Title: Examining the feasibility of conducting a randomised control trial to evaluate the effectiveness of a focussed 15-minute one-to-one consultation to improve blood glucose control in pre-diabetes

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Key trial contacts

Chief Investigator	Mr Nick Gregory (BSc, MPhil) Carwyn James Building Aberystwyth University SY23 3FD nig5@aber.ac.uk 07825538040
Academic Supervisors	Dr Rhys Thatcher Carwyn James Building Aberystwyth University SY23 3FD ryt@aber.ac.uk 01970 628630 Dr Simon Payne Carwyn James Building Aberystwyth University SY23 3FD smp14@aber.ac.uk 01970 628629
Sponsor	Mr Mitchell Parker Aberystwyth University SY23 3FL ethics@aber.ac.uk 01970 621789
Key Protocol Contributors	Mr Sam Chapman Carwyn James Building Aberystwyth University SY23 3FD sac37@aber.ac.uk Dr Thomas Wilson Aberystwyth University SY23 3FL

	tpw2@aber.ac.uk Dr Heather Cox Church Surgery Portland Street Aberystwyth Heather.Cox@wales.nhs.uk

Protocol Contents

Abbreviations

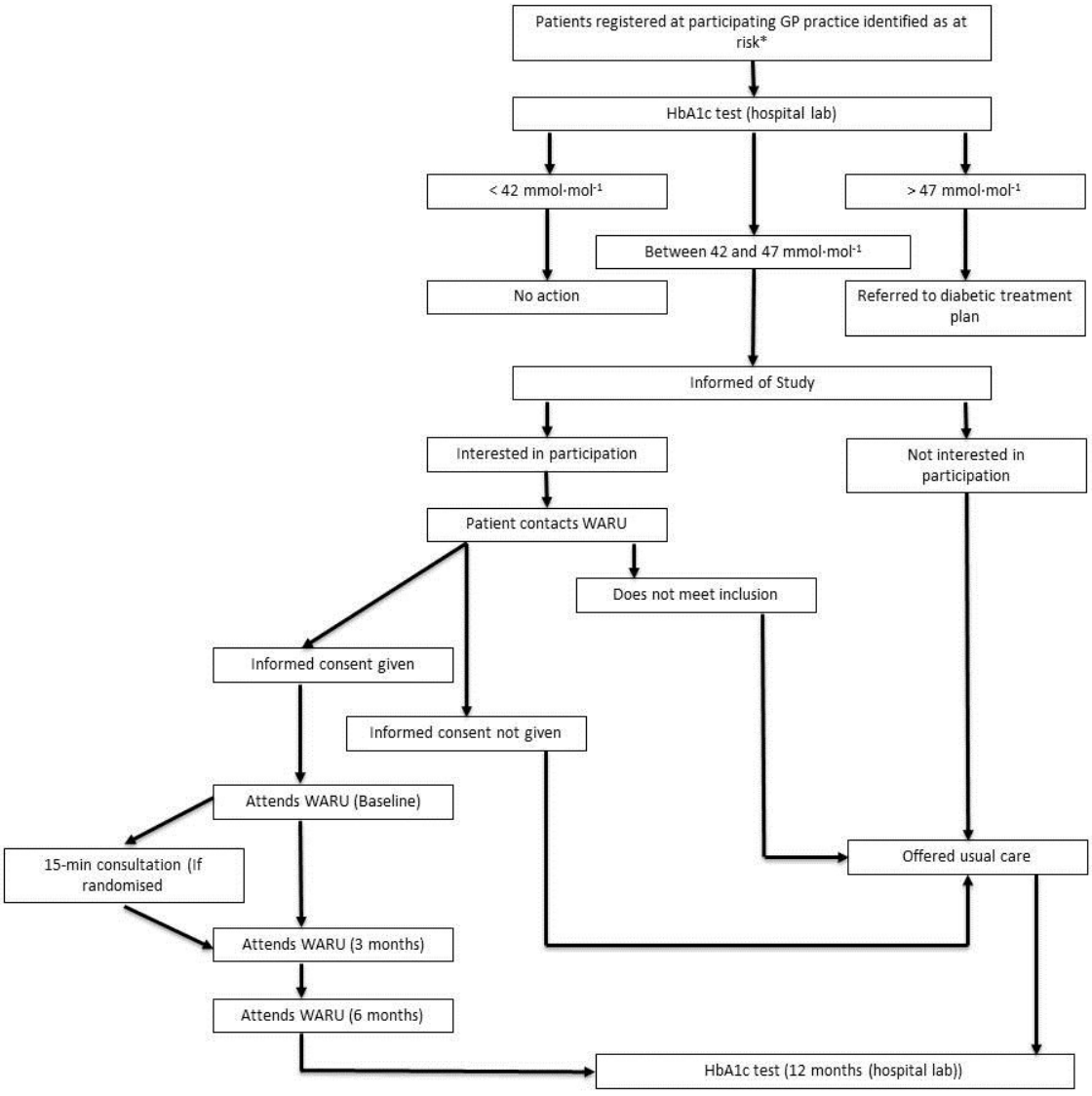
Glycated Haemoglobin	HbA1c
Body Mass Index	BMI
General Practitioner	GP
Wellbeing Assessment Research Unit	WARU
National Health Service	NHS
International Physical Activity Questionnaire	IPAQ
Intervention	INT
Control	CON
Institute of Biological, Environmental and Rural Sciences	IBERS
Flow Infusion Electrospray-High Resolution Mass Spectrometry	FIE-HRMS
Flow Infusion Electrospray- Mass Spectrometry	FIE-MS
Gas Chromatography-Mass Spectrometry	GC-MS
Statistical Package for the Social Sciences	SPSS
Analysis of Variance	ANOVA
Principal Component Analysis	PCA

Study Abstract

This research will assess the feasibility of conducting a randomised control trial to evaluate the effectiveness of a 15-minute one-to-one consultation to improve blood glucose control in pre-diabetes. The consultation will take the form of a 15-minute one-to-one consultation between a health-care practitioner and the patient in a primary care setting. Patients with a glycated haemoglobin (HbA1c) of between 42 and 47 $mmol \cdot mol^{-1}$ will be identified in general practise and will be eligible to participate. They will attend testing sessions at baseline (before the consultation), and at three months and six months post consultation. BMI, waist and hip girth, blood pressure and body composition will be recorded and blood analysed for HbA1c, cholesterol (total and HDL) and dietary components. For a three-week period following each visit, urine will be collected, a 5-ml sample on nine occasions, and physical activity will be recorded in a sub group of participants. Urine will be analysed by flow infusion electrospray mass spectrometry (FIE-MS) to determine the metabolic content, providing an indication of the diet over the three-week sampling period. The research objectives are to assess the effectiveness of recruitment strategy and willingness of patients to engage in, and adhere to, the research process; to determine the impact of consultation on health outcome measures, including HbA1c, and to establish participant and practitioner perspectives of the consultation.

1. Study Flow Chart

Figure 1: Study Schedule. * at risk is a clinical decision made by the GP based on a combination of: BMI <30, inactive lifestyle, family history.



2. Background and Rationale

Pre-diabetes is defined as a higher than normal blood glucose concentration and is associated with an increased risk of developing diabetes; of those identified as pre-diabetic 5 – 10% will develop diabetes within 12 months while a similar percentage will revert to normal blood glucose levels (Tabak et al., 2012). Furthermore, those with pre-diabetes are at an increased risk of developing a range of complications (e.g. Ford et al., 2010). It has been reported that the prevalence of pre-diabetes in England increased dramatically between 2003 and 2011, with the prevalence in those over the age of 16 years, increasing from 11.6% to 35.3% (Mainous et al., 2014). If unchecked the increase in the diabetic and pre-diabetic populations will pose an unsustainable burden on the health care service. It is widely accepted that diet and physical activity play an important role in reducing the risk of developing diabetes. The Diabetes Prevention Program Research Group has shown that diabetes may be preventable by lifestyle intervention targeting diet and exercise (Knowler et al., 2002). Despite this, three in every four adults in the UK are not consuming the recommended five portions of fruit and vegetables per day and one in every three are not reaching the minimum recommendations for physical activity (Statistics on Obesity, Physical Activity and Diet, 2017), figures which go some way to explain the increase in prevalence of pre-diabetes. In 2015 a North Ceredigion GP Cluster initiated a pre-diabetes intervention which targeted patient education and lifestyle modification (Thatcher & Gregory, 2017. Welsh Endocrine and Diabetes Society, Spring Meeting, Cardiff). The intervention comprised of a 30-minute one-to-one consultation with a practice nurse for those identified as having a glycated haemoglobin (HbA1c) of between 42 and 47 $mmol \cdot mol^{-1}$. The 30-minute consultation included the collection of baseline data on diet and exercise and stressed the importance of avoiding developing diabetes and what steps could be taken to avoid this. The design did not include a control group, as such, direct comparisons with usual care cannot be made, however, twelve months post the consultation there were statistically significant

reductions in BMI, waist circumference and HbA1c. Of the 130 participants who had an HbA1c of between 42 and 47 mmol·mol^{-1} at the start of the study 79 remained in the pre-diabetic range while 44 fell below 42 mmol·mol^{-1}, none progressed to >47 mmol·mol^{-1} and there were no follow up data for seven. The current proposal will develop the initial work done by the GP Cluster and inform the development of a randomised control trial. As the consultation will no longer involve collecting baseline data (see 'Plan of investigation') the time required has been reduced from 30 minutes to 15 minutes. Feedback from participants on the consultation will be used to inform the development of the consultation in relation to content and mode of delivery.

3. Assessment and Management of Risk

Blood Sampling:

A 6 mL blood sample will be collected during each visit to the Well-being Assessment Research Unit (WARU). All blood samples will be collected within a Category 2 laboratory. Blood sampling carries a small risk of bruising or infection however members of the research team responsible for collecting blood samples are trained in venepuncture and have an abundance of previous venepuncture experience from previous research projects. Therefore with good practice, the risk is minimal. Blood samples will be labelled anonymously and stored appropriately.

Randomisation:

Participants will be randomised into either the 'Intervention' or 'No intervention' group following the baseline visit to WARU. Whilst half of the cohort will not receive the intervention, usual GP care will not be withheld at any point

Participant Burden:

(A) Participation in the study will result in some additional burden to participant's daily lives although every effort has been made to keep this to a minimum. The research team will be as accommodating as possible when booking participants in for visits to the WARU.

(B) The collection of urine in the home (for the purposes of dietary analysis) has been tested rigorously in previous studies by Aberystwyth University. Previous work has shown the urine collection and storage process to be acceptable, easily conducted and understandable by a cohort of 16 free living individuals. Participants are asked to collect 3 urine samples per week for 3 weeks following each visit to the WARU. All samples are to be collected by participants the first time they urinate in the morning and therefore should not result in additional disruption to their day. The urine collection tubes will be coded anonymously with individual participant numbers and refrigerated by the participant in sealed containers until returned to the WARU by free post or in person depending on participant preference. In total, 27 urine samples will be collected across a period of 6 months.

(C) A randomly allocated sub-group of participants will be asked to wear a physical activity monitor (ActiGraph) for one week following each visit to the WARU. The monitors can simply be worn around the waist like a belt and will not interfere with daily life when worn. Participants will be asked to wear the monitor throughout the day from the time they get out of bed until they return to bed. They do not need to wear the monitor whilst washing. Participants will be asked to record the times they do not wear the monitor during the day using a simple recording sheet provided by the research team. The ActiGraph can be returned to the WARU by free post or in person depending on participant preference.

The research team will be available to assist participants via email, telephone or in person with queries relating to the dietary monitoring protocol and/or physical activity monitoring protocol.

Autonomy:

Participants will be made aware at the outset of the study that their participation is voluntary and are free to withdraw at any time without giving prior notice or reason for withdrawal. Non participation in the study or withdrawing on-going participation from the study will not compromise any current or future care participants receive from the UK National Health Service or future involvement in studies conducted by Aberystwyth University.

Confidentiality:

Participating GP surgeries will only be informed of their patient's participation in the study following receipt of informed consent. All data storage and handling will follow the principles of good clinical practice. All human tissue samples will be labelled anonymously and stored in accordance with the Human Tissue Act (2004).

4. Objectives and Outcome Measures

Primary Objectives:

The primary aim of the research is to assess the feasibility of conducting a randomised control trial to evaluate the effectiveness of a focused 15-minute one-to-one consultation in a primary care setting with a health-care professional to improve blood glucose control in pre-diabetes.

The study aims to quantify the following:

- the number of patients with an HbA1c between 42 and 47 $mmolmol^{-1}$ during the recruitment phase
- the percentage of patients eligible to participate who gave consent to be part of the study
- the percentage of patients who completed baseline testing; 3 month; and 6 month testing

Secondary Objectives

Secondary research questions aim to determine the impact of the consultation on the following measures at 3 and 6 months:

HbA1c

Cholesterol

BMI

Waist and hip girth

Blood pressure

Body composition

Physical activity level

Dietary habits

5. Study Design

This feasibility study will use a randomised control design to assess the effectiveness of a 15 minute one to one consultation compared to no treatment.

6. Study Setting:

All research activity included in the baseline, 3 month and 6 month visits will be completed within the Carwyn James Building, Aberystwyth University. The 15 minute pre-diabetes consultations will take place within Church Surgery, Aberystwyth.

7. Participant Eligibility

Participants will be eligible for participation if they are registered with Church Surgery and have an HbA1c (recorded within the last year) of between 42 and 47 $mmol^{-1}$.

8. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Age > 18, < 80	Under judicial control
Able to provide consent	Unable to understand and follow instructions due to cognition or language problems or provide consent
Registered with a mid-Wales GP surgery	
HbA1c between 42 mmol·mol-1 and 47 mmol·mol-1	

9. Participant Identification and Recruitment

Patients registered with a mid-Wales general practice who are considered at risk of developing diabetes will be identified on surgery's patient database systems based on a body mass index (BMI) > 25 kg/m^2 or an existing glycated haemoglobin (HbA1c; recorded within the last 12 months) of between 42 $mmol \cdot mol^{-1}$ and 47 $mmol \cdot mol^{-1}$. Database searches will be completed by trained surgery employees. Patients identified as being at risk of diabetes based on BMI (without a < 12 month HbA1c) will be invited by letter to their registered surgery to have their blood tested for HbA1c. Eligible patients, with HbA1c between 42 $mmol \cdot mol^{-1}$ and 47 $mmol \cdot mol^{-1}$, will be informed by their surgery via a second letter that they are at increased risk of diabetes and informed of the study. The letter will include key information relating to diabetes, steps that can

be taken to avoid developing diabetes, information on the purpose and procedures of the research study and contact information for the research team. Patients wishing to confirm their interest in participating or to receive further information can do so via telephone, email or visiting the university research facility in person.

10. Screening

Potential participants will initially be screened on patient records to identify those with a body mass index (BMI) > 25 kg/m^2 or an existing glycated haemoglobin (HbA1c; recorded within the last 12 months) of between 42 $mmol \cdot mol^{-1}$ and 47 $mmol \cdot mol^{-1}$. Screening will be completed by trained surgery employees. Patients identified as being at risk of diabetes based on BMI (without a < 12 month HbA1c) will be invited by letter to their registered surgery to have their blood tested for HbA1c. Patients contacted for screening who do not respond will not be contacted again. A record of contacts made is kept on the patient database.

11. Study Payment

Participants will not receive payment or expenses for participating in the study.

12. Consent

Further information regarding the study can be sought via telephone, email or visiting the university research facility in person. Any questions the participant may have can be asked at any point prior to giving consent using any of these methods. Patients are free to withhold consent without giving reason. In accordance with the Welsh Language Act 1993, all correspondence will be translated into Welsh. For patients confirming their involvement, verbal and written informed consent will be sought in person at the start of their first visit to the Well-being Assessment Research Unit (WARU) before being inducted into the study (> 24 hours between receipt of the

study invite letter & participant information sheet and signing informed consent). Those who decline involvement will receive usual care from their GP.

13. Study Procedures

Participants will be required to visit the WARU (Carywn James Building, Penglais Campus, Aberystwyth University, SY23 3FD) on 3 separate occasions, for baseline, 3 month and 6 month testing. During the baseline visit, the procedures and protocol of the study will be explained and informed consent will be received. Participant's height (Holtain Ltd, Crymych, UK) and body mass (wearing loose fitting clothing; Seca 899, Hamburg, Germany) will be collected to calculate body mass index (BMI) and waist and hip girth recorded (Seca 201, Seca Gmbh & Co, Hamburg, Germany). Next, participants will be asked to sit quietly for 10 minutes in the laboratory before blood pressure is recorded from the upper non-dominant arm (Omron M3, Omron Healthcare Ltd, Milton Keynes, UK). Participants will remain seated prior to a 6 mL blood sample being obtained from the antecubital vein and collected into a heparinised vacutainer (BD Vacutainer Systems, Plymouth, UK), with minimal stasis, using standard venepuncture methods performed by a trained member of the research team. Should patients HbA1c be outside the required values during the baseline visit, they will be informed and will take no further part in the research. WARU will inform the participant's GP if their HbA1c is indicative of diabetes. Body composition will be analysed using bioelectrical impedance (Bodystat 1500, Bodystat Ltd, Douglas, British Isles).

Upon completion of this phase of data collection, participants will be provided with a series of validated questionnaires to complete (to be completed at every visit unless otherwise stated). These include; the International Physical Activity Questionnaire- Short Form (IPAQ-SF), Food Frequency Questionnaire (FFQ; EPIC-Norfolk; baseline and 6 months), SF-36 (36-Item Short Form Survey Instrument) and components of the Personal Diabetes Questionnaire (baseline). Participants will complete the questionnaires unassisted although members of the research team will be available to answer any questions the participant may have relating to the questionnaires. Lastly, participants will receive instructions on the use of the urine collection kit for dietary monitoring (see below) and the ActiGraph for physical activity monitoring (if randomised; see below). Participants will then be free to leave the laboratory. An additional acceptability questionnaire designed by the research team will be given to participants at the end of the 6 month visit and will include questions relating to the WARU visits, 15 minute consultation (if received), urine collection and ActiGraph use. Visits will last between approximately 120 minutes and 150 minutes depending on the time taken for participants to complete the relevant questionnaires.

Following completion of the baseline visit, participants will be randomised into either the intervention group (INT) or the control group (CON). Randomisation will be achieved using a minimisation software package (Minim) and will ensure that there will be only minor differences between groups in the variables used in the allocation process. Participants in INT will receive a focussed 15 minute one to one consultation with a practice nurse at their registered general practice. The consultation derives from the original 30 minute protocol employed during a previous study conducted by the present research team (Thatcher and Gregory, 2017) which used 104 GP-registered patients. The first half of the 30 minute consultation in that study (led by general practise) collected baseline data (height, weight, waist circumference, blood pressure)

and the second half provided patients with lifestyle advice on preventing diabetes. The consultation to be used in the proposed study does not require general practise to collect baseline data and therefore the consultation time has been reduced from 30 minute to 15 minutes. The consultation will provide the participant with one to one information regarding the benefits of physical activity and healthy eating. Emphasis will placed on the importance of achieving at least 150 minutes of moderate physical activity each week as well as adhering to healthy dietary habits, based on the NHS Eatwell Guide (Eatwell Guide, 2016). Furthermore, participants will have the opportunity to discuss prediabetes with a trained practice nurse and ask any questions they may have. Participants placed in CON will not receive the consultation and will only attend visits to the WARU. Due to logistical and financial implications, a subgroup of participants will also be randomised for additional physical activity monitoring. 5 participants from INT and 5 from CON will receive an Actigraph (see below for further information on the Actigraph).

Dietary Monitoring:

Metabolic fingerprinting and metabolic profiling of human urine is able to provide a comprehensive and quantitative snapshot of dietary exposure for 12 – 24 hrs prior to urine collection. While a single sample snapshot is not representative of an individuals' habitual dietary exposure, a series of snapshots over a prolonged time period can give a robust overview of an individual's nutritional health. Previous work by IBERS has demonstrated a community based urine collection protocol (n = 16) as a successful and non-disruptive method for monitoring habitual diet. Participants will be provided with a urine collection kit consisting of; of 14 cm non-sterile urine collection straws 4 mL additive free evacuated vacutainer tubes and a125 mL collection container. Once urine has been collected, the sealed vacutainer tubes will be stored in an absorbent pouch within a sealed leak-proof bag and kept in the refrigerator. All urine storage equipment and instructions are fully compliant with the UN3373 standard for Category B

biological substances. Participants will receive instructions to fill the collection container with a mid-stream urine sample (in order to minimise the possibility of bacterial contamination from urethral contaminants; Gilbert, 2006). Any excess urine produced which is not collected in the container should be deposited within the lavatory. The tip of the transfer straw will be submerged into the urine and a 4mL vacutainer tube inserted into the transfer straw to draw the urine into the vacutainer. Any remaining urine in the container will be deposited within the lavatory. The collection container can be rinsed with tap water after each urine sample and reused for each sample collected. Vacutainer tubes will be labelled with anonymous information including participant number, sample number, weekday/weekend sample and week number. Samples will be stored in a refrigerator at 4ºC for a maximum of 10 days before the sample are returned to the lab either in person or by free post for freezing at -80ºC to await analysis. Participants will record the collection details of their urine samples onto a sample collection sheet (see appendices) which notes the sample number and the date and time of collection. Participants will collect 3 samples a week for 3 weeks following each WARU visit. Participants must collect two urine samples within the week on non-consecutive days (e.g. Tuesday & Thursday) and collect a third sample on either day of the weekend (Saturday/Sunday). In total, participants will collect 27 urine samples during their participation in the study. Urine samples will be analysed using laboratory based Flow Infusion High Resolution Mass Spectrometry (FIE-HRMS) which is an established method for dietary analysis using urine samples.

Physical Activity Monitoring:

Physical activity and sedentary lifestyle will be determined using ActiGraph (ActiGraph LLC, Pensacola, FL, USA) following baseline, 3 months and 6 month WARU visits. Participants will be provided with written and verbal instructions on how to operate the device. Participants will choose one week within the three week urine collection period to wear the ActiGraph.

Participants can choose any day within the week to begin wearing the ActiGraph but must then wear it for the following 7 days unless unfeasible to do so (e.g. swimming, bathing or showering). In this instance, participants will record at what time and the amount of time they are not wearing the ActiGraph. Should participants forget to wear the device; the same procedure will be followed. Should participants miss a whole day; they must record for an extra day directly after the 7th day. An additional sheet will be provided for participants to record any time when the device is not worn. Participants do not need to wear the ActiGraph when sleeping although they must record the time they go to sleep and at what time they wake up. Participants must fit the ActiGraph in the morning as soon as it is feasible to do so. Participants can return the ActiGraph at the end of the 7 day recording period either in person or be post.

14. Randomisation Procedure

Randomisation will be achieved using a minimisation software package (Minim) and will ensure that there will be only minor differences between groups in the variables used in the allocation process. Participant details will be recorded after the first visit and inputted into the randomisation package. Following randomisation of the first participant, remaining participants will be randomly allocated into either the intervention or control based upon age (ages 60 + in both groups / equal distribution of sex and BMI 30 kg/m^2 + in both groups). Randomisation will be conducted primarily by the academic supervisor. Church surgery will be informed of the patients who have been randomised to receive the intervention and referral arrangements made.

15. Baseline Data

The data to be collected at baseline and in subsequent visits are directly related to pre-diabetes or to factors which contribute to diabetes risk (e.g. dietary habits and physical activity).

-Blood test: (non-fasted) measure of glycated haemoglobin, cholesterol and metabolites indicative of dietary intake

-Anthropometry: Measures body weight and size. Being overweight is a risk factor associated with diabetes

-Blood pressure: cardiovascular health is detrimentally affected by poor lifestyle and diabetes risk

-Body composition Provides an analysis of fat mass and percentage body fat

-Urine collection: Allows for the accurate analysis of dietary behaviours

-ActiGraph: Allows for the accurate recording of physical activity

-Physical Activity Questionnaire: Provides a measure of physical activity levels

-Food frequency questionnaire: Provides a measure of dietary habits

-Health survey: Provides a indication of current perceived health status

-Components of the Personal Diabetes Questionnaire: Provides a indication of an individual's readiness to change their lifestyle behaviours following information regarding their diabetes risk

16. Clinical Study Assessments (Frequency and Duration)

Procedure	Frequency	Duration	Researcher
Venous Blood sample for measure of HbA1c (if surgery does not have a value < 12 months)	1	10 minutes	Performed by a practice nurse or GP at a mid-Wales General Practise
Recording height and weight	3	5 minutes	Nicholas Gregory or other member of the research team. This will take place in the Carwyn James Building at Aberystwyth University
Recording waist and hip girth	3	5 minutes	Nicholas Gregory or other member of the research team. This will take place in the Carwyn James Building at Aberystwyth University
Recording blood pressure	3	15 minutes	Nicholas Gregory or other member of the research team. This will take place in the Carwyn James Building at Aberystwyth University
Venous blood sample	3	10 minutes	Nicholas Gregory or other member of the research team. This will take place in the Carwyn James Building at Aberystwyth University
Body composition analysis	3	10 minutes	Nicholas Gregory or other member of the research team. This will take place in the Carwyn James Building at Aberystwyth University
Provision of urine sample for dietary analysis	27	5 minutes	Performed by the participant 3 x per week for 3 weeks after each WARU visit. Samples collected at home.
Actigraph (if randomised to receive)	3	7 days	Performed by the participant. Actigraph worn by the subject around the waist during waking hours. Worn for one week (within each 3 week urine sampling phase) after each

			WARU visit

17. Qualitative Assessments (Frequency and Duration)

Procedure	Frequency	Duration	Researcher
Providing information prior to gaining informed consent	1	30 minutes	Nicholas Gregory or other member of the research team. This will take place in the Carwyn James Building at Aberystwyth University
Administration of the International Physical Activity Questionnaire Short Form	3	10 minutes	Nicholas Gregory or other member of the research team. This will take place in the Carwyn James Building at Aberystwyth University
Administration of the Food Frequency Questionnaire	2	15 minutes	Nicholas Gregory or other member of the research team. This will take place in the Carwyn James Building at Aberystwyth University
36-Item Short Form Health Survey Instrument	3	10 minutes	Nicholas Gregory or other member of the research team. This will take place in the Carwyn James Building at Aberystwyth University
Components of the Personal Diabetes Questionnaire	1	10 minutes	Nicholas Gregory or other member of the research team. This will take place in the Carwyn James Building at Aberystwyth University
15 minutes pre-diabetes consultation (if randomised to receive)	1	15 minutes	Performed by a practice nurse at a mid-Wales General Practise
End of Study Feedback questionnaire	1	10 minutes	Nicholas Gregory or other member of the research team. This will take place in the Carwyn James Building at Aberystwyth University

18. Withdrawal Criteria

Participants are free to withdraw from the study at any time without giving prior warning or reason for withdrawal. Participants will not be replaced if withdrawn. Recruitment will continue for the first 6 months of the study. New participants will receive unique individual participant numbers.

19. Storage and Analysis of Clinical Samples

Blood Treatment:

A 1 mL aliquot of whole blood will be transferred from the heparinised vacutainer into a 1.5 mL Eppendorf. The remaining whole blood will be centrifuged at 1500 g for 10 minutes at 4˚C. The separated plasma will be pipetted evenly into two separate eppendorfs and frozen at -80˚C for subsequent analysis of metabolic content using FIE-MS and GC-MS. Two 1.5 µL aliquots of whole blood will be transferred from the 1.mL aliquot into separate test cartridges and will be analysed for HbA1c and lipid profile by an automated point of care blood analyser (Afinion 2, Abbot, Cheshire, UK).

Urine Treatment:

Urine samples will be centrifuged at 1500 g for 10 minutes at 4˚C. 1ml of supernatant will be pipetted evenly into two separate eppendorfs and frozen at -80˚C prior to analysis of metabolic content using FIE-MS and GC-MS.

20. End of Trial

The testing stage of this study will be defined as finished when the last participant completes the final visit (6 month testing). Additionally, the research will be stopped if there is a lack of

recruitment after 6 months or if a clinical or research incident prompts a review.

21. Statistics and Data Analysis

A computerized statistical package will be used to analyse all data associated with the primary and secondary outcomes (SPSS version 17.0, SPSS inc., Chicago, IL). Normally distributed data will be presented as mean ± SD. Scores from the questionnaires will be calculated based upon their respective scoring protocols. A two factor mixed model ANOVA will be conducted on all physiological measures and questionnaire responses to determine any differences between groups over time. Significant differences identified by the ANOVA will be further analysed by post hoc independent or paired t-tests with Bonferroni correction. Data mining of urine samples using methods such as PCA will be employed to determine if foods can be discriminated. Statistical significance will be accepted at $P < 0.05$.

22. Sample Size Calculation

The sample size was decided based upon potential numbers of eligible patients provided to the research team by the participating general practice. Potential numbers are based upon the amount of registered patients with a BMI > 25 kg/m2 or an existing HbA1c < 12 months. As this is a feasibility study for a future large scale randomised control trial, no formal sample size calculation has been employed.

23. Planned Recruitment Rate

Previous work completed by the research team demonstrated an approximate 50% uptake in consultation offers in patients with pre-diabetes (n = 420). Our partnering surgery currently have 737 patients with a BMI >25 kg/m^2. A further 216 patients have an HbA1c (recorded within the last year) within the eligible range. Furthermore, Church surgery identifies approximately 6 new

'at risk' individuals each week. Therefore, we estimate it will take one month to recruit 40 patients into the study.

24. Data Management

All electronic data will be stored on a password protected computer housed within the office of the chief researcher. Manual files will be kept locked within a filing cabinet within the office of the chief investigator. The office will remain locked when the chief investigator is not present. The chief investigator and their supervisor will be the only individuals who have direct access to the office where the data is stored. Data will be published in an anonymous form. All data handled during the study will be identified by a numeric code assigned to each participant upon entry to the study. Aberystwyth University operates its own confidentiality policy which all staff and postgraduate students are trained in. The chief investigator educational supervisor and MRes student will have access to participants' name, contact details, and some additional personal information (e.g. age, identifying gender). The chief investigator will be responsible for communication between the participant and the research team. Participants will consent to the storage of their personal data when signing the informed consent form.

Data will be retained for 7 years following completion of the study. Anonymised data will be stored on a password protected computer accessible only to chief investigator and educational supervisor. After 7 years, the data will be deleted off of the computer hard drive. Paper based materials will be kept within locked filing cabinets within the Carwyn James Building and then destroyed via confidential waste processes according to Aberystwyth University's Data Protection policy.

25. Monitoring, Audit and Inspection

The research will be monitored within the Institute of Biological, Environmental and Rural Sciences (IBERS). Regular meetings between the chief investigator (Nicholas Gregory), educational supervisors (Dr Rhys Thatcher and Dr Simon Payne), MRes student (Sam Chapman) and collaborators (Dr Heather Cox and Dr Thomas Wilson) will ensure academic progress and rigour. Additional post-graduate monitoring is conducted regularly within Aberystwyth University by academic individuals outside of the research team. Health and Safety is overseen in IBERS by Health and Safety officers. Furthermore, regular meetings between the chief investigator, educational supervisors, MRes student and collaborators will take place every 3 months and additionally when necessary to discuss any issues that may arise and to monitor progress.

26. Ethical and Regulatory Considerations

The study will be subject to ethical review by Aberystwyth University Research Ethics System and by an NHS Research Ethics committee. The study will not commence until approvals have been granted. Data generated by the study will be stored and protected in accordance with the Data Protection Act 1998 and the study conducted in accordance with the Declaration of Helsinki 2013.

27. Dissemination Policy

Participants will be informed of the results in the form of a summary report at the end of the study, upon request, written in a lay person format. Participants will be informed if the research progresses to publication. The research team will aim to publish the findings of the research in scientific journals and present at relevant conferences. An overview of the results will also be published on university and departmental websites.