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Does synbiotic supplementation improve the effects of a ketogenic diet?

Submission date
17/02/2026

Recruitment status
Recruiting

Registration date
01/04/2026

Overall study status
Ongoing

Last Edited
01/04/2026

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
A ketogenic diet involves limiting your carbohydrate intake in food and drinks to less than 50g a day. This is called “ketogenic” because is causes your body to increase the production of ketones (by your liver). Ketones provide energy and also act as important signalling molecules and messengers. Ketogenic diets are being used by millions of people around the world for a variety of different reasons. Some people are using them to help with blood sugar control and/or because they find them helpful for weight management. Others follow a ketogenic diet because of their cognitive and/or neurological effects. In the UK, around 13% of the population are estimated to be following a low carbohydrate diet.

Although ketogenic diets are helpful for some outcomes, one potentially negative consequence from consuming a ketogenic diet is an increase in circulating low-density lipoprotein (LDL) cholesterol concentrations (“bad cholesterol”). Over years and decades, an increase in LDL cholesterol may increase the risk of cardiovascular disease.

Our data indicate that the increase in LDL cholesterol might be due to changes in the composition and function of intestinal microorganisms (e.g., gut bacteria). In the SynKeto project, we will examine if taking a daily supplement (a synbiotic) helps to maintain normal healthy gut bacteria and microorganisms – and whether this prevents the typical increase in LDL cholesterol when people start to follow a ketogenic diet. A synbiotic is a combination of a probiotic and prebiotic fibre (see Appendix). If taking a synbiotic is effective, then it may allow people to get the potential benefits of a ketogenic diet without the potential downsides.

Who can participate?
We are looking for approximately 64 men and women who are aged 18-65 years old, free from any chronic health conditions and dietary restrictions.

What does the study involve?
This study is an intervention study, and the total period of involvement will be over approximately 14 weeks. This includes a 12-week period where participants will have to change their diet and take a daily supplement. During an initial screening visit, we will first check participants are eligible to take part in the study. If participants are eligible and would like to

take part, we will ask them to provide written informed consent before we set them up with some equipment to assess diet and physical activity levels, as well as continuous monitors to measure normal glucose and ketone levels. Approximately 1 to 2 weeks later, participants will complete their first main trial visit which will include various measurements including blood, fat and stool samples and body composition scans. After this visit participants will start the 12-week intervention period and will be asked to adhere to a ketogenic diet and daily supplement. Neither the participants nor the research team will be aware who will consume the placebo and who will consume the synbiotic over the 12-week period. After 6 weeks participants will complete an interim visit, involving blood and stool samples and further body composition scans and monitoring of physical activity and glucose and ketone levels. At the end of the 12-week intervention participants will complete a final main trial visit, identical to that completed before the start of the 12-week intervention period.

What are the possible benefits and risks of participating?
By participating in this study individuals will contribute to science and our understanding of how ketogenic diets affect cholesterol, and whether a synbiotic is useful in preventing an increase in LDL cholesterol. This could help millions of people who choose to use ketogenic diets and help clinicians who recommend a ketogenic diet for their patients.

Participants will also be reimbursed for travel expenses, parking permits and will be provided with a monetary allowance towards groceries for the 12-week intervention period. Participants will also be offered an inconvenience payment in the form of Love2Shop gift vouchers, worth £200, on study completion.

Finally, participants will be given a copy of some results within 2-4 weeks of completing the study:
• Diet
• Physical activity levels
• Blood pressure
• Body composition analysis (the amount of muscle and fat that you have, and bone density)
• Cognitive performance

Where is the study run from?
The study will be run from the Human Physiology Laboratories within the Centre for Nutrition, Exercise & Metabolism at the University of Bath (UK).

When is the study starting and how long is it expected to run for?
February 2026 to December 2028.

Who is funding the study?
The study is mainly funded by a government research council, the Biotechnology and Biological Sciences Research Council (BBSRC), with a small contribution from a commercial partner (IFF), as part of a BBSRC Industrial Partnership Award.

Who is the main contact?
The Principal Investigator and Primary Contact for this study is Dr Lucy Rogers (LR2013@bath.ac.uk)

Contact information

Type(s)

Public, Scientific, Principal investigator

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Integrated Research Application System (IRAS)
363636

Central Portfolio Management System (CPMS)
71432

Grant Code
UKRI547

Study information

Scientific Title
The effect of synbiotic supplementation on hypercholesterolaemia during a ketogenic diet: a randomised controlled trial

Study objectives
To establish if SYNBIOTIC supplementation (Polydextrose & Bifidobacterium animalis subsp. lactis B420) maintains gut microbial composition and prevents negative changes to LDL-C and lipoprotein profile during a ketogenic diet

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 16/12/2025, Wales REC 7 (21 Cowbridge Road East, Cardiff, CF10 3NQ, United Kingdom; -; Wales.REC7@wales.nhs.uk), ref: 25/WA/0351

Primary study design
Interventional

Allocation

Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Treatment

Study type(s)
Treatment

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

Interventions
Here is your text with formatting cleaned, clarified, and made consistent, while keeping all original meaning intact and using no special formatting:

DESIGN: The study will be a two-arm, 12week, parallelgroup, doubleblind randomised controlled trial (RCT) in men and women aged 18–65 years (N=64). One group will consume a daily synbiotic supplement (Polydextrose and Bifidobacterium animalis subsp. lactis B420), and the other group will consume a matched placebo. All participants will follow a lowcarbohydrate ketogenic diet. A subset of participants (50%) will be invited to complete a feedingtrial assessment before and after the supplementation period. These participants will remain in the laboratory for an additional 10 hours so that postprandial changes (responses to feeding) can be examined.

TIMELINE: Eligibility will be checked and confirmed during a screening visit (Visit 1, V1). Participants will then be provided with equipment to assess their diet and physical activity, as well as continuous monitors to measure normal glucose and ketone levels. Approximately two weeks later, participants will attend a main trial day (Visit 2), which will include various measurements such as blood samples and a DEXA scan. Participants will also be asked to provide a stool sample. After the first main trial day, participants will begin the 84day (12week) ketogenic diet and supplement period. After about 42 days (6 weeks), participants will attend an interim visit (Visit 3) where some measures will be repeated, including the DEXA scan and assessments of diet, glucose/ketones, and physical activity. Participants will continue on the ketogenic diet and daily supplement, and these measures will be repeated again during the final 14 days of the study. On day 84 (12 weeks), participants will attend a final main trial (Visit 4).

MEASURES: The study will examine the effect of synbiotic supplementation on LDLC concentrations and lipoprotein profile using NMR spectroscopy. Gut microbial composition will be characterised using metagenomic analysis. Validated biomarkers will be used to assess cholesterol and bile acid synthesis, and stable isotopes will be used to examine cholesterol absorption. To assess dynamic changes, including metabolic handling of the prebiotic (polydextrose), postprandial fermentation will be assessed via expired hydrogen and methane, along with circulating concentrations of shortchain fatty acids (SCFAs) and bile acids, including

the interconversion of 13Clabelled polydextrose into systemic SCFAs. Distal effects of synbiotic supplementation will be examined in adipose tissue biopsies taken under basal conditions and 6 hours after meal ingestion. In vitro approaches will also be used to investigate key pathways, including experiments using media conditioned with ex vivo serum from the human RCT (for example, fasted versus fed).

Intervention Type
Other

Primary outcome(s)
1. Primary Outcome Plasma LDL-Cholesterol measured using NMR spectroscopy at Baseline, Week 12

Key secondary outcome(s)
1. Secondary Outcomes Plasma Lipoprotein Profile measured using NMR spectroscopy at Baseline, Week 12

2. Gut Microbiome measured using Faecal metagenomics at Baseline, Week 12

3. Cholesterol Synthesis Biomarkers measured using Gas chromatography Mass Spectrometry at Baseline, Week 12

4. Bile Acid Synthesis Biomarkers measured using Gas chromatography Mass Spectrometry at Baseline, Week 12

5. Faecal Cholesterol Excretion measured using Gas chromatography Mass Spectrometry at Baseline, Week 12

6. Intestinal Cholesterol Absorption measured using Gas chromatography Mass Spectrometry at Baseline, Week 12

7. Faecal short-chain fatty acids and bile acids measured using Gas chromatography Mass Spectrometry at Baseline, Week 12

8. Serum short-chain fatty acids and bile acids measured using Gas chromatography Mass Spectrometry at Baseline, Week 12

Completion date
01/12/2028

Eligibility

Key inclusion criteria
1. Age 18-65 years
2. Body Mass Index (BMI) of 20.0-34.9 kg/m²
3. Able to provide informed consent
4. Willing and able to comply with all study procedures including, maintenance of habitual dietary intake, physical activity, and medication use during the study period.

Healthy volunteers allowed
Yes

Age group
Mixed

Lower age limit
18 Years

Upper age limit
65 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Any reported condition or behaviour deemed to either pose undue personal risk to the participant or that would introduce bias and affect study outcomes
2. Any diagnosed disease(s) or prior surgical procedure that would affect study outcomes (e.g., Type 1 or Type 2 Diabetes Mellitus, cholecystectomy)
3. Severe hypertension (systolic blood pressure ≥ 180 mmHg and/or diastolic blood pressure ≥ 120 mmHg)
4. Taking prescribed medications that will interfere with the study outcomes (e.g., lipidlowering medication)
5. Current use of nonprescribed supplements that could interfere with the study outcomes (e.g., laxatives)
6. Use of antibiotic medication in the last 3 months
7. Frequent use of prebiotic/fibre supplements or probiotic supplements in the last month (>15 times over the past month)
8. Already consuming a low carbohydrate ketogenic diet
9. Current or recent tobacco or recreational drug use (within prior 3 months)
10. Known negative reaction to lidocaine anaesthetic and/or taking warfarin
11. Not weight stable in the prior 3 months (>3% weight change)
12. Unable to understand the required instructions
13. Vegetarian or vegan
14. Women: Pregnant or planning to become pregnant
15. Women: Postmenopausal (absence of menses for >12 months)

Date of first enrolment
01/02/2026

Date of final enrolment
30/12/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
GP practices across BANES and Wiltshire
-
-
England
-

Sponsor information

Organisation
University of Bath

ROR
https://ror.org/002h8g185

Funder(s)

Funder type
Government

Funder Name
Biotechnology & Biological Sciences Research Council

Results and Publications

Individual participant data (IPD) sharing plan
Once the research is published, anonymised datasets will be made available via the University of Bath data repository.

IPD sharing plan summary
Stored in publicly available repository