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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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3 **The Children and Young People's Health Partnership Evelina London Model of Care: economic**
4 **evaluation protocol of a complex system change**
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33 **Abstract**
34

35 **Introduction:** The Children and Young People's Health Partnership (CYPHP) Evelina London Model of
36 Care is a new approach to integrated care delivery for children and young people with common
37 health complaints and chronic conditions. CYPHP includes population health management (services
38 shaped by data-driven understanding of population and individual needs, applied in this case to
39 enable proactive case-finding and tailored biopsychosocial care), specialist clinics with
40 multidisciplinary health teams, and training resources for professionals working with children and
41 young people. This complex health system strengthening program has been implemented in South
42 London since April 2018, and will be evaluated using a cluster randomised control trial (cRCT) with
43 an embedded process evaluation. This protocol describes the within- and beyond-trial economic
44 evaluation of CYPHP.
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48 **Methods and analysis:** The economic evaluation will identify, measure, and value resources and
49 health outcome impacts of CYPHP compared with Enhanced Usual Care (EUC) from a National Health
50 Service/ Personal Social Service and a broader societal perspective. The study population includes
51 90,000 children and young people under 16 years of age in 23 clusters (groups of GP practices) to
52 assess health service use and costs, with more detailed cost-effectiveness analysis of a targeted
53 sample of 2,138 children and young people with asthma, eczema, or constipation (tracer conditions).
54 For the cost-effectiveness analysis, health outcomes will be measured using the Pediatric Quality of
55 Life Inventory (PedsQL) and quality-adjusted life years (QALYs) using the Child Health Utility measure
56 (CHU-9D). To account for changes in parental wellbeing, the Warwick-Edinburg Mental Wellbeing
57 Scale (WEMWBS) will be integrated with QALYs in a cost-benefit analysis. The within-trial economic
58 evaluation will be complemented by a novel long-term model that expands the analytic horizon to
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3 10 years. Analyses will adhere to good practice guidelines and National Institute for Health and Care
4 Excellence (NICE) public health reference case.
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6 **Strength and limitations of this study:**
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- 8 • Robust study design: CYPHP will be evaluated using a cluster randomised control trial (cRCT)
9 with an embedded process evaluation.
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- 11 • Multiple analytic perspectives: Both the NHS and Personal Social Services (PSS) perspective
12 and a societal perspective, accounting for costs falling on parents and schools, will be
13 adopted.
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- 15 • Long analytic horizon: The within-trial economic evaluation will be complemented by a novel
16 long-term model that expands the analytic horizon to 10 years
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- 18 • Impact of Covid-19 on CYPHP service delivery: Differences in the frequency and duration of
19 each CYPHP component before and after Covid-19 may be observed, which will be assessed
20 in sensitivity analyses.
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24 **Word count:** 293 abstract ; main text 3639
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26 Key words: Integrated care, cost-effectiveness, decision modelling, paediatrics
27

28 **References:** 53
29

30 **Ethics and dissemination:** Ethics approval obtained from South West-Cornwall & Plymouth Research
31 Ethics Committee. Results will be submitted for publication in peer-reviewed journals, made
32 available in briefing papers for local decision-makers, and provided to the local community through
33 website and public events. Findings will be generalisable to community-based models of care,
34 especially in urban settings.
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36 **Trial registration number:** NCT03461848; Pre-results.
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38 **Patient and public involvement:** Patients or the public were involved in the design, or conduct, or
39 reporting, or dissemination plans of our research
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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, *specialist 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
<ul style="list-style-type: none"> ▪ EUC ▪ Universal services: <ul style="list-style-type: none"> • 1. In-reach clinics ▪ Specialist (tracer conditions) services: <ul style="list-style-type: none"> • 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 ▪ 5. Multidisciplinary team case-planning and Lunch-and-learn sessions 	<ul style="list-style-type: none"> ▪ Universal services: <ul style="list-style-type: none"> • 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: <ul style="list-style-type: none"> ▪ Health Check ▪ Health Packs for CYP and their parents, comprising condition-specific self-management support, health promotion, and health education material

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

CYP access CYPHP universal services via paediatrician or GP referrals. For specialist services, entry sources include direct referrals (from GP, paediatrician, 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 paediatricians, 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 trials¹ 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
3.Specialist team training	•CYPHP nurses, primary care, secondary care staff, etc.	Minutes	Study's accounting data, service
	•School staff	Rent	CYPHP nurse's caseload notes, service
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)

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- *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 Simerica 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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3 1 **The Children and Young People's Health Partnership Evelina London Model of Care: economic**
4 2 **evaluation protocol of a complex system change**
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32 26 **Abstract**

33 27 **Introduction:** The Children and Young People's Health Partnership (CYPHP) Evelina London Model of
34 28 Care is a new approach to integrated care delivery for children and young people with common
35 29 health complaints and chronic conditions. CYPHP includes population health management (services
36 30 shaped by data-driven understanding of population and individual needs, applied in this case to
37 31 enable proactive case-finding and tailored biopsychosocial care), specialist clinics with
38 32 multidisciplinary health teams, and training resources for professionals working with children and
39 33 young people. This complex health system strengthening program has been implemented in South
40 34 London since April 2018, and will be evaluated using a cluster randomised control trial (cRCT) with
41 35 an embedded process evaluation. This protocol describes the within- and beyond-trial economic
42 36 evaluation of CYPHP.
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44 38 **Methods and analysis:** The economic evaluation will identify, measure, and value resources and
45 39 health outcome impacts of CYPHP compared with Enhanced Usual Care (EUC) from a National Health
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3 39 Service/ Personal Social Service and a broader societal perspective. The study population includes
4 40 90,000 children and young people under 16 years of age in 23 clusters (groups of GP practices) to
5 41 assess health service use and costs, with more detailed cost-effectiveness analysis of a targeted
6 42 sample of 2,138 children and young people with asthma, eczema, or constipation (tracer conditions).
7 43 For the cost-effectiveness analysis, health outcomes will be measured using the Pediatric Quality of
8 44 Life Inventory (PedsQL) and quality-adjusted life years (QALYs) using the Child Health Utility measure
9 45 (CHU-9D). To account for changes in parental wellbeing, the Warwick-Edinburg Mental Wellbeing
10 46 Scale (WEMWBS) will be integrated with QALYs in a cost-benefit analysis. The within-trial economic
11 47 evaluation will be complemented by a novel long-term model that expands the analytic horizon to
12 48 10 years. Analyses will adhere to good practice guidelines and National Institute for Health and Care
13 49 Excellence (NICE) public health reference case.

17 50 **Ethics and dissemination:** The study has received ethical approval from South West-Cornwall &
18 51 Plymouth Research Ethics Committee (REC Reference: 17/SW/0275. Results will be submitted for
19 52 publication in peer-reviewed journals, made available in briefing papers for local decision-makers,
20 53 and provided to the local community through website and public events. Findings will be
21 54 generalisable to community-based models of care, especially in urban settings.

24 55 **Trial registration number:** NCT03461848; Pre-results.

27 57 **Strength and limitations of this study:**

- 29 58
- 30 59 • Robust study design: CYPHP will be evaluated using a cluster randomised control trial (cRCT)
31 60 with an embedded process evaluation.
 - 32 61 • Multiple analytic perspectives: Both the NHS and Personal Social Services (PSS) perspective
33 62 and a societal perspective, accounting for costs falling on parents and schools, will be
34 63 adopted.
 - 35 64 • Long analytic horizon: The within-trial economic evaluation will be complemented by a novel
36 65 long-term model that expands the analytic horizon to 10 years
 - 37 66 • Impact of Covid-19 on CYPHP service delivery: Differences in the frequency and duration of
38 67 each CYPHP component before and after Covid-19 may be observed, which will be assessed
39 68 in sensitivity analyses.
 - 40 69 • Measurement of intervention effects: The intensity of the different intervention
41 70 components may have varied across GP practices and the measurement of health effects
42 71 with the CHU-9D for children below 5 may lack reliability.
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51 76 **Key words:** Integrated care, cost-effectiveness, decision modelling, paediatrics

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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

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

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

136 2. METHODS AND ANALYSIS

137 2.1. Study design

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

148 **Table 1. Key features of the CYPHP intervention and evaluation**

149 Targeted recruitment sample without loss to follow-up	1,496
150 Route to change	<ul style="list-style-type: none"> • 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
151 Main strengths	<ul style="list-style-type: none"> • Opportunistic randomised controlled trial • Rich data with both patient-reported and routine service use data • Embedded process evaluation to assess CYPHP implementation success
152 Stakeholder involvement	CYPHP was developed with children and young people, carers, frontline practitioners, and health service commissioners

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154 2.2. Intervention and control arms

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3 151 The study structure and components of CYPHP and EUC are described in **Figure 1**. As the
4 152 intervention arm provides CYPHP on top of EUC, EUC is delivered at all practices. CYPHP offers
5 153 universal services (available to all CYP, with any childhood condition) and targeted services (available
6 154 only to CYP with tracer conditions - **asthma, constipation, and/or eczema**). EUC is comprised of
7 155 several patient self-management support tools for families and resources available to health
8 156 providers to provide higher quality and more joined-up care for CYP.

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11 157 Specifically, CYPHP includes:

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- CYPHP *universal services*

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 1. *In-reach clinics*, integrated child health clinics co-delivered by patch-pediatricians
15 160 and GPs (patch paediatricians are linked to a cluster of general practices) as part of
16 161 a multidisciplinary CYP health team located in the community.
 - 17 162 2. *Lunch-and-learn sessions*, where a multidisciplinary group of CYP health
18 163 professionals, including pediatricians and primary care staff share knowledge,
19 164 review cases, create common professional cultures, build and reinforce team
20 165 working practices.

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- CYPHP *targeted services (tracer conditions only)*

- 24 167
 - 25 168 3. *Specialist nurse-led services*, usually delivered by a CYPHP nurse trained in
26 169 biopsychosocial care (mental health and other specialists are available too if
27 170 needed) at the CYP's home, during a visit at a community-based clinic, or through a
28 171 phone call or message. It includes health promotion and self-management advice
29 172 on tracer conditions. Patients are triaged and care is planned based on a pre-
30 173 assessment biopsychosocial Health Check (CYPHP Health Check) and patient
31 174 records. The CYPHP Health Check is administered to patients with asthma,
32 175 constipation, or eczema. It uses validated questionnaires when possible to measure
33 176 biopsychosocial health. Child's ongoing conditions are assessed with the Patient
34 177 Oriented Eczema Measure (POEM)(22) for children with eczema, the Asthma
35 178 Control Test (ACT)(23) for asthma, and a bespoke CYPHP constipation
36 179 questionnaire (validation work underway). The Strengths and Difficulties
37 180 Questionnaire (SDQ)(24) is used as an emotional and behavioural screening
38 181 questionnaire. Finally, a set of bespoke social questions to understand a family's
39 182 broader situation and factors that may affect their health and care, such as financial
40 183 worries and days lost of school or work, are also included. Participants who consent
41 184 as research subjects, do also complete the Paediatric Quality of Life Inventory
42 185 (PedsQL)(25) and the Child Health Utility 9-D (CHU-9D)(26).

- 43 186
 - 44 187 4. *Population health management*, where CYP with tracer conditions are sent text
45 188 messages and a letter from their GP, encouraging them to participate in early
46 189 intervention and care. Recipients are identified based on analyses of electronic health
47 190 records and actively reached out to connect them with the healthcare system and
48 191 improve the management of their conditions before they exacerbate.

- 49 192
 - 50 193 5. *Specialist team training*, including education and training for primary care, secondary
51 194 care, or school staff on evidence-based, holistic, and CYP-friendly care for tracer
52 195 conditions, is delivered by CYPHP professionals.

53 193 *Multidisciplinary team case-planning* is important for CYPHP delivery, present in both universal and
54 194 targeted services. It includes case planning and both formal and informal education and training for
55 195 professionals providing CYPHP.

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

199 **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	.

200

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

206 **2.3. Patient and Public Involvement**

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

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214 **2.4. Economic evaluation within the trial**

215 **2.4.1. Population-level cost analysis**

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3 216 The goal of the population-level analysis is to assess the impact of CYPHP compared to EUC on
4 217 healthcare costs of health service use. This analysis will use the whole study population, which
5 218 includes children and young people, 0-15 years of age, registered with a Southwark or Lambeth GP
6 219 practice. Health service use will include primary care consultations, visits with pediatricians, hospital
7 220 outpatient, hospital inpatient, and accident and emergency care during 6 and 12 months. Patient-
8 221 level costs will be obtained by multiplying unit costs by utilisation. National unit costs for children's
9 222 services will be obtained from the Unit Costs of Health and Social Care 2019 by the Personal Social
10 223 Services Resource Unit (28) and the NHS reference costs for 2015-16 (29). Due to the often-skewed
11 224 cost distribution with a large number of zeros and a long right-hand tail, the modified Park Test and
12 225 Pregibon Link test will assess the most appropriate distribution and link to calibrate a Generalized
13 226 linear model (GLM) for costs, for example, with a gamma distribution and a log-link (30,31). The cost
14 227 model will adjust for a binary variable indicating whether the children or young person belonged to
15 228 the intervention or control arm and any demographic variables that show imbalance between the
16 229 two groups.

20 230 **2.4.2. Tracer conditions: cost-effectiveness/utility and cost-benefit analyses**

21 231 This within-trial economic evaluation will also compare CYPHP with EUC for patients under 16 with
22 232 asthma, constipation, and/or eczema. Three types of economic evaluation will be conducted. The
23 233 cost-effectiveness analysis, using point improvement in the PedsQL scale as the primary outcome,
24 234 and the cost-utility analysis, based on quality-adjusted life years (QALYs) from the CHU-9D, will
25 235 adopt an NHS and Personal Social Services (PSS) perspective. PSS includes a range of services
26 236 provided by local authorities for vulnerable groups, including the mentally and physically disabled,
27 237 older people, and neglected children. The cost-benefit analysis will take a societal perspective and
28 238 additionally account for costs falling on parents, and schools, as well as valuing parental wellbeing
29 239 with the Warwick-Edinburg Mental Wellbeing Scale (WEMWBS). These analyses will adhere to
30 240 guidelines for conducting economic evaluations alongside clinical trials and the most recent National
31 241 Institute for Health and Care Excellence (NICE) public health reference case(32–35).

32 242 **Costing: Identification, measurement, and valuation of resources**

33 243 Costing involves identifying, measuring, and valuing the resources used to deliver and participate in
34 244 the intervention, and consequential health and social services use. In a complex system change such
35 245 as CYPHP, the comprehensive identification of resources requires close collaboration with the
36 246 implementation and the process evaluation teams.

37 247

38 248 ***Identification of resource use***

39 249 CYPHP health and social care costs borne by the NHS and PSS mainly include time spent by medical
40 250 professionals and service managers delivering CYPHP services, along with consequential health and
41 251 social services utilisation by patients (**Table 3**). From a societal perspective, time spent by school
42 252 staff participating in CYPHP and time away from work or school by parents and CYP are also
43 253 accounted for. Because both intervention and control practices include EUC, EUC's delivery costs will
44 254 be disregarded. Service use and time away from school and work will be considered for both CYPHP
45 255 and EUC.

46 256 ***Measurement of resource use***

47 257 Resources used to implement CYPHP will be gathered from seven data sources, including the study's
48 258 accounting data, service caseloads, CYPHP nurse's personal caseload notes, study questionnaires,
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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	
<hr/>			
<i>CYP and family</i>			
	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

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3 312 schoolwork, sleep, daily routine, and social activities. The tool is designed to be administered to CYP
4 313 between 7-17 years of age, and a proxy version to be completed by parents is available for younger
5 314 children(39,40). The Warwick-Edinburg Mental Wellbeing Scale (WEMWBS) (41) will serve as a well-
6 315 being questionnaire for parents. All questionnaires were administered at baseline and at two follow-
7 316 up points (6 and 12 months). Questionnaires completed during the first phase of the Covid-19
8 317 pandemic [12 March 2020 – 6 July 2020], will be repeated after this period, and follow-up measures
9 318 delayed. Multiple imputation will be used for questionnaires with missing values.

12 319 In the cost-benefit analysis, QALYs and WEMWBS will be combined by converting both to Pound
13 320 Sterling values. QALYs will be monetised by using the government sector willingness-to-pay of
14 321 £20,000 to £30,000 per QALY gained(42). For WEMWBS, the monetary values published by Simetrica
15 322 and HACT for each Short-version WEMWBS (SWEMWBS) score will be employed and converted to
16 323 cost year 2020/2021 (43). The SWEMWBS score can be obtained from the original WEBWMS using
17 324 seven of its 14 statements about thoughts and feelings.

20 325 **Statistical analyses**

22 326 The intention-to-treat population will be used in statistical analyses. First, differences between
23 327 protocolized and actual intervention components (including inputs, frequency and duration of each
24 328 component) will be assessed (**Table 2**). Second, univariate analyses will be conducted to describe
25 329 sample mean differences and variability across time between treatment and control group for each
26 330 outcome. Three time points will contribute to analysis; baseline, 6-months, and 12 months. Third, to
27 331 adjust for treatment group imbalances, four multilevel regression models will be estimated; one
28 332 each for total costs, QALYs, PedsQL score, and monetary benefits (£ corresponding to QALYs and
29 333 WEBWMS scores together)(44). Each model will include a variable indicating participation in
30 334 intervention or control and variables that, despite randomization, may still be unequally distributed
31 335 between intervention and control groups such as age, gender and deprivation level for the patient-
32 336 level models. For the regression model predicting QALYs, the baseline QALYs will also be controlled
33 337 for(45). Benefits will be estimated using ordinary least squares, and costs with a GLM model with a
34 338 gamma distribution and a log-link. Both the use of a GLM and limited dependent variable mixture
35 339 models will be considered when modelling QALYs(46). All models will cluster standard errors to
36 340 account for correlation of patients in the same CYPHP cluster.

41 341 For each outcome variable and intervention and control groups separately, mean predicted values
42 342 will be generated. Three incremental cost-effectiveness ratios (difference between intervention and
43 343 control in mean predicted costs over difference in mean predicted outcomes) will be computed, one
44 344 for the cost-effectiveness analysis (based on PedsQL scores), another for the cost-utility analysis
45 345 (using QALYs), and a third one for the cost-benefit analysis (£). These three ICERs will be generated
46 346 based on 6 and 12-months data.

48 347 The pattern and amount of missing data between treatment and control groups by study variable
49 348 will be assessed. If data is missing completely at random for both treatment and control groups and
50 349 the percentage of missing data is below 5%, missing data will be ignored. If data is missing at random
51 350 (MAR), multiple imputation accounting for clustering (such as fixed effects) will be used (47). When
52 351 the data is MAR, multiple imputation can lead to consistent, asymptotically efficient, and
53 352 asymptotically normal estimates(48).

56 353 **Handling uncertainty**

58 354 The level of decision uncertainty arising from sampling and assumptions on key parameter estimates
59 355 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

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3 400 Federations, Provider Trusts, CYP and their families. With CYPHP, healthcare utilisation costs may
4 401 remain stable if primary care visits increase, but hospitalisations and emergency room visits
5 402 decrease. Parents and children's costs related to time lost from work or school are also expected to
6 403 decline with CYPHP if CYP's tracer conditions are well managed. Our planned analyses will allow both
7 404 to be studied and accounted for.

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10 405 The long-term model will assess the cost-effectiveness of CYPHP compared to EUC beyond the trial
11 406 duration to fully capture intervention effects on children with asthma, constipation and/or eczema.
12 407 Existing cost-effectiveness studies assessing interventions for CYP with these tracer conditions rarely
13 408 include a long-term model, and the duration of RCTs of education, coaching, nurse-led clinics or
14 409 treatments for the tracer conditions tend to be under three years (51–56). CYPHP is expected to
15 410 foster long-lasting improvements beyond 12 months in health outcomes due to changes in disease
16 411 management behaviour among the CYP and family, and also health professionals. The natural
17 412 progression of the tracer conditions indicates that a substantial percentage of children continue to
18 413 experience symptoms beyond 12 months, and sometimes even into adulthood. Asthma in childhood
19 414 persists into adulthood for 79% of the cases (57). About half of children with atopic eczema still have
20 415 the problem as adults (58,59). Twenty five percent of children with functional constipation continue
21 416 to experience symptoms as adults (60,61).

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25 417 This study will contribute rigorous evidence about health economics of children's integrated
26 418 healthcare in the UK, where there has been a notable paucity of high-quality evidence. Results from
27 419 this study will directly inform decisions on children's healthcare provision in South East London and
28 420 will provide rigorous evidence to inform policy nationally and internationally.

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30 421 **Ethics and dissemination:** Ethics approval was obtained from South West-Cornwall & Plymouth
31 422 Research Ethics Committee. Results will be submitted for publication in peer-reviewed journals,
32 423 made available in briefing papers for local decision-makers, and provided to the local community
33 424 through website and public events. Findings will be generalisable to community-based models of
34 425 care, especially in urban settings.

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38 39 427 **References**

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49 586 Marina Soley-Bori: Conceptualization, Methodology, Writing - Original Draft, Writing - Review &
50 587 Editing, Investigation, Visualisation; Raghu Lingam: Writing - Review & Editing, Funding acquisition;
51 588 Rose-Marie Satherley: Writing - Review & Editing, Investigation. Julia Forman: Writing - Review &
52 589 Editing. Lizzie Cecil: Writing - Review & Editing. Julia Fox-Rushby: Conceptualization, Methodology,
53 590 Supervision, Writing - Review & Editing; Ingrid Wolfe: Writing - Review & Editing, Funding
54 591 acquisition.

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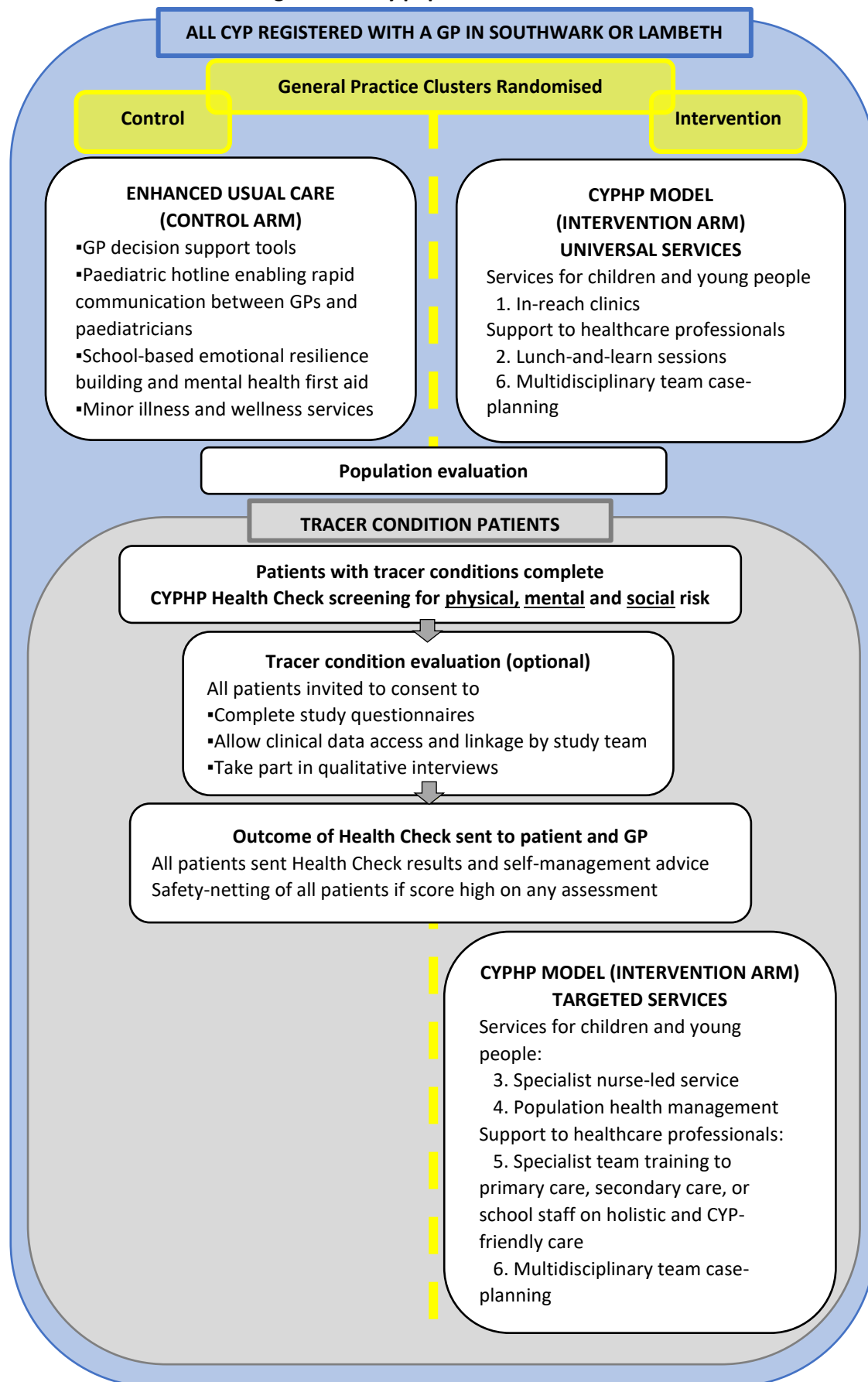
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Figure 1. Study population and intervention flow



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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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4 2 **evaluation protocol of a complex system change**
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32 26 **Abstract**

33 27 **Introduction:** The Children and Young People's Health Partnership (CYPHP) Evelina London Model of
34 28 Care is a new approach to integrated care delivery for children and young people with common
35 29 health complaints and chronic conditions. CYPHP includes population health management (services
36 30 shaped by data-driven understanding of population and individual needs, applied in this case to
37 31 enable proactive case-finding and tailored biopsychosocial care), specialist clinics with
38 32 multidisciplinary health teams, and training resources for professionals working with children and
39 33 young people. This complex health system strengthening program has been implemented in South
40 34 London since April 2018, and will be evaluated using a cluster randomised control trial (cRCT) with
41 35 an embedded process evaluation. This protocol describes the within- and beyond-trial economic
42 36 evaluation of CYPHP.
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44 38 **Methods and analysis:** The economic evaluation will identify, measure, and value resources and
45 39 health outcome impacts of CYPHP compared with Enhanced Usual Care (EUC) from a National Health
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3 39 Service/ Personal Social Service and a broader societal perspective. The study population includes
4 40 90,000 children and young people under 16 years of age in 23 clusters (groups of GP practices) to
5 41 assess health service use and costs, with more detailed cost-effectiveness analysis of a targeted
6 42 sample of 2,138 children and young people with asthma, eczema, or constipation (tracer conditions).
7 43 For the cost-effectiveness analysis, health outcomes will be measured using the Pediatric Quality of
8 44 Life Inventory (PedsQL) and quality-adjusted life years (QALYs) using the Child Health Utility measure
9 45 (CHU-9D). To account for changes in parental wellbeing, the Warwick-Edinburg Mental Wellbeing
10 46 Scale (WEMWBS) will be integrated with QALYs in a cost-benefit analysis. The within-trial economic
11 47 evaluation will be complemented by a novel long-term model that expands the analytic horizon to
12 48 10 years. Analyses will adhere to good practice guidelines and National Institute for Health and Care
13 49 Excellence (NICE) public health reference case.

17 50 **Ethics and dissemination:** The study has received ethical approval from South West-Cornwall &
18 51 Plymouth Research Ethics Committee (REC Reference: 17/SW/0275. Results will be submitted for
19 52 publication in peer-reviewed journals, made available in briefing papers for local decision-makers,
20 53 and provided to the local community through website and public events. Findings will be
21 54 generalisable to community-based models of care, especially in urban settings.

24 55 **Trial registration number:** NCT03461848; Pre-results.

27 57 **Strength and limitations of this study:**

- 29 58
- 30 59 • Robust study design: CYPHP will be evaluated using a cluster randomised control trial (cRCT)
31 60 with an embedded process evaluation.
 - 33 61 • Multiple analytic perspectives: Both the NHS and Personal Social Services (PSS) perspective
34 62 and a societal perspective, accounting for costs falling on parents and schools, will be
35 63 adopted.
 - 37 64
 - 38 65 • Long analytic horizon: The within-trial economic evaluation will be complemented by a novel
39 66 long-term model that expands the analytic horizon to 10 years
 - 41 67
 - 42 68 • Impact of Covid-19 on CYPHP service delivery: Differences in the frequency and duration of
43 69 each CYPHP component before and after Covid-19 may be observed, which will be assessed
44 70 in sensitivity analyses.
 - 45 71
 - 46 72 • Measurement of intervention effects: The intensity of the different intervention
47 73 components may have varied across GP practices and the measurement of health effects
48 74 with the CHU-9D for children below 5 may lack reliability.

50 75

52 76 **Key words:** Integrated care, cost-effectiveness, decision modelling, paediatrics

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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 glycosylated 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)

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

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

139 2. METHODS AND ANALYSIS

140 2.1. Study design

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

151 **Table 1. Key features of the CYPHP intervention and evaluation**

152 Targeted recruitment sample without loss to follow-up	1,496
153 Route to change	<ul style="list-style-type: none"> • 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
154 Main strengths	<ul style="list-style-type: none"> • Opportunistic randomised controlled trial • Rich data with both patient-reported and routine service use data • Embedded process evaluation to assess CYPHP implementation success
155 Stakeholder involvement	CYPHP was developed with children and young people, carers, frontline practitioners, and health service commissioners

152 2.2. Intervention and control arms

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2
3 153 The study structure and components of CYPHP and EUC are described in **Figure 1**. As the
4 154 intervention arm provides CYPHP on top of EUC, EUC is delivered at all practices. CYPHP offers
5 155 universal services (available to all CYP, with any childhood condition) and targeted services (available
6 156 only to CYP with tracer conditions - **asthma, constipation, and/or eczema**). EUC is comprised of
7 157 several patient self-management support tools for families and resources available to health
8 158 providers to provide higher quality and more joined-up care for CYP.

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11 159 Specifically, CYPHP includes:

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13 160 ▪ CYPHP *universal services*

- 14 161 1. *In-reach clinics*, integrated child health clinics co-delivered by patch-pediatricians
15 162 and GPs (patch paediatricians are linked to a cluster of general practices) as part of
16 163 a multidisciplinary CYP health team located in the community.
17 164 2. *Lunch-and-learn sessions*, where a multidisciplinary group of CYP health
18 165 professionals, including pediatricians and primary care staff share knowledge,
19 166 review cases, create common professional cultures, build and reinforce team
20 167 working practices.

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23 168 ▪ CYPHP *targeted services (tracer conditions only)*

- 24 169 3. *Specialist nurse-led services*, usually delivered by a CYPHP nurse trained in
25 170 biopsychosocial care (mental health and other specialists are available too if
26 171 needed) at the CYP's home, during a visit at a community-based clinic, or through a
27 172 phone call or message. It includes health promotion and self-management advice
28 173 on tracer conditions. Patients are triaged and care is planned based on a pre-
29 174 assessment biopsychosocial Health Check (CYPHP Health Check) and patient
30 175 records. The CYPHP Health Check is administered to patients with asthma,
31 176 constipation, or eczema. It uses validated questionnaires when possible to measure
32 177 biopsychosocial health. Child's ongoing conditions are assessed with the Patient
33 178 Oriented Eczema Measure (POEM)(22) for children with eczema, the Asthma
34 179 Control Test (ACT)(23) for asthma, and a bespoke CYPHP constipation
35 180 questionnaire (validation work underway). The Strengths and Difficulties
36 181 Questionnaire (SDQ)(24) is used as an emotional and behavioural screening
37 182 questionnaire. Finally, a set of bespoke social questions to understand a family's
38 183 broader situation and factors that may affect their health and care, such as financial
39 184 worries and days lost of school or work, are also included. Participants who consent
40 185 as research subjects, do also complete the Paediatric Quality of Life Inventory
41 186 (PedsQL)(25) and the Child Health Utility 9-D (CHU-9D)(26).

- 42 187 4. *Population health management*, where CYP with tracer conditions are sent text
43 188 messages and a letter from their GP, encouraging them to participate in early
44 189 intervention and care. Recipients are identified based on analyses of electronic health
45 190 records and actively reached out to connect them with the healthcare system and
46 191 improve the management of their conditions before they exacerbate.

- 47 192 5. *Specialist team training*, including education and training for primary care, secondary
48 193 care, or school staff on evidence-based, holistic, and CYP-friendly care for tracer
49 194 conditions, is delivered by CYPHP professionals.

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53 195 *Multidisciplinary team case-planning* is important for CYPHP delivery, present in both universal and
54 196 targeted services. It includes case planning and both formal and informal education and training for
55 197 professionals providing CYPHP.

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

201 **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	.

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

209 **2.3. Patient and Public Involvement**

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

216 **2.4. Economic evaluation within the trial**

217 **2.4.1. Population-level cost analysis**

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

232 **2.4.2. Tracer conditions: cost-effectiveness/utility and cost-benefit analyses**

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

242 **Costing: Identification, measurement, and valuation of resources**

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

247

248 ***Identification of resource use***

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

256 ***Measurement of resource use***

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

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

267 **Valuation of resource use**

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

276 **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

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3 314 children(39,40). The WEMWBS (41) will serve as a well-being questionnaire for parents. All
4 315 questionnaires were administered at baseline and at two follow-up points (6 and 12 months).
5 316 Questionnaires completed during the first phase of the Covid-19 pandemic [12 March 2020 – 6 July
6 317 2020], will be repeated after this period, and follow-up measures delayed.

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9 318 In the cost-benefit analysis, QALYs and WEMWBS will be combined by converting both to Pound
10 319 Sterling values. QALYs will be monetised by using the government sector willingness-to-pay of
11 320 £20,000 to £30,000 per QALY gained(42). For WEMWBS, the monetary values published by Simetrica
12 321 and HACT for each Short-version WEMWBS (SWEMWBS) score will be employed and converted to
13 322 cost year 2020/2021 (43). The SWEMWBS score can be obtained from the original WEBWMS using
14 323 seven of its 14 statements about thoughts and feelings.

16 324 **Statistical analyses**

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18 325 The intention-to-treat population will be used in statistical analyses. First, differences between
19 326 protocolized and actual intervention components (including inputs, frequency and duration of each
20 327 component) will be assessed (**Table 2**). Second, univariate analyses will be conducted to describe
21 328 sample mean differences and variability across time between treatment and control group for each
22 329 outcome. Three time points will contribute to analysis; baseline, 6-months, and 12 months. Third, to
23 330 adjust for treatment group imbalances, four multilevel regression models will be estimated; one
24 331 each for total costs, QALYs, PedsQL score, and monetary benefits (£ corresponding to QALYs and
25 332 WEBWMS scores together)(44). Each model will include a variable indicating participation in
26 333 intervention or control and variables that, despite randomization, may still be unequally distributed
27 334 between intervention and control groups such as age, gender and deprivation level for the patient-
28 335 level models. For the regression model predicting QALYs, the baseline QALYs will also be controlled
29 336 for(45). Benefits will be estimated using ordinary least squares, and costs with a GLM model with a
30 337 gamma distribution and a log-link. Both the use of a GLM and limited dependent variable mixture
31 338 models will be considered when modelling QALYs(46). All models will cluster standard errors to
32 339 account for correlation of patients in the same CYPHP cluster.

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37 340 For each outcome variable and intervention and control groups separately, mean predicted values
38 341 will be generated. Three incremental cost-effectiveness ratios (difference between intervention and
39 342 control in mean predicted costs over difference in mean predicted outcomes) will be computed, one
40 343 for the cost-effectiveness analysis (based on PedsQL scores), another for the cost-utility analysis
41 344 (using QALYs), and a third one for the cost-benefit analysis (£). These three ICERs will be generated
42 345 based on 6 and 12-months data.

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45 346 The pattern and amount of missing data between treatment and control groups by study variable
46 347 will be assessed. If data is missing completely at random for both treatment and control groups and
47 348 the percentage of missing data is below 5%, missing data will be ignored. If data is missing at random
48 349 (MAR), multiple imputation accounting for clustering (such as fixed effects) will be used (47). When
49 350 the data is MAR, multiple imputation can lead to consistent, asymptotically efficient, and
50 351 asymptotically normal estimates(48).

53 352 **Handling uncertainty**

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55 353 The level of decision uncertainty arising from sampling and assumptions on key parameter estimates
56 354 with policy impact will be assessed. Confidence intervals for ICERs based on the non-parametric
57 355 bootstrap method will be generated(49), along with acceptability curves to reflect the probability of
58 356 CYPHP being cost-effective as the willingness-to-pay per QALY (or other health outcome) increases.
59 357 Deterministic sensitivity analyses on chosen variables (such as intervention set-up costs, intensity of

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3 358 services delivered, and social care costs) will assist in identifying key drivers of the results. Subgroup
4 359 analysis of cost-effectiveness results by tracer condition and quintiles of IMD will be conducted as
5 360 long as a sufficient sample size is available.

7 361 **2.5. Long-term modelling of health and costs beyond the trial**

9 362 A state-transition model reflecting natural disease progression will be developed for each tracer
10 363 condition to predict the cost-effectiveness of CYPHP compared to EUC beyond the trial duration.
11 364 Trial data will be used to define the health states, transition probabilities among states, and to
12 365 calculate the costs and effects from an NHS/PSS perspective. Existing literature and publicly available
13 366 statistics (e.g., Office of National Statistics and existing UK cohort studies) will also be used to gather
14 367 transition probabilities across states beyond 12 months. A functional form characterizing the
15 368 sustainability of intervention effects into the longer run (changes in health-related quality of life and
16 369 health services utilisation) will be inferred based on 6 months and 12 months trial data. The effect of
17 370 alternative analytic horizons on the cost-effectiveness of CYPHP versus EUC will be tested in
18 371 sensitivity analyses, including 2, 5, and 10 years.

22 372 **DISCUSSION**

24 373 The CYPHP Evelina London model is a health-systems strengthening programme to advance towards
25 374 integrated and high-quality care for children and young people in the UK. By offering universal and
26 375 targeted services, CYPHP aims to overcome patient- and provider-level barriers to effective
27 376 management of physical and mental health and foster optimal health behaviour. The aims of this
28 377 economic evaluation are to establish the impact of CYPHP on healthcare costs at the population
29 378 level and the cost-effectiveness of the intervention among CYP with tracer conditions. Asthma,
30 379 constipation, and eczema serve as examples of common long-term conditions among CYP. Lessons
31 380 from managing these conditions should inform a broader health system response to the
32 381 epidemiological transition to chronic diseases.

35 382 **Strengths and weaknesses**

37 383 Beyond temporary trial suspension, Covid-19 may have affected our study in at least two ways. First,
38 384 CYPHP delivery may not return to normal after the pandemic. Differences in the frequency and
39 385 duration of each CYPHP component before and after Covid-19 will be assessed in sensitivity
40 386 analyses. Second, some follow-up questionnaires were due during Covid-19. When possible, data
41 387 were collected, and an additional data point after Covid-19 was included for these participants to
42 388 isolate changes in health status due to the pandemic. Besides the effects of Covid-19, the intensity of
43 389 services delivered as part of CYPHP may not be fully standardised across GP practices. Variability in
44 390 service intensity across practices and its impact on cost-effectiveness results will be assessed in
45 391 sensitivity analyses. Additionally, health utility outcome measurement for children below 5 may lack
46 392 reliability as the questionnaire has not been psychometrically tested for this younger age group
47 393 (26,50). This measurement challenge will be addressed by using multiple economic evaluation
48 394 perspectives and health outcomes (such as the PedsQL) to provide a comprehensive and transparent
49 395 assessment of the effects of the intervention.

53 396 By carrying out three economic evaluations (cost-effectiveness, cost-utility, and cost-benefit) under
54 397 two different perspectives (NHS and PSS, and societal), we aim to inform stakeholders with various
55 398 interests, including Clinical Commissioning Groups and evolving Integrated Care System, GP
56 399 Federations, Provider Trusts, CYP and their families. With CYPHP, healthcare utilisation costs may
57 400 remain stable if primary care visits increase, but hospitalisations and emergency room visits
58 401 decrease. Parents and children's costs related to time lost from work or school are also expected to

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3 402 decline with CYPHP if CYP's tracer conditions are well managed. Our planned analyses will allow both
4 403 to be studied and accounted for.

6 404 The long-term model will assess the cost-effectiveness of CYPHP compared to EUC beyond the trial
7 405 duration to fully capture intervention effects on children with asthma, constipation and/or eczema.
8 406 Existing cost-effectiveness studies assessing interventions for CYP with these tracer conditions rarely
9 407 include a long-term model, and the duration of RCTs of education, coaching, nurse-led clinics or
10 408 treatments for the tracer conditions tend to be under three years (51–56). CYPHP is expected to
11 409 foster long-lasting improvements beyond 12 months in health outcomes due to changes in disease
12 410 management behaviour among the CYP and family, and also health professionals. The natural
13 411 progression of the tracer conditions indicates that a substantial percentage of children continue to
14 412 experience symptoms beyond 12 months, and sometimes even into adulthood. Asthma in childhood
15 413 persists into adulthood for 79% of the cases (57). About half of children with atopic eczema still have
16 414 the problem as adults (58,59). Twenty five percent of children with functional constipation continue
17 415 to experience symptoms as adults (60,61).

21 416 This study will contribute rigorous evidence about health economics of children's integrated
22 417 healthcare in the UK, where there has been a notable paucity of high-quality evidence. Results from
23 418 this study will directly inform decisions on children's healthcare provision in South East London and
24 419 will provide rigorous evidence to inform policy nationally and internationally.

27 420 **Ethics and dissemination:** Ethics approval was obtained from South West-Cornwall & Plymouth
28 421 Research Ethics Committee. Results will be submitted for publication in peer-reviewed journals,
29 422 made available in briefing papers for local decision-makers, and provided to the local community
30 423 through website and public events. Findings will be generalisable to community-based models of
31 424 care, especially in urban settings.

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Figure 1. Study population and intervention flow

For peer review only

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15 629 **Authors contributions**

16 630 Marina Soley-Bori: Conceptualization, Methodology, Writing - Original Draft, Writing - Review &
17 631 Editing, Investigation, Visualisation; Raghu Lingam: Writing - Review & Editing, Funding acquisition;
18 632 Rose-Marie Satherley: Writing - Review & Editing, Investigation. Julia Forman: Writing - Review &
19 633 Editing. Lizzie Cecil: Writing - Review & Editing. Julia Fox-Rushby: Conceptualization, Methodology,
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Figure 1. Study population and intervention flow

