Type 2 diabetes is an increasing problem worldwide and is particularly prevalent among the aging population. Over 2.5 million individuals in the UK are affected, costing the NHS around £10 billion per year (almost 10% of its budget). The risk of diabetes is thought to increase with age because of a progressive decline in the capacity of cells in the pancreas (beta-cells) to secrete insulin, the hormone that controls glucose levels. This in turn results to poor glucose control. The decline in beta-cell function can be accelerated by a poor diet and lifestyle, thus increasing the risk of developing type 2 diabetes. This is more evident in poorer communities where those on lower incomes tend to exhibit less nutritious dietary habits, placing them at greater risk of non-communicable diseases.

Most staple affordable foods have a poor nutritional profile and contain high proportions of rapidly digestible starch. Starch is the main carbohydrate component in the diet and in most plant-based foods. High intakes of readily digestible carbohydrates can lead to fluctuating and elevated fasting and post-prandial glycaemic responses, demonstrated to be a significant factor for noncommunicable diseases.

There is much evidence that diets rich in a type of carbohydrate called resistant starch have a positive impact on controlling of blood glucose levels and hence reduce susceptibility to type 2 diabetes. Resistant starches not completely digested in upper parts of the digestive tract and is fermented by bacteria in the colon. The products of fermentation, known as short-chain fatty acids, are thought to improve beta-cell function and thus insulin secretion. There are a variety of fruits and vegetables that contain various amounts of resistant starch, but UK diets are generally low in resistant starch. Thus, by promoting the widespread consumption of resistant starch, there is the potential to lower type 2 diabetes incidence in the long term. Moreover, another approach to tackle this risk is to reduce the glycaemic impact of commonly consumed foods. Diets rich in complex carbohydrate structures that are digested and absorbed slowly result in reduced glycaemic responses. Such carbohydrates are typically partially resistant to digestion by intestinal amylase. Reducing glycaemic responses and preventing substantial blood glucose fluctuations post-meal can positively impact metabolic health.

Our study will centre on peas, chickpeas, and pea flour, which have naturally occurred variants or mutants with diverse types of resistant starch. These products will be fed to human volunteers to determine the digestibility of the starch in vivo, together with a full spectrum of short- and medium-term physiological responses relevant to beta-cell function and control of blood glucose levels to be monitored. We will also study the best way to process/prepare the peas and chickpea products, as some resistant starch respond differently to these procedures and so they can be used in a wide range of foods. This project will provide new insights into the relationship between resistant starch and susceptibility to type 2 diabetes.

Pilot STUDY 1: Evaluating the impact of resistant starch from peas on gastric emptying

Study design

Randomised, controlled, double-blind, crossover study.

Target sample size

10 male and female volunteers. This was a pilot study in a new area, so a formal power calculation was not possible.

Inclusion criteria

BMI 20–35 kg/m²

Age 18–65 years (inclusive)

Exclusion criteria

Weight change ≥3 kg in the preceding 2 months

Current smokers

Substance abuse

Excess alcohol intake

Pregnancy

Diabetes
Cardiovascular disease
Cancer
Gastrointestinal disease (e.g. inflammatory bowel disease, irritable bowel syndrome)
Kidney disease
Liver disease
Pancreatitis
Use of medications likely to interfere with energy metabolism, appetite regulation or hormonal balance (anti-inflammatory drugs, steroids, antibiotics, androgens, phenytoin, erythromycin, thyroid hormones)

Interventions
After a screening visit, participants attend four study visits in random order at the NIHR Imperial Clinical Research Facility at Hammersmith Hospital, with a washout of at least 7 days between visits. At each visit, an intravenous cannula is inserted for blood sampling, and participants receive a standardised test breakfast together with 100 mg 13C-octanoic acid (a non-invasive stable isotope tracer used to measure gastric emptying). The test breakfast contains one of the following:

Wild-type whole peas (control)
Resistant starch whole peas
Resistant starch pea flour
Resistant starch pea food products (bread, soup, yoghurt, fruit juice, biscuit bar)

The dose of resistant starch is 10 g. The control product provides the same available (digestible) starch content as the intervention products. A standardised lunch is given approximately 180 min post-ingestion, and an ad libitum meal is provided at the end of the study visit.

Primary outcome measure
Gastric emptying rate, assessed by 13C-octanoic acid breath test. Breath samples are collected at baseline (−10 and 0 min) and every 15 min until the end of the study visit.

Secondary outcome measures
Postprandial appetite and satiety, assessed by visual analogue scale every 60 min throughout the study visit
Ad libitum food intake at the end of the study visit
Postprandial hormones, metabolites and inflammatory markers in blood samples taken at baseline (−10 and 0 min) and at 15, 30, 60, 90, 120, 180, 195, 210, 240, 300 and 360 min following the test breakfast
Breath hydrogen concentration measured at 60 min intervals throughout the study visit
Urinary metabolites from a 360 min urine collection following the test breakfast

Pilot STUDY 2: Evaluating the impact of resistant starch from peas on small intestinal digestion
Study design
Randomised, controlled, double-blind, crossover study.

Target sample size
10 male and female volunteers. This was a pilot study in a new area, so a formal power calculation was not possible.

Inclusion criteria
• BMI 20–35 kg/m²
• Age 18–65 years (inclusive)

Exclusion criteria
• Weight change ≥3 kg in the preceding 2 months
• Current smokers
• Substance abuse
• Excess alcohol intake
• Pregnancy
• Diabetes

• Cardiovascular disease
• Cancer
• Gastrointestinal disease (e.g. inflammatory bowel disease, irritable bowel syndrome)
• Kidney disease
• Liver disease
• Pancreatitis
• Use of medications likely to interfere with energy metabolism, appetite regulation or hormonal balance (anti-inflammatory drugs, steroids, antibiotics, androgens, phenytoin, erythromycin, thyroid hormones)

Interventions
After a screening visit, participants are admitted to the NIHR/Wellcome Trust Imperial Clinical Research Facility at Hammersmith Hospital for a single 4-day inpatient stay (3 nights). Enteral feeding tubes are placed by a gastroenterologist using CORPAK self-tracking tubes (no x-ray required) to allow sampling of gastric and small intestinal contents and remain in place for the duration of the 4-day visit. An intravenous cannula is inserted into one arm for blood sampling.

On each of the 4 study days, participants receive a test breakfast in random order, containing one of the following:
1. Wild-type whole peas (control)
2. Resistant starch whole peas
3. Resistant starch pea flour (two types)
4. Resistant starch pea food products (bread, soup, yoghurt, fruit juice, biscuit bar)

The dose of resistant starch is 10 g. The control product provides the same available (digestible) starch content as the intervention products.

Primary outcome measure
Assessment of early-phase digestion of the pea products, measured by microscopy and metabolomic profiling of gastric content samples. Gastric content samples are collected at baseline (–10 and 0 min) and every 15 min for 180 min following each test breakfast.

Secondary outcome measures
Postprandial hormones, metabolites and inflammatory markers in blood samples taken at baseline (–10 and 0 min) and at 15, 30, 60, 90, 120 and 180 min following each test breakfast

Pilot STUDY 3: Evaluating the impact of resistant starch from peas on starch delivery to the colon

Study design
Randomised, controlled, double-blind, crossover study.

Target sample size
10 male and female volunteers. This was a pilot study in a new area, so a formal power calculation was not possible.

Inclusion criteria
• BMI 20–35 kg/m²
• Age 18–65 years (inclusive)

Exclusion criteria
• Weight change ≥3 kg in the preceding 2 months
• Current smokers
• Substance abuse
• Excess alcohol intake
• Pregnancy
• Diabetes
• Cardiovascular disease
• Cancer

• Gastrointestinal disease (e.g. inflammatory bowel disease, irritable bowel syndrome)
• Kidney disease
• Liver disease
• Pancreatitis
• Use of medications likely to interfere with energy metabolism, appetite regulation or hormonal balance (anti-inflammatory drugs, steroids, antibiotics, androgens, phenytoin, erythromycin, thyroid hormones)

Interventions
After a screening visit, participants attend four study visits in random order, with a washout of at least 7 days between visits. At each visit they receive a test breakfast containing one of the following:
1. Resistant starch whole peas
2. Wild-type whole peas
3. Resistant starch pea flour
4. Wild-type pea flour

The dose of resistant starch is 10 g. The control products provide the same available (digestible) starch content as the intervention products. The pea products are grown in a 13C-enriched atmosphere, producing starch enriched ~1–2% above natural abundance, which allows digestion to be assessed by isotope ratio mass spectrometry. Small amounts of naturally occurring stable isotopes of glucose and acetate are also administered at 40 min and 180 min post-breakfast to quantify exogenous production.

Primary outcome measure
13C breath enrichment (measured by isotope ratio mass spectrometry), used to assess digestion and colonic delivery of resistant starch from peas. Breath 13C samples are collected at baseline (–10 and 0 min), then every 15 min for 360 min post-ingestion, then hourly at home until bedtime and again on waking the following morning.

Secondary outcome measures
• Plasma glucose and short-chain fatty acid (SCFA) appearance, quantified using stable isotope tracers
• Postprandial hormones, metabolites and inflammatory markers in blood samples taken at 0, 15, 30, 60, 90, 120, 180, 240, 300 and 360 min
• Breath hydrogen concentration measured at 60 min intervals during the study visit
• Urinary metabolites from a 24 h urine collection following the test breakfast
• Gut microbial composition from a stool sample collected the evening after each test breakfast

Pilot STUDY 6: Evaluating the impact of pea products, high in resistant starch content, on blood glucose.

Study design
Randomised, controlled, double-blind, crossover study.
Target sample size
20 male and female volunteers. This was a pilot study in a new area, so a formal power calculation was not possible.

Inclusion criteria
BMI 20–35 kg/m²
Age 18–65 years (inclusive)

Exclusion criteria
Weight change ≥3 kg in the preceding 2 months
Current smokers
Substance abuse
Excess alcohol intake
Pregnancy
Diabetes
Cardiovascular disease
Cancer

Gastrointestinal disease (e.g. inflammatory bowel disease, irritable bowel syndrome)
Kidney disease
Liver disease
Pancreatitis
Any known allergies
Use of medications likely to interfere with energy metabolism, appetite regulation or hormonal balance (anti-inflammatory drugs, steroids, antibiotics, androgens, phenytoin, erythromycin, thyroid hormones)

Interventions
After a screening visit, participants attend up to 11 study visits in random order at the NIHR/Wellcome Trust Imperial Clinical Research Facility at Hammersmith Hospital, with a washout of at least 3 days between visits. At each visit, an intravenous cannula is inserted for blood sampling, and participants receive a standardised test breakfast incorporating one of the following:
A. Negative control: 50 g or 25 g glucose drink
B. Positive control: normal pea food products (bread, pasta, crackers, muffins)
C. Intervention: high–resistant starch pea food products (bread, pasta, crackers, muffins)
The dose is based on 50 g dry weight resistant starch peas. The control products provide the same available (digestible) starch content as the intervention products.
Primary outcome measure
Postprandial plasma glucose response, measured from blood samples taken at −15, 0, 15, 30, 60, 90 and 120 min following the test breakfast.

Secondary outcome measures
Postprandial serum insulin response, measured at −15, 0, 15, 30, 60, 90 and 120 min following the test breakfast
Postprandial appetite and satiety, assessed by visual analogue scale every 30 min throughout the study visit
Breath hydrogen concentration, measured every 30 min throughout the study visit
Urinary metabolites from a 120 min urine collection following the test breakfast

STUDY 7: Evaluating the effects on glucose homeostasis using a portfolio of food staples made by high resistant starch flour.

Study design
Randomised, controlled, double-blind, 3-arm crossover trial with 28-day supplementation periods.
Target sample size
35 male and female volunteers. Power calculation based on Petropoulou et al., 2020 (Nature Food), Study 1 pea flour data, using G*Power: 27 participants required to detect the effect of interest; 35 recruited to account for an anticipated 30% dropout. Primary outcomes for the power calculation were plasma glucose and serum insulin; secondary outcomes included gut microbiota and incretin gut hormones.
Inclusion criteria

BMI 20–35 kg/m²
Age 18–70 years (inclusive)

Exclusion criteria

Weight change ≥3 kg in the preceding 2 months
Current smokers
Substance abuse
Excess alcohol intake
Pregnancy
Diabetes
Cardiovascular disease
Cancer
Gastrointestinal disease (e.g. inflammatory bowel disease, irritable bowel syndrome)
Kidney disease
Liver disease

Pancreatitis
Any known allergies
Use of medications likely to interfere with energy metabolism, appetite regulation or hormonal balance (anti-inflammatory drugs, steroids, antibiotics, androgens, phenytoin, erythromycin, thyroid hormones)

Interventions
After a screening visit, participants complete three 28-day supplementation periods in random order, with a washout of at least 14 days between periods. Participants consume the assigned food products at home daily for the 28 days. Each set of food products comprises bread, pasta, biscuits, soup, breakfast cereal, bars and snacks. The three arms are:

Positive control: products made with wild-type pea flour (30% pea flour, 70% durum wheat flour; 8 g dry pea material per product)
Intervention: products made with resistant starch pea flour (30% pea flour, 70% durum wheat flour; 8 g dry pea material per product)
Negative control: commonly consumed equivalent products without pea flour (e.g. standard pasta), matched for digestible starch content where possible

Before and after each 28-day supplementation period, participants attend the clinical research facility for an oral glucose tolerance test-style assessment day, including a standardised test breakfast made from the relevant intervention products.

Primary outcome measure
Postprandial plasma glucose and serum insulin response to a standardised test breakfast, measured before and after each 28-day supplementation period. Blood samples are taken at −30, −15, 0, 15, 30, 60, 90, 120, 180, 240 and 300 min relative to the test breakfast.

Secondary outcome measures
Gut microbiota composition, assessed from stool samples collected before each study visit
Incretin and gut hormone responses, measured from postprandial blood samples
Inflammatory markers, measured from postprandial blood samples
Continuous glucose profiles, measured by blinded Dexcom continuous glucose monitor (CGM) during the 28-day supplementation period and at the clinical research facility
Postprandial appetite and satiety, assessed by visual analogue scale every 60 min throughout the assessment day
Ad libitum food intake at the end of the assessment day (standardised pasta and tomato sauce meal)
Breath hydrogen concentration, measured at 0, 15, 60, 120, 180, 240 and 300 min during the assessment day
Urinary metabolites from a 360 min urine collection following the test breakfast
Habitual dietary intake, assessed via a 3-day food and drink diary completed before each assessment day