A randomised controlled study to evaluate an integrated care pathway for children with chronic disease – connecting the dots in healthcare provision

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1. INTRODUCTION

Children with chronic healthcare conditions have better health-related outcomes when their care is managed in a coordinated way.[1] Specifically for children with Attention Deficit Hyperactivity Disorder (ADHD) there are improvements in functional outcomes when families receive more personalized and coordinated care.[2] Children with common chronic conditions, such as ADHD, place an increased burden on ambulatory care hospital services.[3] Increased demand has led to longer waitlist times to access specialists and appropriate intervention services;[4] placing vulnerable children at increased risk of poorer short-term (e.g. increased risk of mental health, social difficulties) and long-term (e.g. convictions, arrests) health and social outcomes.[5] Traditional approaches to increasing frequency and service of delivery are expensive and can have minimal impact on caregiver burden.[6]

An improved approach to the public health care system that is sustainable, cost-effective, provides efficient evidence-based care and improves the quality of life outcomes for children with chronic disease has the potential to reduce waitlist times to access health services, increase consumer satisfaction; and prevent costs associated with poorly managed chronic diseases into adulthood. A community based service-integration approach, rather than self-directed care is proposed as increased service linkages are more likely to occur for children from low-income families.[7] This randomised control trial protocol investigates the cost-effectiveness of an integrated care pathway between hospital and primary care partnerships in improving health and social outcomes in children with chronic disease.

2. BACKGROUND

Chronic conditions such as Attention Deficit Hyperactivity Disorder (ADHD) and intellectual impairment (II), have prevalence rates of approximately 5%[8] and 1-3%[9] in the population, respectively. Such a demand has led to longer waitlist times to see a specialist and access appropriate services within the public health sector in

Australia. In addition, poorer short-term (e.g. increased risk of mental health, social difficulties) and long-term (e.g. convictions, arrests) outcomes have been reported for vulnerable children with multiple risk factors (i.e. income, education, social support).[5] Traditional approaches to increasing frequency and service of healthcare delivery are expensive and have been shown to have minimal impact on caregiver burden[6] and changes to caregiver perception of their reduced influence over their current circumstances, including behavioural issues and overall well-being of their children.[10,11] Research has shown that caregivers who have higher levels of external locus-of-control may be more likely to have issues with taking action to influence their children's behaviours.[10] There is also emerging literature that suggests that locus-of-control may act as a mediator in the relationship between parenting and the caregivers' mental health.[11] These findings suggest that a caregivers' locus-of-control may influence their ability to undertake services and therapies which require regular and active involvement in the management of their child's chronic disease and well-being. Given this context, a different approach to health care systems in the management of chronic disease in children which includes caregiver/family involvement will likely improve both child and caregiver health and social outcomes.[12]

The Chronic Care Model[13] is the most well-known model used to address healthcare systems in the management of chronic diseases. Improved quality of life, clinical outcomes and a reduction in health costs have been seen in adults with chronic diseases (e.g. diabetes, heart disease, chronic obstructive pulmonary disease) when the Chronic Care Model[13] was utilised. Different components (e.g. care coordination) of the Chronic Care Model[13] have been successfully used in the management of children with asthma and ADHD.[8,14,15] However, no studies to date have utilised components of the Chronic Care Model[13] to address health care outcomes in vulnerable children with chronic disease.

The success of a health systems approach needs to be balanced against clinical, mortality and cost-effectiveness data for long-term sustainability within a publicly funded health system. Similar to features of the Chronic Care Model,[13] community based service-integration approaches have been shown to reduce neonatal and maternal morbidity in developing countries[16] and increase the number of service linkages for low income families in a developing country.[7] Features of community based service integration approaches include health worker visits in the community, training of community staff, health promotion, availability of resources to link into existing community services and the allocation of a case manager to the child and family. However, despite reported success in reducing morbidity and increasing access for vulnerable children in developing or low income families, both studies described above do not provide cost-effectiveness data on the community service-integration models used. Nevertheless, reduced health care system costs (e.g. reduced inpatient days, reduced out of pocket expenses) has been shown when care coordination between community and tertiary care providers is provided to children with medically complex conditions.[17] No such information is available for children with chronic disease. Further short and long-term health economics information, which includes financial impacts within the school, family and health care environments are required, particularly for children with chronic disease. Such health economics information is a gap in current literature and needs to be addressed to ensure publically funded community service-integrated models of care are cost-effective and sustainable in the long-term.

Based on available literature and increasing financial pressures to cost-effectively sustain a public health care system for children with chronic diseases, an integrated health care pathway which incorporates the care coordination features of the Chronic Care Model[13] and includes caregiver involvement as an essential component has the potential to improve health and social benefits in an already at risk population. The development of an Integrated Children's Clinic Care (ICCC) pathway which incorporates features of the Chronic Care Model[13] and involvement of caregivers was developed to improve health and social benefits for children with chronic disease. This protocol paper outlines a randomised control trial evaluating the cost-effectiveness of the ICCC pathway. The ICCC centres around an allied health liaison officer facilitating key components of the Chronic Care Model[13] in primary, community and acute care facilities across two Australian health districts of varying socioeconomic status'.

3. AIM OF STUDY

To determine the effectiveness of an integrated care pathway led by an allied health liaison officer in the management of chronic disease in children.

4. OBJECTIVES

a) To determine if the ICCC results in better health outcomes for children with chronic conditions, compared to a self-directed care pathway.
b) To determine the cost-effectiveness of the ICCC using health economics data.

5. HYPOTHESIS

5b. Primary Hypotheses

a) Children who access the ICCC will have improved quality of life (child and family impact) scores than children who access the self-directed care pathway.
b) The ICCC pathway is more cost-effective than a self-directed care pathway.
c) The well-being (i.e. levels of stress, locus of control) of caregivers of children who access the ICCC will be better than the well-being of caregivers of children accessing the self-directed care pathway.

5b. Secondary Hypotheses

H_a : Children who access the ICCC will have better school attendance records than children who access the self-directed care pathway.
H_a : Children who access the ICCC will be linked in with more community services than children who access the self-directed care pathway.

6. STUDY DESIGN

Open, unblinded, multi-site randomised controlled trial.

7. STUDY SETTING

Caboolture Hospital, Gold Coast University Hospital (GCUH) Paediatric Outpatient Clinics and General Practice facilities in Caboolture [Social Economic Index for Areas (SEIFA)=0.1%] and Gold Coast (SEIFA=0.01-0.09%), Australia.

8. STUDY POPULATION

Children (0-16yrs) with a newly diagnosed developmental chronic condition.

9. ELIGIBILITY CRITERIA

9a. Inclusion criteria

Children 0 to 16 years seen by Paediatrician at Caboolture Hospital or GCUH and newly diagnosed with a chronic condition where community based health or family support services are part of the management plan. Chronic conditions are expected to last more than 6 months and to produce consequences that impact on the child's quality of life.[18]

Examples of chronic conditions include (but are not limited to): Autism Spectrum Disorder (ASD), Attention Deficit Hyperactivity Disorder (ADHD), Intellectual Impairment (II), Specific Language Impairment (SLI), Oppositional Defiance Disorder (ODD), Fetal Alcohol Spectrum Disorder (FASD), Cerebral Palsy (CP).

9b. Exclusion criteria

- Children with acute medical conditions requiring urgent intervention where community follow-up is deemed inappropriate by the treating Paediatrician.
- Children with a chronic medical condition primarily managed by medical consultation alone and those conditions where hospital based multidisciplinary teams provide coordinated care.
- Examples of excluded chronic conditions include: cancer, cystic fibrosis, asthma, epilepsy.

10. STUDY OUTCOMES

10a. Primary Outcome

Measures taken at 1 week, 3, 6, 12 months include**:**

- Pediatric Quality of Life (PedQOL) Child - Score 0 to 100. (Parent or child completed)
- PedQOL Family Impact - Score 0 to 100. (Parent completed)
- Subjective Units of Distress Scale (SUDS) - Score 0 to 100. (Parent completed)
- Child Behaviour Checklist (CBCL) – Percentiles. (Parent completed)
- Rotter's Locus of Control Scale - Score 0 to 23 (Parent completed)

10b. Secondary Outcome(s)

Measures taken at 1 week, 3, 6, 12 months include the number of**:**

- GP visits
- Hospital admissions
- Specialist appointments
- Absent school days
- Caregiver missed employment days
- School suspensions including duration in days
- Services currently accessed at the time.

11. STUDY PROCEDURES

11a. Recruitment of participants

Children attending paediatric outpatient clinics with the Paediatrician at Caboolture Hospital or GCUH will be approached to participate in the study at the conclusion of their appointment by the Allied Health Liaison Officer (AHLO). Informed consent will be gained at this time with caregivers provided with a caregiver information sheet and study brochure. The researcher will verbally go through the caregiver information sheet, study brochure and consent form for all caregivers of eligible participants. All caregivers will be asked to initial and date on each page of the caregiver information sheet and study brochure to acknowledge that they have understood the study requirements. When necessary, particularly for children of non-English speaking backgrounds, interpreter services will be used to aid in providing informed consent.

For caregivers who identify with literacy issues, the AHLO will ensure extra time is used to explain the study and obtain informed consent.[19] Before finalising consent, the AHLO will be required use the "teach back" method and ask the caregiver to explain in their own words what the research study is asking them to do, including risks and processes involved.[20]

It is anticipated that a high proportion of caregivers will consent to be a part of this trial; however, we anticipate a high drop-out rate due to the length of the trial, anticipated social issues and previously documented high drop-out rates in a similar study.[7] A high attrition rate (approximately 50%) has been factored into the sample size calculations below.

11b. Randomisation

A randomization list, created by an independent biostatistician will be used. Block size permutation of n=7 will be utilized to ensure equal distribution of participants into each pathway. Assessment allocation (integrated versus self-directed care pathway) will be concealed in sequentially numbered opaque envelopes and assigned to enrolled children immediately after informed consent is gained to participate in the research trial. The envelope will be opened in front of the caregiver and child. This would mean that the caregiver, child and AHLO involved in the trial will not be blinded to group assignment. Blinding in this trial is not feasible due to the nature of the integrated care pathway (i.e. caregivers will expect a multidisciplinary appointment with a General Practitioner).

11c. Study procedure

An outline of the trial can be found in Figure 1 below. Please note that a text message will be sent to the caregiver 24 hours before a planned phone review to serve as a reminder and/or provide an opportunity for the caregiver to negotiate an appropriate time/date for the phone review. It is anticipated that a text message will facilitate increased participation and reduce attrition rates over the period of the study. A maximum of 3 phone attempts will be made at any review time point.

Integrated Children's Care Clinic (ICCC) Pathway

1 week-post Paediatrician appointment:

a) The AHLO will make contact with the child's GP to arrange a multidisciplinary long face-to-face meeting to help facilitate recommendations by the Paediatrician. This may include access to community allied health services. The child and caregiver will be seen by the GP at the conclusion of the multidisciplinary meeting for a consult. The AHLO will complete the following with the caregiver/child post GP consult (based on 7 day period):
    - Ask how many services the child is currently accessing
    - Number of days caregiver missed employment
    - Collect baseline demographics data (family structure, primary carer education, primary carer employment status and mental health status). Please note: if caregiver reports emotional distress, then AHLO will recommend for caregiver to see their GP for further assistance.
    - Complete Pediatric Evaluation of Disability Inventory (PEDI) if child is between 6 months to 7 years.

b) The AHLO will contact Education Queensland to request for number of school attendance and absent days, including any formal suspensions (if applicable).

c) The AHLO will go through the following checklist to ensure completion. Liaison with other professionals and agencies will occur, as appropriate. Each process used and outcome will be documented to guide process evaluation for the AHLO role.[21]
    - Completion of forms – literacy assistance
    - Identification and acceptance to community agencies
        - Disability Services Queensland (DSQ), Child Development Services (CDS), Autism Queensland, Cerebral Palsy League of Queensland (CPLQ), Special Education Unit (SEU)
    - Check progress of financial assistance with Centrelink or similar agency
        - Carer's Allowance
    - School supports, if appropriate
    - Navigation on use of eligible initiatives

- Better Start, Chronic Disease Management Plan, Mental Health Care Plan, ATSI Plan

d) The AHLO will submit Medicare forms to obtain information on:
- Number of GP visits
- Hospital admissions
- Specialist appointments

e) Medical Students from each hospital will call the primary caregiver to complete:
- Peds Quality of Life (Peds QOL) Child and Family Impact Modules
- Subjective Units of Distress Scale (SUDS)
- Locus of Control Questionnaire

3 months (+/- 14 days) post Paediatrician appointment:

a) The AHLO will contact Education Queensland to request for number of school attendance and absent days, including any formal suspensions (if applicable).

b) The AHLO will submit Medicare forms to obtain information on:
- Number of GP visits
- Hospital admissions
- Specialist appointments

f) The AHLO will help arrange a GP long face-to-face consultation appointment to review the child to check on progress of management plan in relation to the child's chronic disease. Each process used, if appropriate, and outcome of actions will be documented to guide process evaluation for the AHLO role.[21] The AHLO will complete the following with the caregiver/child post GP consult:
  - Ask how many services the child is currently accessing
  - Number of days caregiver missed employment
  - Child Behaviour Checklist (CBCL)

6 months (+/- 14 days) post Paediatrician appointment:

a) The AHLO will contact Education Queensland to request for number of school attendance and absent days, including any formal suspensions (if applicable).

b) The AHLO will submit Medicare forms to obtain information on:
  - Number of GP visits
  - Hospital admissions
  - Specialist appointments

c) The AHLO will help arrange a GP long face-to-face consultation appointment to review the child. The AHLO will make phone contact with the caregiver to complete the following with the caregiver:
  - Ask how many services the child is currently accessing
  - Number of days caregiver missed employment
  - Child Behaviour Checklist (CBCL)

d) Medical Students from each hospital will call the primary caregiver to complete:
  - Peds Quality of Life (Peds QOL) Child and Family Impact Modules
  - Subjective Units of Distress Scale (SUDS)
  - Locus of Control Questionnaire

12 months (+/- 14 days) post Paediatrician appointment:

a) Medical Students from each hospital will call the primary caregiver to complete:
   - Peds Quality of Life (Peds QOL) Child and Family Impact Modules
   - Subjective Units of Distress Scale (SUDS)
   - Locus of Control Questionnaire

Self-Directed Care Pathway

1 week-post Paediatrician appointment:

a) The AHLO will complete the following with the caregiver/child (based on 7 day period):
   - Ask how many services the child is currently accessing
   - Number of days caregiver missed employment
   - Collect baseline demographics data (family structure, primary carer education, primary carer employment status and mental health status)
   - Complete Pediatric Evaluation of Disability Inventory (PEDI) if child is between 6 months to 7 years.

b) The AHLO will contact Education Queensland to request for number of school attendance and absent days, including any formal suspensions (if applicable).

c) The AHLO will submit Medicare forms to obtain information on:
   - Number of GP visits
   - Hospital admissions
   - Specialist appointments

d) Medical Students from each hospital will call the primary caregiver to complete:
   - Peds Quality of Life (Peds QOL) Child and Family Impact Modules
   - Subjective Units of Distress Scale (SUDS)
   - Locus of Control Questionnaire

3 months (+/- 14 days) post Paediatrician appointment:

a) The AHLO will contact Education Queensland to request for number of school attendance and absent days, including any formal suspensions (if applicable).

b) The AHLO will submit Medicare forms to obtain information on:
   - Number of GP visits
   - Hospital admissions
   - Specialist appointments

c) The AHLO will complete the following with the caregiver via phone call:
   - Ask how many services the child is currently accessing
   - Number of days caregiver missed employment
   - Child Behaviour Checklist (CBCL)

6 months (+/- 14 days) post Paediatrician appointment:

a) The AHLO will contact Education Queensland to request for number of school attendance and absent days, including any formal suspensions (if applicable).

b) The AHLO will submit Medicare forms to obtain information on:
   - Number of GP visits
   - Hospital admissions

- Specialist appointments

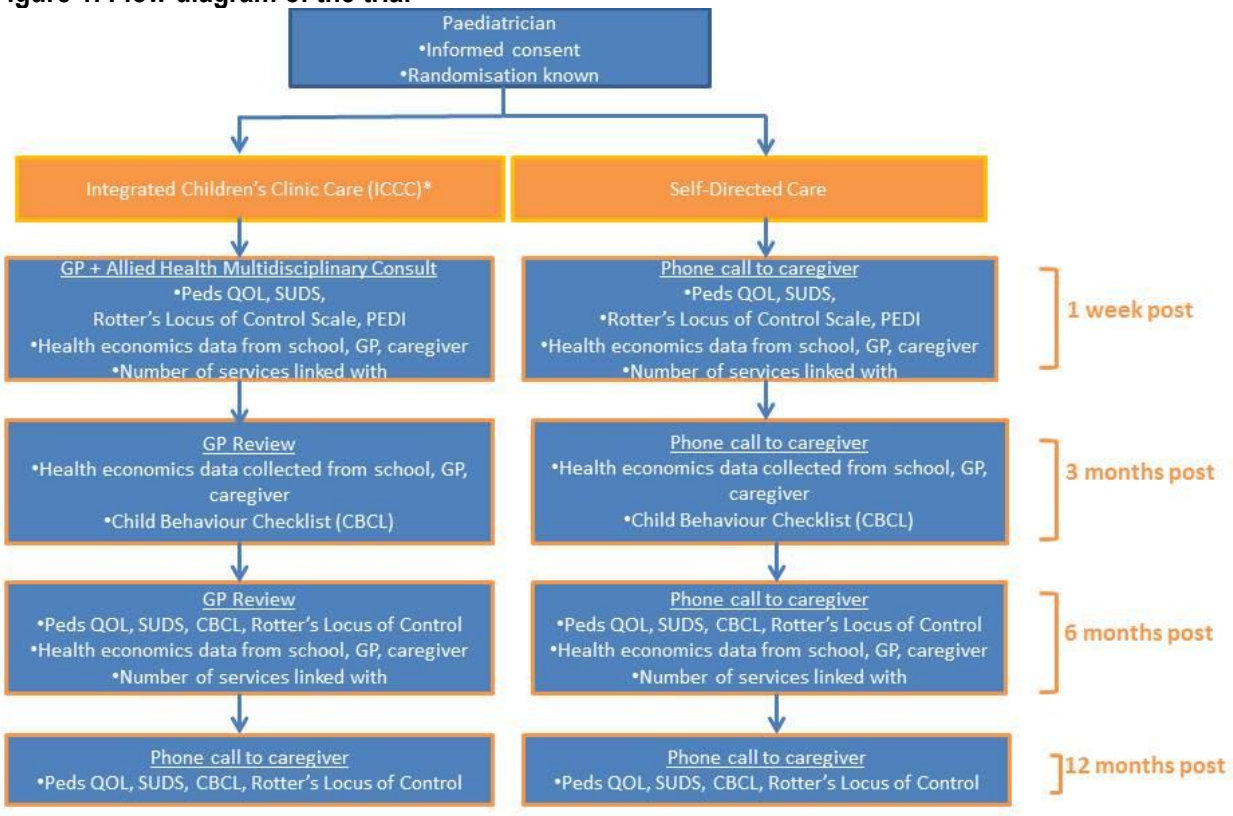
c) The AHLO will make phone contact with the caregiver to complete the following with the caregiver:
   - Ask how many services the child is currently accessing
   - Number of days caregiver missed employment
   - Child Behaviour Checklist (CBCL)

d) Medical Students from each hospital will call the primary caregiver to complete:
   - Peds Quality of Life (Peds QOL) Child and Family Impact Modules
   - Subjective Units of Distress Scale (SUDS)
   - Locus of Control Questionnaire

12 months (+/- 14 days) post Paediatrician appointment:

a) Medical Students from each hospital will call the primary caregiver to complete:
   - Peds Quality of Life (Peds QOL) Child and Family Impact Modules
   - Subjective Units of Distress Scale (SUDS)
   - Locus of Control Questionnaire

Figure 1. Flow diagram of the trial



*Allied Health Liaison Officer (AHLO) helps family navigate: school (e.g. individual educational plan, supports), allied health (e.g. public/private), community resources (e.g. neighbourhood centre, Moreton Bay libraries), Centrelink (e.g. allowances) in conjunction with GP, Paediatrician and/or other relevant staff in community.

11d. Measurement tools used

The following measures will be used to determine if the ICCC pathway results in better health outcomes for children with chronic conditions, compared to the self-directed care pathway

- Pediatric Quality of Life Measures, Child & Family Impact (Score 0 – 100)

- Subjective Units of Distress Scale (Score 0 – 100)
- Child Behaviour Checklist (Score 0 – 100)
- Rotter's Locus of Control Scale (Score 0 – 23)

To determine the cost-effectiveness of the ICCC pathway, the following information will be used:

- Number of: GP visits, hospital admissions, specialist appointments, missed school days, sick days, caregiver missed employment days.

11e. Safety considerations/Patient safety

Children randomised to the self-directed pathway will be allowed to change to ICCC pathway after 6 months, if they wish. However, their recorded data at 12 months will not be used in the final analyses. An indigenous GP practice will be enlisted to ensure children who identify as Aboriginal or Torres Strait Islander patients have the opportunity to choose a GP practice which is culturally appropriate. Identified information will only be shared and viewed by investigators involved in patient care or 'data collection.' De-identified information will only be seen by investigators on the project. Data will be stored in locked cabinet at Caboolture Hospital for 5 years post study completion, as per NHMRC guidelines.

12. STATISTICAL CONSIDERATIONS AND DATA ANALYSIS

12a. Sample size and statistical power

We plan for a total sample size of 112 children (80 % power to detect a mean effect difference of 15 between groups on the quality of life scale) at 0.05 significance level. This sample size has been adjusted for an anticipated high attrition rate of 50%. A 2-sample test of proportions will be used to compare baseline characteristics of both groups.

12b. Statistical methods

All analyses will be conducted using an "intention to treat" (ITT) analysis where all subjects will be compared in the groups which they were originally assigned (regardless of withdrawal or lost to follow-up). For our primary objective, Mann Whitney U test will be used to determine if differences in quality of life measures exist between the ICCC versus self-directed care groups.

For our secondary objective, we will perform univariable analysis to determine which health economic parameters (e.g. missed school days, number of hospital admissions) are related to higher quality of life scores. Stepwise regression will then examine the various combinations via of health economic parameters to generate aROC curves to determine a clinical prediction index for higher quality of life scores. Parameters chosen will be based on using factors that were significant plus those with $P < .25$ level in the univariable analysis and other variables known to have a strong association with poorer health outcomes (e.g. multiple co-morbidities) within the literature. An aROC of ≥0.75 will be considered a clinically relevant cut-off score.[22]

13. ETHICAL CONSIDERATIONS

The study will be conducted in full conformance with principles of the "Declaration of Helsinki" and Good Clinical Practice (GCP).

Low literacy levels:

For caregivers who identify with literacy issues, the AHLO will ensure extra time is used to explain the study and obtain informed consent.[19] Before finalising consent, the AHLO will be required use the "teach back" method and ask the caregiver to explain in their own words what the research study is asking them to do,

including risks and processes involved.[20] For children age ≥12 years, assent will be obtained for participation in the study in conjunction with caregiver consent.

Patient confidentiality:
Identified information (including datasheet forms and consent forms) will only be shared and viewed by investigators involved in patient care or during the data collection phase. Once randomised, patient data will be de-identified and coded according to group allocation. This information will be stored on an excel spreadsheet with a locked code and will only be available to investigators on the project. All hard data will be stored in locked cabinet at Caboolture Hospital for 5 years, as per NHMRC guidelines.

14. OUTCOMES AND SIGNIFICANCE

An integrated care pathway which maximises current community resources and fosters stronger partnerships between primary care and hospital providers has the potential to achieve better integrated health systems and improved health outcomes for children and families with chronic disease within the Australian healthcare context. Possible benefits resulting from this study can include:

- Sustained reduction to Paediatrician's outpatient waiting list as a result of better managed care in the primary care sector (i.e. reduced review referrals requested from GPs)
- Elimination of long wait lists in the long-term, which would allow allied health practitioners to re-focus their skills to more core acute care services within a hospital facility (e.g. management of malnutrition)
- Increased consumer satisfaction of health services
- Stronger relationships between hospital and primary care providers, including public-private health practitioners with a shared electronic database.
- Cost-effective use of public health funding by re-directing funding to a more efficient care pathway that have demonstrated outcomes for children and families managing chronic diseases.

15. REFERENCES

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Statistical Analysis Plan

Study title
Effect of care coordination for children with special health needs without complexity (CSHCN-WC): a multi-center randomized control trial

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Aim
To determine if care coordination improves health-related quality of life for children with special healthcare needs without complexity.

Primary hypotheses
The null hypothesis for each of the two primary outcomes, is that there is no difference in mean pediatric quality of life (PedQL) scores between the trial arms at the primary endpoint (i.e. 12 months). The alternative hypothesis is that there is a difference between the two trial arms.

Study design
Two-arm (integrated care coordination vs standard care), multi-center, open-label, randomized controlled trial

Level of statistical significance
$P<0.05$; two-sided

Sample size
We based our sample size of N=112 on the power of 80% to detect a clinically relevant mean difference between the intervention and control groups, that being 15 units on the PedQL modules with an alpha of 5% and an attrition rate of 50% at 12 months.

Baseline data
Demographic, clinical and self-efficacy data

Randomization
Randomization was undertaken following the recruitment of eligible participants. Participants were then allocated to one of the two trial arms using a permuted block-randomized (1:1) list with a block size of two. This list was created away from the study sites by a statistician using Stata Version 16.

Follow-up trial period
Twelve months

Stopping rules
None

Study population to be analysed
An intention-to-treat analysis was used. All patients who were randomized to one of the two trial arms were subjected to an intention-to-treat analysis.

Interim analysis
Not planned

Primary outcomes
Overall pediatric quality of life as measured by the Pediatric Quality of Life (PedQL) Inventory Version 4.0 (English UK) generic score scales; PedQL Family Impact Module Version 2.0 (English, UK).

Secondary outcomes
Child behaviours, caregiver levels of stress and caregiver's locus of control, as measured by the Child Behavior Checklist (CBCL), Subjective Units of Distress Scale (SUDS) and Rotter's Locus of Control, number of federally funded primary care appointments, specialist appointments, hospital admissions, days absent from school.

Timing of statistical analysis
Data cleansing was conducted on a continual basis throughout the follow-up period of 12 months. Statistical analysis was undertaken and completed thereafter.

Presentation of results
Data is presented by way of their values, confidence intervals and p values.

Comparison of baseline characteristics
Participant baseline characteristics have been presented in a table. Data have been reported as mean with standard deviation (SD) when continuous. Categorical data have been reported as counts and percentages. Differences between continuous variables have been assessed using the Student t-test, whereas Fisher's exact has been used for categorical variables.

Reporting primary outcomes
Means and standard deviations of PedQL Overall and PedQL Family Impact in each study arm will be reported.

Relationship between primary outcome and explanatory variables
General estimating equations have been used to model all primary and secondary outcome variables. In addition to the interaction between group and time variables, model covariates have been identified as significant from univariable analyses. No covariates have been included in the multivariable models on a theory-driven basis. For each of multivariable model, an unstructured correlation has been specified and robust standard errors have been calculated.

Adjustment for multiplicity
We will control for Type 1 errors by adjusting our primary outcomes for different confounders.

Reporting guidelines
Dissemination of study results will comply with the CONSORT Transparent Reporting of Trials (2010) statement.

Missing data
The presence of missing data has been handled by using a repeated measures analysis in the form of generalised estimating equations. Consequently, no observations were excluded if a patient failed to generate data at one or two time-points.

Statistical software
Statistical analyses performed using Stata version 16 (StataCorp, 4905 Lakeway Drive, College Station, Texas 77845 USA http://www.stata.com)

Health economic analysis plan

Carer sick days and child missed school days were summarised using descriptive statistics. Data were censored at time of last contact, with monthly estimates for each group extrapolated to a 12 month period. Bootstrapping used 10,000 replications applied to estimate 95% confidence intervals using the percentile method.

A within-trial cost-effectiveness analysis was conducted to generate an Incremental Cost-Effectiveness Ratio (ICER) for the ICCC intervention relative to control (usual care). A health system perspective was adopted in the base case analysis, with a societal perspective (including carer productivity costs) included in a sensitivity analysis. The time horizon was 12 months, consistent with the period of the trial. As such, discounting was not required. Health system costs included costs of appointments (including specialist, allied health and primary care), hospital admissions and other services including imaging and pathology. As cost data will be sourced from routinely collected datasets, missing data due to loss to follow up were not an issue. Quality Adjusted Life Years (QALYs) were adopted as the measure of effectiveness. Utility values (to estimate QALYs) were derived from the PedsQL survey responses using the mapping algorithm developed by Mpundu-Kaambwa et al (2017). Patients with no follow-up (i.e. 6 month or 12 month) PedsQL data were excluded from the cost-effectiveness analysis. For patients with missing 6 month or 12 month scores, PedsQL scores were imputed using multiple imputation methods. QALYs were derived by estimating the area under the curve using the methods described by Manca et al (2005). A non-parametric probabilistic sensitivity analysis were performed using bootstrapping of cost and QALY pairs with 10,000 replications. This generated 10,000 ICERs which were plotted on a cost-effectiveness plane and used to estimate mean and 95% confidence intervals for Net Monetary Benefit, along with cost-effectiveness acceptability curves.

References:

Manca A, Hawkins N, Sculpher MJ. Estimating mean QALYs in trial-based cost-effectiveness analysis: the importance of controlling for baseline utility. Health economics. 2005 May;14(5):487-96.

Mpundu-Kaambwa C, Chen G, Russo R, Stevens K, Petersen KD, Ratcliffe J. Mapping CHU9D Utility Scores from the PedsQL TM 4.0 SF-15. Pharmacoeconomics. 2017 Apr 1;35(4):453-67.