Mixed-method impact and implementation evaluation of the “Pharmacy First” Services for management of common conditions

Study information
Full name: Mixed-method impact and implementation evaluation of the “Pharmacy First” Services for management of common conditions
Short name: Evaluation of Pharmacy First
Dates: 01 February 2024 to 31 January 2027
Protocol version: 1.3
IRAS number: 342442
Funder: This research is funded by the National Institute for Health and Care Research (Health Services and Delivery Research, NIHR160217)

Study summary

Background

On 31st January 2024, the Government launched Pharmacy First (PF) across England, which enables community pharmacists to supply prescription-only medicines, including antibiotics, to treat seven common health conditions: earache, uncomplicated urinary tract infections in women, sore throat, sinusitis, impetigo, shingles and infected insect bites, after consultation with a community pharmacist. It is hoped that PF will enable faster care and reduce pressure on general practitioners (GPs).

Aims and objectives

The evaluation will investigate whether PF has the intended effect of enabling faster care and reducing pressure on GPs. The aim is to evaluate the impact of PF on the volume of prescribing, case mix of GP consultations, A&E and hospital use, equity of access, antimicrobial resistance trends and cost for different groups of patients in different contexts.

The specific objectives are:

1. To develop a theory of change to guide the evaluation, informed by an implementation science framework and in consultation with stakeholders.

2. To complete a scoping evidence review and stakeholder interviews to understand current clinical pathways, existing legal frameworks and instructions on prescribing relevant to the seven PF conditions, and to contribute to parameterising the economic evaluation, where appropriate.

3. To establish data access and linkage to obtain data for the quantitative impact analysis and subsequent economic evaluation.

4. To describe the uptake of PF nationally, regionally and locally for the seven conditions.

5. To assess how health care use changes after the introduction of PF.

6. To evaluate how antimicrobial use and safety changes following introduction of PF.

7. To assess the impact of PF on national trends in antimicrobial use and resistance for key antibiotic/bacterial organism combinations using national surveillance systems.

8. To understand how and why the programme is and is not taken up by different pharmacies and in different areas.

9. To understand the perceptions and experiences of service users.

10. To assess national budget impact of PF from the NHS and personal social services (PSS) perspective.

11. To estimate the impact of PF on patients’ health and costs from an NHS and PSS perspective to generate estimates of cost-effectiveness/net benefit.

12. To assess the adherence of implementation to the original service specification (fidelity) and identify scope for adapting the PF specification and delivery to improve impact, equity and cost-effectiveness.

Methods

This study is a 36 month, mixed-methods evaluation combining quantitative and qualitative data. Methods comprise evidence synthesis, semi-structured interviews, focus groups, interrupted time series analysis (ITSA) and an economic evaluation. Findings will be brought together and interpreted using an implementation science framework, the Consolidated Framework for Integration Research (CFIR), supplemented by Proctor’s implementation outcomes framework.

The evaluation comprises five work packages:

Work package 1: Literature review, scoping and theory of change, designed to undertake initial orientation and scoping by (i) conducting a review of the published and grey literature on pre-existing PGD and Pharmacist Independent Prescriber (PIP) programmes within the UK; (ii) conducting interviews with English policy officials, national GP leaders and frontline pharmacists; (iii) conducting interviews with Scottish and Welsh policy advisers, GP leaders and frontline pharmacists; and thereby (iv) contributing to the development of other work packages.

Work package 2: Development of data linkages, and analysis of uptake and impact on consultation patterns, workload and patient safety, including antimicrobial use, designed to (i) establish data access and linkage; (ii) describe the uptake of PF nationally, regionally and locally; (iii) evaluate how health care usage changes after the introduction of PF and the impact of PF on inequalities; (iv) evaluate how safety outcomes and antimicrobial use change following introduction of PF; and (v) describe the impact of PF on antimicrobial use and resistance (AMR) trends.

Work package 3: Economic evaluation aims to assess the economic impact of PF. It will: (i) assess the national budget impact of PF from the NHS and personal social services (PSS) perspective; and (ii) estimate the impact of PF on patients’ health and costs from an NHS and PSS perspective to generate estimates of cost-effectiveness/net benefit.

Work package 4: Implementation and fidelity of the roll out has three objectives: (i) to understand how and why PF is and is not taken up including the fidelity of the scheme to the original specification; (ii) to evaluate the effects of PF on the access to, and acceptability of, community pharmacy services to populations historically marginalized in terms of primary health care access; and (iii) to assess pharmacists’ and GPs’ perceptions of the safety of the scheme.

Work package 5: Mixed-methods analysis, consolidation of findings and identification of policy implications, has two objectives: (i) to undertake an integrated evaluation of the implementation of PF structured using the CFIR and Pearson’s outcomes framework; and (ii) to provide insight as to how to improve the PF scheme, assuming it is sufficiently cost-effective to be continued.

Co-production with lay researchers

The evaluation will be co-produced with lay researchers representing diverse groups of service users including those who have been historically marginalised in research and medically underserved, such as those from low socio-economic background, people affected by homelessness, people from racially marginalised groups and vulnerable migrants. Co-researchers will contribute to the evaluation by orienting work packages, participating in the ethics application process, designing inclusive data collection tools, participating in research activities (e.g. conducting interviews and focus groups), interpreting data, and formulating reports. They will also organise citizens' forums in the regions where the research is being conducted to elicit a diverse array of perspectives.

Impact and dissemination

We will provide interim and final reports, translating the study findings into accessible, usable and high-impact learning for practice. The findings should contribute to improvements in access to primary health care, better antimicrobial use and refinements to PF (if PF is judged cost-effective). As well as publishing in specialist journals and the NIHR library, we will disseminate findings through briefings to policy officials, scientific meetings, pharmacy and general practice networks, patient organisations and the mass media. Further, our knowledge translation activities will include two animated outputs co-produced with lay co-researchers, and a podcast series documenting the process and challenges of the evaluation.

Funder

The study is funded by the National Institute for Health and Care Research (NIHR) Health and Social Care Delivery Research Programme (award: NIHR160217).

Contents

Background and rationale

Under the Government’s NHS Primary Care Recovery Plan, NHS England (NHSE) has commissioned Pharmacy First (PF)(1). Since the 31st of January 2024, pharmacies participating in PF are able to supply prescription-only medicines for seven common conditions: earache, uncomplicated urinary tract infections (UTIs) in women, sore throat, sinusitis, impetigo, shingles and infected insect bites, after consultation with a community pharmacist (2). PF builds on the NHS Community Pharmacist Consultation Service (CPCS), in which patients registered with a General Practitioner (GP) can be referred to community pharmacies for minor illness advice and treatment.

In the new PF service, users can walk into pharmacies to access care, assuming self-care has been unsuccessful. PF aims to reduce demand on GPs and Accident and Emergency (A&E), thus improving timeliness of treatment. PF will initially use Patient Group Directives (PGDs), which allow specified health professionals to supply and/or administer medicines without a prescription. An enhanced role for community pharmacy has been shown to improve access to health care in socioeconomically disadvantaged areas, improving equity of access (3,4). The impact of PF on patients, workforce, care pathways and cost may differ geographically, across the seven conditions, and over time, hence the need for national evaluation.

The Government estimates that PF may release up to 10 million GP appointments annually (2) enabling GPs to provide more timely access to those with more urgent need. However, there is also a need to ensure PF does not have any unintentional effects such as avoidable adverse health sequelae. Similar initiatives have shifted care for minor ailments to pharmacies for over two decades, introducing treatment of head lice, threadworm, bacterial conjunctivitis, insect bites and cystitis (5). PGDs for these and other conditions have been implemented in some community pharmacies across Scotland, Wales and some areas of England. Research on PGDs has tended to focus on safety, antibiotic use or impact on the health system in a single area, thus limiting generalisability (5–7).

The extent to which PF will shift demand for services for the seven named conditions away from higher cost settings is uncertain. However, evidence from early adopting areas will be able to inform our understanding of the PF service, and thence our research design. In a Scottish study of PF for UTIs, impetigo and chronic obstructive pulmonary disease, two-thirds of GPs found it useful, reducing pressure on their appointments (8). In the Welsh ‘sore throat test and treat’ service, pharmacists managed 91% of consultations in the pharmacy, and referred only 9.3% people to a GP and 0.2% to A&E (9).

The extent to which PF will affect other outcomes of interest is also uncertain. It is not known if PF will unmask unmet need, whereby overall demand for treating these seven conditions with antibiotics will increase. In turn, there is a concern that widening access to antibiotics may increase antimicrobial resistance (AMR)(10), by increasing population carriage of organisms resistant to first line antibiotics, thus increasing second line antimicrobial use (AMU) in the community. It will be critical to monitor population level AMU and AMR.

Aim, research question, and objectives

The evaluation team will conduct a broad, mixed-method evaluation of the implementation and impact of PF’s roll-out. We aim to evaluate its take-up, safety, equity, cost effectiveness and acceptability, as well as the implications for antibiotic use and thence AMR. The evaluation aims to answer the following overarching research question: how are the seven PF minor illness PGDs being implemented across England and what are their impacts on volume

of prescribing, case mix of GP consultations, A&E and hospital use, equity of access, cost for different groups of patients in different contexts?

The specific objectives of the evaluation are to:

1. To develop a theory of change to guide the evaluation, informed by an implementation science framework and in consultation with stakeholders.

2. To complete a scoping evidence review and stakeholder interviews to understand current clinical pathways, existing legal frameworks and instructions on prescribing relevant to the seven PF conditions, and to contribute to parameterising the economic evaluation, where appropriate.

3. To establish data access and linkage to obtain data for the quantitative impact analysis and subsequent economic evaluation.

4. To describe the uptake of PF nationally, regionally and locally for the seven conditions.

5. To assess how health care use changes after the introduction of PF.

6. To evaluate how antimicrobial use and safety changes following introduction of PF.

7. To assess the impact of PF on national trends in antimicrobial use and resistance for key antibiotic/bacterial organism combinations using national surveillance systems.

8. To understand how and why the programme is and is not taken up by different pharmacies and in different areas.

9. To understand the perceptions and experiences of service users.

10. To assess national budget impact of PF from the NHS and personal social services (PSS) perspective.

11. To estimate the impact of PF on patients’ health and costs from an NHS and PSS perspective to generate estimates of cost-effectiveness/net benefit.

12. To assess the adherence of implementation to the original service specification (fidelity) and identify scope for adapting the PF specification and delivery to improve impact, equity and cost-effectiveness.

Plan of investigation

Study design

This study is a 36 month, mixed-methods evaluation combining quantitative and qualitative data to assesses implementation and impact of PF, and explore what works, for whom, and why, at local (ward or Primary Care Network), Integrated Care System (ICS), regional and national levels. Data collection will be completed by mid-2026 and a final report submitted in

January 2027, plus interim reporting. Since the roll-out of PF is in its early stages, some of the design and methods are unavoidably open to revision. Emerging findings and insights from early work packages will shape lines of enquiry and design decisions in the research to follow. Findings will be brought together and interpreted using an implementation science framework, the Consolidated Framework for Integration Research (CFIR), supplemented by Proctor’s implementation outcomes framework (see below).

The study design has been guided by several outcomes of interest:

- change in pharmacy, general practice, and A&E case mixes
- comparative feasibility and cost of implementing PF for the seven conditions
- volume of antibiotics and antivirals dispensed
- differences in the roll-out of PF and its impact depending on the age, sex, socioeconomic group, ethnicity, or geography (especially urban/rural divides) of service users
- impact on enrolled services in terms of staff, risk, data, safety, and behavioural implications
- differences between how PF is implemented and the stated intention
- potential consequences of PF for inequalities in access to health services and outcomes
- impact on national antimicrobial use and resistance for key antibiotic/bacterial organism combinations

Theoretical framework

The evaluation will be guided by the Consolidated Framework for Implementation Research (CFIR)(11). This will help identify the key factors likely to affect the implementation of PF. The CFIR is a meta-theoretical framework comprising 39 constructs arranged across five domains (outer setting, inner setting, individual characteristics, intervention characteristics and implementation process). It is a practical guide for systematically assessing barriers and facilitators that affect implementation outcomes, especially at different levels (national/local). The CFIR has been used to assess the implementation of a range of new policy and practice interventions using mixed method and qualitative designs (11–13). The CFIR draws attention to the likelihood that PF will vary in its impacts depending on context and on how it is implemented in different places, and prompts the researcher to identify the factors that bring this about.

While the CFIR helps understanding of the factors that affect implementation, it provides less direct information on outcomes. Hence, we will also use Proctor’s framework of implementation outcomes (14). Proctor’s framework comprises eight discrete outcomes for evaluation: acceptability, adoption (also referred to as uptake), appropriateness, costs, feasibility, fidelity, penetration (integration of a practice within a specific setting) and sustainability (also referred to as maintenance or institutionalization).

The findings from the work package 1 literature review and scoping interviews of the factors that have affected implementation of PGDs across the UK and which appear likely to shape future implementation of PF will be mapped to the CFIR domains and constructs. From this, we will be able to develop an understanding of the key characteristics of the intervention (the PF service) that could affect implementation. We will also contribute to parameterising the economic evaluation, where appropriate. The later interviews in work package 4 will further establish the factors across the other CFIR domains and constructs that interviewees believe

may impede or support future policy outcomes. These findings will be used to develop an initial theory of change for PF which will be periodically revised in light of emerging findings.

Methods

The evaluation uses evidence synthesis, semi-structured interviews, focus groups, interrupted time series analysis (ITSA) and an economic evaluation. It comprises five Work Packages (WPs), described below, which integrate to answer all research questions.

Work packages

Work Package 1: Literature review, scoping and theory of change (led by Glover and Lalani with input from Anderson and Pacho)

Summary: this work package comprises initial orientation and scoping to guide the evaluation.

Aims

1. To complement the clinically-oriented NHSE literature reviews developed to inform the design of the PF service by reviewing peer reviewed and grey literature on pre-existing PGD and Pharmacist Independent Prescriber (PIP) programmes.
2. To provide deeper understanding of the factors that affect implementation of PGDs.
3. To describe the evidence underpinning the roll-out of PF and services like PF in England, Wales and Scotland, including the intended goals and expectations of such initiatives.
4. To develop an initial theory of change for PF.
5. To contribute to other WPs.

Methods and analysis

1. Literature review: Undertake a review of peer reviewed and grey literature on pre-existing PGD and PIP programmes, to complement the clinically-oriented NHSE literature reviews developed to inform the design of the PF service, to which we will request access. We will also request unpublished policy documents related to the development of PF. We will review literature on established PGDs, such as those for oral contraception, eye infections and head lice, to provide deeper understanding of the factors that affect implementation of PGDs. Along with the CFIR, the findings from the literature review will inform the development of the interview guide for the scoping interviews listed below.

2. Scoping interviews (England): We will conduct semi-structured interviews (n=25) with purposively selected stakeholders involved in strategic, implementation, and delivery roles at ICS and national level (policymakers at DHSC and NHSE, and key actors at the General Pharmaceutical Council (GPhC), Royal Pharmaceutical Society (RPS), the National Pharmacy Association (NPA), Pharmacists Defence Association (PDA), Community Pharmacy England (CPE), and selected chairs of Local Pharmaceutical Committees (LPCs) within ICS areas as well as national GP/Primary Care leaders. In our interview sample, we will also include front-line pharmacists identified through snowball sampling (both those delivering the service and those not). At these interviews, we will ask for grey literature and other additional documents to support our literature review, with the expectation that these

experts will be well-placed to describe and provide internal literature and assessments on the evidence underpinning the roll-out of PF. We will re-interview a sub-set of these interviewees to contribute to WP4 in mid-2026, asking them to especially reflect on the PF implementation process over time and the extent to which the Programme has been able to be implemented as intended.

3. Scoping interviews (Scotland & Wales): We will conduct semi-structured interviews (n=25-50) with purposively identified stakeholders involved in strategic, implementation and delivery roles in Welsh and Scottish government, Community Pharmacy Scotland and Wales, and RPS Wales and Scotland, national GP/Primary Care leaders as well as front-line pharmacists delivering services similar to PF in each country. As with section 2, we will ask for grey literature and other additional documents to support our literature review, with the expectation that these experts will be well-placed to describe and provide internal literature and assessments on the evidence underpinning the roll-out of PF.

All scoping interviews will be undertaken following informed consent, using a semi-structured topic guide, and will be analysed deductively and inductively using the CFIR as a coding framework to manage and organise the data in the first instance. Interviews will be held online or in person, dependent on participants’ preferences.

4. Programme theory of change: We will use findings from the literature reviews and scoping interviews (sections 1 – 3) and the CFIR to develop an initial theory of change for PF. This will inform the other WPs. The goal will be to map all areas where care pathways change and to validate these in qualitative research interviews in WP4.

WP2: Development of data linkages, and analysis of uptake and impact on consultation patterns, workload and patient safety, including antimicrobial use (led by Avery, with substantial input from Ashiru-Oredope, Sonnex, and MacKenna)

Summary: guided by the theoretical frameworks and underpinnings developed in WP1, this work package will evaluate the uptake of PF nationally and its impact across health services, including GPs, A&E and hospitals, on consultation patterns, workload and patient safety, including AMR.

Aims

1. To establish data access and linkage.
2. To describe the uptake of PF nationally and regionally.
3. To evaluate how health care usage changes after the introduction of PF and the impact of PF on access to health care
4. To evaluate safety outcomes and how antimicrobial use changes following introduction of PF.
5. To link analysis of antibiotic use to AMR**.**

Methods

1. Establish data access and linkage

There will be two main sources of data for the analyses of administrative and clinical data: GP electronic records, linked to A&E and hospital admission data (for determining changes in primary care activity associated with introduction of the PF scheme), and pharmacy-level

data captured as a consultation record at the point of service use (for describing uptake of PF by community pharmacies, activities undertaken and structural and area characteristics).

We will establish data access and record linkage using OpenSAFELY, a secure, open-source software platform for analysis of electronic health records data. OpenSAFELY was established in the early days of the pandemic and has been used to generate analyses since then to support the response to COVID-19. The first OpenSAFELY analysis was published in Nature (15) with a substantial body of work now published in other high impact academic journals such as BMJ and Lancet. OpenSAFELY is now being used by approximately 30 organisations including leading academic institutions, arm’s length bodies (e.g., National Institute for Health and Care Excellence, UK Health Security Agency (UKHSA), NHSE) and others like the Nuffield Trust. It is currently deployed in the data warehouses of the two major GP clinical systems (EMIS and TPP) giving access to the NHS records of over 58 million people (>99% of registered GP patients in England). These data, unavailable elsewhere, can be linked to hospital admission data and A&E attendance. On 18 November 2023, NHSE confirmed publicly that OpenSAFELY can now be used for research beyond COVID-19.

We will work with OpenSAFELY to:

- complete information governance to secure data access
- develop software to interrogate the proposed structured messages that will be sent between community pharmacies and GPs
- train staff to use the OpenSAFELY dashboard
- describe the data elements/variables (e.g., possible values, distribution, etc.) in an OpenSAFELY “short data report” to support all researchers using the platform. As PF is a new service, there may be discrepancies between planned and actual data recording
- develop an OpenSAFELY PF “variables library”. This will be made publicly available for inspection and re-use
- develop descriptive epidemiological dashboards in OpenSAFELY describing the clinical and demographic subgroups of patients accessing the PF service over time
- request anonymised patient-level data from pharmacy consultation records, and
- investigate linking OpenSAFELY data to UKHSA AMR data.

General practices are now required to collect data such as call volume, timing of calls and percentage of calls answered but it is not currently clear whether there is any access to these data at national level for research. Increasingly, many practices utilise online triage systems too. Thus, we will also investigate the feasibility of accessing and analysing such data.

2. Describe the uptake of PF nationally, regionally and locally

Pharmacy level data will be used to undertake a descriptive analysis of the following at national, NHS regional, Integrated Care System (ICS), and local levels (e.g., ward or Primary Care Network (PCN) level), at monthly intervals from 1st February 2024:

- Number of community pharmacies (CPs) providing PF for at least one condition
- Number and proportion of PF consultations broken down by:
  - location of pharmacy (urban versus rural)
  - deprivation level using pharmacy postcode linked to Index of Multiple Deprivation
  - number of patients seen by CP who have no registered GP

  - numbers of patients accessing each of the PF conditions
  - number and type of medicine supplied via PGD
  - number of advisory consultations, or advice plus OTC supply events for each PF condition (where a consultation record for these exists)
  - how patients were referred to each PF service (walk-in, GP or NHS111)
  - number of CP referrals to GP, A&E or other health service per PF condition
- Characteristics of patients receiving PF consultations, which we expect as a minimum will include information on age, gender/sex and ethnicity
- Characteristics of patients accessing GP services (via OpenSAFELY) for the seven PF conditions before and after introduction of PF to allow for comparison to CP characteristics.

3. Describe how health care usage changes after the introduction of PF and the impact of PF on access to health care

We hypothesise that the rollout of PF will be associated with a reduction in GP appointments for the seven conditions included in PF, with this reduction being associated with increased GP appointments for other conditions. We do not anticipate total GP consultations falling because of PF, but patient access for GP appointments may improve for patients who have previously struggled to gain timely access. We will also assess whether PF results in changes in A&E contacts and hospital admissions for the conditions covered by the scheme.

(a) Change in GP consultations

Following initiation of PF, we will examine changes in GP consultation rates for each of the seven conditions included in the scheme; we will also investigate changes in total GP consultations and sub-group analyses by deprivation, and urban versus rural settings. The main analysis will be done at the level of individual general practices using patient-level data. Based on permissions already in place for use of OpenSAFELY, we will be able to do this for virtually all general practices in England covering a population of 58 million. A similar approach will be taken to examining changes in A&E and hospital attendance (see (b) below), antimicrobial use (at general practice level) and safety (see section 4 below).

We will identify GP consultations for each of the seven common conditions based on the relevant SNOMED CT codes (the computer codes that clinicians use when recording consultations) for each condition. Consultation rates will be calculated monthly per head of population in each general practice.

(i) Data analysis

We plan to undertake analysis from up to 24 months before the PF start date, and for as long as follow up data are available before undertaking the final analysis. We will use a quasi-experimental approach, using interrupted time series analysis (ITSA), with the intervention start date set as 1st February 2024 (16). Analysis will also be undertaken at the local level (e.g. PCN) to obtain disaggregate effect estimates, allowing variation in effects to be explored, subject to enough data being available to avoid the identification of individuals.

The ITSA will use generalised linear mixed models for the monthly GP consultation rates for each condition, to estimate changes in the level and trend in consultation rates after the PF intervention compared with before. Calendar time will be included as a covariate along with adjustment for seasonal effects and any within-practice covariates (such as number of full-time equivalent GPs) identified prior to the analysis. We will take account of within practice

clustering. We will take a similar quasi-experimental approach for analyses of changes in A&E and hospital contacts; changes in telephone contacts to general practices (if these data are available), and antimicrobial use (at general practice level). Further analyses will be conducted, taking account of sociodemographic characteristics of patients, to examine any impact on access and outcome inequalities. Intervention effects will be presented as rate ratios with 95% confidence intervals. Data will be analysed using the statistical package Stata (or similar). Given we will be testing for effects on multiple outcomes for multiple conditions (for changes in consultations and other variables outlined below), there is a risk of false discovery of effects (multiple testing bias). We will interpret findings in the context of effect sizes and how many significant effects we would expect to detect due to chance alone.

(ii) *Sample size calculation*

Virtually all general practices in England with patients that access PF will be included in the final evaluation (as well as practices where patients do not access PF). There is a lack of robust literature on sample size calculations for ITSA (and related analyses); there is a complex relationship between number of time points, sample size per time point and expected effect size (16). In general, however, with over 24 time points >80% power can be achieved with as few as 150 subjects per time point. As we plan to include a minimum of 24 time points (and a maximum of 48) and include around 6500 general practices, we are confident this study will be sufficiently powered to detect relevant changes in the outcomes of interest.

(b) Change in A&E and hospital admissions

We hypothesise that A&E visits and hospital admissions for the seven conditions in the PF scheme should not increase and may decrease if PF allows improved access to treatment. To evaluate any changes over time in A&E use and hospital admissions associated with the PF conditions, the number of A&E attendances and hospital admissions related to the seven PF conditions within England will be analysed using secondary care data, available via OpenSAFELY, and linked to the primary care records. Quasi-experimental methods such as ITSA (see above) will be undertaken to estimate changes in rates following the PF intervention.

(c) Change in GP phone contacts

If feasible after exploration in section 1 above, we will examine changes in general practice phone call and online triage data following the introduction of PF. This will include call volume and percentage of calls answered. We will use quasi-experimental methods as outlined previously to examine whether these variables change in association with the introduction of PF. This work will also be linked to the qualitative analysis in WP4.

Additionally, national data on time from appointment booking to appointment date for general practice are available. These data will be interrogated and if possible, an ITSA approach used to determine if there is a change in GP appointment waiting time after the introduction of PF. We hypothesise that the introduction of PF may reduce the GP appointment waiting time.

(d) Potential impact of PF on access to healthcare

We will identify the sociodemographic, geo-spatial and local population behavioural covariates, at neighbourhood levels, which are influencing the uptake and impact of PF, and the extent to which they are doing so.

We will perform a detailed analysis using a national health surveillance platform developed during the UKRI COVID-19 Rapid-Response grant “The CIVIC Project: A Sustainable Platform for COVID-19 syndromic-surveillance via Health, Deprivation and Mass Loyalty-Card Datasets”. This unique platform, implemented in collaboration with the Office for National Statistics, the NHS, UKHSA and a range of private sector data partners (including Boots UK, Tesco, Co-op), allows for the analysis of an unparalleled range of small-area (neighbourhood) population data across the UK, and hence to examine the socio-demographic, health and behavioural factors across the population that may relate to both uptake and ongoing effectiveness of the PF initiative (17). This dataset is updated at least six-monthly and will allow us to examine changes before and after the introduction of PF.

We will predominantly focus on candidate factors influencing the uptake of PF (at local GP/pharmacy levels) and related to inequality that are underpinned by prior theoretical literature (18). These include local age distributions; gender; cultural backgrounds; ethnicity; mobility levels; population density; indices of multiple deprivation; pharmacy footfall; pharmacy usage patterns; seasonal non-stationary disease prevalence; mental health; and a range of behavioural factors related to purchase of over-the-counter medication.

We will develop a range of predictive models (candidates include Linear Regression, Random Forests, XGBoost, Neural Networks) that link socio-demographic factors to the impact of PF in each neighbourhood. Models will be optimised via a rigorous process of nested-cross validation, before exhaustive testing on hold-out data sets to identify the best performing model. Variable Importance Analysis (19) will then be applied to this model, summarizing the influence that each explanatory variable (e.g., deprivation levels) is estimated to have on uptake of PF across UK neighbourhoods.

4. Evaluate how safety outcomes and antimicrobial use change following introduction of Pharmacy First

We aim to describe antimicrobial use and evaluate the PF safety risks primarily using OpenSAFELY data.

(a) Antimicrobial usage

We will describe changes in patterns of antimicrobial use before and after the introduction of PF, for antimicrobial agents used in the PF scheme. Details of all antimicrobial agents supplied through PF will be added to patients’ GP electronic records and so will be accessible through OpenSAFELY. We will use quasi-experimental approaches (as described above) to determine whether the introduction of PF is associated with changes in antimicrobial use (combining GP and PF prescriptions at practice level). This will include:

- changes in duration for each of the antimicrobials prescribed for a condition included in the PF service
- using the limited data available on private prescriptions available at pharmacy-level for antimicrobials (e.g. for UTI treatment), we will evaluate how monthly numbers of these prescriptions change after introduction of PF

(b) Safety

We will use linked PF records, general practice and secondary care data, to evaluate changes in indicators of patient safety, including unintended consequences of antimicrobial use in PF. This will include:

- As per section (3b) above, a reduction or no change in A&E or hospital admissions for the seven conditions in PF will be considered to demonstrate overall safety of the service
- Specific access to subsequent healthcare immediately following PF: for example, UTIs: access to other healthcare settings (GP, A&E, hospital admission) within 30 days of access to PF for the same or related conditions, such as pyelonephritis or sepsis will be quantified. A comparison will be made to initial UTI consultations occurring in general practice during the timeframe
- the frequency with which medication was supplied via PF where a documented allergy or contra-indication (as specified by the PF PGD for each medication) exists in the GP record.
- Identify the number of patients who received multiple courses of antibiotics, more frequently than the exclusion criteria allow in the clinical pathway for each condition.
    - If this misuse is considered high, we will follow up on the number of patients where use of PF has possibly masked an underlying condition, e.g. for PF UTI treatment we will quantify the number of new diagnoses of type 1 or 2 diabetes occurring following multiple UTIs

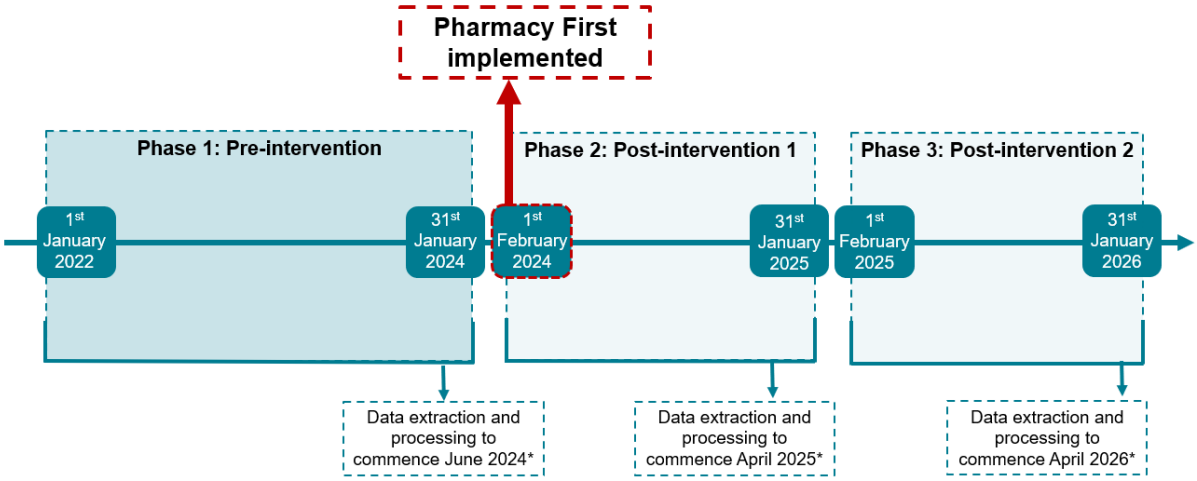
5. National surveillance of antimicrobial use and resistance

Capturing information related to national antimicrobial consumption and resistance following the roll-out of the PF service in England is crucial to identify and respond to any impact of those changes on AMR. The public, patients, health care professionals and policy makers need to know whether current policy initiatives aimed at widening the range of access to antimicrobials have adverse impacts on the goals of the UK AMR National Action Plan (20).

We plan to analyse the impact of PF on trends in:

- the number and type of antibiotics dispensed in the community in England (total and by patient age, per 1,000 population), with sub-group analysis by region/ICS, age group, and antibiotic class (in the context of national surveillance), including antimicrobials approved for use in the seven PF conditions using UKHSA’s routine antimicrobial surveillance data (obtained from ePACT2 from NHS BSA)
- the number of community-associated urine samples positive (by causative organism, age group, sex, ethnicity and deprivation) and the urine isolate AMR rates (by causative organism) using UKHSA’s Second Generation Surveillance System (SGSS) data
- the number of positive bacterial community-associated respiratory samples (by causative organism, age group, sex, ethnicity and deprivation) and the respiratory isolate AMR rates (by causative organism) using SGSS data.

Quasi-experimental analyses will be conducted using ITSA, or similar methods as described above *‘(3a) Change in GP consultations’*, and building on previous research in this area (21–23), at two timepoints: one year and two years after PF introduction (Figure 1), comparing monthly data up to two years after roll-out of PF with two years pre-PF for the seven PF conditions and in total.



* >8 week time lag after end of period required to ensure data completeness

Figure 1. Interrupted time series analysis data extraction plan (ePACT2, NHS BSA and Second Generation Surveillance System, UKHSA)

Work Package 3: Economic Evaluation (led by Elliott)

Summary: this work package will assess the economic impact of PF. It will develop a model informed by the literature reviewed in WP1, and broader health economic theory on rational choice behaviour, principal-agent problems and supplier-induced demand, informed by extra-welfarist approaches to economic evaluation.

Aims

1. To map the current processes of care with and without PF for the seven conditions and reflect these in the theoretical model.
2. To assess the national budget impact of PF from the NHS and PSS perspective.
3. To estimate the impact of PF on patients' health and costs from an NHS and PSS perspective to generate estimates of cost-effectiveness/net benefit.

Methods

Literature review and analysis plan

We will undertake a rapid literature review of economic studies that focus on other PF-type services to identify evidence on their relative cost-effectiveness. This will be combined with evidence from WP1 to inform our analytic, costing and model design. Informed by work in WP1 and WP2 to understand patterns of PF uptake, we will identify approaches to constructing counterfactual aggregate measures, subject to data availability (including comparative ITSA and staggered difference-in-difference).

The literature reviews in WP1 and WP3 will be combined with key informant feedback to support design of the economic evaluations in a number of ways. They will inform model approach and structures, target population characteristics, treatment pathways, resource use and relevant outcomes. We will be guided by findings from this process to determine which population sub-groups should be represented in the economic evaluation, and/or need to be analysed separately. Data availability from WP2 for different population sub-groups will determine, to an extent, whether we are able to carry out specific sub-group analyses. We will work with key informants to carry out exploratory analyses where appropriate.

PF Costs
These costs will comprise PF intervention delivery costs, delivery costs for the various models of PF, and downstream costs incurred as a result of PF or usual care.

PF intervention delivery costs
The cost of implementing and running PF will be based on data gathered through semi-structured interviews with key stakeholders (undertaken in WP1). The PF service will be associated with a professional fee paid from the NHS to pharmacists. We will carry out a top-down micro-costing study to estimate the actual costs incurred during the delivery of the PF intervention. Resource use categories will be refined through consultation with service providers. Resource use for delivering the PF intervention will be estimated by accessing relevant reports and expert input in WP1. The following resource items will be measured for the PF: implementation and service delivery costs, including NHS costs; workforce changes associated with PF; pharmacy costs; and data system maintenance.

We will work with our WP1 stakeholders to identify pharmacies providing PF. If content to share information, they will be asked about the amount and allocation of PF funding, and the costs (monetary and non-monetary) of set up and implementation. Appropriate sensitivity analyses will be conducted to assess the robustness of findings to the assumed costs.

Current care intervention delivery costs
Current care will potentially incorporate GP care, self-care, self-care plus GP care, and self-care followed by A&E. We will identify how current care is currently delivered as part of WP1 and attach costs to these care pathways. These data will be used in the economic evaluation.

Downstream costs
The impact of the PF intervention on prescribing, primary care consultations and any subsequent care, including secondary care, will be obtained via data extraction methods detailed below. This will include costs associated with AMR and safety-related events that have been recorded.

National budget analysis
The combination of the costs above will inform a national budget analysis to determine the impact of introducing PF on healthcare resource use. We will also conduct cost-consequences analyses for each PF condition (and a composite of all seven). Due to the availability of data, the population of interest for the analysis is every patient registered with a general practice in England. This may exclude those people who use PF but are not registered with a general practice; this is mitigated by reviewing the literature in WP1 to identify the characteristics, location and patterns of health care use, including use of CP, of those unlikely to be registered with general practices.

We will focus on budget impacts from the NHS perspective, using national data from OpenSAFELY. We will assess aggregate changes in prescribing activity, use of community health and social care services, primary care contacts, A&E visits and hospitalisations associated with each condition in PF and deemed to be related to the PF conditions. These changes in activity will be costed using national unit costs from routine sources.

Changes in cost of activity over time and by patient characteristics

We will examine changes in the cost of activity over time and by patient characteristics: age, gender, SEG, ethnicity, serious mental illness, learning disabilities, pharmacy density and geography.

Mapping processes of care and construction of economic models to support incremental economic analysis: *general methodological approach to building disease-specific models*

Cohort-level state transition models for each condition will be developed and reported according to standard validation and reporting criteria.(24,25) Each PF condition is acute and we expect the time to resolution to be less than one year, so the evaluation time horizon will be one year. We will recruit service providers (community pharmacists and GPs) and patients through our stakeholder contacts in WP1 to map the processes of care for each condition.

To estimate the patient-level outcome and costs associated with each PF condition, it is necessary to design a treatment pathway, or “model” that reflected the likely events that occur when people experience one of these conditions. This includes what acute events happen, how commonly, and how serious these are likely to be for the patient in terms of short and long-term quality of life, mortality risk and health care resource consumption. These models (also called cohort-level state transition (Markov) models) will be developed to generate estimates of patient outcomes (measured as quality-adjusted life-years (QALYs)) and cost to the NHS in England and patient outcomes (measured as QALYs) associated with the seven PF conditions.

The economic models needed to reflect the likely events that occur when people experience a PF condition:

- What happens and how serious is it for the patient?
- Is this likely to result in primary or secondary care management?
- Is this event likely to increase risk of mortality or reduce quality of life in the short-term?
- How is long-term quality of life, mortality risk and health care resource consumption likely to be affected by this acute event?

States included will be specific to the PF condition under investigation. The length of time (also called sojourn time) a person spends in one health state is referred to as “cycle length”, and will reflect the natural potential rate of change from one state to another. A half-cycle correction will be used to account for the timing of events within a health state sojourn time. Each model will start with initial self-diagnosis of the PF condition health state. Each model will contain an absorbing health state (“dead”). We will determine the impact by estimating the effect on costs and QALYs using a one-year time horizon. We will take the perspective of the NHS in terms of direct costs of managing the consequences of the PF condition. Total QALYs will be calculated as the time in each state weighted by the state-specific utility score. The costs and outcomes will be discounted at the recommended rate of 3.5% per annum (2). The cost year used will be 2024/25. Where it is necessary to inflate costs, the Hospital & Community Health Services (HCHS) index will be used to inflate costs up to 2014/15 and then the newer NHS Cost Inflation Index (NHSCII) will be used to inflate from 2014/15 to 2024/25 (3). The models will be developed and reported according to standard validation and reporting criteria (4,5). Validation will be carried out by a team member not involved in the model building. Face validity will be ascertained through feedback from service providers and patients during the model building process.

Where possible, we will use and adapt existing published models to optimise design. For example, Elliott is building a model with the University of Queensland to evaluate a pharmacy-led UTI intervention similar to PF.

A literature search for each model will be conducted through Medline, Embase, HTA database (01/01/2010 to 31/03/2018 when database was last updated), NHS EED (01/01/2010 to 2015 when database was last updated) and Web of Science using treatment pathway-specific search terms. If a relevant systematic review has been carried out, the search will be updated and this will be detailed in the specific search strategy. Inclusion criteria for studies cannot be too restrictive due to the range of types of parameters required, and the lack of data available for some parameters. Inclusion criteria will be:

- Publication language – English
- Publication date – any, although preference given to newer studies
- Country – any, although preference given to UK-based studies
- Population – reflective of patient group in the model, otherwise general population samples of adults including male and female participants
- Publication type – papers published in peer-reviewed journals preferable, but grey literature included if necessary
- Study design – any relevant to parameter of interest, although preference given to large sample sizes
- Setting – any health care or community setting, preference given to setting relevant to the PF condition pathway
- Systematic reviews – included and preferable to single-study sources
- Animal studies - human studies only

We will use standard hierarchies of evidence to ensure the best quality data are used. Quality of data used will be explicitly discussed in each model. After excluding duplicate records, studies will be included if they examined the incidence, prevalence, treatment or resource use of the consequences of each PF condition pathway. Reference lists of the retrieved references will be hand-searched.

Data required for the economic models are the probabilities of outcomes associated with a PF condition, subsequent events after the condition has been self-diagnosed, the health status associated with a particular health state (e.g. health status for an adult woman with a UTI), and the resources consumed in a particular health state (e.g. NHS costs of treating a UTI). These data will be obtained via the WP2 analyses, literature review and, if necessary, expert opinion. These data will come preferentially from up-to-date UK sources that reflect the characteristics of the patient populations of interest. If possible, individual patient data will be used, with associated measures of mean and variation. If these are not available, point estimates will be used, with carefully specified deterministic ranges, using standard methods for allocating distributions to these data. If necessary, expert opinion or explicitly stated assumptions will be used to generate some parameters, which will be discussed with the project team, and clinical and lay experts, and if necessary, the effect of these assumptions will be tested in sensitivity analysis.

All data categories will reflect real-life patient cohort characteristics (age, sex, relevant diagnosis) as closely as available. Where possible, UK-based studies will be used to define initial cohort characteristics. This allows age-specific health status and mortality to be assigned. The values used for age-specific general population utility and mortality will be taken from large United Kingdom (UK)-based studies and routine datasets (6). As the models

simulate cohorts, rather than individuals, a single mean age and sex-split is specified for each. Where sex-specific parameters are used (e.g. for general population life expectancy), we use an average of values for men and women, weighted according to the stated proportion of each in the overall cohort.

We will use published estimates of health status to attach a utility to each health status in the Markov model. Preferentially, we will use utility estimates derived from UK populations using (Euroqol-5 dimension 3-level) EQ-5D-3L(9) or (Euroqol-5 dimension 5-level) EQ-5D-5L(10) for generic health status as the utility elicitation method, with UK tariffs, using the National Institute for Health and Care Excellence (NICE)-recommended 5L to 3L crosswalk algorithm to estimate QALYs(11, 12) as recommended in the NICE reference case (13). If the utility estimates are derived from non-UK populations, we will use UK tariffs where possible.

Incremental economic analysis

We will estimate the effect of PF versus current care via their impact on quality-adjusted life years (QALYs) and costs using a one-year time horizon, taking the NHS perspective in terms of direct costs of delivering PF or current care and managing the downstream costs. The QALYs and costs will not need to be discounted due to the one-year time-horizon (26). The incremental costs and outcomes associated with each of the seven PF conditions will be incorporated additively, weighted according to the number of people who access each of the seven pathways, into a composite economic model to allow derivation of the difference in patient outcome and costs between PF and current care.

If there is an overall increase in consultations for any of the PF conditions, suggesting previously unmet need that is now being met professionally, we will design the model such that we can estimate the QALY and cost differences associated with previously untreated episodes of the PF condition(s). This will enable estimation of the costs and outcomes of PF versus current care for the seven conditions, including the impact on previously unmet need.

For the probabilistic analysis, distributions appropriate for input parameters will be chosen (27). The probabilistic analysis will be based on 10,000 samples. Deterministic and probabilistic sensitivity analyses will be carried out to understand the robustness of the incremental cost-effectiveness ratio to alternative parameter values or assumptions. Cost-effectiveness acceptability curves (28) will be constructed to express the probability that the intervention is cost-effective as a function of the decision-maker’s ceiling cost-effectiveness ratio (29). Net benefit, a monetary value of QALYs will also be generated.

Costs associated with any change to AMR (based on volume of antibiotics dispensed) attributable to changes in prescribing practice will be accounted for in a sensitivity analysis, with the costing approach informed by a review of the relevant literature (30,31).

WP4: implementation and fidelity of the roll out (led by Glover, Lalani and Pacho)

Summary: this work package will use the CFIR to identify and assess the contribution of the external and internal factors that have affected uptake of PF from the perspective of professionals and service users.

Aims:

1. To understand how and why PF is and is not taken up including the fidelity of the scheme.
2. To evaluate the effects of PF on the access to, and acceptability of, community pharmacy services to populations historically marginalized in terms of primary health care access.
3. To assess pharmacists’ and GPs’ perceptions of the safety of the scheme.

Methods:

Professionals and policy makers: interview, focus group discussion and non-participant observation of pharmacists

We aim to understand how and why the programme is and is not taken up using three approaches: (1) interviewing professionals (n=50-100) (GPs, pharmacists and policymakers); (2) conducting focus group discussion with GPs and pharmacists; and (3) undertaking non-participant observation of pharmacists working in private pharmacies.

Interviewees will be purposively sampled from early adopter sites (i.e. community pharmacies and neighbouring GP surgeries), as well as from high and low adopter sites, taking care to include participating and non-participant pharmacies and pharmacists. Early, high and low adopter sites will be identified using the data sources in WP2 or best available data from public domains. We will identify around 45-50 early, high and low adopter sites and aim to recruit around 75 GPs and pharmacists among them. That said, in qualitative research it is not usually possible to do more than estimate the number of interviews needed before starting data collection. We will continue to undertake interviews, analysing them as we go, until there is a consensus in the WP4 research team that ‘saturation’ (i.e., no new themes or insights are emerging) has been achieved in relation to the topics listed below. These interviews will cover pharmacies’ capacity, capability and experiences of the new PF minor ailments service as well as the acceptability of the scheme. Data will be collected on these professionals’ perceptions of, and explanations for, changes in service use that can help interpret quantitative analysis of service use (WP2). Interviews will also provide an opportunity to assess the impact of the service on self-care by asking about the experiences of professionals telling patients that they were unsuitable for PF or who did not get a prescription medicine. We will also explore: pharmacists’ willingness to participate in the programme; whether willingness to participate is linked to previous workload; the perceived impact of PF on other work within pharmacies; and whether and, if so, how they think PF has increased or decreased access to primary care among more disadvantaged and marginalised populations. We will also conduct follow-up interviews with the policymakers interviewed in WP1 to determine the implementation progress over time, assessing the fidelity of the programme. These interviews will be carried out as outlined under WP1. Interviews will be conducted either in-person or online using platforms such as Zoom or MS Teams.

Focus group participants will be sampled from early adopter sites (i.e. localities currently implementing Pharmacy First) across England. We plan to undertake up to five in-person focus group discussion at both high and low adopter sites (defined above). Each focus group comprises a balanced mix (up to seven individuals) of community pharmacists and clinicians working at neighbouring GP/surgeries, lasting up to 60 minutes. The focus group will explore barriers and facilitators for professionals to implementing Pharmacy First services, including capacity, referral pathway, minimising risks and reassuring patient safety and perceived impacts of PF on their work. Focus group will be conducted in-person at venues preferred by all participants.

We will conduct non-participant observation of community pharmacists implementing PF as part of their daily practices. Twenty Sites for non-participant observation will be sampled from high and low adopter (defined above) among community pharmacies currently delivering PF across England. The observation activity will involve a trained researcher staying at the pharmacy for half a day (up to 4 hours) and taking note of relevant information on the frontline implementation of PF, including the layout and general setting of pharmacies, the routine administration of PF and how PF is integrated into everyday services delivered by community pharmacists. Researchers will NOT be involved in: pharmacy practices, professional advice, consultation with PF service users and interaction with pharmacy users. To make sure that pharmacy users are aware of our proposed observation, visible information on our research activities will be provided before users entering the pharmacy (e.g. a sign showing ‘researcher on-site’ at the entrance of a pharmacy, a quick-response (QR) code linking to an animation explaining this Pharmacy First evaluation project). If community pharmacists consent to both non-participant observation and interviews, any queries arising from observation will be prompted in the interview conducted after the observation. Non-participant observation will be conducted in person upon obtaining the consent of community pharmacies and community pharmacists.

Interviews and focus groups with service users
Among the 45-50 sites where there are early and/or high adopters of the service identified in WP2, we will undertake interviews (around 30) and focus groups (n=10) with service users with help from co-researchers, whom we will train to capture the experiences of those who do and do not use the service, noting any reported changes in health-seeking behaviour. We will recruit after a PF consultation, through People in Research, via targeted local leafleting, and through local Facebook and other social media groups. Guided by the analysis in WP2, which should be able to identify areas and/or pharmacies with high numbers of consultations among unregistered patients, we will be able to include historically marginalised in research and medically underserved populations. We will pay particular attention to issues raised in our current work on pre-PF pilots and self-care (32), such as non-medication safety risks among some communities regarding mischaracterising UTIs as sexually transmitted infections.

We will use our links with grassroots organisations (e.g. Revolving Doors, Diversity Matters, Nottingham Severe Multiple Disadvantage Partnership) as well as follow the lead of co-researchers on how to recruit. We will ensure that British Sign Language (BSL) interpreters are ready when needed and that will be made clear in the recruitment documents (flyers etc.). Unlike general practices, the evidence indicates that community pharmacies are disproportionately represented in more deprived communities and are thus good venues for recruiting from otherwise under-served groups.

Qualitative safety evaluation
The interviews with pharmacists will also include their perceptions of safety and how safety I and safety II principles develop in the PF roll-out (33). Specifically, we will assess mechanisms for: recording and reporting adverse drug reactions; interactions and contra-indications (safety I); and assuring and improving the quality of care and safety such as adherence to PF guidelines and reasons (if any) for deviation, as well as issues of misdiagnosis and delayed referral (safety II). We also hope to garner insights into the extent of anxiety and fear of litigation among pharmacists participating in this programme in terms of concerns about supplying antibiotics (and any subsequent adverse effects) as well as consequences for electing not to supply – a concern cited by pharmacists in early studies on emergency hormonal contraception PGDs (34). Additionally, we will gather GPs’ and

patients' views on consent, access to electronic records, and broader perceptions of the risks to patient safety (misdiagnosis, delayed referral and adverse drug reactions) of accessing PF services locally.

Work Package 5: mixed-methods analysis, consolidation of findings and identification of policy implications (led by Glover and Mays)

Summary: this work package will integrate findings from all strands of the evaluation bringing together evidence on the uptake of the programme among pharmacists and patients, acceptability among stakeholders, feasibility (e.g., capacity and capability of workforce, joined up electronic systems), fidelity to the original aims, nature and volume of consultations, antibiotic use, impact on other services, cost-effectiveness, integration into routine pharmacy practice and likely sustainability. It will start as soon as findings begin to emerge and run throughout the rest of the study.

Aims:

1. To produce an integrated, multi-faceted evaluation of the implementation of PF, structured using the CFIR.
2. To provide insight as to how to improve the PF scheme, assuming it is sufficiently cost-effective to be continued.

Methods:
Activity in this work package will take place at transition points between different types of data collection and analysis, such as towards the end of the analysis of the initial round of interviews in WP1 but before the initial analysis plans in WP2 have been finalised. This is to enable discussion within the research team and more widely of the implications of the interview findings for the following analysis of administrative data. For example, the interviews may identify that pharmacists have reservations about managing patients on one of the seven clinical pathways. This would inform the analysis of consultations and prescribing patterns for that condition. It might be expected that this pathway would contribute less to PF activity than the other six.

At these transition points, meetings of the entire research team will take place at which analyses from the preceding period will be presented and their implications both for ensuing analyses and for interim reporting will be identified.

WP5 will comprise a continuous process of *integration* and *triangulation* of the findings from the different types of data analysed during the evaluation. This process will be underpinned by a system of cross-work package team membership. Each WP team will nominate a team member to join the WP planning, analysis and interpretation meetings of at least one other WP. Since WP2 is the most extensive and multi-faceted WP, its meetings will be attended by a team member from all the other WPs, including WP5. The WP5 team will comprise Glover and Mays, and a representative from each of the other WPs. Mays and Glover, as co-PIs, will attend selected meetings of all the other WPs throughout the study. We will also relate the findings of the current study to other similar studies. The literature reviews in WPs1 and 3 will provide the basis for these comparisons.

Co-production with lay researchers

We aim to actively recruit co-researchers who have particular experience and knowledge relevant to this evaluation. In particular, we will recruit co-researchers representing diverse

groups of service users including those who have been historically marginalised in research and medically underserved. Research identifies populations historically marginalised in terms of primary health care access, such as those from low socio-economic background, people affected by homelessness, people from racially marginalised groups, vulnerable migrants and people with drug and/or alcohol dependency (35). In addition, WP1 will include a literature review of any noted local impacts of pre-existing PGDs and programmes similar to PF on health inequalities, and semi-structured interviews with stakeholders who will provide their perspectives on the role of PGD and programmes similar to PF in reducing health inequalities and organisational barriers to providing care to disadvantaged populations. This will help us adapt the list of historically marginalised in research and medically underserved groups to ensure that our understanding of health inequalities is comprehensive.

We will start recruitment of co-researchers via People in Research, grassroot organisations (e.g. Revolving Doors, Diversity Matters, Nottingham Severe Multiple Disadvantage Partnership), respondent-driven sampling involving referral chains (snowball sampling, also called word of mouth), and community outreach. We will offer flexibility around the time of day of the meetings with an option of one-to-one meetings for those unable to join otherwise.

Co-researchers will contribute to the evaluation by orienting work packages, participating in the ethics application process required in WP4, designing inclusive data collection tools, participating in research activities (e.g. conducting interviews and focus groups), interpreting data and formulating reports. Coresearchers will also organise citizens' forums in the regions where the research is being conducted to elicit a diverse array of perspectives. Ensuring accessibility and inclusivity of the citizens' forums, we have budgeted for BSL interpreters and interpreters from other languages to English to help with facilitation. Co-researchers will be fully involved in all dissemination activities, such as attending and presenting at conferences and contributing to publications.

To support co-researchers, we will provide two half-day research methods training sessions, including on qualitative interviews, focus groups and data analysis. In addition, to build leadership capacity, co-researchers will be offered confidence building training and ongoing support provided by Diversity Matters. Team members listed as co-applicants, as well as academic staff recruited for new roles, will receive Inclusive Public Engagement (IPE) training and ongoing support around cultural humility, helping them to develop the ability to spot when they are not engaging well with communities, and to learn, democratic, participatory methods, which allow the amplification of marginalised knowledge, beliefs and perspectives.

Data management

Once we have LSHTM ethics approval in place, we will establish data sharing agreements between the partners to ensure easy and transparent access to all data and intellectual property management. This will be established in WP2 alongside OpenSAFELY’s scoping work. Identifiable data, including qualitative interview data, will be managed and stored in line with LSHTM, Nottingham, Manchester, and UKHSA data management policies, and aligned with GDPR.

Study timetable

The study duration is from 1st February 2024, with a final report submitted in January 2027.


2024
2025
2026
2027
Work Package (lead institutions)
Milestones and tasks
Q1 Q2 Q3 Q4 Q5 Q6 Q7 Q8 Q9 Q10 Q11 Q12 Q1 (end Jan)
Grant management (All organisations)
Cross-university kick-off and comms plan
Ethical approval for qualitative research
Management committee meetings
Study steering group oversight meetings
Recruitment of RFs
Data-sharing and management plans
Patient and public coproduction and cocreation
WP1 (LSHTM)
Theory of change framework
Review of literature (including grey literature) on existing PGDs
Key informant interviews (policy/GP/pharmacy, England) and data analysis
Key informant interviews (policy/pharmacy, Scotland and Wales) and data analysis
Literature review for health economic parameterisation
Interim report and draft publications
Work Package 2
(Nottingham, UKHSA, Bennett, Manchester)
Months 1-6: Literature review of other PF-type service studies
Months 1-6: Development of analysis plan alongside OpenSAFELY dashboard/data linkage. Ethical approval
Months 6-9: training of UoN staff by Bennett Institute on the use of OpenSAFELY dashboard
Months 1-12: Development of health inequality impact analysis plan alongside OpenSAFELY dashboard/data linkage
Months 9-15: Describe the uptake of PF nationally, regionally and locally in the first 12 months
Month 15-18: Interim internal report to inform subsequent data analysis and feed into economic evaluation
Month 15-27: Describe how healthcare usage changes after the introduction of PF - Change in GP consultations
Month 15-27: Describe how healthcare usage changes after the introduction of PF - Change in A&E and hospital admissions
Month 15-27: Describe how healthcare usage changes after the introduction of PF - Change in GP phone calls
Months 15-19: Describe impact of PF on health inequalities
Months 24-30: Evaluate how antimicrobial use, and safety changes following introduction of Pharmacy First. This will feed into National surveillance of antimicrobial use and resistance led by UKHSA (see final line in WP2)
Months 27-30: Describe the uptake of PF nationally, regionally and locally in months 12-24 of the service
Months 31-36: Draft reports and papers for publication
Ongoing national surveillance of antimicrobial use and resistance: quasi-experimental analyses using interrupted time series analysis, or similar methods, at three timepoints: baseline, one-year and two years after PF introduction
Work Package 3 (Manchester/LSHTM)
Months 1-6: Literature review of other PF-type service economic studies
Months 1-6: HEAP design and explore alternative approaches to constructing counterfactual aggregate measures subject to data availability (including comparative ITSA)
Months 9-24: Costing the PF intervention (implementation and service delivery costs, including NHS costs, workforce changes associated with PF, pharmacy costs, data system maintenance, and changes in safety)
Months 7-15: Work with expert patients and clinicians to map the processes of care in current care-PF and current care+PF for the seven conditions
Months 7-24: Construction of economic models to support incremental economic analysis
Months 16-33: National budget analysis determine the impact of introducing PF on healthcare resource use, and conduct cost consequences analyses for each PF condition (and a composite of all 7)
Months 24-33: Decompose changes in activity over time and by age, gender, SEG, ethnicity, serious mental illness, learning disabilities, pharmacy density, and geography
Months 25-33: Incremental economic analysis
Months 31-36: Develop a resource to allow local commissioners to understand their PF service uptake in the various groups of their community, across the seven conditions; how this impacts costs, effectiveness, and safety; and to help them target further uptake activities, if appropriate.
Months 31-36: Draft reports and papers for publication
Work Package 4 (LSHTM)
Develop topic guide, informed by CFIR and WPs 1-3
Recruit professionals and service users
Conduct focus groups and interviews with service users, focusing on underserved communities, for example, traveller communities, people experiencing homelessness, and asylum seekers. Interviews would include perceptions on acceptability of the scheme and factors affecting access as well as safety.
Interview professionals (GPs, pharmacists, and A&E staff) in early adopting areas including assessing acceptability and perceptions of safety.
Policymaker interviews - focus on scheme fidelity
Analyse qualitative data
Draft publications
Work Package 5 (LSHTM/ALL)
Analyse uptake of PF against CFIR
interim cross-WP internal analyses report
Research team meetings - synthesising findings (cross-consortium group (CG) - learnings discussions)
CG
CG
CG
CG
CG
Final report
Lead organisation(s)
All
LSHTM
Nottingham/UKHSA/Bennett
Manchester
Nottingham/Manchester
Nottingham/LSHTM
Manchester/LSHTM

Equality, diversity and inclusion (EDI)

The team’s EDI strategy has three strands:

Diversity of People: We have convened a team with disciplinary, gender, ethnic, and geographic diversity. We seek to increase diversity through inclusive recruitment processes for new roles.

Diversity of Thought: The LSHTM 2022 early career researcher survey found senior faculty can support early- and mid-career researchers by (a) mentorship, and (b) facilitating career opportunities. This mirrors the NIHR’s 5-point EDI strategy, which aims to embed evidence-based EDI strategies, and improve and invest in the NIHR talent pipeline. To address (a) we will introduce the Parity Action Compassion Empowerment (PACE) reciprocal mentoring model, developed by Johnson, who will train senior faculty to provide inclusive career mentoring. Early/mid-career researchers will receive training to fully capitalise upon reciprocal mentorship. To address (b) we have included early (Pacho/Taylor/Allen), and mid-career (Glover/Lalani/Sonnex) co-applicants supervised by senior co-investigators.

Diversity of Methods: All researchers will receive EDI and PPIE training delivered by our EDI and PPIE leads (Johnson/Pacho), to design an inclusive evaluation applying democratic, participatory methods. This seeks to amplify marginalised knowledges, beliefs, and perspectives, e.g., of racialised and socioeconomically deprived communities, and integrate them with more mainstream experiences of the NHS, community pharmacy, general practice, and PF.

Dissemination, outputs and anticipated impact

We will use our wide-ranging networks of contacts during the evaluation to ensure that our findings reach key stakeholders and in a form that enables them to derive applicable insights.

Outputs

Across all work packages, we will work with policymakers to deliver interim reports, ad hoc briefings and presentations. In addition:

- **WP1** will produce: an interim report in Dec 2024 with qualitative findings designed to help shape WPs 2, 3, and 4; a literature review; and a qualitative findings paper for publication
- **WP2** will produce: open licence codes; interim reports; peer-reviewed articles; an ‘information for action’ briefing for local commissioners and national bodies to better understand the impact of PF services on antibiotic use across different community health care settings; and data for subsequent economic evaluation in WP3.
- **WP3** will produce: estimates of national budget impact; estimates of cost-effectiveness; a resource to allow local commissioners to understand PF service uptake in the various sub-groups of their populations, across the seven conditions, including how uptake impacts costs and effectiveness to help them target further uptake activities, if appropriate.

- **WP4** will produce: peer-reviewed publications on acceptability, access, and safety, paying particular attention to marginalised populations and traditionally underserved communities.
- **WP5** will produce: interim cross-WP internal analyses; a final cross-cutting report to DHSC, NHS England and other government agencies; ad hoc presentations and briefings for DHSC and arm’s length bodies about interim and late-stage findings; similar presentations and briefings for community pharmacy organisations and patient organisations; peer reviewed publications bringing together all aspects of the evaluation.

Impact

We expect broad and varied interest in the evaluation findings, from: policymakers and service delivery leads at DHSC, NHSE, the Treasury, AMR programme and policy leads at DHSC and UKHSA, the English Surveillance Programme for Antimicrobial Utilisation and Resistance oversight group, as well as managers involved in local implementation, Community Pharmacy England, ICSs, commissioners of pharmacy services, the RPS, the Royal College of General Practitioners, patients who access the service, the wider public, and international colleagues. We will also set up a project-specific website hosted at LSHTM. We will be responsive to decision points in the PF service roll-out and provide timely outputs including: a public-facing dashboard tracking service user access; interim and final reports; and ad hoc delivery of targeted feedback upon policymaker and partner request.

Population impact: We expect this evaluation to aid in AMU optimisation, thus minimising AMR risk, at the population-level. Also, we aim to inform better implementation of PF; we will achieve this by working with key stakeholders.

Wider research impact: Interdisciplinary research based on a mixed methods study design will allow multiple subject, method, and disciplinary experts to deliver a robust evaluation of the impact and implementation of PF’s expansion. Without this multi-institute collaboration, the evaluation as laid out in the commissioning brief would not be feasible (35). The findings will provide robust evidence upon which policymakers may consider how best to enhance the future role of community pharmacy in the NHS in England.

Global impact: Our research could be reused and adapted in similar health systems’ contexts. For example, the data dashboard, and the methods and codes used to interrogate it (though not the patient data), will be publicly available, allowing for a generalised and modifiable model that could be implemented in other country contexts. This would save future researchers’ time, save funders’ money, and advance the field considerably.

Dissemination

We will publish our final study in the NIHR library, publicised through networks and press offices, integrate public engagement and dissemination activities into the evaluation, led by Johnson and Pacho, and present at relevant academic meetings, publishing pre-prints and peer- reviewed open access scientific journal articles. We will also produce animated videos co-developed with lay researchers and a podcast delivered quarterly on the progress of the evaluation team in order to disseminate knowledge to the wider public.

Project management and governance

Team management

Mays and Glover have worked together for eight years in the Policy Innovation and Evaluation Research Unit (PIRU), a NIHR PRP Policy Research Unit with long-standing expertise in mixed-methods evaluations of complex policies. They bring insights from their evaluation of the implementation of the UK’s antimicrobial resistance (AMR) national action plan (NAP), during which they have undertaken scoping and evaluative work commissioned by the DHSC on local PF-type PGDs in Cornwall, Scotland and the Isle of Wight.

The management committee (comprising WP leads and sub-leads) will meet frequently and intensively in the first quarter to resolve organisational and administrative issues, but then quarterly thereafter, to deal with administrative aspects of the study. The research team will meet quarterly to discuss the synthesis of findings. Two of these meetings each year will be cross-consortium group learning discussions and will involving PPIE and other stakeholders – see under WP5 above.

Study advisory groups

A Study Steering Committee (SSC), accountable to the NIHR’s HS&DR Programme, will provide ongoing support for project design, analysis, and dissemination. Thus far we have recruited from experts in health care evaluation, pharmacy practice, primary medical services and plan to add additional members from patient representative organisations. NIHR requires an independent chair who can be drawn from any of the groups represented in the SSC. The full membership of this group will be identified during the scoping phase but a number of members have already been identified and are listed in the table below.

Member	Institution	Role
Nick Barber (Chair)	UCL	Emeritus Professor Practice & Policy
Justin Waring	University of Birmingham	Director of BRACE, Professor of Medical Sociology
Jenni Burt	THIS Labs	Director of Science
Catherine Goodman	LSHTM	Professor
Efi Mantzourani	Cardiff University	Reader in Pharmacy Practice
Wasim Bakir	NHSE	Senior Pharmacist, Pharmacy Integration Fund
Kieran Hand	NHSE	AMR programme: National Pharmacy Clinical Lead
Alastair Buxton	Community Pharmacy England	Director of NHS Services
Susan Hopkins	UKHSA	Chief Medical Advisor
Reena Barai	SG Barai Pharmacy	Independent Pharmacy Owner
Claire Nevinson	Boots UK	Chief Pharmacist
Adam Osprey	Community Pharmacy Scotland	Policy and Development pharmacist
Tim Dalton	Greater Manchester Primary Care Provider Board	GP and chair of Primary Care Provider Board
Mark Koziol	Pharmacists Defence Association	Chairman
Kelvin Jordan	Keele University	Professor of Biostatistics

Ethics and regulatory approvals

The study will be undertaken to the highest standard of ethics and research governance, in compliance with data protection regulations and policies relating to the conduct of research of LSHTM and the universities of Nottingham and Manchester. Approvals will be obtained from LSHTM, University of Nottingham and University of Manchester research ethics committees and from the Health Regulatory Authority.

Applications for ethical approval will be prepared at the earliest possible opportunity. Recruitment and consent processes for all primary data collection will ensure participation is informed and voluntary, and anonymity in reporting will be guaranteed. All potential participants will receive information about the study (purpose, design, timescales, what involvement would entail, how data will be managed, etc.) before deciding whether to take part. We will work within best practice guidance and statutory regulations for all data access, storage and processing. Each participant will be assigned a unique identifier, which will be stored separately to all research data. Data will be held on a secure database on password-protected computers on university networks, and access will be restricted to the research team.

Governance approvals may also be required to carry out some the qualitative work in WP4 – interviews with community pharmacists and GPs. We have held discussions with the Health

Research Authority (HRA) in England and NHS Research Scotland to establish the scope and extent of the approvals required.

Ethical considerations – primary research with vulnerable populations

The study will include focus groups and in-depth one-to-one interviews with diverse service users, including people affected by homelessness and vulnerable migrants. Recruitment of vulnerable and/or marginalised groups can be more difficult by their often being absent from mainstream health services (37). In addition, factors such as low income, poor access to transport and poor literacy pose barriers to participation in research (38,39). For those reasons, we will be intentional in our recruitment processes, ensuring that we work with a diverse group of lay co-researchers, recruited through grassroots organisations (e.g. Revolving Doors, Diversity Matters, Nottingham Severe Multiple Disadvantage Partnership) to make all the study materials accessible and to inform our topic guides. We will ensure that BSL interpreters are ready when needed, which will be made clear in the recruitment documents (flyers, etc.). Working closely with grassroots organisations, we will be made aware of the particular challenges the research participants may face.

We recognise that a person's capacity to exercise autonomy and ability to protect their interests through informed consent can be impaired by vulnerability (37,40-42), and that individual capacity is not absolute and is likely to fluctuate (43). Researchers will have the required experience and training to be able to assess potential participants’ capacity and, based on that, make a judgement about whom to include in or exclude from research.

Interviewees and focus group participants will be informed that they can withdraw from the interviews at any point without giving a reason. We will ensure that the interviews and focus groups are conducted at a time convenient for the interviewees. Both, the focus group discussions and in-depth interviews with service users are likely to concern sensitive issues, such as poor health or barriers to accessing health care, and, therefore, may cause emotional distress. If needed, research participants will be offered counselling services.

There are some additional ethical considerations associated with participation in the focus groups, such as a high degree of disclosure within a group, individual participants having less control than in a one-to-one interview during which it may be easier to divert the discussion away from an uncomfortable topic, difficulties around ensuring that everyone’s voice is heard and the impossibility of an anonymous withdrawal of participation. The group context may also create a sense of public vulnerability (44). In efforts to mitigate the harm and prevent participants from experiencing distress, the focus group moderator will state the rules of conduct and stress the impossibility of ensuring anonymity. Further, at the start of the interview, the interviewer will emphasise the non-judgemental character of the research. Participants will be informed that they are allowed to refuse to answer particular questions or withdraw from the research during the focus groups and interviews without providing a reason. Essential to preventing participants’ distress are the researcher's interviewing skills and receiving appropriate ethical approvals. The researcher who will moderate the focus groups and interview participants has experience in conducting qualitative research and has also completed Good Research Practice and Research Ethics Training provided by LSHTM.

Team and expertise

The wider team has expertise in: complex impact and implementation evaluations Mays and Glover), policy analysis and implementation (Mays), antimicrobial resistance (Glover), pharmacy, pharmaceutical public health including national AMR and AMU surveillance

(Ashiru-Oredope), pharmacy practice research (Thornley, Anderson), GP prescribing and safety (Avery), health services research and safety (Lalani), health equity and justice (Pacho), PPI and EDI (Pacho, Johnson), data linkage (MacKenna, Goulding, Sonnex, Allen, Taylor), health economics and safety (Elliott), health economics (O’Neill, and Allen) and statistics (Coupland).

Named collaborators include: Muller-Pebody (Epidemiology), Lonsdale (Pharmacy First Lancashire and South Cumbria Trust), Buxton (Pharmacist and Director of NHS Services at PSNC), and Dineen-Griffin (evaluation lead of UTI CP service in Australia) who will responsively provide expert advice on *ad hoc* issues and join the SSC where appropriate. We have liaised with relevant stakeholders, including RCGP, RPS, NHSE, DHSC, and UKHSA, BSAC, RCGP, Community Pharmacy England, BSAC, and others to understand the complexity of PF and develop relationships with key stakeholders to support the research.

Success criteria and barriers to proposed work

A clear measure of success would be the team’s ability to implement all the elements in the proposal to a high standard in the time available while ensuring a high level of local and national engagement with the findings and their implications for policy and practice. With each WP designed to contribute to understanding the potential consequences of PF for inequalities in access to health services and outcomes, the success of the evaluation would be also defined in terms of being able to advise policymakers on the role of PF in improving or worsening inequalities and organisational barriers and facilitators to providing care to disadvantaged populations.

References

1. NHS England. High quality care for all, now and for future generations: Transforming urgent and emergency care services in England - Urgent and Emergency Care Review End of Phase 1 Report [Internet]. NHS England; 2013 Nov [cited 2023 Nov 1]. Report No.: 00691–00694. Available from: https://www.nhs.uk/NHSEngland/keoghreview/Documents/UECR.Ph1Report.FV.pdf

2. 23/73 Evaluating “Pharmacy First” Services for management of common conditions [Internet]. [cited 2023 Nov 1]. Available from: https://www.nihr.ac.uk/documents/2373-evaluating-pharmacy-first-services-for-management-of-common-conditions/33430

3. Iacobucci G. Primary care access plan could help narrow health inequalities, says pharmacy leader. BMJ. 2023 May 15;p1108.

4. Pharmacy can narrow health inequalities — here’s how. Pharm J [Internet]. 2023; Available from: http://dx.doi.org/10.1211/pj.2023.1.186186

5. Pumtong S, Boardman HF, Anderson CW. A multi-method evaluation of the Pharmacy First Minor Ailments scheme. Int J Clin Pharm. 2011 Apr 28;33(3):573–81.

6. Whittington Z, Cantrill J, Hassell K, Bates F, Noyce P. Community pharmacy management of minor conditions - The “Care at the chemist” scheme. Pharm J. 2001 Mar 31;266(7141):425–8.

7. Burgin C, Motta M, Wilcock M. The Pharmaceutical Journal. 2023 [cited 2023 Nov 1].

How COVID-19 affected pharmacy supply of antibiotics for uncomplicated urinary tract infections. Available from: https://pharmaceutical-journal.com/article/opinion/how-covid-19-affected-pharmacy-supply-of-antibiotics-for-uncomplicated-urinary-tract-infections

8. Stewart F, Caldwell G, Cassells K, Burton J, Watson A. Building capacity in primary care: the implementation of a novel “Pharmacy First” scheme for the management of UTI, impetigo and COPD exacerbation. Prim Health Care Res Dev. 2018/01/24 ed. 2018 Nov;19(6):531–41.

9. Mantzourani E, Wasag D, Cannings-John R, Ahmed H, Evans A. Characteristics of the sore throat test and treat service in community pharmacies (STREP) in Wales: crosssectionalanalysis of 11 304 consultations using anonymized electronic pharmacy records. J Antimicrob Chemother. 2022 Dec 23;78(1):84–92.

10. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ. 2010 May 18;340(may18 2):c2096–c2096.

11. Aerts N, Van Royen K, Van Bogaert P, Peremans L, Bastiaens H. Understanding factors affecting implementation success and sustainability of a comprehensive prevention program for cardiovascular disease in primary health care: a qualitative process evaluation study combining RE-AIM and CFIR. Prim Health Care Res Dev. 2023 Mar 8;24:e17.

12. King ES, Moore CJ, Wilson HK, Harden SM, Davis M, Berg AC. Mixed methods evaluation of implementation and outcomes in a community-based cancer prevention intervention. BMC Public Health. 2019 Aug 5;19(1):1051.

13. Morgan D, Kosteniuk J, O’Connell ME, Kirk A, Stewart NJ, Seitz D, et al. Barriers and facilitators to development and implementation of a rural primary health care intervention for dementia: a process evaluation. BMC Health Serv Res. 2019 Oct 17;19(1):709.

14. Proctor E, Silmere H, Raghavan R, Hovmand P, Aarons G, Bunger A, et al. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. Adm Policy Ment Health. 2011 Mar;38(2):65–76.

15. Williamson, E.J., Walker, A.J., Bhaskaran, K. *et al.* Factors associated with COVID-19-related death using OpenSAFELY. *Nature* **584**, 430–436 (2020). https://doi.org/10.1038/s41586-020-2521-4

16. Kontopantelis E, Doran T, Springate DA, Buchan I, Reeves D. Regression based quasi-experimental approach when randomisation is not an option: interrupted time series analysis. BMJ. 2015 Jun 9;350:h2750.

17. Dolan E, Goulding J, Marshall H, Smith G, Long G, Tata L. Assessing the value of integrating national longitudinal shopping data into respiratory disease forecasting model [Internet]. 2022 [cited 2023 Nov 1]. Available from: https://europepmc.org/article/PPR/PPR568260

18. Todd A, Copeland A, Husband A, Kasim A, Bambra C. The positive pharmacy care law: an area-level analysis of the relationship between community pharmacy distribution,

urbanity and social deprivation in England. BMJ Open. 2014 Aug 12;4(8):e005764.

19. Smith G, Mansilla R, Goulding J. Model Class Reliance for Random Forests. In: Advances in Neural Information Processing Systems [Internet]. Curran Associates, Inc.; 2020 [cited 2023 Nov 1]. p. 22305–15. Available from: https://proceedings.neurips.cc/paper/2020/hash/fd512441a1a791770a6fa573d688bff5-Abstract.html

20. Department of Health and Social Care, Confronting antimicrobial resistance 2024 to 2029. 2024. Accessed April 29, 2024. https://assets.publishing.service.gov.uk/media/663b9c451c82a7597d4f32fe/Confronting-antimicrobial-resistance-2024-to-2029.pdf

21. Bou-Antoun S, Costelloe C, Honeyford K, Mazidi M, Hayhoe BWJ, Holmes A, et al. Age-related decline in antibiotic prescribing for uncomplicated respiratory tract infections in primary care in England following the introduction of a national financial incentive (the Quality Premium) for health commissioners to reduce use of antibiotics in the community: an interrupted time series analysis. J Antimicrob Chemother. 2018 Jun 28;73(10):2883–92.

22. Balinskaite V, Bou-Antoun S, Johnson AP, Holmes A, Aylin P. An Assessment of Potential Unintended Consequences Following a National Antimicrobial Stewardship Program in England: An Interrupted Time Series Analysis. Clin Infect Dis. 2018 Oct 18;69(2):233–42.

23. Balinskaite V, Johnson AP, Holmes A, Aylin P. The Impact of a National Antimicrobial Stewardship Program on Antibiotic Prescribing in Primary Care: An Interrupted Time Series Analysis. Clin Infect Dis Off Publ Infect Dis Soc Am. 2019 Jul 2;69(2):227–32.

24. Vemer P, Corro Ramos I, van Voorn G a. K, Al MJ, Feenstra TL. AdViSHE: A Validation-Assessment Tool of Health-Economic Models for Decision Makers and Model Users. PharmacoEconomics. 2016 Apr;34(4):349–61.

25. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. BMC Med. 2013 Mar 25;11(1):80.

26. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. BMC Med. 2013 Mar 25;11(1):80.

27. Caldwell D. Decision Modelling for Health Economic Evaluation. A Briggs, M Sculpher, K Claxton. Int J Epidemiol. 2007 Apr 1;36(2):476–7.

28. Fenwick E, Byford S. A guide to cost-effectiveness acceptability curves. Br J Psychiatry J Ment Sci. 2005 Aug;187:106–8.

29. Fenwick E, Claxton K, Sculpher M. Representing uncertainty: the role of costeffectiveness acceptability curves. Health Econ. 2001 Dec;10(8):779–87.

30. Wozniak TM, Dyda A, Merlo G, Hall L. Disease burden, associated mortality and

economic impact of antimicrobial resistant infections in Australia. Lancet Reg Health – West Pac [Internet]. 2022 Oct 1 [cited 2023 Nov 1];27. Available from: https://www.thelancet.com/journals/lanwpc/article/PIIS2666-6065(22)00136-5/fulltext

31. Shrestha P, Cooper BS, Coast J, Oppong R, Do Thi Thuy N, Phodha T, et al. Enumerating the economic cost of antimicrobial resistance per antibiotic consumed to inform the evaluation of interventions affecting their use. Antimicrob Resist Infect Control. 2018 Aug 9;7:98.

32. Pacho A, Mays N, Glover R; “the best self-care for me […] would be to go and see a specialist”. Evaluating the UK’s antimicrobial resistance policy to encourage self-care for minor infections: a qualitative study with women from racialised minorities and in low-income households who experience urinary tract infections. *Journal of Health Services Research & Policy* (Under peer review).

33. Jones CEL, Phipps DL, Ashcroft DM. Understanding procedural violations using Safety-I and Safety-II: The case of community pharmacies. Saf Sci. 2018 Jun;105:114–20.

34. Seston EM, Holden K, Cantrill J. Emergency hormonal contraception: the community pharmacy perspective. J Fam Plann Reprod Health Care. 2001 Oct;27(4):203–8.

35. Gibson H, Sanders C, Blakeman T, Ashcroft D, Fudge N, Howells K. Providing care to marginalised communities: a qualitative study of community pharmacy teams. Br J Gen Pract [Internet]. 2022 Oct 6 [cited 2023 Nov 16]; Available from: https://bjgp.org/content/early/2023/10/10/BJGP.2023.0267

36. Baird B, Buckingham H, Charles A, Edwards N, Murray R. A vision for community pharmacy. Nuffield Trust and The King’s Fund; 2023.

37. Smith, L.J. (2008), How ethical is ethical research? Recruiting marginalized, vulnerable groups into health services research. Journal of Advanced Nursing, 62: 248-257. https://doi.org/10.1111/j.1365-2648.2007.04567.x

38. Cassell J. & Young A. (2002) Why we should not seek individualinformed consent for participation in health services research. Journal of Medical Ethics28, 313–317
39. Rogers W.A. (2004) Evidence based medicine and justice: a frame-work for looking at the impact of EBM on vulnerable or disad-vantaged groups.Journal of Medical Ethics30, 141–145

40. Steinke E.E. (2004) Research ethics, informed consent and participant recruitment. Clinical Nurse Specialist18(2), 88–9.

41. Ulrich C., Wallen G. & Grady C. (2002) Research vulnerability and patient advocacy: balance-seeking perspectives for the clinical nurse scientist? Editorial Nursing Research51(2), 71–72.

42. Royal College of Nursing (2004)Research Ethics. RCN Guidance for Nurses. RCN, London.

43. Hannigan B. & Allen D. (2003) A tale of two cities: research governance issues arising from two ethnographic investigations into the organisation of health and social care. International Journal of Nursing Studies40, 685–695.
44. Sim, J., Waterfield, J. Focus group methodology: some ethical challenges. Qual Quant 53, 3003–3022 (2019). https://doi.org/10.1007/s11135-019-00914-5