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Symptom reporting, healthcare-seeking behaviour and antibiotic use for common infections: protocol for Bug Watch, a prospective community cohort study

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3 **Symptom reporting, healthcare-seeking behaviour and antibiotic use for common infections:**
4 **protocol for Bug Watch, a prospective community cohort study**
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10 *On behalf of the Preserving Antibiotics through Safe Stewardship (PASS) study research group:*
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Abstract

Introduction

Antimicrobial resistance is a significant worldwide problem largely driven by selective pressure exerted through antibiotic use. Preserving antibiotics requires identification of opportunities to safely reduce prescriptions, for example in the management of mild common infections. However, more information is needed on how infections are usually managed and what proportion lead to consultation and antibiotic use. The aim of this study is to quantify consultation and prescribing patterns in the community for a range of common acute infection syndromes (respiratory, gastrointestinal, skin/soft tissue, mouth/dental, eye and urinary tract). This will inform development of interventions to improve antibiotic stewardship as part of a larger programme of work, Preserving Antibiotics through Safe Stewardship (PASS).

Methods and analysis

This will be an online prospective community cohort study in England. We will invite 19,510 adults who previously took part in a nationally-representative survey (the Health Survey for England) and consented to be contacted about future studies. Adults will also be asked to register their children. Data collection will consist of a baseline registration survey followed by weekly surveys sent by email for six months. Weekly surveys will collect information on symptoms of common infections, healthcare seeking behaviour, and use of treatments including antibiotics. We will calculate the proportions of infection syndromes that lead to GP consultation and antibiotic prescription. We will investigate how healthcare-seeking and treatment behaviours vary by demographics, social deprivation, infection profiles, and knowledge and attitudes towards antibiotics, and will apply behavioural theory to investigate barriers and enablers to these behaviours.

Ethics and dissemination

This study has been given ethical approval by the UCL Research Ethics Committee (ID 11813/001). Each participant will provide informed consent upon registration. We will disseminate our work through publication in peer-reviewed academic journals. Anonymised data will be made available through the UK Data Service (<https://www.ukdataservice.ac.uk/>).

Strengths and limitations of this study

- This study will use a novel and efficient method for large-scale collection of information about symptoms and related health-seeking behaviours.
- It will address an important aspect of primary care (antibiotic use) by collecting data on a comprehensive set of symptoms of common infections, but will not cover sexually-transmitted infections.
- Collecting data over an entire year will allow seasonal variations to be explored.
- Participants will be recruited from a sample that is representative of the population living in private households in England.
- The prospective community cohort design will enable information to be captured about symptoms irrespective of medical consultation.

Introduction

The emergence of antimicrobial resistance (AMR) is a significant worldwide problem. It is largely driven by selective pressure exerted through antibiotic use and has led to some infections becoming untreatable with existing antimicrobials.[1] Preserving antibiotics for the future depends on achieving a safe balance between potential population harms of prescribing antibiotics and risks to the individual of not prescribing. The set of actions that promote this responsible use of antibiotics is referred to as antibiotic stewardship.[2]

Improving stewardship requires identification of opportunities to safely reduce prescriptions of antibiotics. An example of this may lie in the management of acute common infections in the community. Respiratory infections are the most common reason for GP consultation, but most patients safely manage these infections without consulting their GP or taking an antibiotic.[3] There is limited information, however, on how the public manage other infections, what proportion lead to consultation and antibiotic use, or how these proportions vary according to infection syndrome or patient characteristics.

The aim of the Bug Watch study is to quantify consultation and antibiotic prescribing patterns in the community for a range of acute common infections (respiratory, gastrointestinal, skin/soft tissue, mouth/dental, eye and urinary tract). Bug Watch is part of a larger programme of work, Preserving Antibiotics through Safe Stewardship (PASS), which aims to inform the development of multifaceted behavioural interventions that will strengthen antibiotic stewardship across a range of healthcare settings. Results from Bug Watch will be synthesised with insights from qualitative interviews to identify opportunities for improved antibiotic stewardship in the community and general practice and inform development of interventions.

Methods and analysis

Study design and setting

This will be an online prospective community cohort study in England. Data collection will consist of a baseline registration survey followed by weekly surveys for six months. Weekly surveys will collect information on symptoms of common infections, healthcare seeking behaviour, and use of treatments including antibiotics.

Recruitment

We will recruit participants through the Health Survey for England (HSE). HSE is an annual survey first conducted in 1991 that monitors changes in the health and lifestyles of people living in England.[4] It is commissioned by NHS Digital and run by NatCen Social Research and the UCL Research Department of Epidemiology and Public Health. The sample of individuals included in HSE each year is designed to be representative of the population living in private households in England. Full details of the methods for HSE sample have been described previously.[5]

We will invite all adults who took part in the HSE in 2013, 2014 or 2015 and who consented to be contacted about future research studies (with the exception of 50-53 year olds from the 2015 survey who were recruited to a different study). This comprises 19,510 adults, of whom we estimate 15,819 (81%) will still be resident at the address on record when they are contacted. Parents or guardians will

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3 be invited to register up to four children aged under sixteen, and all information for children will be
4 reported by the adult who registered them. Anyone aged sixteen or over living in the same household
5 will be invited to register separately.
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7 Recruitment will be conducted in four waves starting in March, June, September and November 2018.
8 Initial invitations to take part in Bug Watch will be sent by post. Those who wish to sign up will be
9 directed to a web link. A second reminder letter will be sent to those who have not registered
10 approximately three weeks after the initial invitation was sent. Where possible, invitation reminders will
11 also be sent by email or SMS text message. Individuals who are invited and do not wish to take part in
12 the study will be removed from contact lists.
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15 *Participant materials and incentives*

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17 The initial invitation letter will include a participant information sheet which will describe the purpose of
18 the study, what participants will be asked to do, and the contact details of the study team. It will also
19 include a paper copy of a “symptom diary”, which will be designed to help participants to keep track of
20 the symptoms of infection that will be collected in the weekly surveys.
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23 Study invitations will direct those interested in participating to a UCL web page. This page will include
24 the registration survey URL as well as a short video describing the study. Those wishing to register
25 children will also be able to download an information sheet for children. We will design this sheet so
26 that it is suitable to be read by anyone aged approximately eight years or older. Following registration,
27 participants will be sent a reusable laminated copy of the symptom diary, a pen, and a Bug Watch-
28 branded magnet.
29

30 During follow-up, participants will be sent approximately two email newsletters. These newsletters will
31 provide updates about the study such as rates of weekly survey completion. To avoid influencing the
32 behaviour of participants during follow-up, the newsletters will not include details about the main study
33 outcomes.
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36 All participants will receive a £5 voucher to thank them for registering. At the end of follow-up, those
37 who have completed at least 50% of their weekly surveys will be sent an additional £5 voucher. They will
38 also be entered into a prize draw to win a further £50 voucher.
39

40 *Data collection*

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42 All data will be collected using REDCap electronic data capture tools hosted on the UCL Data Safe
43 Haven.[6] REDCap (Research Electronic Data Capture) is a secure, web-based application for research
44 studies. The UCL Data Safe Haven provides a technical solution for storing, handling and analysing
45 identifiable data. It has been certified to the ISO27001 information security standard and conforms to
46 NHS Digital’s Information Governance Toolkit. Data analysis will also be conducted within the UCL Data
47 Safe Haven, from which personal information will not be removed.
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50 Online registration will take approximately 15 minutes per person. Participants will be asked to provide
51 consent, confirming that they have read and understood the information sheets. Parents or legal
52 guardians will be asked to give formal consent for children under the age of 16. For children that are
53 able to give assent, the parent or legal guardian will be asked to discuss with them whether they wish to
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3 take part or not. Consent for linking data to the broader HSE survey data and for contact for qualitative
4 interviews will also be requested.
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6 Full details of the baseline data collection are shown in Table 1. The baseline survey will collect
7 information on contact details, demographics, household composition, general health, oral health and
8 GP consultations. It will also include questions about knowledge and attitudes towards antibiotics,
9 adapted from Wave 3 of the Wellcome Trust Monitor survey, and the EQ-5D-3L instrument for
10 measuring health-related quality of life.[7][8] The Wellcome Trust Monitor survey is designed to be
11 representative of the UK adult population and measures trends in public attitudes towards science.
12 Wave 3 of the survey, conducted in 2015, included a set of questions about knowledge and attitudes
13 towards antibiotics. The EQ-5D-3L is a standardised measure of health status developed by the EuroQol
14 Group that provides a simple, generic measure of health for clinical and economic appraisal.[8]
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18 On the first Monday after registration, participants will be sent an email reminding them to start
19 keeping track of symptoms of infection. Following this, they will be sent weekly emails each Monday
20 with a link to a survey to fill in details about symptoms from the previous seven days and how they
21 managed them. These emails will be sent each week for six months, and each survey will be open for
22 one week. Participants will be given the opportunity to complete feedback forms about Bug Watch after
23 approximately six weeks of participation, and again after all weekly surveys have been sent.
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26 The symptoms that will be monitored in Bug Watch are shown in Table 2. For each day that a symptom
27 is reported, participants will be asked to rate its severity (mild, moderate or severe) and to complete the
28 EQ-5D-3L. They will also be asked to report what they did about their symptoms including whether they
29 took time off work (or school), sought medical advice, or took any treatments. When antibiotics are
30 reported, further details will be collected about the type of antibiotic, duration, who it was prescribed
31 by (or how otherwise obtained) and adherence to treatment.
32

33
34 At the end of a series of symptoms, participants will be asked to complete a set of questions about what
35 influenced how they managed their symptoms, specifically whether or not they consulted their GP and
36 sought antibiotics. We will apply the COM-B (Capability, Motivation, Opportunity, Behaviour) model of
37 behaviour change [9] to explore the wide-range of potential individual, socio-cultural and environmental
38 barriers/enablers to these behaviours. The survey will include at least one item mapping onto each
39 domain of the COM-B model (Table 3). Items will be in the form of belief statements to which
40 participants rate their agreement on Likert-type scales from 1- Strongly Disagree to 5 - Strongly Agree.
41

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43 In all surveys, we will make use of “skip logic” to ensure that participants are only shown questions that
44 are relevant to them. For example, they will first be asked if they have any symptoms, and only if they
45 do will they be shown specific symptom categories. Weekly surveys will therefore take no longer than a
46 minute if no symptoms are reported, and approximately 5-10 minutes if symptoms are reported.
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48 *Statistical analysis*

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50 We will describe the demographic characteristics of the Bug Watch cohort and assess its
51 representativeness by comparing with the characteristics of the broader HSE sample and/or published
52 national statistics. We will also assess the representativeness of the knowledge and attitudes towards
53 antibiotics of the cohort by comparing with the Wellcome Trust Monitor Survey.[7]
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3 Symptoms reported will be combined into infection syndromes. We will create descriptive profiles of
4 infection syndromes including types of symptom reported, duration, timing and severity. We will
5 calculate the proportions of infection syndromes that lead to people consulting their GP and receiving
6 antibiotics. Antibiotic use will be described in terms of type of antibiotic, duration, who it was prescribed
7 by (or how otherwise obtained) and adherence to treatment. Other health-seeking behaviours,
8 behavioural influences (barriers and enablers within the COM-B model), and treatments taken to
9 manage symptoms will also be described.
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12 We will use regression methods to investigate how healthcare-seeking and treatment behaviours vary
13 by age, gender, ethnicity, presence of other illnesses, social deprivation, infection profile, and
14 knowledge and attitudes towards antibiotics. We will also assess the impact of different types of
15 infection on quality of life using the EQ5D-3L scores, and on reported work and school absences. We will
16 use these measures to estimate the overall impact of community infection at the population level. Full
17 statistical methods will be presented with relevant analyses.
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20 *Patient and public involvement*

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22 Participants were not directly involved in design of this study although feedback will be collected at two
23 time points during follow up. Newsletters will be sent to give participants updates during the study, and
24 a summary of the main findings will be available at the end. As part of the wider PASS study, a subset of
25 participants will be invited to take part in qualitative interviews that will draw on behavioural theory to
26 investigate the drivers of health-seeking behaviours. Findings from Bug Watch and the related
27 interviews will inform stakeholder panels to develop stewardship interventions through a user-centred
28 design approach.
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31 **Ethics and dissemination**

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33 This study has been given ethical approval by the UCL Research Ethics Committee (ID 11813/001). Each
34 participant will provide informed consent upon registration. We will disseminate our work through
35 publication in peer-reviewed academic journals and presentation at conferences. Findings will
36 contribute to interventions and educational materials developed through the wider PASS study.
37 Anonymised data from Bug Watch will be made available through the UK Data Service
38 (<https://www.ukdataservice.ac.uk/>) for use by other researchers.
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Authors' contributions

Written on behalf of the Preserving Antibiotics through Safe Stewardship (PASS) study research group. CMS is responsible for data collection, management and analysis, and drafted the protocol. ACH, EBF, and the PASS study investigators developed the concept for the study. All authors contributed to the study design and development of the questionnaires. AC, FM and SH led recruitment. All authors have checked and approved the protocol to be published.

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Competing interests

None declared.

Word count 2068

Table 1: Baseline data collection

Section	Fields included
Consent	<ul style="list-style-type: none"> • Consent to participate in Bug Watch (required) • Permission to be contacted for qualitative interviews; for data to be linked to the Health Survey for England; to be contacted about a urinary tract infection sub-study (optional)
Contact details	<ul style="list-style-type: none"> • ID number (from invitation letter) • Name • Email address • Postal address
Demographics	<ul style="list-style-type: none"> • Date of birth • Sex • Country of birth • Ethnic group • Work status (employed, in education, unemployed, retired, etc.) • Full or part time work • Is a healthcare worker
General health	<ul style="list-style-type: none"> • Long term illnesses or health problems • Recurrent urinary tract infections • Currently pregnant; which trimester • Smoking status • Seasonal influenza vaccine in the last year • EQ-5D-3L
GP consultations	<ul style="list-style-type: none"> • Number of GP consultations in last 12 months
Antibiotics	<ul style="list-style-type: none"> • Ever been prescribed antibiotics; number in last 12 months • Ever been prescribed antibiotics but thought it was not the right treatment • When last took antibiotics; were they prescribed (if not, where from); were all taken • Ever asked for an antibiotic prescription; was it given; needed to persuade • Which conditions think can be treated with antibiotics • Understanding of term "antibiotic resistance"
Oral health	<ul style="list-style-type: none"> • Rate dental health (global item) • Has dentures • Dental symptoms in last 12 months • Problems caused by mouth/ teeth/ dentures in last 12 months (impact on quality of life)
Household composition	<ul style="list-style-type: none"> • Number of adults (aged 16+) • Number of children, number to be registered (up to 4)

NB: Questions are filtered and adapted based on previous responses so that they are only shown to participants when relevant. For example, "Currently pregnant" is not shown if sex is given as male.

Table 2 Symptoms of infection to be collected in Bug Watch

Respiratory	Gastrointestinal	Eye	Urinary tract	Skin/ soft tissue	Mouth/ dental	General/ non-specific
Runny nose	Nausea	Red eye	Painful urination	Rash (general)	Toothache	Fever
Blocked nose	Vomiting	Conjunctivitis	Frequent urination	Rash (local)	Mouth ulcer	Chills
Sneezing	Stomach/ abdominal pain	Stye	Urgent urination	Itchy (general)	Gum abscess	Muscle aches
Dry cough	Diarrhoea			Itchy (local)		Night sweats
Coughing up phlegm			Cloudy/ dark/ smelly urine	Boils/ abscesses		Fatigue
Short of breath			Blood in urine	Infected wound/ cut		Headache
Ear ache/ pain			Bladder pain	Mastitis		Migraine
Fluid leaking from ear			Kidney pain	Chicken pox		Loss of appetite
Sinus pain/ congestion				Shingles		

Table 3: Example items exploring barriers/enablers to GP consulting and antibiotic seeking behaviours, based on the COM-B model of behaviour change [9] (asked at the end of a series of symptoms in Bug Watch)

COM-B Domain	Example barrier/enabler belief statements
Capability (psychological)	<p>'I thought antibiotics would be effective in treating my symptoms'</p> <p>'I did not know what other treatments were available'</p>
Capability (physical)	<p>'I felt too unwell to travel to the GP practice'</p>
Opportunity (social)	<p>'I was encouraged by others to go see my GP'</p> <p>'My GP discussed alternatives ways of managing my symptoms'</p> <p>'I was involved in the decision of whether or not to take antibiotics'</p>
Opportunity (physical)	<p>'I was unable to take time off work to recover without taking antibiotics'</p> <p>'Other treatments were too expensive'</p> <p>'It was easy to get a GP appointment'</p>
Motivation (reflective)	<p>'I felt confident in safely treating my symptoms without antibiotics'</p> <p>'I did not think I would get better as quickly without antibiotics'</p>
Motivation (automatic)	<p>'I was worried about my symptoms'</p> <p>'I always go see my GP when I have these types of symptoms'</p> <p>'I felt reassured that I could safely manage my symptoms without antibiotics'</p>

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract p1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found p2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported p3
Objectives	3	State specific objectives, including any prespecified hypotheses p3
Methods		
Study design	4	Present key elements of study design early in the paper p3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection p3,4,5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up p3,4,5
		(b) For matched studies, give matching criteria and number of exposed and unexposed NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable p4,5, Table 1, Table 2
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group p4,5, Table 1, Table 2
Bias	9	Describe any efforts to address potential sources of bias p5,6
Study size	10	Explain how the study size was arrived at p3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why p5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding
		(b) Describe any methods used to examine subgroups and interactions
		(c) Explain how missing data were addressed
		(d) If applicable, explain how loss to follow-up was addressed
		(e) Describe any sensitivity analyses
Results - NA		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included

1		(b) Report category boundaries when continuous variables were categorized
2		(c) If relevant, consider translating estimates of relative risk into absolute risk for
3		a meaningful time period
4		
5	Other analyses	17 Report other analyses done—eg analyses of subgroups and interactions, and
6		sensitivity analyses
7		
8	Discussion - NA	
9	Key results	18 Summarise key results with reference to study objectives
10	Limitations	19 Discuss limitations of the study, taking into account sources of potential bias or
11		imprecision. Discuss both direction and magnitude of any potential bias
12		
13	Interpretation	20 Give a cautious overall interpretation of results considering objectives,
14		limitations, multiplicity of analyses, results from similar studies, and other
15		relevant evidence
16		
17	Generalisability	21 Discuss the generalisability (external validity) of the study results
18		
19	Other information	
20	Funding	22 Give the source of funding and the role of the funders for the present study and, if
21		applicable, for the original study on which the present article is based p8
22		

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

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Keywords:	Epidemiology < INFECTIOUS DISEASES, INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, PRIMARY CARE

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Abstract

Introduction

Antimicrobial resistance is a significant worldwide problem largely driven by selective pressure exerted through antibiotic use. Preserving antibiotics requires identification of opportunities to safely reduce prescriptions, for example in the management of mild common infections in the community. However, more information is needed on how infections are usually managed and what proportion lead to consultation and antibiotic use. The aim of this study is to quantify consultation and prescribing patterns in the community for a range of common acute infection syndromes (respiratory, gastrointestinal, skin/soft tissue, mouth/dental, eye and urinary tract). This will inform development of interventions to improve antibiotic stewardship as part of a larger programme of work, Preserving Antibiotics through Safe Stewardship (PASS).

Methods and analysis

This will be an online prospective community cohort study in England. We will invite 19,510 adults who previously took part in a nationally-representative survey (the Health Survey for England) and consented to be contacted about future studies. Adults will also be asked to register their children. Data collection will consist of a baseline registration survey followed by weekly surveys sent by email for six months. Weekly surveys will collect information on symptoms of common infections, healthcare-seeking behaviour, and use of treatments including antibiotics. We will calculate the proportions of infection syndromes that lead to GP consultation and antibiotic prescription. We will investigate how healthcare-seeking and treatment behaviours vary by demographics, social deprivation, infection profiles, and knowledge and attitudes towards antibiotics, and will apply behavioural theory to investigate barriers and enablers to these behaviours.

Ethics and dissemination

This study has been given ethical approval by the UCL Research Ethics Committee (ID 11813/001). Each participant will provide informed consent upon registration. We will disseminate our work through publication in peer-reviewed academic journals. Anonymised data will be made available through the UK Data Service (<https://www.ukdataservice.ac.uk/>).

Strengths and limitations of this study

- This study will use a novel and efficient method for large-scale collection of information about symptoms and related healthcare-seeking behaviours.
- It will address an important aspect of primary care (antibiotic use) by collecting data on a comprehensive set of symptoms of common infections, but will not cover sexually-transmitted infections.
- Collecting data over an entire year will allow seasonal variations to be explored.
- Participants will be recruited from a sample that is representative of the population living in private households in England.
- The prospective community cohort design will enable information to be captured about symptoms irrespective of medical consultation.

Introduction

The emergence of antimicrobial resistance (AMR) is a significant worldwide problem. It is largely driven by selective pressure exerted through antibiotic use and has led to some infections becoming untreatable with existing antimicrobials.[1] Preserving antibiotics for the future depends on achieving a safe balance between potential population harms of prescribing antibiotics and risks to the individual of not prescribing. The set of actions that promote this responsible use of antibiotics is referred to as antibiotic stewardship.[2]

Improving stewardship requires identification of opportunities to safely reduce prescriptions of antibiotics. Although overprescribing of antibiotics for patients presenting at primary care with common infections has been widely reported,[3] there is also evidence for a significant clinical “iceberg” of infection.[4,5] For example, previous studies have shown that most patients safely manage respiratory and gastrointestinal symptoms without consulting their GP or taking an antibiotic.[4,5] This suggests that inappropriate antibiotic prescriptions could be reduced through improved management of common infections and associated symptoms in the community. There is limited information, however, on how the public manage symptoms of other infections, what proportion of infections lead to consultation and antibiotic use, or how these rates vary according to type of symptoms or patient characteristics. Establishing this requires information to be captured on patients in the community, including those who do not seek healthcare, and identification of healthcare-seeking behaviours, ideally through prospective follow-up.

The aim of the Bug Watch study is to quantify consultation and antibiotic prescribing patterns in the community for a range of acute common infections (respiratory, gastrointestinal, skin/soft tissue, mouth/dental, eye and urinary tract). Bug Watch is part of a larger programme of work, Preserving Antibiotics through Safe Stewardship (PASS), which aims to inform the development of multifaceted behavioural interventions that will strengthen antibiotic stewardship across a range of healthcare settings. Results from Bug Watch will be synthesised with insights from qualitative interviews to identify opportunities for improved antibiotic stewardship in the community and general practice and inform development of interventions.

Methods and analysis

Study design and setting

This will be an online prospective community cohort study in England. Data collection will consist of a baseline registration survey followed by weekly surveys for six months. Weekly surveys will collect information on symptoms of common infections, healthcare-seeking behaviour, and use of treatments including antibiotics.

Recruitment

We will recruit participants through the Health Survey for England (HSE). HSE is an annual survey first conducted in 1991 that monitors changes in the health and lifestyles of people living in England.[6] It is commissioned by NHS Digital and run by NatCen Social Research and the UCL Research Department of Epidemiology and Public Health. The sample of individuals included in HSE each year is designed to be representative of the population living in private households in England. Full details of the methods for HSE sample have been described previously.[7]

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3 We will invite all adults who took part in the HSE in 2013, 2014 or 2015 and who consented to be
4 contacted about future research studies (with the exception of 50-53 year olds from the 2015 survey
5 who were recruited to a different study). This comprises 19,510 adults, of whom we estimate 15,819
6 (81%) will still be resident at the address on record when they are contacted. Parents or guardians will
7 be invited to register up to four children aged under sixteen, and all information for children will be
8 reported by the adult who registered them. Anyone aged sixteen or over living in the same household
9 will be invited to register separately.
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12 Recruitment will be conducted in four waves starting in March, June, September and November 2018.
13 Initial invitations to take part in Bug Watch will be sent by post. Those who wish to sign up will be
14 directed to a web link. A second reminder letter will be sent to those who have not registered
15 approximately three weeks after the initial invitation was sent. Where possible, invitation reminders will
16 also be sent by email or SMS text message. Individuals who are invited and do not wish to take part in
17 the study will be removed from contact lists.
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20 *Participant materials and incentives*

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22 The initial invitation letter will include a participant information sheet which will describe the purpose of
23 the study, what participants will be asked to do, and the contact details of the study team. It will also
24 include a paper copy of a “symptom diary”, which will be designed to help participants to keep track of
25 the symptoms of infection that will be collected in the weekly surveys.
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27 Study invitations will direct those interested in participating to a UCL web page. This page will include
28 the registration survey URL as well as a short video describing the study. Those wishing to register
29 children will also be able to download an information sheet for children. We will design this sheet so
30 that it is suitable to be read by anyone aged approximately eight years or older. Following registration,
31 participants will be sent a reusable laminated copy of the symptom diary, a pen, and a Bug Watch-
32 branded magnet.
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35 During follow-up, participants will be sent two email newsletters. These newsletters will provide
36 updates about the study such as rates of weekly survey completion. To avoid influencing the behaviour
37 of participants during follow-up, the newsletters will not include details about the main study outcomes.
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40 All participants will receive a £5 voucher to thank them for registering. At the end of follow-up, those
41 who have completed at least 50% of their weekly surveys will be sent an additional £5 voucher to thank
42 them for participating. They will also be entered into a prize draw to win a further £50 voucher.
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44 *Data collection*

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46 All data will be collected using REDCap electronic data capture tools hosted on the UCL Data Safe
47 Haven.[8] REDCap (Research Electronic Data Capture) is a secure, web-based application for research
48 studies. The UCL Data Safe Haven provides a technical solution for storing, handling and analysing
49 identifiable data. It has been certified to the ISO27001 information security standard and conforms to
50 NHS Digital’s Information Governance Toolkit. Data analysis will also be conducted within the UCL Data
51 Safe Haven, from which personal information will not be removed.
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54 Online registration will take approximately 15 minutes per person. Participants will be asked to provide
55 consent, confirming that they have read and understood the information sheets. Parents or legal
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guardians will be asked to give formal consent for children under the age of 16. For children that are able to give assent, the parent or legal guardian will be asked to discuss with them whether they wish to take part or not. Consent for linking data to the broader HSE survey data and for contact for qualitative interviews will also be requested.

Full details of the baseline data collection are shown in Table 1. The baseline survey will collect information on contact details, demographics, household composition, general health, oral health and GP consultations. It will also include questions about knowledge and attitudes towards antibiotics, adapted from Wave 3 of the Wellcome Trust Monitor survey, and the EQ-5D-3L instrument for measuring health-related quality of life.[9][10] The Wellcome Trust Monitor survey is designed to be representative of the UK adult population and measures trends in public attitudes towards science. Wave 3 of the survey, conducted in 2015, included a set of questions about knowledge and attitudes towards antibiotics. The EQ-5D-3L is a standardised measure of health status developed by the EuroQol Group that provides a simple, generic measure of health for clinical and economic appraisal.[10]

On the first Monday after registration, participants will be sent an email reminding them to start keeping track of symptoms of infection. Following this, they will be sent weekly emails each Monday with a link to a survey to fill in details about symptoms from the previous seven days and how they managed them. These emails will be sent each week for six months, and each survey will be open for one week. One reminder email will be sent on the Thursday of each week if the survey has not been completed. Participants will be given the opportunity to complete feedback forms about Bug Watch after approximately six weeks of participation, and again after all weekly surveys have been sent.

The symptoms that will be monitored in Bug Watch are shown in Table 2. For each day that a symptom is reported, participants will be asked to rate its severity (mild, moderate or severe) and to complete the EQ-5D-3L. They will also be asked to report what they did about their symptoms including whether they took time off work (or school), sought medical advice, or took any treatments. When antibiotics are reported, further details will be collected about the type of antibiotic, duration, who it was prescribed by (or how otherwise obtained) and adherence to treatment.

At the end of a series of symptoms, participants will be asked to complete a set of questions about what influenced how they managed their symptoms, specifically whether or not they consulted their GP and sought antibiotics. We will apply the COM-B (Capability, Motivation, Opportunity, Behaviour) model of behaviour change [11] to explore the wide-range of potential individual, socio-cultural and environmental barriers/enablers to these behaviours. The survey will include at least one item mapping onto each domain of the COM-B model (Table 3). Items will be in the form of belief statements to which participants rate their agreement on Likert-type scales from 1- Strongly Disagree to 5 - Strongly Agree.

In all surveys, we will make use of “skip logic” to ensure that participants are only shown questions that are relevant to them. For example, they will first be asked if they have any symptoms, and only if they do will they be shown specific symptom categories. Weekly surveys will therefore take no longer than a minute if no symptoms are reported, and approximately 5-10 minutes if symptoms are reported.

Statistical analysis

We will describe the demographic characteristics of the Bug Watch cohort and assess its representativeness by comparing with the characteristics of the broader HSE sample and published

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3 national statistics. We will also assess the representativeness of the knowledge and attitudes towards
4 antibiotics of the cohort by comparing with the Wellcome Trust Monitor Survey.[9]
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6 Symptoms reported will be combined into infection syndromes (i.e., combinations of symptoms
7 associated with an episode of infection). We will create descriptive profiles of infection syndromes
8 including types of symptom reported, duration, timing and severity. We will calculate the proportions of
9 infection syndromes that lead to people consulting their GP and receiving antibiotics. Antibiotic use will
10 be described in terms of type of antibiotic, duration, who it was prescribed by (or how otherwise
11 obtained) and adherence to treatment. Other healthcare-seeking behaviours, behavioural influences
12 (barriers and enablers within the COM-B model), and treatments taken to manage symptoms will also
13 be described.
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16 We will use Poisson regression to calculate rates of infection, consultation and antibiotic prescribing.
17 These analyses will be weighted by the population structure of England, and will account for the
18 clustered nature of the data. We will use logistic regression to investigate how GP consultation and
19 antibiotic prescribing varies by age, gender, ethnicity, presence of other illnesses, social deprivation,
20 infection syndrome, and knowledge and attitudes towards antibiotics. Continuous variables will be
21 converted into categorical variables. We will also assess the impact of different types of infection on
22 quality of life using the EQ5D-3L scores, and on reported work and school absences. We will use these
23 measures to estimate the overall impact of community infection at the population level. Full statistical
24 methods will be presented with relevant analyses.
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28 *Patient and public involvement*

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30 Participants were not directly involved in design of this study although feedback will be collected at two
31 time points during follow up. Newsletters will be sent to give participants updates during the study, and
32 a summary of the main findings will be available at the end. As part of the wider PASS study, a subset of
33 participants will be invited to take part in qualitative interviews that will draw on behavioural theory to
34 investigate the drivers of healthcare-seeking behaviours (full methods will be published elsewhere).
35 Findings from Bug Watch and the related interviews will inform stakeholder panels to develop
36 stewardship interventions through a user-centred design approach.
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39 **Ethics and dissemination**

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41 This study has been given ethical approval by the UCL Research Ethics Committee (ID 11813/001). Each
42 participant will provide informed consent upon registration. We will disseminate our work through
43 publication in peer-reviewed academic journals and presentation at conferences. Findings will
44 contribute to interventions and educational materials developed through the wider PASS study.
45 Anonymised data from Bug Watch will be made available through the UK Data Service
46 (<https://www.ukdataservice.ac.uk/>) for use by other researchers.
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Authors' contributions

Written on behalf of the Preserving Antibiotics through Safe Stewardship (PASS) study research group. CMS is responsible for data collection, management and analysis, and drafted the protocol. ACH, EBF, and the PASS study investigators developed the concept for the study. All authors contributed to the study design and development of the questionnaires. AC, FM and SH led recruitment. All authors have checked and approved the protocol to be published.

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Competing interests

None declared.

Word count 2110

Table 1: Baseline data collection

Section	Fields included
Consent	<ul style="list-style-type: none"> • Consent to participate in Bug Watch (required) • Permission to be contacted for qualitative interviews; for data to be linked to the Health Survey for England; to be contacted about a urinary tract infection sub-study (optional)
Contact details	<ul style="list-style-type: none"> • ID number (from invitation letter) • Name • Email address • Postal address
Demographics	<ul style="list-style-type: none"> • Date of birth • Sex • Country of birth • Ethnic group • Work status (employed, in education, unemployed, retired, etc.) • Full or part time work • Is a healthcare worker
General health	<ul style="list-style-type: none"> • Long term illnesses or health problems • Recurrent urinary tract infections • Currently pregnant; which trimester • Smoking status • Seasonal influenza vaccine in the last year • EQ-5D-3L
GP consultations	<ul style="list-style-type: none"> • Number of GP consultations in last 12 months
Antibiotics	<ul style="list-style-type: none"> • Ever been prescribed antibiotics; number in last 12 months • Ever been prescribed antibiotics but thought it was not the right treatment • When last took antibiotics; were they prescribed (if not, where from); were all taken • Ever asked for an antibiotic prescription; was it given; needed to persuade • Which conditions think can be treated with antibiotics • Understanding of term "antibiotic resistance"
Oral health	<ul style="list-style-type: none"> • Rate dental health (global item) • Has dentures • Dental symptoms in last 12 months • Problems caused by mouth/ teeth/ dentures in last 12 months (impact on quality of life)
Household composition	<ul style="list-style-type: none"> • Number of adults (aged 16+) • Number of children, number to be registered (up to 4)

NB: Questions are filtered and adapted based on previous responses so that they are only shown to participants when relevant. For example, "Currently pregnant" is not shown if sex is given as male.

Table 2 Symptoms of infection to be collected in Bug Watch

Respiratory	Gastrointestinal	Eye	Urinary tract	Skin/ soft tissue	Mouth/ dental	General/ non-specific
Runny nose	Nausea	Red eye	Painful urination	Rash (general)	Toothache	Fever
Blocked nose	Vomiting	Conjunctivitis	Frequent urination	Rash (local)	Mouth ulcer	Chills
Sneezing	Stomach/ abdominal pain	Stye	Urgent urination	Itchy (general)	Gum abscess	Muscle aches
Dry cough	Diarrhoea			Itchy (local)		Night sweats
Coughing up phlegm			Cloudy/ dark/ smelly urine	Boils/ abscesses		Fatigue
Short of breath			Blood in urine	Infected wound/ cut		Headache
Ear ache/ pain			Bladder pain	Mastitis		Migraine
Fluid leaking from ear			Kidney pain	Chicken pox		Loss of appetite
Sinus pain/ congestion				Shingles		

Table 3: Example items exploring barriers/enablers to GP consulting and antibiotic seeking behaviours, based on the COM-B model of behaviour change [11] (asked at the end of a series of symptoms in Bug Watch)

COM-B Domain	Example barrier/enabler belief statements
Capability (psychological)	<p>'I thought antibiotics would be effective in treating my symptoms'</p> <p>'I did not know what other treatments were available'</p>
Capability (physical)	<p>'I felt too unwell to travel to the GP practice'</p>
Opportunity (social)	<p>'I was encouraged by others to go see my GP'</p> <p>'My GP discussed alternatives ways of managing my symptoms'</p> <p>'I was involved in the decision of whether or not to take antibiotics'</p>
Opportunity (physical)	<p>'I was unable to take time off work to recover without taking antibiotics'</p> <p>'Other treatments were too expensive'</p> <p>'It was easy to get a GP appointment'</p>
Motivation (reflective)	<p>'I felt confident in safely treating my symptoms without antibiotics'</p> <p>'I did not think I would get better as quickly without antibiotics'</p>
Motivation (automatic)	<p>'I was worried about my symptoms'</p> <p>'I always go see my GP when I have these types of symptoms'</p> <p>'I felt reassured that I could safely manage my symptoms without antibiotics'</p>

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract p1 (b) Provide in the abstract an informative and balanced summary of what was done and what was found p2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported p3
Objectives	3	State specific objectives, including any prespecified hypotheses p3
Methods		
Study design	4	Present key elements of study design early in the paper p3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection p3,4,5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up p3,4,5 (b) For matched studies, give matching criteria and number of exposed and unexposed NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable p4,5, Table 1, Table 2
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group p4,5, Table 1, Table 2
Bias	9	Describe any efforts to address potential sources of bias p5,6
Study size	10	Explain how the study size was arrived at p3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why p5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses
Results - NA		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included

1		(b) Report category boundaries when continuous variables were categorized
2		(c) If relevant, consider translating estimates of relative risk into absolute risk for
3		a meaningful time period
4		
5	Other analyses	17 Report other analyses done—eg analyses of subgroups and interactions, and
6		sensitivity analyses
7		
8	Discussion - NA	
9	Key results	18 Summarise key results with reference to study objectives
10	Limitations	19 Discuss limitations of the study, taking into account sources of potential bias or
11		imprecision. Discuss both direction and magnitude of any potential bias
12		
13	Interpretation	20 Give a cautious overall interpretation of results considering objectives,
14		limitations, multiplicity of analyses, results from similar studies, and other
15		relevant evidence
16		
17	Generalisability	21 Discuss the generalisability (external validity) of the study results
18		
19	Other information	
20	Funding	22 Give the source of funding and the role of the funders for the present study and, if
21		applicable, for the original study on which the present article is based p8
22		

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

BMJ Open

Symptom reporting, healthcare-seeking behaviour and antibiotic use for common infections: protocol for Bug Watch, a prospective community cohort study

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Manuscripts

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3 **Symptom reporting, healthcare-seeking behaviour and antibiotic use for common infections:**
4 **protocol for Bug Watch, a prospective community cohort study**
5
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7

8 **Authors and affiliations**
9

10 *On behalf of the Preserving Antibiotics through Safe Stewardship (PASS) study research group:*
11

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Abstract

Introduction

Antimicrobial resistance is a significant worldwide problem largely driven by selective pressure exerted through antibiotic use. Preserving antibiotics requires identification of opportunities to safely reduce prescriptions, for example in the management of mild common infections in the community. However, more information is needed on how infections are usually managed and what proportion lead to consultation and antibiotic use. The aim of this study is to quantify consultation and prescribing patterns in the community for a range of common acute infection syndromes (respiratory, gastrointestinal, skin/soft tissue, mouth/dental, eye and urinary tract). This will inform development of interventions to improve antibiotic stewardship as part of a larger programme of work, Preserving Antibiotics through Safe Stewardship (PASS).

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- It will address an important aspect of primary care (antibiotic use) by collecting data on a comprehensive set of symptoms of common infections, but will not cover sexually-transmitted infections.
- Collecting data over an entire year will allow seasonal variations to be explored.
- Participants will be recruited from a sample that is representative of the population living in private households in England.
- The prospective community cohort design will enable information to be captured about symptoms irrespective of medical consultation.

Introduction

The emergence of antimicrobial resistance (AMR) is a significant worldwide problem. It is largely driven by selective pressure exerted through antibiotic use and has led to some infections becoming untreatable with existing antimicrobials.[1] Preserving antibiotics for the future depends on achieving a safe balance between potential population harms of prescribing antibiotics and risks to the individual of not prescribing. The set of actions that promote this responsible use of antibiotics is referred to as antibiotic stewardship.[2]

Improving stewardship requires identification of opportunities to safely reduce prescriptions of antibiotics. Although overprescribing of antibiotics for patients presenting at primary care with common infections has been widely reported,[3] there is also evidence for a significant clinical “iceberg” of infection.[4,5] For example, previous studies have shown that most patients safely manage respiratory and gastrointestinal symptoms without consulting their GP or taking an antibiotic.[4,5] This suggests that inappropriate antibiotic prescriptions could be reduced through improved management of common infections and associated symptoms in the community. There is limited information, however, on how the public manage symptoms of other infections, what proportion of infections lead to consultation and antibiotic use, or how these rates vary according to type of symptoms or patient characteristics. Establishing this requires information to be captured on patients in the community, including those who do not seek healthcare, and identification of healthcare-seeking behaviours, ideally through prospective follow-up.

The aim of the Bug Watch study is to quantify consultation and antibiotic prescribing patterns in the community for a range of acute common infections (respiratory, gastrointestinal, skin/soft tissue, mouth/dental, eye and urinary tract). Bug Watch is part of a larger programme of work, Preserving Antibiotics through Safe Stewardship (PASS), which aims to inform the development of multifaceted behavioural interventions that will strengthen antibiotic stewardship across a range of healthcare settings. Results from Bug Watch will be synthesised with insights from qualitative interviews to identify opportunities for improved antibiotic stewardship in the community and general practice and inform development of interventions.

Methods and analysis

Study design and setting

This will be an online prospective community cohort study in England. Data collection will consist of a baseline registration survey followed by weekly surveys for six months. Weekly surveys will collect information on symptoms of common infections, healthcare-seeking behaviour, and use of treatments including antibiotics.

Recruitment

We will recruit participants through the Health Survey for England (HSE). HSE is an annual survey first conducted in 1991 that monitors changes in the health and lifestyles of people living in England.[6] It is commissioned by NHS Digital and run by NatCen Social Research and the UCL Research Department of Epidemiology and Public Health. The sample of individuals included in HSE each year is designed to be representative of the population living in private households in England. Full details of the methods for HSE sample have been described previously.[7]

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3 We will invite all adults who took part in the HSE in 2013, 2014 or 2015 and who consented to be
4 contacted about future research studies (with the exception of 50-53 year olds from the 2015 survey
5 who were recruited to a different study). This comprises 19,510 adults, of whom we estimate 15,819
6 (81%) will still be resident at the address on record when they are contacted. Parents or guardians will
7 be invited to register up to four children aged under sixteen, and all information for children will be
8 reported by the adult who registered them. Anyone aged sixteen or over living in the same household
9 will be invited to register separately.
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12 As this is a largely descriptive study, and the primary outcome is calculation of rates, we did not require
13 a formal power calculation. Based on their experience of previous population surveys, NatCen estimated
14 that approximately 25% of those who received a letter would sign up (~4,000), and approximately 50%
15 of those who signed up would complete follow-up (~2,000 people completing six months of follow-up).
16 This would equate to approximately 1,000 person-years of follow-up, which would allow calculation of
17 crude rates of 500 cases per 1,000 person-years with a 95% CI of 457-546; 200 cases per 1,000 person-
18 years, 95% CI 173-230; and 100 cases per 1,000 person-years 95% CI 81-122.
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21 Recruitment will be conducted in four waves starting in March, June, September and November 2018.
22 Initial invitations to take part in Bug Watch will be sent by post. Those who wish to sign up will be
23 directed to a web link. A second reminder letter will be sent to those who have not registered
24 approximately three weeks after the initial invitation was sent. Where possible, invitation reminders will
25 also be sent by email or SMS text message. Individuals who are invited and do not wish to take part in
26 the study will be removed from contact lists.
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29 *Participant materials and incentives*

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31 The initial invitation letter will include a participant information sheet which will describe the purpose of
32 the study, what participants will be asked to do, and the contact details of the study team. It will also
33 include a paper copy of a "symptom diary", which will be designed to help participants to keep track of
34 the symptoms of infection that will be collected in the weekly surveys.
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37 Study invitations will direct those interested in participating to a UCL web page. This page will include
38 the registration survey URL as well as a short video describing the study. Those wishing to register
39 children will also be able to download an information sheet for children. We will design this sheet so
40 that it is suitable to be read by anyone aged approximately eight years or older. Following registration,
41 participants will be sent a reusable laminated copy of the symptom diary, a pen, and a Bug Watch-
42 branded magnet.
43

44 During follow-up, participants will be sent two email newsletters. These newsletters will provide
45 updates about the study such as rates of weekly survey completion. To avoid influencing the behaviour
46 of participants during follow-up, the newsletters will not include details about the main study outcomes.
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49 All participants will receive a £5 voucher to thank them for registering. At the end of follow-up, those
50 who have completed at least 50% of their weekly surveys will be sent an additional £5 voucher to thank
51 them for participating. They will also be entered into a prize draw to win a further £50 voucher.
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53 *Data collection*

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3 All data will be collected using REDCap electronic data capture tools hosted on the UCL Data Safe
4 Haven.[8] REDCap (Research Electronic Data Capture) is a secure, web-based application for research
5 studies. The UCL Data Safe Haven provides a technical solution for storing, handling and analysing
6 identifiable data. It has been certified to the ISO27001 information security standard and conforms to
7 NHS Digital's Information Governance Toolkit. Data analysis will also be conducted within the UCL Data
8 Safe Haven, from which personal information will not be removed.
9

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11 Online registration will take approximately 15 minutes per person. Participants will be asked to provide
12 consent, confirming that they have read and understood the information sheets. Parents or legal
13 guardians will be asked to give formal consent for children under the age of 16. For children that are
14 able to give assent, the parent or legal guardian will be asked to discuss with them whether they wish to
15 take part or not. Consent for linking data to the broader HSE survey data and for contact for qualitative
16 interviews will also be requested.
17

18
19 Full details of the baseline data collection are shown in Table 1. The baseline survey will collect
20 information on contact details, demographics, household composition, general health, oral health and
21 GP consultations. It will also include questions about knowledge and attitudes towards antibiotics,
22 adapted from Wave 3 of the Wellcome Trust Monitor survey, and the EQ-5D-3L instrument for
23 measuring health-related quality of life.[9][10] The Wellcome Trust Monitor survey is designed to be
24 representative of the UK adult population and measures trends in public attitudes towards science.
25 Wave 3 of the survey, conducted in 2015, included a set of questions about knowledge and attitudes
26 towards antibiotics. The EQ-5D-3L is a standardised measure of health status developed by the EuroQol
27 Group that provides a simple, generic measure of health for clinical and economic appraisal.[10]
28

29
30 On the first Monday after registration, participants will be sent an email reminding them to start
31 keeping track of symptoms of infection. Following this, they will be sent weekly emails each Monday
32 with a link to a survey to fill in details about symptoms from the previous seven days and how they
33 managed them. These emails will be sent each week for six months, and each survey will be open for
34 one week. One reminder email will be sent on the Thursday of each week if the survey has not been
35 completed. Participants will be given the opportunity to complete feedback forms about Bug Watch
36 after approximately six weeks of participation, and again after all weekly surveys have been sent.
37

38
39 The symptoms that will be monitored in Bug Watch are shown in Table 2. For each day that a symptom
40 is reported, participants will be asked to rate its severity (mild, moderate or severe) and to complete the
41 EQ-5D-3L. They will also be asked to report what they did about their symptoms including whether they
42 took time off work (or school), sought medical advice, or took any treatments. When antibiotics are
43 reported, further details will be collected about the type of antibiotic, duration, who it was prescribed
44 by (or how otherwise obtained) and adherence to treatment.
45

46
47 At the end of a series of symptoms, participants will be asked to complete a set of questions about what
48 influenced how they managed their symptoms, specifically whether or not they consulted their GP and
49 sought antibiotics. We will apply the COM-B (Capability, Motivation, Opportunity, Behaviour) model of
50 behaviour change, which has been validated for studies of the general population, [11] to explore the
51 wide-range of potential individual, socio-cultural and environmental barriers/enablers to these
52 behaviours. The survey will include at least one item mapping onto each domain of the COM-B model
53 (Table 3). Items will be in the form of belief statements to which participants rate their agreement on
54 Likert-type scales from 1- Strongly Disagree to 5 - Strongly Agree.
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3 In all surveys, we will make use of “skip logic” to ensure that participants are only shown questions that
4 are relevant to them. For example, they will first be asked if they have any symptoms, and only if they
5 do will they be shown specific symptom categories. Weekly surveys will therefore take no longer than a
6 minute if no symptoms are reported, and approximately 5-10 minutes if symptoms are reported.
7

8 *Statistical analysis*

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10 We will describe the demographic characteristics of the Bug Watch cohort and assess its
11 representativeness by comparing with the characteristics of the broader HSE sample and published
12 national statistics. We will also assess the representativeness of the knowledge and attitudes towards
13 antibiotics of the cohort by comparing with the Wellcome Trust Monitor Survey.[9]
14
15

16 Symptoms reported will be combined into infection syndromes (i.e., combinations of symptoms
17 associated with an episode of infection). We will create descriptive profiles of infection syndromes
18 including types of symptom reported, duration, timing and severity. We will calculate the proportions of
19 infection syndromes that lead to people consulting their GP and receiving antibiotics. Antibiotic use will
20 be described in terms of type of antibiotic, duration, who it was prescribed by (or how otherwise
21 obtained) and adherence to treatment. Other healthcare-seeking behaviours, behavioural influences
22 (barriers and enablers within the COM-B model), and treatments taken to manage symptoms will also
23 be described.
24
25

26 We will use Poisson regression to calculate rates of infection, consultation and antibiotic prescribing.
27 These analyses will be weighted by the population structure of England (age, sex, index of multiple
28 deprivation, region – as indicted by representativeness) and will account for the clustered nature of the
29 data. We will use logistic regression to investigate how GP consultation and antibiotic prescribing varies
30 by age, gender, ethnicity, presence of other illnesses, social deprivation, infection syndrome, and
31 knowledge and attitudes towards antibiotics. Continuous variables will be converted into categorical
32 variables. We will also assess the impact of different types of infection on quality of life using the EQ5D-
33 3L scores, and on reported work and school absences. We will use these measures to estimate the
34 overall impact of community infection at the population level. Full statistical methods will be presented
35 with relevant analyses.
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39 *Patient and public involvement*

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41 Participants were not directly involved in design of this study although feedback will be collected at two
42 time points during follow up. Newsletters will be sent to give participants updates during the study, and
43 a summary of the main findings will be available at the end. As part of the wider PASS study, a subset of
44 participants will be invited to take part in qualitative interviews that will draw on behavioural theory to
45 investigate the drivers of healthcare-seeking behaviours (full methods will be published elsewhere).
46 Findings from Bug Watch and the related interviews will inform stakeholder panels to develop
47 stewardship interventions through a user-centred design approach.
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50 **Ethics and dissemination**

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52 This study has been given ethical approval by the UCL Research Ethics Committee (ID 11813/001). Each
53 participant will provide informed consent upon registration. We will disseminate our work through
54 publication in peer-reviewed academic journals and presentation at conferences. Findings will
55 contribute to interventions and educational materials developed through the wider PASS study.
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Anonymised data from Bug Watch will be made available through the UK Data Service (<https://www.ukdataservice.ac.uk/>) for use by other researchers.

For peer review only

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Authors' contributions

Written on behalf of the Preserving Antibiotics through Safe Stewardship (PASS) study research group. CMS is responsible for data collection, management and analysis, and drafted the protocol. ACH, EBF, and the PASS study investigators developed the concept for the study. All authors (CMS, AC, CF, SH, FL, FM, SM, JSM, MJR, LS, GT, ACH, EBF) contributed to the study design and development of the questionnaires. AC, FM and SH led recruitment. All authors (CMS, AC, CF, SH, FL, FM, SM, JSM, MJR, LS, GT, ACH, EBF) have checked and approved the protocol to be published.

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Competing interests

None declared.

Word count 2241

Table 1: Baseline data collection

Section	Fields included
Consent	<ul style="list-style-type: none"> • Consent to participate in Bug Watch (required) • Permission to be contacted for qualitative interviews; for data to be linked to the Health Survey for England; to be contacted about a urinary tract infection sub-study (optional)
Contact details	<ul style="list-style-type: none"> • ID number (from invitation letter) • Name • Email address • Postal address
Demographics	<ul style="list-style-type: none"> • Date of birth • Sex • Country of birth • Ethnic group • Work status (employed, in education, unemployed, retired, etc.) • Full or part time work • Is a healthcare worker
General health	<ul style="list-style-type: none"> • Long term illnesses or health problems • Recurrent urinary tract infections • Currently pregnant; which trimester • Smoking status • Seasonal influenza vaccine in the last year • EQ-5D-3L
GP consultations	<ul style="list-style-type: none"> • Number of GP consultations in last 12 months
Antibiotics	<ul style="list-style-type: none"> • Ever been prescribed antibiotics; number in last 12 months • Ever been prescribed antibiotics but thought it was not the right treatment • When last took antibiotics; were they prescribed (if not, where from); were all taken • Ever asked for an antibiotic prescription; was it given; needed to persuade • Which conditions think can be treated with antibiotics • Understanding of term "antibiotic resistance"
Oral health	<ul style="list-style-type: none"> • Rate dental health (global item) • Has dentures • Dental symptoms in last 12 months • Problems caused by mouth/ teeth/ dentures in last 12 months (impact on quality of life)
Household composition	<ul style="list-style-type: none"> • Number of adults (aged 16+) • Number of children, number to be registered (up to 4)

NB: Questions are filtered and adapted based on previous responses so that they are only shown to participants when relevant. For example, "Currently pregnant" is not shown if sex is given as male.

Table 2 Symptoms of infection to be collected in Bug Watch

Respiratory	Gastrointestinal	Eye	Urinary tract	Skin/ soft tissue	Mouth/ dental	General/ non-specific
Runny nose	Nausea	Red eye	Painful urination	Rash (general)	Toothache	Fever
Blocked nose	Vomiting	Conjunctivitis	Frequent urination	Rash (local)	Mouth ulcer	Chills
Sneezing	Stomach/ abdominal pain	Stye	Urgent urination	Itchy (general)	Gum abscess	Muscle aches
Dry cough	Diarrhoea			Itchy (local)		Night sweats
Coughing up phlegm			Cloudy/ dark/ smelly urine	Boils/ abscesses		Fatigue
Short of breath			Blood in urine	Infected wound/ cut		Headache
Ear ache/ pain			Bladder pain	Mastitis		Migraine
Fluid leaking from ear			Kidney pain	Chicken pox		Loss of appetite
Sinus pain/ congestion				Shingles		

Table 3: Example items exploring barriers/enablers to GP consulting and antibiotic seeking behaviours, based on the COM-B model of behaviour change [11] (asked at the end of a series of symptoms in Bug Watch)

COM-B Domain	Example barrier/enabler belief statements
Capability (psychological)	<p>'I thought antibiotics would be effective in treating my symptoms'</p> <p>'I did not know what other treatments were available'</p>
Capability (physical)	<p>'I felt too unwell to travel to the GP practice'</p>
Opportunity (social)	<p>'I was encouraged by others to go see my GP'</p> <p>'My GP discussed alternatives ways of managing my symptoms'</p> <p>'I was involved in the decision of whether or not to take antibiotics'</p>
Opportunity (physical)	<p>'I was unable to take time off work to recover without taking antibiotics'</p> <p>'Other treatments were too expensive'</p> <p>'It was easy to get a GP appointment'</p>
Motivation (reflective)	<p>'I felt confident in safely treating my symptoms without antibiotics'</p> <p>'I did not think I would get better as quickly without antibiotics'</p>
Motivation (automatic)	<p>'I was worried about my symptoms'</p> <p>'I always go see my GP when I have these types of symptoms'</p> <p>'I felt reassured that I could safely manage my symptoms without antibiotics'</p>

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract p1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found p2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported p3
Objectives	3	State specific objectives, including any prespecified hypotheses p3
Methods		
Study design	4	Present key elements of study design early in the paper p3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection p3,4,5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up p3,4,5
		(b) For matched studies, give matching criteria and number of exposed and unexposed NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable p4,5, Table 1, Table 2
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group p4,5, Table 1, Table 2
Bias	9	Describe any efforts to address potential sources of bias p5,6
Study size	10	Explain how the study size was arrived at p3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why p5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding
		(b) Describe any methods used to examine subgroups and interactions
		(c) Explain how missing data were addressed
		(d) If applicable, explain how loss to follow-up was addressed
		(e) Describe any sensitivity analyses
Results - NA		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included

		(b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion - NA		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based p8

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.