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Probiotics to reduce infections in care home residents

Submission date	Recruitment status	[X] Prospectively registered
14/07/2016	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
20/07/2016	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
06/08/2024	Infections and Infestations	

Plain English summary of protocol

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
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Additional identifiers

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 objectives
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

Primary study design
Interventional

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

Study type(s)
Treatment

Health condition(s) or problem(s) studied
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(s)
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

Key secondary outcome(s)
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

Completion date
01/07/2019

Eligibility

Key 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

Healthy volunteers allowed
No

Age group
Senior

Sex
All

Total final enrolment
310

Key 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

Date of first enrolment
01/12/2016

Date of final enrolment
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
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Sponsor information

Organisation
Cardiff University

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

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?
Results article	results	07/07/2020	08/07/2020	Yes	No
Results article		04/03/2021	06/08/2024	Yes	No
Results article		01/05/2021	06/08/2024	Yes	No
Protocol article	protocol	20/06/2019	09/06/2020	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Relationships Between Age, Frailty, Length of Care Home Residence and Biomarkers of Immunity and Inflammation in Older Care Home Residents in the United Kingdom	17/03/2021	06/08/2024	Yes	No