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A multifaceted intervention to reduce antibiotic prescribing among CHIldren with acute COugh and respiratory tract infection: the CHICO cluster RCT

Peter S Blair, Grace J Young, Clare Clement, Padraig Dixon, Penny Seume, Jenny Ingram, Jodi Taylor, Jeremy Horwood, Patricia J Lucas, Christie Cabral, Nick A Francis, Elizabeth Beech, Martin Gulliford, Sam Creavin, Janet A Lane, Scott Bevan and Alastair D Hay

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A multifaceted intervention to reduce antibiotic prescribing among CHIldren with acute COugh and respiratory tract infection: the CHICO cluster RCT

Peter S Blair,[1*] Grace J Young,[2] Clare Clement,[2] Padraig Dixon,[3] Penny Seume,[4] Jenny Ingram,[1] Jodi Taylor,[2] Jeremy Horwood,[4] Patricia J Lucas,[5] Christie Cabral,[4] Nick A Francis,[6] Elizabeth Beech,[7] Martin Gulliford,[8] Sam Creavin,[4] Janet A Lane,[2] Scott Bevan[2] and Alastair D Hay[4]

[1]Centre for Academic Child Health, University of Bristol, Bristol Medical School, Bristol, UK
[2]Bristol Trials Centre (Bristol Randomised Trials Collaboration), Bristol Medical School, Department of Population Health Sciences, University of Bristol, Bristol, UK
[3]Nuffield Department of Primary Care Health Sciences, University of Oxford, Radcliffe Primary Care Building, Oxford, UK
[4]Centre for Academic Primary Care, Bristol Medical School, Population Health Sciences, University of Bristol, Bristol, UK
[5]School for Policy Studies, University of Bristol, Bristol, UK
[6]Primary Care and Population Sciences, University of Southampton, Aldermoor Health Centre, Southampton, UK
[7]NHS England and NHS Improvement, South West, UK
[8]School of Population Health and Environmental Sciences, King's College London, London, UK

[*]Corresponding author

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Prioritisation Committee A (out of hospital) – May 2018–March 2022 and NICE diagnostic advisory committee – October 2022 to the present. Martin Gulliford was a member of the HSDR Funding Committee – May 2016–May 2019.

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Abstract

A multifaceted intervention to reduce antibiotic prescribing among CHIldren with acute COugh and respiratory tract infection: the CHICO cluster RCT

Peter S Blair,[1*] Grace J Young,[2] Clare Clement,[2] Padraig Dixon,[3] Penny Seume,[4] Jenny Ingram,[1] Jodi Taylor,[2] Jeremy Horwood,[4] Patricia J Lucas,[5] Christie Cabral,[4] Nick A Francis,[6] Elizabeth Beech,[7] Martin Gulliford,[8] Sam Creavin,[4] Janet A Lane,[2] Scott Bevan[2] and Alastair D Hay[4]

[1]Centre for Academic Child Health, University of Bristol, Bristol Medical School, Bristol, UK
[2]Bristol Trials Centre (Bristol Randomised Trials Collaboration), Bristol Medical School, Department of Population Health Sciences, University of Bristol, Bristol, UK
[3]Nuffield Department of Primary Care Health Sciences, University of Oxford, Radcliffe Primary Care Building, Oxford, UK
[4]Centre for Academic Primary Care, Bristol Medical School, Population Health Sciences, University of Bristol, Bristol, UK
[5]School for Policy Studies, University of Bristol, Bristol, UK
[6]Primary Care and Population Sciences, University of Southampton, Aldermoor Health Centre, Southampton, UK
[7]NHS England and NHS Improvement, South West, UK
[8]School of Population Health and Environmental Sciences, King's College London, London, UK

[*]Corresponding author p.s.blair@bristol.ac.uk

Background: Clinical uncertainty in primary care regarding the prognosis of children with respiratory tract infections contributes to the unnecessary use of antibiotics. Improved identification of children at low risk of future hospitalisation might reduce clinical uncertainty. A National Institute for Health and Care Research-funded 5-year programme (RP-PG-0608-10018) was used to develop and feasibility test an intervention.

Objectives: The aim of the children with acute cough randomised controlled trial was to reduce antibiotic prescribing among children presenting with acute cough and respiratory tract infection without increasing hospital admission.

Design: An efficient, pragmatic open-label, two-arm trial (with embedded qualitative and health economic analyses) using practice-level randomisation using routinely collected data as the primary outcome.

Setting: General practitioner practices in England.

Participants: General practitioner practices using the Egton Medical Information Systems® patient-record system for children aged 0–9 years presenting with a cough or upper respiratory tract infection. Recruited by Clinical Research Networks and Clinical Commissioning Groups.

Intervention: Comprised: (1) elicitation of parental concerns during consultation; (2) a clinician-focused prognostic algorithm to identify children with acute cough and respiratory tract infection at low, average

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or elevated risk of hospitalisation in the next 30 days accompanied by prescribing guidance, (3) provision of a printout for carers including safety-netting advice.

Main outcome measures: Co-primaries using the practice list-size for children aged 0–9 years as the denominator: rate of dispensed amoxicillin and macrolide items at each practice (superiority comparison) from *NHS Business Services Authority ePACT2* and rate of hospital admission for respiratory tract infection (non-inferiority comparison) from Clinical Commissioning Groups, both routinely collected over 12 months.

Results: Of the 310 practices required, 294 (95%) were recruited (144 intervention and 150 controls) with 336,496 registered 0–9-year-olds (5% of all 0–9-year-old children in England) from 47 Clinical Commissioning Groups. Included practices were slightly larger than those not included, had slightly lower baseline dispensing rates and were located in more deprived areas (reflecting the distribution for practice postcodes nationally). Twelve practices (4%) subsequently withdrew (six related to the pandemic). The median number of times the intervention was used was 70 per practice (by a median of 9 clinicians) over 12 months. There was no evidence that the antibiotic dispensing rate in the intervention practices [0.155 (95% confidence interval 0.135 to 0.179)] differed to controls [0.154 (95% confidence interval 0.130 to 0.182), relative risk= 1.011 (95% confidence interval 0.992 to 1.029); $p = 0.253$]. There was, overall, a reduction in dispensing levels and intervention usage during the pandemic. The rate of hospitalisation for respiratory tract infection in the intervention practices [0.019 (95% confidence interval 0.014 to 0.026)] compared to the controls [0.021 (95% confidence interval 0.014 to 0.029)] was non-inferior [relative risk = 0.952 (95% confidence interval 0.905 to 1.003)]. The qualitative evaluation found the clinicians liked the intervention, used it as a supportive aid, especially with borderline cases but that it, did not always integrate well within the consultation flow and was used less over time. The economic evaluation found no evidence of a difference in mean National Health Service costs between arms; mean difference −£1999 (95% confidence interval −£6627 to 2630).

Conclusions: The intervention was feasible and subjectively useful to practitioners, with no evidence of harm in terms of hospitalisations, but did not impact on antibiotic prescribing rates.

Future work and limitations: Although the intervention does not appear to change prescribing behaviour, elements of the approach may be used in the design of future interventions.

Trial registration: This trial is registered as ISRCTN11405239 (date assigned 20 April 2018) at www.controlled-trials.com (accessed 5 September 2022). Version 4.0 of the protocol is available at: https://www.journalslibrary.nihr.ac.uk/ (accessed 5 September 2022).

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List of abbreviations

AMR	antimicrobial resistance
AMS	antimicrobial stewardship
BRTC	Bristol Randomised Trials Collaboration
CCG	Clinical Commissioning Group
CHICO RCT	CHIldren with COugh Randomised Controlled Study
CI	confidence interval
CONSORT	Consolidated Standards of Reporting Trials (Guidelines)
CPAG	Clinician and Pharmacist Advisory Group
CRN	Clinical Research Network
DMC	Data Monitoring Committee
EMIS®	Egton Medical Information Systems
FTE	full-time equivalent
GP	general practitioner
HTA	Health Technology Assessment
IMD	Index of Multiple Deprivation
ISRCTN	International Standard Randomised Controlled Trials Number
ITT	intention to treat
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute of Health and Care Research
NPT	normalisation process theory
PAG	Parent Advisory Group
PPI	patient and public involvement
RCT	randomised controlled trial
REC	Research Ethics Committee
RTI	respiratory tract infection
SAE	serious adverse event
SD	standard deviation
TARGET	name given to the 5-year National Institute of Health and Care Research funded programme of research underpinning the children with cough trial to develop an intervention to improve the targeting of antibiotics for children with respiratory tract infections (Ref No: RP-PG-0608-10018)
TMG	Trial Management Group
TSC	Trial Steering Committee

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Plain language summary

Coughs and colds (also known as respiratory tract infections) are the most common reason that children are taken to family doctors and nurses in primary care. These clinicians are not always sure how best to treat them and often use antibiotics 'just in case'. There are now concerns that clinicians are using antibiotics too often, and that this is increasing the number of resistant bugs (bacteria that cannot be killed by antibiotics). We wanted to see if using a scoring system of symptoms and signs of illness to help clinicians identify children very unlikely to need hospital care as well as listening to parents' concerns and giving them a personalised leaflet with care and safety advice, reduced antibiotic use. We recruited practices rather than patients, so did not need individual patient consent. The two main outcomes were the rate of antibiotics dispensed for children and number of children admitted to hospital for respiratory tract infections, using routinely collected data for 0–9-year-olds. We recruited 294 general practitioner practices, which was 95% of the total needed; 144 were asked to use the intervention and 150 to continue providing usual care (controls); only 12 practices subsequently withdrew (6 related to the pandemic). The average number of times the intervention was used was 70 per practice (by an average of 9 clinicians) over 12 months. There was no evidence that the antibiotic dispensing rate in the intervention practices differed from control practices. Further analyses showed an overall reduction in dispensing levels and intervention usage during the pandemic. The rate of hospitalisation for respiratory tract infection in the intervention practices was similar to the control practices. In the interviews, we found that clinicians liked the intervention and used it as a supportive aid during consultations, especially for borderline cases, rather than a tool to change prescribing behaviour.

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Scientific summary

Background

Respiratory tract infections (RTIs) in children are common and present major resource implications for primary care. Unnecessary use of antibiotics is associated with the development of antimicrobial resistance. Qualitative work from our National Institute for Health and Care Research (NIHR) TARGET Programme for Applied Research in 2016 identified clinician uncertainty regarding children's prognosis as a major driver of antibiotic prescribing and that improved identification of children at very low risk of future hospitalisation could increase confidence to withhold antibiotics. We developed an intervention that included: (1) eliciting carer concerns during consultation; (2) a clinician-focused algorithm to predict future hospitalisation for children with cough and RTI and (3) a carer-focused personalised printout recording decisions made at the consultation and safety-netting information. The intervention was not intended to replace but rather supplement clinical judgement.

In the feasibility trial, we found a recruitment differential at baseline in that intervention children were significantly more unwell than those recruited to the control group. We also found that recruitment procedures and using a stand-alone tool increased consultation times by 5 minutes. Learning from this, we proposed a more 'efficient' study design. We recruited practices rather than individual patients via Clinical Commission Groups (CCGs) and the national NIHR Clinical Research Network (CRN) and rather than trawl through the practice notes to collect primary outcome data, we utilised routinely collected data by the National Health Service (NHS) and CCGs. We also took a 'lighter touch' to data collection using short baseline and follow-up questionnaires filled in by designated practice champion [general practitioner (GP), nurse, practice manager or pharmacist] and embedded the intervention within the practice system rather than as a stand-alone tool. We hoped that this would not only mitigate recruitment differential but would also be resource efficient.

Objectives

Our aim was to assess whether embedding a multifaceted intervention into general practice for children (aged 0–9 years) presenting with acute cough and RTI would reduce antibiotic dispensing (superiority comparison) without impacting (non-inferiority comparison) on hospital attendance for RTI. We included a qualitative study to explore the use of the intervention, how it was embedded into practice and whether it was used appropriately and an economic evaluation of a between-arm comparison of secondary and primary care costs from an NHS perspective. We also report on the barriers and facilitators of using an efficient design.

Methods

The CHIldren with Cough (CHICO) randomised controlled trial (RCT) was an efficient, pragmatic, open-label, two-arm (intervention vs. control) trial of children in England aged 0–9 years presenting with an acute cough and RTI. The study received ethical approval (ref: 18/LO/0345) on 14 November 2018. Recruitment of practices was via CCGs and CRNs, between October 2018 and October 2020. Inclusion criteria were GP practices using the Egton Medical Information Systems (EMIS®) patient record system (used in 56% of English practices) where the local CCG had agreed to provide primary outcome data and the practice consented to take part. Practices were excluded if they were participating in any antimicrobial stewardship activities during the study period (12 months) involving potentially confounding concurrent intervention studies or were merging or planning to merge with another practice. Randomisation of

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practices on a 1 : 1 basis was stratified by CCG and minimised for list size and previous dispensing rate in the 12 months before data collection was conducted by the independent Bristol Randomised Trials Collaboration (BRTC) unit.

A practice champion was appointed at each intervention practice to distribute training materials within the practice, co-ordinate training of prescribing staff, encourage all clinicians to use the intervention appropriately and report from the EMIS® system how many times the intervention was used. Intervention practices were sent instructions including screenshots on how to install the intervention on the EMIS® system. E-mail support was offered to the practice champion to help implement this and encourage appropriate use of the tool.

When a child was in the age range, the healthcare professional received a ‘soft’ (i.e. a reminder) pop-up on their screen asking if the child was presenting with RTI. The pop-up gave the option of opening the CHICO Intervention. The Intervention screen would also open if the healthcare professional input a RTI-specific EMIS® code during the consultation. The algorithm included seven predictors two of which (age of patient and history of asthma) were already available for automatic entry, the other five predictors (short illness duration, temperature, intercostal or subcostal recession on examination, wheeze and moderate or severe vomiting) were entered during consultation. The algorithm reported whether the child was at elevated, average or very low risk of hospitalisation in the following 30 days along with antibiotic prescribing guidance. The health professional also had the option to print a short personalised letter with safety-netting guidance for the carer. The intervention was used in practices over a 1-month period.

The clinicians in practices randomised to the comparator arm were asked to treat children presenting with acute cough and RTI as they would normally.

The co-primary outcomes for children aged 0–9 years over a 12-month period were the rate of dispensed amoxicillin and macrolide items prescribed, for all indications (superiority comparison) collected routinely by NHS Business Services Authority (NHSBSA) ePACT2 and the rate of hospital admission for RTI (non-inferiority comparison) routinely collected by CCGs. The denominator was those 0–9-year-olds registered at each practice. Baseline data surrounding the characteristics of the practice and follow-up data after 12 months were collected. A secondary outcome looking at the rate of accident and emergency (A&E) attendances for RTI was collected in a similar way to hospitalisations.

A roll-out to three CCGs was performed initially to address any teething issues with the intervention, the internal pilot phase lasted 3 months and included a further four CCGs to help establish best practice for recruiting and communicating with practices before widening to the remaining CCGs.

Both sample size calculations assumed 90% power and a conservative two-sided alpha of 0.025 to take account of the two co-primary outcomes, an intracluster correlation coefficient of 0.03 and an estimated coefficient of variation of 0.65 along with an assumption of 750 children aged 0–9 years registered per practice. A 10% difference in dispensing data and no more than a 1% difference in hospital admission yielded 155 practices per arm. All primary and secondary analyses were conducted on an intention-to-treat (ITT) basis. A full CHICO statistical analysis plan was developed and agreed by the Trial Steering Committee (TSC) and Data Monitoring Committee (DMC). Mixed models were used to account for the within- and between-CCG level variation, incorporating the latter as a random effect. A random-effects Poisson regression model was used to analyse both co-primaries by arm, including list size as the exposure and baseline rate as a covariate. All analyses were carried out in Stata 17.0 and the results were described in terms of ‘strength of evidence’ rather than significance.

For the qualitative analysis, anonymised transcripts from interviews with clinicians (GPs and practice nurses) were checked for accuracy and then imported into NVivo Pro (version 10/11) using thematic analysis and the four normalisation process theory (NPT) constructs to develop themes across the data sets. For the economic evaluation, the comparison of between-arm costs used a two-way mixed-effect linear regression that accounted for the nesting of practices in CCG clusters. The primary economic analysis regressed total costs on arm and covariates for list size and dispensing rate, both of which were used for minimisation at randomisation.

Results

In 2018, there were around 200 CCGs in England, 110 were assessed as eligible (≥ 15 EMIS® practices), 52 consented to take part and 47 provided at least one practice. We also used all 15 CRNs in England to help with recruitment. Recruitment took 24 rather than 12 months continuing to October 2020 (due to slow response of some CCGs and impact of the COVID-19 pandemic). Of the 310 practices required, 294 (95%) were recruited (144 intervention and 150 controls) representing 336,496 registered 0–9-year-olds (5% of all 0–9-year-old children in England). Included practices were slightly larger and had slightly lower baseline dispensing rates, compared with practices not included from their CCG. They were also located more commonly in deprived areas reflecting the geographical distribution of practice postcodes nationally. Of the 294 practices, 12 (4%) subsequently withdrew (6 related to the pandemic).

The two arms were well balanced with respect to baseline characteristics. There were four serious adverse events (three intervention, one control) reported, none related to the intervention. Across the 121 (84%) intervention practices that provided at least 1 month of intervention usage data, a total of 11,944 intervention uses were recorded {median 70 [interquartile range (IQR) 9–142])}. Twenty practices (17%) recorded zero usage over the 12-month period. The median number of users per practice was nine (IQR 3–16). Of these, 74% were GPs, 14% were nurses, 6% were office staff, 3% were other clinicians, 3% were locum GPs and 1% were pharmacists. The baseline and follow-up data collection periods spanned October 2017–October 2021 thus included the COVID-19 pandemic which began in the spring of 2020. Both the use of the intervention and antibiotic dispensing data followed the expected seasonal winter peak until the pandemic during which the intervention usage dramatically fell and seasonal pattern disappeared with a notable decrease in antibiotic dispensing during pandemic lockdowns.

The main ITT analysis showed no evidence that the antibiotic dispensing rate in the intervention practices {0.155 [95% confidence interval (CI) 0.135 to 0.179])} differed from the controls [0.154 (95% CI 0.130 to 0.182)] with a relative risk (RR) of 1.011 (95% CI 0.992 to 1.029); $p = 0.253$. On average, this translates into 15 amoxicillin/macrolide items dispensed a year, per 100 registered patients aged 0–9 years. The pre-planned per-protocol analysis produced strong evidence of increased dispensing in the intervention arm [0.166 vs. 0.154, RR = 1.052 (95% CI 1.029 to 1.076), $p < 0.001$], although many non-compliant practices joined in the latter half of the study, when COVID-19 had lowered all dispensing rates leading to a surplus of 'low dispensing' practices in the control arm. There was weak evidence that the intervention decreased dispensing in the older children [RR = 0.965 (95% CI 0.935 to 0.997), $p = 0.030$] but increased dispensing in the younger children [RR = 1.037 (95% CI 1.014 to 1.060), $p = 0.001$]. Accounting for COVID-19 by including an indicator variable did not alter the primary finding. A post hoc analysis, removing all follow-up data after March 2020, led to reduced dispensing in the intervention arm [0.192 vs. 0.204, RR = 0.967 (95% CI 0.946 to 0.989), $p = 0.003$]; this equates to a 5.9% reduction but this observation is both post hoc and underpowered. Sensitivity analyses surrounding patient age, exclusion of pilot practices, a focus on amoxicillin only, delayed implementation and replacing the CCG random effects with Primary Care Network (PCN) random effects did not materially change dispensing rates. Some pre-defined subgroup analyses did interact with the treatment effect, with evidence of increased dispensing rates in the intervention arm among practices located in areas with a higher level of deprivation ($p = 0.004$), practices with more than one site ($p < 0.001$) and practices with a higher proportion of prescribing nursing staff ($p < 0.001$).

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We found no difference in the rate of hospitalisations at 0.019 (95% CI 0.014 to 0.026) and 0.021 (95% CI 0.014 to 0.029) for the intervention and control arms, respectively [incidence rate ratio (IRR) was 0.952 (95% CI 0.905 to 1.003)]. As 1.003 lies below the 1.01 non-inferiority margin we set, the intervention was considered non-inferior to the controls. Pre-specified sensitivity analyses did not change these results. The usual winter peak of hospital admissions was absent during the pandemic. The secondary outcome of A&E attendance rates were 0.049 (95% CI 0.037 to 0.066) and 0.045 (95% CI 0.032 to 0.063) for the intervention and control arms, respectively. The IRR was 1.013 (95% CI 0.980 to 1.047); $p = 0.437$.

Twenty-six clinicians (20 GPs and 6 practice nurses) were interviewed via telephone from 24 practices and 13 CCGs. The qualitative findings confirmed that intervention clinicians started using the tool and then stopped over time. The clinicians liked the intervention and used it as a supportive aid during consultations rather than a tool to change behaviour. They really liked the safety-netting advice leaflet, and this was seen to be the most useful intervention component, especially for facilitating discussions with parents about treatment decisions. The intervention was believed to be more useful in patients who were seen as 'borderline'. Clinicians initially welcomed CHICO in theory but for some it proved difficult to align the intervention flow with that of the consultation, especially if the data entry of the patient's record was normally made after the consultation. In the follow-up questionnaire, when asked if they would use the intervention again, 73% of the practitioners said that they would.

For the economic evaluation, NHS costs were calculated from the costs of the intervention itself, prescriptions of amoxicillin and macrolides per the co-primary outcome, A&E attendances and hospital admissions. Data were complete. There was no evidence of a difference in mean NHS costs in those practice randomised to use the intervention compared to those that did not. This conclusion held under various sensitivity analyses, including a per-protocol analysis.

The 'efficient design' was viable and relatively easy to implement. Recruited practices included 5% of all 0–9-year-old children in England with wide geographical cover. Engagement with CRNs and installation of the intervention was straightforward although the impact of updates to practice IT systems and lack of practice IT skills required extended support in some practices. Engagement with CCGs and their understanding of their role in research was variable. Data on the co-primary outcomes using routine dispensing information from the NHSBSA ePACT system and routine hospital attendance from CCGs were almost 100%.

Conclusions

This study did not produce evidence that embedding a multifaceted intervention into general practice for children presenting with acute cough and RTI could reduce antibiotic dispensing or impact on hospital attendance for RTI. Inference of the findings was made difficult as the pandemic affected intervention usage, dispensing levels and hospital attendance. The clinicians liked the intervention and used it as a supportive aid during consultations rather than a tool to change behaviour. The use of an efficient design was successful in this trial suggesting using routinely collected data for primary outcomes at the practice level is viable in England and should be promoted for primary care research where appropriate. Although the intervention does not appear to change prescribing behaviour, elements of the approach may be used in the design of future interventions.

Trial registration

This trial is registered as ISRCTN11405239 (date assigned 20 April 2018) at www.controlled-trials.com (accessed 5 September 2022). Version 4.0 of the protocol is available at: https://www.journalslibrary.nihr.ac.uk/ (accessed 5 September 2022).

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Chapter 1 Introduction

Structure of this report

In *Chapter 1*, the background to the research and rationale for reducing antibiotic prescriptions through use of a complex intervention is presented. *Chapter 2* describes the methods employed including the details of the intervention, recruitment, outcome measures, how the data were collected, the internal pilot and the study design. *Chapter 3* presents the clinical results of the study, *Chapter 4* the qualitative findings and *Chapter 5* the economic evaluation. *Chapter 6* discusses the efficient design of the study including the facilitators and barriers to such a design. *Chapter 7* presents the discussion and conclusions.

Background

Antibiotic prescribing

Respiratory tract infections (RTIs) in children present a major resource implication for primary healthcare services internationally for five reasons. First, they are extremely common and costly to service providers, families and employers.[1,2] Second, there is clinical uncertainty in primary care regarding the diagnosis and best management of RTIs, as reflected by the variation in the use of antibiotics in primary care for RTIs between nations,[3] general practitioner (GP) practices[4] and clinicians.[5] Third, antibiotic prescribing by primary care clinicians in the United Kingdom (UK) remains significantly higher than in some of our European neighbours.[6] Fourth, the overuse and misuse of existing antibiotics, combined with the slowing in the development of new antibiotics, are associated with the development and proliferation of antimicrobial resistance between[7] and within[8] nations as well as individuals.[6,9,10] Finally, the use of antibiotics leads to the subsequent 'medicalisation of illness' in which patients believe they should consult for similar symptoms in the future.[11] A number of key publications have highlighted the need for more research to define the appropriate use of antibiotics and healthcare resources for RTIs if the public health disaster of ineffective antibiotics for serious infections is to be averted.[12–14]

Findings from the TARGET programme

The design of the CHIldren with Cough (CHICO) trial's intervention was borne out of evidence from the TARGET programme's earlier work streams. This has involved data synthesis of qualitative and quantitative evidence,[15–19] a qualitative investigation to understand both parents' information needs and influences on clinical decisions surrounding antibiotic prescribing, quantitative evidence in terms of a large multicentre, prospective cohort study (over 8300 children) to derive and internally validate a clinical rule to predict hospitalisation of children with RTIs,[20,21] and the development of an intervention informed by a critical synthesis of all findings.[22] This culminated in a feasibility cluster randomised controlled trial (RCT) study to measure the acceptability of using symptoms, signs and demographic characteristics to predict hospital admittance in children presenting to primary care with RTI.[23,24] Findings across the TARGET programme were synthesised using Greene and Kreuter's Precede-Proceed model which integrates across several behavioural theories into a unified model.[25]

Qualitative work from the National Institute for Health and Care Research (NIHR) TARGET programme for Applied Research in 2016 identified clinician uncertainty as a major driver of antibiotic prescribing. Primary care clinicians acknowledge that they prescribe antibiotics for a range of medical and non-medical reasons, particularly in children, who are seen as vulnerable[26] and whose clinical state can change rapidly. Many clinicians report that they prescribe antibiotics just in case to mitigate perceived risk of future hospital admission and complications.[19,26] Our earlier programme work indicated that improved identification of children at very low risk of future hospitalisation could increase confidence

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to withhold antibiotics in low-risk groups.[15,16] Clinical prediction rules are designed to reduce clinical uncertainty in an outcome (such as a child's risk of hospitalisation) by assessing the strength of association between the risk of it occurring and baseline characteristics (e.g. sociodemographic characteristics or symptoms and signs of illness).

Clinical prediction rule for hospitalisation

The TARGET cohort study aimed to identify symptoms, signs and demographic characteristics that may predict hospitalisation and poor prognosis of a child. In particular, such an algorithm could potentially identify a large group of children at very low risk of hospitalisation and therefore are potentially unlikely to require antibiotics.

In line with expectations, just under 1% of the children were admitted to hospital up to 30 days after their consultation with the primary care clinician. We found seven characteristics independently associated with increased risk of hospitalisation for their acute cough or RTI during the subsequent 30 days. These are described by the STARWAVe mnemonic: Short illness duration (parent reported ≤ 3 days), Temperature (parent reported severe in previous 24 hours or ≥ 37.8° on examination), Age of patient (< 2 years), Recession (intercostal or subcostal on examination), Wheeze (on listing to chest with stethoscope), Asthma (currently diagnosed) and Vomiting (parent reported moderate or severe in the 24 hours prior to consultation). The area under the receiver operating characteristic (ROC) curve for the coefficient-based algorithm was 0.82 [95% confidence interval (CI) 0.77 to 0.87].

The prediction rule identifies children at very low, medium and high risk of future hospitalisation with advice given on how the clinician can use this information in conjunction with their own clinical judgement to decide the best course of action for each child. Assigning one point per predictive characteristic, a points-based algorithm was used to quantify absolute probabilities to three groups: (1) 'very low' (0.3%, 95% CI 0.2% to 0.4%) scoring 0 or 1 point; (2) 'normal' (1.5%, 1.0% to 1.9%) scoring 2 or 3 points and (3) 'high' (11.8%, 7.3% to 16.2%) scoring ≥ 4 points. The rule can potentially be effective in both reducing the overall prescription of antibiotics by increasing clinician confidence that they are not needed 'just in case' in the very low-risk group (just under 70% of children are in this group), as well as better identify those children in need of close monitoring (2% of children are in the high-risk group). Children in the medium-risk group (29%) have a similar risk of future hospitalisation as all children combined, so management should follow current National Institute for Health and Care Excellence (NICE) guidelines,[27] which state that clinicians should decide on the use of immediate, delayed or no antibiotics based on their assessment of the child's illness severity.

The interaction within the consultation

Our finding from our qualitative reviews was that clinicians could misinterpret parent's communication about their concerns or ideas regarding their child's illness as pressure for antibiotics and in some cases this led to unnecessary or unwanted antibiotics being prescribed.[26] Clinician communication was focused on differentiating minor and more serious illnesses, with the message (both implicit and explicit) that viral illnesses were minor while those that were 'serious' were treated with antibiotics. Clinicians and parents were often talking at cross purposes about the seriousness of the illness; parents emphasising the severity of the symptoms to demonstrate the impact on child health and to justify the consultation; clinicians seeking to justify a no-antibiotic treatment decision by minimising the problem.

The findings of our qualitative study suggested that parents want better information on the symptoms and signs of serious RTIs and when to consult,[28] along with more useful advice on home management of symptoms.[29] Parents did not want to know the absolute risk of hospitalisation for their child but they did want advice and information specific to their child.[29] When parents did consult, clinician explanations of diagnosis and treatment recommendations were not well understood by parents, and they remained unclear about how to manage a RTI and when to consult.[27–29] Clinicians reported that most often they gave a simple viral diagnosis, communicating that the illness was self-limiting and did not need antibiotic treatment.[29] However, if the child's illness appeared severe to the parent, or the parent was concerned about particular symptoms or impacts which were not addressed by the clinician, the parent reported viewing a simple viral diagnosis as inadequate. Parents' concerns encompassed things that fell outside a simple biomedical model for RTIs, including both child health and psychosocial impacts, but reported that clinicians rarely addressed these.

The feasibility study and an 'efficient' design

In the feasibility trial, the intervention group antibiotic prescribing rate at consultation was 25% (compared to 37% in our earlier cohort study); however, among the control group, the overall prescribing rate was even lower at 16%. The paradoxical effects found in the feasibility study were largely explained by a post-randomisation recruitment differential, with possible Hawthorne effects.[24] In the intervention arm, there was a significantly higher recruitment rate, difference in clinician type (proportionally more practice nurses recruiting), the children were significantly younger and importantly the intervention children were more unwell at baseline (significantly higher respiratory rate, significantly higher wheeze prevalence and significantly higher parent and clinician global illness severity scores). Learning from these lessons, we proposed a more 'efficient' study design that would not only mitigate recruitment differential but would also be resource efficient, using an intervention designed to be replicable for the National Health Service (NHS). Rather than recruit patients and collect consent during consultation we conducted the CHICO RCT at the practice level (as a cluster RCT) using Clinical Commission Groups (CCGs) and the national NIHR Clinical Research Network (CRN) to recruit practices. Rather than trawl through the practice notes to collect primary outcome data we utilised routinely collected data (dispensing data collected by NHS Business Services Authority (NHSBSA) ePACT2[30] and hospitalisation rates for RTI collected by CCGs). We also took a 'lighter touch' to data collection using short baseline and follow-up questionnaires filled in by the practice champion (GP, nurse, practice manager or pharmacist) and embedded the intervention within the practice system rather than as a stand-alone tool. This both reduced the time it takes to open and close the tool and had the advantage of utilising data already within the system and incorporating data entered as part of the trial into the practice system, thus, not duplicating clinical work. The barriers and facilitators to this efficient design approach are reported in *Chapter 6*.

Rationale

Antimicrobial resistance is recognised by the UK government, governments around the world and the World Health Organization (WHO) as one of the most pressing public health threats of our time. Around 80% of antibiotics prescribed for human consumption are prescribed in primary care,[31] and it has been estimated that around 50% of antibiotic prescribing in this setting is unnecessary.[32] Approaches to modify antibiotic prescribing in primary care have been developed and evaluated, and prescribing rates in England have declined slightly using figures from 2014 to 2015,[31] although antibiotic prescribing rates in the UK continue to be substantially higher than many other European countries.[6] The UK Five Year Anti-Microbial Resistance (AMR) Strategy 2013–2018 aims to conserve the effectiveness of existing antibiotics through effective antimicrobial stewardship, including reducing the inappropriate use of antibiotics. There is, therefore, an urgent need for an efficient intervention that can be rolled out at scale that safely addresses many of the key drivers of antibiotic prescribing in children. Recent papers suggest cluster randomised trials aimed at reducing antibiotics may be implemented efficiently in large samples from routine care settings by using primary care electronic health records in the UK.[33–35] We are aware of two ongoing studies: the first investigating the effects of an integrated package of interventions (including delayed prescribing; patient decision aids; communication training; patient information leaflets; and near-patient testing with C-reactive protein)[36] and the second (an 'efficient design' study) investigating the effects of a multifaceted intervention consisting of practice antibiotic prescribing feedback, delivery of educational and decision support tools and a webinar to explain and promote the intervention.[37] Both studies focus on the general rather than the paediatric population and have different components compared to our complex intervention. Primary care clinicians[38] and the research community[39] have called for the development of a sound evidence base, currently unavailable,

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to help them identify children at low and high risk of complications, especially serious complications such as pneumonia, that require hospitalisation. At a minimum, it is essential to demonstrate that any change in practice does not increase the number of children with serious complications. A change in practice should improve health outcomes for children, while distinguishing children for whom antibiotics are certainly not needed and providing precise information regarding the symptoms denoting poor prognosis for which parents should be vigilant.

Aims and objectives

Aim

The aim of the CHICO RCT is to reduce antibiotic prescribing among children presenting with cough or RTI without increasing hospital admission for this condition. Objectives pertain to the practice level, as no data was collected on individual participants.

Primary objectives

To determine:

P1. Whether the CHICO intervention decreases the number of paediatric formulation antibiotic suspension items dispensed for RTIs to children presenting with acute cough and RTI to primary care (superiority comparison).
P2. Whether the CHICO intervention results in no change in hospital admissions for children with a hospital diagnosis of RTI (non-inferiority comparison).

Secondary objectives

To determine:

S1. Whether the CHICO intervention results in no change in the accident and emergency (A&E) attendance rates of children with a hospital diagnosis of RTI (superiority comparison).
S2. The costs to the NHS for using the CHICO intervention.
S3. Whether any intervention effect is modified by the proportion of locums used.
S4. Whether any intervention effect is modified by the practices' prior antibiotic prescribing rate.
S5. Whether any intervention effect differs between GP and nurse prescribers.
S6. Whether any intervention effect differs between practices with 1 versus 2+ sites.
S7. Whether any intervention effect differs within child age groups.
S8. Whether any intervention effect differs between practices and over time.
S9. Whether the embedded CHICO intervention is acceptable to, and used by, primary care clinicians (GPs and nurses) in consultations with carers and their children and how does this vary between practices.

Chapter 2 Methods

Study design

The CHICO RCT is an efficient, pragmatic, open-label, parallel, two-arm (intervention vs. control) cluster randomised trial with an embedded qualitative study and health economics. The trial aimed at reducing antibiotic prescribing among children presenting with acute cough and RTI, with randomisation at the practice level, using routine antibiotic dispensing to assess effectiveness and hospitalisation data for RTI to assess non-inferiority. Randomisation of practices, to the two arms, was 1 : 1 with no involvement, or consent, from participants within them. The CHICO trial protocol has been published.[40]

Ethics approval and registration

The study received North of Scotland Research Ethics Committee (REC) approval on 29 October 2018 and by Health Research Authority at London-Camden and Kings Cross REC (ref: 18/LO/0345) on 14 November 2018. Trial Registration Number: ISRCTN11405239. This contains all items required to comply with the WHO Trial Registration Data Set. Any amendments to the protocol were reported accordingly to the regulatory bodies.

Practice systems

Egton Medical Information Systems (EMIS®) or EMIS® Health or EMISWeb (formerly known as Egton Medical Information Systems) supplies electronic patient record systems and software used in primary care in England. It is used in more than half the practices (56%) in England.[41] The intervention was embedded in the EMIS® system including pop-ups to identify children that may be eligible for the trial. The facilitators and barriers to this approach are reported in the results section.

As a separate scoping exercise to inform future dissemination, we contacted users or experts in *SystmOne* (covers 34% of practices)[41] and reported in the results section the potential of embedding the intervention in this system.

Recruitment sites and site training

Given we needed access to CCGs to obtain primary outcome data, we endeavoured to recruit CCGs to the study first and then the practices within these CCGs. In 2018, there were over 200 CCGs in England and between 10 and 80 practices per CCG. For recruitment of CCGs, we focused on those having 15 or more EMIS® practices. One of our co-investigators (EB) is a national project lead for healthcare-acquired infections and antimicrobial resistance at NHS England and co-ordinated expressions of interest from CCGs prior to the start of the trial.

The intervention clinicians were provided with print and online evidence-based information to describe how the intervention works. This included an overview of the intervention (see *Figure 1*), a flowchart of how the intervention works in EMIS®, a description of how the algorithm is scored and how to use the parent leaflet (see *Appendix 1*).

A practice champion was appointed at each practice to distribute training materials within the practice, co-ordinate training of practice prescribing staff, encourage all clinicians to use the intervention

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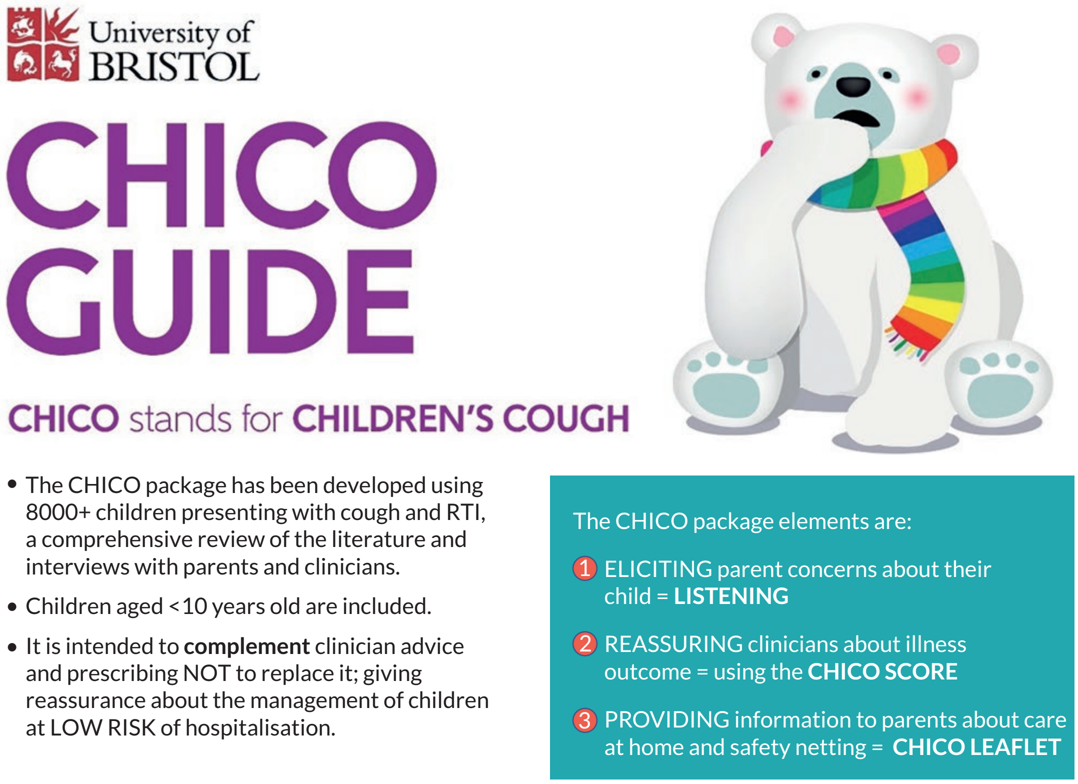

University of
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CHICO
GUIDE

CHICO stands for CHILDREN'S COUGH

- The CHICO package has been developed using 8000+ children presenting with cough and RTI, a comprehensive review of the literature and interviews with parents and clinicians.
- Children aged < 10 years old are included.
- It is intended to **complement** clinician advice and prescribing NOT to replace it; giving reassurance about the management of children at LOW RISK of hospitalisation.

The CHICO package elements are:

① ELICITING parent concerns about their child = **LISTENING**

② REASSURING clinicians about illness outcome = using the **CHICO SCORE**

③ PROVIDING information to parents about care at home and safety netting = **CHICO LEAFLET**

FIGURE 1 Children with cough clinician guide (overview of the intervention).

appropriately and report from the EMIS® system how many times the intervention was used. In the training package for clinicians, it was emphasised that the primary purpose of the intervention was to support the care of the larger proportion of children (69%) who have a very low risk of hospitalisation and this intervention was but one tool in their armoury for clinical decision making. The clinicians in practices randomised to the comparator arm were asked to treat children presenting with acute cough and RTI as they would normally.

Participants and recruitment

Recruitment of practices was via CCGs and the 15 CRNs across England using established channels of communication. NIHR CRNs support health and care organisations to be research active[42] and can help recruit practices at a national level, including those serving diverse socioeconomic populations, improving the generalisability of findings.[43] CCGs are generally less involved in research but as they communicate regularly with practices can be used to help with recruitment.

A roll-out to three CCGs was performed initially to address any teething issues with the intervention, the internal pilot phase lasted 3 months and included a further four CCGs to help establish best practice for recruiting and communicating with practices before widening to the remaining CCGs.

After the pilot phase, CCGs in other regions of England were approached prioritising those with > 15 EMIS® practices which could potentially be recruited to the study.

Eligibility

Inclusion criteria

General practitioner practices in England using the EMIS® electronic patient record system to house the intervention, where the local CCG has agreed to provide primary outcome data and the practice consented to take part. Children aged 0–9 years presenting with a cough or RTI to the participating practice were flagged for eligibility in CHICO via a pop-up on the EMIS® consultation screen (for practices in the intervention arm of the study). No identifiable information was collected at participant level for the study. The number of times the intervention was used at practice level, over a 12-month period, was collected via an EMIS® search.

Exclusion criteria

Practices were excluded if they were participating in any antimicrobial stewardship activities during the study period involving concurrent intervention studies, where there was a potential to confound or modify the effects of our intervention. Practices involved in the CHICO feasibility study or were merging or planning to merge with another practice were also excluded.

Children aged 10–14 were considered for inclusion but at this age an increasing number are given antibiotics in tablet form and given the much lower consultation rate in older children the research team decided to exclude this group from the study population.

Study population

The study population was children aged 0–9 years presenting with acute cough and RTI. The primary outcomes were antibiotic dispensing rates (amoxicillin and macrolide items) and hospitalisation rates for RTI over a 12-month period at each practice divided by the number of 0–9-year-olds registered at that practice.

Intervention

Overview

The intervention consists of (1) eliciting explicit carer concerns during consultation, (2) a clinician-focused algorithm to predict risk of hospitalisation for children with acute cough and RTI in the following 30 days and (3) a carer-focused personalised printout recording decisions made at the consultation and safety-netting information.[22] The algorithm was to be used as one tool among many the clinicians already have, to decide whether the child needs antibiotics. In the training package for clinicians it was emphasised that the primary purpose of the algorithm was not so much to identify the small proportion of children (2%) at higher risk of hospitalisation but rather the much larger proportion of children (69%), who have a very low risk of hospitalisation.

Installation

Practices randomised to the intervention were sent instructions including screenshots on how to install the intervention application on the EMIS® system. E-mail support was offered to the practice champion to help implement this and encourage appropriate use of the tool. Requests to access a practice EMIS® system remotely to assist installation, subject to appropriate data security clearance, were also used if the installation ran into any problems.

Detail of intervention workflow during a consultation

- Step 1: Soft Pop-up. Small CHICO pops up when child aged 0–9 years presents; clinician may click to open CHICO input screen.
- Step 2: CHICO Trigger. Specific EMIS® codes automatically trigger CHICO input screen.
- Step 3: CHICO Input screen: closed questions (clinical prediction rule) and elicitation of parent concerns.
- Step 4: CHICO Output. Step 4a – Additional hover text.
- Step 5: CHICO Letter + printout. Populate EMIS® record, generate Microsoft Word document (via mail merge) for printing.

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Once imported, the intervention was embedded within the primary care information system. The steps above outline how the intervention worked in practice. When a child was in the age range of 0–9 years, the healthcare professional received a soft pop-up on their screen asking if the child was presenting with RTI. The pop-up gave the option of opening the CHICO Intervention (see *Appendix 2*, *Figures 23* and *24*). The Intervention screen would also open if the healthcare professional input a RTI-specific EMIS® code during the consultation. An embedded form was presented to record the presence or absence of particular symptoms and signs. Two of the seven predictors (age of patient and history of asthma) were already available for automatic entry. The other five predictors (short illness duration, temperature, intercostal or subcostal recession on examination, wheeze and any vomiting) were recorded during the consultation. Clinical details that are required to complete the STARWAVe algorithm were documented in a standardised EMIS® proforma and the electronic medical record, then identified whether the consulting patient was at elevated, average or very low risk of hospitalisation using a 7-point scoring system. The health professional was also prompted to elicit explicit concerns of the carer. The output page appeared as a small pop-up on the screen (see *Table 1*), requiring no action from the healthcare professional but informed them of the child's risk of hospitalisation.

When the Intervention input page had been saved the health professional had the option to print a short, personalised letter for the carer. This letter captured the following information:

1. patient's name and age;
2. pre-specified brief description of the function of the consultation;
3. parent/carer's concerns; manually typed in by the healthcare professional;
4. healthcare professional's advice regarding raised parent's concerns;
5. name of healthcare professional.

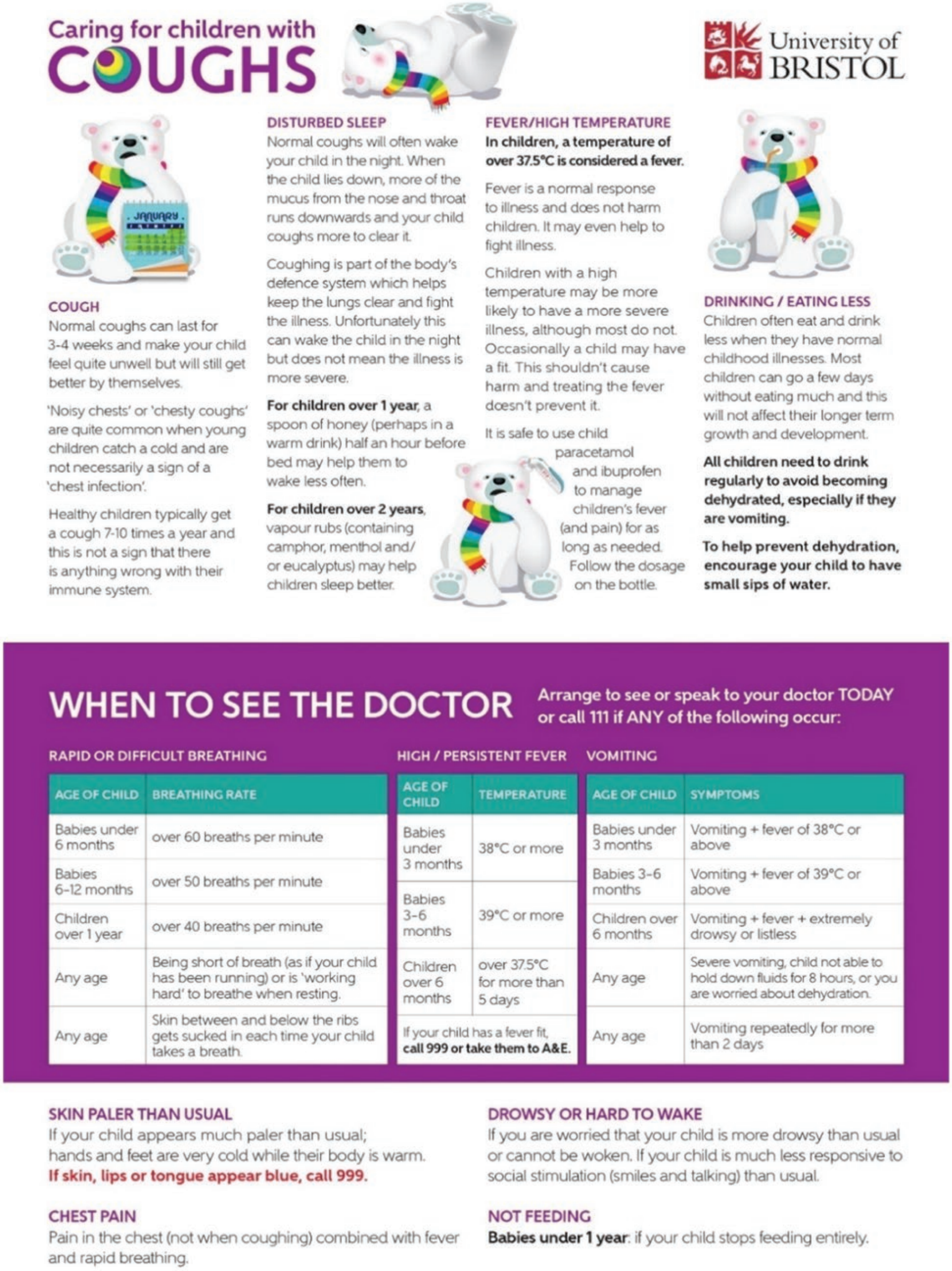
This personalised letter (project website upload) was provided to the carer alongside the 'Caring for CHICO' safety-netting leaflet (see *Figure 2*) providing further information regarding common carer concerns. The leaflet was based on one which was co-designed with parents and drew on our earlier work on the natural course of a typical RTI illness, typical duration of cough, caring for a child with a cough and safety-netting advice about when to re-consult. A slightly amended version was used in this intervention and made available in print or electronic format.[44]

Monitoring intervention use

An internal dashboard system was used for reporting frequency of use of the intervention by clinicians to practices during the 12-month participation period; where a 'use' of the intervention was defined as entering five or more symptom codes into the template as part of the consultation. Practices were provided with searches (EMIS® queries) which practice champions were requested to run monthly and feed back to the study team.

TABLE 1 Children with cough risk outputs

CHICO result	Pop-up text
Low-risk group	Very reassuring CHICO score: 0 or 1 CHICO predictors: > 99.6% of children will recover from this illness with home care. Consider a no- or delayed-antibiotic prescribing strategy. CHICO leaflet and letter covers common concerns and safety netting advice.
Average-risk group	Reassuring CHICO score: 2 or 3 CHICO predictors: > 98% of children will recover from this illness with home care. Consider no- or delayed-antibiotic prescribing strategy. CHICO leaflet and letter covers common concerns and safety-netting advice.
Elevated-risk group	Safety-netting needed: 4+ CHICO predictors: This is more than average, but > 87% of children will still recover from this illness with home care. Highlight SAFETY NETTING advice in CHICO leaflet.



Caring for children with

COUGHS

University of BRISTOL

COUGH

Normal coughs can last for 3-4 weeks and make your child feel quite unwell but will still get better by themselves.

'Noisy chests' or 'chesty coughs' are quite common when young children catch a cold and are not necessarily a sign of a 'chest infection'.

Healthy children typically get a cough 7-10 times a year and this is not a sign that there is anything wrong with their immune system.

DISTURBED SLEEP

Normal coughs will often wake your child in the night. When the child lies down, more of the mucus from the nose and throat runs downwards and your child coughs more to clear it.

Coughing is part of the body's defence system which helps keep the lungs clear and fight the illness. Unfortunately this can wake the child in the night but does not mean the illness is more severe.

For children over 1 year, a spoon of honey (perhaps in a warm drink) half an hour before bed may help them to wake less often.

For children over 2 years, vapour rubs (containing camphor, menthol and/ or eucalyptus) may help children sleep better.

FEVER/HIGH TEMPERATURE

In children, a temperature of over 37.5°C is considered a fever.

Fever is a normal response to illness and does not harm children. It may even help to fight illness.

Children with a high temperature may be more likely to have a more severe illness, although most do not. Occasionally a child may have a fit. This shouldn't cause harm and treating the fever doesn't prevent it.

It is safe to use child paracetamol and ibuprofen to manage children's fever (and pain) for as long as needed. Follow the dosage on the bottle.

DRINKING / EATING LESS

Children often eat and drink less when they have normal childhood illnesses. Most children can go a few days without eating much and this will not affect their longer term growth and development.

All children need to drink regularly to avoid becoming dehydrated, especially if they are vomiting.

To help prevent dehydration, encourage your child to have small sips of water.

WHEN TO SEE THE DOCTOR

Arrange to see or speak to your doctor TODAY or call 111 if ANY of the following occur:

RAPID OR DIFFICULT BREATHING

AGE OF CHILD	BREATHING RATE
Babies under 6 months	over 60 breaths per minute
Babies 6–12 months	over 50 breaths per minute
Children over 1 year	over 40 breaths per minute
Any age	Being short of breath (as if your child has been running) or is 'working hard' to breathe when resting.
Any age	Skin between and below the ribs gets sucked in each time your child takes a breath.

HIGH / PERSISTENT FEVER

AGE OF CHILD	TEMPERATURE
Babies under 3 months	38°C or more
Babies 3–6 months	39°C or more
Children over 6 months	over 37.5°C for more than 5 days
If your child has a fever fit, **call 999 or take them to A&E.**	

VOMITING

AGE OF CHILD	SYMPTOMS
Babies under 3 months	Vomiting + fever of 38°C or above
Babies 3–6 months	Vomiting + fever of 39°C or above
Children over 6 months	Vomiting + fever + extremely drowsy or listless
Any age	Severe vomiting, child not able to hold down fluids for 8 hours, or you are worried about dehydration.
Any age	Vomiting repeatedly for more than 2 days

SKIN PALER THAN USUAL

If your child appears much paler than usual; hands and feet are very cold while their body is warm. **If skin, lips or tongue appear blue, call 999.**

CHEST PAIN

Pain in the chest (not when coughing) combined with fever and rapid breathing.

DROWSY OR HARD TO WAKE

If you are worried that your child is more drowsy than usual or cannot be woken. If your child is much less responsive to social stimulation (smiles and talking) than usual.

NOT FEEDING

Babies under 1 year: if your child stops feeding entirely.

FIGURE 2 Children with cough safety-netting leaflet.

Encouraging intervention use

To accomplish this, the monthly searches returned by the practice champions were checked by the study team and relayed back to the practice if the intervention had not been used. In addition, practice champions were to review the search results and remind clinicians to use the intervention. CCGs were asked to support the study at both CCG levels and to endorse the use of the intervention within practices using local engagement processes and Anti-Microbial Stewardship (AMS) activities. Working with the AMS teams already established among practices and CCG pharmacists we selected CCG AMS leads to promote the use of the intervention at practice level.

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Fidelity of the intervention

The consistency and reliability (fidelity) measures focused on intervention exposure and the quality of the intervention delivered (using the process interviews as part of the qualitative investigation). Using our light-touch approach to data collection meant it was challenging to measure fidelity.

Capturing intervention usage

Monthly searches collected data on intervention usage, defined as 5+ symptom codes being entered into the CHICO template (see *Appendix 2*). There may have been consultations that were missed (false negatives) and some that were included with fewer than five symptoms (false positives) but these were difficult to quantify. In addition, in the follow-up questionnaire sent after 12 months participation in CHICO, there were questions about the use of the intervention for practices in the intervention arm of the study. Additional questions were added, concerning change in use during the pandemic, from April 2020 (project web upload).

Usual care (control practices)

The control arm for CHICO trial was usual care for this condition. The clinicians from practices randomised to the control arm were just asked to treat children presenting with cough or RTI as they normally would. Baseline and follow-up questionnaire data on control practices were collected but no data directly from the clinicians aside from routinely requesting information on serious adverse events (SAEs).

Outcome measures

Primary outcome measures

There were two primary outcomes:

P1. The rate of amoxicillin and macrolide items dispensed, calculated using the number of items dispensed to 0–9-year-olds and the number of children aged 0–9 registered at each practice over a 12-month period (testing for superiority). The number of items dispensed, for all indications, was used as a proxy measure due to the limitations of routine data.
P2. The rate of hospitalisations for RTI, calculated using the number of hospitalisations for RTI among children aged 0–9 years and the number of children aged 0–9 registered at each practice over a 12-month period (testing for non-inferiority).

Secondary outcome measures

S1. A&E attendance rates for RTI, calculated using the number of A&E attendances for RTI among children aged 0–9 years and the number of children aged 0–9 registered at each practice over a 12-month period.
S2. An exploration into the usage of the intervention, in terms of both usage over a 12-month period and seasonality, and the effects it has on primary outcome P1.
S3. A between-arm comparison of mean NHS costs in a cost-consequence analysis (health economics).
S4. Acceptability of the intervention and variation in use determined by qualitative interviews with the clinicians.

Subgroup analyses (potential effect modifiers for P1)

S1. Comparison of primary outcome P1 stratified by categorisation of proportion of locums (median) used over the 12 months the practice is in the study.
S2. Comparison of primary outcome P1 stratified by categorisation of proportion of nurses (median)

used over the 12 months the practice is in the study. This was originally planned as a dichotomisation of practices into those with GP prescribers only and those with nurse or other prescribers as well. However, given that the majority of practices had nurse prescribers, it seemed sensible to look at nurses as a proportion of staff.

S3. Comparison of primary outcome P1 stratified by categorisation of practice dispensing rates taken from the 12 months prior to the data collection from each practice.

S4. Comparison of primary outcome P1 dichotomised by those practices with one site only and those with multiple sites.

S5. Comparison of primary outcome P1 dichotomised by those practices with follow-up periods before the COVID-19 pandemic and those with follow-up months on or after March 2020.

S6. Comparison of primary outcome P1 dichotomised by those practices with a high level of deprivation versus those with a low level of deprivation.

Data collection

In this efficient design the data were mainly being collected from the practices and CCGs rather than patients and clinicians.

Expression of interest

As part of the recruitment of CCGs to the study, a form was completed by interested CCGs denoting their willingness to participate. One of our co-investigators (EB) is a national project lead for healthcare-acquired infections and antimicrobial resistance at NHS England and co-ordinated expressions of interest from CCGs prior to the start of the trial. Eligible practices were contacted via the CCGs and CRNs to take part in the trial. When GP practices were invited to participate, they were advised on the general principles of the trial, namely that the research will investigate methods to optimise the management of childhood RTI as well to agree to provide a practice champion as our primary contact and willingness of a member of staff to take part in qualitative interviews. If they were randomised to the intervention arm, the practices would need to agree to install the CHICO intervention on EMIS® and for the practice champion to monitor its use and send monthly updates. If practices wished to take part in the study, they completed an expression of interest form confirming agreement.

Randomisation data

When CCGs agreed to take part in the CHICO trial, the latest 12 months of data available, for amoxicillin and macrolide prescribing, was collected for all practices in their area. The latest month of list size data was used as the denominator to calculate the rate of dispensing over the 12-month period. This was then used to divide the data into those with a HIGH or LOW dispensing rate for stratification purposes in the randomisation process. In a similar way, practices within the CCG were split into those with a HIGH or LOW list size, relative to other practices within their CCG. These HIGH/LOW categorisations were not shared with the trial team until a practice agreed to take part and were ready to be randomised.

Baseline questionnaire

A brief questionnaire was sent to each practice to collect data on the characteristics of all practices prior to randomisation. Data were collected on the numbers of staff at the practice (by job type), questions regarding triaging of RTI conditions and postcode (for calculating the Index of Multiple Deprivation).

Routine data

For each practice, baseline data and follow-up data after 12 months were collected along with data for the two primary outcomes (dispensing and hospitalisations) and the secondary outcome (A&E attendances). The items of amoxicillin and macrolides dispensed, each month, were collected for the 12 months prior to randomisation and the 12 months after the implementation period. A short 'implementation period' (usually around 1 month) was allowed prior to the 12-month data collection

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period, giving time for the practices to install the intervention and encourage staff to use it. Any data collected during this period were not used in the analysis. For example, if a practice was randomised on the 10th of January their typical month 1 of follow-up would be February, as routine data were available for each calendar month. The data were obtained from NHSBSA ePACT2 system.[30]

For the same 24-month period, data were collected on hospitalisations and A&E attendances, via a secure NHS e-mail inbox. These data were collected directly from each CCG. Data analysts from each CCG were asked to provide the number of hospitalisations for RTI, the number of hospitalisations with a 'missing' diagnosis and the total number of hospitalisations. Similar data were collected on A&E attendances. List size data, per month and 5-year epoch, were obtained from the NHS digital website.[45]

Intervention usage

Practices were provided with an EMIS® search, which looked at the number of times the intervention template was opened. This was collected for each of the 12 months the intervention practices were in the study. Qualitative interviews with clinicians (GPs and practice nurses) and other practice staff (managers, pharmacists) and CCG staff (medicines managers) explored the use of the intervention, how it was embedded into practice and whether it was used appropriately.

Follow-up questionnaire

Like the baseline questionnaire, practices were asked to complete a follow-up questionnaire 12 months later. This included additional data on items such as the number of locums used during the 12 months of follow-up as well as questions around COVID-19 and how it had affected their triaging. Intervention practices were also asked what they thought of the intervention and if they would want to use it again.

Safety data (serious adverse events)

Intervention and control practices were asked to report SAEs immediately on the practice becoming aware of the event. The CHICO team sent a reminder e-mail, quarterly during follow-up, to remind practices to report SAEs. An additional reminder was sent 3 months after the practice had completed their time in the study. As the trial was collecting data on A&E attendances and hospitalisations routinely, only the following events required reporting.

Intervention and control practices

Fatal SAEs: During the trial the practice should report any deaths that are related to a RTI or its complications that occur in patients under 10 years of age to the CHICO research team. This is only applicable to patients who had attended a consultation at the practice in the 90 days prior to the date of death for a RTI-related medical complaint.

Intervention practices only

Related SAEs: During the trial any medical event that meets the standard definition of an SAE (e.g. is life-threatening), and the attending clinician at the practice suspects may be related to the use of the CHICO intervention should be reported to the CHICO research team. An event may be related if it is possibly, probably or definitely due to an adverse impact on the care of the child following using the information provided in the CHICO intervention.

Fidelity data

The fidelity measures focused on intervention exposure and the quality of the intervention delivered (using the process interviews as part of the qualitative investigation).

Sample size

Both sample size calculations assumed 90% power and a conservative two-sided alpha of 0.025 to take account of the two co-primary outcomes. Both sample sizes also assumed an intracluster correlation coefficient of 0.03 (as suggested in discussion with Professor Sandra Eldridge, an expert in cluster randomised trials and complex designs), an estimated coefficient of variation of 0.65 (to take account of differences in cluster size) and an assumption of 750 children aged 0–9 years registered per practice (based on Bristol and Bath CCG data from 2016). Expected differences assumed: (1) a reduction in dispensing rate from 33 prescriptions per 100 registered children aged 0–9 years to 29 (or fewer) prescriptions (i.e. ≥ 10% overall reduction); and (2) a hospitalisation rate that was no more than 2% in the intervention arm, compared with the control arm which is estimated to be 1%. This was based on a non-inferiority margin of 1%; however, the investigators wanted to err on the side of caution and used a two-sided alpha for the sample size calculation. This gave an overall sample size requirement of 310 practices; 155 intervention and 155 control practices. Although not pre-specified, estimates of the intraclass correlation coefficient (ICC) were carried out for the primary outcomes. Mixed-effects linear regression models were used, instead of Poisson models, to allow for the calculation of an ICC using the 'estat icc' command in Stata. Only control practices were used to estimate the ICC and CCGs with less than five practices were not included in the calculation as these were unlikely to provide a true estimate of within-cluster variability.

Random allocation

General practitioner practices were randomised on a 1 : 1 basis by the independent Bristol Randomised Trials Collaboration (BRTC) unit using a web-based system, to ensure allocation concealment. All children registered at a GP practice randomised to the intervention arm followed current standard management along with the additional intervention tool. All children registered at a GP practice randomised to the control arm received current standard management. Randomisation was at the practice level. It was stratified by CCG and then further minimised for by practice list size of children (HIGH/LOW) and the baseline dispensing rates of amoxicillin and macrolides antibiotics given to 0–9-year-olds over the previous 12 months (HIGH/LOW), relative to other practices within the CCG. The trial manager was responsible for inputting these variables into the randomisation system.

Blinding

Due to the nature of the intervention delivery, it was not possible to blind the practices to their allocation of either control or intervention group. Administrative staff had access to individual data items, for entry into the database. The trial statistician and trial manager had access to data, by arm, to be able to monitor hospitalisations and report to the Data Monitoring Committee (DMC). No other member of the research team had access to these data until the findings were revealed.

Statistical methods

A full CHICO statistical analysis plan was developed and agreed by the Trial Steering Committee (TSC) and DMC.[46] All primary and secondary analyses were conducted on an intention-to-treat (ITT) basis. A full CHICO statistical analysis plan was developed and agreed by the TSC and DMC chairs 4 months prior to the end of follow-up and 7 months prior to the final analysis commencement. The analysis plan also included details on the proposed health economic and qualitative outcomes.

Summary of baseline data and flow of participants

A Consolidated Standards of Reporting Trials (CONSORT) diagram was used to present the reasons why CCGs and practices were not recruited (due to ineligibility or declining). It was also used to present the number of withdrawals and the number used in the analysis, by arm.

Descriptive statistics were used to summarise characteristics of practices and compare them between groups in a baseline table. Categorical variables were summarised using frequencies and proportions while continuous variables were summarised using medians and interquartile ranges (IQRs; given their skewed nature). Had any differences, between the groups, been in excess of 0.5 standard deviations

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(SDs)/IQRs or 10% or more they would have been controlled for in sensitivity analyses. However, this was not the case.

Primary outcome analysis

The co-primary outcomes were the rate of amoxicillin and macrolide items (antibiotics) dispensed, for all indications, and the rate of hospitalisations for RTI. The denominator for each of these outcomes was the mean number of children aged 0–9 years registered at the practice over the 12-month follow-up period. In the analysis plan, the team pre-specified that the median list size would be used; however, given the number of practices that merged it seemed more accurate to calculate the mean. All analyses were carried out in Stata 17.0 and the results were described in terms of 'strength of evidence' rather than significance. No formal methods of imputation were carried out as the primary outcome was obtainable for over 99% of practices.

Mixed models were used to account for the within and between CCG level variation, incorporating the latter as a random effect. A random-effects Poisson regression model was used to analyse both of these co-primary outcomes. This has the advantage of incorporating person/years follow-up (number of children at a practice) and examining clustering by practice. The dispensing record of the practices in the 12 months prior to randomisation was used as a minimisation variable and thus balance the dispensing records at baseline. This was adjusted for, in the primary analysis of dispensing rates, to resolve any residual difference. While the dispensing outcome will be testing for superiority, the hospitalisation outcome will be testing for non-inferiority where a difference of no more than 1% higher in the intervention arm is reasonable to suggest non-inferiority. Therefore, emphasis was placed on the CI when assessing this outcome.

Secondary outcome analysis

The rate of A&E attendances for RTI was calculated in the same way as the rate of hospitalisations, although it was a test for superiority rather than non-inferiority.

Intervention usage was explored across the seasons and across the 12 months of follow-up. Its impact on dispensing was explored and the correlation was presented using scatter plots and Pearson's correlation coefficient.

Sensitivity analyses

Dispensing outcome

1. A per-protocol analysis was utilised to exclude non-compliers in the intervention arm. The level of compliance was calculated as the number of times the intervention was used over a 12-month period divided by the list size of 0–9-year-olds at the practice. Practices were considered compliers if this figure was greater than or equal to 0.05. Practices who did not provide intervention usage data were also excluded from this analysis along with any practices that had merged with another CHICO practice during the follow-up period of the trial.
2. When calculating the level of compliance, it became clear that COVID-19 had been the cause of the majority of 'non-compliers'. Therefore, a post hoc sensitivity analysis was included that looked at the complier average causal effect (CACE). This analysis utilised data from those who did not comply with the intervention and attempted to find a comparable group in the control arm. This was carried out using the instrumental variable analysis approach, using the 'ivpoisson gmm' command in Stata.
3. When the influences of COVID-19 were known, after analysis, a post hoc analysis was included to account for COVID-19. In this analysis, follow-up months prior to March 2020 were included and follow-up months on, or after, March 2020 were excluded. The exposure time variable (list size) was scaled up/down to account for the number of months included; for example, for a practice that began follow-up in January 2020 and completed it in December 2020, the first 2 months of data were utilised as: the number of items dispensed during January and February, across the exposure: list size*(2/12).

4. Small elements to the CHICO intervention were adapted during the pilot phase of the study, such as the generation of a frequently asked questions (FAQ) document; therefore, the dispensing primary outcome was repeated, without the pilot data.
5. At the time of writing the analysis plan, the COVID-19 pandemic had been present in the UK for over a year. The team added a sensitivity analysis that would add a COVID-19 time variable, ranging from 1 to 12, to account for the months of follow-up affected by COVID-19 (on or after March 2020); for example, for practices commencing follow-up between January 2020 and December 2020 the COVID-19 variable would be 10. This variable was added as a covariate in a sensitivity analysis.
6. The amoxicillin and macrolide item data are separated by 5-year epochs and the CHICO trial was primarily interested in the 0–4 and 5–9 year age groups. However, the team also collected data on dispensed items with a 'missing' age group. Therefore, in a sensitivity analysis, these additional items were included in the 0–9 age group.
7. A post hoc analysis was included to look at amoxicillin prescribing rates only (excluding macrolides).
8. The primary analysis was repeated for 0–4-year-olds only, utilising the 0–4 age epoch data on dispensing and the list size of 0–4-year-olds at the practice.
9. The primary analysis was repeated for 5–9-year-olds only, utilising the 5–9 age epoch data on dispensing and the list size of 5–9-year-olds at the practice.
10. After follow-up had ended, but before final analysis commenced, a post hoc analysis was added to replace the random effects for CCG with a random effect for Primary Care Network (PCN). PCNs are groups of practices working together to focus on local patient care so, in a similar way to a CCG, this sensitivity analysis accounted for the within and between variation across PCNs. PCNs are often made up of practices across different CCGs and do not lie within CCGs; therefore, the analysis was unable to account for both at the same time.
11. During analysis, an additional post hoc sensitivity analysis was included to adjust for the potential confounding effects of a delay between the baseline 12-month collection period and the 12-month follow-up period.

Hospitalisation/accident and emergency outcome

1. For hospitalisation and A&E data, diagnosis codes are sometimes missing. Therefore, data were collected on the number of 'diagnosis missing' hospital/A&Es as well as the total number of hospital/A&Es. Using the proportion of lower respiratory tract infection (LRTI) attendances out of those with a diagnosis we could then deduce the proportion of 'diagnosis missing' attendances that were likely to be attributable to RTI and include these in a sensitivity analysis.
2. The previous sensitivity analysis was repeated and included all 'diagnosis missing' attendances, rather than just a proportion.
3. As with the dispensing outcome, the team added a sensitivity analysis that would add a COVID-19 time variable, ranging from 1 to 12, to account for the months of follow-up affected by COVID-19 (on or after March 2020); for example, for practices commencing follow up between January 2020 and December 2020 the COVID-19 variable would be 10. This variable was added as a covariate in a sensitivity analysis.
4. Complete data were provided for 46 out of 47 CCGs who provided practices for the study. As monthly data were suppressed to avoid identification of patients (where $n < 5$), CCGs were asked to also provide annual data to avoid inaccurate summations of $n < 5$. Unfortunately, West Hampshire CCG did not provide these data. Therefore, their annual data may be a misrepresentation of the true figure and their data were removed in a sensitivity analysis.

Subgroup analyses

Subgroup analyses were carried out for dispensing rates (P1). Formal tests of interaction between the potential effect modifiers and treatment pathway were carried out to test whether the treatment effect differed between the different subgroups. These effect modifiers are listed in *Subgroup analyses (potential effect modifiers for P1)*. These variables were dichotomised to aid presentation and interpretation, taking

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the median value where the variable was continuous. Models with and without an interaction term were compared using a likelihood ratio test and this *p*-value was presented.

Internal pilot study

An internal pilot phase lasting 3 months and using 4 CCGs to recruit 60 practices was planned and conducted to help establish the best methods for recruiting and communicating with practices before widening to the remaining CCGs.

Stop/go assessment

There were four stop/go criteria (see *Table 2*).

Our progression criteria at the pilot stage were based on:

1. the percentage of practices recruited against the initial practice target of 60;
2. the percentage of GP practices with a named practice champion;
3. the percentage of intervention GPs/nurses using the intervention at least once;
4. the percentage of antibiotic dispensing data we can obtain for each practice.

Internal pilot areas of assessment

In addition to stop/go criteria, the internal pilot was used to assess areas where we could improve recruitment, communication with practice champions and use of the intervention. This included:

1. the number of eligible practices within the 20 CCGs already approached and whether at this stage we needed to approach further CCGs to increase the number of practices in the study;
2. the recruitment rate of eligible practices within the four CCGs in the pilot phase, again as an indicator of whether we need to approach further CCGs;
3. the recruitment of practice champions, a focus on their role and how we maximise strategies to encourage use of the intervention;

TABLE 2 Stop/go criteria for the internal pilot

Criteria (all must be met, failure of one or more triggers action)	Proposed action
≥ 80% or 48+ practices recruited	Continue as planned
≥ 80% or 48+ practices naming a champion	
≥ 80% of GPs/nurses using the intervention	
≥ 90% or 54+ practices we can obtain antibiotic dispensing data	
70–79% or 42–47 practices recruited	TSC and HTA discuss problems with the TMG and implement remedies
70–79% or 42–47 practices naming a champion	
70–79% of GPs/nurses using the intervention	
80–89% or 48–53 practices we can obtain antibiotic dispensing data	
< 70% or < 42 practices recruiting	Discuss plans with TSC and NIHR HTA. Consider further pilot or stopping trial
< 70% or < 42 practices naming a champion	
< 70% of GPs/nurses using the intervention	
< 80% or < 48 practices we can obtain antibiotic dispensing data	

HTA, Health Technology Assessment.

4. the efficiency of embedding the intervention in practice systems and resolution of any barriers or delays;
5. the number of times the intervention is used between practices and over time;
6. the timeliness of the primary outcome data and consistency of format between CCGs;
7. the timeliness of the secondary outcome data and consistency of format between CCGs.

Trial oversight

The University of Bristol was the sponsor for this trial and was responsible for overall oversight of the trial. The TSC provided independent supervision of the trial and monitored trial progress. The TSC had an independent Chair, GP and clinical academic Hazel Everitt (Associate Professor at the University of Southampton) and four other independent members. These are an independent statistician (Dr Beth Stuart from the University of Southampton), a second clinician (Professor Gail Hayward from the University of Oxford) and two patient and public involvement (PPI) representatives. Meetings were held at least annually. The DMC monitored patient safety and trial data efficacy and consisted of an independent chair (Jill Mollison from the University of Oxford), two other independent members (Oliver van Hecke and Sena Jawad) and the trial statistician. The three independent members were nominated in 2018 prior to any data collection activity according to NIHR research governance guidance. The DMC received and reviewed reports on the data accruing to this trial and made recommendations on the conduct of the trial to the TSC. In the final months of follow-up, the chair stepped down from their position and another independent member (Oliver van Hecke) took up the position. Given that the CHICO trial was nearing completion, a new independent member was not sought, this approach was agreed by the funder.

All SAEs were recorded and notified as appropriate to the relevant authorities.

Safety

The trial is a low-risk study (risks to participants are no higher than that of standard medical care); thus, SAEs were only reported if fatal or serious AND potentially related to trial participation.

As one of the outcomes for the trial is hospitalisation, it was expected some participants would be admitted to hospital (e.g. due to a deterioration of their underlying illness). Hospitalisation due to RTI is an expected SAE and would **not** be subject to expedited reporting.

For SAE reporting, safety forms were completed for each event by the practice healthcare practitioner and subsequently reviewed by the study clinicians. All SAEs were reported by arm to the DMC prior to scheduled meetings. If there were any safety concerns, the DMC would report to the study Chief Investigator and TSC for further action.

Monitoring for SAEs took place for the duration of the 12-month data collection phase and a further 90 days after this period to allow for the collection of information about any fatalities up to 90 days after consultation.

All practices were regularly prompted by the CHICO study team during their participation in the trial to remind them to report any SAEs and to confirm if zero SAEs arose during the reporting period.

Hospitalisation and A&E attendance data were reported each month for participating practices by their local CCG organisation.

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Patient and public involvement

Patient and public involvement was represented by a Parent Advisory Group (PAG). The CHICO intervention was developed in collaboration with the PAG during the final year of the CHICO feasibility trial (Workstream 4 of the Applied Health TARGET programme).

We met with the parent group several times during the development of the intervention and design of the study. They felt that it was important to conduct a national study and to use a whole practice intervention. They also thought it would be acceptable to conduct the future study without consenting individual patients, as this took time within GP consultations, and that using a prediction tool on the computer during consultation would be fine and would provide reassurance. They strongly endorsed and encouraged us to use the well-designed parent leaflet as it provided very useful information.

Patient and public involvement was maintained throughout the trial through a group of three parents, two of whom (in rotation) attended and contributed to all the TSC meetings including the final results reveal meeting.

Clinical and Practitioner Advisory Group

As the intervention focus was on GP practices and not on recruiting individual patients, we made extensive contact with the Clinical and Practitioner Advisory Group (CPAG) during the trial period, which was important for the study. The CPAG was made up of clinical staff from seven Bristol practices, including GPs, nurse practitioners with paediatric expertise, practice pharmacists and a practice paramedic. We held several meetings with the group in May 2018 and subsequently communicated by e-mail. Advice was sought on the use of hard or soft pop-ups and trigger codes in a consultation, format of the template and the personalised letter. We discussed potential barriers and how to overcome them and any staff training needs to use CHICO. We also ran some ‘think aloud’ sessions with several GPs to see the intervention in action in EMIS® and gather their thoughts about any problems or changes needed. Input on the draft design of follow-up questionnaires was also requested from the CPAG, including how easy it would be for practices to answer the questions.

Chapter 3 Clinical results

Internal pilot review

A TSC took place on 25 February 2019 to assess the stop/go criteria for the RCT pilot, based on the practices recruited between October and December 2018 (see *Table 3*).

In addition to the stop/go criteria above, other assessment areas listed in *Internal Pilot areas of assessment* were used to improve recruitment and resolve any barriers implementing the intervention. Criteria (1) suggested more than 4 CCGs would be required to recruit at least 48 practices; thus, a further 3 CCGs were recruited to the pilot.

The TSC was supportive of the progress that had been made at that time and the achievement of the stop/go criteria. The CHICO trial continued to recruit practices from the pilot CCGs and went on to recruit additional CCGs and practices after the pilot ended.

Recruitment

The CHICO trial recruited CCGs, and randomised practices within them, between October 2018 and October 2020. There was a 3-month pause in recruitment between March 2020 and June 2020, at the onset of the COVID-19 pandemic, while the study team, TSC and funders re-assessed the feasibility and safety of the intervention during the pandemic. By mid-June 2020, there seemed to be an appetite for restarting recruitment again with perceived capacity in practices and new expressions of interest from some regions such as the South-West. A budgeting exercise suggested an un-costed 4-month extension could support the study to reach the target recruitment figure by the end of September 2020. Recruitment restarted again on 16th June, following a non-substantial amendment (following the COVID-related halt) being approved by the sponsor. In total, 52 CCGs agreed to take part in the study but only 47 of the CCGs (see *Figure 3*) provided the 294 practices (see *Figure 4*). Practices were randomised between October 2018 and October 2020, with the 12-month follow-up period continuing until September 2021.

Trial flow

In total, 125 CCGs were assessed for eligibility (see *Figure 5*). For the CHICO intervention to work, practices had to be using EMIS®.

TABLE 3 Internal pilot stop/go criteria review

Criteria (all must be met, failure of one or more triggers action)	Met	Detail
1. ≥ 80% or 48+ practices recruited from 7 CCGs	☑	By 31 December, 48 practices had been randomised.
2. ≥ 80% or 48+ practices naming a champion	☑	All 48 practices recruited had a named champion.
3. ≥ 80% of GPs/nurses using the intervention[a]	☑	The team received responses from 18/23 intervention practices. Of these, 16 met the criteria.
4. ≥ 90% or 54+ practices we can obtain antibiotic dispensing data	☑	100% of baseline dispensing data were available when the criteria were assessed.

[a] Defined as 'at least 50% of all clinical staff at the practice using the intervention at least once during the first month post-installation'.

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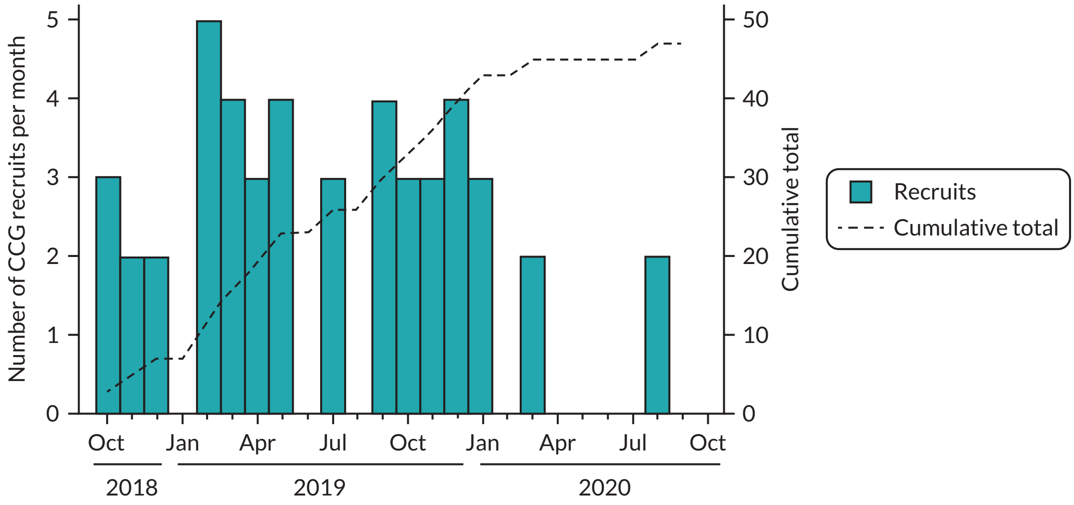

FIGURE 3 Children with cough recruitment of CCGs.

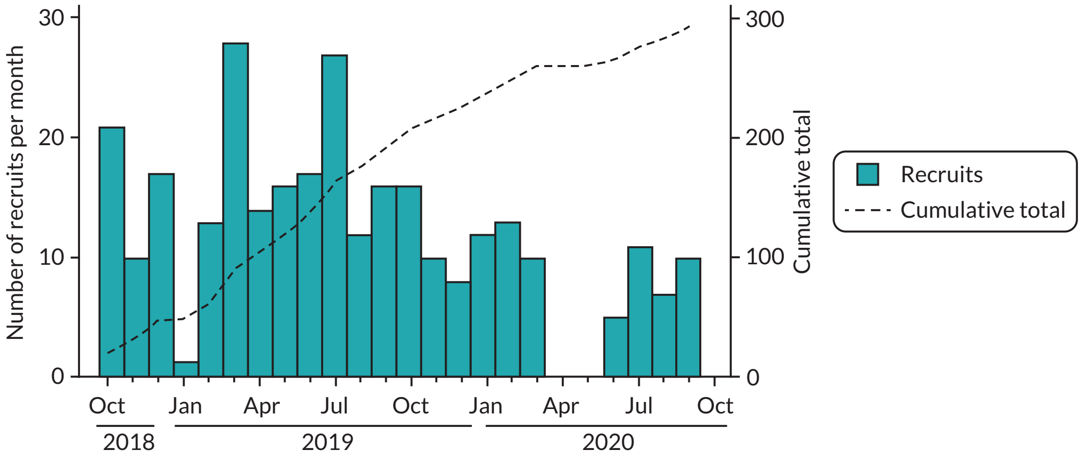

FIGURE 4 Children with cough recruitment of practices.

The majority of CCGs found to be ineligible (*n* = 14) did not have enough practices using EMIS®. Of the 110 eligible CCGs that were then approached, 52 (47%) consented to take part. Practices from within those CCGs were then approached and asked for expressions of interest. An additional 33 practices expressed interest but were not recruited, as their CCG had not consented to take part. The majority of practices were excluded due to having no capacity to take part (*n* = 57) or because they stopped responding to communications (*n* = 42). By the end of recruitment, the CHICO study had randomised 294 practices, 144 to the intervention arm and 150 to the control arm.

Over the course of the trial, there were 12 practice withdrawals, 8 in the intervention arm of the trial and 4 in the control arm (see *Table 4*). The majority of withdrawals in the intervention arm were listed as 'pandemic related', which included lack of time/resources to take part in the trial but also a lack of children consulting with a cough. Other reasons include issues with installing the intervention, a complete change in staff at the practice and a merger (two practices in the control arm merged together to form one larger practice).

Of the 144 practices randomised to the intervention arm, 100% provided baseline data and routine data on dispensing rates and hospitalisations could be obtained for 100% of practices. Intervention usage data were complete (12 months of data) for 115 (80%) practices and partially complete for 16 (11%) of practices. The other 13 (9%) of practices provided no intervention usage data. The follow-up questionnaire was then completed by 130 (90%). Similar proportions of follow-up data were available for the control arm (89%), with one missing due to the Gloucestershire practice merger.

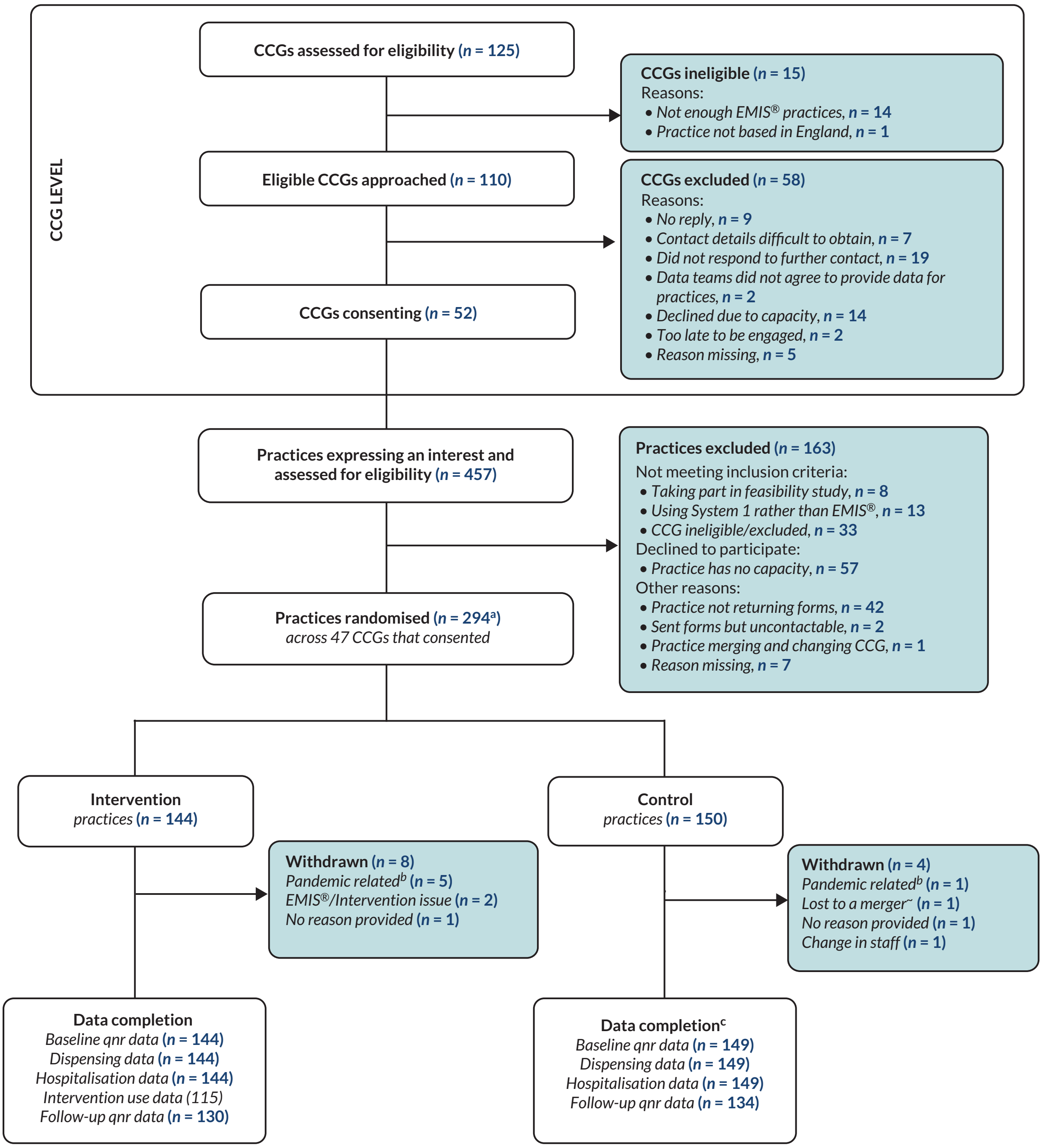
CCG LEVEL
CCGs assessed for eligibility (n = 125)
CCGs ineligible (n = 15)
Reasons:
• Not enough EMIS® practices, n = 14
• Practice not based in England, n = 1
Eligible CCGs approached (n = 110)
CCGs excluded (n = 58)
Reasons:
• No reply, n = 9
• Contact details difficult to obtain, n = 7
• Did not respond to further contact, n = 19
• Data teams did not agree to provide data for practices, n = 2
• Declined due to capacity, n = 14
• Too late to be engaged, n = 2
• Reason missing, n = 5
CCGs consenting (n = 52)
Practices expressing an interest and assessed for eligibility (n = 457)
Practices excluded (n = 163)
Not meeting inclusion criteria:
• Taking part in feasibility study, n = 8
• Using System 1 rather than EMIS®, n = 13
• CCG ineligible/excluded, n = 33
Declined to participate:
• Practice has no capacity, n = 57
Other reasons:
• Practice not returning forms, n = 42
• Sent forms but uncontactable, n = 2
• Practice merging and changing CCG, n = 1
• Reason missing, n = 7
Practices randomised (n = 294[a]) across 47 CCGs that consented
Intervention practices (n = 144)
Control practices (n = 150)
Withdrawn (n = 8)
Pandemic related[b] (n = 5)
EMIS®/Intervention issue (n = 2)
No reason provided (n = 1)
Withdrawn (n = 4)
Pandemic related[b] (n = 1)
Lost to a merger~ (n = 1)
No reason provided (n = 1)
Change in staff (n = 1)
Data completion
Baseline qnr data (n = 144)
Dispensing data (n = 144)
Hospitalisation data (n = 144)
Intervention use data (115)
Follow-up qnr data (n = 130)
Data completion[c]
Baseline qnr data (n = 149)
Dispensing data (n = 149)
Hospitalisation data (n = 149)
Follow-up qnr data (n = 134)

FIGURE 5 The CHICO trial CONSORT flowchart. EMIS®, Egton Medical Information Systems® (electronic health records); qnr, questionnaire; [a] One of the practices randomised is made up of two practices who work closely and were due to merge; [b] Reasons include lack of staff, lack of resources or lack of consultations for CHICO; [c] Two practices within the control arm merged, therefore their outcome data was compiled into one practice.

Randomisation

Randomisation of practices was stratified by CCG and minimised for list size and previous dispensing rate. *Table 5* shows that the stratification across CCGs allowed for a relatively equal share of intervention and control practices across each CCG.

However, some CCGs were only able to recruit one or two practices, which hindered this process. During the 2-year recruitment period, almost half of the CCGs underwent a merger, either with other

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TABLE 4 Withdrawals

	Intervention, *N* (%)	Control, *N* (%)	*p*-value[a]
CCG withdrawals	0 (0)	0 (0)	–
Practice withdrawals	8 (6)	4 (3)	0.211
Pandemic related	5 (3)	1 (1)	0.089
Intervention/EMIS® issues	2 (1)	0 (0)	0.148
No reason provided	1 (1)	1 (1)	0.977
Complete change of staff	0 (0)	1 (1)	0.326
Merged with another practice	0 (0)	1 (1)	0.326
Loss to follow-up[b]	14 (10)	16 (11)	0.789

a Chi-square.
b Refers to those practices that did not complete a follow-up questionnaire.

CCGs in the study or with CCGs outside of the study. Details of these mergers can be found in the footnote of *Table 5*. There were five errors when randomising practices that will have affected the minimisation process, which are summarised in *Table 6*.

TABLE 5 Recruited CHICO practices, per CCG

	Total	Intervention	Control
	N	*n* (%)	*n* (%)
Bristol, North Somerset and South Gloucestershire	39	20 (51)	19 (49)
Birmingham and Solihull	9	5 (56)	4 (44)
Brent[a]	17	7 (41)	10 (59)
Buckinghamshire	2	0 (0)	2 (100)
Cambridge and Peterborough	2	1 (50)	1 (50)
Cannock Chase	1	0 (0)	1 (100)
Canterbury and Coastal[b]	2	1 (50)	1 (50)
Devon	3	1 (33)	2 (67)
Dudley[c]	13	5 (38)	8 (62)
East Berkshire[d]	5	2 (40)	3 (60)
East Lancashire	7	4 (57)	3 (43)
East Staffordshire	4	3 (75)	1 (25)
Eastbourne[e]	1	1 (100)	0 (0)
Gloucestershire	5	3 (60)	2 (40)
Guildford and Waverly[f]	1	0 (0)	1 (100)
Hastings and Rother[e]	5	2 (40)	3 (60)
Herts Valley	7	5 (71)	2 (29)
Kernow	4	2 (50)	2 (50)
Leeds	1	0 (0)	1 (100)

TABLE 5 Recruited CHICO practices, per CCG (*continued*)

	Total	Intervention	Control
	N	***n* (%)**	***n* (%)**
Liverpool	15	7 (47)	8 (53)
Manchester	12	7 (58)	5 (42)
Medway[b]	6	4 (67)	2 (33)
Morecambe Bay	14	6 (43)	8 (57)
Newcastle and Gateshead	1	1 (100)	0 (0)
North East Essex	3	2 (67)	1 (33)
North Hampshire[g]	1	1 (100)	0 (0)
North Staffordshire	2	1 (50)	1 (50)
North West Surrey[f]	4	1 (25)	3 (75)
Nottingham[h]	3	1 (33)	2 (67)
Oxfordshire	15	8 (53)	7 (47)
Salford	1	0 (0)	1 (100)
Sandwell and West Birmingham[c]	2	2 (100)	0 (0)
Shropshire[i]	4	3 (75)	1 (25)
Somerset	27	14 (52)	13 (48)
South East Hampshire[g]	4	2 (50)	2 (50)
South East Staffordshire and Seisdon	2	1 (50)	1 (50)
South Cheshire[j]	3	1 (33)	2 (67)
Southwark[k]	6	3 (50)	3 (50)
Staffordshire and Surrounds	3	2 (67)	1 (33)
Stoke on Trent	1	1 (100)	0 (0)
Sunderland	8	4 (50)	4 (50)
Thanet[b]	1	1 (100)	0 (0)
Vale of York	2	0 (0)	2 (100)
Walsall[c]	9	5 (56)	4 (44)
Wandsworth[l]	2	1 (50)	1 (50)
West Hampshire[g]	9	5 (56)	4 (44)
West Kent[b]	6	4 (67)	2 (33)

a Became part of North West London CCG in April 2021.
b Became part of Kent and Medway CCG in April 2020.
c Became part of Black Country and West Birmingham CCG in April 2021.
d Became part of Frimley CCG in April 2021.
e Became part of East Sussex CCG in April 2020.
f Became part of Surrey Heartlands CCG in April 2020.
g Became part of Hampshire, Southampton and Isle of Wight CCG in April 2021.
h Became part of Nottinghamshire CCG in April 2020.
i Became part of Shropshire CCG in April 2021.
j Became part of Cheshire CCG in April 2020.
k Became part of South East London CCG in April 2020.
l Became part of South West London CCG in April 2020.

Note
Clinical Commissioning Groups are grouped according to their status in October 2018.

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TABLE 6 Randomisation stratification/minimisation errors

Error	Practices affected	Potential issue
Randomised three times (due to false error message).	1	The randomisation system will have counted the same practice three times, therefore this will have affected the minimisation.
Typo when entering the CCG number.	3	The stratification/minimisation process was not successful in these practices as they were entered as a new CCG.
Practice entered as having a 'High' list size, when in fact it had a 'Low' list size.	1	This will have affected the minimisation for this CCG.

Baseline data

Baseline comparisons for the CHICO study are given in *Table 7*. The team pre-specified in the analysis plan[46] that any baseline characteristics that differed by more than 10% (categorical variables), half a SD or half an IQR (continuous variables) would be investigated. None of the baseline characteristics met these criteria so no investigations were carried out. The two arms were well balanced with respect to baseline characteristics, suggesting that stratification by CCG and minimisation had been successful. Of the practices randomised, 62% had a high list size relative to other practices within their CCG suggesting that smaller practices were less likely to be recruited. In a similar way, 42% of the practices randomised had a high baseline dispensing rate, relative to other practices within their CCG suggesting that high prescribers were less likely to be recruited.

The median number of GPs was 6 per arm and this was well recorded (290/294). However, there were varying completion rates for the numbers of each type of staff, at each practice, therefore these figures may not be a true representation of practice staff. The Index of Multiple Deprivation was used to assess whether the CHICO study was recruiting practices from high or low levels of deprivation is based on data available from 2019.[47] In general, there was a larger proportion of practices in quintiles 1 and 2 (higher levels of deprivation) than quintiles 4 and 5 (lower levels of deprivation) reflecting an excess of practices located in urban areas and a similar distribution to the geographical location of all GP practices in England.

The Income Deprivation Affecting Children Index (IDACI)[48] measures the proportion of all children aged 0–15 living in income-deprived families and this was 15% in both arms. There were 43 practices that were randomised on, or after, March 2020. The other 251 were randomised before March 2020. The proportion of RTIs consulted over the phone changed immensely; going from ~25% mostly/always consulting over the phone pre-COVID-19 to ~65% during the pandemic.

Serious adverse events

There were four events that were reported during the CHICO study (see *Table 8*). There was one hospitalisation in the intervention arm. There were three deaths reported, two of which were in the intervention arm; all unrelated to the intervention.

Intervention usage

Complete 12-month intervention usage data were available for 115/144 (80%) practices. Data from these practices allowed us to look at intervention usage over time, both in terms of calendar year (January–December) and follow-up time point (months 1–12). Twelve practices (8%) provided between 6 and 11 months of intervention usage data and four (2%) practices provided < 6 months of data.

TABLE 7 Practice-level baseline characteristics, by arm

	Intervention		**Control**	
	***N*[a]**	***Median (IQR) or n (%)***	***N*[a]**	***Median (IQR) or n (%)***
***Randomisation variables*[b]**				
High list size, relative to others in their CCG (%)	144	92 (64%)	150	91 (61%)
High dispensing rate, relative to others in their CCG (%)	144	60 (42%)	150	66 (44%)
***Baseline practice level*[c]**				
List size[d]*: all ages 0–9*	144	*974.5 (701.3–1422.3)*	150	*997.0 (645.1–1375.3)*
List size[d]*: age 0–4 epoch*	144	*479.8 (338.8–682.0)*	150	*474.2 (307.9–662.3)*
List size[d]*: age 5–9 epoch*	144	*485.2 (348.8–779.5)*	150	*515.0 (334.3–723.0)*
Median dispensing rate (IQR), per 100 list size	144	*19.0 (14.3–24.9)*	150	*17.7 (14.3–23.9)*
CHICO leaflet in use at the practice	142	12 (8%)	142	10 (7%)
Distance to the nearest children's A&E (miles)	142	*4.7 (2.3–9.0)*	145	*4.0 (2.2–11.5)*
IMD quintile based on practice postcode[e]				
Quintile 1 *(most deprived)*	144	37 (26%)	150	40 (27%)
Quintile 2		29 (20%)		31 (21%)
Quintile 3		31 (22%)		29 (19%)
Quintile 4		28 (19%)		26 (17%)
Quintile 5 *(least deprived)*		19 (13%)		24 (16%)
Income deprivation affecting children index score	144	*0.15 (0.08–0.25)*	150	*0.15 (0.08–0.26)*
Practice staff				
Median # of GPs	143	6.0 (4.0–10.0)	147	6.0 (4.0–9.0)
Median # of GPs (1.0FTE)	123	4.1 (2.5–6.0)	125	4.0 (3.0–6.0)
Median # of Salaried Nurses	114	2.0 (1.0–4.0)	124	2.0 (1.0–4.0)
Median # of Salaried Nurses (1.0FTE)	81	1.7 (1.0–2.6)	91	1.5 (0.8–3.0)
Median # of Sessional Nurses	68	0.0 (0.0–1.0)	65	0.0 (0.0–0.0)
Median # of Sessional Nurses (1.0FTE)	44	0.0 (0.0–0.2)	33	0.0 (0.0–0.3)
Median # Pharmacist Prescribers	89	1.0 (0.0–1.0)	101	1.0 (0.0–1.0)
Median # Pharmacist Prescribers (1.0FTE)	58	0.4 (0.0–0.8)	60	0.5 (0.1–1.0)
Median # of Locums	102	4.0 (1.0–6.0)	101	3.0 (2.0–6.0)
Patient management				
Patient management (not mutually exclusive)				
No triage	141	35 (25%)	145	46 (32%)
Nurse face-to-face	141	17 (12%)	145	20 (14%)
GP face-to-face	141	47 (33%)	145	47 (32%)
Receptionist telephone triage	141	44 (31%)	145	48 (33%)
Nurse telephone triage	141	17 (12%)	145	26 (18%)
GP telephone triage	141	74 (52%)	145	81 (56%)
Other[g]	141	16 (11%)	145	20 (14%)

continued

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TABLE 7 Practice-level baseline characteristics, by arm (*continued*)

	Intervention		**Control**	
	***N*[a]**	***Median (IQR) or n (%)***	***N*[a]**	***Median (IQR) or n (%)***
Proportion of RTIs consulted over the phone (*pre-COVID*)				
None	120	21 (18%)	125	25 (20%)
Very few		32 (27%)		33 (26%)
Some cases		35 (29%)		35 (28%)
Most cases		25 (21%)		24 (19%)
Always		7 (6%)		8 (6%)
Of these, how many are completely dealt with on the phone? (*pre-COVID*)				
None	116	24 (21%)	119	31 (26%)
Very few		48 (41%)		45 (38%)
Some cases		35 (30%)		40 (34%)
Most cases		8 (7%)		3 (3%)
Always		1 (1%)		0 (0%)
Proportion of RTIs consulted over the phone (*post-COVID*)				
None	22	1 (5%)	21	1 (5%)
Very few		3 (14%)		1 (5%)
Some cases		4 (18%)		5 (24%)
Most cases		7 (32%)		5 (24%)
Always		7 (32%)		9 (43%)
Of these, how many are completely dealt with on the phone? (*post-COVID*)				
None	22	1 (5%)	21	2 (10%)
Very few		7 (32%)		1 (5%)
Some cases		9 (41%)		15 (71%)
Most cases		5 (23%)		2 (10%)
Always		0 (0%)		1 (5%)

a The number of practices who we have data for (denominator).
b When CCGs accepted participation in the trial, the previous 12 months of list sizes and dispensing figures (in 0–9-year-olds) was used to split the practices into HIGH and LOW categories, relative to other practices within their CCG. This information was used in the minimisation method of randomisation.
c Collected from baseline practice questionnaires unless stated otherwise.
d Collected from NHS digital data.[45]
e Index of Multiple Deprivation.[48]
f The IDACI measures the proportion of all children aged 0–15 living in income-deprived families.
g Other options includes: online (askmyGP®), emergency care practitioner and pharmacist.

The remaining 13 (9%) intervention practices did not provide any intervention usage data. Across the 121 practices that provided at least 1 month of intervention usage data, we recorded a total of 11,944 uses of the intervention. The median usage across the practices with 12 months of data (*n* = 115) was 70 uses (IQR 9–142). Twenty practices (17%) recorded zero usage over the 12-month period. All of these 20 practices started follow-up after May 2019 and 13 (65%) began follow-up from March 2020.

TABLE 8 Serious adverse events

SAE	Arm of the study	SAE description	Outcome
SAE-001	Intervention	Patient admitted to hospital for RTI	Based on information available the event was not considered related to the intervention
SAE-002	Control	Fatality – no details of cause but patient history suggests unrelated to RTI	Not considered related to the intervention
SAE-003	Intervention	Fatality (unrelated to RTI, intervention not used)	Not considered related to the intervention
SAE-004	Intervention	Fatality (unknown whether a RTI consultation took place within 90 days of the fatality)	Not considered related to the intervention

Users of the intervention

Using the EMIS® user mnemonic (a unique username for each healthcare practitioner using system), the CHICO template recorded 1399 individual users of the intervention. The median number of users per practice (*n* = 131) was 9 (IQR 3–16). This figure remained the same when looking at practices providing 12 months of data (*n* = 115); median 9 (IQR 3–17). *Figure 6* shows the job roles of the intervention users. Of the 1399 users identified, the job role type was available for 1341 of them. Of these, 994 (74%) were GPs, 187 (14%) were nurses, 77 (6%) were office staff, 40 (3%) were clinicians, 34 (3%) were locum GPs and 7 (1%) were pharmacists. There was also one consultant and one phlebotomist.

There were four individual users who used the intervention more than 100 times; two GPs, one nurse and one clinician. Overall, the GPs and nurses used the intervention the most, with a median of five uses per GP/nurse over the 12-month period (see *Figure 7*). Office staff (e.g. analysts and medical secretaries) used it the least, averaging one use per member of staff.

Usage of the intervention over the 12 months of participation in the study

Practices with 12 months of intervention usage data available allowed for a detailed inspection of trends over months 1–12 of follow-up. Panel A of *Figure 8* shows usage over the 12-month period for all 115 practices. Due to COVID-19, it is difficult to determine what a typical pattern of intervention usage may look like. *Table 9* provides the median use per month based on the individual practices presented in *Figure 8*. Panel B of *Figure 8* and row 2 of *Table 9* show the data for the 29 practices that completed

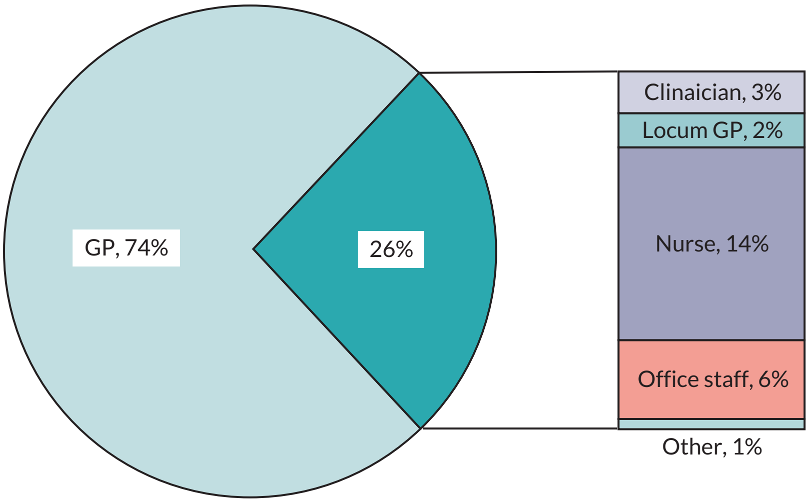

FIGURE 6 Job roles of those using the intervention.

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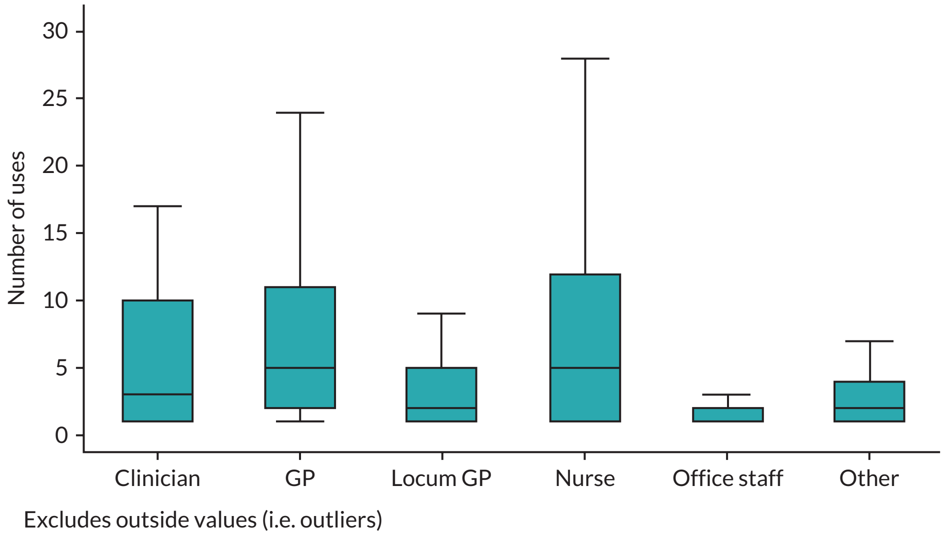

FIGURE 7 Uses of the intervention, per job role.

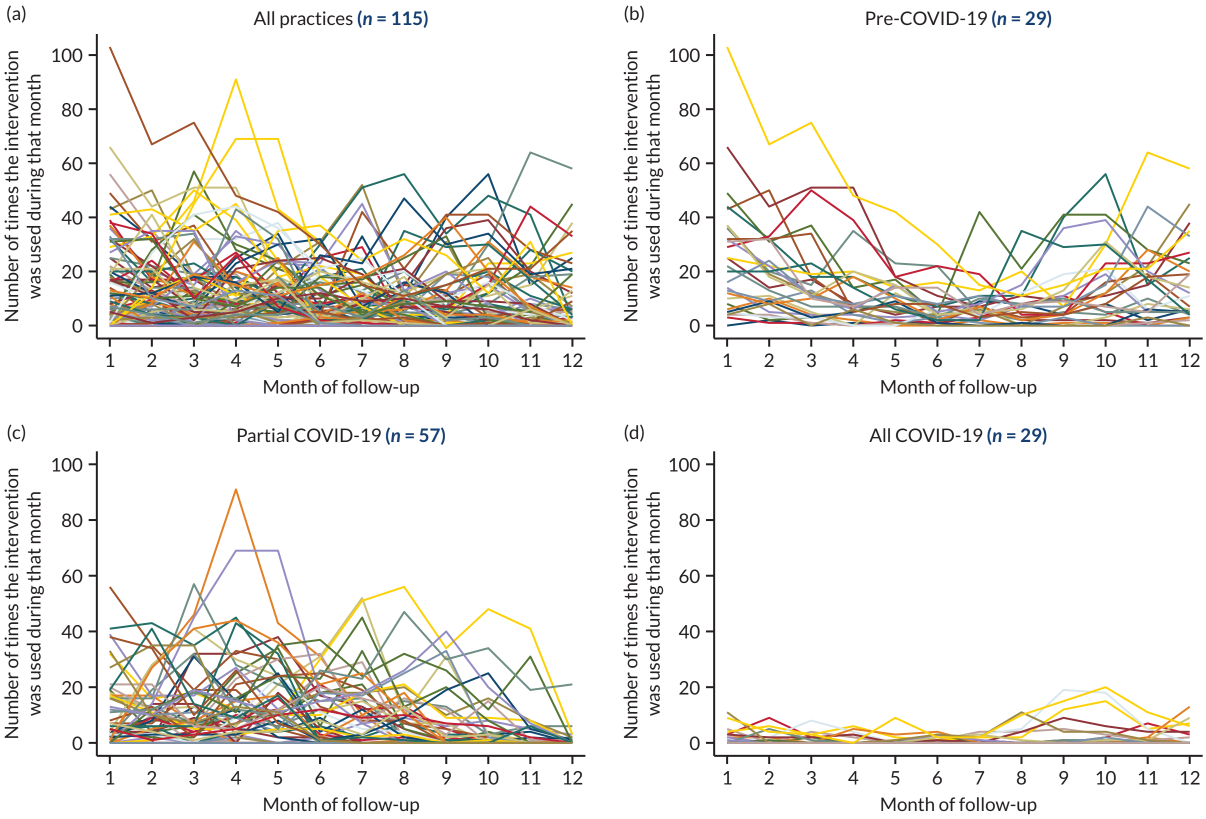

FIGURE 8 Intervention usage, by follow-up month for (a) all practices, (b) pre-COVID-19 (completed before March 2020), (c) partial COVID-19 (≥ 1 month from March 2020), (d) all COVID-19 (complete follow-up from March 2020).

follow-up prior to March 2020 and were, therefore, unaffected by COVID-19 lockdowns. Generally, the majority of use was at the start of follow-up, in months 1 (median = 22) and 2 (median = 18). However, for these 29 practices who completed follow-up prior to the pandemic, month 1 had to be between November 2018 and March 2019. Therefore, the increased usage in months 1 and 2 may coincide with the seasons, rather than indicate an increased usage at the start of follow-up. Panel C shows the practices that had 1–11 months of follow-up data on, or after, March 2020 (*n* = 57). Given the variety of months affected by COVID-19, it is difficult to spot trends or patterns in the intervention usage data.

TABLE 9 Median intervention usage over the 12 months of follow-up

	Month of follow-up											
	M1	**M2**	**M3**	**M4**	**M5**	**M6**	**M7**	**M8**	**M9**	**M10**	**M11**	**M12**
All practices (*n* = 115)	4	6	4	5	5	2	2	2	0	1	1	0
Pre-COVID-19[a] (*n* = 29)	22	18	11	7	8	4	6	6	7	11	10	7
Partial COVID-19[b] (*n* = 57)	4	9	7	9	10	6	5	2	0	0	0	0
All COVID-19[c] (*n* = 29)	0	0	0	0	0	0	0	0	0	0	0	0

a Completed follow-up prior to March 2020.
b Between 1 and 11 months were on, or after, March 2020.
c All follow-up was on, or after, March 2020.

For practices with complete follow-up on or after March 2020 (*n* = 29), the median usage was 0 for all months and panel D of *Figure 8* shows how the maximum usage recorded over that period was 20.

Usage of the intervention across the seasons

If we combine all practices and look at the data across calendar months, we can see the seasonal effects on intervention usage. In *Figure 9*, we can see the seasonal variation between October 2018 and February 2020, with increased usage during the winter months and fewer uses during the summer months. This suggests that usage did correlate with the number of children presenting with RTIs. However, from March 2020 the effects of COVID-19 lockdowns are clear, with very little usage of the intervention. There is a small increase in May, June and July 2021, when restrictions were relaxed and RTIs were more prevalent in the population.

Looking at usage per calendar month, with all years combined, the seasonal variation is clear (see *Figure 10* and *Table 10*). Looking specifically at practices that completed follow-up before COVID-19 (*n* = 29), median usage was highest in November (19), December (14) and January (15). This was also evident in practices with at least 1 month on, or after, March 2020 (*n* = 57). For practices with all

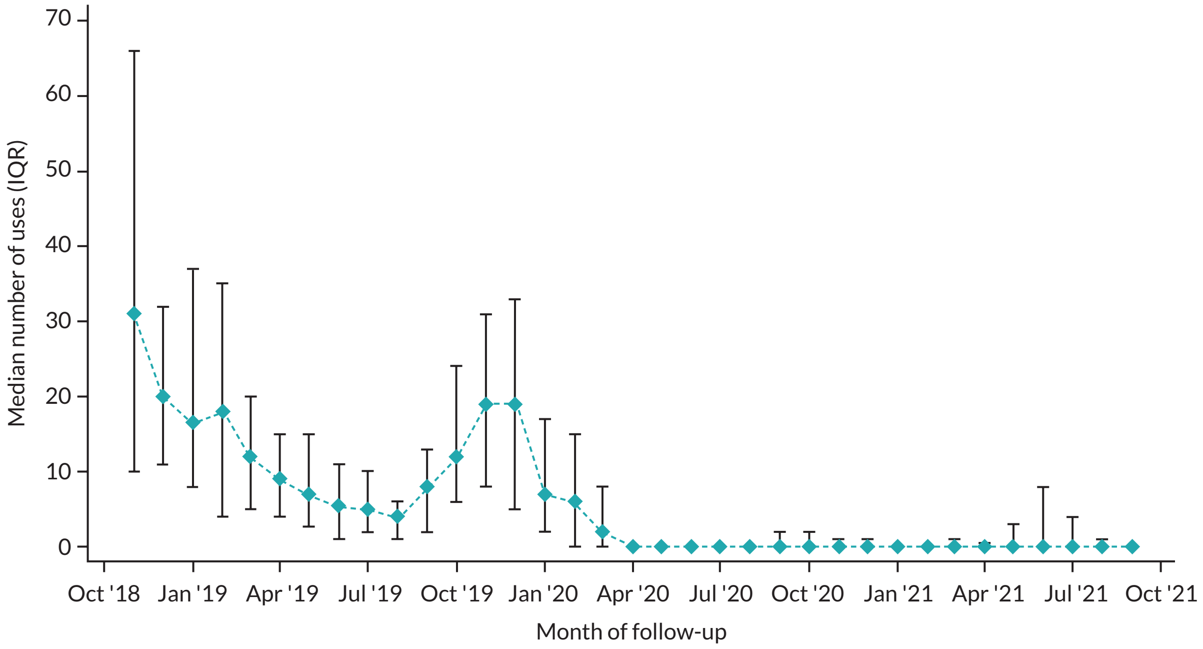

FIGURE 9 Intervention usage over time, with each practice (*n* = 115) contributing 12 months of data.

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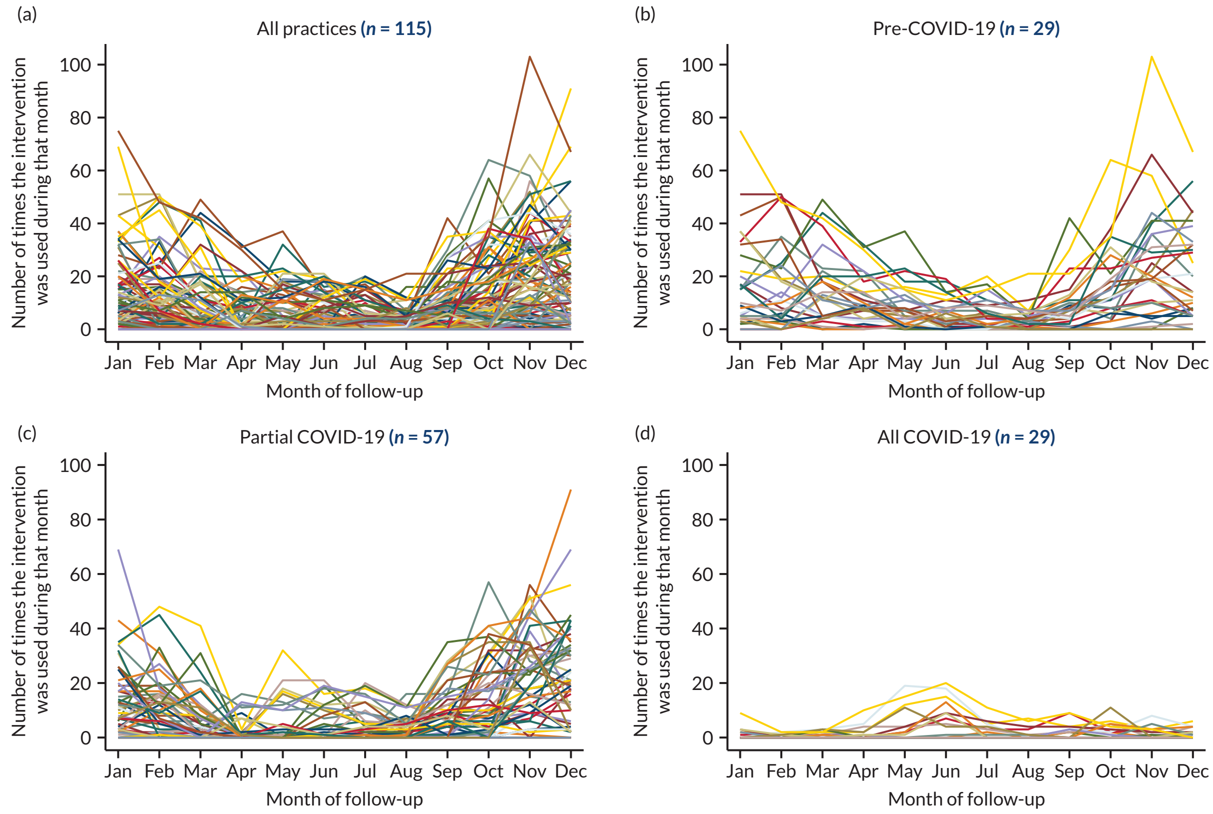

FIGURE 10 Intervention usage, by calendar month for (a) all practices, (b) pre-COVID-19 (completed before March 2020), (c) partial COVID-19 (≥ 1 month from March 2020), (d) all COVID-19 (complete follow-up from March 2020).

TABLE 10 Median intervention usage per calendar month

	Month of follow-up											
	January	**Febuary**	**March**	**April**	**May**	**June**	**July**	**August**	**September**	**October**	**November**	**December**
All practices (*n* = 115)	5	3	2	0	0	0	1	1	4	5	10	10
Pre-COVID-19[a] (*n* = 29)	15	11	12	9	7	4	5	3	7	12	19	14
Partial COVID-19[b] (*n* = 57)	7	6	3	0	0	0	0	1	5	8	18	19
All COVID-19[c] (*n* = 29)	0	0	0	0	0	0	0	0	0	0	0	0

a Completed follow-up prior to March 2020.
b Between 1 and 11 months were on, or after, March 2020.
c All follow-up was on, or after, March 2020.

12 months of follow-up data on, or after March 2020 (*n* = 29), median usage bucked the usual seasonal trends, with summer months providing the highest number of uses.

Compliance with the intervention

The definition of compliance was pre-defined in the statistical analysis plan as the number of uses of the intervention divided by the list size of 0–9-year-olds. *Figure 11* shows the relationship between these

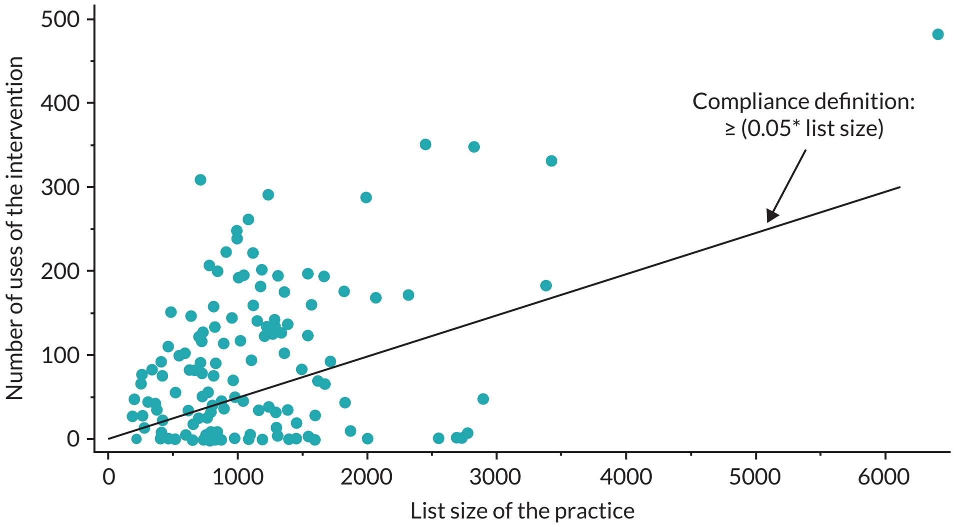

FIGURE 11 Assessing compliance with the intervention.

two variables. For the per-protocol analysis, the CHICO trial team pre-specified that a practice would be compliant if the intervention was used in at least 5% of children (0.05*list size). However, this definition may be impacted by COVID-19. The green line indicates the boundary line for practices considered compliant (dots on or above the line).

We had planned to look at the proportion of prescribing staff that were using the intervention at least once. As described previously (see *Baseline data*), the reporting of the number of staff at each practice was quite poor.

Plotting the number of staff (*x*-axis) versus the number of individual users of the intervention (*y*-axis), it is clear that, in many cases, the number of users exceeds the number of prescribing staff at the practice (see *Figure 12*). Given the underreporting, the 'number of staff' figures were not utilised when looking at compliance with the intervention.

Relationship between compliance and change in dispensing

Figure 13 looks at the relationship between the level of compliance (annual intervention usage/list size) and the change in dispensing (follow-up rate – baseline rate). Panel A shows the relationship for all intervention practices with compliance data (n = 129).

The line of best fit suggested that increased compliance led to increased antibiotic usage; Pearson's correlation coefficient 0.241, p = 0.006. However, as described in *Usage of the intervention across the seasons*, practices that had follow-up during COVID-19 often reported 0 compliance, yet had a decrease in dispensing due to lockdowns. Therefore, panel B is perhaps a better representation of the relationship between intervention usage and change in dispensing rate. In this panel, the focus is on those practices that completed follow-up prior to COVID-19, n = 31. The relationship here is in the opposite direction, with increased intervention usage leading to a decrease in dispensing; Pearson's correlation coefficient −0.326, p = 0.074. After removing the outlier (compliance = 0.42), the correlation observed was weakened to −0.222, p = 0.238.

Dispensing: primary outcome, sensitivity and subgroup analyses

Impact of COVID-19 on dispensing

Figure 14 combines all baseline and follow-up data for all practices, in both arms, and shows the seasonal effects on dispensing. Between October 2017 and February 2020, the dispensing rates reached highs of over 0.35 in the winter and approximately 0.10 in the summer. The effects of COVID-19, and its

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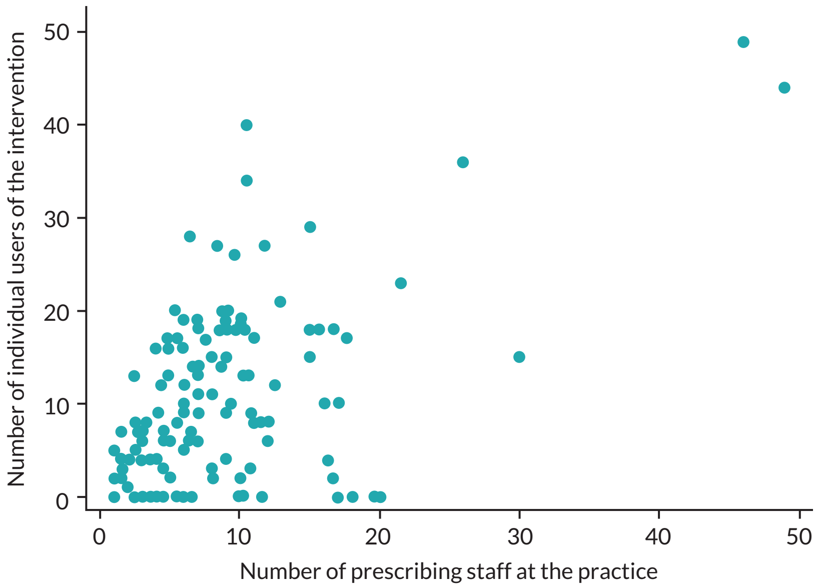

FIGURE 12 Number of individual users compared to the number of prescribing staff.

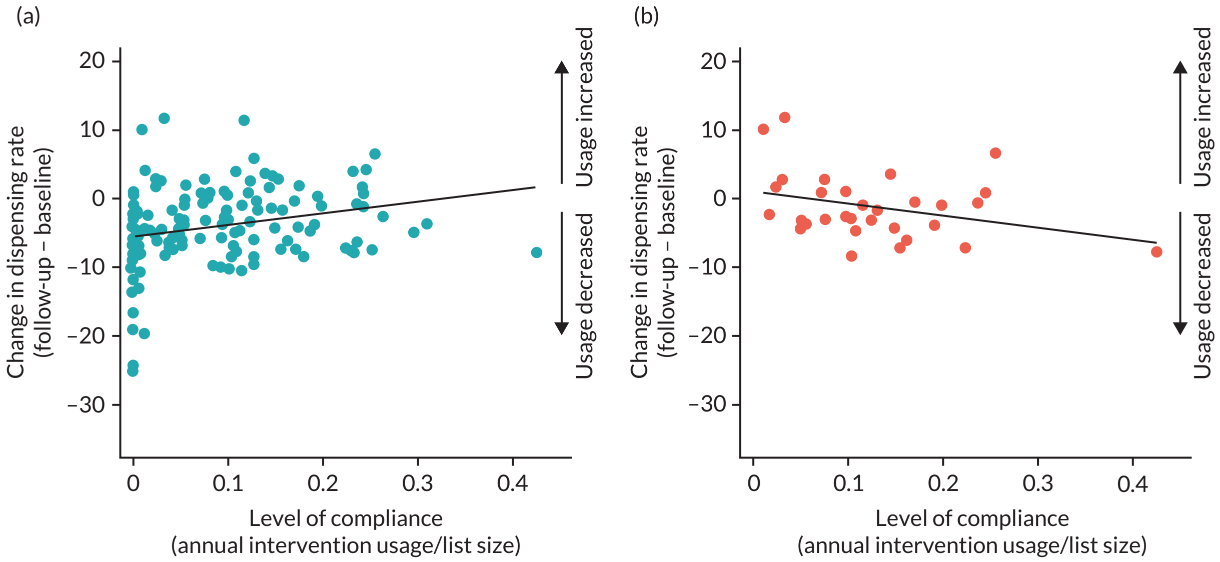

FIGURE 13 Correlation between compliance and change in dispensing in (a) all intervention practices with compliance data and (b) restricted to those with follow-up prior to COVID-19.

associated lockdowns, on dispensing are clear from March–July 2020 when it dropped to 0.05. When restrictions were relaxed in late spring/summer of 2021, there was an unseasonably high dispensing rate. Focusing specifically on the control practices (reflecting usual care) comparing the 12 months (March 2019–February 2020) prior to the pandemic to the first 12 months (March 2020–February 2021) during the pandemic (taking account of seasonal variability), the dispensing rates halved from 20.55 items per 100 children (95% CI 19.64 to 21.46) to 9.84 items per 100 children (95% CI 9.18 to 10.50). A similar reduction was observed in the intervention arm.

In the sample size calculation, for the dispensing rate outcome, the team had hypothesised a 4% absolute rate reduction, from 0.33 to 0.29 (equivalent to 4 prescriptions per 100 patients, per year). Given the low dispensing rates during COVID-19, it would have been difficult to distinguish any differences between the arms of the trial between March 2020 and April 2021.

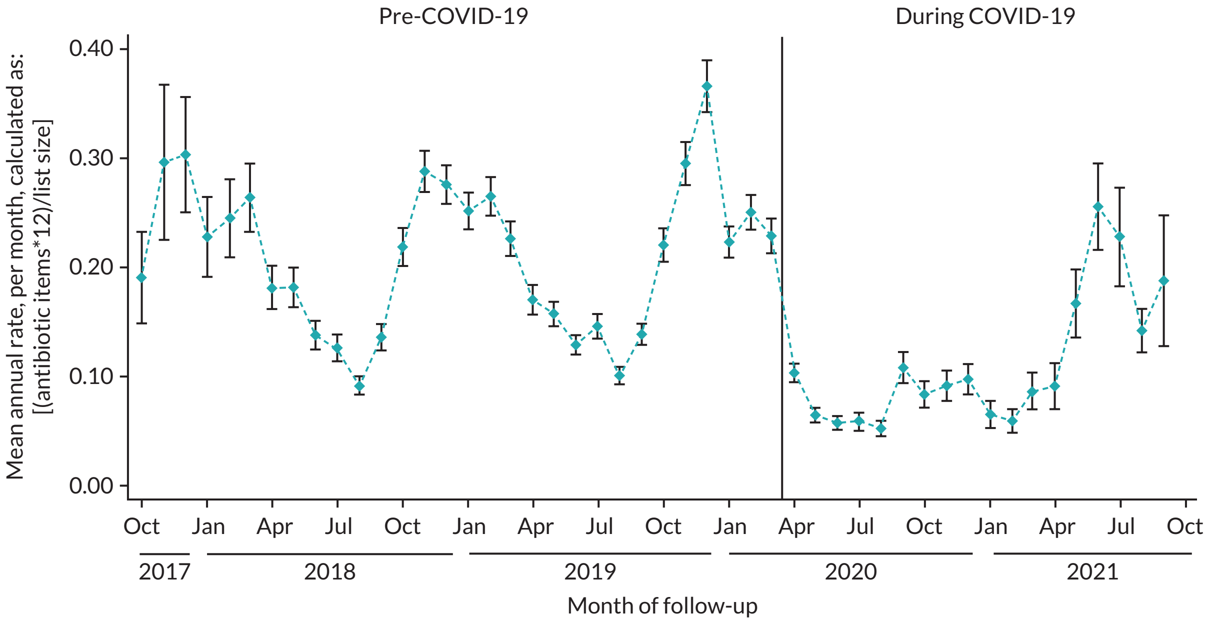

FIGURE 14 Mean dispensing rate (95% CI) during the CHICO baseline and follow-up periods. Each practice contributed 24 months of follow-up data.

Dispensing rate comparison

Figure 15 displays the follow-up data separated by arm. There were fewer practices at either end of the follow-up that could contribute data for these time points; therefore, the CIs are larger at either end. However, even with this uncertainty, there did not appear to be a difference over time between the arms.

There were 144 practices in the intervention arm with data on dispensing and 149 in the control arm (1 lost due to a merger). Using the list size of 0–9-year-olds as the denominator and adding random effects at the CCG level, the incidence rate, of amoxicillin/macrolide dispensing, was 0.155 and 0.154 in the intervention and control arms, respectively (see *Table 11*). After adjustment for the baseline dispensing rate, this gave an incidence rate ratio (IRR) of 1.011 (0.992, 1.029). There was no evidence of a difference between the arms for the dispensing rate outcome.

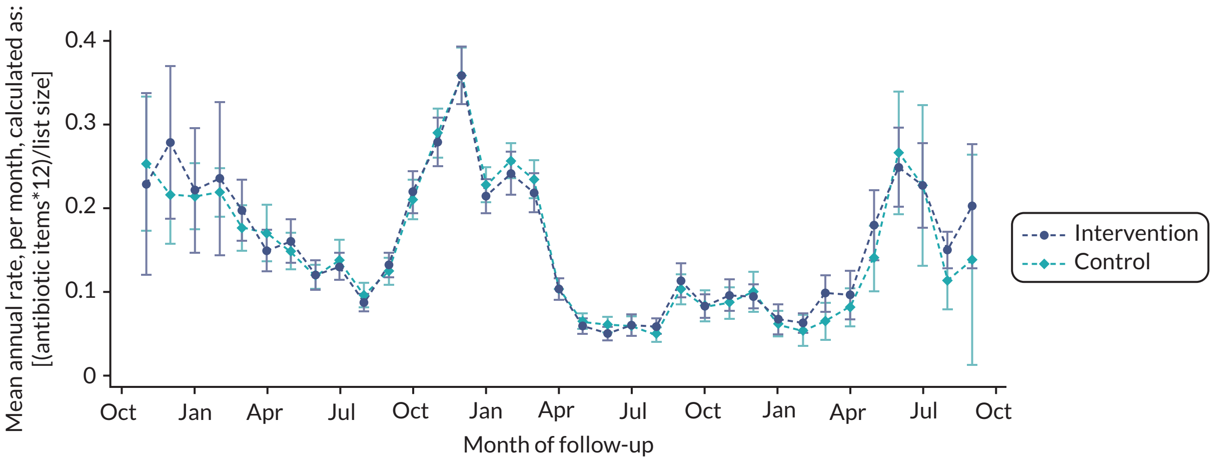

FIGURE 15 Mean dispensing rate (95% CI) during the CHICO follow-up period (October 2018–October 2021), by arm. Each practice contributed 12 months of follow-up data.

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TABLE 11 Dispensing rate comparison

	Intervention rate (95% CI)	Control rate (95% CI)	IRR (95% CI)[a]	*p*-values[a]
Dispensing outcome	0.155 (0.135 to 0.179)	0.154 (0.130 to 0.182)	1.011 (0.992 to 1.029)	0.253

a Random-effects Poisson regression, adjusting for baseline dispensing rate and incorporating the CCG as a random effect.

Sensitivity analyses for the dispensing primary outcome

There were six pre-specified sensitivity analyses for the dispensing rate primary outcome (see *Table 12*) and five post hoc analyses that were added during follow-up data collection or after presenting the results to the team. Firstly, a pre-specified per-protocol analysis was carried out that excluded 'non-compliant' practices from the intervention arm. Practices were considered non-compliant if the number of uses of the intervention divided by the list size of 0–9-year-olds was less than 5% (n = 50). Intervention practices were also excluded where the intervention usage was unknown (n = 15) or where an intervention practice merged with another practice that had previously taken part in the control arm (n = 1). In total, there were 66 exclusions from this analysis leaving 78 intervention practices to compare with the 149 in the control arm.

The per-protocol analysis produced strong evidence against the null hypothesis of equal dispensing in both arms of the study, with a higher rate of dispensing in the intervention arm (restricted to compliers). However, when investigated further, a lot of the practices that were non-compliant had joined in the latter half of the study, when COVID-19 had lowered all dispensing rates *Figure 16*. Therefore, this sensitivity analysis was not considered to be suitable as it falsely inflates the intervention arm dispensing rate as equivalent practices in the control arm were still included.

Therefore, a post hoc CACE analysis was included to allow for compliance to be incorporated but avoid bias caused by only removing practices from one arm of the study. This analysis provided a similar point estimate as the per protocol but with large CIs and therefore no evidence of a difference.

A pre-specified sensitivity analysis had attempted to account for COVID-19 effects, by including a variable in the model which provided the number of years of follow-up that were on, or after, March 2020 (1–12). This analysis produced very similar results as the primary outcome. A post hoc sensitivity analysis was carried out which only utilised follow-up month data prior to COVID-19 and excluded follow-up months after February 2020. The exposure (list size) was then scaled down to the number of months of available data. This provided evidence of a difference, in favour of the intervention [0.192 vs. 0.204, RR = 0.967 (95% CI 0.946 to 0.989). p = 0.003]; assuming 1000 children (0–9-year-olds) per practice this equates to 192 items (intervention) compared to 204 items (controls) per practice or a 5.9% reduction. However, interpretation of this finding is limited given the lack of power and the post hoc nature of this observation.

As previously described in *Internal pilot review*, there were 48 practices that were recruited as part of a CHICO internal pilot. These practices were removed in a sensitivity analysis as the intervention was adapted for the main trial. Excluding these practices provided an IRR of 1.026 (95% CI 1.005 to 1.048), which provided weak evidence to suggest that the intervention may have led to higher dispensing rates.

Another sensitivity analysis incorporated dispensed amoxicillin/macrolide items with 'missing' age. This produced equally higher rates of dispensing in both arms, providing the same conclusion as the primary analysis. We felt that a post hoc analysis may have helped to distinguish whether there was any difference in amoxicillin dispensing only. This analysis did provide a slightly lower dispensing rate in the intervention arm but there was no statistical evidence of a difference.

A difference was seen between the arms when splitting the primary outcome into two separate epochs; 0–4 and 5–9. In the 0–4 group, there was evidence to suggest an increase in dispensing in the

TABLE 12 Sensitivity analysis for the CHICO trial dispensing outcome

	N (I : C)	Intervention rate (95% CI)	Control rate (95% CI)	IRR (95% CI)[a]	*p*-values[a]
Primary analysis	144 : 149	0.155 (0.135 to 0.179)	0.154 (0.130 to 0.182)	1.011 (0.992 to 1.029)	0.258
Per protocol[b]	*78 : 149*	*0.166 (0.141 to 0.196)*	*0.154 (0.130 to 0.182)*	*1.052 (1.029 to 1.076)*	< 0.001
Post hoc 1: CACE analysis[c]	*144 : 149*			*1.056 (0.890 to 1.254)*	*0.530*
COVID-19 month indicator[d]	*144 : 149*			*1.002 (0.984 to 1.021)*	*0.790*
Post hoc 2: Pre-COVID months[e]	*105 : 121*	*0.192 (0.163 to 0.227)*	*0.204 (0.171 to 0.244)*	*0.967 (0.946 to 0.989)*	*0.003*
Excluding pilot practices[f]	*117 : 128*	*0.155 (0.134 to 0.179)*	*0.154 (0.129 to 0.183)*	*1.026 (1.006 to 1.048)*	*0.012*
Including 'age unknown'[g]	*144 : 149*	*0.187 (0.164 to 0.213)*	*0.187 (0.160 to 0.219)*	*1.002 (0.986 to 1.018)*	*0.835*
Post hoc 2: Amoxicillin[h]	*144 : 149*	*0.120 (0.105 to 0.138)*	*0.121 (0.103 to 0.143)*	*0.994 (0.974 to 1.014)*	*0.555*
0–4-year-olds only	*144 : 149*	*0.224 (0.195 to 0.258)*	*0.222 (0.187 to 0.264)*	*1.037 (1.014 to 1.060)*	*0.001*
5–9-year-olds only	*144 : 149*	*0.093 (0.080 to 0.107)*	*0.093 (0.079 to 0.110)*	*0.965 (0.935 to 0.997)*	*0.030*
Post hoc 4: PCN level[i]	*144 : 149*	*0.155 (0.143 to 0.168)*	*0.154 (0.140 to 0.169)*	*0.942 (0.916 to 0.969)*	< 0.001
Post hoc 5: Delay[j]	*144 : 149*			*1.043 (1.023 to 1.063)*	< 0.001

[a] Random-effects Poisson regression, adjusting for baseline dispensing rate and incorporating the CCG as a random effect.
[b] Excluding those in the intervention arm who did not comply with the intervention (number of uses/list size < 0.05) or where their compliance was unknown and excludes a practice that merged with another practice that had taken part in the control arm.
[c] Complier average causal effect analysis.
[d] Including a numerical variable (0–12) to indicate how many months were affected by COVID-19.
[e] Excluding follow-up months affected by COVID-19.
[f] Excluding practices from the internal pilot ($n = 27 : n = 21$).
[g] Adding in all amoxicillin/macrolide items where the age was unknown (worst-case scenario).
[h] Focusing on amoxicillin items only.
[i] Replacing CCG with PCN as the cluster variable.
[j] Some practices asked to delay their start date and a covariate was included to indicate the number of months they delayed.

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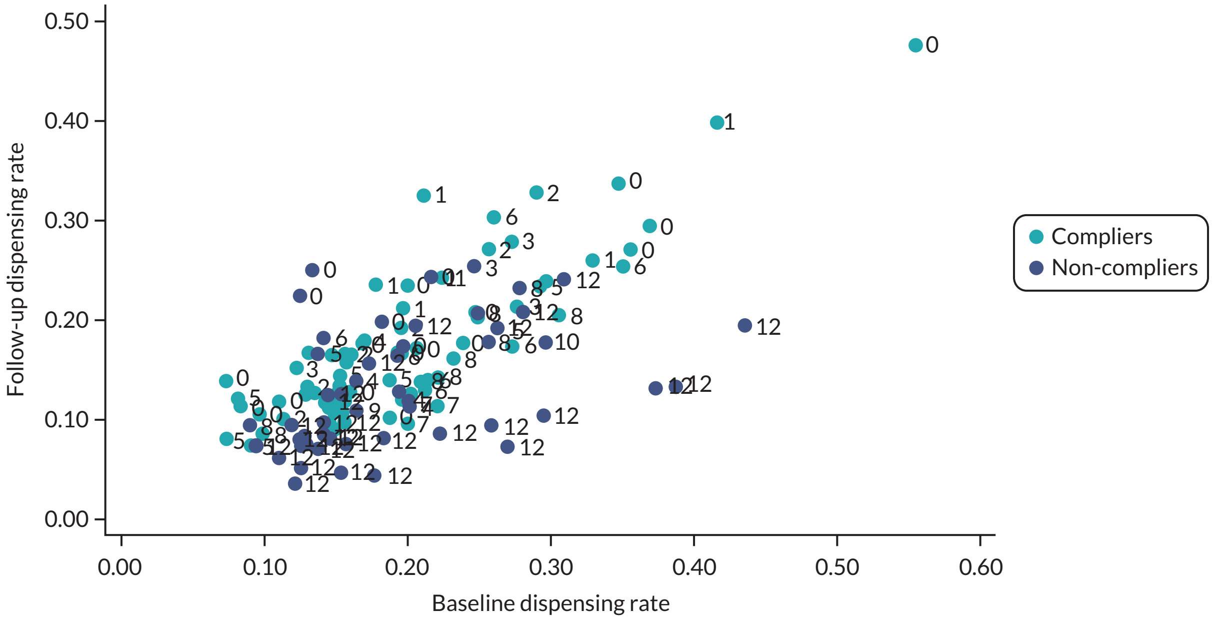

FIGURE 16 Baseline and follow-up dispensing rates across the intervention arm compliers and non-compliers. Marker labels indicate the number of months on or after March 2020 (COVID-19).

intervention arm. Conversely, in the 5–9-year-old group, there was evidence to suggest a decrease in dispensing rate in the intervention arm. This may be because clinical staff, using the intervention, had more confidence when using the intervention in the older age group but this is conjecture.

Another sensitivity analysis replaced the CCG random effects with PCN random effects. The 293 practices were part of 174 unique PCNs, with between 1 and 6 practices in each. Adding PCN as a random effect gave an IRR of 0.942 (95% CI 0.916 to 0.969), providing evidence of lower dispensing in the intervention practices, compared with controls.

The final sensitivity analysis included a covariate to indicate the number of months between baseline and follow-up (implementation period). This was 1 month for 253/293 (86%) of practices, 2 months for 14 (5%) of practices (10 intervention: 4 control) and between 3 and 21 months for the remaining 26 (9%) practices (all intervention). This adjusted analysis provided evidence of a difference, in favour of the control arm.

Subgroup analyses for the dispensing primary outcome

There were six pre-specified subgroup analyses for the dispensing primary outcome,[46] which utilised practice-level data to split the data into two subgroups and look for an interaction between the subgroup and trial arm effects, on dispensing rates (see *Table 13*).

In *Table 13*, when assessing the impact of the proportion of locums at the practice, there was some evidence to suggest that practices with more locums had a treatment effect in favour of the intervention. There was strong evidence of an interaction between trial arm and proportion of nurses. For those practices with a low proportion of nurses (< 17% of staff), there was a 0.15 dispensing rate in the intervention arm and a 0.17 dispensing rate in the control arm. In practices with a higher proportion of nurses (≥ 17%) the opposite was true; 0.16 and 0.14, respectively. This suggests that the intervention was successful at decreasing dispensing rates in practices with a lower proportion of nurses. Equally, it suggested that the intervention increased the dispensing rate in practices with a high proportion of nurses. A similar interaction was found when looking at the number of sites a practice has. In those with more than one site, the intervention had a negative impact on dispensing, suggesting that the intervention training may be difficult to implement across multiple sites.

TABLE 13 Pre-specified subgroup analyses for the dispensing outcome

Variable	*N* (I : C)	Intervention mean (SD)	Control mean (SD)	Subgroup-specific IRR (95% CI)[a]	Interaction IRR (95% CI)[b]	*p*[c]
Proportion of locums						
< 25%	54 : 41	0.15 (0.12, 0.18)	0.15 (0.12, 0.18)	0.94 (0.90 to 0.97)	0.84 (0.74 to 0.95)	0.005
≥ 25%	48 : 58	0.17 (0.14, 0.20)	0.18 (0.15, 0.21)	0.96 (0.93 to 0.99)		
Proportion of nurses						
< 17%	81 : 72	0.15 (0.13, 0.17)	0.17 (0.15, 0.19)	0.92 (0.90 to 0.95)	1.40 (1.21 to 1.62)	< 0.001
≥ 17%	62 : 74	0.16 (0.13, 0.19)	0.14 (0.11, 0.18)	1.05 (1.02 to 1.08)		
Past dispensing rate						
< 18%	68 : 80	0.12 (0.11, 0.13)	0.12 (0.10, 0.13)	1.03 (1.00 to 1.06)	1.00 (1.00 to 1.00)	0.557
≥ 18%	76 : 69	0.19 (0.17, 0.21)	0.21 (0.18, 0.23)	0.99 (0.97 to 1.02)		
Practices site[d]						
1 site	95 : 90	0.15 (0.13, 0.17)	0.16 (0.13, 0.20)	0.93 (0.90 to 0.95)	1.15 (1.10 to 1.20)	< 0.001
≥ 2 sites	34 : 37	0.17 (0.14, 0.20)	0.15 (0.12, 0.18)	1.03 (0.99 to 1.07)		
Follow-up completed before the COVID-19 pandemic						
Yes	31 : 26	0.16 (0.13, 0.20)	0.16 (0.14, 0.18)	0.99 (0.96 to 1.04)	1.02 (0.97 to 1.07)	0.391
No	113 : 123	0.15 (0.13, 0.18)	0.15 (0.13, 0.18)	1.01 (0.99 to 1.03)		
Level of deprivation						
Low (rank ≥ 14387)	72 : 74	0.15 (0.12, 0.18)	0.15 (0.13, 0.18)	0.96 (0.93 to 0.98)	1.00 (1.00 to 1.00)	0.004
High (rank < 14387)	72 : 75	0.16 (0.14, 0.19)	0.15 (0.12, 0.19)	1.06 (1.03 to 1.09)		

a The treatment effect (IRR) in each subgroup.
b The interaction IRR (subgroup*trial arm), treating the subgroup of interest as a continuous variable where possible.
c Taken from a likelihood ratio test comparing models with/without the interaction term included, treating the subgroup of interest as a continuous variable where possible.
d Taken from the practice follow-up questionnaire.

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There was also some evidence to suggest that the intervention was more successful in practices with lower levels of deprivation and had a negative impact on those that had high levels of deprivation.

There was no evidence of an interaction when looking at past dispensing habits or separating practices into those affected/not affected by COVID-19.

Hospitalisations: primary outcome and sensitivity analyses

Impact of COVID-19 on hospitalisations for respiratory tract infection

In a similar way to dispensing rates, there was seasonal variation in hospitalisation for RTI across all CHICO practices (see *Figure 17*). Between October 2017 and March 2020, the hospitalisation rates, for RTI, reached highs of nearly 0.06 in the winter and approximately 0.02 in the summer. The effects of COVID-19, and its associated lockdowns, on hospitalisations are clear from April 2020 onwards when it dropped to < 0.01. When restrictions were relaxed in late spring/summer of 2021, hospitalisations climbed back towards normal levels; apart from July 2021 where they were unseasonably high.

Hospitalisation rate comparison

Hospitalisation rates appeared to be very similar between the arms, over the 3-year follow-up period (see *Figure 18*).

We pre-specified a non-inferiority margin of 0.01 for this outcome. Therefore, when comparing intervention with the control the IRR upper CI needed to be less than 1.01 to conclude non-inferiority. The rate of hospitalisations were 0.019 and 0.021 for the intervention and control arms, respectively (see *Table 14*). The IRR was 0.952 (95% CI 0.905, 1.003). As 1.003 lies below the 1.01 non-inferiority margin the intervention was considered non-inferior to the control.

Three pre-specified sensitivity analyses were carried out to test the robustness of the non-inferiority result. As West Hampshire did not provide accurate annual figures, their data were removed in a post hoc sensitivity analysis. First, a proportion of the hospitalisations with a missing diagnosis were included as RTI diagnoses. This provided very similar results to the primary outcome; IRR 0.950 (95% CI 0.903

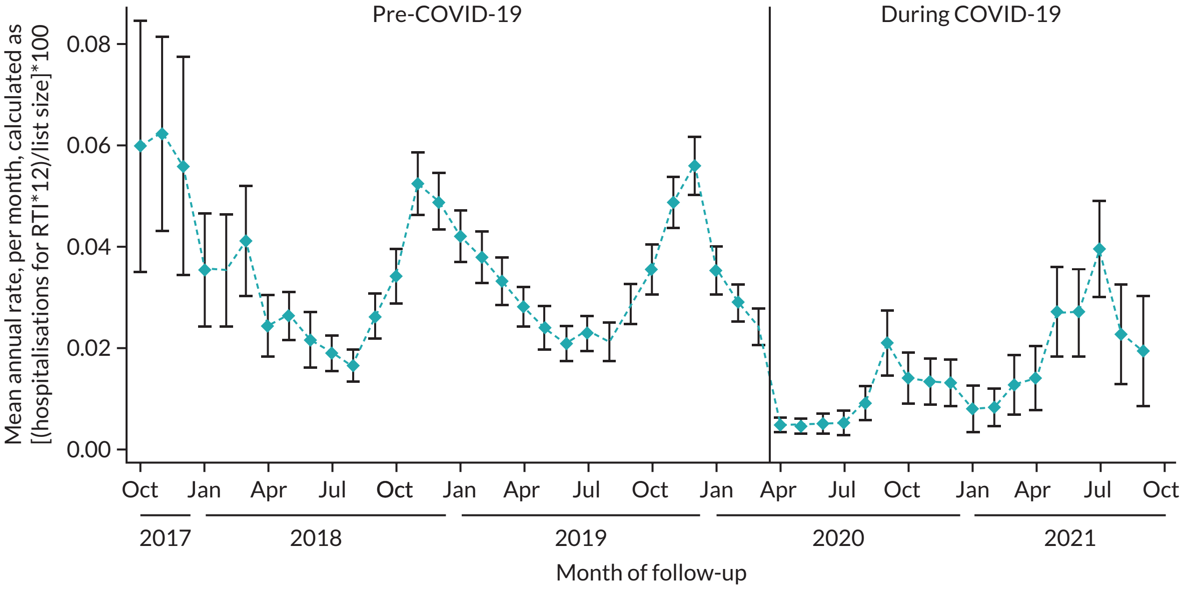

FIGURE 17 Mean hospitalisation rate (95% CI) during the CHICO baseline and follow-up periods. Each practice contributed 24 months of data.

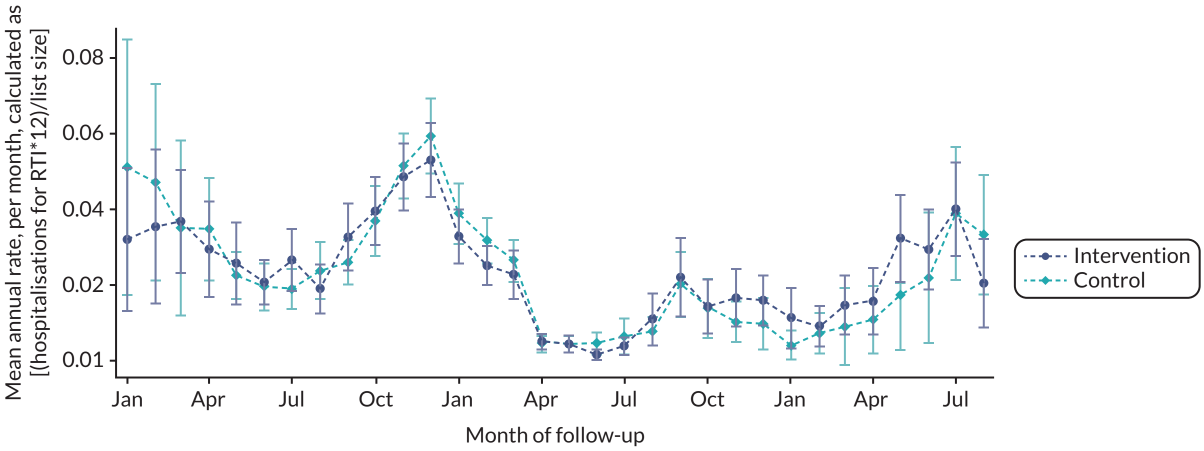

FIGURE 18 Mean hospitalisation rate (95% CI) during the CHICO follow-up period (January 2019–August 2021), by arm. October 2018–December 2018 and September 2021 have been excluded due to low numbers. Each practice contributed up to 12 months of follow-up data.

TABLE 14 Hospitalisation rate comparison

	Intervention rate (95% CI)	Control rate (95% CI)	IRR (95% CI)[a]
Primary analysis	0.019 (0.014 to 0.026)	0.021 (0.014 to 0.029)	0.952 (0.905 to 1.003)
Including % missing diagnoses[b]	*0.020 (0.014 to 0.026)*	*0.021 (0.015 to 0.032)*	*0.950 (0.903 to 1.000)*
Including all missing diagnoses[c]	*0.021 (0.015 to 0.028)*	*0.023 (0.015 to 0.034)*	*0.967 (0.920 to 1.016)*
COVID-19 month indicator[d]			*0.936 (0.889 to 0.986)*
Excluding West Hampshire[e]	*0.018 (0.013 to 0.024)*	*0.019 (0.013 to 0.026)*	*0.951 (0.900 to 1.004)*

a Random-effects Poisson regression, adjusting for baseline hospitalisation rate and incorporating the CCG as a random effect.
b A proportion of hospitalisations with a missing diagnosis were included as RTI diagnoses: (RTI hospitalisation/total hospitalisations)*missing diagnosis hospitalisations.
c All hospitalisations with a missing diagnosis were included a RTI diagnoses.
d Including a numerical variable (0–12) to indicate how many months were affected by COVID-19.
e Excluding West Hampshire practices (I = 4, C = 5), who did not provide annual data.

to 1.000). Second, all hospitalisations with a missing diagnosis were included as RTI diagnoses, akin to a worst-case scenario. While there were still more hospitalisations in the control arm, the CI for this sensitivity analysis was (0.920, 1.016), slightly above the non-inferiority margin. Including a variable from 1 to 12 months, as with the dispensing outcome, to account for the number of months affected by COVID-19 provided results that agreed with the non-inferiority conclusion. We observed the same effect following the removal of West Hampshire practices.

Accident and emergency attendances: secondary outcome and sensitivity analyses

As A&E attendances were collected in the same way as hospitalisations, they were also analysed in the same way.

Impact of COVID-19 on accident and emergency attendances for respiratory tract infection

In a similar way to dispensing and hospitalisations, there was obvious seasonal variation in A&E attendances for RTI across all CHICO practices (see *Figure 19*). Between October 2017 and March 2020,

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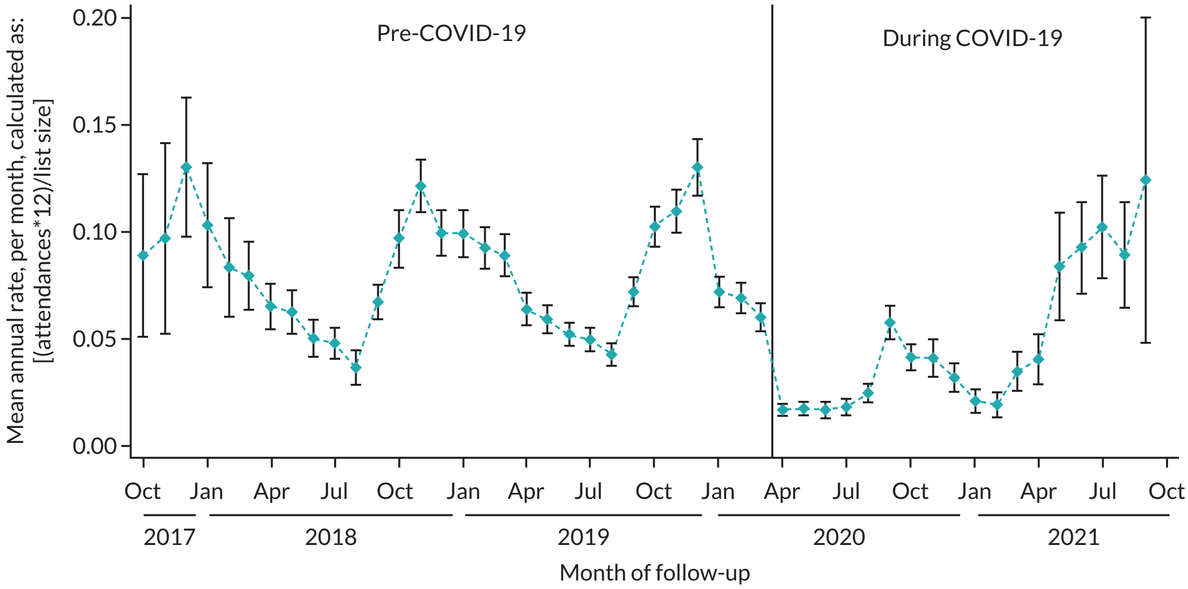

FIGURE 19 Mean A&E attendance rate (95% CI) during the CHICO baseline and follow-up periods. Each practice contributed 24 months of data.

the A&E attendance rates, for RTI, reached highs of nearly 13% in the winter and approximately 4% in the summer. The effects of COVID-19, and its associated lockdowns, on A&E attendances is clear from April 2020 onwards when it dropped to 2%. When restrictions were relaxed in late spring/summer of 2021, they became unseasonably high.

Accident and emergency attendance rate comparison

As with the dispensing and hospitalisation rates the A&E attendance rates appeared to be very similar between the arms, over the 3-year follow-up period (see *Figure 20*).

The rate of A&E attendances was 0.049 and 0.045 for the intervention and control arms, respectively (see *Table 15*). The IRR was 1.013 (95% CI 0.980, 1.047; *p* = 0.437), providing no evidence of a difference between the groups.

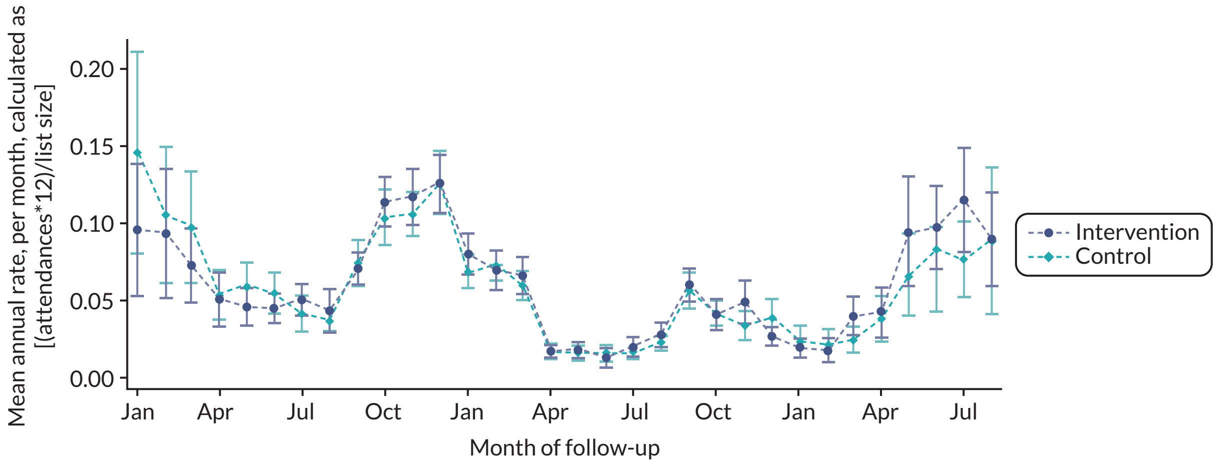

FIGURE 20 Mean A&E attendance rate (95% CI) during the CHICO follow-up period (January 2019–August 2021), by arm. October 2018–December 2018 and September 2021 have been excluded due to low numbers. Each practice contributed up to 12 months of follow-up data.

TABLE 15 Accident and emergency rate comparison

	Intervention rate (95% CI)	Control rate (95% CI)	IRR (95% CI)[a]	*p*-value
Secondary analysis	0.049 (0.037 to 0.066)	0.045 (0.032 to 0.063)	1.013 (0.980 to 1.047)	0.437
Including % missing diagnoses[b]	*0.060 (0.045 to 0.082)*	*0.054 (0.038 to 0.078)*	*1.006 (0.977 to 1.037)*	*0.680*
Including all missing diagnoses[c]	*0.134 (0.093 to 0.193)*	*0.120 (0.080 to 0.182)*	*0.976 (0.956 to 0.996)*	*0.017*
COVID-19 month indicator[d]			*1.012 (0.980 to 1.047)*	*0.445*
Excluding West Hampshire[e]	*0.050 (0.037 to 0.067)*	*0.045 (0.032 to 0.063)*	*1.021 (0.987 to 1.056)*	*0.226*

[a] Random-effects Poisson regression, adjusting for baseline A&E attendance rate and incorporating the CCG as a random effect.
[b] A proportion of A&E attendances with a missing diagnosis were included as RTI diagnoses: (RTI attendances/total attendances)*missing diagnosis attendances.
[c] All A&E attendances with a missing diagnosis were included a RTI diagnoses.
[d] Including a numerical variable (0–12) to indicate how many months were affected by COVID-19.
[e] Excluding West Hampshire practices (I = 4, C = 5).

As with the hospitalisation outcome, various sensitivity analyses were carried out to account for the various misgivings in the data. As with hospitalisations, there were A&E attendances with missing diagnoses. Including a proportion of these as RTI-related gave very similar results to the main secondary outcome; however including all of them led to a higher number of A&E attendances in the intervention arm. This was true for both hospitalisations and A&E attendances suggesting that there may have been a higher proportion of 'missing' diagnoses in the intervention arm, compared with the control. Including a variable from 1 to 12, to account for the number of months affected by COVID-19, provided results that agreed with the secondary outcomes results. As did the removal of West Hampshire practices.

Exploratory calculations of the intracluster correlation coefficient

Of the 149 control practices, 55 were excluded when estimating the ICC as they were from a CCG with $n < 5$ practices. Using a mixed-effects linear regression model with follow-up rate as the dependent variable, baseline rate as a covariate and CCG as the random effect the ICC for practices within clusters for the dispensing and hospitalisation outcomes was ~0.05 and ~0.32, respectively. While an estimate has been made, these results should be viewed with caution given the small size of each cluster and the effects of COVID-19 on hospitalisation and dispensing rates.

Acceptability of the intervention

As part of the follow-up questionnaire, practices were asked how they found the intervention in terms of (1) ease of use, (2) helpfulness and (3) willingness to use it again. Practices were asked 'Did you find the intervention…?' and they provided the following responses (see *Figure 21*). The majority (92%) found the intervention 'OK' or 'easy' to use and over half found it 'helpful'. For practices that found the intervention unhelpful, reasons provided were conflicts with other templates: 'Sepsis template', 'Didn't work with the contradictory COVID templates released nationally', or dislike of the intervention: 'GPs felt like this was an extra layer of intervention required on top of usual care', 'The problems that often the doctor had to close the EMIS® window before printing the leaflets off – if they forgot the patient had often disappeared – it was too late', 'It is hard to know the extent to which the information given to

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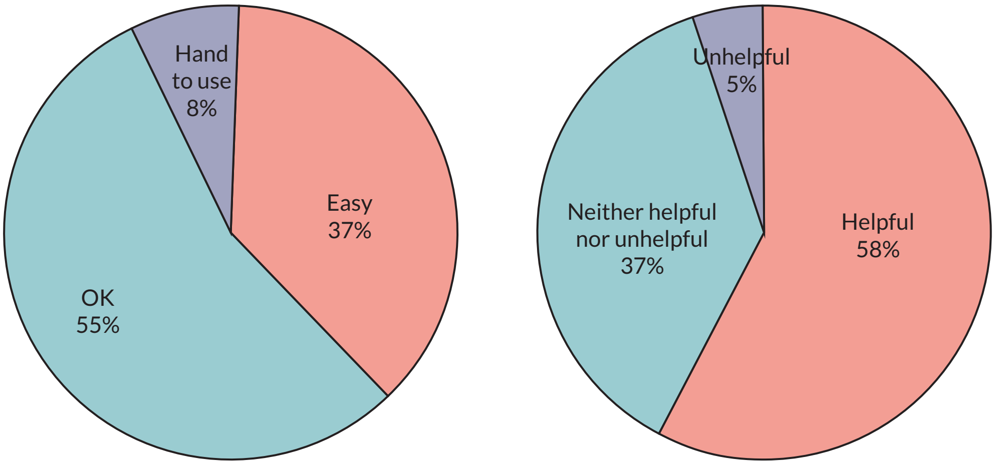

FIGURE 21 Acceptability of the intervention.

parents influence their subsequent behaviour'. When asked if they would use the intervention again, if it became available, 85/117 (73%) said that they would.

COVID-19 impact

From March 2020, the intervention was used very infrequently (see *Figure 9*). Although various sensitivity and subgroup analyses were carried out in an attempt to account for COVID-19, if practices were not using the intervention then it does call into question the validity of the results. Points to note are:

- As seen in *Impact of COVID-19 on dispensing*, *Impact of COVID-19 on hospitalisations for respiratory tract infection* and *Impact of COVID-19 on accident and emergency attendances for respiratory tract infection*, COVID-19 had a big impact on dispensing, hospitalisation and A&E rates, causing a drop in rates during lockdowns and an unseasonably high rate during the summer of 2021. Although this should have affected the two arms in a similar way, it would have made any differences between the two arms difficult to distinguish.
- How patients were triaged was also impacted. From April 2020, in the follow-up questionnaire, practices were asked if the proportion of patients triaged over the telephone had changed due to the pandemic and 141/181 (78%) agreed that it had. Post March 2020, intervention practices were asked if there had been any months where they had been unable to use the intervention due to COVID-19. Of the 80 practices that answered this question, 17 (21%) said that there had been months where they were unable to use the intervention and 24 (30%) said there had been months with limited usage. Prior to March 2020, the median usage per month, per practice, was nine uses. Post March 2020, the median usage was zero.
- Adverse impact to recruitment of practices during wave 1 of COVID, resulted in requiring an extra 4 months (un-costed) extension to achieve the target number of practices.
- COVID-19 and subsequent vaccination programs may have contributed to the poor follow-up and communication from several practices, due to staff unavailability and other priorities.
- Estimated reduction in dispensing antibiotics may not be clearly attributed to use of the intervention, as this could be partly affected by school closures during the pandemic causing a slowdown in RTI infections and children not visiting GP practices as frequently.
- A reduction in intervention usage occurred during the pandemic when changing patterns of consultations in practices affected the number of children being seen face to face, although an alternative one-page guidance for using the intervention in remote consultations was provided.
- There may have been an increase in A&E attendances during the pandemic if patients were unable to be seen in GP practices, this could affect the secondary outcome S1.
- In some intervention practices, COVID-19 pop-ups prevented the CHICO pop-up from being displayed.

Protocol deviations

There was only one protocol deviation noted; during randomisation, four input errors were identified. Corrective and preventative actions were put in place. Both the Chief Investigator and the sponsor concluded the input errors would have minimal impact on the data integrity for the study, and the sample size would ensure there was no impact on the balance of the arms of the study (reviewed and approved on 16 April 2019).

SNOMED/Egton Medical Information Systems upgrade impact

The CHICO intervention resources were created using Template manager (the module for creating templates, protocols and concepts in EMIS®). The EMIS® set-up guide is described in *Appendix 3*. Certain known errors in EMIS® prevented a handful of practices from being able to implement the CHICO resources at all. The SNOMED upgrade by EMIS® adversely affected intervention practices being able to calculate the CHICO score. Therefore, a SNOMED-compliant version of the CHICO resources had to be written and tested before implementing new practices.

Scoping exercise for *SystmOne*

SystmOne covers 34% of GP practices In England, and although these practices were excluded from the trial, a scoping exercise was undertaken to investigate the possibility of creating the intervention using this practice system should the results indicate the intervention would be adopted by the NHS. Discussing the intervention with *SystmOne* users there did not seem to be any barriers to using the intervention in this system. A *SystmOne* Resources set-up guide was created to describe how the resources (a clinical template, letter templates, protocol and a set of clinical reports) could be distributed and imported into practices (see *Appendix 4*). The resources were demonstrated to a study clinician; however, there would need to be further testing by clinicians using *SystmOne* before distributing. In addition, both for the EMIS® and *SystmOne* versions of the resources, the list of medicines prescribed for asthma (such as drugs for prophylaxis of asthma), would need to be updated to reflect current prescribing behaviour.

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Chapter 4 Qualitative study

Introduction

To explore the use of the intervention, how it was embedded into practice and whether it was used appropriately, we conducted interviews with clinicians (GPs and practice nurses). Data collection and analysis were informed by normalisation process theory (NPT),[39,49] which was developed to explain the social processes leading to the routine embedding of innovative health technologies or complex interventions in healthcare.

Normalisation process theory proposes that implementation of interventions is dependent on the ability of participants to fulfil four criteria which can be understood using the core constructs of NPT, which are 'coherence' (sense making — understanding and opinion of the intervention purpose), 'cognitive participation' (buy-in — the work people do to develop new practices), 'collective action' (the work to operationalise practices) and 'reflexive monitoring' (ways in which people appraise how new practices are working).

Methods

Recruitment and sampling

Clinicians involved in implementing the CHICO intervention were invited to take part in semistructured interviews. To capture maximum variation in views and experience and reflect a range of practices (those with high and low patient lists and antibiotic prescribing rates, serving areas of high and low socioeconomic deprivation) and clinicians (GPs and practice nurses with a range of years' experience) were purposively sampled. The socioeconomic status of practices was estimated using the Index of Multiple Deprivation decile[47] based on the practice post code. The sample size was determined by data saturation, such that no new themes were emerging from the data by the end of data collection.[50] Potential participants were contacted by the qualitative researcher (CLCL) via e-mail and invited to take part in the interview. Clinicians from 56 practices were invited to participate. Participants were asked to provide their audio-recorded verbal consent to take part immediately before the interview.

Interviews

The interviews were all conducted by telephone by the qualitative researcher (CLCL), who is an experienced social scientist. The first set of interviews was conducted during the trial pilot phase and findings were fed back to the Trial Management Group (TMG) to optimise the intervention implementation and guided changes during the remainder of the study. The second phase of interviews was conducted after practices had been using the intervention for 12 months. A flexible topic guide was used to assist questioning during interviews but allow participants to introduce and discuss topics not anticipated by the researchers (see *Box 1*).

BOX 1 Interview discussion topic guide

- Experience and views of CHICO intervention
    - First impressions
    - Preparedness for the intervention
    - Views on credibility and usefulness
    - Frequency of use and changes over time
    - Who used for and why?
    - How is it used in consultation?
    - Parents' responses
- Impact of CHICO
    - Benefits of CHICO intervention

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    - What has not worked well/been less successful
    - Influences on prescribing behaviour
    - Influences on views on hospitalisation
    - Impact on consultation time
    - Any changes made to how CHICO intervention is used
    - Suggested changes to the CHICO intervention
- Views of potential for change in practice
    - Impact on practice
    - Any changes needed for wider implementation?
    - Potential barriers to roll-out
    - Other current influences on antibiotic prescribing
- Any other issues

Topic guides were modified as necessary throughout the course of the study to reflect findings as they emerged. With informed consent from participants, interviews were audio recorded using a digital voice recorder, transcribed using a professional transcription service and anonymised to protect confidentiality. Interviews lasted between 15 and 37 minutes, with an average time of 25 minutes.

Analysis of the interviews

Anonymised transcripts were checked for accuracy and then imported into NVivo Pro (version 10/11)[51] data analysis software to aid the management and analysis of the data. Analysis began shortly after data collection started and was ongoing and iterative. Ongoing analysis informed further data collection; for instance, analytic insights from data gathered in earlier interviews helped identify any changes that needed to be made to the topic guide during later interviews, for example, to explore new or underexplored topics raised in earlier interviews. Thematic analysis[52] was used to scrutinise the data to identify and analyse patterns and themes of salience for participants across and within the data set. Transcripts were coded inductively to establish an initial analysis framework and three researchers (CLCL, JH and CC) coded a subset of three transcripts; any discrepancies were discussed to ensure a coding consensus and maximise rigour.[53] The remaining transcripts were analysed (by CLCL) using the agreed analysis framework. The four NPT constructs were used to further develop themes across the data sets. To ensure that findings were trustworthy and credible, preliminary findings were discussed with the multidisciplinary trial management team.

Results

Participants

Twenty-six clinicians (20 GPs and 6 practice nurses) were interviewed from across 24 practices and 13 CCGs (see *Table 16*). Findings are presented for each of the NPT constructs, illustrated with anonymised verbatim quotations.

Coherence (sense making)

Clinicians welcomed the CHICO intervention as it aimed to help with ongoing issues being faced by practices such as the prevalence of children presenting with a cough and perceived parent concerns with not receiving antibiotics.

> *It was something that we were particularly interested in doing anyway. We do see lots of children, obviously, with coughs and colds and some parents generally are concerned. Some parents do understand that infections can be viral, but some do also expect an antibiotic if it's had a chesty cough for a certain period of time.*
>
> *(GP 14)*

> *Just a couple of weeks ago before CHICO was installed, they [nurses] were having numerous complaints from parents saying they felt cheated out of antibiotics.*
>
> *(GP 5)*

TABLE 16 Interview participant characteristics

Characteristic	Number of participants
Years of experience	
0–5	2
6–10	7
11–15	6
16–20	1
21–25	8
31+	2
Above CCG median practice patient list size	14
Below CCG median practice patient list size	12
Above CCG median antibiotic prescribing rate	11
Below CCG median antibiotic prescribing rate	15
Practice deprivation score	
High	7
Medium	9
Low	10

The intervention also aligned with existing strategies and efforts to reduce unnecessary antibiotic prescribing. Clinicians were already familiar with similar protocols and templates commonly used in primary care and believed the intervention would fit within their usual practice.

> *I thought it was good using that kind of direction that we were moving anyway to prescribe less antibiotics. So it was just something that was in time and in tune with what we needed to do.*
>
> *(GP 21)*

> *It seemed like it would be a simple intervention to use that could be used, you know just within a consultation so we always like that … It's almost part of what we would normally do.*
>
> *(GP 11)*

Cognitive participation (buy-in)

Clinicians felt they were well prepared for using the intervention and liked the training and materials. They found the training guides useful to refer to throughout the study and liked the ability to practice using a training patient. Although a website that held background information on the study and published literature on the intervention development was available, most clinicians did not feel the need to visit it.

> *I think [we were] really well prepared. The training results are really good but having a test patient was really good.*
>
> *(GP 11)*

> *The leaflets that you gave out and the information and the CHICO guides were given, were quite self-explanatory and all seemed quite straightforward.*
>
> *(Nurse 17)*

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Collective action (using children with cough in practice)

Most clinicians liked the intervention and thought it was quick and easy to use and used it as a supportive aid within consultations and described it as a safety net. It was a way of reassuring themselves and parents of the appropriateness of some treatment decisions.

> *I thought it was good, it was easy to use and yes, I thought it was a good idea.*
>
> *(Nurse 20)*

> *I think if you are not prescribing antibiotics, then it's a good safety netting tool. So, you can confidently say to the patient that you don't feel antibiotics are indicated.*
>
> *(GP 19)*

> *It's very reassuring for the professional and of course when you've printed out the leaflet that this is the scoring we have done; it is very reassuring for parents as well.*
>
> *(GP 16)*

Launching children with cough

During the pilot phase, clinicians were prompted to use the intervention through a 'pop-up', which appeared for all children under the age of 10. This limited the use of the intervention for some because it was launched at a point too early in the consultation to be useful and some clinicians did not like it. Based on this finding, the timing of the CHICO template was changed in the main trial phase and clinicians preferred the new form of launching the intervention using a code such as 'cough'.

> *It seems the hard pop up was useful, but it comes up too early. So, it comes up before you know what's actually wrong with the child.*
>
> *(Nurse 8)*

> *Initially … the flags … came up whenever you had an interactions with a 10-year-old. We had to remove it because it just drove everyone nuts.*
>
> *(GP 4)*

> *When you type in 'cough', a little box would come up with a CHICO template opening up, and then we were quite happy to proceed with completing it.*
>
> *(GP 14)*

However, some practices retained the automatic pop-up to help remind clinicians to use the intervention.

> *We've kept the automatic launch on, even though it is a bit annoying … We thought the best way to try and get people to use it and remember it for the whole year was keep it as automated.*
>
> *(GP 13)*

Prognostic algorithm

Most clinicians like the template where they entered the patient's symptoms and signs. They found it easy and straightforward to use without adding any more time to consultations.

> *It was fairly quick to use … it also allowed you to enter free text, and it had all the relevant questions.*
>
> *(GP 14)*

> *I think in practise I think the templates are not cumbersome. They are not bulky, and it can fit into the time that we have to see patients.*
>
> *(GP 4)*

However, some clinicians felt the template did not capture all the relevant symptoms and they needed to record these separately in the patient's record. This required 'moving between two screens' (GP 11), which could be problematic.

> *It was quite useful template to record the information. It could have been a little bit more sort of, bit more history of presenting complaint and there was the examination obviously and certain questions to ask but I often found then I went back into the patients notes and wrote a bit more information about the consultation, so, you couldn't put everything in the template. I found I either use the template and then probably it was a bit of a sketchy history, or, I had to then go into the patients note or save the template and then do a history of presenting complaints and I found it made it a bit more disjointed.*
>
> *(GP 19)*

Clinicians liked that the template helped to elicit parent concerns which were believed to be important but could be forgotten.

> *I think the parent concerns are good because that's just making it a bit more patient centred and maybe we forget to ask that sometimes.*
>
> *(GP 11)*

> *I suppose I wouldn't necessarily ask about what are you particularly worried about directly.*
>
> *(Nurse 17)*

> *'Ask the parent or carer what they were most worried about that day'. I think that's an invaluable question, really, because you just don't quite know what the parent is actually worried about … so I think that was really valuable, and again, a good prompt that some doctors may or may not actually ask.*
>
> *(GP 14)*

Clinicians had mixed views about the risk management advice aspect of the intervention. Few of the clinicians remembered this aspect and some did not find it useful. The perceived usefulness of the prognostic algorithm depended on the severity of the child's symptoms. Clinicians found it most useful with children who were 'borderline' cases for hospitalisation or prescribing antibiotics.

> *It gives the clinician visual cues about the severity of it, which is very good.*
>
> *(GP 1)*

> *I've never seen CHICO give me any kind of management advice.*
>
> *(GP 12)*

> *I've tended not to take that much notice of that. I don't know if that was just because originally it was quite interesting, but now it's always the same, because the majority of what we see is mild viral self-limiting respiratory illnesses. Most parents hadn't even considered that their child might need hospital, or whether that would play any part in how we manage them.*
>
> *(GP 13)*

> *I personally would probably [have] used it more for the borderline ones.*
>
> *(GP 14)*

Letter/advice leaflet

The advice leaflet was believed to be the most useful intervention component and clinicians liked it for a range of reasons. The leaflet was a good safety-netting tool and a way of facilitating conversations with parents and reinforcing the clinician's decision not to prescribe antibiotics.

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> *I didn't find CHICO useful for the score. I found it helpful for the leaflet. I think my whole use was centred around the leaflet.*
>
> *(GP 11)*

> *It really helped with safety netting if you weren't giving them antibiotics, so it gave you a lot more confidence that parents knew what the signs were … so I think that was the best bit of the intervention.*
>
> *(GP 16)*

> *So, if there was a feeling that it was going to be a difficult consultation to try and steer them [parents] away from antibiotics based on the clinical assessment then that would be a really good adjunct tool for that.*
>
> *(GP 25)*

Clinicians felt that parents were more satisfied with receiving the leaflet that explained the clinician's decisions and having information they could take home with them. The safety-netting advice was a way of educating and empowering parents, which could have longer-term implications for reducing repeat visits to practices.

> *I think it just makes patients feel more satisfied that they're not going away empty handed. They've been given something, and I feel kind of that what I've said to them has been enhanced by going away with a leaflet.*
>
> *(GP 11)*

> *I think on one of the occasions it was particularly good because I think the mother of my patient did struggle with the idea why antibiotics might be useful down the line but weren't now and I think that was quite helpful.*
>
> *(GP 16)*

> *I hope over time it [leaflet] will empower parents a bit to not actually contact us as early as they tend to do in this area with coughs in their children. There's the first line on the leaflet saying, 'Normal coughs can last three to four weeks.' That's actually what we've been trying to educate patients about for ages. The bit about how many times you get a cough a year, and all this is quite normal. I think probably that has been one of the most helpful things as well that healthy children do get a lot of coughs. It doesn't necessarily mean there's anything wrong with their child. It's just normal.*
>
> *(GP 13)*

Nurses found being able to give the parents the leaflet particularly useful as they felt they faced increased scrutiny and push back from parents if they did not prescribe antibiotics.

> *What we find quite often as an ANP [Advanced Nurse Practitioner] is if we refuse them antibiotics, then they go and make an appointment with the doctor and get antibiotics. So, you know, you're always aware in the back of your mind that that kind of thing is going to rumble on and then you know, they'll just go and see and then just keep seeing people until they get what they want … I would say that it gave us that extra back-up to say no.*
>
> *(Nurse 24)*

As with the prognostic algorithm, the advice leaflet was seen to be more useful in children considered to be 'borderline'.

> *Like especially when there is a borderline whether to go to the hospital or not and the score is a bit on the lesser side and parents are not keen to go to the hospital and at that time, this has particularly helped. The leaflet you're giving them the clear-cut advice of when to go and when to seek advice.*
>
> *(GP 23)*

Challenges with children with cough in practice

Clinicians highlighted some challenges with using the CHICO intervention in practice, which led to reduced use or not using all the intervention components. These included the use of the intervention not being aligned to some clinicians' usual consultation practice. Some clinicians would usually complete the patient record at the end of the consultation or after the patient had left meaning they were not able to use the algorithm to support decision-making or provide the parent with the personalised letter and advice leaflet. Difficulties aligning the intervention with their consultation flow led some clinicians to stop using the intervention. However, in some cases, clinicians did provide parents with pre-printed advice leaflets.

> *I do my typing up at the end of the consultation so it [intervention] doesn't alter my thought processes, 'am I going to prescribe them antibiotics or not'. I have already made that decision from taking the history and doing the examination. It is just back-up at the end of the consultation, because, like I say, I do my typing up at the end. It doesn't actually give you the scoring until you click, 'save' so that pop-up comes right up right at the end. I have already made my decision by then.*
>
> *(GP 3)*

> *If I then while the child is with me code something like upper respiratory tract infection or chest infection, then the pop up comes again and then I fill it in. But the problem is that I don't always do that bit until after the kid has gone … I get a pop up saying do I want to print a leaflet about antibiotics or not. But usually, my patient's long gone by that stage.*
>
> *(GP 12)*

> *The hardest thing I think is that to load the letters you have to save and actually you save when the patient's out of the door normally and so it's just a bit clunky so you're having to save earlier than you would like to and then go back in and edit in order to launch the leaflet … Most of us find that it gets in the way of our consultation and so therefore we don't use it, but we like the leaflet, and we give that out.*
>
> *(GP 11)*

> *Unfortunately the leaflet thing probably got a little bit overlooked because you do the whole template, finish the consultation with the patient and then they would go and then you'd finish writing up your notes which I think most practitioners would do, finish writing up the notes when they've gone and then you click on save and then up comes the 'would you like to print a leaflet' and it's 'oh, I've forgotten to do that'.*
>
> *(Nurse 17)*

Some clinicians did not like focusing on the computer and having to input information when the patient was present as they wanted to pay attention to the patient and to maintain a face-to-face contact.

> *Normally for most consultations, I'll type it up after they've gone so that if we can maintain eye contact and have the conversation with the parent rather than typing.*
>
> *(GP 13)*

Some practices conducted their consultations remotely, which meant clinically assessing the symptoms required for the prognostic algorithm was challenging. This was more of an issue with telephone consultations as some symptoms could still be assessed using video where the child could still be 'seen' and 'heard'.

> *Can assess using video, can see the child … breathlessness, wheezing.*
>
> *(GP 18)*

> *I mean we do a lot of video consultations as well 'cause then you can see whether the child's running around and what they're doing and what have you, so yes it could easily be adapted I would have thought.*
>
> *(Nurse 20)*

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It was also difficult to provide parents with the printed letters and leaflets in some practices, either because of the remote consultation or because of printing issues. However, some clinicians had found ways around this including using pre-printed versions of the leaflet provided by the study team, saving a PDF version that could then be printed off without using the intervention and e-mailing or texting the leaflets to parents.

> *Often, I would just give them a nice – you know, they were very attractive leaflets and a bit more probably, yeah more striking than the black and white paper printout.*
>
> *(GP 19)*

> *We've started to e-mail the leaflet to patients ... using a text messaging service ... So we have used the leaflets via telephone consultation as well, so you can do that, so that bit is good.*
>
> *(GP 22)*

> *So, a lot of the time we're texting leaflets now. I don't know whether that would be something –we use something called [ACCU RX]... that is a technical service, and you can embed leaflets and... that would be quicker... so if we wanted to upload CHICO we could.*
>
> *(GP 11)*

> *I have to say I really – I do like it but what I do is - we've got the CHICO leaflet embedded in EMIS® so sometimes I just give that without using – We've also got it, I think there's a link to it on our website so we don't so much do the CHICO intervention we just say, 'Actually, there's this really nice leaflet ... have a look on our website.' Some of my colleagues do ... sometimes I just have some printed leaflets and give it to them without having to use the intervention.*
>
> *(GP 15)*

Frequency of use

How often clinicians believed they used the CHICO intervention was variable with some reporting frequent use early on, but that use reduced over time. This could depend on clinicians remembering to use it, how busy the practice was, and increased familiarity with the algorithm outcomes.

> *Used on a daily basis.*
>
> *(GP 15)*

> *She [nurse practitioner] uses it for every single patient.*
>
> *(GP 5)*

> *In the latter months we sometimes would forget to do the CHICO template ... The more you use it, the more you get used to it and you get a feel of what the score might be and what the outcome might be.*
>
> *(GP 14)*

Perceived impact on behaviour/practice

Some clinicians believed the intervention influenced their prescribing behaviour. However, others believed that it supported rather than changed their prescribing decisions and did not change their behaviour.

> *I'm not sure it massively did [affect prescribing]. Perhaps not directly I would say ... We probably went on the history and the physical examination.*
>
> *(Nurse 17)*

> *The main thing we used it for was safety netting and we do that anyway, so it's really just enhancing. Not like we're saying 'okay we are going to ignore everything in front of us because CHICO is telling us to do this.' It really just fits in with what we do anyway.*
>
> *(GP 11)*

> *You know your clinical judgement supersedes any guidelines but they're always there to support your decision making from that aspect.*
>
> *(GP 25)*

Use during the COVID-19 pandemic (interviews took place during or just after the first wave)

Changes with practice pathways such as increased nurse triaging and the use of COVID-19 protocols led to reduced use of the CHICO intervention during the pandemic. Anyone presenting with a cough was assessed for potential COVID-19 infection and referred for a COVID-19 test.

> *COVID did definitely affect it. So, I mean just I guess thinking of cough, you're thinking of COVID so I don't think we've used it for a year I would say. I would say that. But before that we used it quite frequently.*
>
> *(GP 21)*

> *I didn't and I'm not sure others did because first of all we were doing remote consultation, especially the first wave and the first wave also I was isolated at home so I wouldn't have used it then and I would definitely tell anybody with a cough to get a test and refer them to the clinic we have in ((city)).*
>
> *(GP 25)*

The need to conduct consultations in restricted spaces with no computers or materials such as leaflets meant clinicians were unable to use the CHICO prognostic algorithm and they could not print out the personalised letters or use pre-printed leaflets.

> *The problem it was that was slightly that we were seeing patients with coughs and temperatures in a red room. So, we'd cleared everything from that clinical room to keep things as, so we didn't have the leaflets readily available and also we weren't logging onto that computer cause we were trying to keep it that everything we touched we had to clean down, so, I must admit, I don't think we did use it when patients cause we had to have a red room cause, you know, anyone presenting with a temperature or a cough, which included children with those symptoms, so, yeah, I don't think we'd probably used it quite as much during COVID.*
>
> *(GP 19)*

> *Part of the reason that we wouldn't use it during COVID is that we're seeing our patients now … we're seeing outside in the car park, so we don't have our computer in front of us.*
>
> *(GP 15)*

The increased use of remote consultations during the COVID-19 pandemic further highlighted the challenges discussed. However, having used it during remote consultations during this period, clinicians did perceive some benefits to using the intervention remotely including less need to focus on a face-to-face consultation.

> *It fit more naturally with remote working because its easier to get whatever you need on the screen, and you're not worried about eye contact and body language.*
>
> *(GP 25)*

There were also fewer children presenting with respiratory illnesses which reduced the opportunity to use the CHICO intervention during the pandemic.

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> *That's where it all stopped because majority of our consultations since the COVID started last year, they all went into the telephone consultation and so that's where we have not used much of CHICO template at all.*
>
> (GP 23)

> *We get a lot of virally coughs and colds and things in children but since lockdown and since COVID, there's been hardly any and I suppose that's because people aren't going out and they're not going to nurseries are they and they're not picking it up … So there's hardly – well we haven't hardly any children in now.*
>
> (Nurse 20)

Both GPs and nurse practitioners found the intervention useful. However, some clinicians believed the intervention would be more useful and have more impact for trainee doctors to support decision-making and help guide patient management. Trainee doctors are likely to be less experienced with sick children and believed to be more likely to prescribe antibiotics and could therefore benefit more from the intervention.

> *Doctors in training have found this a much more useful than some of the experienced doctors … 'cause sometimes they haven't seen lots of children and they really appreciate having a system whereby it helps to guide their management.*
>
> (GP 22)

> *Of course it was useful for us also but sometimes we are seeing registrars might be more inclined to prescribe antibiotics and everything but that was a good guide regarding the intervention.*
>
> (GP 23)

Reflexive monitoring (appraisal of CHICO)

When appraising the CHICO intervention and making recommendations for future implementation, participants suggested expanding the template to encompass more information. This could help overcome issues with having to record information in multiple places and switching screens.

> *Maybe a box, history of presenting complaints, so if there was other information – because I think if you're filling in a template, especially when we're busy in the winter, it be good if we could record all the information in that template and then not have to go back into the notes to record things that we think is important to record.*
>
> (GP 19)

> *But if you're using a template, you want it to capture all the information. So, adding those two, heart rate, respiratory rate and oxygen saturations would help it to be more complete.*
>
> (GP 13)

Clinicians also recommended adapting the intervention to be more conducive to remote consultations. This could include informing parents about how to assess symptoms and having parent-reported criteria rather than having the clinician-assessed criteria. However, some clinicians worried about relying on parent-reported symptoms as these could be less accurate and more subjective.

> *Adapting the template to remote consultation will be a good thing … have parent observed criteria rather than clinician observed.*
>
> (GP 23)

> *I think the tool is little bit reliant on clinical aspect as well which you may not have so it's difficult to judge on chest signs and symptoms and respiratory distress and that sort of thing, wheeze, based on a conversation with a parent and even temperature. They may not have a temperature probe so you*

> *may not be able to get particular aspects of it but then some bits you will be able to get. But if it can be tweaked to amend for things that may not happen on remote working then that may obviously help.*
>
> *(GP 25)*

And asking if they would use the intervention in the future

> *I would have no problem with starting to use it again now because I feel you know, now we're gonna start getting back to normal and coughs will just be coughs and colds and it would be really useful to have that back again.*
>
> *(Nurse 24)*

Discussion and conclusions

Summary of the findings and implications

The use of NPT allowed for examination of issues with both the design of the intervention and its implementation. Interview data indicated that while the NPT constructs of coherence and cognitive participation were fulfilled, this was not the case for cognitive participation, with negative consequences for implementation.

The qualitative findings help explain why no difference was found between the control and intervention groups. They confirmed that clinicians used the intervention at the start of the trial, but usage waned over time. Clinicians initially welcomed CHICO in theory but in practice, it proved difficult to align the intervention flow with that of the clinician's usual consultation practice. Most clinicians liked the algorithm template and found it straightforward to use, without adding any more time to consultations. However, having to close the patient's record before the end of the consultation to complete the intervention process did not always align with clinicians' usual processes and was problematic. The COVID-19 pandemic also impacted use of the intervention due to changes to practice pathways, increased use of remote consultations and reduced numbers of children presenting with RTIs.

While some clinicians reported that the intervention influenced prescribing decisions and found it most useful in 'borderline cases', others reported that they used it as a supportive aid during consultations rather than a tool to change prescribing behaviour. CHICO helped elicit parent concerns and reassure clinicians and parents of the appropriateness of some treatment decisions. Clinicians particularly liked the safety-netting parental advice leaflet, as it helped explain treatment decisions and home care with parents and this was seen to be the most useful intervention component. To increase use of the intervention, findings suggest it may need to be adapted for use within remote consultations and to fit better with clinicians' consultation flow.

Strengths and limitations of the qualitative study

Strengths include interviewing both GPs and nurses who used the intervention from a diverse range of practices. The use of NPT to inform data collection and analysis enabled a focus on issues with both the intervention design and the way it was implemented in practice.

Limitations include possible memory bias as most clinicians were interviewed towards the end of the trial, which may have been some time after they had last used the intervention. In addition, we did not interview those clinicians who have never used the tool, and this could have provided useful insights into the barriers of using the tool. Insight into whether and when clinicians would choose to use or ignore the tool is also missing, which limits understanding of its use in different situations. A further limitation that parents of children that CHICO was used with were not interviewed which should be taken into consideration when interpreting the results. However, clinicians did discuss how the intervention was received by parents, which provided some useful insight into parents' views.

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As we were examining the experience of using the intervention, we did not interview people who did not use the intervention. However, as interviews were conducted with those who used the intervention early on but then their use reduced over time, we have provided insight into why clinicians may not engage with the intervention.

Conclusions

Clinicians found the CHICO intervention useful, and it helped discussions with parents about concerns and treatment decisions. Some clinicians believed the intervention influenced their prescribing behaviour and found it most useful in 'borderline cases'. However, others believed that it supported rather than changed their prescribing decisions and did not change their prescribing behaviour. Clinicians usage of the intervention reduced over time and this was further impacted by the COVID-19 pandemic and subsequent increase in remote consultations and reduction in RTIs.

To increase use of the intervention, findings suggest it may need to be adapted to align more with clinician's consultation flow and allow use during remote consultations.

Chapter 5 Economic evaluation

Introduction

The economic evaluation of the CHICO trial comprised a between-arm comparison of secondary and primary care costs from an NHS perspective. This analytical approach was informed by the experiences of the related CHICO feasibility trial, as well as the design used for the present trial.

The feasibility trial recruited children aged between 3 months and 11 years with acute cough and RTI. Quality of life was calculated in the feasibility trial using the CHU9D instrument, which is validated for children aged 5–11 years. In the event, only some 25% of children recruited to the feasibility trial were in this age range, and only 9% of participants provided sufficient baseline and follow-up CHU9D data to enable calculated of quality-adjusted life-years (QALYs). This experience indicated the challenges of collecting and calculating data on quality of life and cognate measures such as QALYs in very young populations presenting to primary care with RTIs.

In relation to the present trial, the co-primary outcomes of the trial are rates of amoxicillin and macrolide items dispensed to children aged 0–9 years, and rates of LRTI hospitalisations. Given that both outcomes embody elements of resource consumption (dispensing of medication and hospitalisation), a between-arm comparison of these and other costs was considered the most appropriate way of addressing our secondary aim (S2) of clarifying whether and by how much NHS costs might change in the event of a deployment of the intervention algorithm into routine clinical practice.

The following sets out our approach to identify, quantify and value NHS costs incurred in each arm of the trial, which was undertaken following the publication of the trial's protocol and was undertaken following the steps described in the statistical analysis plan[45] agreed with the trial's DMC. Our reporting of this economic evaluation follows the updated guidance contained in the Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement.[54]

Resource use and valuation

The NHS costs included in the between-arm inferential comparison were those of the intervention itself, costs of dispensed amoxicillin and macrolides, A&E attendances and hospital admissions. These costs were calculated from an NHS perspective. As the follow-up period does not extend beyond 1 year, discounting of costs was not applied. Each cost item is considered in turn below. Costs are reported on 2020/21 prices.

Costs of the intervention

The costs of the intervention comprised the non-research related costs involved at the practice level that arose from integrating the intervention into local computers, and training costs borne at the practice level. We consider possible other intervention-related costs that may arise in the event of a large-scale (e.g. national) deployment in *Chapter 7 Discussion*, but for the between-arm cost analysis we restricted our focus to those costs incurred in the trial itself.

To reflect experiences at some but not all practices in the trial, we made the conservative assumption that time will be required to manage and troubleshoot the integration of the algorithm at the practice level. We assumed that this would be undertaken by a practice manager working for 1 hour in total. This amounts to a cost of £54 per practice in 2020/21 prices, corresponding to a salary of Band 6 on the Agenda for Change (AFC) pay scale.[55]

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For training time involved in using the intervention, we assumed that it would take some time for prescribing clinicians to understand the rationale for the intervention and to become familiar with its use. This is also a conservative assumption since the 'implementation' period of the trial allowed time for practices to install the intervention and to encourage its use by staff. We assumed that the time involved would be equivalent to that of a single consultation. The median number of GP prescribers of amoxicillin and macrolides per practice in the trial was 4. Given a cost per consultation of £39 in 2020/21 prices, we therefore calculated practice-level training costs as 4*£39 = £156.

The costs of the intervention were therefore estimated as £210 per practice. In sensitivity analysis, to test our conservative assumptions on GP training and manager integration of the intervention, we re-ran our main results attributing no costs to the intervention itself.

Costs of amoxicillin and macrolides

Data on both the volume and cost of prescriptions at each practice were taken from the BNFePACT2 (Electronic Prescribing Analysis and Cost) system. The volume data were specific to each practice, collected routinely every month and reflected dispensed amoxicillin and macrolide prescriptions given to children aged 0–9 years, for each practice, and obtained from ePACT2.

Data on the net ingredient cost of amoxicillin and macrolides (see *Appendix 6*, *Table 20*) were also obtained from the ePACT system. The cost data were not specific to each practice. Instead, they represented cost of all amoxicillin and macrolides dispensed to this age group in England during the 2020/21 financial year. Using these cost data, therefore, assumes that the costs and composition of prescriptions – reflecting the relative mix of specific medications as well as their formulation, dose and presentation – of all GP practices in England are similar to those of practices included in the trial.

The use of net ingredient cost reflects a basic cost of the drug concerned. Given the unavailability of details on formulation, presentation, dose and other information, it does not account for container costs, dispensing costs and net fees or net prescription charges income.

Costs of accident and emergency attendances

As noted in *Chapter 3*, the collection of data on A&E attendances is routinely undertaken each month by each CCG. We used these data to identify the volume of attendances. These were costed using NHS Reference Costs 2019/20[56] and inflated to 2020/21 prices. The inflation index is used as the average of the last 5 years (2016/17–2020/21 financial years) of the NHS cost inflation index.[55]

We did not have information on whether an attendance led to a subsequent admission, the type of investigation conducted or the nature of treatment received while attending. Reference costs also does not distinguish between attendances related to paediatric or adult populations. We, therefore, created an average unit cost, weighted by the number of attendances reported for all admissions. However, we excluded dental admissions, and those where the patient was reported as dead on arrival. The unit cost in 2020/21 prices was £186.

Costs of hospital admissions

Volumes of per-practice hospital admissions related to RTI were also obtained from data routinely collected by CCGs. These were also costed using NHS Reference Costs 2019/20, inflated to 2020/21 prices as for A&E attendance using NHS cost inflation index as described above.[54]

The data available to the trial indicated that an admission had taken place, but did not otherwise identify the specific diagnosis associated with an admission nor whether the admission was associated with non-elective long or short stay, or day care. We therefore costed admissions as follows. Within each of non-elective long-stay, non-elective short-stay and day care episodes, we calculated an average of all unit costs that relate to acute respiratory symptoms. We weighted each unit cost by the respective volume of finished consultant episodes. Finished consultant episodes are completed episodes of treatment received by a patient under the care of a single consultant, and are a fundamental way of tracking activity in the NHS. These unit costs were then weighted by the total finished consultant episodes of each of non-elective long-stay care, non-elective short-stay care and day care to give a total average unit cost for LRTI-related hospital admissions.

Clinical Commissioning Groups were asked to identify hospital admissions for children for a broad list of conditions that may have been associated with RTIs. We developed estimates of unit costs that specifically focused on admissions pertaining to these types of infection.

A currency, in NHS reference costs, is a unit of healthcare activity such as a finished consultant episode. The currency codes used and their associated descriptions in, for example, the costing of non-elective long-stay care are summarised (see *Appendix 6*, *Table 21*). For the primary economic analysis, we estimated the cost of a hospital admission as £1209. We also conducted a sensitivity analysis in which we repeated this calculation of unit costs, but only including those service descriptions that specifically mention RTIs. In this case, the unit cost was estimated as £1165.

Analysis and sensitivity analysis

The comparison of between-arm costs used a two-way mixed-effect linear regression that accounted for the nesting of practices in CCG clusters. The analysis used this model for mean between-arm cost differences given the sample size of the trial and the desirable coverage properties for these kinds of parametric estimators even when within-arm cost data happen to be skewed.[57,58] The primary analysis model regressed total costs on arm and covariates for list size and dispensing rate, both of which were used for minimisation at randomisation. We conducted sensitivity analyses that repeated this regression but (a) from a per-protocol perspective, following the same analysis steps described in *Chapter 2 Methods* but applied to the between-arm comparison of costs (b) using unit costs for hospital admissions where the currency description of care episodes specifically mentions 'RTI' as in *Table 18* below (c) excluding intervention costs from the between-arm comparison.

Results

Data completeness and description of cost data

We used data from 293 of 294 randomised practices; the 294th practice merged with another trial practice after randomisation and was analysed as part of the larger, merged entity. Data were complete on all resource items used to undertake the between-arm cost comparison.

The volume of resource use in each arm is shown in *Table 17*. All cost data reported below are in 2020/21 prices. All practices reported some costs, ranging between £188 (for a practice in the control arm) and a maximum cost of £452,029 (for a practice in the intervention arm).

TABLE 17 Volumes of resource use

Cost category	Per practice mean resource use in control arm	Per practice mean resource use intervention arm
Amoxicillin	142.59 (116.83)	139.54 (101.04)
Macrolides	38.60 (38.67)	40.18 (38.50)
A&E attendance	53.05 (50.68)	57.31 (50.97)
Hospital admissions	24.16 (35.20)	22.02 (31.98)

Note
Volumes of intervention use not included here as a single unit cost the intervention was included for all practices in the intervention arm. Usage of the intervention is described in *Chapter 2 Intervention usage*, and is used in the per-protocol analysis described later.

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Costs were similar between arms. Mean (£39,826) and median (£29,162) unadjusted per-practice NHS costs during the 12 months of trial follow-up were somewhat lower in the intervention arm than in the control arm (mean £38,246, median £28,216). The distribution of per-practice costs was also similar between arms (see *Figure 22*).

There was no evidence of a between-arm difference when comparing cost categories (see *Table 18*).

Note that the costs of the intervention itself are modest compared to other cost categories, especially that of hospitalisation and A&E attendance.

Primary economic analysis

The primary analysis model regressed total costs on trial allocation and on covariates for list size and dispensing rate (see *Table 19*), adjusting for variance in 47 CCG clusters.

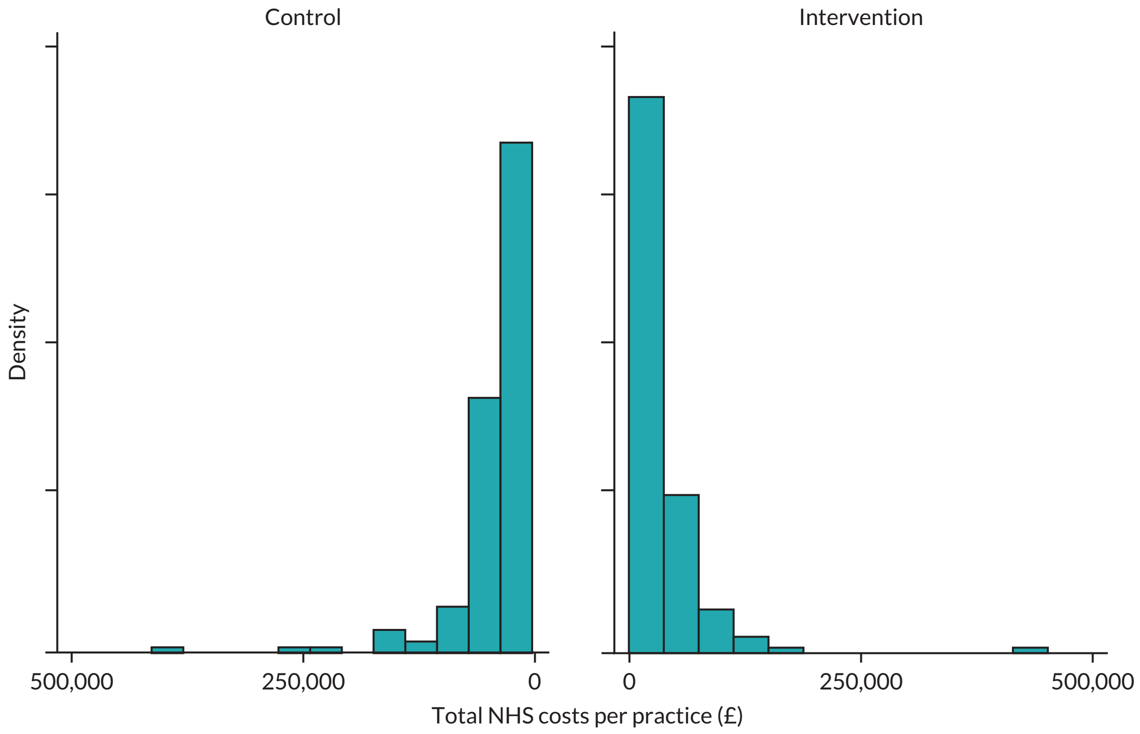

FIGURE 22 Distribution of total costs in control and intervention arms.

TABLE 18 Between-arm comparison of cost components

Cost category	Unadjusted control practices mean cost (SD)	Unadjusted intervention practices mean cost (SD)	Adjusted between-arm cost difference	95% CI
Dispensed amoxicillin and macrolides	£736 (£676)	£740 (£638)	£11	−£29 to £52
A&E attendance	£9880 (£9439)	£10,673 (£9493)	£629	−£257 to £1515
Hospital admissions	£29,209 (£42,557)	£26,662 (£38,664)	−£2924	−£7233 to £1386
Intervention cost	£0	£210 (–)	£210	–

Note
Confidence intervals on differences between arms in cost were calculated from mixed-effect linear regression of cost, adjusted for baseline dispensing rate and list size.

TABLE 19 Results of economic analysis

Analysis	Adjusted between-arm cost difference	95% CI
Primary economic analysis	−£1999	−£6627 to £2630
Sensitivity analyses		
Per-protocol analysis	−£1724	−£7663 to £4216
LRTI-specific hospital unit costs	−£1892	−£6366 to £2582
Assuming intervention costs of £0	−£2908	−£7221 to £1404

Confidence intervals on differences between arms in cost were calculated from mixed-effect linear regression of cost, adjusted for baseline dispensing rate and for list size.

Although mean NHS costs were lower in the intervention arm, primarily because of the impact of lower hospitalisation costs, all results were consistent with a null effect of the intervention on NHS costs.

This conclusion did not change in any of the sensitivity analyses. Hospitalisation was the largest cost element, and the results of analysis in which a narrower definition of unit costs attributable to admissions was used were similar to the primary analysis. Costs attributable to the intervention itself included training time as well as potential integration and troubleshooting time. Our sensitivity analysis in which we assumed zero costs of the intervention, a possible consequence of long-term use and familiarity of the intervention, was similar to the other between-arm cost comparisons. As noted in *Chapter 3*, the pre-specified per-protocol analysis is likely to be biased by the effect of non-compliance among practices that joined in the second half of the study, during which period the COVID-19 pandemic had reduced dispensing rates.

Discussion

Given the light-touch design of the trial, the economic evaluation of the RCT was limited to a between-arm comparison of mean NHS costs. NHS costs were calculated from the costs of the intervention itself, prescriptions of amoxicillin and macrolides per the co-primary outcome, A&E attendances and hospital admissions. Data were complete. All models – the primary adjusted analysis and sensitivity analyses – were consistent with no effect of the intervention on NHS costs.

Strengths of the economic evaluation

The design of the trial permitted the efficient analysis of very large volumes of data, encompassing millions of dispensed items, and tens of thousands of intervention usages, A&E attendance and hospital admissions. The reliance on routine data for all elements of the economic evaluation met the protocol's objective of assessing the costs of the intervention to the NHS, while reducing the overall costs of the trial.

Limitations of the economic evaluation

The CHICO feasibility trial confirmed the difficulty of obtaining comprehensive, useable quality-of-life data in this young patient population. This reflected both the absence of quality-of-life instruments designed for young children (especially those aged 0–4 years), issues in interpreting quality-of-life measures in this population and the completeness of data collected from parents on behalf of participating children. By design, we did not measure the quality of life of children in this trial. This meant that the present analysis was limited to a comparison of costs, rather than a full economic evaluation.

Without patient-specific information, it was necessary to make assumptions about the type and costs of care received for those children attending A&E and those admitted to hospital. We used

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volume-weighted unit costs to account for uses of this service. This was likely to cause material bias for between-arm cost comparisons only if the composition of care (with respect to complications, comorbidities and any attendant complexity) was markedly different in one arm or another.

Our unit cost data on dispensed amoxicillin and macrolides also involved a compositional assumption. We used unit costs drawn from all dispensed amoxicillin and macrolides in England in the 2020–21 financial year. We, therefore, assumed that the practices included in the trial had the same costs as all other practices in England. We also lacked data on the precise formulation and presentation of dispensed items, but it is not clear that including this information would have had a noticeable impact on between-arm comparisons.

The analysis reported here was – by design – limited to a within-trial evaluation of the impact of the intervention on NHS costs during the 12-month period of trial follow-up. Distal impacts of the intervention on antimicrobial resistance and its associated costs over the long term, a critical motivation for undertaking this work, were not accounted for in the within-trial cost comparison. We also did not intend to evaluate the wider costs to the NHS of a full national roll-out, not least because this would be to presuppose both the efficacy outcome of the trial as well as the interest and capacity of systems providers to integrate the intervention.

Nevertheless, the research team did undertake very preliminary, high-level assessments of how costs might be impacted by a wider deployment of the intervention. Based on discussions with CCG 'Research and Development' staff, it appears that costs related to licensing, maintenance and support would be modest, especially when considered on a per-practice basis. The level of these costs would also depend on the specific way in which providers implemented and provided the intervention to practices. Nevertheless, there appear to be few grounds on which a wider use of the intervention would drastically increase NHS costs relative to the experiences observed in the CHICO trial.

Conclusion

There was no evidence of a difference in mean NHS costs in those practice randomised to use the intervention compared to those that did not. This conclusion held under various sensitivity analyses, including a per-protocol analysis.

Chapter 6 Facilitators and barriers to an efficient design

The problems with conducting research in primary care

Primary care is a difficult environment in which to conduct research. Effective recruitment strategies generally require practitioner involvement[59] but this is difficult in the time allowed for consultations and can lead to the exclusion of patients for whom recruitment might be more challenging and therefore increase the risk of selection bias.[60] In England, general practices are already divided into those who are willing to conduct research and those who are not, which challenges the external validity of any successful trial when rolling out an intervention.[61] The time pressure can be compounded if the intervention is not fully integrated into the practice computer systems; a stand-alone tool takes time to open and close, may not draw upon information already collected within the system and may be less amenable to modification on a wider scale. In primary care research, there are also difficulties in collecting patient outcomes. This is largely dependent on physical access to patient notes and is both costly and time-consuming.

In this section, we look at some of the facilitators and barriers to an efficiently designed trial including semistructured interviews with three members of a CRN network and two from CCGs involved in the set-up of CHICO using a framework approach.[62]

Recruiting practices

Practices were recruited using the national network of all 15 CRNs in England and 47 of the 211 CCGs covering the English regions in 2019. Of the 310 practices required, 294 were recruited over a 24-month period (initially we allowed 12 months for this).

Facilitators to recruitment

The 15 CRNs were helpful with the recruitment of practices; presenting our study at CRN meetings and using the national CRN lead for support helped facilitate a co-ordinated national approach. Some CRNs contact practices that opt-in to conduct research while others contact all the practices in their area. Feedback from 11 of the 15 CRNs suggested around half the practices had joined the Research Sites Initiative scheme (NIHR-funded scheme to enable research delivery) and were often the first to be contacted. Recruitment via CCGs had a wider reach of practices than via CRNs, although CCG participation in recruitment was more variable depending on capacity. Working with these two networks provided a large geographical spread across England (see *Appendix 5*) and provided us with over a quarter of the practices (26%) in the most deprived socioeconomic quintile.

Using quarterly study newsletters for practices, CRNs and CCGs with league tables monitoring levels of recruitment improved responses.

Barriers to recruitment

Recruitment took longer than expected, partly because we had to recruit CCGs first (who provide hospitalisation data for practices). It was difficult to know which individuals to contact and how to do so (some CCGs did not appear to be public-facing), response times were often slow, their role in research was often misunderstood, staff changes hindered communication and a number of CCGs merged during the study period. Some CCGs were averse to getting involved in research or cited lack of capacity as a reason to be excluded from the research.

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> *I mean in reality they [CCG] don't play a major part in – and never actually have a major role in research. It's not a core business of a CCG like it would be in a provider. So we don't have a research department, which is probably why the CHICO trial ended up at my door because it was about prescribing.*
>
> *[P4 CCG]*

At the start of recruitment, October 2018, there were 211 CCGs across England. By the end of follow-up, September 2021, there were only 106 CCGs. While this did reduce the number of CCG contacts required to obtain the data, it sometimes resulted in change of staff who were not familiar with the trial or its requirements.

The level of engagement was much better with CRNs although access to practices was not straightforward. Limiting the contact to practices that want to opt-in to research via some of the CRNs missed the opportunity of letting research-naïve practices know about light-touch efficient design studies. Although other CRNs contacted all practices.

> *I would say that about a third of the practices were what I would call research naïve or inexperienced, green as in they hadn't really had a sort of established relationship with us in the past.*
>
> *[P2 CRN]*

Of the 294 practices we recruited, we are aware of at least 22 practices (7%) who merged during their baseline/follow-up annual data capture. We excluded practices who anticipated a merger with another practice but had no control over this once the practice was randomised, especially in the rare instances when the merging practices were randomised to different arms of the trial. The length of time from expression of interest from practices to randomisation was longer than expected due to the delayed site agreements returned from the practices.

Using routinely collected data for the primary outcomes

The co-primary outcomes in the trial were (1) practice-dispensed prescription data for amoxicillin and macrolide antibiotics for children 0–9 years retrieved from the NHSBSA ePACT2[30] reporting system and (2) hospital admission rate for RTI among 0–9 years routinely collected by all English CCGs. The ascertainment of these data was 99.7% (293/294) for antibiotic dispensing and hospitalisation rates. Data for one practice were only lost due to a merger.

Facilitators to collecting routine data

Using aggregated data avoids the need for the consulting physician to solicit individual consent, reduces or eliminates the risk of selection bias and removes the task of accessing individual patient notes. Routine data are often collected monthly so data completeness and quality can be monitored throughout the collection period, which was particularly important in this trial to scrutinise and report any sudden changes in hospital admission rates to the DMC. The routinely collected data can be imported to data management software; thus, there is less likelihood of data entry errors and missing data are rare. The cost of research staff and time taken to collect the primary outcome data was much reduced compared to a traditional trial. In total 11/294 practices asked to be withdrawn from the study (3.7%) and 14/294 (4.8%) were lost to follow-up from the study; the main reasons cited being lack of capacity and prioritising the COVID-19 pandemic. A further advantage of collecting routine data is that withdrawal of a practice does not necessarily mean a loss of the primary outcome data for that practice (if the data are already in the public domain).

Barriers to collecting routine data

A potential problem with aggregate data collected from a third party is where data are suppressed, owing to a low number of events, although in this study data were collected over a 12-month period largely avoiding this problem. Some liaison was needed between the trial team and the CCGs to know exactly what data were available and in what format this could be presented needing additional time to import and utilise data from different formats. Dispensed prescription data, practice list size data and hospital admission data are reliable as they feed into financial transactions; however, data reporting A&E attendance were less so due to a limited coding set. Many A&E attendances do not have a diagnosis coded; therefore, the number of attendances attributable to RTI is likely to be inaccurate.

Integrating the intervention within the electronic medical record system

The trial only included practices using the EMIS® system. The practice champion was given written instructions on how to install the intervention within EMIS®. Intervention use was monitored using searches on the EMIS® system, run by the practice champion and shared with the research team.

Facilitators to integrating the intervention

Installation of the intervention was relatively straightforward for EMIS®. Practice systems allow for user-friendly manipulation so interventions can be integrated and interfaced with system data already collected; thus, negating any additional clinical workload. Screen pop-ups can also be used to notify clinicians of eligible patients for the study.

Barriers to integrating the intervention

Familiarity with the EMIS® system varied between practices; thus the level of support required from the research team to help install the intervention and download usage also varied. Provision to help install or use third-party algorithms is not offered by system providers. EMIS® upgrades to the system during the trial meant that rewriting installation instructions, resources and testing had to be carried out and fed back to the practices. For instance, the READ codes used to identify clinical terms within consultations were upgraded to SNOMED codes by EMIS® in the early months of 2020, which meant the algorithm had to be amended so the intervention would function correctly. We found that our funded provision of IT support throughout the study was crucial to the smooth running of the integrated intervention. Although pop-ups can be used, some clinicians found them irritating and switched them off while other practices had so many pop-ups (especially during the COVID-19 pandemic) that the CHICO pop-up was often obscured.

A light-touch approach to data collection

Clinicians were not required to provide any data about individual participants (apart from reporting SAEs), those in the intervention group were asked to familiarise themselves with the tool and use it, while those in the control arm were asked to provide usual care. Data collection from the practices directly was limited to short baseline and follow-up questionnaires. Data on intervention usage were downloaded from EMIS® and the co-primary outcome was downloaded from ePACT2 and the relevant CCGs.

Facilitators to a light-touch approach

The light-touch approach reduced the time needed during consultation to record information, the trawling of patient notes and provided a more objective data resource downloaded from the system rather than from individual input. Practice champions, familiar with practice systems, played an important role in obtaining the required data and training clinicians in the use of the intervention. Baseline questionnaires were received from 294/294 practices (100%), follow-up questionnaires were received from 265/294 practices (90%) while intervention usage was collected from 116/144 of the intervention practices (81%), indicating the data burden was not too onerous. Training consisted of a brief conversation between the practice champion and clinicians, signposting to further information available if needed and a 1-month run-in period before data collection where clinicians could familiarise themselves with the intervention. Feedback suggested the clinicians were happy in terms of training to use the intervention tool.

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Barriers to a light-touch approach

Conversely, this approach reduced the level of interpretation that can be gleaned from the data. Removing patient-level recruitment results in a loss of denominator data, in our case not knowing how many individual children consulted for RTI and cough. As a proxy, we used the number of children registered at each practice. Given the diversity of the practices included in the trial, we are assuming that those children taking part in the trial were no different from children in the general population, but we have no way of testing this assumption. We also lost detail that may be taken from the consultation of whether antibiotics were prescribed immediately or delayed relying instead on the number of antibiotics being dispensed. The lack of contact with control practices (apart from reminders to provide SAE reports) also ran the risk of practices wanting to withdraw from the study, especially with changes of staff. Several strategies were needed to obtain follow-up paperwork back from practices, including help from the CRN network and the managed recovery team, newsletters and time and resources spent trying to contact the practices at varying times and days. Consideration also needs to be given to the ethical implications of not seeking consent from individual patients. We asked sites to display posters informing patients the research was taking place and no concerns were raised but we did not proactively seek a response on this issue.

Chapter 7 Discussion

Summary and interpretation of the main findings

There was no evidence overall that the antibiotic dispensing rate, for amoxicillin or macrolides, in the intervention practices differed from practices in the control arm. There were no differences seen in the rate of hospitalisations for RTI between study arms. Subgroup analyses did show decreased dispensing rates in the intervention arm for older children and increased rates in the younger children. This analysis also showed decreased dispensing rates in the intervention arm for practices restricted to one site, in less deprived areas and proportionally fewer nurse practitioners. Conversely, the intervention arm increased practice dispensing rates in those practices with more than one site, situated in the more deprived areas and where there was a higher proportion of nurse practitioners. Intervention use was low in relation to the likely number of children in whom it could have been used. The impact of the COVID-19 pandemic on the trial was noticeable in terms of the primary outcomes and made interpretation of the findings more difficult. Impact of the COVID-19 pandemic on dispensing rates and intervention usage

Follow-up data were collected from practices over a 35-month period from November 2018 to September 2021 which included a 19-month period from March 2020, when the pandemic spread across England. Taking account of seasonal fluctuation, by focusing on the 12-month periods before and after 1 March 2020, the average dispensing rate in the control practices halved from 20.55 items per 100 children (95% CI 19.64 to 21.46) to 9.84 items per 100 children (95% CI 9.18 to 10.50). A similar reduction was also evident among the intervention practices but would make any differences between the two arms more difficult to distinguish. The pandemic also had an impact on intervention usage. Prior to March 2020, the median usage per month, per intervention practice, was nine uses. Post March 2020, the median usage per month, per practice, was zero. Half of the practices questioned responded that there had been months where they were unable to use the intervention or they had limited usage. The qualitative interviews with the clinicians also suggested the changing patterns of consultations in practices affected the number of children being seen face to face, while school closures caused a slowdown in RTI infections and thus reduced consultations. A post hoc sensitivity analysis focused on the months of data collected prior to the pandemic and showed reduced dispensing in the intervention arm compared to the control arm, that did provide statistical evidence of a difference. However, the absolute difference was so small the clinical benefit would be negligible. There was also a correlation between increased intervention usage and decreased dispensing rates in the pre-pandemic data collected but again the number of practices was too low to draw any conclusions. Although the impact of the pandemic does not invalidate our main findings, it does question just how negative these findings may have been in the absence of the pandemic.

Impact of the COVID-19 pandemic on hospitalisation rates

The effects of COVID-19, and its associated lockdowns on hospitalisation admission were clear. From April 2020, the rates dropped and only started to climb back towards normal levels in the summer of 2021 when the rates were unseasonably high. A similar pattern was observed for A&E attendance. Despite these uncommon fluctuations, the rates for attendance and admission were similar for both arms of the trial.

How the intervention was received

Intervention usage over time

The intervention was used nearly 12,000 times in the trial with a median average of 70 uses per practice. It was difficult to gauge usage over the 12-month follow-up period, given the seasonal influence and impact of the pandemic, although the data suggest usage fell after the first few months

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and slightly picked up towards the end of follow-up. The qualitative interviews confirmed that clinicians used the intervention at the start of the trial, but usage waned over time. We did not collect data on how many RTI consultations were conducted in the trial. A rough estimate can be made from the dispensing data and intervention practice characteristics if we assume the dispensed items were all for RTI consultations and 50% of the children consulting were given these items. The dispensing rate in the intervention arm was 15.5 items per 100 children, given the median number of 0–9-year-olds was 975 children in 144 intervention practices, this yields 21,762 dispensed items and 43,524 consultations for RTI. This is purely speculative but would suggest the 11,944 uses of the intervention was around 1 in every 4 consultations. The qualitative interviews suggested some clinicians found the intervention most useful in 'borderline cases', which suggests clinicians may have been selective in terms of when they used the tool and partly explains the low usage.

Acceptance of the intervention

Generally the intervention was easy to use and few thought it unhelpful; nearly three-quarters suggested they would use the intervention again, if it became available. The qualitative interviews suggested the clinicians liked the algorithm template and found it straightforward to use, without adding any more time to consultations. Clinicians particularly liked the safety-netting parental advice leaflet, as it helped explain treatment decisions and home care with parents and this was seen to be the most useful intervention component. While some clinicians reported that the intervention influenced prescribing decisions, others reported that they used it as a supportive aid during consultations rather than a tool to change prescribing behaviour. Some clinicians reported the intervention interrupted the consultation flow, having to close the patient's record before the end of the consultation to complete the intervention process, which did not always align with clinicians' usual processes.

Strengths and limitations

The CHICO study demonstrated that an efficiently designed practice-level large trial in primary care using routinely collected data was feasible and potentially good value for money. The average cost of an NIHR RCT was £1.25 million in 2019–20,[63] whereas the cost of the CHICO RCT, which included over 300,000 children (5% of the entire national 0–9-year-old population) was below £1 million. The study was geographically widespread recruiting 4% of all GP practices in England. Using different recruitment strategies[64] and existing networks such as the CRNs helped recruit some research-naïve practices and gave us a sample that reflected the national breakdown of practices located in more socioeconomically deprived areas. Conducting the trial at the practice level removed the need for patient recruitment and potential for recruitment differential between arms while focusing the clinician's time on using the intervention, reflecting real-life practice. Utilising routinely collected data as the primary outcome reduced problems with missing data while removing the burden of searching through patient notes. Integrating the intervention within the practice system both exploited the data already available and added to the patient's record avoiding duplicating of effort and saved time. Primary care practices are often very busy and the average length of face-to-face consultation in the UK is around 10 minutes; less than half the time given to patients in, for example, Sweden and the USA.[65] Thus, embedding the intervention and avoiding patient recruitment protected the limited time available within the consultation. The NIHR is keen to see more efficient, innovative studies which provide robust evidence to inform clinical practice and policy,[66] and this trial is a good example of that.

Efficient design studies are not suitable if individual patient consent is required and face their own challenges in the changing landscape of primary care in England. Around 2.5% of practices close or merge each year while some new practices open and recognition of the current research portfolio within practices, especially when signing up to a trial, needs to be part of this process.[67] We were also surprised by the wide variability in practice list size, 8% of practices in the study having three sites or more. The expansion of multisite practices has implications for future trials in terms of factoring in variable list sizes for sample size calculations and checking that multiple sites use the same electronic record systems. For these larger multiple-site practices further provision may be needed; in terms of training, monitoring and data collection a practice champion might be required for each of the different sites.

Growing demands on primary care services have also led to policymakers promoting telephone and video consultations, even before the COVID-19 pandemic, and these sometimes do not lend themselves to enlisting patients in research.[68] Interventions like ours, that require face-to-face consultations, cannot be used if the child cannot be assessed and future studies need to take into account this changing landscape of consultations. Embedding the intervention within the record system makes it easier for clinicians to use and to monitor use but also means that IT support is needed, especially if the system manufacturers make changes that might impact on intervention use. Utilising CCGs to collect one of the primary outcomes also added an extra layer of recruitment in that we needed to get CCGs on board before we could recruit practices in their area. The number of CCGs in England almost halved during the study period due to organisational restructuring which made it difficult to administer the trial. There was also a lack of uniformity when approaching these commissioning groups and their role in research needed clarifying.[69] Another limitation of the design was the allowance for a delayed start date. While this was rare in the control arm (3%), a quarter of intervention practices delayed their start date resulting in a 'gap' between their baseline and follow-up period. In the majority of cases, this was to allow the practice more time to implement the intervention due to staffing/resource issues caused by COVID-19.

One of the main limitations of a light-touch approach to data collection is the loss of detail available for analysis. Losing denominator data such as patients consulting for different conditions will depend on the hypothesis being tested and needs to strike a balance between the accuracy of what you are trying to measure and whether a proxy marker will deliver the population impact of the intervention. Using the number of 0–9-year-olds registered at the practice as a denominator accounted for variation in practice size but meant we could not measure the number of children consulting for RTI, which is both a more precise denominator and a metric for measuring intervention usage. The routinely collected dispensing data served as a robust proxy marker for prescribing data but cannot distinguish between immediate and delayed prescriptions, nor antibiotics prescribed for non-RTI indications. Fidelity in this study was also difficult to measure; we monitored intervention usage from symptoms recorded but not how the different components of this complex intervention were used or how long this took. Our light-touch approach meant we did not record the number of RTI consultations or have any means to investigate the nature of these consultations and how this was associated with intervention usage which would have been particularly useful given the impact of the COVID-19 pandemic. We estimate that our intervention was used in approximately one in four consultations. The qualitative interviews suggest clinicians often used the intervention for borderline cases which reflects our advice that the intervention should just be one tool used in the toolbox to deal with these consultations and partly explains why the average use of the intervention was just 70 per practice over 12 months. Finally, an unavoidable limitation is that we have not included the effects of antimicrobial resistance. Antimicrobial resistance is a long-term problem where the overuse of antibiotics may lead to greater resistance for many common diseases, which in turn will have long-term and extensive adverse impacts on health. This RCT is part of a preventative strategy to reduce this potential by testing the efficacy of a tool that may reduce the use of antibiotics. To test any effects on whether we are reducing the problem of antimicrobial resistance would need a different study design over many more years.

Comparison with other literature

Antimicrobial stewardship interventions can seek to either change the type of antibiotic prescribed, and/or reduce the quantity of antibiotics prescribed. Most existing literature focuses on the latter (quantity) with a recent systematic review synthesising the evidence for interventions targeted at reducing antibiotic prescribing for respiratory infections.[70] This identified four types of intervention with moderate-strength evidence of reduced antibiotic prescribing compared with usual care. These were: (1) clinic-based parent education (21% overall prescribing reduction; similar return visits); (2) public patient education campaigns combined with clinician education (7% reduction in overall prescribing);

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(3) procalcitonin point-of-care testing in adults (12–72% overall prescribing reduction); and (4) electronic decision support systems (5–9% reduction in overall prescribing).

We previously showed that interventions were most likely to be effective in children with respiratory infections if they (1) target both parents and clinicians during consultation; (2) provide automatic prescribing prompts; and (3) include clinician leadership in the intervention design.[16]

The present study used an electronic decision support system intended to reduce antibiotic prescribing (and therefore dispensing) in children at very low risk of hospitalisation in the 30 days following consultation, finding no evidence of overall reductions in antibiotic dispensing.

We are aware of one other UK study resembling CHICO. The REDUCE cluster randomised trial also randomised GP practices to receive an electronic medical record embedded decision support tool aiming to reduce antibiotic prescribing for respiratory infections. It found evidence that the intervention was effective in adults (15–84 years) but, as with our study, did not find evidence of reduced prescribing in children (0–14 years, nor adults aged > 84 years). This study also monitored safety by reporting hospital admissions for serious bacterial infections, finding no evidence these were increased in the intervention group.[71]

The reduction in consultation and antibiotic dispensing rates we observed between pre-pandemic and pandemic periods is consistent with that reported in a number of other studies, both in the UK and globally.[72–74]

Implications for policy, clinical practice and research

While showing promise in some subgroups, we did not find evidence to support the widespread adoption of the CHICO intervention in routine clinical practice. We suspect the main reasons for ineffectiveness were: (1) relatively low frequency of intervention use in relation to the number of children presenting in whom it could have been used; (2) the purpose of the algorithm element of the intervention not being entirely clear to intervention clinicians (to identify children at very low risk of future hospitalisation in whom antibiotics could be safely withheld); and (3) problems with delivery timing of the intervention (often not being presented to the clinician until after the consultation end).

Electronic medical record providers could improve intervention effectiveness if platforms could improve timing of intervention delivery (e.g. decision aids appearing before consultations are closed). Although the intervention does not appear to change prescribing behaviour, elements of the approach may be used in the design of future interventions. Further research is also needed to develop and evaluate effective electronic record-based antimicrobial stewardship interventions for children, who appear to be a ‘hard to reach’ group with regard to this methodology.

Conclusion

Embedding a multifaceted intervention into general practice for children presenting with acute cough and RTI did not reduce antibiotic dispensing or impact on hospital attendance for RTI. There was weak evidence of reduced dispensing levels in the intervention arm prior to the COVID-19 pandemic although the numbers were small. Inference of the findings was made difficult as the pandemic affected intervention usage, dispensing levels and hospital attendance, and it could be argued that the pandemic critically impacted the ability of the trial to demonstrate its intended outcome. The clinicians liked the intervention and used it as a supportive aid during consultations rather than a tool to change behaviour. The use of an efficient design was successful in this trial suggesting using routinely collected data for primary outcomes at the practice level is viable in England. An infrastructure for recruiting practices is in place and with more investment should be promoted for primary care research where appropriate.

Acknowledgements

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Contributions of authors

Peter S Blair (https://orcid.org/0000-0002-7832-8087) (Professor of Epidemiology and Statistics) was chief investigator for the trial, and as such participated in its design, was responsible for oversight of the trial and wrote this final report.

Grace J Young (https://orcid.org/0000-0002-5210-1183) (Medical Statistician) was the trial statistician, involved in writing the statistical analysis plan, co-ordinating data collection and conducting the statistical analysis.

Clare Clement (https://orcid.org/0000-0002-5555-433X) (Qualitative Researcher) was the qualitative researcher for the trial, involved in managing and conducting the qualitative analysis.

Padraig Dixon (https://orcid.org/0000-0001-5285-409X) (Health Economist) was a co-applicant, and health economist for the trial, involved in designing, managing and conducting the health economic evaluation.

Penny Seume (https://orcid.org/0000-0001-9407-5828) (Trial Manager) was responsible for managing the trial, acquisition of data and contributing to aspects of trial design.

Jenny Ingram (https://orcid.org/0000-0003-2366-008X) (Qualitative Researcher) was a co-applicant, and one of the lead qualitative researchers for the trial, involved in the design of the trial and qualitative analysis.

Jodi Taylor (https://orcid.org/0000-0001-7171-8923) (Head of Trial Operations) contributed to aspects of the trial design, and was involved in the day-to-day management of the trial.

Jeremy Horwood (https://orcid.org/0000-0001-7092-4960) (Qualitative Researcher) was a co-applicant, and one of the lead qualitative researchers for the trial, involved in the design of the trial and qualitative analysis.

Patricia J Lucas (https://orcid.org/0000-0002-0469-8085) (Behavioural Scientist) was a co-applicant and involved in the design of the trial, behavioural modelling and development of the intervention.

Christie Cabral (https://orcid.org/0000-0002-9884-0555) (Qualitative Researcher) was a co-applicant and involved in the design of the trial, development of the intervention and qualitative analysis.

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Nick A Francis (https://orcid.org/0000-0001-8939-7312) (Professor of Primary Care Research) was a co-applicant and involved in the design of the trial and provided expertise in practice-based RTI interventions.

Elizabeth Beech (https://orcid.org/0000-0001-7288-1167) (NHS Antimicrobial Stewardship Lead) was a co-applicant, involved in the design of the trial, acquisition of data and provided expertise in the collection of routine data.

Martin Gulliford (https://orcid.org/0000-0003-1898-9075) (Professor of Public Health) was a co-applicant, involved in the design of the trial and provided expertise on routine data analysis.

Sam Creavin (https://orcid.org/0000-0002-6772-7111) (GP and Clinical Research Fellow) was a co-applicant, involved in the design of the trial and provided expertise in EMIS® systems and development of the intervention.

Janet A Lane (https://orcid.org/0000-0002-7578-4925) (Reader in Trials Research, codirector of the BRTC) was a co-applicant, contributed to the trial design and was involved in management of the study.

Scott Bevan (https://orcid.org/0000-0002-4567-5111) (Trial Manager) was responsible for managing the trial during the first 18 months and contributed to aspects of trial design.

Alastair D Hay (https://orcid.org/0000-0003-3012-375X) (GP and Professor of Primary Care Research) was a co-applicant and clinical lead, who initiated the idea and led the development with a NIHR Programme grant. He was involved in the design of the trial, further development of the intervention and co-wrote parts of the final report.

All authors read, approved and/or commented on the final report.

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Dissemination

We are planning to write to all the GP practices, CCGs and CRNs that have been involved in the study with a brief summary of the main findings the day before either the final report or the peer-reviewed paper is published. We have also submitted two abstracts of our main findings (quantitative and qualitative) for oral presentation to the Society of Academic Primary Care (SAPC) national conference held in Lancaster in July 2022:

Blair PS, Young G, Seume P, Ingram J, Clement C, Taylor J, Cabral C, Lucas PJ, Beech E, Horwood J, Dixon P, Gulliford M, Francis N, Creavin S, Lane AJ, Bevan S, Hay AD. (2022), Evaluation of a complex intervention to improve antibiotic prescribing for CHIldren presenting to primary care with acute

COugh and respiratory tract infection: the CHICO randomised controlled trial. *Submitted to the Society for Academic Primary Care (SAPC ASM) 50th Annual Scientific Meeting, University of Central Lancashire, 4–6 July.*

Clement C, Ingram J, Cabral C, Blair PS, Lucas P, Hay AD, Seume P, Horwood J. (2022), What are clinician's views and experiences of implementing a complex intervention to inform antibiotic prescribing in children with respiratory tract infections in primary care? *Submitted to the Society for Academic Primary Care (SAPC ASM) 50th Annual Scientific Meeting, University of Central Lancashire, 4–6 July.*

We have presented one abstract of preliminary findings at the South-West SAPC Conference 2020:

Clement C, Ingram J, Cabral C, Blair PS, Lucas P, Horwood J. (2020), Clinicians views and experiences of implementing a complex intervention to reduce antibiotic prescribing in children with Respiratory Tract Infections in primary care. *Submitted to the Society for Academic Primary Care South-West (SAPC SW) Annual Research Meeting, Bristol, UK, 6 March.*

Two abstracts of preliminary findings at the South-West SAPC Conference 2021:

Seume P, Young G, Ingram J, Lucas P, Taylor J, Hay AD, Dixon P, Creavin S, Horwood J, Lane AJ, Beech E, Blair PS. (2021), An efficiently designed RCT in primary care clustered at the practice level using routinely collected CCG data as the primary outcome: barriers and facilitators from the CHIldren's COugh (CHICO) study. *Submitted to the Society for Academic Primary Care South-West (SAPC SW) Annual Research Meeting, University of Warwick Onlin,e 18 March.*

Clement C, Ingram J, Cabral C, Blair PS, Lucas P, Hay AD, Seume P, Horwood J. (2021), Clinicians' views and experiences of implementing a complex intervention to inform antibiotic prescribing in children with respiratory tract infections in primary care. *Submitted to the Society for Academic Primary Care South-West (SAPC SW) Annual Research Meeting, University of Warwick Online, 18 March.*

One abstract of preliminary findings at the South-West SAPC Conference 2022:

Seume P, Blair PS, Ingram J, Clement C, Young G, Taylor J, Cabral C, Lucas PJ, Beech E, Horwood J, Dixon P, Gulliford M, Francis N, Creavin S, Lane AJ, Bevan S, Hay AD. (2022), A more efficient approach to randomised controlled trials in primary care using routinely collected practice-level data. *Submitted to the Society for Academic Primary Care South-West (SAPC SW) Annual Research Meeting, University of Exeter (Online), 10–11 March.*

We have one paper describing the protocol published:

Seume P, Bevan S, Young G, Ingram J, Clement C, Cabral C, Lucas PJ, Beech E, Taylor J, Horwood J, Dixon P, Gulliford MC, Francis N, Creavin ST, Lane AJ, Hay AD, Blair PS. Protocol for an 'efficient design' cluster randomised controlled trial to evaluate a complex intervention to improve antibiotic prescribing for CHIldren presenting to primary care with acute COugh and respiratory tract infection: the CHICO study. *BMJ Open*. 2020 April **11**(3). http://bmjopen.bmj.com/cgi/content/full/bmjopen-2020-041769.

One paper describing the efficient design has now published:

Blair PS, Ingram J, Clement C, Young G, Seume P, Taylor J, Cabral C, Lucas P, Beech E, Horwood J, Dixon P, Gulliford M, Francis N, Creavin S, Lane A, Bevan S, Hay AD. A more efficient approach to randomised controlled trials in primary care using routinely collected practice-level data. *BMJ Open* 2022;**12**(7):e061574.

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And we have submitted our main findings to the BMJ.

Blair PS, Young G, Clement C, Dixon P, Seume P, Ingram J, Taylor J, Cabral C, Lucas PJ, Beech E, Horwood J, Gulliford M, Francis NA, Creavin S, Lane JA, Bevan S & Hay AD. A multifaceted intervention to improve management of antibiotics for CHIldren presenting to primary care with acute COugh and respiratory tract infection (CHICO): an efficient cluster randomised controlled trial. Submitted to the *BMJ*, August 2022.

We intend to submit a separate qualitative paper.

Data-sharing statement

This study used secondary data which can be obtained from the NHS digital website and NHSBSA ePACT2 website (https://www.nhsbsa.nhs.uk/access-our-data-products/epact2) (accessed 5 September 2022) for practice-level list sizes and dispensing data by practice, respectively. The hospitalisation data are not available for redistribution as it was not agreed as part of the contracts with the CCGs. For any further information, please contact the corresponding author.

Equality, diversity and inclusion

The CHICO research team was a multidisciplinary team made up of clinical academics, child health researchers, clinical trial methodologists, statisticians, health economists, qualitative researchers and a NHS antimicrobial stewardship lead. Practices were recruited from every CRN in England, in an effort to gain a representative sample of general practices and also involve less 'research active' practices. Involvement at the CRN/CCG level, insured that all practices were provided with an opportunity to take part. Any EMIS® practice was eligible but those using alternative electronic health systems could not be included. The patient leaflet was translated into other languages (Punjabi and Urdu) so that non-English-speaking families could take part.

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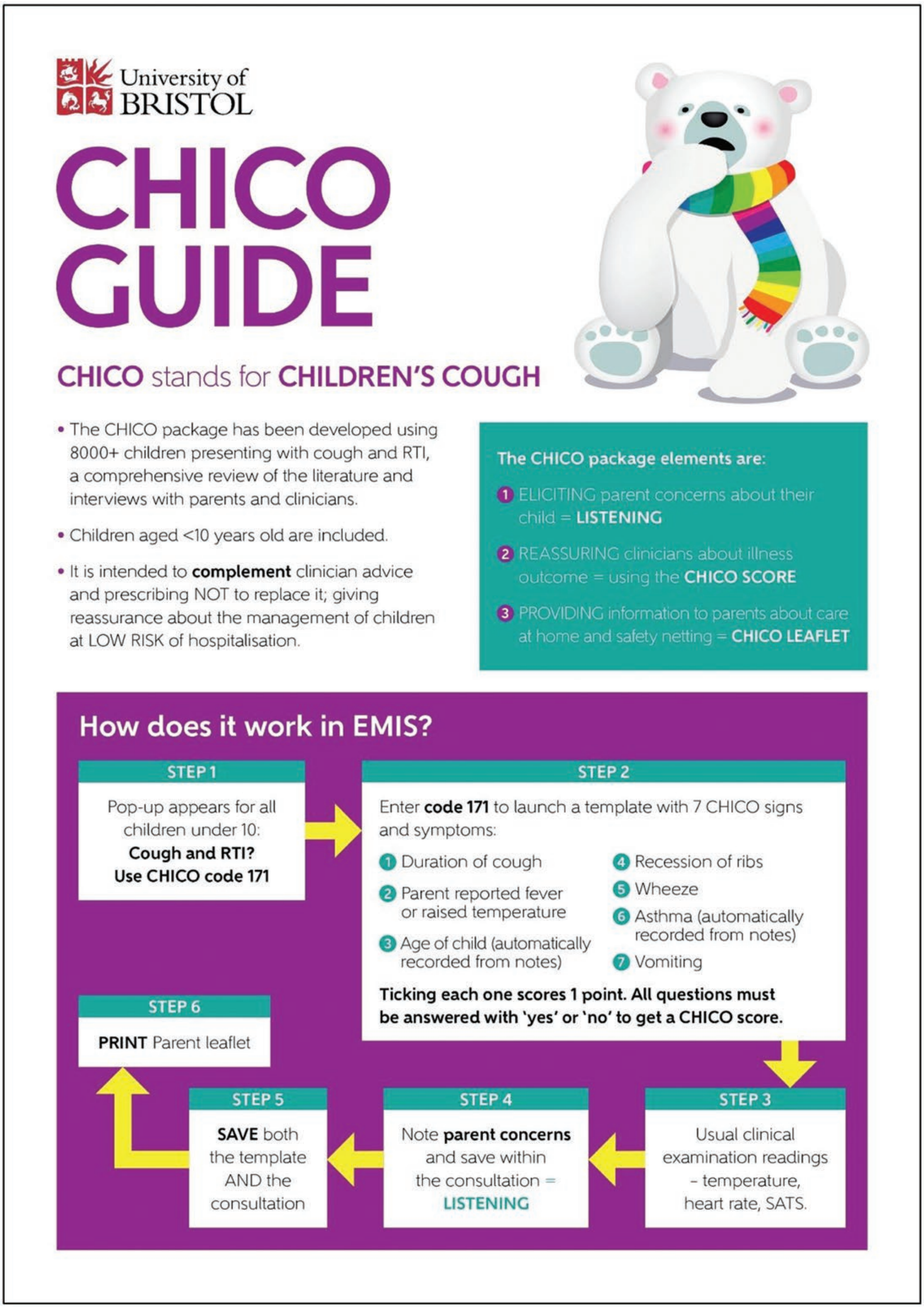
Appendix 1 Clinician's guide



University of BRISTOL

CHICO GUIDE

CHICO stands for **CHILDREN'S COUGH**

- The CHICO package has been developed using 8000+ children presenting with cough and RTI, a comprehensive review of the literature and interviews with parents and clinicians.
- Children aged <10 years old are included.
- It is intended to **complement** clinician advice and prescribing NOT to replace it; giving reassurance about the management of children at LOW RISK of hospitalisation.

The CHICO package elements are:

① ELICITING parent concerns about their child = **LISTENING**

② REASSURING clinicians about illness outcome = using the **CHICO SCORE**

③ PROVIDING information to parents about care at home and safety netting = **CHICO LEAFLET**

How does it work in EMIS?

STEP 1

Pop-up appears for all children under 10:
Cough and RTI?
Use CHICO code 171

STEP 2

Enter **code 171** to launch a template with 7 CHICO signs and symptoms:

① Duration of cough
② Parent reported fever or raised temperature
③ Age of child (automatically recorded from notes)
④ Recession of ribs
⑤ Wheeze
⑥ Asthma (automatically recorded from notes)
⑦ Vomiting

Ticking each one scores 1 point. All questions must be answered with 'yes' or 'no' to get a CHICO score.

STEP 3

Usual clinical examination readings – temperature, heart rate, SATS.

STEP 4

Note **parent concerns** and save within the consultation = **LISTENING**

STEP 5

SAVE both the template AND the consultation

STEP 6

PRINT Parent leaflet

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REASSURING parents about illness outcome = using the CHICO SCORE

The 7 CHICO signs produce a CHICO score to indicate the probability that the child will be hospitalised for RTI in next 30 days.

CHICO SCORE	ADDITIONAL TEXT IN HOVER SCREEN
0 or 1 LOWEST risk group	VERY REASSURING CHICO score: **0 or 1** predictors: > 99.6% of children will recover from this illness with home care. **Consider no** or **delayed antibiotic prescribing strategy.** CHICO leaflet covers common concerns and safety netting.
2 or 3 AVERAGE risk group	REASSURING CHICO score: **2 or 3** predictors: > 98% of children will recover from this illness with home care. **Consider no** or **delayed antibiotic prescribing strategy.** CHICO leaflet covers common concerns and safety netting.
4+ ELEVATED risk group	SAFETY NETTING NEEDED: **4 +** CHICO predictors. This is more than average, but > 87% children will still recover from this illness with home care. **Highlight SAFETY NETTING advice in CHICO leaflet.**

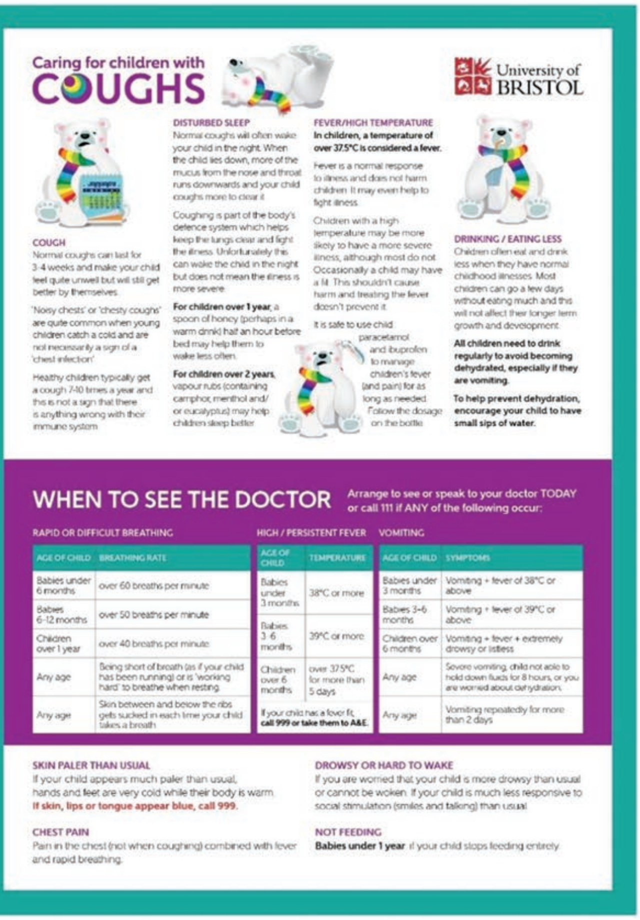
PROVIDING information about care at home/ safety netting = CHICO LEAFLET

Parent leaflet can be generated after saving consultation:
- given as pre-printed leaflet;
- or added to a personal letter.

Leaflet has the 4 most **common concerns** about childhood cough - duration, sleeping, vomiting, not eating or drinking.

With a safety netting section on **'When to see the doctor'**

Two versions of the letter can be printed for patients without and with antibiotic prescriptions.



Caring for children with

COUGHS

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COUGH

Normal coughs can last for 3-4 weeks and make your child feel quite unwell but will still get better by themselves.

'Noisy chests' or 'chesty coughs' are quite common when young children catch a cold and are not necessarily a sign of a 'chest infection'.

Healthy children typically get a cough 7-10 times a year and this is not a sign that there is anything wrong with their immune system.

DISTURBED SLEEP

Normal coughs will often wake your child in the night. When the child lies down, more of the mucus from the nose and throat runs downwards and your child coughs more to clear it.

Coughing is part of the body's defence system which helps keep the lungs clear and fight the illness. Unfortunately this can wake the child in the night but does not mean the illness is more severe.

For children over 1 year, a spoon of honey (perhaps in a warm drink) half an hour before bed may help them to wake less often.

For children over 2 years, vapour rubs (containing camphor, menthol and/ or eucalyptus) may help children sleep better.

FEVER/HIGH TEMPERATURE

In children, a temperature of over 37.5°C is considered a fever.

Fever is a normal response to illness and does not harm children. It may even help to fight illness.

Children with a high temperature may be more likely to have a more severe illness, although most do not. Occasionally a child may have a fit. This shouldn't cause harm and treating the fever doesn't prevent it.

It is safe to use child paracetamol and ibuprofen to manage children's fever (and pain) for as long as needed. Follow the dosage on the bottle.

DRINKING / EATING LESS

Children often eat and drink less when they have normal childhood illnesses. Most children can go a few days without eating much and this will not affect their longer term growth and development.

All children need to drink regularly to avoid becoming dehydrated, especially if they are vomiting.

To help prevent dehydration, encourage your child to have small sips of water.

WHEN TO SEE THE DOCTOR

Arrange to see or speak to your doctor TODAY or call 111 if ANY of the following occur:

RAPID OR DIFFICULT BREATHING

AGE OF CHILD	BREATHING RATE
Babies under 6 months	over 60 breaths per minute
Babies 6-12 months	over 50 breaths per minute
Children over 1 year	over 40 breaths per minute
Any age	Being short of breath (as if your child has been running) or is 'working hard' to breathe when resting
Any age	Skin between and below the ribs gets sucked in each time your child takes a breath

HIGH / PERSISTENT FEVER

AGE OF CHILD	TEMPERATURE
Babies under 3 months	38°C or more
Babies 3-6 months	39°C or more
Children over 6 months	over 37.5°C for more than 5 days
If your child has a fever fit, **call 999 or take them to A&E.**	

VOMITING

AGE OF CHILD	SYMPTOMS
Babies under 3 months	Vomiting + fever of 38°C or above
Babies 3-6 months	Vomiting + fever of 39°C or above
Children over 6 months	Vomiting + fever + extremely drowsy or listless
Any age	Severe vomiting, child not able to hold down fluids for 8 hours, or you are worried about dehydration.
Any age	Vomiting repeatedly for more than 2 days

SKIN PALER THAN USUAL

If your child appears much paler than usual, hands and feet are very cold while their body is warm.
If skin, lips or tongue appear blue, call 999.

CHEST PAIN

Pain in the chest (not when coughing) combined with fever and rapid breathing.

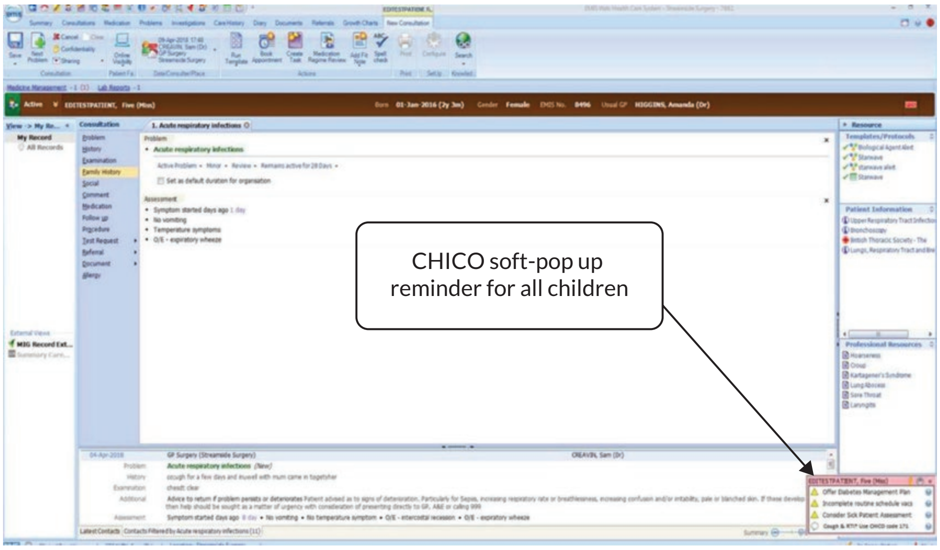
DROWSY OR HARD TO WAKE

If you are worried that your child is more drowsy than usual or cannot be woken. If your child is much less responsive to social stimulation (smiles and talking) than usual.

NOT FEEDING

Babies under 1 year: if your child stops feeding entirely.

Appendix 2 View of template on Egton Medical Information Systems screen during consultation



CHICO soft-pop up reminder for all children

EDITESTPATIENT, Five (Miss)

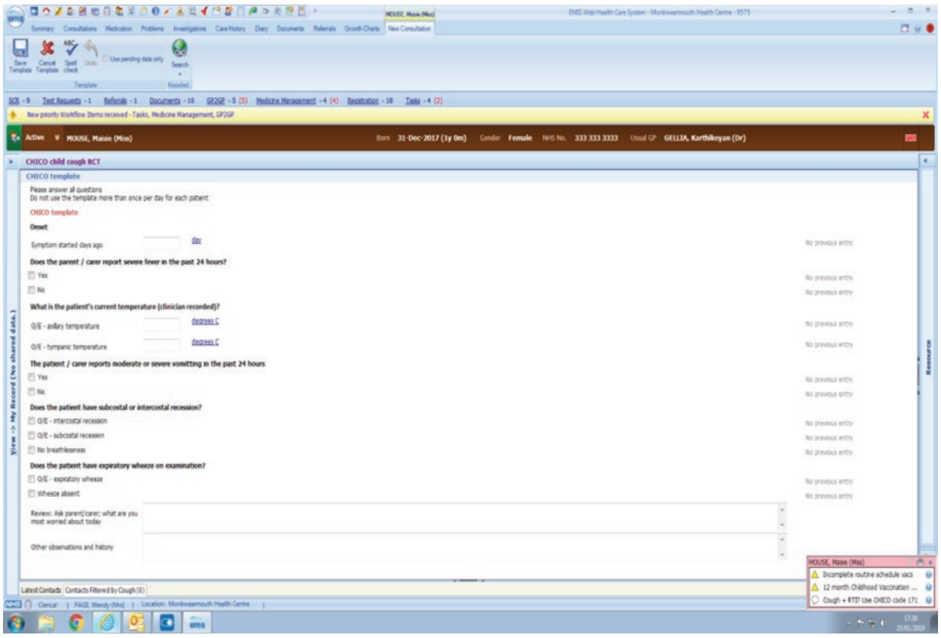
Offer Diabetes Management Plan

Incomplete routine schedule vacs

Consider Sick Patient Assessment

Cough & RTI? Use CHICO code 171

FIGURE 23 Soft pop-up reminder.



Save Template
Cancel Template
Spell check
Undo
Use pending data only
Search
SCR - 9
Test Requests - 1
Referrals - 1
Documents - 10
GP2GP - 5 (5)
Medicine Management - 4 (4)
Registration - 18
Tasks - 4 (2)

New priority Workflow Items received - Tasks, Medicine Management, GP2GP

Active MOUSE, Maisie (Miss) Born 31-Dec-2017 (1y 0m) Gender Female NHS No. 333 333 3333 Usual GP GELLIA, Karthikeyan (Dr)

CHICO child cough RCT

CHICO template

Please answer all questions
Do not use the template more than once per day for each patient

CHICO template

Onset

Symptom started days ago ___ day

Does the parent / carer report severe fever in the past 24 hours?

☐ Yes
☐ No

What is the patient's current temperature (clinician recorded)?

O/E - axillary temperature ___ degrees C
O/E - tympanic temperature ___ degrees C

The patient / carer reports moderate or severe vomiting in the past 24 hours

☐ Yes
☐ No

Does the patient have subcostal or intercostal recession?

☐ O/E - intercostal recession
☐ O/E - subcostal recession
☐ No breathlessness

Does the patient have expiratory wheeze on examination?

☐ O/E - expiratory wheeze
☐ Wheeze absent

Review: Ask parent/carer; what are you most worried about today

Other observations and history

MOUSE, Maisie (Miss)

Incomplete routine schedule vacs

12 month Childhood Vaccination ...

Cough + RTI? Use CHICO code 171

No previous entry
View -> My Record (No shared data.)
Resource
Latest Contacts
Contacts Filtered by Cough (0)
Clinical
PAGE, Wendy (Mrs)
Location: Monkwearmouth Health Centre

FIGURE 24 Algorithm template.

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Appendix 3 Egton Medical Information Systems resources set-up guide

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CHICO: EMIS Web Template Manager Import guide

This EMIS Web Import guide and provides a descriptive step-by-step process for importing the CHICO intervention into EMIS Web.

The CHICO intervention involves a complex algorithm and multiple files to import. The tool will only function properly if the importing steps are followed in the correct order, deviation may prevent further imports.

If you encounter any issues, please contact the CHICO study team: chico-study@bristol.ac.uk or 07811 984 357.

Step 1: Preparing for the import

1.1. **IMPORTANT: For practices already using the intervention, please ensure you Deactivate and Archive all existing CHICO Protocols, Concepts, Data Entry Templates and Document Templates, before importing the updated resources outlined below**

1.2. Save the CHICO SNOMED intervention folder to the computer's desktop and unzip the folder by right clicking and clicking 'Extract all'. You should now have an unzipped CHICO SNOMED Intervention folder saved on the desktop.

1.3. Open EMIS Web with a User profile that has Admin rights, i.e. access to the **Configuration** module

1.4. Click on the **'EMIS Button'** in the top left corner, click on **'Configuration'**, and then select **'Template Manager'** *(figure 1)*.

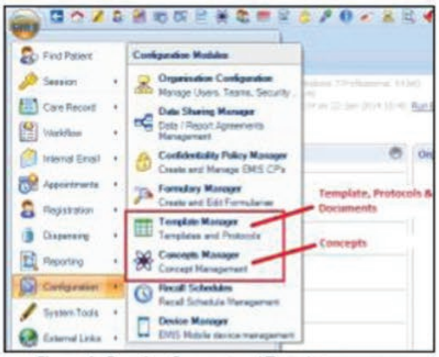
Find Patient
Session
Care Record
Workflow
Internal Email
Appointments
Registration
Dispensing
Reporting
Configuration
System Tools
External Links
Configuration Modules
Organisation Configuration
Manage Users, Teams, Security
Data Sharing Manager
Data / Report Agreements Management
Confidentiality Policy Manager
Create and Manage EMIS CPs
Formulary Manager
Create and Edit Formularies
Template Manager
Templates and Protocols
Concepts Manager
Concept Management
Recall Schedules
Recall Schedule Management
Device Manager
EMIS Mobile device management
Template, Protocols & Documents
Concepts

Figure 1: Opening Concept and Template manager

1.5. Click on the tab **'Templates & Protocols'** *(figure 2)*. Click **'Add'** and **'Folder'** on the navigation pane to create a new folder. Name this folder **'CHICO Research Templates'** *(figure 3)*.

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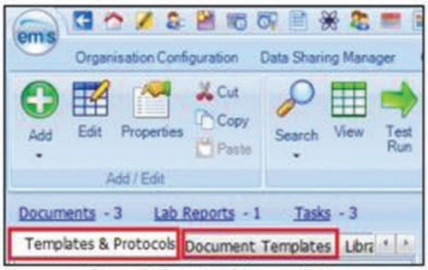

ems
Organisation Configuration
Data Sharing Manager
Add
Edit
Properties
Cut
Copy
Paste
Search
View
Test Run
Add / Edit
Documents - 3
Lab Reports - 1
Tasks - 3
Templates & Protocols
Document Templates
Libra

Figure 2: Template Manager Tabs

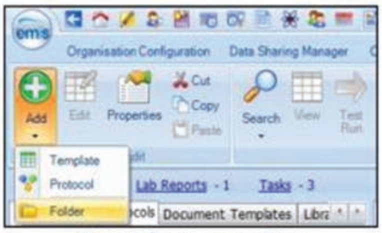

ems
Organisation Configuration
Data Sharing Manager
Add
Edit
Properties
Cut
Copy
Paste
Search
View
Test Run
Template
Protocol
Folder
Lab Reports - 1
Tasks - 3
Document Templates
Libra

Figure 3: Creating a new folder

1.6. Click on the tab **'Document Templates'.** Click **'Add'** and **'Folder'** to create a new folder. Name this folder **'CHICO Research documents'**.

1.7. Click the EMIS button, click on **'Configuration'** and then select **'Concepts Manager'**. Click **'Add'** and **'Folder'** to create a new folder. Name this folder **'CHICO Research concepts'**.

Step 2: Importing Concepts

2.1. In the navigation pane (on the left-hand side), click on the **'CHICO Research Concepts'** folder just created and click the **'Import button'** in the tool bar *(figure 4)*.

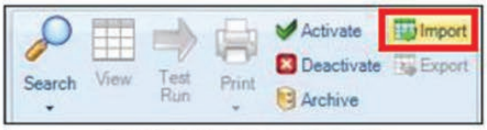
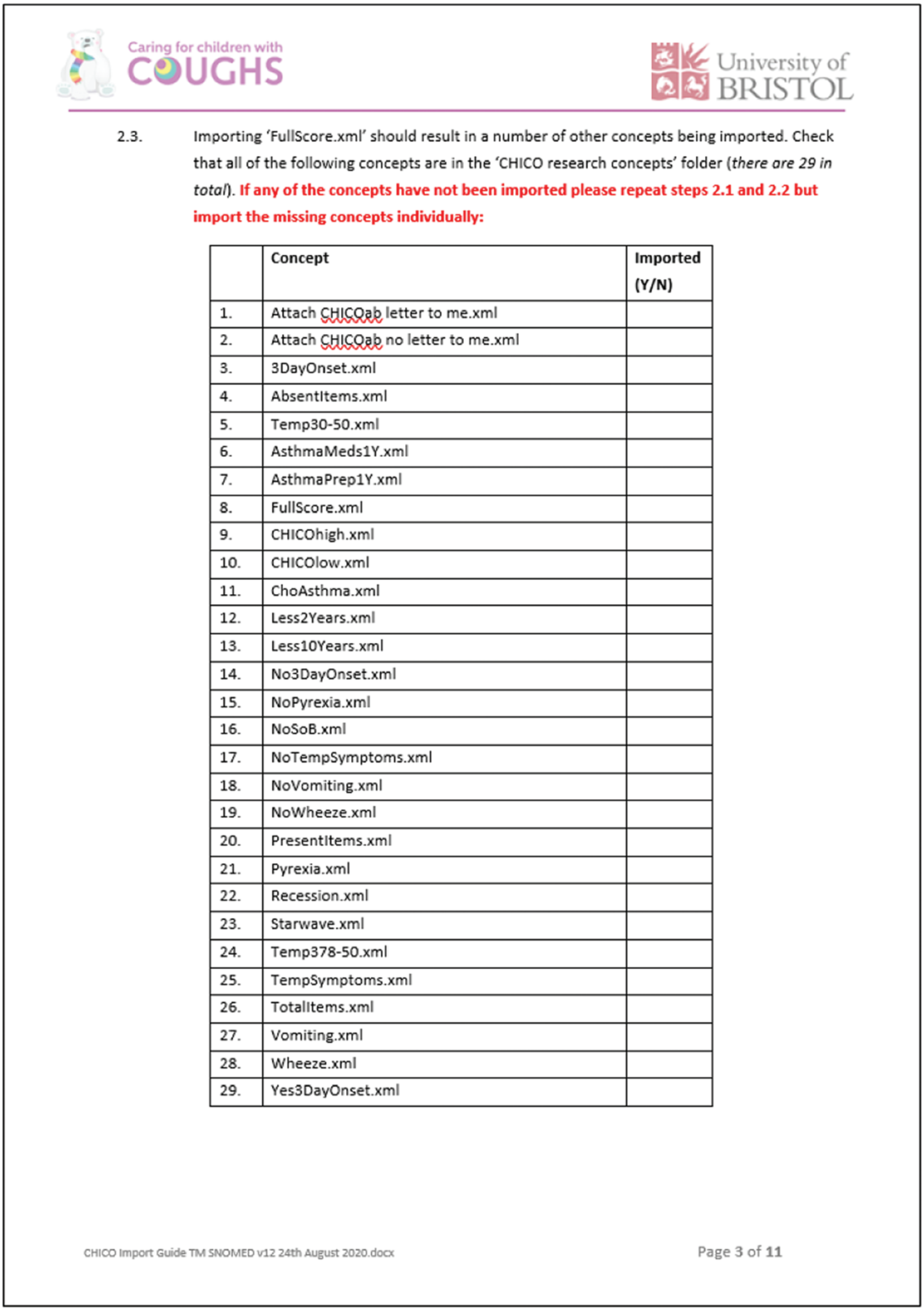

Search
View
Test Run
Print
Activate
Deactivate
Archive
Import
Export

Figure 4: Import button in the tool bar.

2.2. Within the import pop-up, navigate to the unzipped CHICO SNOMED intervention folder on your desktop. Open this folder and then open **'Concepts'** folder. Import the file named **'FullScore.xml'**.



2.3. Importing 'FullScore.xml' should result in a number of other concepts being imported. Check that all of the following concepts are in the 'CHICO research concepts' folder (*there are 29 in total*). **If any of the concepts have not been imported please repeat steps 2.1 and 2.2 but import the missing concepts individually:**

	Concept	**Imported (Y/N)**
1.	Attach CHICOab letter to me.xml	
2.	Attach CHICOab no letter to me.xml	
3.	3DayOnset.xml	
4.	AbsentItems.xml	
5.	Temp30-50.xml	
6.	AsthmaMeds1Y.xml	
7.	AsthmaPrep1Y.xml	
8.	FullScore.xml	
9.	CHICOhigh.xml	
10.	CHICOlow.xml	
11.	ChoAsthma.xml	
12.	Less2Years.xml	
13.	Less10Years.xml	
14.	No3DayOnset.xml	
15.	NoPyrexia.xml	
16.	NoSoB.xml	
17.	NoTempSymptoms.xml	
18.	NoVomiting.xml	
19.	NoWheeze.xml	
20.	PresentItems.xml	
21.	Pyrexia.xml	
22.	Recession.xml	
23.	Starwave.xml	
24.	Temp378-50.xml	
25.	TempSymptoms.xml	
26.	TotalItems.xml	
27.	Vomiting.xml	
28.	Wheeze.xml	
29.	Yes3DayOnset.xml	

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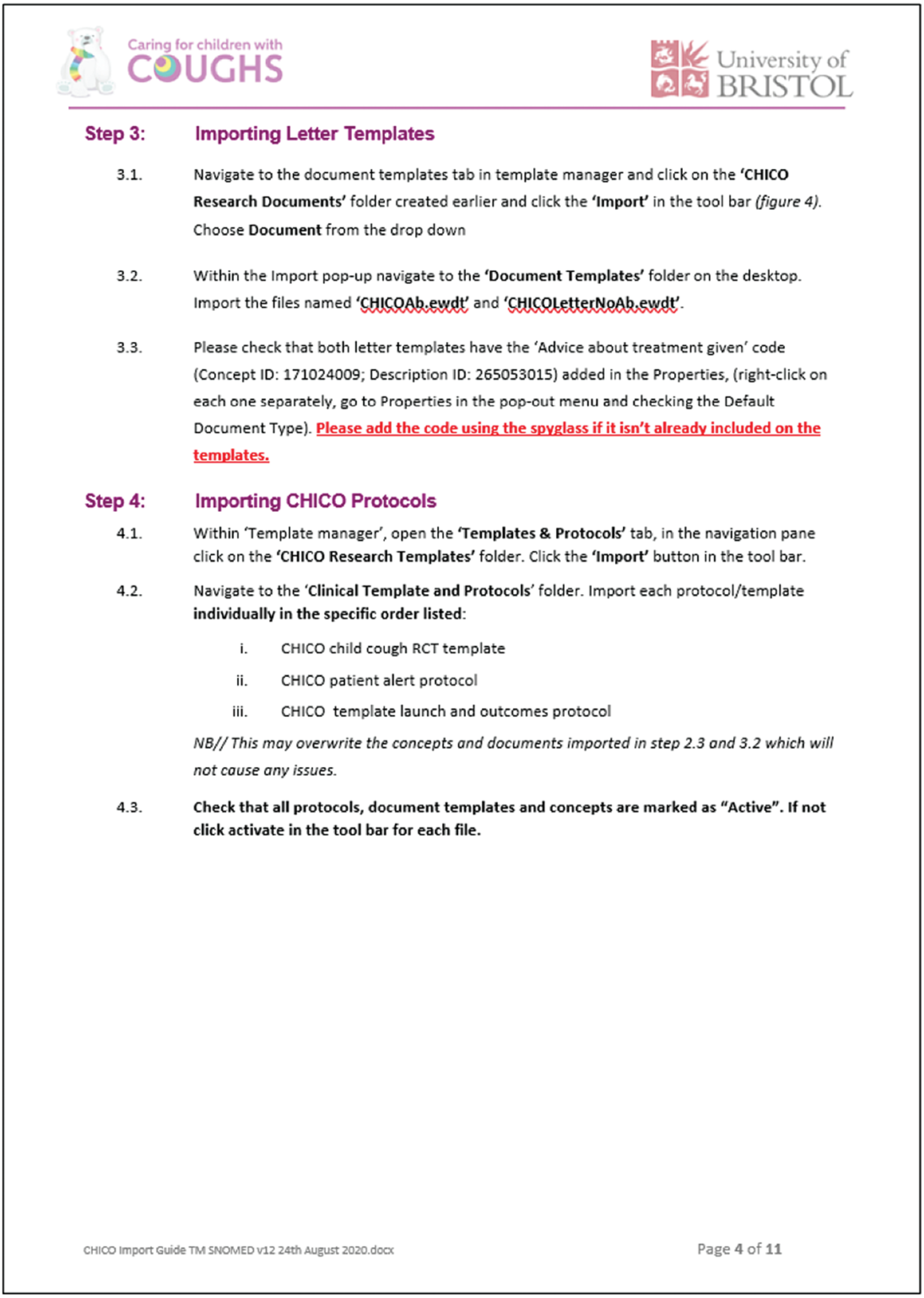

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Step 3: Importing Letter Templates

3.1. Navigate to the document templates tab in template manager and click on the **'CHICO Research Documents'** folder created earlier and click the **'Import'** in the tool bar *(figure 4)*. Choose **Document** from the drop down

3.2. Within the Import pop-up navigate to the **'Document Templates'** folder on the desktop. Import the files named **'CHICOAb.ewdt'** and **'CHICOLetterNoAb.ewdt'**.

3.3. Please check that both letter templates have the 'Advice about treatment given' code (Concept ID: 171024009; Description ID: 265053015) added in the Properties, (right-click on each one separately, go to Properties in the pop-out menu and checking the Default Document Type). **Please add the code using the spyglass if it isn't already included on the templates.**

Step 4: Importing CHICO Protocols

4.1. Within 'Template manager', open the **'Templates & Protocols'** tab, in the navigation pane click on the **'CHICO Research Templates'** folder. Click the **'Import'** button in the tool bar.

4.2. Navigate to the '**Clinical Template and Protocols**' folder. Import each protocol/template **individually in the specific order listed**:

i. CHICO child cough RCT template
ii. CHICO patient alert protocol
iii. CHICO template launch and outcomes protocol

NB// This may overwrite the concepts and documents imported in step 2.3 and 3.2 which will not cause any issues.

4.3. **Check that all protocols, document templates and concepts are marked as "Active". If not click activate in the tool bar for each file.**

CHICO Import Guide TM SNOMED v12 24th August 2020.docx

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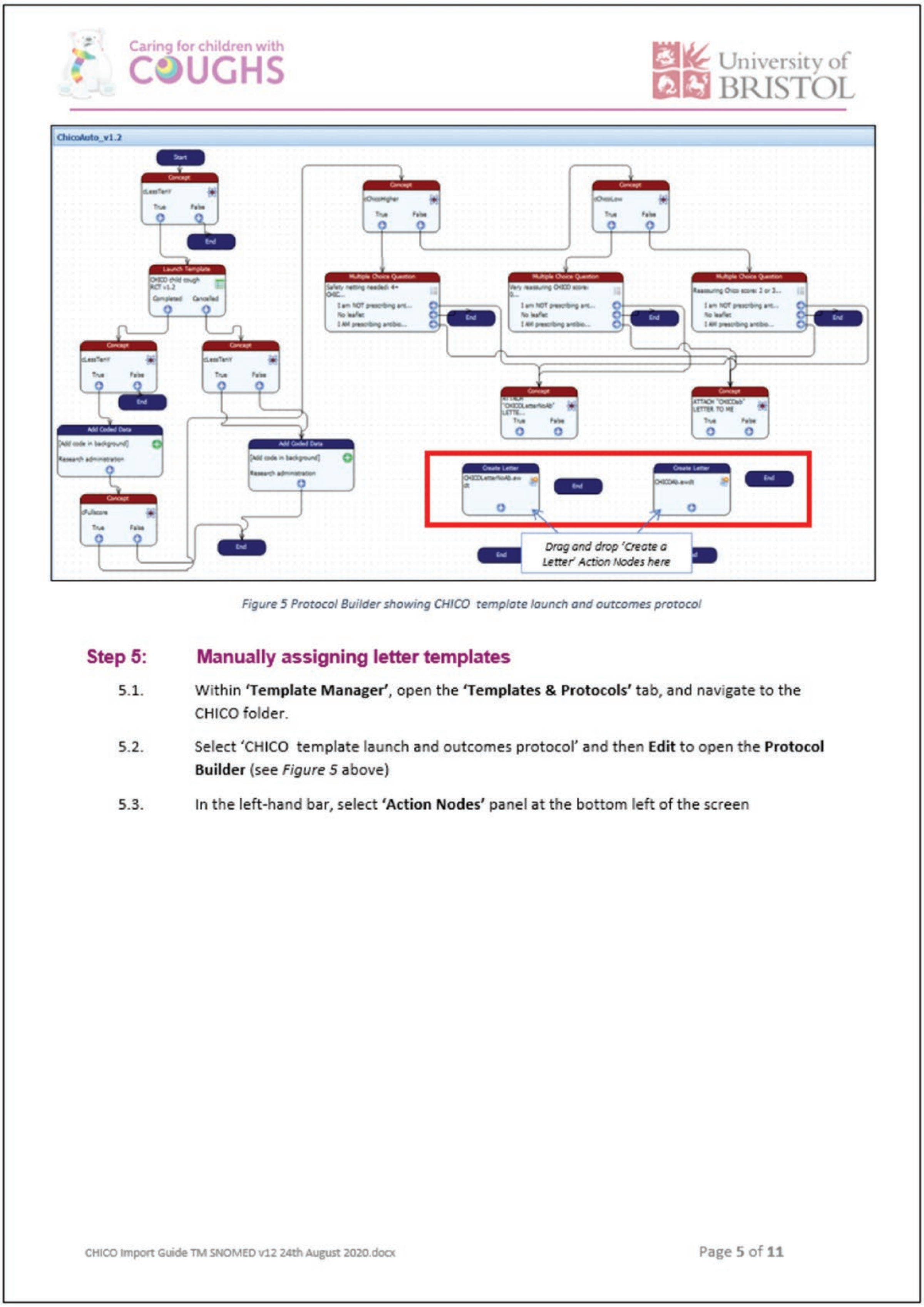
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COUGHS
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BRISTOL
ChicoAuto_v1.2
Start
Concept
cLessTenY
True
False
End
Launch Template
CHICO child cough RCT v1.2
Completed
Cancelled
Concept
cLessTenY
True
False
End
Concept
cLessTenY
True
False
Add Coded Data
[Add code in background]
Research administration
Add Coded Data
[Add code in background]
Research administration
Concept
cFullscore
True
False
End
Concept
cChicoHigher
True
False
Multiple Choice Question
Safety netting needed: 4+ CHIC...
I am NOT prescribing ant...
No leaflet
I AM prescribing antibio...
End
Concept
cChicoLow
True
False
Multiple Choice Question
Very reassuring CHICO score: 0...
I am NOT prescribing ant...
No leaflet
I AM prescribing antibio...
End
Multiple Choice Question
Reassuring Chico score: 2 or 3...
I am NOT prescribing ant...
No leaflet
I AM prescribing antibio...
End
Concept
ATTACH "CHICOLetterNoAb" LETTE...
True
False
Concept
ATTACH "CHICOab" LETTER TO ME
True
False
Create Letter
CHICOLetterNoAb.awdt
End
Create Letter
CHICOAb.awdt
End
End
End

Drag and drop 'Create a Letter' Action Nodes here

Figure 5 Protocol Builder showing CHICO template launch and outcomes protocol

Step 5: Manually assigning letter templates

5.1. Within **'Template Manager'**, open the **'Templates & Protocols'** tab, and navigate to the CHICO folder.

5.2. Select 'CHICO template launch and outcomes protocol' and then **Edit** to open the **Protocol Builder** (see *Figure 5* above)

5.3. In the left-hand bar, select **'Action Nodes'** panel at the bottom left of the screen

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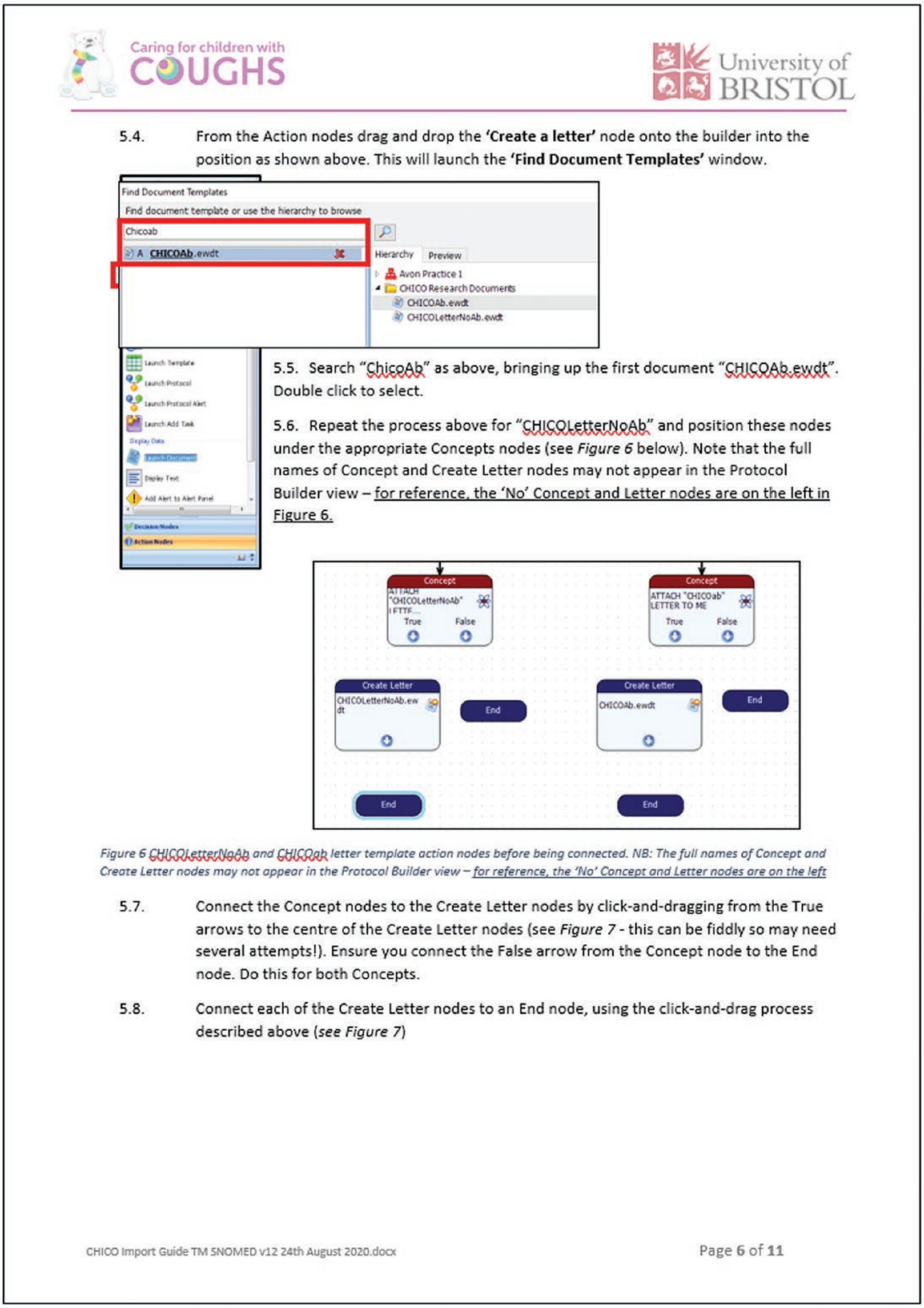

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5.4. From the Action nodes drag and drop the **'Create a letter'** node onto the builder into the position as shown above. This will launch the **'Find Document Templates'** window.

Find Document Templates
Find document template or use the hierarchy to browse
Chicoab
A CHICOAb.ewdt
Hierarchy
Preview
Avon Practice 1
CHICO Research Documents
CHICOAb.ewdt
CHICOLetterNoAb.ewdt
Launch Template
Launch Protocol
Launch Protocol Alert
Launch Add Task
Display Data
Launch Document
Display Text
Add Alert to Alert Panel
Decision Nodes
Action Nodes

5.5. Search "ChicoAb" as above, bringing up the first document "CHICOAb.ewdt". Double click to select.

5.6. Repeat the process above for "CHICOLetterNoAb" and position these nodes under the appropriate Concepts nodes (see *Figure 6* below). Note that the full names of Concept and Create Letter nodes may not appear in the Protocol Builder view – for reference, the 'No' Concept and Letter nodes are on the left in Figure 6.

Concept
ATTACH "CHICOLetterNoAb" LETTE...
True
False
Concept
ATTACH "CHICOab" LETTER TO ME
True
False
Create Letter
CHICOLetterNoAb.ewdt
End
Create Letter
CHICOAb.ewdt
End
End
End

Figure 6 CHICOLetterNoAb and CHICOab letter template action nodes before being connected. NB: The full names of Concept and Create Letter nodes may not appear in the Protocol Builder view – for reference, the 'No' Concept and Letter nodes are on the left

5.7. Connect the Concept nodes to the Create Letter nodes by click-and-dragging from the True arrows to the centre of the Create Letter nodes (see *Figure 7* - this can be fiddly so may need several attempts!). Ensure you connect the False arrow from the Concept node to the End node. Do this for both Concepts.

5.8. Connect each of the Create Letter nodes to an End node, using the click-and-drag process described above (*see Figure 7*)

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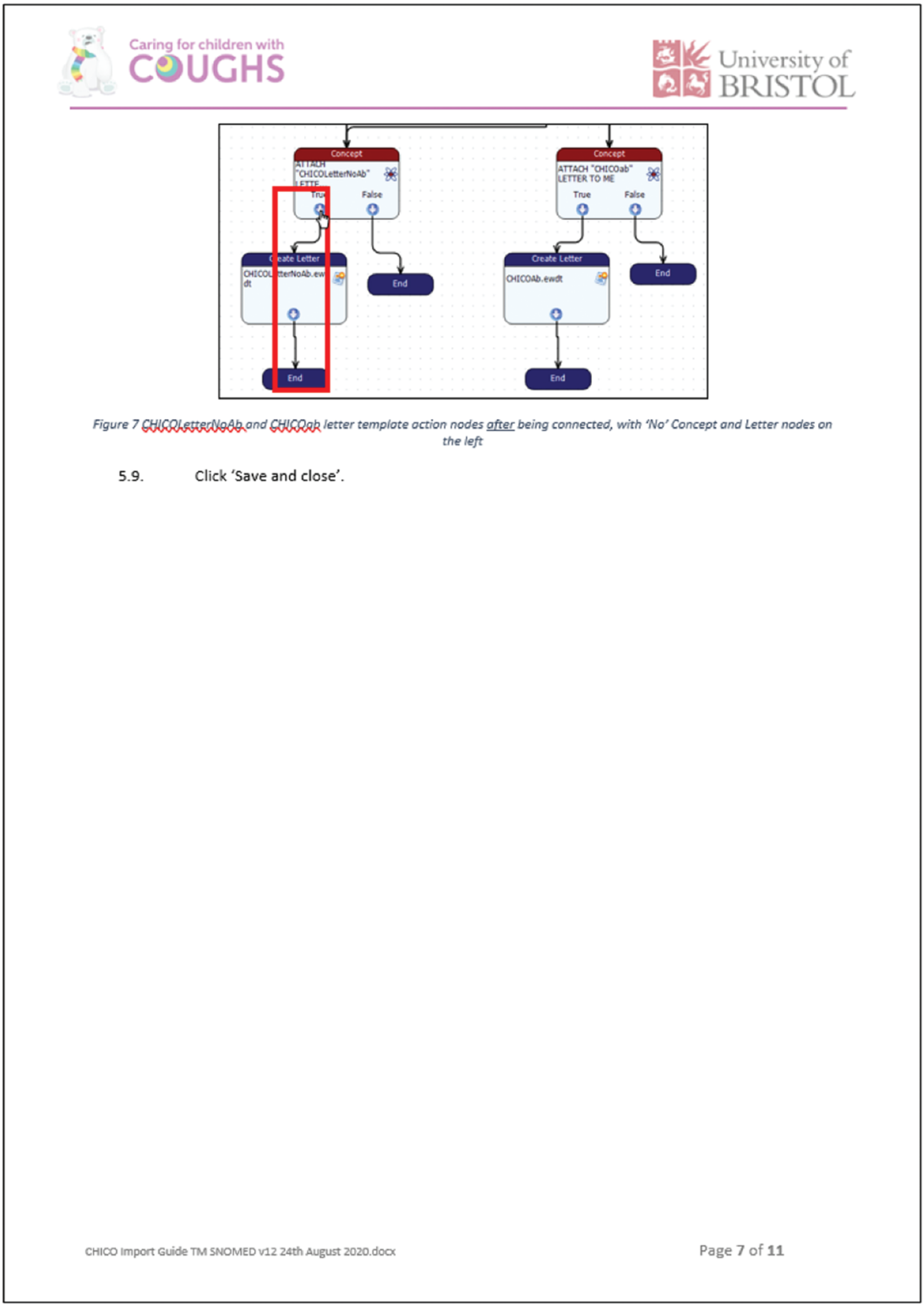

Caring for children with COUGHS
University of BRISTOL
Concept
ATTACH "CHICOLetterNoAb" LETTE
True
False
Concept
ATTACH "CHICOab" LETTER TO ME
True
False
Create Letter
CHICOLetterNoAb.ewdt
End
Create Letter
CHICOAb.ewdt
End
End
End

Figure 7 CHICOLetterNoAb and CHICOab letter template action nodes after being connected, with 'No' Concept and Letter nodes on the left

5.9. Click 'Save and close'.

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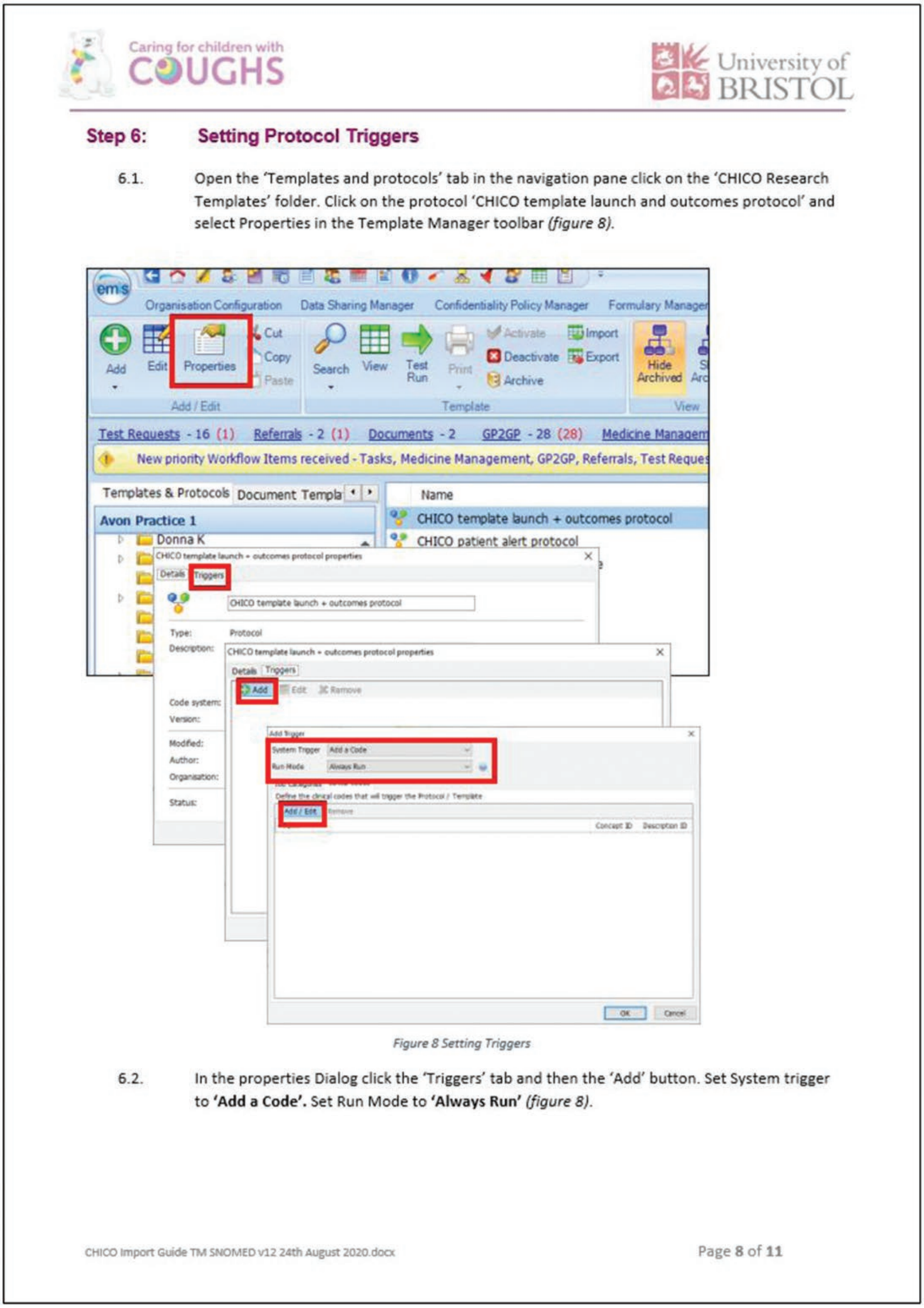
Caring for children with COUGHS
University of BRISTOL
Organisation Configuration
Data Sharing Manager
Confidentiality Policy Manager
Formulary Manager
Add
Edit
Properties
Cut
Copy
Paste
Search
View
Test Run
Print
Activate
Deactivate
Archive
Import
Export
Hide Archived
Add / Edit
Template
View
Test Requests - 16 (1)
Referrals - 2 (1)
Documents - 2
GP2GP - 28 (28)
Medicine Managem
New priority Workflow Items received - Tasks, Medicine Management, GP2GP, Referrals, Test Reques
Templates & Protocols
Document Templa
Avon Practice 1
Donna K
Name
CHICO template launch + outcomes protocol
CHICO patient alert protocol
CHICO template launch + outcomes protocol properties
Details
Triggers
Add
Edit
Remove
Add Trigger
Define the clinical codes that will trigger the Protocol / Template
Add / Edit
Remove
Concept ID
Description ID
OK
Cancel

Step 6: Setting Protocol Triggers

6.1. Open the 'Templates and protocols' tab in the navigation pane click on the 'CHICO Research Templates' folder. Click on the protocol 'CHICO template launch and outcomes protocol' and select Properties in the Template Manager toolbar *(figure 8)*.

Type: Protocol

System Trigger: Add a Code

Run Mode: Always Run

Figure 8 Setting Triggers

6.2. In the properties Dialog click the 'Triggers' tab and then the 'Add' button. Set System trigger to **'Add a Code'.** Set Run Mode to **'Always Run'** *(figure 8)*.

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6.3. In the 'Define the clinical codes that will trigger the protocol / template' section *(figure 8)* select 'Add/Edit' and in the 'Code Selector' window *(figure 9)* search for the following SNOMED terms and add them by double clicking:

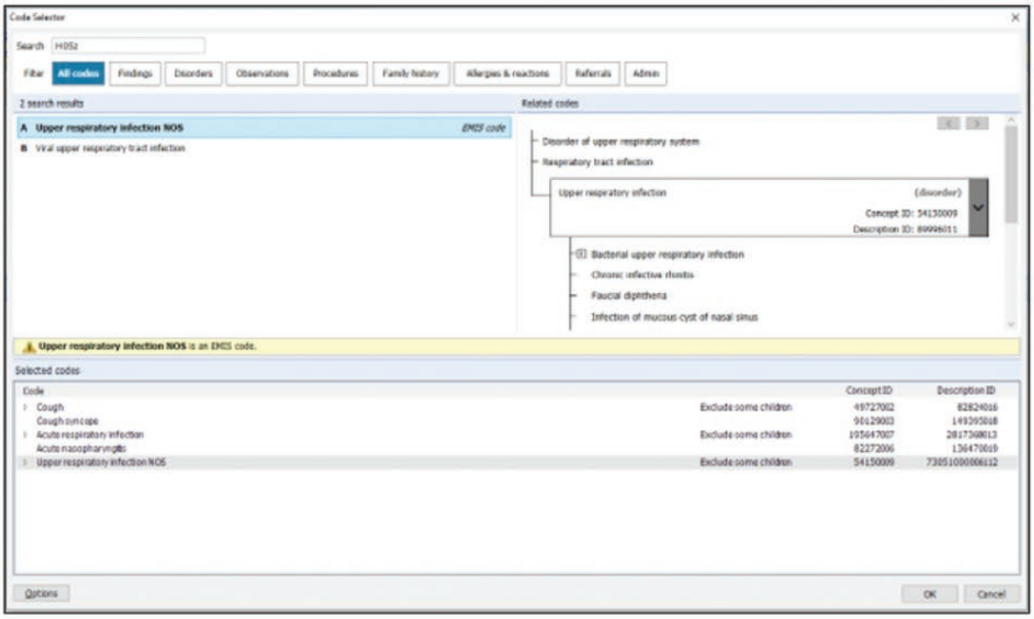
i. *Cough* – ***Right click in Selected codes and click "Include Just this"***

ii. *Cough syncope*

iii. *Acute Respiratory Infections* - ***Right click in Selected codes and click "Include Just this"***

iv. *Acute Nasopharyngitis*

v. *Upper Respiratory Tract Infection NOS* – ***Right click in Selected codes and click "Include Just this"***



A **Upper respiratory infection NOS** *EMIS code*
B Viral upper respiratory tract infection

Disorder of upper respiratory system
Respiratory tract infection
Upper respiratory infection (disorder)
Concept ID: 54150009
Description ID: 89996011
Bacterial upper respiratory infection
Chronic infective rhinitis
Faucial diphtheria
Infection of mucous cyst of nasal sinus

Upper respiratory infection NOS is an EMIS code.

Selected codes

Code		Concept ID	Description ID
Cough	Exclude some children	49727002	82824016
Cough syncope		90129003	149395018
Acute respiratory infection	Exclude some children	195647007	2817368013
Acute nasopharyngitis		82272006	136470019
Upper respiratory infection NOS	Exclude some children	54150009	73051000006112

Figure 9 Code Selector with trigger codes added

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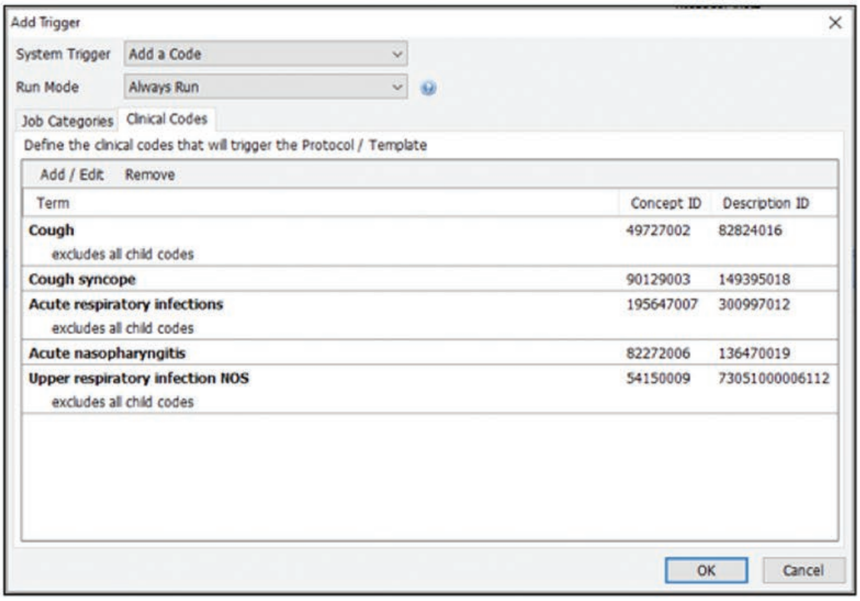
6.4. Click **OK** on the Code Selector, the 'CHICO template launch and outcomes protocol' properties should now appear as below (Figure 10), click **OK** and **OK** again.



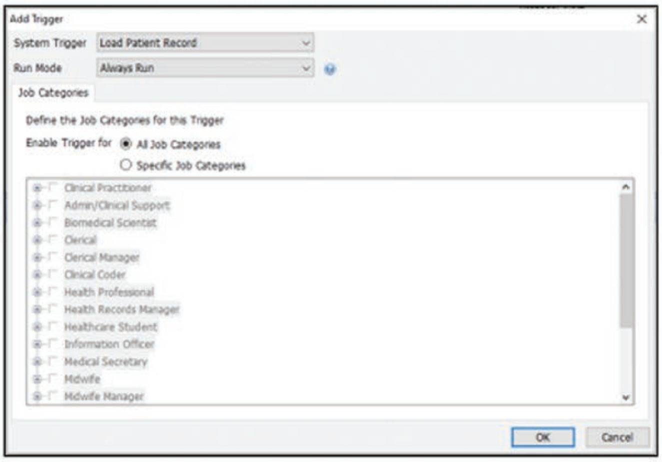
System Trigger: Add a Code
Run Mode: Always Run

Define the clinical codes that will trigger the Protocol / Template

Term	Concept ID	Description ID
Cough excludes all child codes	49727002	82824016
Cough syncope	90129003	149395018
Acute respiratory infections excludes all child codes	195647007	300997012
Acute nasopharyngitis	82272006	136470019
Upper respiratory infection NOS excludes all child codes	54150009	73051000006112

Figure 10: CHICO Auto_V1.2 (SNOMED) properties

6.5. Open the properties for the protocol **'CHICO patient alert'** and click 'Triggers' and the 'Add' button. Set system trigger to **'Load Patient Record'.** Set Run Mode to **'Always Run'** and click OK



System Trigger: Load Patient Record
Run Mode: Always Run

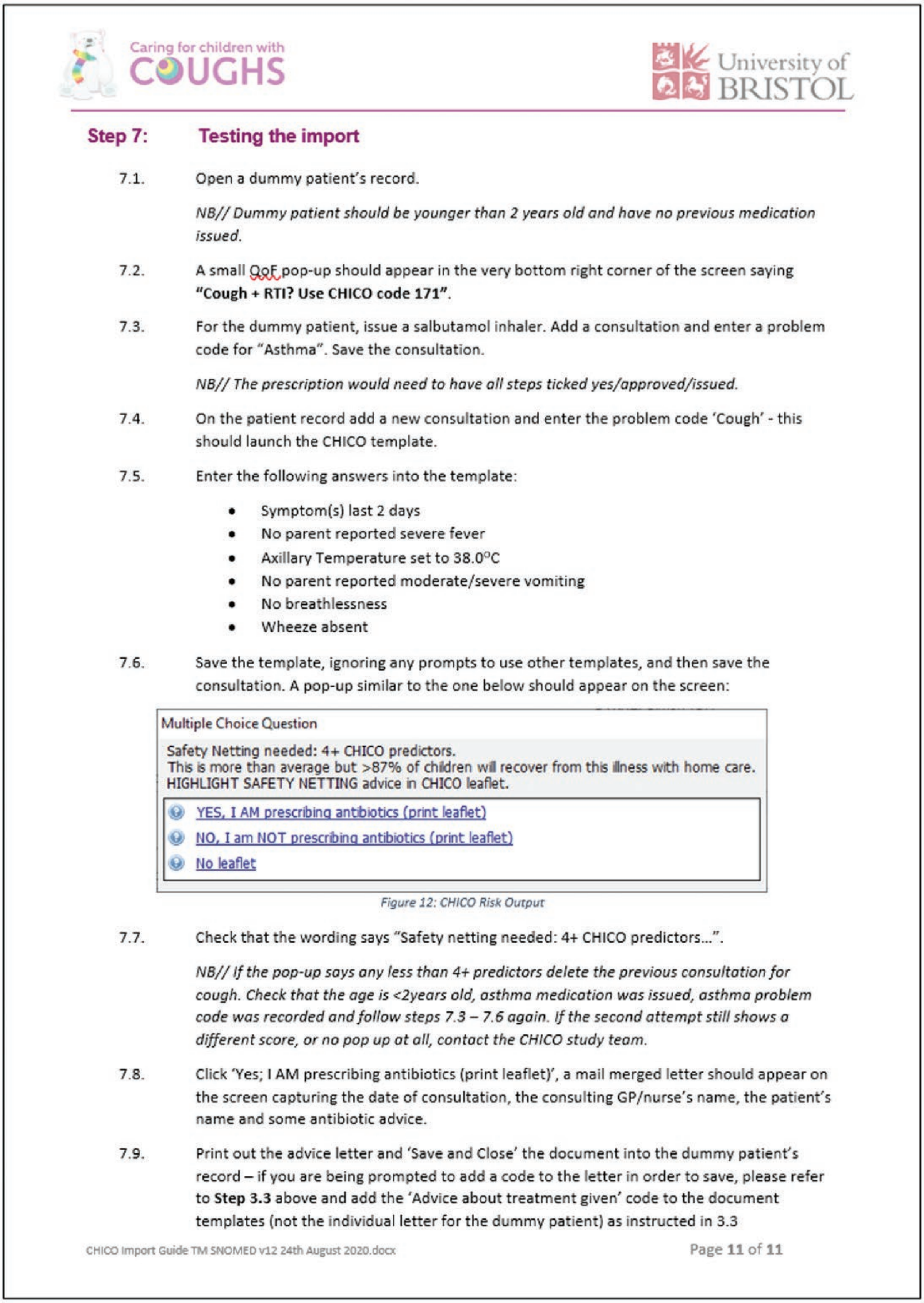
Define the Job Categories for this Trigger

Enable Trigger for ● All Job Categories
○ Specific Job Categories

- ☐ Clinical Practitioner
- ☐ Admin/Clinical Support
- ☐ Biomedical Scientist
- ☐ Clerical
- ☐ Clerical Manager
- ☐ Clinical Coder
- ☐ Health Professional
- ☐ Health Records Manager
- ☐ Healthcare Student
- ☐ Information Officer
- ☐ Medical Secretary
- ☐ Midwife
- ☐ Midwife Manager

Figure 11 Trigger settings for CHICOsoftpopup_V1.2

6.6. **Check that all protocols and templates are activated**. If not activated, you can activate by right clicking each concept/protocol and clicking activate (or using the activate button in the tool bar).



Caring for children with COUGHS

University of BRISTOL

Step 7: Testing the import

7.1. Open a dummy patient's record.

NB// Dummy patient should be younger than 2 years old and have no previous medication issued.

7.2. A small QoF pop-up should appear in the very bottom right corner of the screen saying **"Cough + RTI? Use CHICO code 171"**.

7.3. For the dummy patient, issue a salbutamol inhaler. Add a consultation and enter a problem code for "Asthma". Save the consultation.

NB// The prescription would need to have all steps ticked yes/approved/issued.

7.4. On the patient record add a new consultation and enter the problem code 'Cough' - this should launch the CHICO template.

7.5. Enter the following answers into the template:

- Symptom(s) last 2 days
- No parent reported severe fever
- Axillary Temperature set to 38.0°C
- No parent reported moderate/severe vomiting
- No breathlessness
- Wheeze absent

7.6. Save the template, ignoring any prompts to use other templates, and then save the consultation. A pop-up similar to the one below should appear on the screen:

Multiple Choice Question

Safety Netting needed: 4+ CHICO predictors.
This is more than average but >87% of children will recover from this illness with home care.
HIGHLIGHT SAFETY NETTING advice in CHICO leaflet.

YES, I AM prescribing antibiotics (print leaflet)
NO, I am NOT prescribing antibiotics (print leaflet)
No leaflet

Figure 12: CHICO Risk Output

7.7. Check that the wording says "Safety netting needed: 4+ CHICO predictors...".

NB// If the pop-up says any less than 4+ predictors delete the previous consultation for cough. Check that the age is <2years old, asthma medication was issued, asthma problem code was recorded and follow steps 7.3 – 7.6 again. If the second attempt still shows a different score, or no pop up at all, contact the CHICO study team.

7.8. Click 'Yes; I AM prescribing antibiotics (print leaflet)', a mail merged letter should appear on the screen capturing the date of consultation, the consulting GP/nurse's name, the patient's name and some antibiotic advice.

7.9. Print out the advice letter and 'Save and Close' the document into the dummy patient's record – if you are being prompted to add a code to the letter in order to save, please refer to **Step 3.3** above and add the 'Advice about treatment given' code to the document templates (not the individual letter for the dummy patient) as instructed in 3.3

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Appendix 4 *SystmOne* resources set-up guide

This document describes how to set up the CHICO intervention resources in *SystmOne*. The resources are a clinical Template, two Letter Templates, a Protocol and a set of Clinical Reports.

Preparing for the import

Note: Practices already using the CHICO intervention but needing to upgrade the resources should delete or archive the previous version in SystmOne before importing the new version.

The resources are distributed as a set of files:

- a letter templates file called '*CHICO WordLetterTemplates 151021.xml*' (or similar);
- a clinical template called '*SystmOneTemplates CHICO child cough RCT 151021.xml*' (or similar);
- a reporting file called '*CHICO Exported Reports 151021.rpt*' (or similar);
- a protocol file called '*SystmOneProtocol CHICO patient alert protocol 151021.xml*' (or similar);
- a protocol file called '*SystmOneProtocol CHICO template launch + outcomes protocol 151021.xml*' (or similar).

Save these files onto your computer or a shared drive.

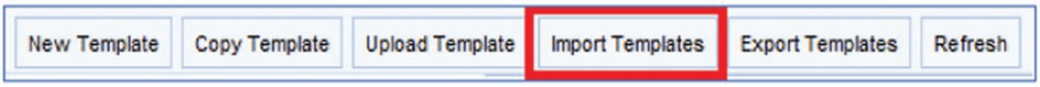
If these resources have been provided in a single compressed (zip) file, right click the file in File Explorer and select 'Extract all' from the pop-up menu. This will create a new folder containing the five individual files.

Setting up the letter templates

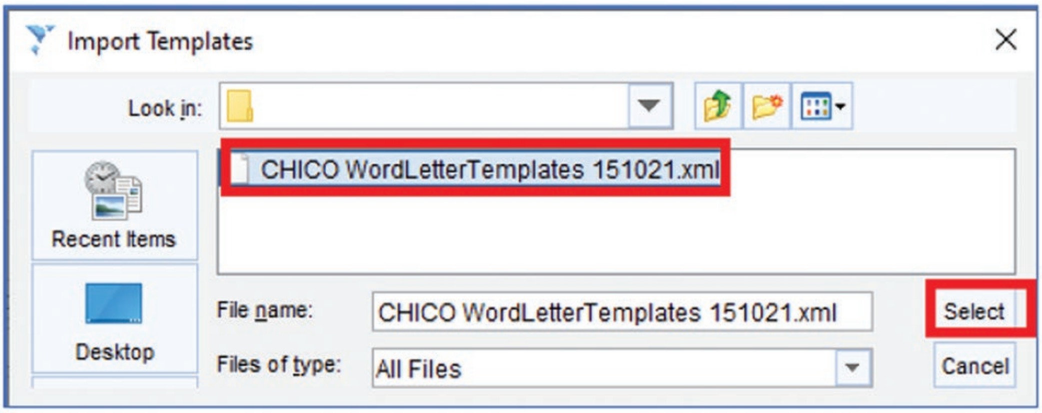
There are two CHICO Letter templates – for when antibiotics are prescribed and not prescribed.

To import the letter templates into *SystmOne*:

- Go to Setup → Referrals and Letters → Word Letter Templates.
- Select Import Templates.



- Select the file called '*CHICO WordLetterTemplates 151021.xml*' (or similar).



CHICO WordLetterTemplates 151021.xml

File name: CHICO WordLetterTemplates 151021.xml

Files of type: All Files

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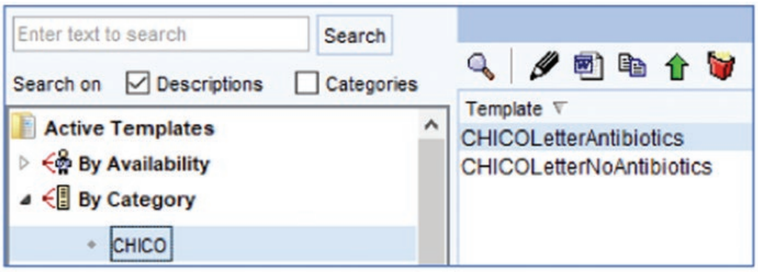
Two Word Letter Templates called ‘*CHICOLetterAntibiotics*’ and ‘*CHICOLetterNoAntibiotics*’ will be created in a category called ‘CHICO’.


Enter text to search
Search
Active Templates
By Availability
By Category
CHICO
Template

Search on ☑ Descriptions ☐ Categories

CHICOLetterAntibiotics
CHICOLetterNoAntibiotics

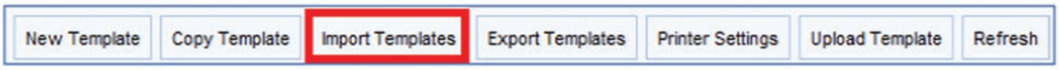
Setting up the clinical template

There are two steps in setting up the clinical template:

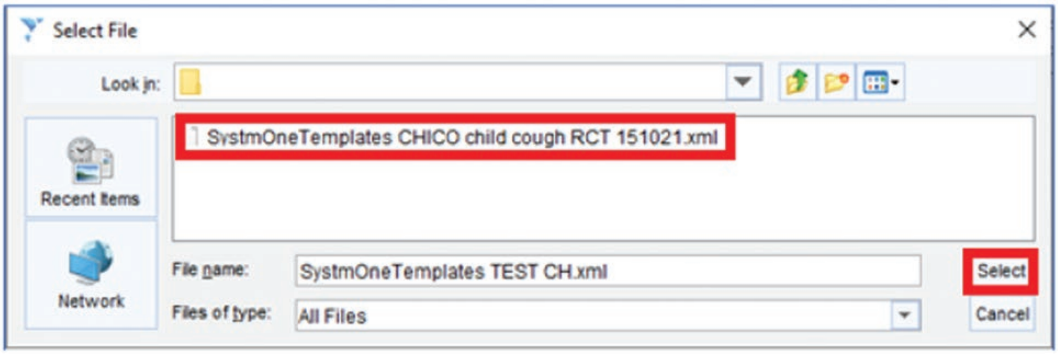
- Importing the Template.
- Publishing the Template.

Importing the template

- Go to Setup → Data Entry → New Template Maintenance.
- Select Import Templates.


New Template
Copy Template
Import Templates
Export Templates
Printer Settings
Upload Template
Refresh

- Select the file called ‘*SystmOneTemplates CHICO child cough RCT 151021.xml*’ (or similar).

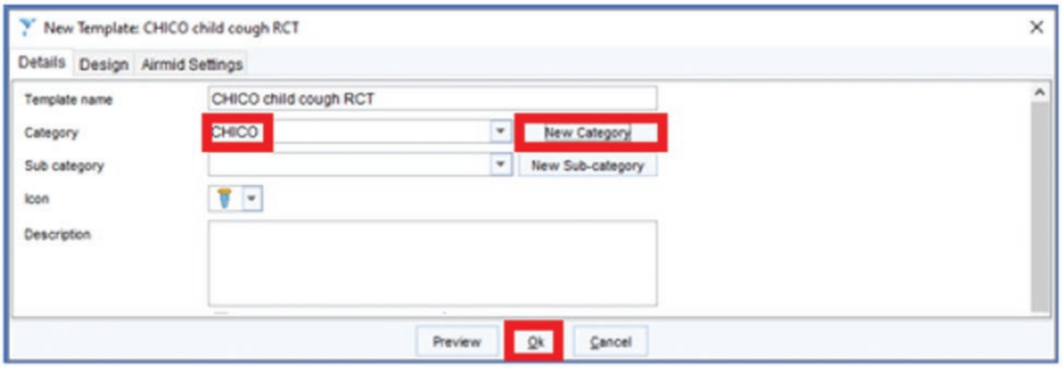

Select File
Look in:
Recent Items
Network
Select
Cancel

SystmOneTemplates CHICO child cough RCT 151021.xml

File name: SystmOneTemplates TEST CH.xml

Files of type: All Files

- The New Template window is displayed. Select the category called ‘CHICO’ if it already exists. Otherwise create and select a ‘New Category’ called ‘CHICO’. Select Ok to complete the template import.


New Template: CHICO child cough RCT
Details
Design
Airmid Settings
New Category
New Sub-category
Preview
Ok
Cancel

Template name: CHICO child cough RCT

Category: CHICO

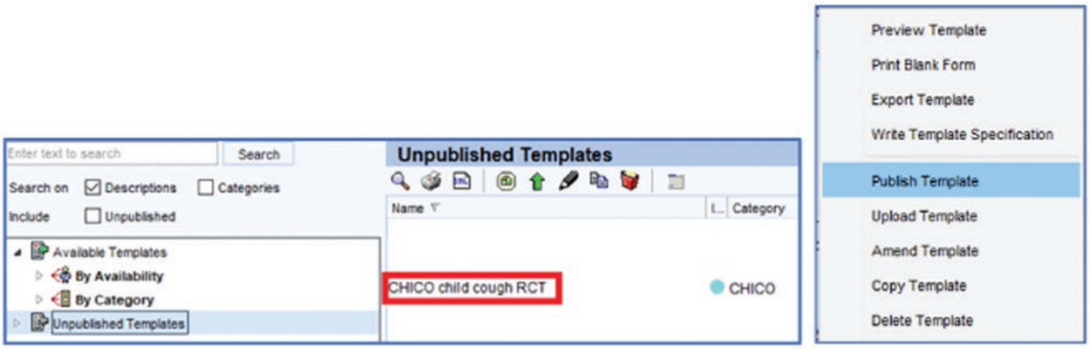
Sub category:

Icon:

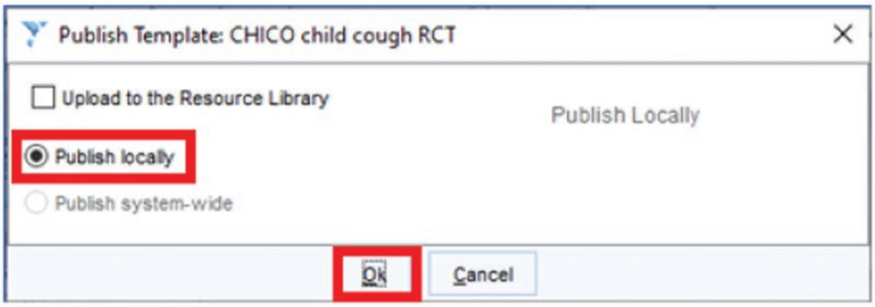
Description:

Publishing the template

- Select 'Unpublished Templates' on the left-hand side of the New Template Maintenance screen. Right click the '*CHICO child cough RCT*' template and select 'Publish Template' from the pop-up menu.

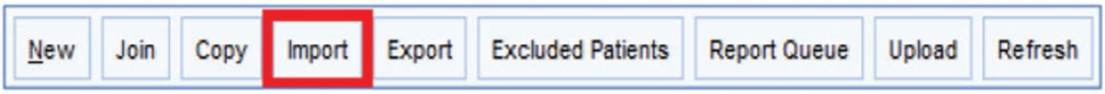

Enter text to search
Search
Search on ☑ Descriptions ☐ Categories
Include ☐ Unpublished
Available Templates
By Availability
By Category
Unpublished Templates
Unpublished Templates
Name
Category
CHICO child cough RCT
CHICO
Preview Template
Print Blank Form
Export Template
Write Template Specification
Publish Template
Upload Template
Amend Template
Copy Template
Delete Template

- Select 'Publish Locally' from the available options. Select Ok.

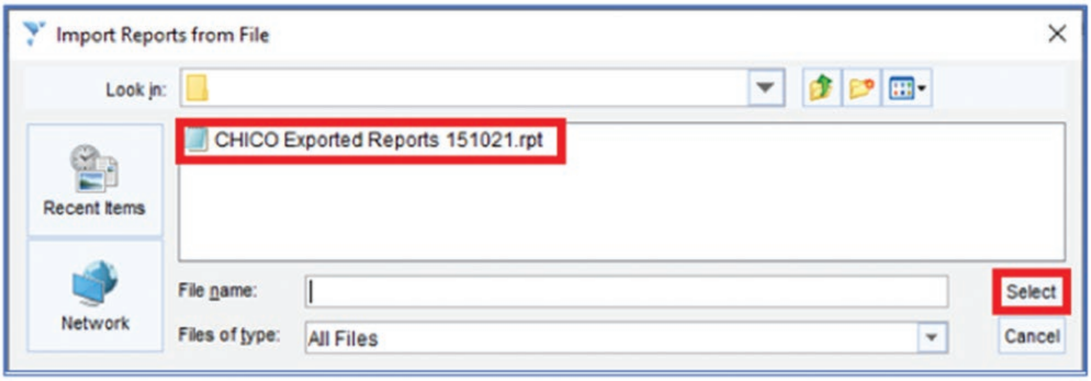

Publish Template: CHICO child cough RCT
☐ Upload to the Resource Library
Publish Locally
● Publish locally
○ Publish system-wide
Ok
Cancel

Setting up the clinical reports

- Go to Reporting → Clinical Reporting.
- Select Import.


New
Join
Copy
Import
Export
Excluded Patients
Report Queue
Upload
Refresh

- Select the file called '*CHICO Exported Reports 151021.rpt*' (or similar).


Import Reports from File
Look in:
CHICO Exported Reports 151021.rpt
Recent Items
Network
File name:
Files of type:
All Files
Select
Cancel

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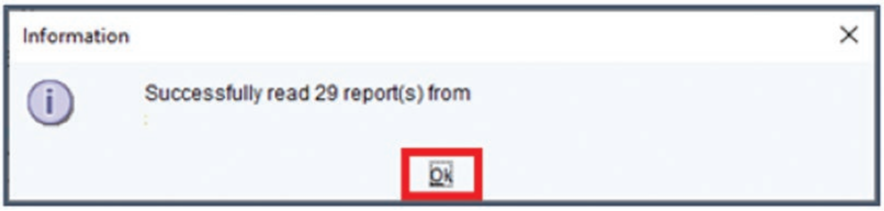
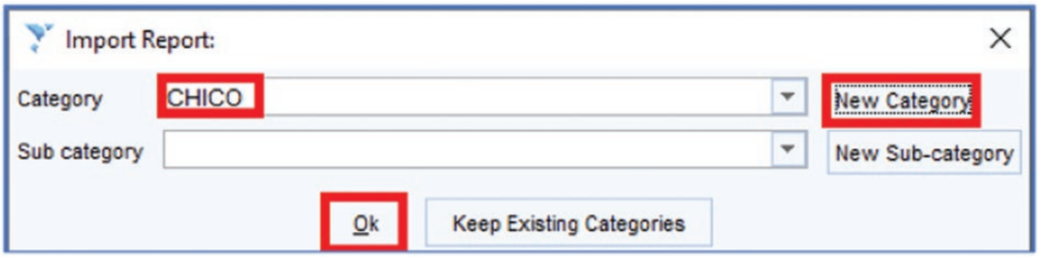
- An import confirmation message is displayed. Select Ok to clear the message.


Information
Ok

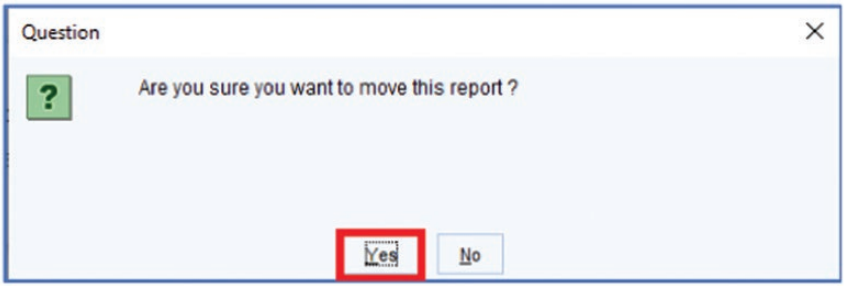
Successfully read 29 report(s) from

- Select the category called 'CHICO' if it already exists. Otherwise create and select a 'New Category' called CHICO. Select Ok.


Import Report:
New Category
New Sub-category
Ok
Keep Existing Categories

Category: CHICO
Sub category:

- A confirmation message is displayed. Select Yes to confirm that you want to move the reports.


Question
Yes
No

Are you sure you want to move this report ?

A set of clinical reports will be created in a category called 'CHICO'.

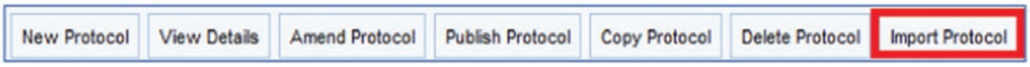
Setting up the protocols

There are three steps in setting up the Protocols:

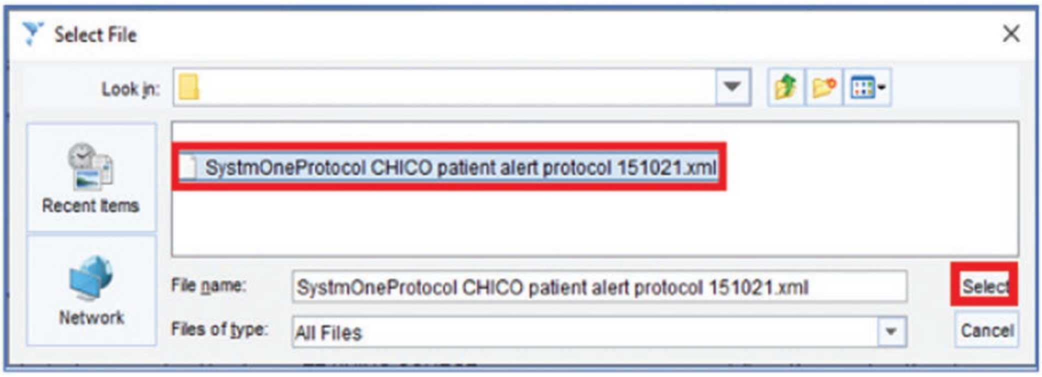
- Importing the Protocols.
- Editing the 'launch + outcomes' Protocol.
- Publishing the Protocols.

Importing the protocols

- Go to Setup → Workflow Support → Protocols.
- Select Import Protocol.


New Protocol
View Details
Amend Protocol
Publish Protocol
Copy Protocol
Delete Protocol
Import Protocol

- Select the file called '*SystmOneProtocol CHICO patient alert protocol 151021.xml*' (or similar).

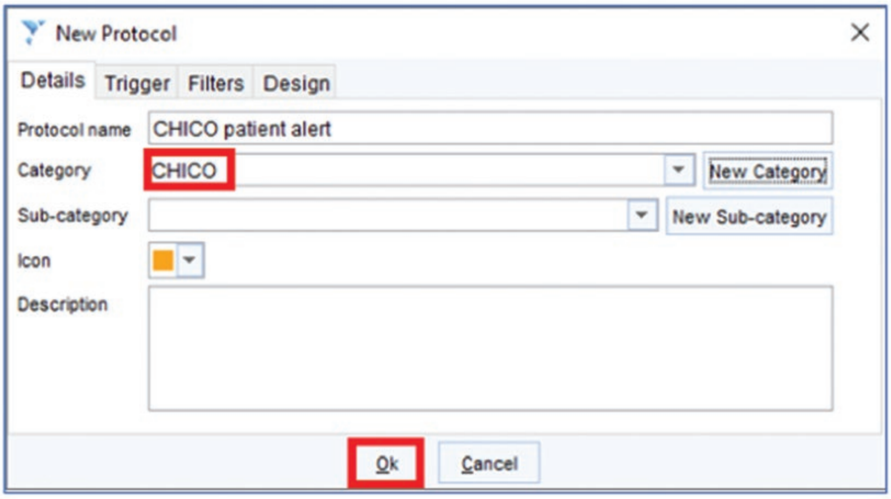

Select File
Look in:
Recent Items
Network
Select
Cancel

SystmOneProtocol CHICO patient alert protocol 151021.xml

File name: SystmOneProtocol CHICO patient alert protocol 151021.xml

Files of type: All Files

- Select the category called 'CHICO' if it already exists or create and select a 'New Category' called 'CHICO'. Select Ok.


New Protocol
Details
Trigger
Filters
Design
New Category
New Sub-category
Ok
Cancel

Protocol name: CHICO patient alert

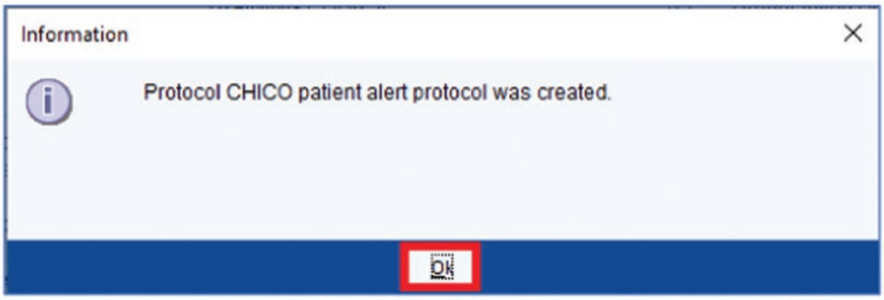
Category: CHICO

Sub-category:

Icon:

Description:

- A confirmation creation message is displayed. Select Ok.


Information
Ok

Protocol CHICO patient alert protocol was created.

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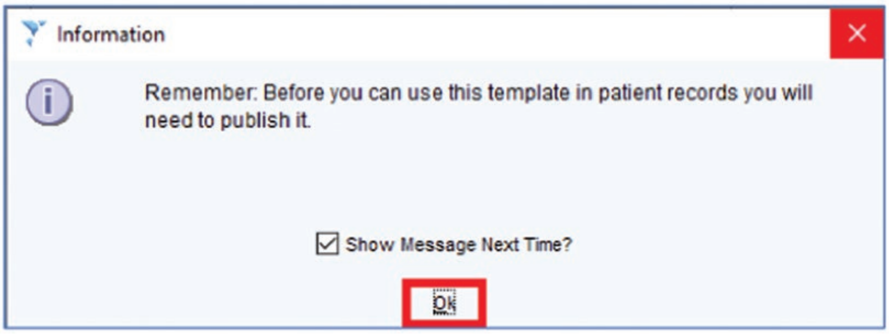
- You may see the following information message in which case select Ok.


Information
Ok

Remember: Before you can use this template in patient records you will need to publish it.

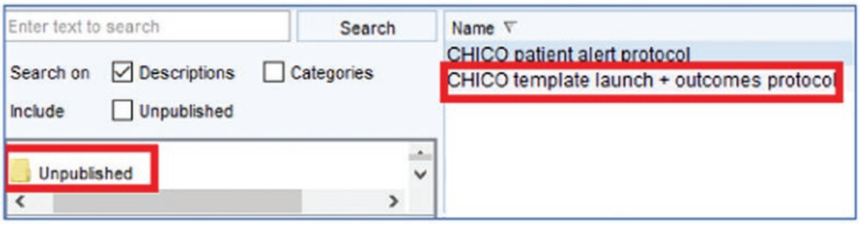
☑ Show Message Next Time?

- Now import the protocol file called '*SystmOneProtocol CHICO template launch + outcomes protocol 151021.xml*' (or similar) in the same way as described above.

Editing the 'launch ± outcomes' Protocol

When the 'launch + outcomes' Protocol is imported, links from it to the clinical template and letter templates are lost. The Protocol therefore must be amended to reinstate the links.

- Select 'Unpublished' on the left-hand side of the Protocols screen. Right click the Protocol called '*CHICO template launch + outcomes protocol*' and select 'Amend Protocol' from the pop-up menu.

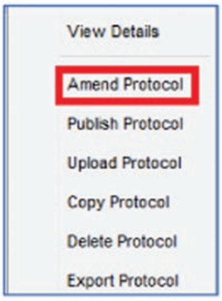

Enter text to search
Search
Name
Unpublished

Search on ☑ Descriptions ☐ Categories

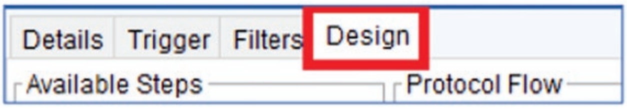
Include ☐ Unpublished

CHICO patient alert protocol

CHICO template launch + outcomes protocol


View Details
Amend Protocol
Publish Protocol
Upload Protocol
Copy Protocol
Delete Protocol
Export Protocol

- Select the tab called Design.

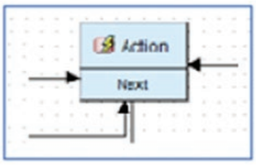

Details
Trigger
Filters
Design
Available Steps
Protocol Flow

Three steps in the design flowchart need to be amended:

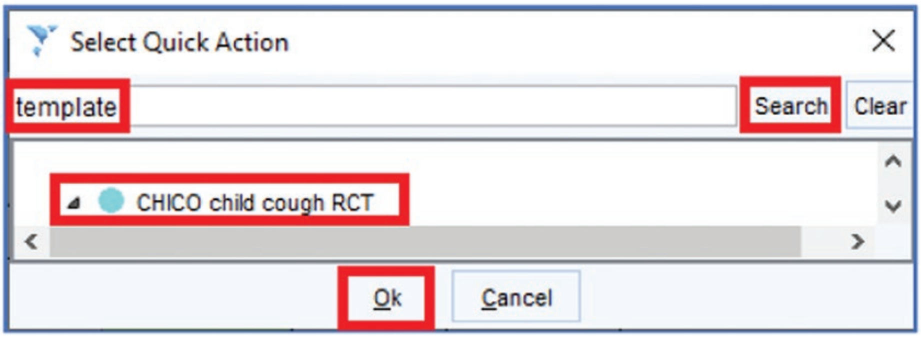
- The Action step that identifies the clinical template.
- The two steps that identify the letter templates.

Linking the clinical template

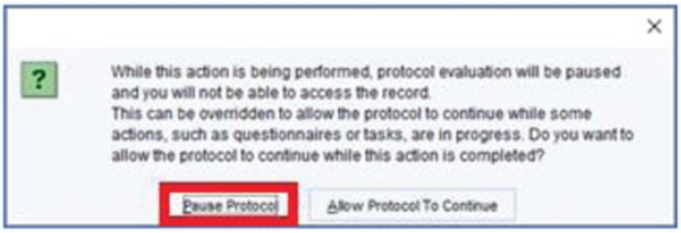
- Double left-click the Action step near the top of the design.


Action
Next

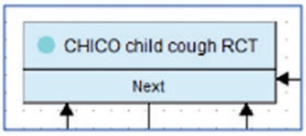
- In the Select Quick Action window, search for 'template' and select the 'CHICO child cough RCT' template. Select Ok.


Select Quick Action
template
Search
Clear
CHICO child cough RCT
Ok
Cancel

- Select Pause Protocol.

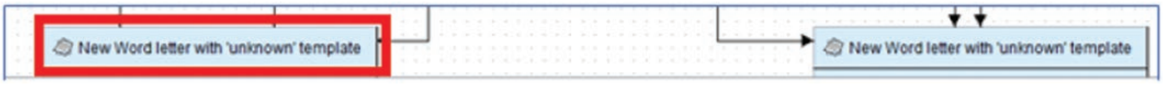

While this action is being performed, protocol evaluation will be paused and you will not be able to access the record.
This can be overridden to allow the protocol to continue while some actions, such as questionnaires or tasks, are in progress. Do you want to allow the protocol to continue while this action is completed?
?
Pause Protocol
Allow Protocol To Continue

- Check that this part of the design now looks like this.


CHICO child cough RCT
Next

Linking the two Letter Templates

- Towards the bottom of the Design, there are two steps with unknown letter templates. Double left-click the one on the left.


New Word letter with 'unknown' template
New Word letter with 'unknown' template

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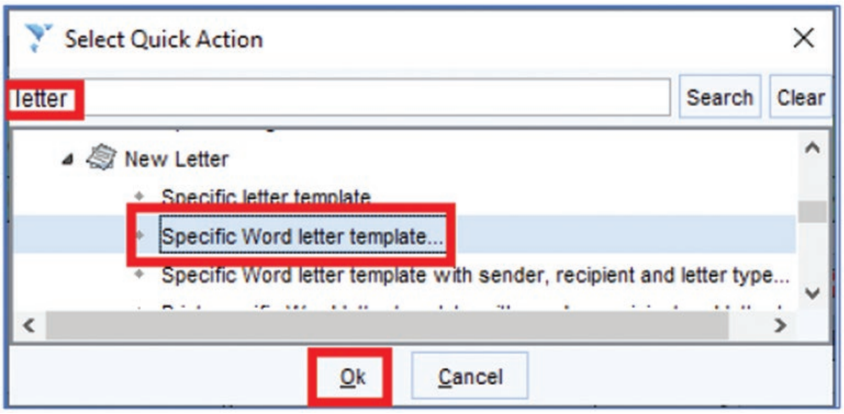
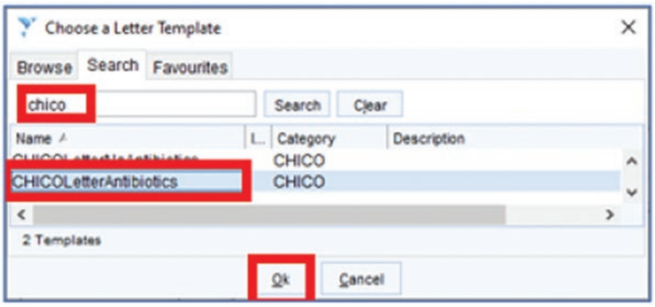
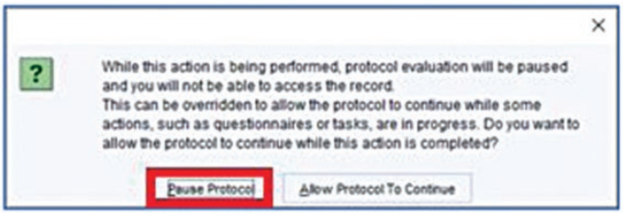
- In the Select Quick Action window, search for ‘letter’ and select New Letter → Specific Word Letter Template. Select Ok.


Select Quick Action
letter
Search
Clear
New Letter
Specific letter template
Specific Word letter template...
Specific Word letter template with sender, recipient and letter type...
Ok
Cancel

- Search for ‘chico’ and select ‘CHICOLetterAntibiotics’. Select Ok.

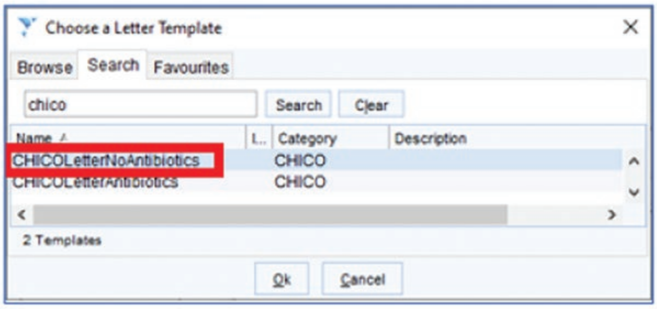

Choose a Letter Template
Browse
Search
Favourites
chico
Search
Clear
Name
L..
Category
Description
CHICO
CHICOLetterAntibiotics
CHICO
2 Templates
Ok
Cancel

- Select Pause Protocol.

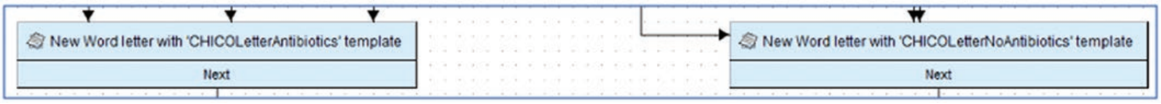

While this action is being performed, protocol evaluation will be paused and you will not be able to access the record.
This can be overridden to allow the protocol to continue while some actions, such as questionnaires or tasks, are in progress. Do you want to allow the protocol to continue while this action is completed?

Pause Protocol
Allow Protocol To Continue

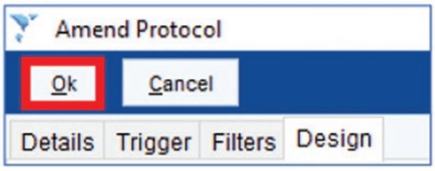
- Repeat the above process for the other unknown template but this time selecting the ‘CHICOLetterNoAntibiotics’ template.


Choose a Letter Template
Browse
Search
Favourites
chico
Search
Clear
Name
L..
Category
Description
CHICOLetterNoAntibiotics
CHICO
CHICOLetterAntibiotics
CHICO
2 Templates
Ok
Cancel

- Check that this part of the design now looks like this making sure that the CHICOLetterAntibiotics is on the left and CHICOLetterNoAntibiotics is on the right.

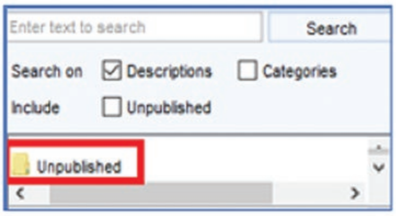

New Word letter with 'CHICOLetterAntibiotics' template
Next
New Word letter with 'CHICOLetterNoAntibiotics' template
Next

- Select Ok in the top-left corner of the Amend Protocol window to save the amended protocol design.

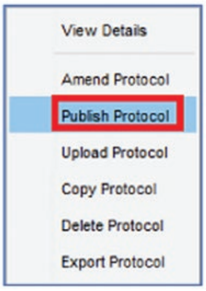

Amend Protocol
Ok
Cancel
Details
Trigger
Filters
Design

Publishing the protocols

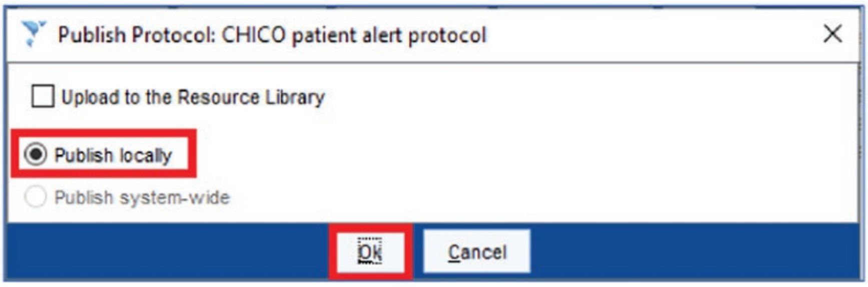
- Select 'Unpublished' on the left-hand side of the Protocols screen.


Enter text to search
Search
Search on
☑ Descriptions
☐ Categories
Include
☐ Unpublished
Unpublished

- Right click the Protocol called '*CHICO patient alert protocol*' and select 'Publish Protocol' from the pop-up menu.


View Details
Amend Protocol
Publish Protocol
Upload Protocol
Copy Protocol
Delete Protocol
Export Protocol

- Select 'Publish locally'. Select Ok.


Publish Protocol: CHICO patient alert protocol
☐ Upload to the Resource Library
● Publish locally
○ Publish system-wide
Ok
Cancel

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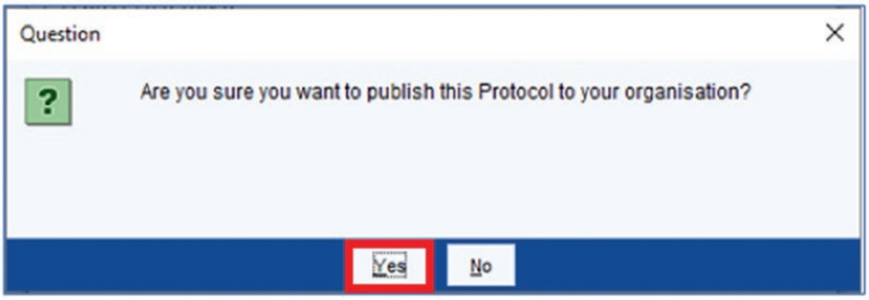
- A confirmation message is displayed. Select Yes.



Are you sure you want to publish this Protocol to your organisation?

- Repeat the above publication sequence for the Protocol called '*CHICO template launch + outcomes*'.

Using *SystmOne* organisation groups

The instructions above describe publishing the clinical Template and Protocols locally.

If the CHICO resources are to be made available to other organisations, you can publish to the appropriate *SystmOne* organisation instead of locally. In addition to publishing the clinical Template and Protocols, the Letter Templates and Clinical Reports will also need to be published to the organisation group.

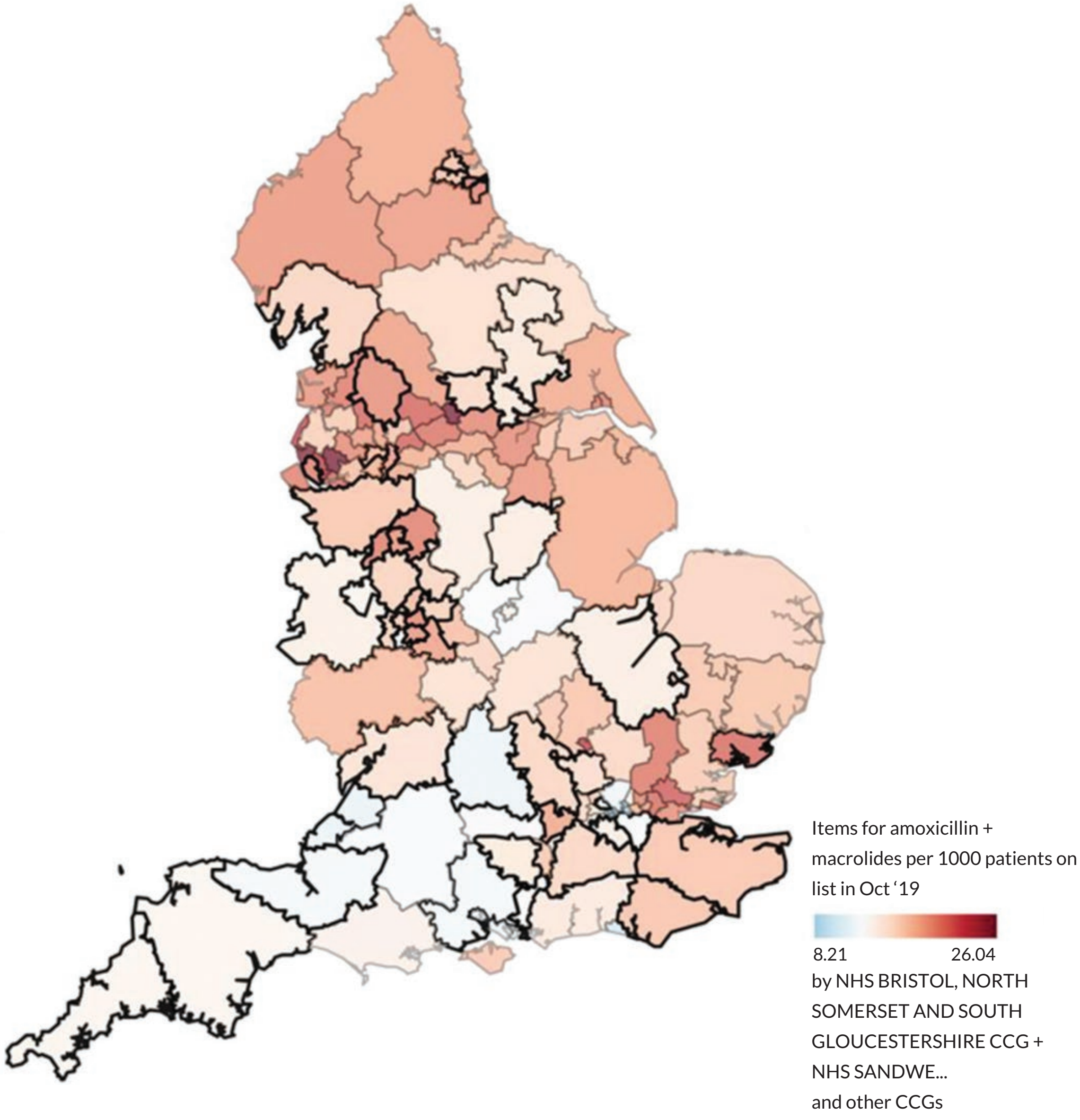
To publish a Letter Template:

- Go to Setup → Referrals and Letters → Word Letter Templates.
- Right-click the letter template and select Publish in the pop-up menu.
- Select the Organisation Group.
- Select Ok.

To publish Clinical Reports:

- Go to Reporting → Clinical Reporting.
- Select the report(s).
- Select the Publish icon .
- Select the Organisation Group.
- Select Ok.

Appendix 5 The Clinical Commissioning Groups taking part in the children with cough study (bold), as defined in 2019


Items for amoxicillin + macrolides per 1000 patients on list in Oct '19
8.21
26.04
by NHS BRISTOL, NORTH SOMERSET AND SOUTH GLOUCESTERSHIRE CCG + NHS SANDWE...
and other CCGs

Clinical Commissioning Groups are shaded in red/pink according to the number of items of amoxicillin and macrolides, per 1000 list size at the mid-point of recruitment, October 2019. Copyright Mapbox, Open Street Map. For up to date data please refer to: https://openprescribing.net/analyse/#org= CCG&orgIds=15E,15C,D2P2L,14Y,06H,04Y,27D,15N, 01A,05D,97R,D4U1Y,11M,D9Y0V,06N,91Q,11N, 15F,99A,14L,01K,13T,06T,05G,W2U3Z,52R,10Q, 01G,05Q,11X,M2L0M,05W,72Q,36L,05V,00P,92A, 03Q&numIds=0501013B0,5.1.5&denom= total_list_size&selectedTab=map.

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Appendix 6 Health economics: unit codes and currency costs

TABLE 20 Unit cost of dispensed amoxicillin and macrolide

Dispensed item	Unit cost – net ingredient cost
Children aged 0–4 years	
Amoxicillin	£1.83
Macrolides	£6.05
Children aged 5–9 years	
Amoxicillin	£3.06
Macrolides	£12.28

TABLE 21 Currency codes used to create a weighted average unit cost for hospital admissions

Currency code	Currency description	Finished consultant episodes
PD11A	Paediatric, Acute Upper RTI or Common Cold, with CC Score 4+	723
PD11B	Paediatric, Acute Upper RTI or Common Cold, with CC Score 1–3	1916
PD11C	Paediatric, Acute Upper RTI or Common Cold, with CC Score 0	1608
PD12A	Paediatric, Asthma or Wheezing, with CC Score 4+	460
PD12B	Paediatric, Asthma or Wheezing, with CC Score 1–3	2850
PD12C	Paediatric, Asthma or Wheezing, with CC Score 0	2024
PD13A	Paediatric Cystic Fibrosis, with CC Score 5+	188
PD13B	Paediatric Cystic Fibrosis, with CC Score 2–4	124
PD13C	Paediatric Cystic Fibrosis, with CC Score 1	41
PD13D	Paediatric Cystic Fibrosis, with CC Score 0	26
PD14A	Paediatric Lower Respiratory Tract Disorders without Acute Bronchiolitis, with CC Score 11+	1198
PD14B	Paediatric Lower Respiratory Tract Disorders without Acute Bronchiolitis, with CC Score 8–10	1331
PD14C	Paediatric Lower Respiratory Tract Disorders without Acute Bronchiolitis, with CC Score 4–7	3466
PD14D	Paediatric Lower Respiratory Tract Disorders without Acute Bronchiolitis, with CC Score 2–3	4048
PD14E	Paediatric Lower Respiratory Tract Disorders without Acute Bronchiolitis, with CC Score 1	3839
PD14F	Paediatric Lower Respiratory Tract Disorders without Acute Bronchiolitis, with CC Score 0	6192
PD15A	Paediatric Acute Bronchiolitis with CC Score 5+	1252
PD15B	Paediatric Acute Bronchiolitis with CC Score 2–4	3007

continued

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TABLE 21 Currency codes used to create a weighted average unit cost for hospital admissions (*continued*)

Currency code	Currency description	Finished consultant episodes
PD15C	Paediatric Acute Bronchiolitis with CC Score 1	3179
PD15D	Paediatric Acute Bronchiolitis with CC Score 0	7174
PD65A	Paediatric Upper Respiratory Tract Disorders with CC Score 5+	215
PD65B	Paediatric Upper Respiratory Tract Disorders with CC Score 2–4	390
PD65C	Paediatric Upper Respiratory Tract Disorders with CC Score 1	272
PD65D	Paediatric Upper Respiratory Tract Disorders with CC Score 0	535

CC, complication and comorbidity.

EME
HSDR
HTA
PGfAR
PHR

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