

CYSTINOSIS: CLINICAL DECISION SUPPORT PROGRAMME

Draft clinical recommendations from the expert faculty

INTRODUCTION

The recommendations in this document were made by a global steering committee of international clinicians with expertise in managing cystinosis. They aim to support specialist and non-specialist healthcare professionals in their daily clinical practice when treating young adults and adult patients with cystinosis; for simplicity the term ‘adult’ is used to encompass both age groups.

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. We would encourage a thoughtful transition of adolescent patients to adult services in a timely manner. We have identified recommendations supported by evidence-based clinical guidance and additional published data. However, where such evidence is lacking, we offer guidance based on collective expert opinion.

1. CLINICAL GUIDANCE & RESOURCES AROUND CYSTINOSIS

The KDIGO guidance is followed both internationally and in the majority of European countries. However, we advise that other international recommendations, national guidance and other sources should also be consulted including:

- Nephropathic cystinosis: an international consensus document
- Specific guidelines for adult and adolescent patients
- Specific recommendations for the management of bone disease.

Supporting References:

- Emma F, et al. Nephropathic cystinosis: an international consensus document. *Nephrol Dial Transplant* 2014;29(Suppl 4):iv87–94. <https://www.ncbi.nlm.nih.gov/pubmed/25165189>
- Langman CB, et al. Controversies and research agenda in nephropathic cystinosis: conclusions from a “Kidney Disease: Improving Global Outcomes” (KDIGO) Controversies Conference. *Kidney Int* 2016;89(6):1192–203. <https://www.ncbi.nlm.nih.gov/pubmed/27181776>
- Ariceta G, et al. Cystinosis in adult and adolescent patients: Recommendations for the comprehensive care of cystinosis. *Nefrologia* 2015;35(3):304–21. <https://www.ncbi.nlm.nih.gov/pubmed/26523297>

2. GENERAL CONSIDERATIONS WHEN TREATING A PATIENT WITH CYSTINOSIS

Cystinosis is a rare multi-system disorder with overall incidence rates reported in France, Denmark, Sweden, Germany and Australia of between 1:115,000 and 1:260,000 live births. Because of its rarity, there can be a lack of awareness of the short- and long-term consequences and multi-organ impact of the disease, even among adult nephrologists.

In our opinion, an adult nephrologist or a metabolic physician with specific experience of cystinosis should take the lead and be the key clinician coordinator in the care of these patients, ideally in a centre of excellence, where a multidisciplinary healthcare team experienced in managing these patients is available. This will ensure that practical management strategies such as optimal dosing regimens, which includes monitoring of WBC cystine levels, improved adherence to therapy, as well as awareness of the long-term consequences and treatment of the disease in the different organ systems, is adequately monitored. Other healthcare specialties may also be involved, for example to provide education and support post-transplant or to optimise patient adherence for the long-term. We note that the multidisciplinary team structure, however, will vary case-by-case, hospital-to-hospital and country-to-country.

It is important to ensure that young adults with cystinosis are transitioned from paediatric to adult care through a formal paediatric to adult transition service, to ensure optimal long-term outcomes.

Supporting References:

- Elmonem MA, et al. Cystinosis: a review. *Orphanet J Rare Dis* 2016;11:47. <https://www.ncbi.nlm.nih.gov/pubmed/27102039> for incidence rates
- Langman CB, et al. Controversies and research agenda in nephropathic cystinosis: conclusions from a “Kidney Disease: Improving Global Outcomes” (KDIGO) Controversies Conference. *Kidney Int* 2016;89(6):1192–203. <https://www.ncbi.nlm.nih.gov/pubmed/27181776>

Mutidisciplinary approach

We recommend a leader to co-ordinate the care of the complex issues experienced by patients with cystinosis. This may be a nephrologist or a metabolic specialist. Several other specialists from the multidisciplinary team are required to be involved in the care of adults cystinosis patients:

Nephrologist

We recommend that a nephrologist is integral in the care of this condition. The frequency for review will vary according to patient need and range from 2 times/year to more if required.

Metabolic specialist

A metabolic specialist may lead the care of an adult cystinosis patient in combination

with a nephrologist, with special attention to endocrine functions, with review required at least annually or more frequently as required. It is the opinion of some of the experts that patients should be followed by a metabolic specialist or an endocrinologist for thyroid functions and diabetes; typically, annually or twice a year depending on individual centres and healthcare systems.

Ophthalmologist

We recommend that a cystinosis patient be reviewed by an ophthalmologist annually or more frequently if required.

Specialist renal nurse

Some experts work closely with a specialist renal nurse and recommend that they should always be present to help coordinate and assist with patient queries and offer support. However, we recognise that this function is not offered by all centres and healthcare systems.

Cardiology input

Cardiology input should be as appropriate for patients with chronic renal disease.

Neurologist

We advise an annual visit for clinical evaluation in adult patients, with additional clinical examinations as required.

Patient/parent/carer

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 discussions and decisions regarding their care with the consent of the patient.

Other

We advise that a patient should also receive dietetic support to assess nutritional status (especially if the patient experiences weight loss, has diabetes mellitus and/or renal failure). As approximately 30% of adult patients will have respiratory issues, support from a pulmonologist may be required. We would also advise psychology, neurology, and speech and language, occupational therapy follow-up, and input to social services.

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.

3. MULTI-ORGAN INVOLVEMENT

Fertility impact & family-planning

Based on our clinical experience we recommend that the following family-planning advice and support is offered to cystinosis patients who may wish to have children.

For female and male patients

For female patients

Female patients should be advised that the likelihood of becoming pregnant, including potential for a successful pregnancy outcome, is dependent upon their renal health. Female patients with cystinosis should still expect to be fertile. The patient should be made aware that they will need to stop cystine-depletion therapy on confirmation of pregnancy to prevent foetal exposure to cystine-depleting therapy. There is a lack of data around cystine-depleting therapy and breast-feeding and therefore cystine-depletion therapy should be avoided during breastfeeding. Finally, the advice and discussion should be tailored according to the individual female patient's renal function; as per conventional chronic kidney disease (CKD) and post-transplant advice.

For male patients

Male patients should be advised that though previously thought to be infertile, in vitro fertilization techniques with intracytoplasmic sperm injection, may be an option if they wish to father children with their own sperm.

Additionally, potential preservation in a sperm bank could be a possibility for a few individuals. 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 specialities, such as endocrinology or obstetrics and gynaecology, for further support and advice.

Renal considerations

Based on the current guidance and available evidence we recommend monitoring renal function and disease progression according to the individual patient's circumstance. As well as monitoring cystine levels in WBCs, we advise specific monitoring requirements for different patient scenarios based on our clinical experience, as follows:

1. For patients with Fanconi syndrome

We recommend the use of appropriate electrolyte supplementation for countering acidosis, chronic hypokalaemia, hypophosphatemia and carnitine, if needed. We do not advise using indomethacin in adults.

2. For patients on dialysis

Both dialysis modes are suitable depending on the medical and social situation of the patient. For patients on haemodialysis, we recommend tailoring the ultrafiltration and dialysate electrolytes according to individual patient need.

Tailoring the ultrafiltration and monitoring of potassium and phosphate levels by adapting supplementation accordingly is advised. We recommend that these patients are informed that transplantation is the optimal treatment option, if feasible.

3. For patients before renal transplantation

We advise following current KDIGO pre-transplant recommendations for monitoring renal function in these patients.

For patients with CKD before transplantation: we suggest close monitoring of serum creatinine for calculation of eGRF values to monitor renal function. Serum creatinine may not correctly reflect kidney function in those patients with muscle wasting. For those patients with end stage renal disease (ESRD), we suggest carefully monitoring of potassium and phosphate levels and adapting supplementation to control acidosis and parathyroid hormone (PTH).

4. For patients after renal transplantation

We advise following current KDIGO post-transplant recommendations for monitoring renal function with the addition of monitoring cystine levels in WBCs in these patients. Close attention should be paid to polyuria immediately post transplantation.

We recommend starting Cystine-depletion therapy (CDT) treatment as soon as possible once the patient can take oral medication. Additional electrolyte supplementation may be required.

We also strongly recommend educating transplant patients on the long-term benefits of adhering to both their CDT and immunosuppressive therapeutic regimens.

Nervous System and neurocognitive aspects

Based on our clinical experience we recommend that routine assessment of distal muscle strength, motor-function ability and memory testing is performed at every patient visit together with directed discussion around possible neurological signs and symptoms.

Specifically for the central nervous system: we recommend a clinical examination is undertaken and any history of headache investigated as intracranial hypertension may be observed. Regular ophthalmological examinations are also 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. A brain MRI can be performed to look for brain atrophy, white matter signal anomalies, or ischemic lesions; calcifications may be observed by tomodensitometry.

In the peripheral nervous system: we recommend use of a rating scale to evaluate and monitor signs and symptoms in chronic muscular disorders.

To assess the impact on neurocognition: we recommend the MMSE is used for neurocognitive evaluation, particularly if there is some relevant patient complaint,

for example, underperforming in school, visuo-spatial or behaviour issues. Such an evaluation needs to at least include an assessment of visual-spatial abilities, visual-motor coordination, and short-term memory evaluation.

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. Further assessments may include the following:

- Swallowing test
- MMSE
- MFM
- 6 Minute-Walking-Test
- cranial MRI
- ENMG

However, we acknowledge that the frequency of the neurology assessment will vary from centre-to-centre and from country-to-country.

Supporting References:

- Ariceta G, Camacho JA, Fernandez-Obispo M et al. Cystinosis in adult and adolescent patients: Recommendations for the comprehensive care of cystinosis. *Nefrologia* 2015; 35: 304–321

Muscle involvement

Regular exercise should be encouraged, with access to physiotherapy, to support with potential muscle wasting and skeletal deformities. 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.¹³ In addition, and based on our clinical experience, we advise that healthcare professionals follow recommendations from neurology and speech and language colleagues when requesting neurological tests such as ENMG and video-fluoroscopy for swallowing, and to determine the frequency of assessment.

Supporting References:

- Huckabee M-L, et al. The Test of Masticating and Swallowing Solids (TOMASS): reliability, validity and international normative data. *Int J Lang Commun Disord* 2018;53(1):144–156. <https://www.ncbi.nlm.nih.gov/pubmed/28677236>
- Ariceta G, et al. Cystinosis in adult and adolescent patients: Recommendations for the comprehensive care of cystinosis. *Nefrologia* 2015;35(3):304–21. <https://www.ncbi.nlm.nih.gov/pubmed/26523297>

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ENMG may be performed:

- At baseline when signs of muscle weakness and wasting appear
- As part of a neurological examination
- Not as part of routine follow-up, but to differentiate muscle or peripheral nerve involvement

Swallowing:

- Swallowing problems may be best assessed by a swallowing test and video fluoroscopy
- The Test of Masticating and Swallowing Solids (TOMASS) may be used¹⁹
 - Drink 100 mL of water; measure duration of drinking (choking present?)
 - A cracker (standardised; 5 cm²) is offered, with the request: 'Please eat this as soon as you can'
 - After eating, the subject is asked to say their own name (assessment of voice)
 - 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

For clinical muscle testing, rating scales (e.g. the Medical Research Council [MRC] Muscle Scale) can be used to detect distal muscular weakness and wasting. Alternatively, the Motor Function Measure (MFM) rating scale, or the 6 Minute-Walking-Test can be used to precisely monitor the severity and progression of motor function in neuromuscular disease.

ENMG can also be performed to monitor the myogenic syndrome. We do not recommend routine serum creatine kinase assessment and muscle biopsies as part of regular neuromuscular follow-up. Muscle biopsy should not be performed in all patients as it is invasive and should be performed only in rare cases for specific indications.

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.

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

We recommend conducting ENMG at baseline. The patient should have regular clinical follow-up on an annual basis.

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: ideally video-

fluoroscopy of swallowing (if available) or fibre-optic endoscopic evaluation of swallowing.

Supporting References:

- Huckabee ML, McIntosh T, Fuller L et al. The Test of Masticating and Swallowing Solids (TOMASS): reliability, validity and international normative data. *Int J Lang Commun Disord* 2018; 53: 144–156
- Ariceta G, Camacho JA, Fernandez-Obispo M et al. Cystinosis in adult and adolescent patients: Recommendations for the comprehensive care of cystinosis. *Nefrologia* 2015; 35: 304–321

Ophthalmological considerations

Based on our clinical experience we recommend that healthcare professionals work with an ophthalmologist, ideally experienced with cystinosis, to monitor the ocular impact of the disease for all ocular structures. The frequency of ocular assessment should be individualised to the needs of the patient and to the condition of their eyes: typically, 6 months to a year, but occasionally every 3 months.²⁰

We suggest an ophthalmology assessment includes examination of the eyes with digital images from a slit lamp and fundus photography, as a minimum to allow monitoring of changes over time. The full ophthalmological examination should include anterior and posterior segments, combined with complementary examinations (such as anterior-segment and/or posterior-segment optical coherence tomography [OCT]), or visual field, if necessary.

Supporting References:

- Gahl WA, et al. Corneal crystals in nephropathic cystinosis: natural history and treatment with cysteamine eyedrops. *Mol Genet Metab* 2000;71:100–20. <https://www.ncbi.nlm.nih.gov/pubmed/11001803>
- Pinxten AM, et al. Clinical practice: A proposed standardized ophthalmological assessment for patients with cystinosis. *Ophthalmol Ther* 2017;6:93–104. <https://www.ncbi.nlm.nih.gov/pubmed/28477325>

For the Anterior segment:

Assessment should include photophobia, visual acuity test, slit lamp examination for corneal depositions/neovascularization/keratopathy, and intraocular pressure (IOP).

For the Posterior segment:

Despite the photophobia symptoms, the dilated funduscopy is advised to investigate the crystals particularly on the surface of the retina, depigmentation, pigment epithelial alterations, 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.

Finally, we advise that changes in cornea cystinosis score (Gahl's score) and photophobia score can be useful to monitor a patient's adherence with the cysteamine eye drops regimen.^{21,22}

Complaints related to dry eyes are frequent and can be improved by using hydrating eye drops.

Cardio-respiratory considerations

We recommend following current guidance for dialysis and post-transplant patients for cardiology and respiratory function examinations in all cystinosis patients, both symptomatic and asymptomatic. 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 dyspnoea or obstructive lung disease is observed.

Supporting References:

- Ariceta G, et al. Cystinosis in adult and adolescent patients: Recommendations for the comprehensive care of cystinosis. *Nefrologia* 2015;35(3):304–21. <https://www.ncbi.nlm.nih.gov/pubmed/26523297>

Endocrine aspects

In our clinical experience, hypothyroidism is the most common endocrine disorder found in patients with cystinosis. Diabetes mellitus is also common in adult patients, especially post-transplant, and hypogonadism may also be found particularly in male patients.

Supporting References:

- Ariceta G, et al. Cystinosis in adult and adolescent patients: Recommendations for the comprehensive care of cystinosis. *Nefrologia* 2015;35(3):304–21. <https://www.ncbi.nlm.nih.gov/pubmed/26523297>

We advise monitoring and managing endocrine disorders as follows:

Hypothyroidism

- Common in adults
- Check every 6 months from an early age using total thyroxine (FT3, T4) and thyroid-stimulating hormone (TSH) thyroid function tests
- Thyroid supplementation may be required

Diabetes mellitus

- Common in adults, especially after transplantation
- Blood sugar should be checked at every visit, ideally 3–6 monthly; it may be necessary to alter immunosuppressive calcineurin inhibitor (CNI) regimens in transplant patients or to initiate insulin therapy

Hypogonadism

- Hypogonadism is an important problem particularly in adolescent males, and patients should be given appropriate fertility counselling
- 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 such as when puberty is delayed. If appropriate, discussions on banking sperm may be considered

Gastrointestinal and hepatological involvement

Since these complications are less common in adult cystinosis patients, we recommend that annual liver function tests (LFTs), as well as amylase and pancreatic enzymes, are sufficient to monitor for gastrointestinal (GI) and hepatological symptoms.

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

We also note that many GI side effects such as heartburn can be related to the treatment the patient has to take, e.g. Cystine-depletion therapy (CDT), potassium bicarbonate/citrate supplements.

Dermatological considerations

We advise performing an annual skin examination, especially in those patients who have undergone transplantation. Skin examination can easily be performed in an out-patient visit. We also note that cystinosis-specific changes, such as skin striae and molluscoid swellings (purple lesions at the knee or elbow), are a first sign of CDT overdose and require immediate attention that should not wait until the next annual review.

The use of a sunscreen, with at least sun protection factor (SPF) 50, as part of a sun protection strategy, is particularly important for patients post-renal transplantation. However, we recommend use of high-protection sunscreen as a preventive measure against skin cancer for all patients with cystinosis.

Supporting References:

- Kasiske BL, et al. KDIGO Clinical practice guidelines for the care of kidney transplant recipients: a summary. *Kidney Int.* 2010; 77(4):299-311. <https://www.ncbi.nlm.nih.gov/pubmed/19847156>
- Elmonem MA, et al. Cystinosis: a review. *Orphanet J Rare Dis* 2016;11:47. <https://www.ncbi.nlm.nih.gov/pubmed/27102039>

Dental care

In our clinical opinion dental health is affected in patients with cystinosis, and we recommend regular rigorous dental hygiene and regular dental check-ups in all patients.

Enamel defects and caries are common problems 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.

Supporting References:

- Bassim CW, et al. Craniofacial and dental findings in cystinosis. *Oral Dis* 2010;16(5):488–95. <https://www.ncbi.nlm.nih.gov/pubmed/20233313>

4. PATIENT WELL BEING

Quality of life and psychological well-being

In our clinical experience patients with a rare, chronic and severe disease such as cystinosis require a multidisciplinary team approach to clinical management, and 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.

Based on experiences with more common diseases, e.g. type 1 diabetes, several approaches can support patients' adherence and quality of life.

Core elements are:

- A multi-professional team approach, where all members are familiar with all aspects of the disease
- Setting and following common targets, and good communication
- Engage the patient's friends and relatives, and provide ongoing education and psychological support
- Availability of patient groups
- Specific psychological support to cope with all aspects pertaining to medication, halitosis, early complications, long-term risks, psychosocial integration, anxiety, depression, burn-out, stigmatisation, late-onset systemic abnormalities, work, partnership, insurances, legal issues, and long-term disabilities.

The psychosocial team members should be trained and experienced in the care and support of patients with severe chronic diseases. In addition, they need a deep understanding of the current therapy and its impact on every-day life.

There are several validated screening tests available to monitor the psychological well-being of patients with a chronic disease. Many have also been translated into different languages:

- Motivational interviewing
- Screening for wellbeing; depression; anxiety
- Screening for disease-specific quality of life
- Screening for generic quality of life

Cystinosis is known to have an impact on several psychosocial aspects for patients:

- High prevalence of depression and anxiety
- Stigmatisation 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)

These factors can all have a negative impact on adherence to therapy and on quality of life (QoL) for patients.

There are many helpful resources to support adult patients with cystinosis:

- Education on practical aspects of therapy in everyday life (not scientific discussion but sharing experiences and training skills, e.g. how to communicate about the disease, the 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
- 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)); although 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 – but not every person with cystinosis wants to be a part of this community
- Patient empowerment with patient-centred communication (motivational interviewing), possible as web-delivered intervention.

The written patient information and resources on <https://cystinosis.org/> are very helpful and motivating. Also, the European cystinosis network at <http://cystinosis-europe.eu> can direct patients to information within their own countries.

Supporting References:

- Cameron F, et al. Lessons from the Hvidoere International Study Group on childhood diabetes: be dogmatic about outcome and flexible in approach. *Pediatr Diabetes* 2013;14:473–80. <https://www.ncbi.nlm.nih.gov/pubmed/23627895>
- Beinart N, et al. Mood and illness experiences of adults with cystinosis. *Ren Fail* 2015;37:835–9. <https://www.ncbi.nlm.nih.gov/pubmed/25715639>
- Doyle M. Peer support and mentorship in a US rare disease community: Findings from the cystinosis in emerging adulthood study. *Patient* 2015;8:65–73. <https://www.ncbi.nlm.nih.gov/pubmed/25231828>
- Cameron FJ, et al. ISPAD Clinical Practice Consensus Guidelines 2014. Diabetes in adolescence. *Pediatr Diabetes* 2014;15(Suppl 20):245–56. <https://www.ncbi.nlm.nih.gov/pubmed/25039664>
- Lansing AH et al. Pilot study of a web-delivered multicomponent intervention for rural teens with poorly controlled type 1 diabetes. *J Diabetes Res* 2016;7485613. <https://www.ncbi.nlm.nih.gov/pubmed/27610391>
- Schaefer MR, Kavookjian J. The impact of motivational interviewing on adherence and symptom severity in adolescents and young adults with chronic illness: A systematic review. *Patient Educ Couns* 2017;100(12):2190–9. <https://www.ncbi.nlm.nih.gov/pubmed/28619271>
<http://www.motivationalinterviewing.org/> Miller / Rollnick: Motivational Interviewing <https://www.psykiatri-regionh.dk/who-5/Pages/default.aspx>; <http://www.phqscreeners.com/select-screener> <http://www.svri.org/sites/default/files/attachments/2016-01-13/HADS.pdf>
- Ware JE Jr, et al. The validity of disease-specific quality of life attributions among adults with multiple chronic conditions. *Int J Stat Med Res* 2016;5(1):17–40. <https://www.ncbi.nlm.nih.gov/pubmed/27087882>
- Németh G. Health related quality of life outcome instruments. *Eur Spine J* 2006;15(Suppl 1):S44–51. <https://www.ncbi.nlm.nih.gov/pubmed/16320032>
- Langman CB, et al. Controversies and research agenda in nephropathic cystinosis: conclusions from a “Kidney Disease: Improving Global Outcomes” (KDIGO) Controversies Conference. *Kidney Int* 2016;89(6):1192–203. <https://www.ncbi.nlm.nih.gov/pubmed/27181776>

Diet and lifestyle

In our clinical experience, cystinosis patients tend to have low appetite so dietary restriction is unnecessary unless the patient has either diabetes mellitus, CKD or ESRD where relevant guidance should be followed. Diet and lifestyle are also especially important in transplanted patients, including regular physical activity.

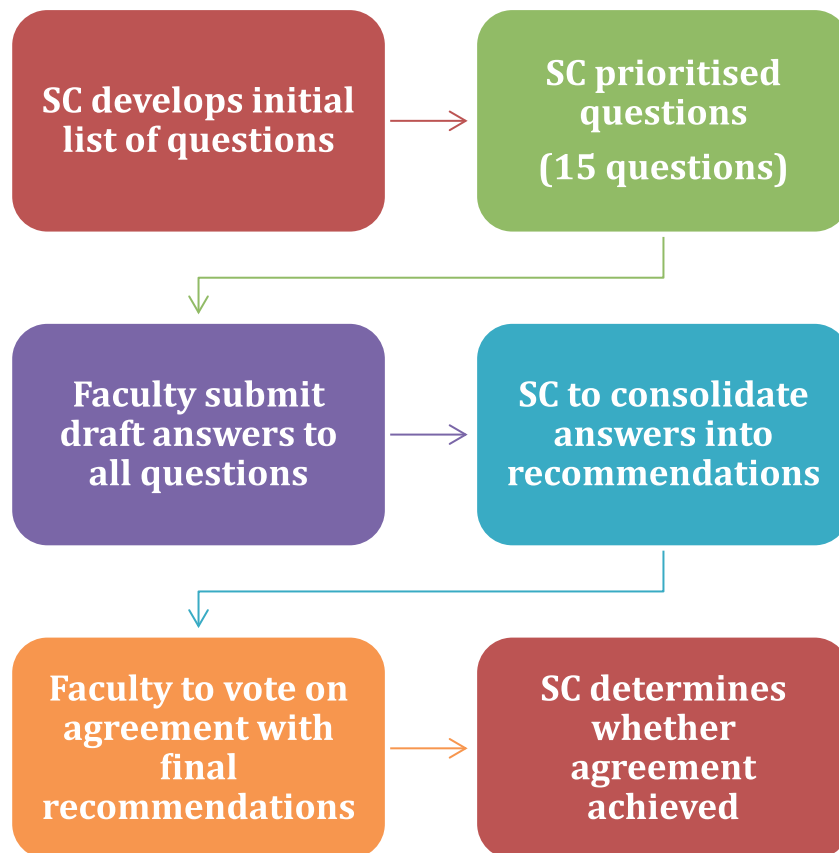
It is important to have a good rapport and honest discussion with patients about how diet and lifestyle impacts on their long-term outcomes. We recommend that the importance of a balanced diet, with optimal nutrition and hydration (and linking with blood test results) is emphasized to the patient at each consultation.

We advise that dietary advice and treatment is provided in collaboration with a specialist dietitian when required. 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.

Supporting References:

- Ariceta G, et al. Cystinosis in adult and adolescent patients: Recommendations for the comprehensive care of cystinosis. *Nefrologia* 2015;35(3):304–21. <https://www.ncbi.nlm.nih.gov/pubmed/26523297>
- Emma F, et al. Nephropathic cystinosis: an international consensus document. *Nephrol Dial Transplant* 2014;29(Suppl 4):iv87–94. <https://www.ncbi.nlm.nih.gov/pubmed/25165189>

STEP-BY-STEP PROCESS



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