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A study to safely remove a penicillin allergy label in hospitalised patients

Submission date
28/06/2021

Recruitment status
No longer recruiting

Registration date
26/08/2021

Overall study status
Completed

Last Edited
16/04/2025

Condition category
Other

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
This research addresses an important problem in health care: the high rate of patients inaccurately diagnosed with penicillin allergy (PenA). More than 1 in 10 patients have a label of PenA in hospitals, meaning they can't be given penicillins. Currently, patients with a PenA label who have an infection or need antibiotics to prevent infection are treated with non-penicillin antibiotics. These are associated with higher chances of negative consequences: longer hospital stays, higher readmission rates, increased risk of serious infections such as MRSA, wound infections after operations, and resistance to antibiotics, making healthcare very difficult. Also, this is likely to cost the NHS several million pounds each year. However, most (9 out of 10) people with a PenA label prove not to actually be allergic when properly tested. Inaccurate PenA labels often happen because side effects and symptoms of infection are mistaken for an allergy. PenA testing involves a careful medical history, review of previous records, allergy skin tests and a 'penicillin oral challenge' (giving penicillin by mouth under supervision). This takes several hours, needs a specialist and can only be done in a small number of allergy clinics. Getting rid of incorrect PenA label is called 'de-labelling'. Because PenA tests are not routinely available to most hospital patients, researchers have developed a simple method to de-label based on a careful review of the clinical history without the need for skin tests.
Based on medical history and previous records, patients are grouped as 'low risk' or 'high risk'. Nearly half of 'PenA' patients are 'low risk'. Studies suggest that giving penicillin by mouth to 'low risk' patients under medical supervision without doing allergy skin tests is safe. This is called a 'direct' oral penicillin challenge (DPC). More research is needed to find out how patients, doctors and hospital managers feel about DPC and how best it can be carried out in hospitals. This will help design new allergy testing pathways.
The aims of this study are to find out what patients, healthcare workers and managers think about DPC to remove incorrect PenA labels, and to design a safe way to start using DPC in hospitals and estimate costs.

Who can participate?
Patients aged 18 years and over with a current penicillin allergy label from different types of wards including surgical and cancer patients who are at a higher risk of serious infections.

What does the study involve?
Patients with a PenA label will be seen by a pharmacist or a nurse and placed in ‘low risk’ and ‘high risk’ groups. ‘Low risk’ patients will be offered the DPC. ‘High risk’ patients and those declining the DPC will be seen in an allergy clinic for further testing. The researchers will collect information by interviewing patients in the ‘low risk’ group and talk to groups of patients, healthcare workers and managers. They will find out how many ‘low risk’ patients are willing to undergo DPC and describe how they get on. They will look at the ways they might offer DPC in hospital and work out what it would cost.

What are the possible benefits and risks of participating?
This study will help to improve antibiotic use in hospitals, improve patient experience and outcomes, reduce rates of serious hospital-acquired infections, and save the NHS money. Patients and patient organisations have helped design this study and will be involved in every stage. The researchers will share their findings with all those involved in the care of patients with infections and PenA and beyond.

Where is the study run from?
University Hospitals Birmingham NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
May 2021 to April 2023

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
293544

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 293544, HS&DR - NIHR129069, CPMS 49718

Study information

Scientific Title
A multicentre study to investigate a protocol-driven multidisciplinary service model to tackle ‘spurious penicillin allergy’ in secondary care (SPACE study)

Acronym
SPACE

Study objectives
Nearly half of the patients carrying a penicillin allergy label in hospitals are stratified as ‘low risk’ (most unlikely to be penicillin allergic). Allergy labels can be safely removed in these patients through a direct penicillin challenge procedure without the need for skin testing. Direct penicillin challenges can be safely conducted by non-specialist healthcare professionals and will be acceptable by the majority of patients. This new service model is cost-effective.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 23/07/2021, London - London Bridge Research Ethics Committee (80 London Road, London, SE1 6LH, United Kingdom; +44 (0)207972 2580; Nrescommittee.london-londonbridge@nhs.net), ref: 21/PR/0814

Study design
Multicentre observational study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Spurious/inaccurate penicillin allergy labels in secondary care

Interventions
The proposed service model for PenA de-labelling in secondary care is as follows:

Using information captured from a structured drug allergy history and review of previous prescription records (where available), patients will be stratified into 'low risk' and 'high risk'. The 'low risk' group will include those describing non-specific symptoms or a 'benign rash' that is not in keeping with an allergic reaction, or those with an 'indeterminate history' >10 years previously that is suggestive of a non-life-threatening reaction. The 'high risk' group includes those with a history suggestive of an immediate allergic reaction or anaphylaxis (serious allergic reaction). Patients giving a history of serious immunological reactions such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, Steven Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), erythema multiforme etc, are excluded. Patients meeting the criteria for 'low risk' will be offered a direct penicillin challenge (DPC). Those declining DPC and patients in the 'high risk' group will be referred to an allergy clinic as per current national guidelines. The risk stratification process is performed by a senior research pharmacist (RP) or a senior research nurse (RN) who have undergone study-specific training and supervised by a consultant.

Intervention Type
Other

Primary outcome measure
The behaviour, attitudes and acceptability of patients, healthcare professionals and managers regarding the use of Direct oral Penicillin Challenge (DPC) in 'low risk' patients, assessed using 1-1 interviews and focus groups between 6 – 18 months of the study

Secondary outcome measures
Measured at a single timepoint:
1. The proportion of 'low risk' patients with a PenA label who would be eligible for a DPC, measured by applying risk stratification criteria (4-18 months)
2. The proportion of 'low risk' patients who would be willing and complete a DPC, measured by the number of 'low risk' patients who give informed consent (4-18 months)
3. The practical aspects of implementing this de-labelling programme in secondary care by investigating factors such as organisational context, treatment pathway, protocol implementation, time taken and resources (based on qualitative and quantitative methods applied in the study)
4. The potential cost-effectiveness of this service model, calculated using health economics methods comparing the cost of standard care provided to PenA patients compared to the new proposed service model between 17-22 months

Overall study start date

01/05/2021

Completion date
30/04/2023

Eligibility

Key inclusion criteria
1. Patients with a current penicillin allergy label
2. Aged ≥18 years
3. Willing and able to give informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
122

Total final enrolment
122

Key exclusion criteria
1. Clinically unstable patients, i.e., unstable cardio-respiratory status (eg: respiratory failure, cardiac failure, pre-hepatic encephalopathy etc)
2. History of serious non-immediate systemic hypersensitivity reactions (HSRs) to penicillin
3. Documented Steven Johnson syndrome (SJS), toxic epidermal necrolysis (TENS), acute exanthematous generalised pustulosis (AEGS), erythema multiforme, haemolytic anaemia, vasculitis, acute interstitial nephritis
4. Those deemed unsuitable for medical reasons (unlikely to comply with study protocol)
5. Pregnant
6. Breastfeeding
7. Concomitant COVID-19 infection (patients from pre-surgical units and Haematology-Oncology units may be considered following recovery from COVID-19)
8. Those participating in any other research currently or those who have participated in research involving medicinal product, medical devices and/or other intervention in the preceding 6 weeks

Added 11/08/2023:
9. Patients currently receiving omalizumab or those who have received omalizumab within 6 months prior to the proposed DPC
10. Patients currently taking antihistamine and unable to temporarily withdraw for the proposed DPC

Date of first enrolment
01/08/2021

Date of final enrolment
31/03/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Heartlands Hospital
University Hospitals Birmingham NHS Foundation Trust
Bordesley Green East
Birmingham
United Kingdom
B9 5SS

Study participating centre
John Radcliffe Hospital
Oxford University Hospitals NHS Trust
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Leeds General Infirmary
Leeds Teaching Hospitals NHS Trust
Great George St
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Sponsor information

Organisation

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Sponsor type
Hospital/treatment centre

Website
http://www.uhb.nhs.uk/

ROR
https://ror.org/014ja3n03

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

Current publication and dissemination plan as of 11/08/2023:
The investigators aim to publish the results of the SPACE study in peer review journals, present at conferences and also disseminate via patient organisations in 2023-24.

Previous publication and dissemination plan:
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/08/2024

Individual participant data (IPD) sharing plan
Data collected for this study will be stored on the NHS networks. Anonymised data will be shared within the SPACE team across all three centres for the study: Birmingham, Oxford and Leeds.

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol file	version 14.0	09/06/2022	14/08/2023	No	No
Plain English results			09/04/2024	No	Yes
Results article		01/04/2025	16/04/2025	Yes	No