The Cost of Implementing Ketogenic Diet Therapy for Children and Young People with Drug-Resistant Epilepsy in the United Kingdom

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Epilepsy is the most common chronic neurological condition in childhood, affecting 112,700 children and young people in the UK,[1] of which approximately 30% have seizures that are resistant to anti-seizure medications.[2] The burden of seizures, anti-seizure medications and psychiatric comorbidities negatively impact health-related quality of life,[3] and have predicted healthcare costs of £16,931 per child over 18 months.[4] Alternative treatment options for children with drug-resistant epilepsy (DRE) are limited. Ketogenic diet therapy (KDT; high-fat, low-carbohydrate diets) is associated with a 'relative risk' of 3.16 of achieving seizure freedom, and 5.80 of ≥50% seizure reduction in children with epilepsy, compared to no change in treatment.[5]

In 2012, the National Institute for Health and Care Excellence (NICE) guidelines for the management of epilepsy in children and young people recommended that KDT should be offered to individuals who have failed to respond effectively to two appropriate anti-seizure medications.[6] Over the past 20 years there has been a dramatic increase in KDT services across the UK and Ireland, and the number of UK KDT referrals has increased seven-fold.[7] Some of this increase could be attributed to these national recommendations.

In 2021, the CG137 NICE guidelines were reviewed and updated, and NICE attempted to evaluate the cost-effectiveness of KDT, highlighting that there is a significant gap in health economic research, with no relevant cost data for the UK.[8] Three cost-utility analyses were included that compared the cost and health benefits of KDT to care as usual for children with DRE, but these were Dutch studies and were not generalisable to UK practice due to differences in healthcare funding models and service delivery models.[9] A research recommendation was made by NICE to determine *'What is the short-term and long-term clinical and cost-effectiveness of ketogenic diets in adults and children with drug-resistant epilepsy'*, which would be essential to inform national guidance in the future.

With a view to addressing this research recommendation, I contacted a health economist at the University of Manchester, Dr Sean Gavan, and Dr Natasha Schoeler, a Research Dietitian at University College London, to explore how we could embark on a project to complete a health economic analysis of the ketogenic diet for the management of DRE. We were successful in applying to the Nutricia Metabolic Research Fund to secure funding for Dr Gavan and Dr Schoeler's support and supervision and I applied to the NIHR pre-doctoral fellowship programme to develop the project.

I have completed some preliminary work to estimate a nationally representative and robust estimate for the cost of implementing KDT, which I plan to submit for publication. This is the first stage in the development of a model-based cost-effectiveness analysis of KDT, compared with care as usual, for children and young people with drug-resistant epilepsy in the UK.

Method

To estimate the direct cost of implementing KDT to the NHS over a 2-year period, a stepwise process was used:

- **Stage 1:** Determining the most common patient pathway.
- **Stage 2:** Estimation of the quantity of the resource components (professionals involved, length of contact, investigations, prescriptions).
- **Stage 3:** Determining the unit cost of each resource component from appropriate sources.
- **Stage 4:** An estimation of the total cost of KDT with sensitivity and scenario analysis (age, dietary type, complexity).

A common patient pathway

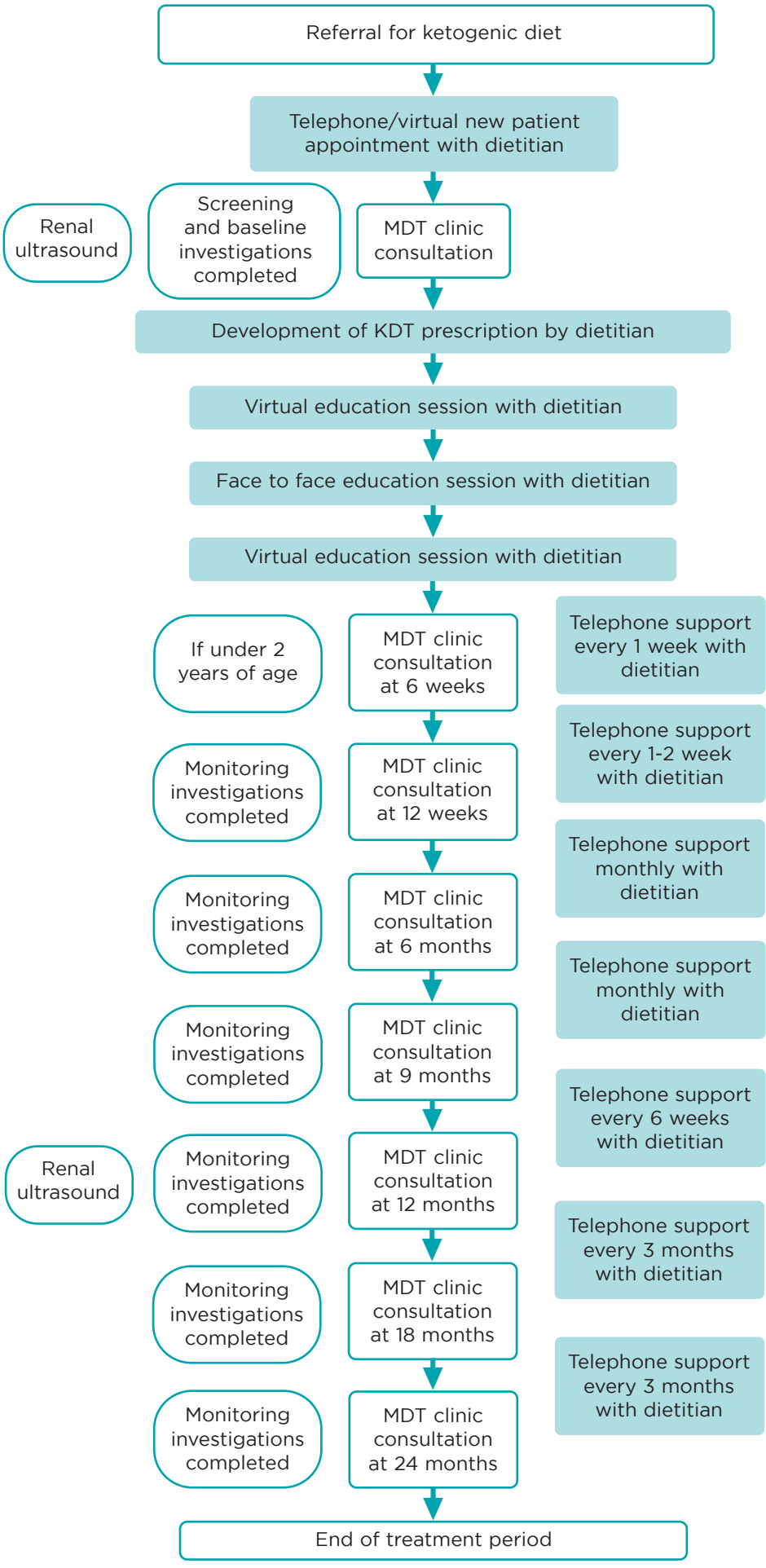
A service pathway conceptual method was used to describe the sequence of clinical actions from decision to start KDT and then all actions within a 2-year treatment schedule. Outpatient dietary initiation was evaluated as this is the most common pathway for dietary initiation in the UK.[7]

To account for national variation in patient pathways, eight centres (8/21) agreed to share their pathways and a flow diagram was then created to demonstrate the most common pathway (see **Figure 1**) followed by children and young people referred for KDT. Each centre was then consulted to obtain additional detail on specific elements of the patient pathway and patient monitoring.

Estimation of the quantity and cost of resource components

Each clinical contact during the treatment period has been quantified and costed, including multidisciplinary and dietetic-led contacts, as well as time to develop the dietary prescription and care plan. In addition, any investigations, including laboratory or point-of-care testing, were included and an estimation of the cost and quantity of prescribed KDT products for each of the dietary types.

Figure 1: Common patient pathway



To ensure a robust cost estimate, differing age groups (infants, school age and teenagers) and different dietary types (classical, modified medium-chain triglyceride [MCT] and modified ketogenic diets), both oral and tube fed, were included to ensure the best and worst case scenarios were accounted for.

Results

The direct treatment costs (clinical contacts), including home monitoring, have been calculated at £4,563.52 for routine care and up to £6,971.01 for children and young people with complex medical backgrounds (see **Figure 2**).

Prescription products to support KDT have the biggest impact on the cost of the total treatment pathway. It is unsurprising that enterally fed children incur the greatest cost from prescribable products, as their full nutritional requirements are provided by foods for special medical purposes (FSMPs). To account for the usual costs of being enterally fed, the cost of FSMPs prior to, and whilst on, KDT were compared. The cost of FSMPs prior to and whilst on KDT was compared. On average enteral feeding products to support KDT increases the prescription cost of FSMPs by 10.6% (range 4.3-18.1%).

With this considered, the average cost of the 2-year pathway, including FSMPs, would be on average £7,320.80 for children under 4 years of age, £9,074.86 for school age children and £11,076.20 for a teenager. This number increases over the life course, as expected, due to increasing calorie requirements for age and growth.

Conclusion

The average cost of the full KDT treatment pathway, including nutritional supplements over 2 years, is £9,452.42 (range £4,802.72–£14,111.07). This cost can be compared to other medical diets – for example, a low protein diet used in the management of inherited metabolic disease is estimated to cost £12,000 to £18,000 per phenylketonuria patient per year.[11]

The burden of seizures has been estimated to cost £16,931 per child over 18 months,[4] which can be extrapolated to £22,574.67 over a 2-year period. Research has shown us that KDT is an effective treatment option for DRE and can reduce seizures by at least 50% in around 60% of cases,[5] reducing the potential financial burden on the NHS for those responders. The cost of KDT is not dissimilar to other alternative treatment options for DRE; including Epidyolex, which as an adjunctive therapy estimated to cost between £5,000 and £10,000 per patient each year.[12] Other non-drug treatment options include vagal nerve stimulation, which has been estimated to cost £21,238[13] and has a similar efficacy rate to KDT.[14]

This project only assesses the cost of KDT and doesn't consider any potential cost savings that an effective treatment could bring, but it is the necessary first step to demonstrate the health economic value of KDT as a treatment option for DRE within the NHS. The results from this study will be used to prime a future grant application to perform a larger model-based cost-effectiveness analysis of KDT compared with usual care, for children and young people with DRE in the UK.

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Figure 2: Total cost of 2-year treatment pathway