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The Probiotics for Antibiotic Associated Diarrhoea (PAAD) study in care homes: determining the effect of probiotics on antibiotic associated diarrhoea

Submission date 05/03/2013	**Recruitment status** Stopped	[X] Prospectively registered [_] Protocol
Registration date 14/03/2013	**Overall study status** Stopped	[_] Statistical analysis plan [_] Results
Last Edited 16/07/2015	**Condition category** Signs and Symptoms	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Infectious diarrhoea is caused by pathogens invading the human host and disrupting the normal colonic flora of the gut or by an overgrowth of existing bacteria. The most common infectious cause of nosocomial or healthcare acquired diarrhoea is Clostridium difficile. In severe cases, the illness leads to dehydration and death. There is very little data on the incidence of antibiotic-associated diarrhoea (AAD) in long term care facilities. Each case causes suffering, potential serious complications and exposes other residents to risk of infection. This adds to the burden on staff in long term care facilities from increased work load, greater patient transfers and reduced morale, all of which becomes worse in a cluster or outbreak. The purpose of this study is to look at whether the co-administration of probiotics with acute antibiotic treatment reduces the incidence of antibiotic-associated diarrhoea among service users at care homes.

Who can participate?
Adults who do not meet any of the exclusion criteria and who are usually resident in participating nursing or dual-registered care homes in the UK who are prescribed antibiotics during the study period. We will also include adults who lack mental capacity for whom we have a personal/professional legal representative.

What does the study involve?
If you are given antibiotics in the course of your usual medical care at any point during the following 12 months and you agree to take part, you will be randomly assigned (equivalent to the toss of a coin) either to the active treatment or the placebo (the placebo will resemble the active treatment in every way except it will not contain any active ingredients). The study preparation will be prepared for you by the care home staff. It will be provided twice every day for 21 days. Relevant details related to your medical history will be recorded. You will be monitored for eight weeks: This includes information being collected on the antibiotics and study preparation you are taking, whether you have had diarrhoea and how you are feeling each week. At the end of the eight weeks information about any other treatments that you have been

given and whether you have had to go to hospital or have other treatment will be collected. If you develop diarrhoea during the eight weeks, the care home staff will collect a sample of your stool and send this to our laboratory for tests.

What are the possible benefits and risks of participating?
There may be some potential benefits for you if the probiotic does prevent or reduce the severity of diarrhoea caused by treatment with antibiotics. However, there will be no direct benefit to you in the event that you are randomly selected to take a placebo. The proposed study does pose ethical issues, namely the conduct of a randomised placebo controlled trial in a population with the potential challenge of mental capacity. For this reason, prior to enrolment and at randomisation, the mental capacity of all service users (SUs) will be assessed by trained staff. The Medicines and Healthcare products Regulatory Agency (MHRA) considers this study to be an efficacy study of VSL#3 in a new and unlicensed indication and have defined this study to be a Type B trial, which identifies the risk to service users as being somewhat higher than that of standard medical care. The study medication will be delivered by appropriately trained and experienced care home- clinical staff or study trained staff, managed and monitored by South East Wales Trials Unit.

Where is the study run from?
Participating nursing or dual-registered care homes in the UK.

When is the study starting and how long is it expected to run for?
Recruitment is expected to start in April 2013 and will end in April 2014. Service users will be followed up for eight weeks from the date of randomisation.

Who is funding the study?
Heath Technology Assessment (HTA)

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2011-006269-17

Protocol serial number
HTA 08/13/24, SPON1069-11

Study information

Scientific Title
A double-blind placebo-controlled randomised clinical trial to study the effect of Probiotics for the prevention or amelioration of Antibiotic Associated Diarrhoea in residents of care homes in South Wales and England

Acronym
PAAD Study

Study objectives
Antibiotics treatment disrupts the normal flora of the gut, sometimes causing diarrhoea. Older patients with frequent hospitalizations and high co-morbidity are at greatest risk of developing antibiotic associated diarrhoea (AAD). Clostridium difficile (C. difficile) is a Gram positive, spore forming bacillus that has most recently been highlighted as a potentially serious threat to hospitalized patients and care home service users, causing high levels of morbidity and, in some cases death. C. difficile associated diarrhoea (CDAD) is the most commonly identified cause of AAD. Surveillance data and UK clinical experience suggests that AAD, including CDAD, could be an important problem in the UK care homes. In addition, there are strong grounds for evaluating probiotics in conjunction with antibiotic treatment to prevent AAD in care home service users, but this has never been evaluated in robust clinical trial.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/081324
Study protocol can be found at:http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0011/52211/PRO-08-13-24.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
South East Wales Ethics Committee Panel B, 15/06/2012, ref: 12/WA/0057

Study design
Multi-centre double-blinded placebo-controlled two-arm individually randomised trial

Primary study design
Interventional

Study type(s)

Prevention

Health condition(s) or problem(s) studied
Antibiotic Associated Diarrhoea

Interventions
Patients randomised to receive either Probiotic VSL# 3 or placebo.

VSL #3 is freeze dried lactose free sachet containing 4.4g of a mixture of 450 billion live lactic acid bacteria and bifidobacteria.

Placebo Formulation (TBC): A lactose free powder 4.4g Sachet, matched for taste, consistency and colour.

Dose One sachet (4.4g of freeze-dried powder), twice daily, per oral.

The trial duration in 24 months, Service users will receive the intervention (IMP or Placebo) for 21 days and will be followed up for 8 weeks.

Updated 24/01/2014: the study was stopped on 31/10/2013 due to emerging evidence that there was no longer sufficient scientific justification to commence recruitment.

Intervention Type
Other

Primary outcome(s)
The occurrence of at least one episode of AAD during the eight weeks following randomisation. AAD is defined as three or more loose stools in a 24-hour period following a period of normal stool consistency.

Key secondary outcome(s))
1. Proportion of stool samples positive for Clostridium difficile toxin A or B from SUs who develop AAD during the eight week follow-up period.
2. Duration, frequency and recurrence of AAD during the eight-week follow-up period.
3. QoL, measured using EQ-5D at the time of randomisation and each week during the eight-week follow-up period.
4. Recovery from illness that triggered antibiotic treatment.
5. Healthcare Resource Use, including GP and practice nurse consultations, other medication, procedures, investigations, hospital appointments, A&E attendances and any hospital inpatient admissions, measured at the end of the eight-week follow-up period.
6. Unplanned hospitalisations, including all-cause and AAD related, during the eight-week follow-up period.
7. Adverse Events: e.g. vomiting, abdominal pain, excessive flatulence, bloating, skin rashes, during the eight-week follow-up period.
8. Adherence to the antibiotic, probiotic/placebo treatment course.
9. All causes of mortality in the 8 week follow up period.

Completion date
31/10/2014

Reason abandoned (if study stopped)

Objectives no longer viable

Eligibility

Key inclusion criteria
1. Resident in a care home for 24 hours or more, with a minimum planned period of residential care of 1 month
2. Able to provide informed consent or have a personal legal representative who can provide consent for inclusion
3. If the service users (SU) takes a regular probiotic but chooses to discontinue the probiotic

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Sex
All

Key exclusion criteria
1. Severely immuno-compromised, e.g. known severe neutropenia
2. Has artificial heart valve in situ
3. Medical history of acute pancreatitis
4. Requires naso-jejunal feeding /nasogastric feeding currently has a colostomy
5. SU without capacity already receiving a probiotic

Date of first enrolment
01/04/2013

Date of final enrolment
01/04/2014

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Cardiff University
Cardiff
United Kingdom
CF14 4YS

Sponsor information

Organisation
Cardiff University (UK)

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Government

Funder Name
NIHR Health Technology Assessment Programme - HTA (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Other publications	project note	01/12/2015		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes