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The Children and Young People's Health Partnership Evelina London Model of Care: economic evaluation protocol of a complex system change

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Abstract

Introduction: The Children and Young People's Health Partnership (CYPHP) Evelina London Model of Care is a new approach to integrated care delivery for children and young people with common health complaints and chronic conditions. CYPHP includes population health management (services shaped by data-driven understanding of population and individual needs, applied in this case to enable proactive case-finding and tailored biopsychosocial care), specialist clinics with multidisciplinary health teams, and training resources for professionals working with children and young people. This complex health system strengthening program has been implemented in South London since April 2018, and will be evaluated using a cluster randomised control trial (cRCT) with an embedded process evaluation. This protocol describes the within- and beyond-trial economic evaluation of CYPHP.

Methods and analysis: The economic evaluation will identify, measure, and value resources and health outcome impacts of CYPHP compared with Enhanced Usual Care (EUC) from a National Health Service/ Personal Social Service and a broader societal perspective. The study population includes 90,000 children and young people under 16 years of age in 23 clusters (groups of GP practices) to assess health service use and costs, with more detailed cost-effectiveness analysis of a targeted sample of 2,138 children and young people with asthma, eczema, or constipation (tracer conditions). For the cost-effectiveness analysis, health outcomes will be measured using the Pediatric Quality of Life Inventory (PedsQL) and quality-adjusted life years (QALYs) using the Child Health Utility measure (CHU-9D). To account for changes in parental wellbeing, the Warwick-Edinburg Mental Wellbeing Scale (WEMWBS) will be integrated with QALYs in a cost-benefit analysis. The within-trial economic evaluation will be complemented by a novel long-term model that expands the analytic horizon to

10 years. Analyses will adhere to good practice guidelines and National Institute for Health and Care Excellence (NICE) public health reference case.

Strength and limitations of this study:

- Robust study design: CYPHP will be evaluated using a cluster randomised control trial (cRCT) with an embedded process evaluation.
- Multiple analytic perspectives: Both the NHS and Personal Social Services (PSS) perspective and a societal perspective, accounting for costs falling on parents and schools, will be adopted.
- Long analytic horizon: The within-trial economic evaluation will be complemented by a novel long-term model that expands the analytic horizon to 10 years
- Impact of Covid-19 on CYPHP service delivery: Differences in the frequency and duration of each CYPHP component before and after Covid-19 may be observed, which will be assessed in sensitivity analyses.

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Key words: Integrated care, cost-effectiveness, decision modelling, paediatrics

References: 53

Ethics and dissemination: Ethics approval obtained from South West-Cornwall & Plymouth Research Ethics Committee. Results will be submitted for publication in peer-reviewed journals, made available in briefing papers for local decision-makers, and provided to the local community through website and public events. Findings will be generalisable to community-based models of care, especially in urban settings.

Trial registration number: NCT03461848; Pre-results.

Patient and public involvement: Patients or the public were involved in the design, or conduct, or reporting, or dissemination plans of our research

1. INTRODUCTION

In 2018 nearly 1400 excess child deaths occurred in the UK compared with Sweden, adjusting for population size (1,2). The UK fares worse than other high-income countries in chronic disease management too. Only 16% of young people in the UK with type 1 diabetes had a glycated haemoglobin A1c under 7·5%, whereas in Germany and Austria this standard was met for 34% of young people (3–5). Poor chronic disease management results in worse health-related quality of life (6,7), and in higher emergency room visits and hospitalisations, which are key healthcare cost drivers (5,8–11). Beyond direct medical costs, poorly controlled chronic conditions result in time lost from school and employment, placing a significant burden on families. For example, the overall cost of caring for children with asthma aged 1–5 years in the 12 months following attendance at hospital for wheeze or asthma is estimated to be 14.53 million GBP (12).

Ensuring good health in childhood is a public health priority both as a rights-based principle (13), and for the health, social, and economic consequences in adulthood (14,15). Notwithstanding the current pandemic, the UK paediatric healthcare delivery model—originally designed to treat acute conditions through high-intensity specialist and inpatient services—now needs to address chronic health care needs and emphasise preventive care. Previous efforts to integrate care for children and young people (CYP) with ongoing conditions have shown potential for improving quality of life and reducing costs, but evidence is limited (16).

The Children and Young People's Health Partnership (CYPHP) Evelina London Model of Care is an innovative approach to integrated healthcare delivery. It was implemented in April 2018 in two London boroughs (Lambeth and Southwark) where A&E attendance for 0-4 year olds and hospital admissions related to asthma were 16% and 25% higher than the national average, respectively. (17). The CYPHP model aims to strengthen the health system by bridging the gap between primary and secondary care, physical and mental health, and links healthcare with local efforts to tackle the socioeconomic determinants of health. Through coordinated, early intervention, and biopsychosocial care delivered in primary care and community settings, CYPHP has been developed to promote better healthcare and self-management for CYP with common health complaints and chronic conditions(18,19).

CYPHP will be implemented across Southwark and Lambeth in two stages. The staged implementation offers a platform for an opportunistic clustered Randomized Control Trial (cRCT) study design for rigorous evaluation purposes, running alongside a service evaluation reporting regularly to a Partnership Board of commissioner, provider, community organisations, and researchers. In the first CYPHP deployment stage (approximately 3 years), general practices were randomised to either CYPHP (intervention) or Enhanced Usual Care (EUC—control). After three years, CYPHP will be implemented in all of the practices.

The aim of the embedded economic evaluation is, first, to assess the impact of CYPHP compared to EUC on patient-level health care costs from an NHS and Personal Social Service (PSS) perspective for the entire trial population. Second, among children with specific targeted tracer conditions, establish the cost-effectiveness and cost-utility of CYPHP compared to EUC also from an NHS and PSS perspective (NICE reference case). To capture the impact of this complex system change across government sectors, parents, and CYP, a cost-benefit analysis of CYPHP compared to EUC from a societal perspective will also be conducted. The cost-effectiveness of CYPHP compared to EUC beyond the trial duration will also be explored with a state-transition model reflecting natural disease progression for each tracer condition. Existing evaluations of interventions to improve outcomes for children with tracer conditions (such as education initiatives) rarely consider effects

beyond 3 years, which may result in a partial characterization of the intervention effects, and as such this method is a novel application in child health economic research.

Both the population and tracer-conditions analyses aim to inform decisions on the current CYPHP provision in Lambeth and Southwark and throughout the South East London Integrated Care System, as well as its potential expansion to other areas if proven efficient.

2. METHODS AND ANALYSIS

2.1. Study design

The study design and intervention components are outlined in detailed in our published trial protocol paper (18). In summary, seventy general practices in Southwark and Lambeth were grouped into 23 virtual clusters, occurring naturally for GP-pediatrician co-located clinics. Twelve of these clusters were assigned to the intervention (CYPHP) and 11 clusters to the control group (EUC). For randomization, clusters were stratified by borough, and restricted randomization was carried out to ensure the number of CYP under 16 years, their socioeconomic status (measured by the Index of Multiple Deprivation and Income Deprivation Affecting Children Index), and number of outpatient referrals were similar between the two study arms. The trial population includes CYP under 16 years of age registered to a general practice in Southwark or Lambeth.

2.2. Intervention and control arms

The components of CYPHP and EUC are described in **Table 1.** As the intervention arm provides CYPHP on top of EUC, EUC is delivered at all practices. CYPHP offers universal services (available to all CYP, with any childhood condition) and targeted services (available only to CYP with tracer conditions - **asthma, constipation, and/or eczema**). EUC is comprised of several patient self-management support tools for families and resources available to health providers to provide higher quality and more joined-up care for CYP.

Specifically, CYPHP includes:

- CYPHP *universal services*
  - *In-reach clinics,* integrated child health clinics co-delivered by patch-pediatricians and GPs (patch paediatricians are linked to a cluster of general practices) as part of a multidisciplinary CYP health team located in the community.
- CYPHP *targeted services (tracer conditions only)*
  - *Specialist nurse-led team services,* usually delivered by a CYPHP nurse trained in biopsychosocial care (mental health and other specialists are available too if needed) at the CYP's home, during a visit at a community-based clinic, or through a phone call or message. It includes health promotion and self-management advice on tracer conditions. Patients are triaged and care is planned based on a pre-assessment biopsychosocial Health Check and patient records.
  - *Population health management,* where CYP with tracer conditions are sent text messages and a letter from their GP, encouraging them to participate in early intervention and care.

Multidisciplinary team case-planning is important for CYPHP delivery, present in both universal and targeted services. It includes case planning and both formal and informal education and training for professionals providing CYPHP. These multidisciplinary sessions for case planning and education and team building are supplemented with *Lunch-and-learn sessions,* where a multidisciplinary group of CYP health professionals, including pediatricians and primary care staff share knowledge, review

cases, create common professional cultures, build and reinforce team working practices. Finally, s*pecialist team training,* including education and training for primary care, secondary care, or school staff on evidence-based, holistic, and CYP-friendly care, is delivered by CYPHP professionals.

For more details on EUC and CYPHP see Newham and colleagues (2019)(18).

Table 1. CYPHP and EUC intervention components

CYPHP	EUC
▪ EUC	
▪ Universal services: • 1. In-reach clinics	▪Universal services: • Decision support tools for GPs (guidelines and referral guidance for common conditions and minor illnesses) easily accessible during a consultation • Paediatric hotline enabling rapid communication between general practices and paediatricians • School-based emotional resilience building and mental health first aid
▪ Specialist (tracer conditions) services: • 2. Specialist nurse-led service based on Health Check and patient records. Case planning, and informal education and training to support multidisciplinary holistic care. • 3. Specialist team training to primary care, secondary care, or school staff on holistic and CYP-friendly care • 4. Population health management	▪ Specialist (tracer conditions) services: ▪ Health Check ▪ Health Packs for CYP and their parents, comprising condition-specific self-management support, health promotion, and health education material
▪ 5. Multidisciplinary team case-planning and Lunch-and-learn sessions	

Note: Tracer conditions=asthma, constipation, and eczema.

CYP access CYPHP universal services via pediatrician or GP referrals. For specialist services, entry sources include direct referrals (from GP, pediatrician, school nurse, or emergency department), self-referrals (availability publicized through community events, posters in GP practices), and proactive case finding (CYP with tracer conditions are sent text messages and a letter from their GP).

Table 2 describes the expected inputs, frequency, and duration of each CYPHP component. All these data elements will be collected, as actual implementation may differ from protocolised implementation.

Table 2. Protocolised inputs, frequency, and duration of CYPHP components

Intervention component	Recipient	Inputs	Frequency	Duration	Comments
1.In-reach clinics	Patients	Labour: GP and patch-paediatrician	Once a month	20-30 min per patient	2-3 hours total
2.Specialist team service	Patients	Labour: CYPHP nurse and mental health specialist Capital: children's centre	Varies	60 min (home), 30 min (general practice or school)	Service type, duration, and location tailored to CYP
3.Specialist team training	Professionals	Labour: CYPHP nurse, primary care and secondary care staff, school staff	Varies	Varies	.

4.Population health management	Patients	Labour: population health clinician, analyst, manager	Varies	Varies	Data: access, storage, analysis Proactive case finding: costs for sending messages
5. Multidisciplinary team case planning and Lunch-and-learn	Children's Health Professionals	Labour: CYPHP nurse, mental health specialist, paediatrician and GP who works alongside CYPHP	Once a week	60 min	.

2.3. Economic evaluation within the trial

2.3.1. Population-level cost analysis

The goal of the population-level analysis is to assess the impact of CYPHP compared to EUC on healthcare costs of health service use. This analysis will use the whole study population, which includes children and young people, 0-16 years of age, registered with a Southwark or Lambeth GP practice. Health service use will include primary care consultations, visits with pediatricians, hospital outpatient, hospital inpatient, and accident and emergency care during 6 and 12 months. Patient-level costs will be obtained by multiplying unit costs by utilisation. National unit costs for children's services will be obtained from the Unit Costs of Health and Social Care 2019 by the Personal Social Services Resource Unit (20) and the NHS reference costs for 2015-16 (21). Due to the often-skewed cost distribution with a large number of zeros and a long right-hand tail, the modified Park Test and Pregibon Link test will assess the most appropriate distribution and link to calibrate a Generalized linear model (GLM) for costs, for example, with a gamma distribution and a log-link (22,23). The cost model will adjust for a binary variable indicating whether the children or young person belonged to the intervention or control arm and any demographic variables that show imbalance between the two groups.

2.3.2. Tracer conditions: cost-effectiveness/utility and cost-benefit analyses

This within-trial economic evaluation will also compare CYPHP with EUC for patients under 16 with asthma, constipation, and/or eczema. Three types of economic evaluation will be conducted. The cost-effectiveness analysis, using point improvement in the PedsQL scale as the primary outcome, and the cost-utility analysis, based on quality-adjusted life years (QALYs) from the CHU-9D, will adopt an NHS and Personal Social Services (PSS) perspective. The cost-benefit analysis will take a societal perspective and additionally account for costs falling on parents, and schools, as well as valuing parental wellbeing with the Warwick-Edinburg Mental Wellbeing Scale (WEMWBS). These analyses will adhere to guidelines for conducting economic evaluations alongside clinical trials[1] and the most recent National Institute for Health and Care Excellence (NICE) public health reference case(24–27).

Costing: Identification, measurement, and valuation of resources

Costing involves identifying, measuring, and valuing the resources used to deliver and participate in the intervention, and consequential health and social services use. In a complex system change such as CYPHP, the comprehensive identification of resources requires close collaboration with the implementation and the process evaluation teams.

Identification of resource use

CYPHP health and social care costs borne by the NHS and PSS mainly include time spent by medical professionals and service managers delivering CYPHP services, along with consequential health and social services utilisation by patients (**Table 3**). From a societal perspective, time spent by school staff participating in CYPHP and time away from work or school by parents and CYP are also accounted for. Because both intervention and control practices include EUC, EUC's delivery costs will be disregarded. Service use and time away from school and work will be considered for both CYPHP and EUC.

Measurement of resource use

Resources used to implement CYPHP will be gathered from seven data sources, including the study's accounting data, service caseloads, CYPHP nurse's personal caseload notes, study questionnaires, primary care data, secondary care data, and interviews with CYPHP nurses (**Table 3**). EMIS will provide location, type, number and length of visits part of in-reach clinics and specialist team services. CYPHP nurse's caseload notes will supply information on specialist team training and multidisciplinary team case-planning. Time spent at lunch-and-learn sessions will be obtained from service caseloads. Patient-level service use will be gathered from primary and secondary care activity files. Family and CYP time away from work or school are questions included in the study questionnaires. Interviews with a random sample of CYPHP nurses to understand their phone usage and transportation to patient visits will also be conducted.

Valuation of resource use

As with the population-level cost analysis, national unit costs for children's services will be obtained from the Unit Costs of Health and Social Care 2019 (20) and NHS reference costs for 2015-16 (21). The Unit Costs of Health and Social Care 2014 version will also be used to value referrals to social care services (28). Unit costs not available from these sources will be collected from trial records directly (e.g. monthly rent of children's health center use). All unit costs will be presented in pounds sterling (£) for a base cost year 2020/2021; the Hospital and Community Health Services pay and price index will be used to adjust for inflation(28). As the horizon of the within-trial analysis is 6 and 12 months, no discounting will be applied to either costs or outcomes.

Table 3. Identification and measurement of costs

Cost components	Description of resources used	Unit of measure	Source, level data collected
Intervention delivery costs			
Set-up costs	Hiring costs, training, materials	Total costs	Study's accounting data
1.In-reach clinics	Paediatrician, general practitioner, mental health specialist, etc.	Minutes	Primary care data (EMIS), patient
2.Specialist nurse-led services	•CYPHP nurses, mental health specialists, etc.	Minutes	Primary care data, patient
	•Phone usage	Minutes/text messages	Interview CYPHP nurse, service
	•Travel to patients (distance and mileage)	Minutes and £	Primary care data and interview CYPHP nurse, service
	•Children's center	Rent	Study's accounting data, service
3.Specialist team training	•CYPHP nurses, primary care, secondary care staff, etc.	Minutes	CYPHP nurse's caseload notes, service
	•School staff	Minutes	
4.Population health management	•Population health clinician, analyst, manager	Minutes	Study's accounting data, service
5.Multidisciplinary team case-planning	•CYPHP nurses, primary care, secondary care staff, etc.	Minutes	CYPHP nurse's caseload notes, service
Lunch-and-learn sessions	Paediatrician, general practitioner, other child health professionals, clerks/administrative, etc.	Minutes	Service Caseloads, service
Overhead costs	Using spaces, data access and storage	£	Study's accounting data
Service use			
	•General practitioner	No. visits	Primary care data and secondary care activity, patient
	•Paediatrician	No. visits	
	•Hospital outpatient	No. visits	
	•Hospital inpatient	No. visits	
	•Accident and emergency	No. visits	
	•Social care services†	Referral yes/no	
CYP and family			
	Time away from school	Hours	Study questionnaires, patient
	Time away from work	Hours	Study questionnaires, parent

Note: †CYPHP nurses may refer CYP and their families to social care services. An indicator for referrals to social services is available in primary care data. EMIS=Egton Medical information Systems. Secondary care data (inpatient stays, A&E attendances, and outpatient visits) will be obtained from Guy's and Sant Thomas' NHS Foundation Trust and King's College Hospital data.

Computation of total costs

Total costs will be computed at the patient level by summing *intervention delivery costs* (only CYP in intervention arm) and *health service use cost* (CYP in intervention and control arms)

- *Intervention delivery costs* will include set-up, CYPHP delivery and overhead costs. Some of these components will vary across patients (e.g., specialist team services), others across clinics (e.g., staff specialist training), and others will be the same for all patients (e.g., overhead costs such as the cost of administration and facilities). Staff specialist training costs, costs of universal services (in-reach clinics), intervention set-up costs, and overheads will each be apportioned. CYP with tracer conditions are the target population of the economic evaluation. The cost of universal services, however, also needs to be considered as CYP with tracer conditions may be referred to specialist team services during an in-reach clinic visit. Different apportioning rules will be used, for example, the costs of universal services could be apportioned by using the percentage of CYP with tracer conditions who were referred by in-reach clinics. Total per-patient apportioned costs will be added to patient-level specialist team services costs.
- *Health service use costs* will result from multiplying the quantity of services used, by their unit cost, and summing across services types for each patient.

Total costs of patients in the control arm will only reflect health service use costs.

In the cost-benefit analysis, total costs will also include costs borne by patients, parent and schools. Patient and parents' costs will be comprised of school and work time lost, respectively. Schools' costs will include time spent by school staff attending specialist team training.

Measurement and valuation of health outcomes

The trial's primary health outcome measure of the tracer conditions evaluation is the Pediatric Quality of Life Inventory (PedsQL), which will be used in the cost-effectiveness analysis. The PedsQL includes 23 items covering physical, emotional, social and school functioning(29) and is available through 6 age-specific questionnaires (0-12 months, 13-24 months, 2-4 years, 5-7 years, 8-12 years, and 13-17 years). The PedsQL has shown to be reliable, valid and responsive to meaningful change across general and disease-specific populations(29–31). The Child Health Utility questionnaire (CHU-9D)—a generic preference-based measure of paediatric health-related quality of life that allows the calculation of quality adjusted life years (QALYs)—will be the health outcome measure for cost-utility analysis. The 9 items of CHU-9D cover feeling worried, sad, tired, annoyed, perceptions of schoolwork, sleep, daily routine, and social activities. The tool is designed to be administered to CYP between 7-17 years of age, and a proxy version to be completed by parents is available for younger children(32,33). The Warwick-Edinburg Mental Wellbeing Scale (WEMWBS) (34) will serve as a well-being questionnaire for parents. All questionnaires were administered at baseline and at two follow-up points (6 and 12 months). Questionnaires completed during the first phase of the Covid-19 pandemic [12 March 2020 – 6 July 2020], will be repeated after this period, and follow-up measures delayed. Multiple imputation will be used for questionnaires with missing values.

In the cost-benefit analysis, QALYs and WEMWBS will be combined by converting both to Pound Sterling values. QALYs will be monetised by using the government sector willingness-to-pay of £20,000 to £30,000 per QALY gained(35). For WEMWBS, the monetary values published by Simetrica and HACT for each Short-version WEMWBS (SWEMWBS) score will be employed and converted to cost year 2020/2021 (36). The SWEMWBS score can be obtained from the original WEBWMS using seven of its 14 statements about thoughts and feelings.

Statistical analyses

The intention-to-treat population will be used in statistical analyses. First, differences between protocolized and actual intervention components (including inputs, frequency and duration of each component) will be assessed (**Table 2**). Second, univariate analyses will be conducted to describe sample mean differences and variability across time between treatment and control group for each outcome. Three time points will contribute to analysis; baseline, 6-months, and 12 months. Third, to adjust for treatment group imbalances, multilevel regression models will be estimated for total costs, QALYs, PedsQL score, and benefits (£ corresponding to QALYs and WEBWMS scores together)(37). All these models will control for variables that, despite randomization, may still be unequally distributed between intervention and control groups such as age, gender and deprivation level for the patient-level models. For the regression model predicting QALYs, the baseline QALYs will also be controlled for(38). Benefits will be estimated using ordinary least squares, and costs with a GLM model with a gamma distribution and a log-link. Both the use of a GLM and limited dependent variable mixture models will be considered when modelling QALYs(39). All models will cluster standard errors to account for correlation of patients in the same CYPHP cluster.

For each outcome variable and intervention and control groups separately, mean predicted values will be generated. Three incremental cost-effectiveness ratios (difference between intervention and control in mean predicted costs over difference in mean predicted outcomes) will be computed, one for the cost-effectiveness analysis (based on PedsQL scores), another for the cost-utility analysis (using QALYs), and a third one for the cost-benefit analysis (£). These three ICERs will be generated based on 6 and 12-months data.

The pattern and amount of missing data between treatment and control groups by study variable will be assessed. If data is missing completely at random for both treatment and control groups and the percentage of missing data is below 5%, missing data will be ignored. If data is missing at random (MAR), multiple imputation accounting for clustering (such as fixed effects) will be used (40). When the data is MAR, multiple imputation can lead to consistent, asymptotically efficient, and asymptotically normal estimates(41).

Handling uncertainty

The level of decision uncertainty arising from sampling and assumptions on key parameter estimates with policy impact will be assessed. Confidence intervals for ICERs based on the non-parametric bootstrap method will be generated(42), along with acceptability curves to reflect the probability of CYPHP being cost-effective as the willingness-to-pay per QALY (or other health outcome) increases. Deterministic sensitivity analyses on chosen variables (such as intervention set-up costs, intensity of services delivered, and social care costs) will assist in identifying key drivers of the results. Subgroup analysis of cost-effectiveness results by tracer condition and quintiles of IMD will be conducted as long as a sufficient sample size is available.

2.3. Long-term modelling of health and costs beyond the trial

A state-transition model reflecting natural disease progression will be developed for each tracer condition to predict the cost-effectiveness of CYPHP compared to EUC beyond the trial duration. Trial data will be used to define the health states, transition probabilities among states, and to calculate the costs and effects from an NHS/PSS perspective. Existing literature and publicly available statistics (e.g., Office of National Statistics and existing UK cohort studies) will also be used to gather transition probabilities across states beyond 12 months. A functional form characterizing the sustainability of intervention effects into the longer run (changes in health-related quality of life and

health services utilisation) will be inferred based on 6 months and 12 months trial data. The effect of alternative analytic horizons on the cost-effectiveness of CYPHP versus EUC will be tested in sensitivity analyses, including 2, 5, and 10 years.

DISCUSSION

The CYPHP Evelina London model is a health-systems strengthening programme to advance towards integrated and high-quality care for children and young people in the UK. By offering universal and targeted services, CYPHP aims to overcome patient- and provider-level barriers to effective management of physical and mental health and foster optimal health behaviour. The aims of this economic evaluation are to establish the impact of CYPHP on healthcare costs at the population level and the cost-effectiveness of the intervention among CYP with tracer conditions. Asthma, constipation, and eczema serve as examples of common long-term conditions among CYP. Lessons from managing these conditions should inform a broader health system response to the epidemiological transition to chronic diseases.

Strengths and weaknesses

Beyond temporary trial suspension, Covid-19 may have affected our study in at least two ways. First, CYPHP delivery may not return to normal after the pandemic. Differences in the frequency and duration of each CYPHP component before and after Covid-19 will be assessed in sensitivity analyses. Second, some follow-up questionnaires were due during Covid-19. When possible, data were collected, and an additional data point after Covid-19 was included for these participants to isolate changes in health status due to the pandemic.

By carrying out three economic evaluations (cost-effectiveness, cost-utility, and cost-benefit) under two different perspectives (NHS and PSS, and societal), we aim to inform stakeholders with various interests, including Clinical Commissioning Groups and evolving Integrated Care System, GP Federations, Provider Trusts, CYP and their families. With CYPHP, healthcare utilisation costs may remain stable if primary care visits increase, but hospitalisations and emergency room visits decrease. Parents and children's costs related to time lost from work or school are also expected to decline with CYPHP if CYP's tracer conditions are well managed. Our planned analyses will allow both to be studied and accounted for.

The long-term model will assess the cost-effectiveness of CYPHP compared to EUC beyond the trial duration to fully capture intervention effects on children with asthma, constipation and/or eczema. Existing cost-effectiveness studies assessing interventions for CYP with these tracer conditions rarely include a long-term model, and the duration of RCTs of education, coaching, nurse-led clinics or treatments for the tracer conditions tend to be under three years (43–48). CYPHP is expected to foster long-lasting improvements beyond 12 months in health outcomes due to changes in disease management behaviour among the CYP and family, and also health professionals. The natural progression of the tracer conditions indicates that a substantial percentage of children continue to experience symptoms beyond 12 months, and sometimes even into adulthood. Asthma in childhood persists into adulthood for 79% of the cases (49). About half of children with atopic eczema still have the problem as adults (50,51). Twenty five percent of children with functional constipation continue to experience symptoms as adults (52,53).

This study will contribute rigorous evidence about health economics of children's integrated healthcare in the UK, where there has been a notable paucity of high-quality evidence. Results from this study will directly inform decisions on children's healthcare provision in South East London and will provide rigorous evidence to inform policy nationally and internationally.

Authors contributions

Marina Soley-Bori: Conceptualization, Methodology, Writing - Original Draft, Writing - Review & Editing, Investigation, Visualisation; Raghu lingam: Writing - Review & Editing, Funding acquisition; Rose-Marie Satherley: Writing - Review & Editing, Investigation. Julia Forman: Writing - Review & Editing. Lizzie Cecil: Writing - Review & Editing. Julia Fox-Rushby: Conceptualization, Methodology, Supervision, Writing - Review & Editing; Ingrid Wolfe: Writing - Review & Editing, Funding acquisition.

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Declaration of interests

The authors declare no conflict of interest

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The Children and Young People's Health Partnership Evelina London Model of Care: economic evaluation protocol of a complex system change

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Abstract

Introduction: The Children and Young People's Health Partnership (CYPHP) Evelina London Model of Care is a new approach to integrated care delivery for children and young people with common health complaints and chronic conditions. CYPHP includes population health management (services shaped by data-driven understanding of population and individual needs, applied in this case to enable proactive case-finding and tailored biopsychosocial care), specialist clinics with multidisciplinary health teams, and training resources for professionals working with children and young people. This complex health system strengthening program has been implemented in South London since April 2018, and will be evaluated using a cluster randomised control trial (cRCT) with an embedded process evaluation. This protocol describes the within- and beyond-trial economic evaluation of CYPHP.

Methods and analysis: The economic evaluation will identify, measure, and value resources and health outcome impacts of CYPHP compared with Enhanced Usual Care (EUC) from a National Health

Service/ Personal Social Service and a broader societal perspective. The study population includes 90,000 children and young people under 16 years of age in 23 clusters (groups of GP practices) to assess health service use and costs, with more detailed cost-effectiveness analysis of a targeted sample of 2,138 children and young people with asthma, eczema, or constipation (tracer conditions). For the cost-effectiveness analysis, health outcomes will be measured using the Pediatric Quality of Life Inventory (PedsQL) and quality-adjusted life years (QALYs) using the Child Health Utility measure (CHU-9D). To account for changes in parental wellbeing, the Warwick-Edinburg Mental Wellbeing Scale (WEMWBS) will be integrated with QALYs in a cost-benefit analysis. The within-trial economic evaluation will be complemented by a novel long-term model that expands the analytic horizon to 10 years. Analyses will adhere to good practice guidelines and National Institute for Health and Care Excellence (NICE) public health reference case.

Ethics and dissemination: The study has received ethical approval from South West-Cornwall & Plymouth Research Ethics Committee (REC Reference: 17/SW/0275. Results will be submitted for publication in peer-reviewed journals, made available in briefing papers for local decision-makers, and provided to the local community through website and public events. Findings will be generalisable to community-based models of care, especially in urban settings.

Trial registration number: NCT03461848; Pre-results.

Strength and limitations of this study:

- Robust study design: CYPHP will be evaluated using a cluster randomised control trial (cRCT) with an embedded process evaluation.
- Multiple analytic perspectives: Both the NHS and Personal Social Services (PSS) perspective and a societal perspective, accounting for costs falling on parents and schools, will be adopted.
- Long analytic horizon: The within-trial economic evaluation will be complemented by a novel long-term model that expands the analytic horizon to 10 years
- Impact of Covid-19 on CYPHP service delivery: Differences in the frequency and duration of each CYPHP component before and after Covid-19 may be observed, which will be assessed in sensitivity analyses.
- Measurement of intervention effects: The intensity of the different intervention components may have varied across GP practices and the measurement of health effects with the CHU-9D for children below 5 may lack reliability.

Key words: Integrated care, cost-effectiveness, decision modelling, paediatrics

1. INTRODUCTION

In 2018 nearly 1400 excess child deaths occurred in the UK compared with Sweden, adjusting for population size (1,2). The UK fares worse than other high-income countries in chronic disease management too. Only 16% of young people in the UK with type 1 diabetes had a glycated haemoglobin A1c under 7·5%, whereas in Germany and Austria this standard was met for 34% of young people (3–5). Poor chronic disease management results in worse health-related quality of life (6,7), and in higher emergency room visits and hospitalisations, which are key healthcare cost drivers (5,8–11). Beyond direct medical costs, poorly controlled chronic conditions result in time lost from school and employment, placing a significant burden on families. For example, the overall cost of caring for children with asthma aged 1–5 years in the 12 months following attendance at hospital for wheeze or asthma is estimated to be 14.53 million GBP (12).

Ensuring good health in childhood is a public health priority both as a rights-based principle (13), and for the health, social, and economic consequences in adulthood (14,15). Notwithstanding the current pandemic, the UK paediatric healthcare delivery model—originally designed to treat acute conditions through high-intensity specialist and inpatient services—now needs to address chronic health care needs and emphasise preventive care. Previous efforts to integrate care for children and young people (CYP) with ongoing conditions have shown potential for improving quality of life and reducing costs, but evidence is limited (16).

The Children and Young People's Health Partnership (CYPHP) Evelina London Model of Care is an innovative approach to integrated healthcare delivery. It was implemented in April 2018 in two London boroughs (Lambeth and Southwark) where A&E attendance for 0-4 year olds and hospital admissions related to asthma were 16% and 25% higher than the national average, respectively. (17). The CYPHP model aims to strengthen the health system by bridging the gap between primary and secondary care, physical and mental health, and links healthcare with local efforts to tackle the socioeconomic determinants of health. Through coordinated, early intervention, and biopsychosocial care delivered in primary care and community settings, CYPHP has been developed to promote better healthcare and self-management for CYP with common health complaints and chronic conditions(18,19). The concept of biopsychosocial care follows many of the tenets of patient centred care as outlined by Tramonti and colleagues (20), however we use a more specific term to describe the model in greater detail.

CYPHP will be implemented across Southwark and Lambeth in two stages. The staged implementation offers a platform for an opportunistic clustered Randomised Control Trial (cRCT) study design for rigorous evaluation purposes, running alongside a service evaluation reporting regularly to a Partnership Board of commissioner, provider, community organisations, and researchers. In the first CYPHP deployment stage (approximately 3 years), general practices were randomised to either CYPHP (intervention) or Enhanced Usual Care (EUC—control). After three years, CYPHP will be implemented in all of the practices.

The aims of the embedded economic evaluation are, first, to assess the impact of CYPHP compared to EUC on patient-level health care costs from an NHS and Personal Social Service (PSS) perspective for the entire trial population. Second, among children with specific targeted tracer conditions, to compare costs and health outcomes and establish the cost-effectiveness (cost per point improvement in the PedsQL) and cost-utility (cost per QALY) of CYPHP versus EUC also from an NHS and PSS perspective (NICE reference case(21)). Third, to capture the impact of this complex system change across government sectors, parents, and CYP, a cost-benefit analysis (cost per monetarized unit of WEMWBS and QALYs) of CYPHP compared to EUC from a societal perspective will also be

conducted. The cost-effectiveness of CYPHP compared to EUC beyond the trial duration will be explored with a state-transition model reflecting natural disease progression for each tracer condition. Existing evaluations of interventions to improve outcomes for children with tracer conditions (such as education initiatives) rarely consider effects beyond 3 years, which may result in a partial characterization of the intervention effects, and as such this method is a novel application in child health economic research. Both the economic evaluation and the state-transition model are essential as they will determine whether potential health gains related to the intervention justify its costs relative to current practice, and therefore whether a decision to provide and roll-out the intervention is justifiable in terms of efficiency.

Both the population and tracer-conditions analyses aim to inform decisions on the current CYPHP provision in Lambeth and Southwark and throughout the South East London Integrated Care System, as well as its potential expansion to other areas if proven efficient.

2. METHODS AND ANALYSIS

2.1. Study design

The study design and intervention components are outlined in detailed in our published trial protocol paper (18). In summary, seventy general practices in Southwark and Lambeth were grouped into 23 virtual clusters, occurring naturally for GP-pediatrician co-located clinics. Twelve of these clusters were assigned to the intervention (CYPHP) and 11 clusters to the control group (EUC). For randomization, clusters were stratified by borough, and restricted randomization was carried out to ensure the number of CYP under 16 years, their socioeconomic status (measured by the Index of Multiple Deprivation and Income Deprivation Affecting Children Index), and number of outpatient referrals were similar between the two study arms. The trial population includes CYP under 16 years of age registered to a general practice in Southwark or Lambeth. Key information on the CYPHP intervention and evaluation are summarized in **Table 1**.

Table 1. Key features of the CYPHP intervention and evaluation

Targeted recruitment sample without loss to follow-up	1,496
Route to change	•A theoretically informed intervention (Theoretical Domains Framework) • Evidence based (based on systematic review on integrated care models for child health(16)) •Integrates care in line with patient, provider, and policy perspectives – providing efficient, preventive access to care, closer to home
Main strengths	• Opportunistic randomised controlled trial •Rich data with both patient-reported and routine service use data •Embedded process evaluation to assess CYPHP implementation success
Stakeholder involvement	CYPHP was developed with children and young people, carers, frontline practitioners, and health service commissioners

2.2. Intervention and control arms

The study structure and components of CYPHP and EUC are described in **Figure 1.** As the intervention arm provides CYPHP on top of EUC, EUC is delivered at all practices. CYPHP offers universal services (available to all CYP, with any childhood condition) and targeted services (available only to CYP with tracer conditions - **asthma, constipation, and/or eczema**). EUC is comprised of several patient self-management support tools for families and resources available to health providers to provide higher quality and more joined-up care for CYP.

Specifically, CYPHP includes:

- CYPHP *universal services*
    1. *In-reach clinics,* integrated child health clinics co-delivered by patch-pediatricians and GPs (patch paediatricians are linked to a cluster of general practices) as part of a multidisciplinary CYP health team located in the community.
    2. *Lunch-and-learn sessions,* where a multidisciplinary group of CYP health professionals, including pediatricians and primary care staff share knowledge, review cases, create common professional cultures, build and reinforce team working practices.
- CYPHP *targeted services (tracer conditions only)*
    3. *Specialist nurse-led services,* usually delivered by a CYPHP nurse trained in biopsychosocial care (mental health and other specialists are available too if needed) at the CYP's home, during a visit at a community-based clinic, or through a phone call or message. It includes health promotion and self-management advice on tracer conditions. Patients are triaged and care is planned based on a pre-assessment biopsychosocial Health Check (CYPHP Health Check) and patient records. The CYPHP Health Check is administered to patients with asthma, constipation, or eczema. It uses validated questionnaires when possible to measure biopsychosocial health. Child's ongoing conditions are assessed with the Patient Oriented Eczema Measure (POEM)(22) for children with eczema, the Asthma Control Test (ACT)(23) for asthma, and a bespoke CYPHP constipation questionnaire (validation work underway). The Strengths and Difficulties Questionnaire (SDQ)(24) is used as an emotional and behavioural screening questionnaire. Finally, a set of bespoke social questions to understand a family's broader situation and factors that may affect their health and care, such as financial worries and days lost of school or work, are also included. Participants who consent as research subjects, do also complete the Paediatric Quality of Life Inventory (PedsQL)(25) and the Child Health Utility 9-D (CHU-9D)(26).

    4. *Population health management,* where CYP with tracer conditions are sent text messages and a letter from their GP, encouraging them to participate in early intervention and care. Recipients are identified based on analyses of electronic health records and actively reached out to connect them with the healthcare system and improve the management of their conditions before they exacerbate.

    5. Specialist team training, including education and training for primary care, secondary care, or school staff on evidence-based, holistic, and CYP-friendly care for tracer conditions, is delivered by CYPHP professionals.

Multidisciplinary team case-planning is important for CYPHP delivery, present in both universal and targeted services. It includes case planning and both formal and informal education and training for professionals providing CYPHP.

Table 2 describes the expected inputs, frequency, and duration of each CYPHP component. All these data elements will be collected, as actual implementation may differ from protocolised implementation.

Table 2. Protocolised inputs, frequency, and duration of CYPHP components

Intervention component	Inputs	Frequency	Duration	Comments
1.In-reach clinics	Labour: GP and patch-paediatrician	Once a month	20-30 min per patient	2-3 hours total
2. Lunch-and-learn sessions	Labour: CYPHP nurse, mental health specialist, paediatrician and GP who works alongside CYPHP	Once a week	60 min	
3.Specialist nurse-led service	Labour: CYPHP nurse and mental health specialist Capital: children's centre	Varies	60 min (home), 30 min (general practice or school)	Service type, duration, and location tailored to CYP
4.Population health management	Labour: population health clinician, analyst, manager	Varies	Varies	Data: access, storage, analysis Proactive case finding: costs for sending messages
5.Specialist team training	Labour: CYPHP nurse, primary care and secondary care staff, school staff	Varies	Varies	.
6. Multidisciplinary team case planning	Labour: CYPHP nurse, mental health specialist, paediatrician and GP who works alongside CYPHP	Once a week	60 min	.

CYP access CYPHP universal services via pediatrician or GP referrals. For specialist services, entry sources include direct referrals (from GP, pediatrician, school nurse, or emergency department), self-referrals (availability publicized through community events, posters in GP practices), and proactive case finding (CYP with tracer conditions are sent text messages and a letter from their GP). Further details on CYPHP's implementation are included in the publicly available handbook(27).

2.3. Patient and Public Involvement

Stakeholders were involved in the development of the theoretical framework for CYPHP, identification of research questions and refining the research methodology. Stakeholders included children and young people, carers, frontline practitioners, and health service commissioners. A patient and public involvement group was developed with children and their families and it was consulted with regard to evaluation design; including appropriateness of outcome measures and consent procedures.

2.4. Economic evaluation within the trial

2.4.1. Population-level cost analysis

The goal of the population-level analysis is to assess the impact of CYPHP compared to EUC on healthcare costs of health service use. This analysis will use the whole study population, which includes children and young people, 0-15 years of age, registered with a Southwark or Lambeth GP practice. Health service use will include primary care consultations, visits with pediatricians, hospital outpatient, hospital inpatient, and accident and emergency care during 6 and 12 months. Patient-level costs will be obtained by multiplying unit costs by utilisation. National unit costs for children's services will be obtained from the Unit Costs of Health and Social Care 2019 by the Personal Social Services Resource Unit (28) and the NHS reference costs for 2015-16 (29). Due to the often-skewed cost distribution with a large number of zeros and a long right-hand tail, the modified Park Test and Pregibon Link test will assess the most appropriate distribution and link to calibrate a Generalized linear model (GLM) for costs, for example, with a gamma distribution and a log-link (30,31). The cost model will adjust for a binary variable indicating whether the children or young person belonged to the intervention or control arm and any demographic variables that show imbalance between the two groups.

2.4.2. Tracer conditions: cost-effectiveness/utility and cost-benefit analyses

This within-trial economic evaluation will also compare CYPHP with EUC for patients under 16 with asthma, constipation, and/or eczema. Three types of economic evaluation will be conducted. The cost-effectiveness analysis, using point improvement in the PedsQL scale as the primary outcome, and the cost-utility analysis, based on quality-adjusted life years (QALYs) from the CHU-9D, will adopt an NHS and Personal Social Services (PSS) perspective. PSS includes a range of services provided by local authorities for vulnerable groups, including the mentally and physically disabled, older people, and neglected children. The cost-benefit analysis will take a societal perspective and additionally account for costs falling on parents, and schools, as well as valuing parental wellbeing with the Warwick-Edinburg Mental Wellbeing Scale (WEMWBS). These analyses will adhere to guidelines for conducting economic evaluations alongside clinical trials and the most recent National Institute for Health and Care Excellence (NICE) public health reference case(32–35).

Costing: Identification, measurement, and valuation of resources

Costing involves identifying, measuring, and valuing the resources used to deliver and participate in the intervention, and consequential health and social services use. In a complex system change such as CYPHP, the comprehensive identification of resources requires close collaboration with the implementation and the process evaluation teams.

Identification of resource use

CYPHP health and social care costs borne by the NHS and PSS mainly include time spent by medical professionals and service managers delivering CYPHP services, along with consequential health and social services utilisation by patients (**Table 3**). From a societal perspective, time spent by school staff participating in CYPHP and time away from work or school by parents and CYP are also accounted for. Because both intervention and control practices include EUC, EUC's delivery costs will be disregarded. Service use and time away from school and work will be considered for both CYPHP and EUC.

Measurement of resource use

Resources used to implement CYPHP will be gathered from seven data sources, including the study's accounting data, service caseloads, CYPHP nurse's personal caseload notes, study questionnaires,

primary care data, secondary care data, and interviews with CYPHP nurses (**Table 3**). EMIS will provide location, type, number and length of visits part of in-reach clinics and specialist team services. CYPHP nurse's caseload notes will supply information on specialist team training and multidisciplinary team case-planning. Time spent at lunch-and-learn sessions will be obtained from service caseloads. Patient-level service use will be gathered from primary and secondary care activity files. Family and CYP time away from work or school are questions included in the study questionnaires. Interviews with a random sample of CYPHP nurses to understand their phone usage and transportation to patient visits will also be conducted.

Valuation of resource use

As with the population-level cost analysis, national unit costs for children's services will be obtained from the Unit Costs of Health and Social Care 2019 (28) and NHS reference costs for 2015-16 (29). The Unit Costs of Health and Social Care 2014 version will also be used to value referrals to social care services (36). Unit costs not available from these sources will be collected from trial records directly (e.g. monthly rent of children's health center use). All unit costs will be presented in pounds sterling (£) for a base cost year 2019/2020; the NHS Cost Inflation Index (NHSCII) will be used to adjust for inflation(36). As the horizon of the within-trial analysis is 6 and 12 months, no discounting will be applied to either costs or outcomes.

Table 3. Identification and measurement of costs

Cost components	Description of resources used	Unit of measure	Source, level data collected
Intervention delivery costs			
Set-up costs	Hiring costs, training, materials	Total costs	Study's accounting data
1.In-reach clinics	Paediatrician, general practitioner, mental health specialist, etc.	Minutes	Primary care data (EMIS), patient
2.Lunch-and-learn sessions	Paediatrician, general practitioner, other child health professionals, clerks/administrative, etc.	Minutes	Service Caseloads, service
3.Specialist nurse-led services	•CYPHP nurses, mental health specialists, etc.	Minutes	Primary care data, patient
	•Phone usage	Minutes/text messages	Interview CYPHP nurse, service
	•Travel to patients (distance and mileage)	Minutes and £	Primary care data and interview CYPHP nurse, service
	•Children's center	Rent	Study's accounting data, service
4.Population health management	•Population health clinician, analyst, manager	Minutes	Study's accounting data, service
5.Specialist team training	•CYPHP nurses, primary care, secondary care staff, etc.	Minutes	CYPHP nurse's caseload notes, service
	•School staff	Minutes	
6.Multidisciplinary team case-planning	•CYPHP nurses, primary care, secondary care staff, etc.	Minutes	CYPHP nurse's caseload notes, service
Overhead costs	Using spaces, data access and storage	£	Study's accounting data
Service use			
	•General practitioner	No. visits	Primary care data and secondary care activity,

	•Paediatrician	No. visits	patient
	•Hospital outpatient	No. visits	
	•Hospital inpatient	No. visits	
	•Accident and emergency	No. visits	
	•Social care services†	Referral yes/no	
CYP and family			
	Time away from school	Hours	Study questionnaires, patient
	Time away from work	Hours	Study questionnaires, parent

Note: †CYPHP nurses may refer CYP and their families to social care services. An indicator for referrals to social services is available in primary care data. EMIS=Egton Medical information Systems. Secondary care data (inpatient stays, A&E attendances, and outpatient visits) will be obtained from Guy's and Sant Thomas' NHS Foundation Trust and King's College Hospital data.

Computation of total costs

Total costs will be computed at the patient level by summing *intervention delivery costs* (only CYP in intervention arm) and *health service use cost* (CYP in intervention and control arms)

- *Intervention delivery costs* will include set-up, CYPHP delivery and overhead costs. Some of these components will vary across patients (e.g., specialist team services), others across clinics (e.g., staff specialist training), and others will be the same for all patients (e.g., overhead costs such as the cost of administration and facilities). Staff specialist training costs, costs of universal services (in-reach clinics), intervention set-up costs, and overheads will each be apportioned. CYP with tracer conditions are the target population of the economic evaluation. The cost of universal services, however, also needs to be considered as CYP with tracer conditions may be referred to specialist team services during an in-reach clinic visit. Different apportioning rules will be used, for example, the costs of universal services could be apportioned by using the percentage of CYP with tracer conditions who were referred by in-reach clinics. Total per-patient apportioned costs will be added to patient-level specialist team services costs.
- *Health service use costs* will result from multiplying the quantity of services used, by their unit cost, and summing across services types for each patient.

Total costs of patients in the control arm will only reflect health service use costs.

In the cost-benefit analysis, total costs will also include costs borne by patients, parent and schools. Patient and parents' costs will be comprised of school and work time lost, respectively. Schools' costs will include time spent by school staff attending specialist team training.

Measurement and valuation of health outcomes

The trial's primary health outcome measure of the tracer conditions evaluation is the Pediatric Quality of Life Inventory (PedsQL), which will be used in the cost-effectiveness analysis. The PedsQL includes 23 items covering physical, emotional, social and school functioning(25) and is available through 6 age-specific questionnaires (0-12 months, 13-24 months, 2-4 years, 5-7 years, 8-12 years, and 13-17 years). The PedsQL has shown to be reliable, valid and responsive to meaningful change across general and disease-specific populations(25,37,38). The Child Health Utility questionnaire (CHU-9D)—a generic preference-based measure of paediatric health-related quality of life that allows the calculation of quality adjusted life years (QALYs)—will be the health outcome measure for cost-utility analysis. The 9 items of CHU-9D cover feeling worried, sad, tired, annoyed, perceptions of

schoolwork, sleep, daily routine, and social activities. The tool is designed to be administered to CYP between 7-17 years of age, and a proxy version to be completed by parents is available for younger children(39,40). The Warwick-Edinburg Mental Wellbeing Scale (WEMWBS) (41) will serve as a well-being questionnaire for parents. All questionnaires were administered at baseline and at two follow-up points (6 and 12 months). Questionnaires completed during the first phase of the Covid-19 pandemic [12 March 2020 – 6 July 2020], will be repeated after this period, and follow-up measures delayed. Multiple imputation will be used for questionnaires with missing values.

In the cost-benefit analysis, QALYs and WEMWBS will be combined by converting both to Pound Sterling values. QALYs will be monetised by using the government sector willingness-to-pay of £20,000 to £30,000 per QALY gained(42). For WEMWBS, the monetary values published by Simetrica and HACT for each Short-version WEMWBS (SWEMWBS) score will be employed and converted to cost year 2020/2021 (43). The SWEMWBS score can be obtained from the original WEBWMS using seven of its 14 statements about thoughts and feelings.

Statistical analyses

The intention-to-treat population will be used in statistical analyses. First, differences between protocolized and actual intervention components (including inputs, frequency and duration of each component) will be assessed (**Table 2**). Second, univariate analyses will be conducted to describe sample mean differences and variability across time between treatment and control group for each outcome. Three time points will contribute to analysis; baseline, 6-months, and 12 months. Third, to adjust for treatment group imbalances, four multilevel regression models will be estimated; one each for total costs, QALYs, PedsQL score, and monetary benefits (£ corresponding to QALYs and WEBWMS scores together)(44). Each model will include a variable indicating participation in intervention or control and variables that, despite randomization, may still be unequally distributed between intervention and control groups such as age, gender and deprivation level for the patient-level models. For the regression model predicting QALYs, the baseline QALYs will also be controlled for(45). Benefits will be estimated using ordinary least squares, and costs with a GLM model with a gamma distribution and a log-link. Both the use of a GLM and limited dependent variable mixture models will be considered when modelling QALYs(46). All models will cluster standard errors to account for correlation of patients in the same CYPHP cluster.

For each outcome variable and intervention and control groups separately, mean predicted values will be generated. Three incremental cost-effectiveness ratios (difference between intervention and control in mean predicted costs over difference in mean predicted outcomes) will be computed, one for the cost-effectiveness analysis (based on PedsQL scores), another for the cost-utility analysis (using QALYs), and a third one for the cost-benefit analysis (£). These three ICERs will be generated based on 6 and 12-months data.

The pattern and amount of missing data between treatment and control groups by study variable will be assessed. If data is missing completely at random for both treatment and control groups and the percentage of missing data is below 5%, missing data will be ignored. If data is missing at random (MAR), multiple imputation accounting for clustering (such as fixed effects) will be used (47). When the data is MAR, multiple imputation can lead to consistent, asymptotically efficient, and asymptotically normal estimates(48).

Handling uncertainty

The level of decision uncertainty arising from sampling and assumptions on key parameter estimates with policy impact will be assessed. Confidence intervals for ICERs based on the non-parametric

bootstrap method will be generated(49), along with acceptability curves to reflect the probability of CYPHP being cost-effective as the willingness-to-pay per QALY (or other health outcome) increases. Deterministic sensitivity analyses on chosen variables (such as intervention set-up costs, intensity of services delivered, and social care costs) will assist in identifying key drivers of the results. Subgroup analysis of cost-effectiveness results by tracer condition and quintiles of IMD will be conducted as long as a sufficient sample size is available.

2.5. Long-term modelling of health and costs beyond the trial

A state-transition model reflecting natural disease progression will be developed for each tracer condition to predict the cost-effectiveness of CYPHP compared to EUC beyond the trial duration. Trial data will be used to define the health states, transition probabilities among states, and to calculate the costs and effects from an NHS/PSS perspective. Existing literature and publicly available statistics (e.g., Office of National Statistics and existing UK cohort studies) will also be used to gather transition probabilities across states beyond 12 months. A functional form characterizing the sustainability of intervention effects into the longer run (changes in health-related quality of life and health services utilisation) will be inferred based on 6 months and 12 months trial data. The effect of alternative analytic horizons on the cost-effectiveness of CYPHP versus EUC will be tested in sensitivity analyses, including 2, 5, and 10 years.

DISCUSSION

The CYPHP Evelina London model is a health-systems strengthening programme to advance towards integrated and high-quality care for children and young people in the UK. By offering universal and targeted services, CYPHP aims to overcome patient- and provider-level barriers to effective management of physical and mental health and foster optimal health behaviour. The aims of this economic evaluation are to establish the impact of CYPHP on healthcare costs at the population level and the cost-effectiveness of the intervention among CYP with tracer conditions. Asthma, constipation, and eczema serve as examples of common long-term conditions among CYP. Lessons from managing these conditions should inform a broader health system response to the epidemiological transition to chronic diseases.

Strengths and weaknesses

Beyond temporary trial suspension, Covid-19 may have affected our study in at least two ways. First, CYPHP delivery may not return to normal after the pandemic. Differences in the frequency and duration of each CYPHP component before and after Covid-19 will be assessed in sensitivity analyses. Second, some follow-up questionnaires were due during Covid-19. When possible, data were collected, and an additional data point after Covid-19 was included for these participants to isolate changes in health status due to the pandemic. Besides the effects of Covid-19, the intensity of services delivered as part of CYPHP may not be fully standardised across GP practices. Variability in service intensity across practices and its impact on cost-effectiveness results will be assessed in sensitivity analyses. Additionally, health utility outcome measurement for children below 5 may lack reliability as the questionnaire has not been psychometrically tested for this younger age group (26,50). This measurement challenge will be addressed by using multiple economic evaluation perspectives and health outcomes (such as the PedsQL) to provide a comprehensive and transparent assessment of the effects of the intervention.

By carrying out three economic evaluations (cost-effectiveness, cost-utility, and cost-benefit) under two different perspectives (NHS and PSS, and societal), we aim to inform stakeholders with various interests, including Clinical Commissioning Groups and evolving Integrated Care System, GP

Federations, Provider Trusts, CYP and their families. With CYPHP, healthcare utilisation costs may remain stable if primary care visits increase, but hospitalisations and emergency room visits decrease. Parents and children's costs related to time lost from work or school are also expected to decline with CYPHP if CYP's tracer conditions are well managed. Our planned analyses will allow both to be studied and accounted for.

The long-term model will assess the cost-effectiveness of CYPHP compared to EUC beyond the trial duration to fully capture intervention effects on children with asthma, constipation and/or eczema. Existing cost-effectiveness studies assessing interventions for CYP with these tracer conditions rarely include a long-term model, and the duration of RCTs of education, coaching, nurse-led clinics or treatments for the tracer conditions tend to be under three years (51–56). CYPHP is expected to foster long-lasting improvements beyond 12 months in health outcomes due to changes in disease management behaviour among the CYP and family, and also health professionals. The natural progression of the tracer conditions indicates that a substantial percentage of children continue to experience symptoms beyond 12 months, and sometimes even into adulthood. Asthma in childhood persists into adulthood for 79% of the cases (57). About half of children with atopic eczema still have the problem as adults (58,59). Twenty five percent of children with functional constipation continue to experience symptoms as adults (60,61).

This study will contribute rigorous evidence about health economics of children's integrated healthcare in the UK, where there has been a notable paucity of high-quality evidence. Results from this study will directly inform decisions on children's healthcare provision in South East London and will provide rigorous evidence to inform policy nationally and internationally.

Ethics and dissemination: Ethics approval was obtained from South West-Cornwall & Plymouth Research Ethics Committee. Results will be submitted for publication in peer-reviewed journals, made available in briefing papers for local decision-makers, and provided to the local community through website and public events. Findings will be generalisable to community-based models of care, especially in urban settings.

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Marina Soley-Bori: Conceptualization, Methodology, Writing - Original Draft, Writing - Review & Editing, Investigation, Visualisation; Raghu Lingam: Writing - Review & Editing, Funding acquisition; Rose-Marie Satherley: Writing - Review & Editing, Investigation. Julia Forman: Writing - Review & Editing. Lizzie Cecil: Writing - Review & Editing. Julia Fox-Rushby: Conceptualization, Methodology, Supervision, Writing - Review & Editing; Ingrid Wolfe: Writing - Review & Editing, Funding acquisition.

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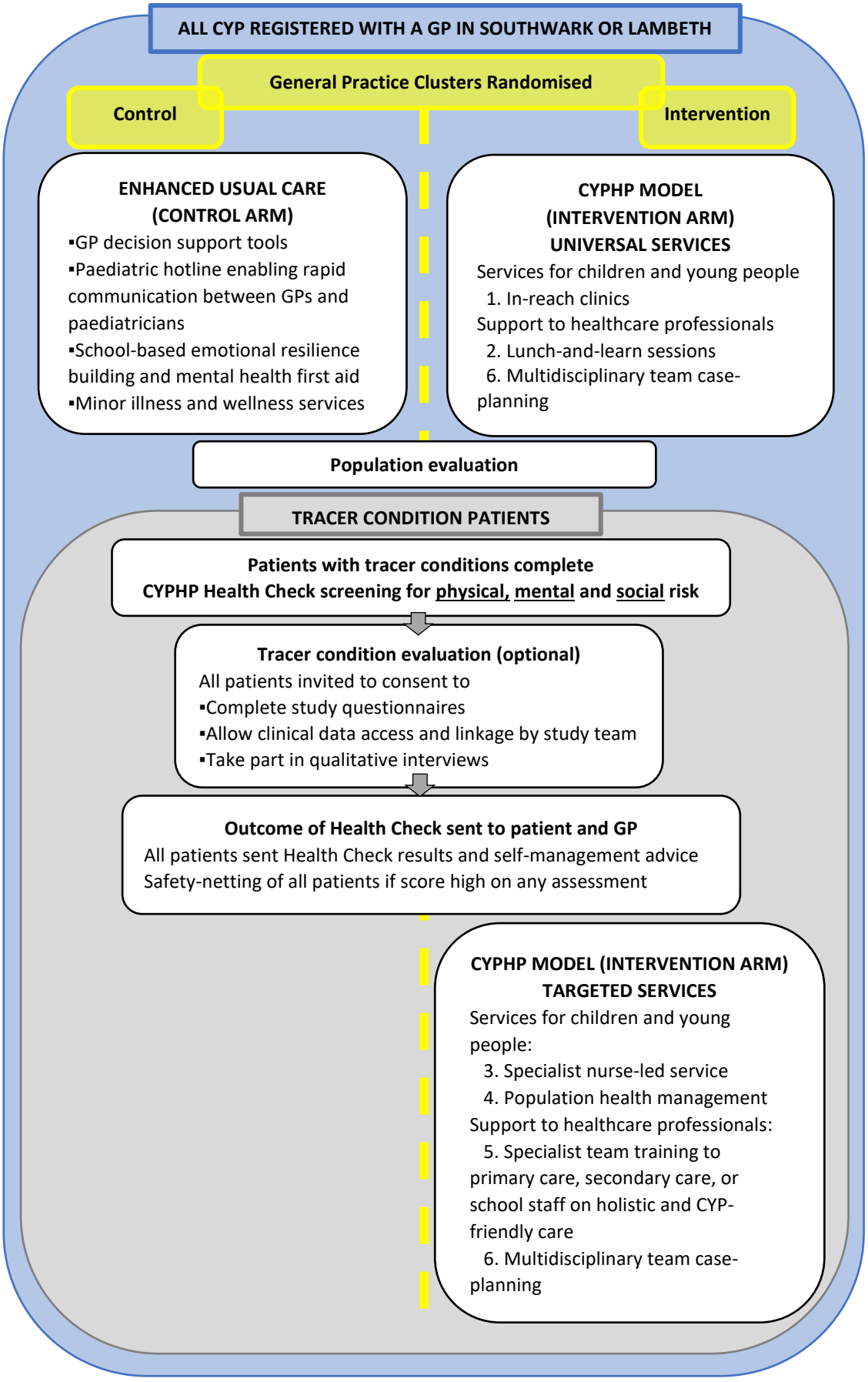
Figure 1. Study population and intervention flow



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The Children and Young People's Health Partnership Evelina London Model of Care: economic evaluation protocol of a complex system change

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The Children and Young People's Health Partnership Evelina London Model of Care: economic evaluation protocol of a complex system change

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Abstract

Introduction: The Children and Young People's Health Partnership (CYPHP) Evelina London Model of Care is a new approach to integrated care delivery for children and young people with common health complaints and chronic conditions. CYPHP includes population health management (services shaped by data-driven understanding of population and individual needs, applied in this case to enable proactive case-finding and tailored biopsychosocial care), specialist clinics with multidisciplinary health teams, and training resources for professionals working with children and young people. This complex health system strengthening program has been implemented in South London since April 2018, and will be evaluated using a cluster randomised control trial (cRCT) with an embedded process evaluation. This protocol describes the within- and beyond-trial economic evaluation of CYPHP.

Methods and analysis: The economic evaluation will identify, measure, and value resources and health outcome impacts of CYPHP compared with Enhanced Usual Care (EUC) from a National Health

Service/ Personal Social Service and a broader societal perspective. The study population includes 90,000 children and young people under 16 years of age in 23 clusters (groups of GP practices) to assess health service use and costs, with more detailed cost-effectiveness analysis of a targeted sample of 2,138 children and young people with asthma, eczema, or constipation (tracer conditions). For the cost-effectiveness analysis, health outcomes will be measured using the Pediatric Quality of Life Inventory (PedsQL) and quality-adjusted life years (QALYs) using the Child Health Utility measure (CHU-9D). To account for changes in parental wellbeing, the Warwick-Edinburg Mental Wellbeing Scale (WEMWBS) will be integrated with QALYs in a cost-benefit analysis. The within-trial economic evaluation will be complemented by a novel long-term model that expands the analytic horizon to 10 years. Analyses will adhere to good practice guidelines and National Institute for Health and Care Excellence (NICE) public health reference case.

Ethics and dissemination: The study has received ethical approval from South West-Cornwall & Plymouth Research Ethics Committee (REC Reference: 17/SW/0275. Results will be submitted for publication in peer-reviewed journals, made available in briefing papers for local decision-makers, and provided to the local community through website and public events. Findings will be generalisable to community-based models of care, especially in urban settings.

Trial registration number: NCT03461848; Pre-results.

Strength and limitations of this study:

- Robust study design: CYPHP will be evaluated using a cluster randomised control trial (cRCT) with an embedded process evaluation.
- Multiple analytic perspectives: Both the NHS and Personal Social Services (PSS) perspective and a societal perspective, accounting for costs falling on parents and schools, will be adopted.
- Long analytic horizon: The within-trial economic evaluation will be complemented by a novel long-term model that expands the analytic horizon to 10 years
- Impact of Covid-19 on CYPHP service delivery: Differences in the frequency and duration of each CYPHP component before and after Covid-19 may be observed, which will be assessed in sensitivity analyses.
- Measurement of intervention effects: The intensity of the different intervention components may have varied across GP practices and the measurement of health effects with the CHU-9D for children below 5 may lack reliability.

Key words: Integrated care, cost-effectiveness, decision modelling, paediatrics

1. INTRODUCTION

In 2018 nearly 1400 excess child deaths occurred in the UK compared with Sweden, adjusting for population size (1,2). The UK fares worse than other high-income countries in chronic disease management too. Only 16% of young people in the UK with type 1 diabetes had a glycated haemoglobin A1c under 7·5%, whereas in Germany and Austria this standard was met for 34% of young people (3–5). Poor chronic disease management results in worse health-related quality of life (6,7), and in higher emergency room visits and hospitalisations, which are key healthcare cost drivers (5,8–11). Beyond direct medical costs, poorly controlled chronic conditions result in time lost from school and employment, placing a significant burden on families. For example, the overall cost of caring for children with asthma aged 1–5 years in the 12 months following attendance at hospital for wheeze or asthma is estimated to be 14.53 million GBP (12).

Ensuring good health in childhood is a public health priority both as a rights-based principle (13), and for the health, social, and economic consequences in adulthood (14,15). Notwithstanding the current pandemic, the UK paediatric healthcare delivery model—originally designed to treat acute conditions through high-intensity specialist and inpatient services—now needs to address chronic health care needs and emphasise preventive care. Previous efforts to integrate care for children and young people (CYP) with ongoing conditions have shown potential for improving quality of life and reducing costs, but evidence is limited (16).

The Children and Young People's Health Partnership (CYPHP) Evelina London Model of Care is an innovative approach to integrated healthcare delivery. It was implemented in April 2018 in two London boroughs (Lambeth and Southwark) where A&E attendance for 0-4 year olds and hospital admissions related to asthma were 16% and 25% higher than the national average, respectively. (17). The CYPHP model aims to strengthen the health system by bridging the gap between primary and secondary care, physical and mental health, and links healthcare with local efforts to tackle the socioeconomic determinants of health. Through coordinated, early intervention, and biopsychosocial care delivered in primary care and community settings, CYPHP has been developed to promote better healthcare and self-management for CYP with common health complaints and chronic conditions(18,19). The concept of biopsychosocial care follows many of the tenets of patient centred care as outlined by Tramonti and colleagues (20), however we use a more specific term to describe the model in greater detail.

CYPHP will be implemented across Southwark and Lambeth in two stages. The staged implementation offers a platform for an opportunistic clustered Randomised Control Trial (cRCT) study design for rigorous evaluation purposes, running alongside a service evaluation reporting regularly to a Partnership Board of commissioner, provider, community organisations, and researchers. In the first CYPHP deployment stage (approximately 3 years), general practices were randomised to either CYPHP (intervention) or Enhanced Usual Care (EUC—control). CYPHP includes the EUC components, but also in-reach clinics, lunch-and-learn sessions, specialist nurse-led services, population health management, specialist team training, and multidisciplinary team case planning. After three years, CYPHP will be implemented in all of the practices.

The aims of the embedded economic evaluation are, first, to assess the impact of CYPHP compared to EUC on patient-level health care costs from an NHS and Personal Social Service (PSS) perspective for the entire trial population. PSS includes a range of services provided by local authorities for vulnerable groups, including the mentally and physically disabled, older people, and neglected children. Second, among children with specific targeted tracer conditions, to compare costs and health outcomes and establish the cost-effectiveness (cost per point improvement in the PedsQL)

and cost-utility (cost per QALY) of CYPHP versus EUC also from an NHS and PSS perspective (NICE reference case(21)). Third, a cost-benefit analysis (cost per monetarized unit of parental wellbeing and children's QALYs) of CYPHP compared to EUC from a societal perspective will be conducted. The cost-benefit analysis will also account for costs falling on parents and schools. The cost-effectiveness of CYPHP compared to EUC beyond the trial duration will be explored with a state-transition model reflecting natural disease progression for each tracer condition. Existing evaluations of interventions to improve outcomes for children with tracer conditions (such as education initiatives) rarely consider effects beyond 3 years, which may result in a partial characterization of the intervention effects, and as such this method is a novel application in child health economic research. Both the economic evaluation and the state-transition model are essential as they will determine whether potential health gains related to the intervention justify its costs relative to EUC, and therefore whether a decision to provide and roll-out the intervention is justifiable in terms of efficiency.

Both the population and tracer-conditions analyses aim to inform decisions on the current CYPHP provision in Lambeth and Southwark and throughout the South East London Integrated Care System, as well as its potential expansion to other areas if proven efficient.

2. METHODS AND ANALYSIS

2.1. Study design

The study design and intervention components are outlined in detailed in our published trial protocol paper (18). In summary, seventy general practices in Southwark and Lambeth were grouped into 23 virtual clusters, occurring naturally for GP-pediatrician co-located clinics. Twelve of these clusters were assigned to the intervention (CYPHP) and 11 clusters to the control group (EUC). For randomization, clusters were stratified by borough, and restricted randomization was carried out to ensure the number of CYP under 16 years, their socioeconomic status (measured by the Index of Multiple Deprivation and Income Deprivation Affecting Children Index), and number of outpatient referrals were similar between the two study arms. The trial population includes CYP under 16 years of age registered to a general practice in Southwark or Lambeth. Key information on the CYPHP intervention and evaluation are summarized in **Table 1**.

Table 1. Key features of the CYPHP intervention and evaluation

Targeted recruitment sample without loss to follow-up	1,496
Route to change	•A theoretically informed intervention (Theoretical Domains Framework) • Evidence based (based on systematic review on integrated care models for child health(16)) •Integrates care in line with patient, provider, and policy perspectives – providing efficient, preventive access to care, closer to home
Main strengths	• Opportunistic randomised controlled trial •Rich data with both patient-reported and routine service use data •Embedded process evaluation to assess CYPHP implementation success
Stakeholder involvement	CYPHP was developed with children and young people, carers, frontline practitioners, and health service commissioners

2.2. Intervention and control arms

The study structure and components of CYPHP and EUC are described in **Figure 1.** As the intervention arm provides CYPHP on top of EUC, EUC is delivered at all practices. CYPHP offers universal services (available to all CYP, with any childhood condition) and targeted services (available only to CYP with tracer conditions - **asthma, constipation, and/or eczema**). EUC is comprised of several patient self-management support tools for families and resources available to health providers to provide higher quality and more joined-up care for CYP.

Specifically, CYPHP includes:

- CYPHP *universal services*
    1. *In-reach clinics,* integrated child health clinics co-delivered by patch-pediatricians and GPs (patch paediatricians are linked to a cluster of general practices) as part of a multidisciplinary CYP health team located in the community.
    2. *Lunch-and-learn sessions,* where a multidisciplinary group of CYP health professionals, including pediatricians and primary care staff share knowledge, review cases, create common professional cultures, build and reinforce team working practices.
- CYPHP *targeted services (tracer conditions only)*
    3. *Specialist nurse-led services,* usually delivered by a CYPHP nurse trained in biopsychosocial care (mental health and other specialists are available too if needed) at the CYP's home, during a visit at a community-based clinic, or through a phone call or message. It includes health promotion and self-management advice on tracer conditions. Patients are triaged and care is planned based on a pre-assessment biopsychosocial Health Check (CYPHP Health Check) and patient records. The CYPHP Health Check is administered to patients with asthma, constipation, or eczema. It uses validated questionnaires when possible to measure biopsychosocial health. Child's ongoing conditions are assessed with the Patient Oriented Eczema Measure (POEM)(22) for children with eczema, the Asthma Control Test (ACT)(23) for asthma, and a bespoke CYPHP constipation questionnaire (validation work underway). The Strengths and Difficulties Questionnaire (SDQ)(24) is used as an emotional and behavioural screening questionnaire. Finally, a set of bespoke social questions to understand a family's broader situation and factors that may affect their health and care, such as financial worries and days lost of school or work, are also included. Participants who consent as research subjects, do also complete the Paediatric Quality of Life Inventory (PedsQL)(25) and the Child Health Utility 9-D (CHU-9D)(26).

    4. *Population health management,* where CYP with tracer conditions are sent text messages and a letter from their GP, encouraging them to participate in early intervention and care. Recipients are identified based on analyses of electronic health records and actively reached out to connect them with the healthcare system and improve the management of their conditions before they exacerbate.

    5. Specialist team training, including education and training for primary care, secondary care, or school staff on evidence-based, holistic, and CYP-friendly care for tracer conditions, is delivered by CYPHP professionals.

Multidisciplinary team case-planning is important for CYPHP delivery, present in both universal and targeted services. It includes case planning and both formal and informal education and training for professionals providing CYPHP.

Table 2 describes the expected inputs, frequency, and duration of each CYPHP component. All these data elements will be collected, as actual implementation may differ from protocolised implementation.

Table 2. Protocolised inputs, frequency, and duration of CYPHP components

Intervention component	Inputs	Frequency	Duration	Comments
1.In-reach clinics	Labour: GP and patch-paediatrician	Once a month	20-30 min per patient	2-3 hours total
2. Lunch-and-learn sessions	Labour: CYPHP nurse, mental health specialist, paediatrician and GP who works alongside CYPHP	Once a week	60 min	
3.Specialist nurse-led service	Labour: CYPHP nurse and mental health specialist Capital: children's centre	Varies	60 min (home), 30 min (general practice or school)	Service type, duration, and location tailored to CYP
4.Population health management	Labour: population health clinician, analyst, manager	Varies	Varies	Data: access, storage, analysis Proactive case finding: costs for sending messages
5.Specialist team training	Labour: CYPHP nurse, primary care and secondary care staff, school staff	Varies	Varies	.
6. Multidisciplinary team case planning	Labour: CYPHP nurse, mental health specialist, paediatrician and GP who works alongside CYPHP	Once a week	60 min	.

Children and young people access universal services through referrals from their pediatrician or GP. For specialist services, entry sources include direct referrals (from GP, pediatrician, school nurse, or emergency department), self-referrals (availability publicized through community events, posters in GP practices), and proactive case finding (CYP with tracer conditions are sent text messages and a letter from their GP). Further details on CYPHP's implementation are included in the publicly available handbook(27).

2.3. Patient and Public Involvement

Stakeholders were involved in the development of the theoretical framework for CYPHP, identification of research questions and refining the research methodology. Stakeholders included children and young people, carers, frontline practitioners, and health service commissioners. A patient and public involvement group was developed with children and their families and it was consulted with regard to evaluation design; including appropriateness of outcome measures and consent procedures.

2.4. Economic evaluation within the trial

2.4.1. Population-level cost analysis

The goal of the population-level analysis is to assess the impact of CYPHP compared to EUC on healthcare costs of health service use. This analysis will use the whole study population, which includes children and young people, 0-15 years of age, registered with a Southwark or Lambeth GP practice. Health service use will include primary care consultations, visits with pediatricians, hospital outpatient, hospital inpatient, and accident and emergency care during 6 and 12 months. Patient-level costs will be obtained by multiplying unit costs by utilisation. National unit costs for children's services will be obtained from the Unit Costs of Health and Social Care 2019 by the Personal Social Services Resource Unit (28) and the NHS reference costs for 2015-16 (29). Due to the often-skewed cost distribution with a large number of zeros and a long right-hand tail, the modified Park Test and Pregibon Link test will assess the most appropriate distribution and link to calibrate a Generalized linear model (GLM) for costs, for example, with a gamma distribution and a log-link (30,31). The cost model will adjust for a binary variable indicating whether the children or young person belonged to the intervention or control arm and any demographic variables that show imbalance between the two groups.

2.4.2. Tracer conditions: cost-effectiveness/utility and cost-benefit analyses

This within-trial economic evaluation will also compare CYPHP with EUC for patients under 16 with asthma, constipation, and/or eczema. Three types of economic evaluation will be conducted. The cost-effectiveness analysis, using point improvement in the PedsQL scale as the primary outcome, and the cost-utility analysis, based on quality-adjusted life years (QALYs) from the CHU-9D, will adopt an NHS and Personal Social Services (PSS) perspective. The cost-benefit analysis will take a societal perspective and value parental wellbeing with the Warwick-Edinburg Mental Wellbeing Scale (WEMWBS). These analyses will adhere to guidelines for conducting economic evaluations alongside clinical trials and the most recent National Institute for Health and Care Excellence (NICE) public health reference case(32–35).

Costing: Identification, measurement, and valuation of resources

Costing involves identifying, measuring, and valuing the resources used to deliver and participate in the intervention, and consequential health and social services use. In a complex system change such as CYPHP, the comprehensive identification of resources requires close collaboration with the implementation and the process evaluation teams.

Identification of resource use

From an NHS and PSS perspective, resources used relate to the delivery of the intervention, health and social care use by patients, and time at school and work lost (**Table 3**). Intervention delivery mostly includes time spent by medical professionals and service managers delivering CYPHP services. From a societal perspective, time spent by school staff participating in CYPHP and time away from work or school by parents and CYP are also accounted for. Because both intervention and control practices include EUC, EUC's delivery costs will be disregarded. Service use and time away from school and work will be considered for both CYPHP and EUC.

Measurement of resource use

Resources used to implement CYPHP will be gathered from seven data sources, including the study's accounting data, service caseloads, CYPHP nurse's personal caseload notes, study questionnaires, primary care data, secondary care data, and interviews with CYPHP nurses (**Table 3**). EMIS will provide location, type, number and length of visits part of in-reach clinics and specialist team

services. CYPHP nurse's caseload notes will supply information on specialist team training and multidisciplinary team case-planning. Time spent at lunch-and-learn sessions will be obtained from service caseloads. Patient-level service use will be gathered from primary and secondary care activity files. Family and CYP time away from work or school are questions included in the study questionnaires. Interviews with a random sample of CYPHP nurses to understand their phone usage and transportation to patient visits will also be conducted.

Valuation of resource use

As with the population-level cost analysis, national unit costs for children's services will be obtained from the Unit Costs of Health and Social Care 2019 (28) and NHS reference costs for 2015-16 (29). The Unit Costs of Health and Social Care 2014 version will also be used to value referrals to social care services (36). Unit costs not available from these sources will be collected from trial records directly (e.g. monthly rent of children's health center use). All unit costs will be presented in pounds sterling (£) for a base cost year 2019/2020; the NHS Cost Inflation Index (NHSCII) will be used to adjust for inflation(36). As the horizon of the within-trial analysis is 6 and 12 months, no discounting will be applied to either costs or outcomes.

Table 3. Identification and measurement of costs

Cost components	Description of resources used	Unit of measure	Source, level data collected
Intervention delivery costs			
Set-up costs	Hiring costs, training, materials	Total costs	Study's accounting data
1.In-reach clinics	Paediatrician, general practitioner, mental health specialist, etc.	Minutes	Primary care data (EMIS), patient
2.Lunch-and-learn sessions	Paediatrician, general practitioner, other child health professionals, clerks/administrative, etc.	Minutes	Service Caseloads, service
3.Specialist nurse-led services	•CYPHP nurses, mental health specialists, etc.	Minutes	Primary care data, patient
	•Phone usage	Minutes/text messages	Interview CYPHP nurse, service
	•Travel to patients (distance and mileage)	Minutes and £	Primary care data and interview CYPHP nurse, service
	•Children's center	Rent	Study's accounting data, service
4.Population health management	•Population health clinician, analyst, manager	Minutes	Study's accounting data, service
5.Specialist team training	•CYPHP nurses, primary care, secondary care staff, etc.	Minutes	CYPHP nurse's caseload notes, service
	•School staff	Minutes	
6.Multidisciplinary team case-planning	•CYPHP nurses, primary care, secondary care staff, etc.	Minutes	CYPHP nurse's caseload notes, service
Overhead costs	Using spaces, data access and storage	£	Study's accounting data
Service use			
	•General practitioner	No. visits	Primary care data and secondary care activity, patient
	•Paediatrician	No. visits	
	•Hospital outpatient	No. visits	

	•Hospital inpatient	No. visits	
	•Accident and emergency	No. visits	
	•Social care services†	Referral yes/no	
CYP and family			
	Time away from school	Hours	Study questionnaires, patient
	Time away from work	Hours	Study questionnaires, parent

Note: †CYPHP nurses may refer CYP and their families to social care services. An indicator for referrals to social services is available in primary care data. EMIS=Egton Medical information Systems. Secondary care data (inpatient stays, A&E attendances, and outpatient visits) will be obtained from Guy's and Sant Thomas' NHS Foundation Trust and King's College Hospital data.

Computation of total costs

Total costs will be computed at the patient level by summing *intervention delivery costs* (only CYP in intervention arm) and *health service use cost* (CYP in intervention and control arms)

- *Intervention delivery costs* will include set-up, CYPHP delivery and overhead costs. Some of these components will vary across patients (e.g., specialist team services), others across clinics (e.g., staff specialist training), and others will be the same for all patients (e.g., overhead costs such as the cost of administration and facilities). Staff specialist training costs, costs of universal services (in-reach clinics), intervention set-up costs, and overheads will each be apportioned. CYP with tracer conditions are the target population of the economic evaluation. The cost of universal services, however, also needs to be considered as CYP with tracer conditions may be referred to specialist team services during an in-reach clinic visit. Different apportioning rules will be used, for example, the costs of universal services could be apportioned by using the percentage of CYP with tracer conditions who were referred by in-reach clinics. Total per-patient apportioned costs will be added to patient-level specialist team services costs.
- *Health service use costs* will result from multiplying the quantity of services used, by their unit cost, and summing across services types for each patient.

Total costs of patients in the control arm will only reflect health service use costs.

In the cost-benefit analysis, total costs will also include costs borne by patients, parent and schools. Patient and parents' costs will be comprised of school and work time lost, respectively. Schools' costs will include time spent by school staff attending specialist team training.

Measurement and valuation of health outcomes

The trial's primary health outcome measure of the tracer conditions evaluation is the Pediatric Quality of Life Inventory (PedsQL), which will be used in the cost-effectiveness analysis. The PedsQL includes 23 items covering physical, emotional, social and school functioning(25) and is available through 6 age-specific questionnaires (0-12 months, 13-24 months, 2-4 years, 5-7 years, 8-12 years, and 13-17 years). The PedsQL has shown to be reliable, valid and responsive to meaningful change across general and disease-specific populations(25,37,38). The Child Health Utility questionnaire (CHU-9D)—a generic preference-based measure of paediatric health-related quality of life that allows the calculation of quality adjusted life years (QALYs)—will be the health outcome measure for cost-utility analysis. The 9 items of CHU-9D cover feeling worried, sad, tired, annoyed, perceptions of schoolwork, sleep, daily routine, and social activities. The tool is designed to be administered to CYP between 7-17 years of age, and a proxy version to be completed by parents is available for younger

children(39,40). The WEMWBS (41) will serve as a well-being questionnaire for parents. All questionnaires were administered at baseline and at two follow-up points (6 and 12 months). Questionnaires completed during the first phase of the Covid-19 pandemic [12 March 2020 – 6 July 2020], will be repeated after this period, and follow-up measures delayed.

In the cost-benefit analysis, QALYs and WEMWBS will be combined by converting both to Pound Sterling values. QALYs will be monetised by using the government sector willingness-to-pay of £20,000 to £30,000 per QALY gained(42). For WEMWBS, the monetary values published by Simetrica and HACT for each Short-version WEMWBS (SWEMWBS) score will be employed and converted to cost year 2020/2021 (43). The SWEMWBS score can be obtained from the original WEBWMS using seven of its 14 statements about thoughts and feelings.

Statistical analyses

The intention-to-treat population will be used in statistical analyses. First, differences between protocolized and actual intervention components (including inputs, frequency and duration of each component) will be assessed (**Table 2**). Second, univariate analyses will be conducted to describe sample mean differences and variability across time between treatment and control group for each outcome. Three time points will contribute to analysis; baseline, 6-months, and 12 months. Third, to adjust for treatment group imbalances, four multilevel regression models will be estimated; one each for total costs, QALYs, PedsQL score, and monetary benefits (£ corresponding to QALYs and WEBWMS scores together)(44). Each model will include a variable indicating participation in intervention or control and variables that, despite randomization, may still be unequally distributed between intervention and control groups such as age, gender and deprivation level for the patient-level models. For the regression model predicting QALYs, the baseline QALYs will also be controlled for(45). Benefits will be estimated using ordinary least squares, and costs with a GLM model with a gamma distribution and a log-link. Both the use of a GLM and limited dependent variable mixture models will be considered when modelling QALYs(46). All models will cluster standard errors to account for correlation of patients in the same CYPHP cluster.

For each outcome variable and intervention and control groups separately, mean predicted values will be generated. Three incremental cost-effectiveness ratios (difference between intervention and control in mean predicted costs over difference in mean predicted outcomes) will be computed, one for the cost-effectiveness analysis (based on PedsQL scores), another for the cost-utility analysis (using QALYs), and a third one for the cost-benefit analysis (£). These three ICERs will be generated based on 6 and 12-months data.

The pattern and amount of missing data between treatment and control groups by study variable will be assessed. If data is missing completely at random for both treatment and control groups and the percentage of missing data is below 5%, missing data will be ignored. If data is missing at random (MAR), multiple imputation accounting for clustering (such as fixed effects) will be used (47). When the data is MAR, multiple imputation can lead to consistent, asymptotically efficient, and asymptotically normal estimates(48).

Handling uncertainty

The level of decision uncertainty arising from sampling and assumptions on key parameter estimates with policy impact will be assessed. Confidence intervals for ICERs based on the non-parametric bootstrap method will be generated(49), along with acceptability curves to reflect the probability of CYPHP being cost-effective as the willingness-to-pay per QALY (or other health outcome) increases. Deterministic sensitivity analyses on chosen variables (such as intervention set-up costs, intensity of

services delivered, and social care costs) will assist in identifying key drivers of the results. Subgroup analysis of cost-effectiveness results by tracer condition and quintiles of IMD will be conducted as long as a sufficient sample size is available.

2.5. Long-term modelling of health and costs beyond the trial

A state-transition model reflecting natural disease progression will be developed for each tracer condition to predict the cost-effectiveness of CYPHP compared to EUC beyond the trial duration. Trial data will be used to define the health states, transition probabilities among states, and to calculate the costs and effects from an NHS/PSS perspective. Existing literature and publicly available statistics (e.g., Office of National Statistics and existing UK cohort studies) will also be used to gather transition probabilities across states beyond 12 months. A functional form characterizing the sustainability of intervention effects into the longer run (changes in health-related quality of life and health services utilisation) will be inferred based on 6 months and 12 months trial data. The effect of alternative analytic horizons on the cost-effectiveness of CYPHP versus EUC will be tested in sensitivity analyses, including 2, 5, and 10 years.

DISCUSSION

The CYPHP Evelina London model is a health-systems strengthening programme to advance towards integrated and high-quality care for children and young people in the UK. By offering universal and targeted services, CYPHP aims to overcome patient- and provider-level barriers to effective management of physical and mental health and foster optimal health behaviour. The aims of this economic evaluation are to establish the impact of CYPHP on healthcare costs at the population level and the cost-effectiveness of the intervention among CYP with tracer conditions. Asthma, constipation, and eczema serve as examples of common long-term conditions among CYP. Lessons from managing these conditions should inform a broader health system response to the epidemiological transition to chronic diseases.

Strengths and weaknesses

Beyond temporary trial suspension, Covid-19 may have affected our study in at least two ways. First, CYPHP delivery may not return to normal after the pandemic. Differences in the frequency and duration of each CYPHP component before and after Covid-19 will be assessed in sensitivity analyses. Second, some follow-up questionnaires were due during Covid-19. When possible, data were collected, and an additional data point after Covid-19 was included for these participants to isolate changes in health status due to the pandemic. Besides the effects of Covid-19, the intensity of services delivered as part of CYPHP may not be fully standardised across GP practices. Variability in service intensity across practices and its impact on cost-effectiveness results will be assessed in sensitivity analyses. Additionally, health utility outcome measurement for children below 5 may lack reliability as the questionnaire has not been psychometrically tested for this younger age group (26,50). This measurement challenge will be addressed by using multiple economic evaluation perspectives and health outcomes (such as the PedsQL) to provide a comprehensive and transparent assessment of the effects of the intervention.

By carrying out three economic evaluations (cost-effectiveness, cost-utility, and cost-benefit) under two different perspectives (NHS and PSS, and societal), we aim to inform stakeholders with various interests, including Clinical Commissioning Groups and evolving Integrated Care System, GP Federations, Provider Trusts, CYP and their families. With CYPHP, healthcare utilisation costs may remain stable if primary care visits increase, but hospitalisations and emergency room visits decrease. Parents and children's costs related to time lost from work or school are also expected to

decline with CYPHP if CYP's tracer conditions are well managed. Our planned analyses will allow both to be studied and accounted for.

The long-term model will assess the cost-effectiveness of CYPHP compared to EUC beyond the trial duration to fully capture intervention effects on children with asthma, constipation and/or eczema. Existing cost-effectiveness studies assessing interventions for CYP with these tracer conditions rarely include a long-term model, and the duration of RCTs of education, coaching, nurse-led clinics or treatments for the tracer conditions tend to be under three years (51–56). CYPHP is expected to foster long-lasting improvements beyond 12 months in health outcomes due to changes in disease management behaviour among the CYP and family, and also health professionals. The natural progression of the tracer conditions indicates that a substantial percentage of children continue to experience symptoms beyond 12 months, and sometimes even into adulthood. Asthma in childhood persists into adulthood for 79% of the cases (57). About half of children with atopic eczema still have the problem as adults (58,59). Twenty five percent of children with functional constipation continue to experience symptoms as adults (60,61).

This study will contribute rigorous evidence about health economics of children's integrated healthcare in the UK, where there has been a notable paucity of high-quality evidence. Results from this study will directly inform decisions on children's healthcare provision in South East London and will provide rigorous evidence to inform policy nationally and internationally.

Ethics and dissemination: Ethics approval was obtained from South West-Cornwall & Plymouth Research Ethics Committee. Results will be submitted for publication in peer-reviewed journals, made available in briefing papers for local decision-makers, and provided to the local community through website and public events. Findings will be generalisable to community-based models of care, especially in urban settings.

Figure 1. Study population and intervention flow

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Figure 1. Study population and intervention flow