ISRCTN16392920 https://doi.org/10.1186/ISRCTN16392920

# Probiotics to reduce infections in care home residents

| Submission date | Recruitment status | |
|---|---|---|
| 14/07/2016 | No longer recruiting | ✓ Prospectively registered |
| | | ✓ Protocol added |
| **Registration date** | **Overall study status** | ? SAP not yet added |
| 20/07/2016 | Completed | ✓ Results added |
| **Last Edited** | **Condition category** | ? Raw data not yet added |
| 24/01/2023 | Infections and Infestations | ✓ Study completed |

## Plain English Summary

Background and study aims
Care home residents (CHR) are prescribed far more antibiotics than the general population because they are more likely to get an infection, caused by a weakened immune system, living close to others and having a number of health conditions (multi-morbidity). In previous research in care homes, it was found that CHR took antibiotics for an average of 17.4 days per year. High antibiotic use increases the risk of bacteria becoming resistant to antimicrobial treatments. Antimicrobial resistance (AMR) can spread within the home and to hospitals and the community. This is thought to get worse as the population ages. Infections in CHR cost the NHS more than £54 million every year in costs of hospitalising residents alone, as infections are the most common reason for CHR hospitalisation. AMR infections are generally more serious and costly, particularly in older people. Reduction in antibiotic use and AMR could improve quality of life, save money, and help preserve the usefulness of existing antibiotics. Other than vaccination and good hygiene practices, there are few methods proven to prevent infection in CHR. Probiotics are live bacteria that are thought to be beneficial for health, possibly by increasing “good” bacteria (that doesn’t damage health) and reducing “bad” bacteria (that is potentially harmful) in the digestive system (gut). They are safe and cheap and most often used as food supplements. Some studies have shown probiotics to be effective at reducing infections and enhancing the immune system response, but research in CHR is currently lacking. The aim of this study is to find out whether taking probiotics every day can reduce infections in care home residents.

Who can participate?
Adults over 65 years of age who live in a care home.

What does the study involve?
Participants are randomly allocated to one of two study groups. Those in the first group take a probiotic containing various kinds of live bacteria every day for 12 months by mouth. Those in the second group take a placebo (dummy) every day for 12 months. The amount antibiotics taken by participants,as well as the amount of infections, are recorded for both groups over 12 months. After three and six months, participants have a sample of blood taken to test how well

their immune system is working and to assess the individual components of their blood. Participants also complete questionnaires at these times to assess their quality of life and wellbeing.

What are the possible benefits and risks of participating?
For participants who receive the probiotics, there is a chance that they will benefit from a lower chance of developing an infection that may require treatment with an antibiotic. Probiotics are classed as a food supplement and there are very few side effects (mainly bloating and flatulence if these occur). Probiotics carry theoretical risks including infection beyond the gut but this is considered unlikely. There is a small risk of pain or bruising when blood samples are taken. Participants are able to choose whether to provide samples or not when taking part in the study.

Where is the study run from?
The study is run from the South East Wales Trials Unit (Cardiff) and takes place in approximately twenty care homes located in England and Wales (UK)

When is the study starting and how long is it expected to run for?
September 2015 to July 2019

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

Who is the main contact?
Professor Christopher Butler

# Contact information

### Type(s)
Scientific

### Contact name
Prof Christopher Butler

### Contact details
Nuffield Department of Primary Care Health Sciences
University of Oxford
Oxford
United Kingdom
OX2 6GG

# Additional identifiers

### EudraCT/CTIS number

### IRAS number

### ClinicalTrials.gov number

### Protocol/serial number
20338

# Study information

### Scientific Title
A double-blind placebo controlled trial to evaluate the efficacy of probiotics (Lactobacillus rhamnosus, LGG and Bifidobacterium animalis subsp. lactis, BB-12) in reducing antibiotic administration for infection in care home residents

### Acronym
PRINCESS

### Study hypothesis
Primary hypothesis:
Daily oral probiotic reduces CAAD for infection vs placebo in Care Home Resident (CHR).

Mechanisms hypothesis:
Daily oral probiotic reduces gastrointestinal colonisation with AMR bacteria, enhances influenza vaccine response and modulates ex-vivo cytokine response to Toll Like Receptor (TLR) agonists vs placebo in CHR.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Wales REC 3, 23/10/2015, ref: 15/WA/0306

### Study design
Randomised; Interventional; Design type: Not Specified, Not Specified

### Primary study design
Interventional

### Secondary study design
Randomised controlled trial

### Study setting(s)
Care home

### Study type(s)
Treatment

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

### Condition
Specialty: Infectious diseases and microbiology

### Interventions

Participants are randomised to one of two groups via an online system which uses the method of minimisation, with a random component set at 80%. There are two minimisation variables: the care home at which the participant is resident, and the participant's gender.

Intervention arm: Once daily oral probiotic (Lactobacillus rhamnosus, LGG and Bifidobacterium animalis subsp. lactis, BB-12) for twelve months.
Placebo arm: Once daily oral placebo for twelve months.

Two follow-up visits will take place, at 3 and 12 months.

## Intervention Type
Other

## Primary outcome measure
1. Cumulative antibiotic administration days for all cause infections over 12 months
2. Total number of days of systemic antibiotic administration as recorded in care home medical records and discharge summaries if the participant is admitted to hospital, over 12 months

## Secondary outcome measures
Secondary outcome measures as of 01/11/2018:
1. Cumulative Antibiotic Administration Days (CAAD) for five sub-categories of Common Infectious Diseases (Respiratory Tract Infection, Urinary Tract Infection, skin, Gastrointestinal Infections and unexplained fever); number, site, duration (mean and cumulative) of infection over 12 months as measured by data recorded at regular intervals by research nurses from care home records.
2. Antibiotic consumption as measured by data recorded at regular intervals by RN from care home records over 12 months
3. Hospitalisation rate as measured by data recorded at regular intervals by RN from care home records over 12 months
4. Mortality as measured by data recorded at regular intervals by RN from care home records over 12 months
5. Health Utility as measured using the EQ-5D at baseline, 3 months and 12 months
6. Wellbeing is measured using the ICECAP-O at baseline, 3 months and 12 months
7. Full blood count (FBC) as measured by laboratory analysis of blood samples taken at baseline and 12 months
8. Vitamin D levels as measured by laboratory analysis of blood samples taken at baseline and 12 months
9. Immunology - Patient's cytokine and chemokine response in whole blood samples stimulated ex-vivo by Toll Like Receptors TLR2 and TLR4 as measured by laboratory analysis of samples taken at baseline and 12 months
10. Measurement of plasma cytokines and chemokines in plasma and whole blood; and measurement of monocyte and neutrophil phagocytosis of E.coli
11. Antimicrobial resistance (AMR) as measured by Culture and antibiotic sensitivity of Gram-negative Enterobacteriaceae and Vancomycin resistant enterococci (VRE) from stool sample at baseline and 12 months
12. Presence of probiotic bacteria Lactobacillus rhamnosus, LGG and Bifidobacterium animalis subsp. lactis, BB-12, plus presence of (antimicrobial resistant) AMR bacteria and C. difficile in stool is measured by laboratory analysis of stool samples taken at baseline, 3 months and 12 months
13. Presence of oral Candida species in saliva is measured by semi-quantitiative laboratory analysis of saliva samples taken at baseline, 3 months and 12 months

14. Influenza vaccine response - Haemagglutination inhibition assay and antibody titers at two points during participation: one immediately prior to the vaccine being administered and one 28 days post vaccine administration

Previous secondary outcome measures:
1. Cumulative Antibiotic Administration Days (CAAD) for five sub-categories of Common Infectious Diseases (Respiratory Tract Infection, Urinary Tract Infection, skin, Gastrointestinal Infections and unexplained fever); number, site, duration (mean and cumulative) of infection over twelve months as measured by data recorded at regular intervals by research nurses from care home records.
2. Antibiotic consumption as measured by data recorded at regular intervals by RN from care home records over 12 months
3. Hospitalisation rate as measured by data recorded at regular intervals by RN from care home records over 12 months
4. Mortality as measured by data recorded at regular intervals by RN from care home records over twelve months
5. Health Utility as measured using the EQ-5D at baseline, three months and twelve months
6. Wellbeing is measured using the ICECAP-O at baseline, three months and twelve months
7. Full blood count (FBC) as measured by laboratory analysis of blood samples taken at baseline and twelve months
8. Vitamin D levels as measured by laboratory analysis of blood samples taken at baseline and twelve months
9. Immunology - Patient's cytokine and chemokine response in whole blood samples stimulated ex-vivo by Toll Like Receptors TLR2 and TLR4 as measured by laboratory analysis of samples taken at baseline and twelve months
10. Blood - Modified expression of Toll Like Receptors (TLR) as measured in circulating white blood cells from whole blood samples taken at baseline and twelve months
11. Antimicrobial resistance (AMR) as measured by Culture and antibiotic sensitivity of Gram-negative Enterobacteriaceae and Vancomycin resistant enterococci (VRE) from stool sample at baseline and twelve months
12. Presence of probiotic bacteria Lactobacillus rhamnosus, LGG and Bifidobacterium animalis subsp. lactis, BB-12, plus presence of (antimicrobial resistant) AMR bacteria and C. difficile in stool is measured by laboratory analysis of stool samples taken at baseline, three months and twelve months
13. Presence of oral Candida species in saliva is measured by semi-quantitiative laboratory analysis of saliva samples taken at baseline, three months and twelve months
14. Influenza vaccine response - Haemagglutination inhibition assay and antibody titers at two points during participation: one immediately prior to the vaccine being administered and one 28 days post vaccine administration

### Overall study start date
01/09/2015

### Overall study end date
01/07/2019

# Eligibility

### Participant inclusion criteria
1. Aged 65 years or older
2. Currently living in a care home setting (residential, nursing or mixed)

3. Participant is willing and able to give informed consent for participation in the trial OR if the participant lacks capacity, a consultee is willing to complete a consultee declaration form

### Participant type(s)
Patient

### Age group
Senior

### Sex
Both

### Target number of participants
Planned Sample Size: 330; UK Sample Size: 330

### Total final enrolment
310

### Participant exclusion criteria
1. Is known to be immunocompromised (requiring immunosuppressants, long term high dose oral, intramuscular or intravenous steroids)
2. Is currently taking regular probiotics and is not willing to adapt to trial protocol
3. Is a temporary care home resident (i.e. less than 1 month of planned transitional/respite residential care)
4. Death is thought to be imminent
5. Lactose intolerant

### Recruitment start date
01/12/2016

### Recruitment end date
31/10/2017

## Locations

### Countries of recruitment
United Kingdom

Wales

### Study participating centre
**South East Wales Trials Unit**
Cardiff University
7th Floor, Neuadd Meirionnydd
Heath Park
Cardiff
United Kingdom
CF14 4YS

# Sponsor information

**Organisation**
Cardiff University

**Sponsor details**
Research Governance and Contracts
30-36 Newport Road
Cardiff
Wales
United Kingdom
CF24 0DE

**Sponsor type**
Hospital/treatment centre

**ROR**
https://ror.org/03kk7td41

# 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

All publications and presentations relating to the trial will be authorised by the Trial Management Group and will follow the PRINCESS publication policy. The trial protocol will be published. The trial results will be published and all who meet the criteria for authorship will be listed as authors. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged. The results will be presented to the DMC prior to publication. Papers will be shared with the funders prior to submission. Funders will have 14 days in which to respond and to bring any matters of factual accuracy relating to the intervention to the attention of the trial team. The funders will have no role in decisions on publication. The funding source and other support will be acknowledged. We are unable to give dates or further details at this stage.

## Intention to publish date

01/07/2020

## Individual participant data (IPD) sharing plan

Not provided at time of registration

## IPD sharing plan summary

Data sharing statement to be made available at a later date

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Protocol article | protocol | 20/06/2019 | 09/06/2020 | Yes | No |
| Results article | results | 07/07/2020 | 08/07/2020 | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |