# TRIAL PROTOCOL

# Snacktivity™ work package 4 (WP4)

A multi-centre, open-label, two-arm, parallel group, individually randomised trial, with an internal pilot and economic evaluation, to test the superiority of Snacktivity™ compared with usual care (current guidelines on physical activity).

**This protocol has regard for the HRA guidance and is compliant with the SPIRIT guidelines (2013)**

***Version Number:*** ***5.0***

**Version Date:** **22 May 2025**

# PROTOCOL DEVELOPMENT

## Protocol amendments

The following amendments and/or administrative changes have been made to this protocol since the implementation of the first approved version.

| Amendment number | Date of amendment | Protocol version number | Type of amendment | Summary of amendment |
|---|---|---|---|---|
| *AM12-NSA12* | *27.02.25* | *3.0* | *Non-Substantial* | *The study team can now offer a £10 e-voucher to those participants who have not returned their accelerometer.* |
| *AM14-NSA14* | *03.04.2025* | *4.0* | *Non-Substantial* | *Participants will be given a £30 voucher if they complete the 3 month follow up and a £30 voucher if they complete the 12 month follow up.* |
| *AM15-NSA15* | *23.05.2025* | *5.0* | *Non-Substantial* | *ISRCTN number updated and text added to allow NHS Research Scotland (NRS) Primary Care Network to screen and invite patients to the study.* |

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| The Funder of the trial has had no role in the trial design, data collection, data analysis or data interpretation. | FUNDED BY NIHR \| National Institute for Health Research |

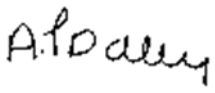
## PROTOCOL SIGN OFF

### Chief Investigator (CI) signature page

I, the Chief Investigator, confirm that I have read and agree with the following protocol, and that I will conduct the trial in compliance with the version of this protocol approved by the REC and any other responsible organisations.

I agree to ensure that the information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the trial publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the trial will be given; and that any discrepancies from the trial as stated in this and any subsequent approved protocol will be explained.

| | |
|---|---|
| Trial name: | Snacktivity work package 4 (WP4) |
| Protocol version number: | Version: 5.0 |
| Protocol version date: | 22/05/2025 |
| | |
| CI name: | Professor Amanda Daley |
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### Sponsor statement

By signing the IRAS form for this trial, Birmingham Community Healthcare NHS Trust, acting as sponsor, confirm approval of this protocol.

### Compliance statement

This protocol describes the Snacktivity™ WP4 trial only. The protocol should not be used as a guide for the treatment of people not taking part in the Snacktivity™ WP4 trial.

The trial will be conducted in compliance with the approved protocol, the UK Policy Framework for Health and Social Care Research, Data Protection Act 2018 and the Principles of Good Clinical Practice (GCP) as set out in the UK Statutory Instrument (2004/1031) and subsequent amendments thereof. Every care has been taken in the drafting of this protocol, but future amendments may be necessary, which will receive the required approvals prior to implementation.

## Principal Investigator (PI) signature page

As Principal Investigator, I confirm that the following protocol has been agreed and accepted, and that I will conduct the trial in compliance with the approved protocol where this does not compromise participant safety.

I agree to ensure that the information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor.

| | |
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| Trial name:<br><br>Protocol version number: | Snacktivity work package 4 (WP4)<br><br>Version: 5.0 |
| Protocol version date: | 22/05/2025 |
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| ISRCTN reference number | 12390945 |
| IRAS reference number | 336675 |

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## ABBREVIATIONS

| Abbreviation | Term |
|---|---|
| **AE** | Adverse Event |
| **API** | Application Programming Interface |
| **BCTU** | Birmingham Clinical Trials Unit |
| **BCHC** | Birmingham Community Healthcare NHS Foundation Trust |
| **BLE** | Bluetooth Low Energy |
| **BMI** | Body Mass Index |
| **CI** | Chief Investigator |
| **CEA** | Cost-Effectiveness Analysis |
| **CSO** | Chief Scientist Office |
| **COVID** | Corona Virus Disease |
| **CRF** | Case Report Form |
| **CRM** | Customer Relationship Management |
| **CRN** | Clinical Research Network |
| **CV** | Curriculum Vitae |
| **CVD** | Cardiovascular Disease |
| **DMC** | Data Monitoring Committee |
| **DMP** | Data Management Plan |
| **DOB** | Date of Birth |
| **DSA** | Data sharing agreement |
| **eConsent** | Electronic Consent |
| **eCRF** | Electronic Case Report Form |
| **GCP** | Good Clinical Practice |
| **GDPR** | General Data Protection Regulation |
| **GP** | General Practitioner |
| **HADS** | Hospital Anxiety and Depression Scale |
| **HCP** | Health Care Professional/Provider |
| **HRA** | Health Research Authority |

| | |
|---|---|
| **HRQOL** | Health-related quality of life |
| **ICECAP-A** | ICEPop CAPability measure for Adults |
| **IP** | Internet protocol |
| **IPAQ** | International Physical Activity Questionnaires |
| **IRAS** | Integrated Research Application System |
| **ISF** | Investigator Site File |
| **LU** | Loughborough University |
| **MET** | Metabolic Equivalents |
| **mHealth** | Mobile health |
| **MHRA** | Medicines and Healthcare products Regulatory Agency |
| **MVPA** | Moderate-Vigorous Physical Activity |
| **NCD** | Non-Communicable Diseases |
| **NHS** | National Health Service |
| **NIHR** | National Institute for Health and Care Research |
| **NRS** | NHS Research Scotland |
| **PA** | Physical Activity |
| **PACES** | Physical Activity Enjoyment Scale |
| **PAG** | Public Advisory Group |
| **PAVS** | Physical Activity Vital Sign |
| **PI** | Principal Investigator |
| **PIS** | Participant Information Sheet |
| **PPI** | Patient and Public Involvement |
| **QALY** | Quality-adjusted life year |
| **RA** | Research Associate |
| **REC** | Research Ethics Committee |
| **RCT** | Randomised Controlled Trial |
| **SAE** | Serious Adverse Event |
| **SAP** | Statistical Analysis Plan |
| **SMS** | Short Messaging Service |

| | |
|---|---|
| **SOP** | Standard Operating Procedure |
| **TMF** | Trial Master File |
| **TMG** | Trial Management Group |
| **TSC** | Trial Steering Committee |
| **UK** | United Kingdom |
| **UoB** | University of Birmingham |
| **UoL** | University of Leicester |
| **WSQ** | Workforce Sitting Questionnaire |

## TRIAL SUMMARY

**Title**

A multi-centre, open-label, two-arm, parallel group, individually randomised trial, with an internal pilot and economic evaluation, to test the superiority of Snacktivity™ compared with usual care (current guidelines on physical activity).

**Objectives**

To assess the effectiveness and cost-effectiveness of the Snacktivity™ intervention compared to usual care (current guidance on physical activity) in adults who do less than the recommended amount of MVPA (moderate-vigorous physical activity) per week.

**Trial design**

A multi-centre, randomised, open-label, two-arm, individually randomised, parallel group, superiority trial with an internal pilot and economic evaluation.

**Participant population and sample size**

724 adults who are aged 18 years and over who do not complete 150 minutes or more of MVPA per week as per the national guidelines.

**Setting**

Recruitment will take place from NHS Trusts/settings and non-NHS settings. NHS settings are defined as any service that is delivered to members of the public by a health care professional/ provider (HCP) employed/funded by the NHS, and includes community health services, primary care and general practices, secondary care and mental health organisations. Non-NHS settings will include recruiting via social media platforms (including via NIHR Be Part of Research), third sector organisations, public health organisations, community support groups and workplaces.

**Eligibility criteria**

Inclusion criteria:

- Aged ≥18 years
- Completes <150 minutes per week of MVPA as assessed by the Physical Activity Vital Sign (PAVS) Questionnaire
- Owns a mobile phone capable of hosting apps (e.g. Apple iOS 13.0+ and Android 4.3+)
- Able to provide informed consent
- Agreement for their HCP to be notified of their involvement in the trial

Exclusion criteria:

- Unable to understand English sufficiently to complete the trial assessments
- Women known to be pregnant or breastfeeding
- Inpatient, bedbound or unable to complete physical activity

**Interventions**

Snacktivity™ intervention versus usual care (the current guidance for physical activity).

**Outcome Measures at three and twelve months after randomisation unless otherwise stated**

**Primary outcome**

The primary outcome is average weekly MVPA at 12 months measured using the Axivity (AX3) device

**Secondary outcomes**

We will assess the following using the Axivity (AX3) device:

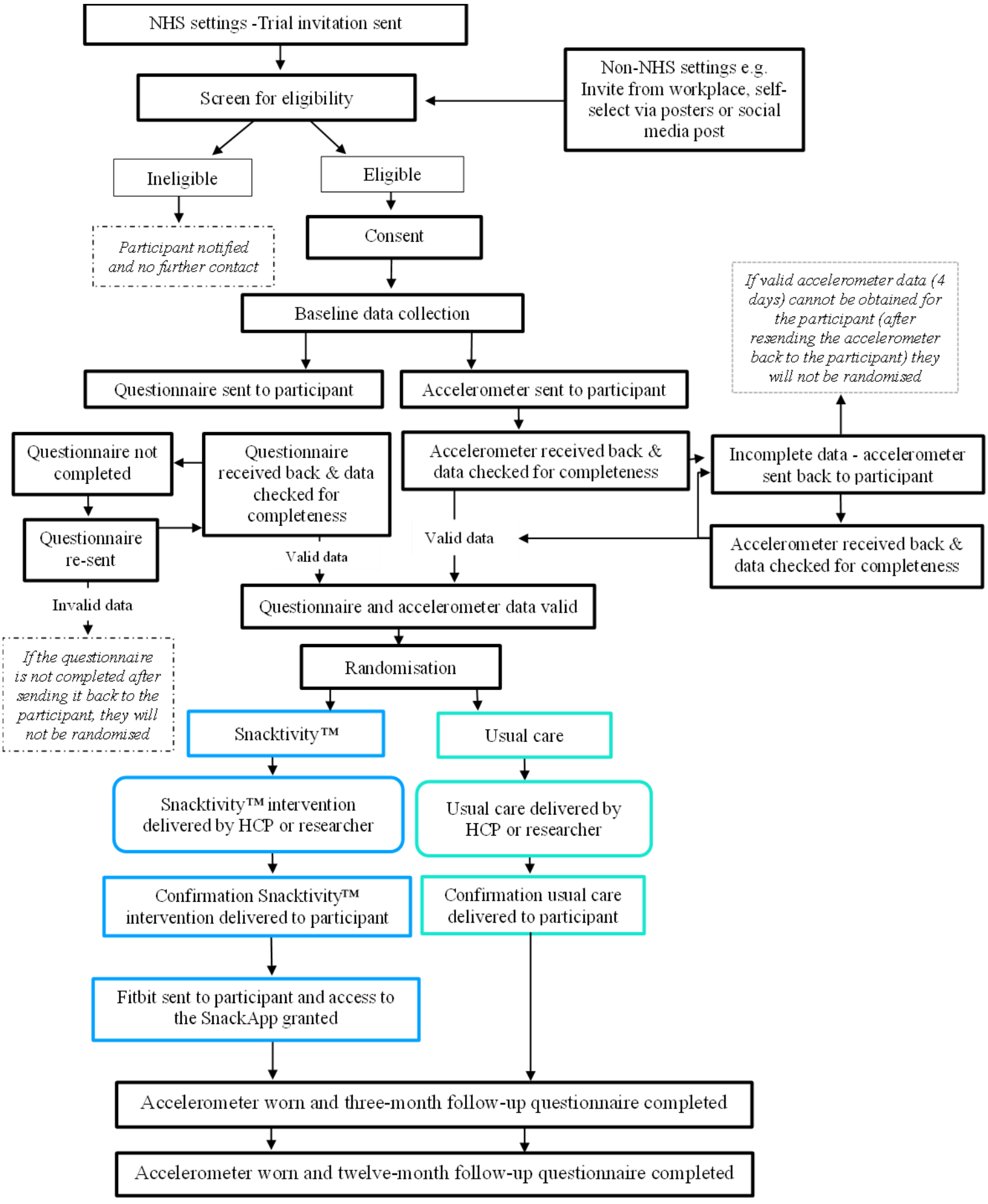
- proportion of participants meeting the guidance amount of 150 minutes of MVPA per week
- average total minutes (sum of light, moderate and vigorous) of physical activity per day
- average number of minutes of light, moderate and vigorous physical activity per day
- average minutes of MVPA accumulated in bouts lasting ≥2, ≥5 and ≥10-minutes per day
- average number of MVPA bouts lasting ≥2, ≥5 and ≥10-minutes per day
- average magnitude of dynamic wrist acceleration per day (as a proxy for total volume of activity)
- average intensity gradient per day (no unit for this variable)
- average minutes of sedentary time per day
- average time (minutes) spent in prolonged sedentary behaviour per day
- average number of prolonged sedentary bouts per day
- average sleep duration (mins/day) and average efficiency (quality) (%/day)

We will also assess:

- weight (objective (or self-reported if participant is unable to provide objective weight))
- depression/anxiety (using the Hospital Anxiety and Depression Scale (HADS))
- quality of life (using the EQ-5D-5L questionnaire)
- self-reported sedentary behaviours (using the Workforce Sitting Questionnaire (WSQ) and International Physical Activity Questionnaire (IPAQ) (sitting question only))
- self-efficacy for physical activity (using the Self-Efficacy for Exercise Questionnaire)
- enjoyment of physical activity (using the Physical Activity Enjoyment Scale (PACES))
- habitual physical activity (using the Self-Report Habit Index (intervention group only))
- participation in Snacktivity™ using Fitbit™ data (to assess intervention adherence) (intervention group only)
- serious adverse events related to participation in physical activity
- cost-effectiveness (using the ICEpop CAPability measure for Adults (ICECAP-A) and a health care resource use questionnaire)

Participant's experiences of the trial will be captured using single item exit questions at three and twelve months follow-up.

## TRIAL SCHEMA



## TABLE OF CONTENTS


**1. BACKGROUND AND RATIONALE ..... 20**
1.1 Background ..... 20
1.2. Trial rationale ..... 20
1.2.1. Justification for participant population ..... 20
1.2.2. Justification for design ..... 20
1.2.3. Justification for choice of intervention(s) ..... 21
1.2.4. Technology in healthcare ..... 21
1.2.5. Justification of choice of primary outcome ..... 22
**2. AIMS AND OBJECTIVES ..... 22**
2.1. Internal pilot objectives ..... 22
2.2. Main trial objectives ..... 22
2.2.1. Clinical aims and objectives ..... 22
2.2.2. Economic aims and objectives ..... 22
**3. TRIAL DESIGN AND SETTING ..... 23**
3.1. Trial design ..... 23
3.2. Trial setting ..... 23
3.3. Assessment of risk ..... 23
**4. ELIGIBILITY ..... 23**
4.1. Inclusion criteria ..... 23
4.2. Exclusion criteria ..... 23
4.3. Co-enrolment ..... 23
**5. CONSENT ..... 24**
5.1 Consent procedure ..... 24
5.2 Ongoing consent ..... 25
**6. ENROLMENT, RANDOMISATION and BLINDING ..... 25**
6.1. Identification ..... 25
6.1.1. NHS Trusts/settings ..... 25
6.1.2. non-NHS settings ..... 26
6.2. Screening and enrolment ..... 26
6.2.1. Potential participants identified and invited to participate using the electronic trial link ..... 26
6.2.2. Potential participants identified and invited to participate using paper invitation packs ..... 27
6.3. Randomisation ..... 27
6.4. Randomisation process ..... 27
6.5. Randomisation method ..... 28
6.6. Blinding ..... 28
6.7. Informing the participant's GP and other parties ..... 28
**7. TRIAL INTERVENTION ..... 28**
7.1. Trial intervention ..... 28
7.2. Snacktivity™ intervention ..... 28

7.2.1. Outline and overview ..... 28
7.2.2. Snacktivity™ Consultation ..... 29
7.2.3. SnackApp and physical activity tracker ..... 29
7.2.4. Commercial development of the SnackApp and MHRA ..... 30
7.2.5. Training of HCPs/Researchers to deliver the Snacktivity™ intervention ..... 30
7.2.6. HCP Snacktivity™ consultations (intervention group) ..... 31
7.2.7. Researcher Snacktivity™ appointments (intervention group) ..... 32
7.2.8. Intervention fidelity ..... 32
7.2.9. Delivery of the Fitbit™ and access to the SnackApp (Intervention group only) ..... 32
7.2.10. Additional support for participants using the Fitbit™ and SnackApp ..... 32
7.3. Usual care ..... 33
7.3.1. HCPs discussing the current guidance for physical activity (usual care group) ..... 33
7.3.2. Researchers discussing the current guidance for physical activity (usual care group) ..... 33
7.4. Continuation of intervention after the trial ..... 33
7.5. Intervention supplies ..... 34
**8. OUTCOME MEASURES ..... 34**
8.1. Pilot trial outcomes ..... 34
8.2. Main trial outcomes ..... 35
8.2.1. Primary outcome(s) ..... 35
8.2.2. Secondary outcomes ..... 35
8.2.3. Cost-effectiveness outcomes ..... 35
8.2.4. Snacktivity™ intervention outcomes ..... 35
**9. TRIAL PROCEDURES ..... 36**
9.1. Baseline Data Collection ..... 36
9.1.1. Questionnaires ..... 36
9.1.2 Accelerometer ..... 36
9.2 Participants not progressing to randomisation ..... 36
9.3 Intervention ..... 37
9.4 Usual care ..... 37
9.5 Three month follow-up ..... 37
9.4.1. Questionnaires ..... 37
9.4.2. Accelerometer ..... 37
9.6 Twelve month follow-up ..... 38
9.5.1. Questionnaires ..... 38
9.5.2. Accelerometer ..... 38
9.7 Schedule of Assessments ..... 38
9.8 Withdrawal and changes in levels of participation ..... 39
**10. ADVERSE EVENT REPORTING ..... 40**
10.1. Definitions ..... 40
10.2. Adverse event reporting in Snacktivity ..... 41
10.3. Serious Adverse Advents reporting in Snacktivity™ ..... 41
10.3.1. Serious Adverse Events not requiring reporting to the trial office ..... 41

10.3.2. Serious Adverse Events requiring non-expedited reporting to the trial office ..... 42
10.3.3. Serious Adverse Events requiring expedited reporting to the trial office ..... 42
10.4. SAE Reporting process ..... 42
10.4.1. Assessment of causality of an SAE ..... 43
10.4.2. Assessment of expectedness of an SAE by the clinical member of the co-investigator group 44
10.4.3. Provision of SAE follow-up information ..... 45
10.5. Reporting SAEs to third parties ..... 45
10.6 Mortality ..... 45
**11. DATA HANDLING AND RECORD KEEPING ..... 45**
11.1. Source data ..... 45
11.2. Case Report Form (CRF) completion ..... 46
11.3. Participant completed questionnaires ..... 47
11.4. Data management ..... 47
11.5. Self-evident corrections ..... 47
11.6. Data security ..... 47
11.6.1 University of Birmingham ..... 47
11.6.2 Loughborough University ..... 48
11.6.3 University of Leicester ..... 48
11.7. Archiving ..... 48
**12. QUALITY CONTROL AND QUALITY ASSURANCE ..... 49**
12.1. Site set-up and initiation ..... 49
12.2. Monitoring ..... 49
12.2.1. On-site monitoring ..... 49
12.2.2. Central monitoring ..... 49
12.3. Audit and inspection ..... 49
12.4. Notification of Serious Breaches ..... 50
**13. END OF TRIAL DEFINITION ..... 50**
**14. STATISTICAL CONSIDERATIONS ..... 50**
14.1. Sample size ..... 50
14.2. Analysis of outcomes ..... 50
14.2.1. Primary outcome ..... 50
14.2.2. Secondary outcomes ..... 51
14.2.3. Planned subgroup analyses ..... 51
14.2.4. Missing data and sensitivity analyses ..... 51
14.3. Planned final analyses ..... 51
**15. HEALTH ECONOMICS ..... 51**
15.1. Within-trial economic evaluation ..... 51
15.2. Model-based economic evaluation ..... 52
**16. SUB-STUDIES ..... 52**
**17. TRIAL ORGANISATIONAL STRUCTURE ..... 53**

17.1. Sponsor ..... 53
17.2. Coordinating centre ..... 53
17.3. Trial Management Group (TMG) ..... 53
17.4. Co-investigator group ..... 53
17.5. Joint Trial Steering Committee and Data Monitoring Committee ..... 53
17.7. Finance ..... 54
**18. ETHICAL CONSIDERATIONS ..... 54**
**19. DATA PROTECTION AND CONFIDENTIALITY ..... 54**
**20. FINANCIAL AND OTHER COMPETING INTERESTS ..... 55**
**21. INSURANCE AND INDEMNITY ..... 55**
21.1 University of Birmingham ..... 55
21.2 Loughborough University ..... 55
21.3 University of Leicester ..... 55
**22. ACCESS TO FINAL DATASET ..... 55**
**23. PUBLICATION PLAN ..... 56**
**24. REFERENCE LIST ..... 57**

# 1. BACKGROUND AND RATIONALE

## 1.1 Background

The population has become less physically active and more sedentary, yet there is compelling evidence that inactivity and high levels of sitting are both independently associated with poorer health and mortality (1-3). Public health guidance in the United Kingdom (UK) and internationally states that over a week, aerobic activity should add up to at least 150-minutes of moderate-vigorous physical activity (MVPA) (4-5). However, meeting this guidance means making large changes for most people and few achieve this regularly. Based on self-report, ~61% of UK adults meet current guidance for aerobic physical activity (6). However, this is likely to be over-reported, as objective assessment shows that only 6% of men and 4% of women in England achieve 150-minutes per week (7). This is of real concern and there is no reason to assume the situation will improve unless effective interventions are put in place. Previous physical activity interventions have only had modest effects, at best, on initiation of physical activity, and we know very little about successful behavioural maintenance (8-9). It is clear that guidance that sets large behavioural goals for physical activity has not been successful in getting the public physically active and a one-size approach may not be optimal.

## 1.2. Trial rationale

### 1.2.1. Justification for participant population

Approximately 6-10% of global mortality associated with non-communicable diseases (NCDs) is due to physical inactivity (1). There is also strong evidence that participation in physical activity promotes physical functioning and improves mental health (10-11). The prevention of NCDs is a major public health goal worldwide, and improving lifestyle behaviours is considered essential to reducing the financial and health burden of NCDs (12). Alongside a large proportion of adults not meeting current physical activity guidelines, there is growing public health concern about the amount of time spent in sedentary behaviours, with adults spending approximately 60-70% of waking hours sedentary (13). Too much time spent sitting has been associated with diabetes, cardiovascular disease (CVD), all-cause and CVD-related mortality (14-15). Public Health England have stated that if 1 in 10 adults aged 40-60 years in England achieved just 10-minutes of brisk walking per day, this would save the National Health Service (NHS) and taxpayers ~£310 million per year (16).

### 1.2.2. Justification for design

In preparation for this trial, and with the support of the patient advisory group, we conducted a series of development studies, including a feasibility randomised controlled trial (RCT) to help plan the trial design. This prior research has guided our understanding of the views of the public about the Snacktivity™ concept, Health Care Professional/Provider (HCPs) experiences of delivering the Snacktivity™ intervention to patients within routine consultations, the feasibility of the trial procedures (including recruitment rate), and the acceptability of the proposed intervention to the public (17-19). In addition, we investigated participants' experiences of using the technology (Fitbit device linked to mobile phone application called SnackApp) developed to support participants' engagement with physical activity/Snacktivity™ (20). Collectively, our work has indicated that the public liked the Snacktivity™ concept and were able to implement the approach within their daily lives, and that HCPs were able to successfully integrate conversations about Snacktivity™ within consultations (21). We did however identify that additional recruitment strategies and monitoring of recruitment progress were required to ensure successful recruitment in a subsequent phase III RCT. Following completion of the randomised feasibility trial (21), the aim of this research is to evaluate the effectiveness and cost-effectiveness of the Snacktivity™ intervention in both NHS and non-NHS

settings in a large RCT. As the feasibility trial identified some challenges to recruitment and data collection procedures, this definitive trial will include an internal pilot to address these, before proceeding to completion of recruitment of the required sample size.

### 1.2.3. Justification for choice of intervention(s)

An alternative 'whole day' approach to physical activity promotion that could engage and motivate the public to be regularly more active (and break up sedentary time), is a concept referred to here as Snacktivity™. Rather than focusing on encouraging 150-minutes per week of physical activity (~30-minutes per day over five days; i.e. make large changes), Snacktivity™ focuses on promoting small, but frequent, doses of regular MVPA throughout the day, such that at least 150-minutes of MVPA is accumulated weekly. A physical activity 'snack' typically lasts between 2 to 5-minutes, e.g., walk-talk conversations, walking coffee breaks, using stairs not the lift, pacing whilst using the telephone, or parking the car a little further away and walking to your destination. An important benefit of Snacktivity™ over current physical activity guidance is that Snacktivity™ encourages breaking up sitting time throughout the day. Snacktivity™ may also help develop people's confidence to become physically active more regularly, and small changes are easier for people to initiate and then maintain, than large changes. How people feel about physical activity is an important predictor of whether they continue to engage and adhere (22). Psychological theory acknowledges that achieving small changes is important for individuals' self-efficacy (23-24). Simple actions may become habitual more quickly than complex ones, suggesting that integration of small physical activity changes, or 'snacks', within everyday routines may be a more feasible approach to developing and sustaining physical activity, than trying to achieve large changes (24). The most common reason for inactivity is a perceived lack of time; Snacktivity™ provides a direct opportunity to address this barrier (25).

An inverse dose-response relationship exists between physical activity and all-cause mortality, therefore for inactive people any increase in physical activity is important (26-27). The relationship is also characterised by a steep early slope meaning the greatest gains in health are experienced when moving people who are sedentary to 2-3 metabolic equivalents (MET)/hours per week (~30-minutes per week), than moving more active people to doing marginally more (26,28). Improved cardio-metabolic and aerobic fitness have been reported from brief bouts of physical activity (29-33).

Notably, updated guidance from health agencies around the world have removed the need for adults to complete physical activity in bouts lasting 10 minutes or more (4,5). Our previous work has shown that the small bout Snacktivity™ approach for promoting physical activity was viewed positively by the public (17-18). An important additional benefit of Snacktivity™ is that it encourages breaking up sitting time throughout the day, meaning that it has the potential to impact two health behaviours simultaneously. Whilst the idea that small bouts of physical activity may improve health is not new, it is not a message that has been highlighted to the public, in part, because of a lack of robust evidence in real world health settings. To date, no RCT has directly investigated whether Snacktivity™ increases participation in MVPA or the number of people meeting the recommended guidelines for physical activity.

### 1.2.4. Technology in healthcare

Given a large proportion of the population are insufficiently physically active and report high volumes of sedentary behaviour, we need interventions with high reach; this objective can be achieved by mobile health (mHealth) interventions. The use of technology to deliver lifestyle interventions has grown exponentially over the past decade. Technology based interventions offer some key advantages over traditional behaviour change interventions. Technology based interventions have the ability to reach a large number of people at a relatively low cost and offers increased access to the public at a time and place that suits their preferences, including the ability to

overcome the need to attend face-to-face sessions to receive the intervention. As a population approach, smartphone-based interventions are attractive as 90% of mobile phone users are in possession of their telephones 24 hours per day. mHealth technology is applicable across the age and cultural spectrums, and studies have shown that this generation find electronic devices that promote physical activity acceptable to them (34-35).

#### 1.2.5. Justification of choice of primary outcome

As this trial is focused on the benefits and impact of Snacktivity™ upon physical activity and health outcomes, and in line with current health guidance for physical activity, we have selected minutes of MVPA as the primary outcome for this trial.

## 2. AIMS AND OBJECTIVES

The overall aim of the trial is to assess the effectiveness and cost-effectiveness of Snacktivity™ to promote physical activity and reduce future risk of disease in the population compared with usual care (current guidance for physical activity).

### 2.1. Internal pilot objectives

The trial includes a 6-month internal pilot phase to assess recruitment and adherence Snacktivity™. The internal pilot aims to assess:

- Recruitment: Aim to recruit ≥30% of the total sample size (≥218/724 participants) in 6 months (this equates to 36-37 participants per month);
- Adherence to Snacktivity™: Defined as a participant achieving a minimum of four bouts of MVPA lasting ≥2-minutes (i.e., activity snacks) on average each day over 12 weeks as per the feasibility trial. This criterion will be based on those who would be expected to have reached 12 weeks follow-up after the trial has been open for 6 months, which we estimate to be approximately 100-120 participants (i.e. 50-60 participants in the Snacktivity™ intervention group).

Data collected during the internal pilot will inform progression to the full trial, which will be based on pre-defined stop-go criteria agreed with the funder (see Outcomes, section 8.1).

### 2.2. Main trial objectives

#### 2.2.1. Clinical aims and objectives

The primary objective is to assess whether Snacktivity™ increases MVPA at 12 months compared to usual care (current guidelines on physical activity) in adults who do less than the current recommended amount of MVPA per week (i.e. complete <150-minutes of MVPA per week).

The trial also aims to assess the:

- Effects of the Snacktivity™ intervention on physical activity and physical activity habits;
- Effects of the Snacktivity™ intervention on sedentary behaviours;
- Effects of the Snacktivity™ intervention on quality of life, depression and anxiety scores;
- Effects of the Snacktivity™ intervention on weight.

#### 2.2.2. Economic aims and objectives

The aim of the economic analysis is to assess the cost-effectiveness of the Snacktivity™ intervention. It has the following objectives:

- To estimate the cost of Snacktivity™ to the health service;

- To measure how Snacktivity™ impacts health care use and levels of productivity;
- To assess if Snacktivity™ leads to improved health-related quality of life (HRQOL) and improved wellbeing;
- To estimate the intervention cost-effectiveness in the short term (12 months) and if appropriate, the long term (lifetime).

# 3. TRIAL DESIGN AND SETTING

## 3.1. Trial design

A multi-centre, open-label, two-arm, parallel group, individually randomised trial, with an internal pilot and economic evaluation, to test the superiority of Snacktivity™ compared with usual care (current guidelines on physical activity).

## 3.2. Trial setting

Recruitment will take place from NHS Trusts/settings and non-NHS settings. NHS settings are defined as any service that is delivered to members of the public by an HCP employed/funded by the NHS, and includes community health services, primary care and general practices, secondary care and mental health organisations. Non-NHS settings will include recruiting via social media platforms (including via the National Institute for Health and Care Research (NIHR) Be Part of Research), third sector organisations, public health organisations, community support groups and workplaces.

## 3.3. Assessment of risk

All clinical trials can be considered to involve an element of risk and in accordance with the Birmingham Clinical Trials Unit (BCTU) standard operating procedures (SOPs), this trial has been risk assessed to clarify any risks relating uniquely to this trial beyond that associated with usual care.

A risk assessment has been conducted and concluded that this trial is: No higher than the risk of current usual care.

# 4. ELIGIBILITY

## 4.1. Inclusion criteria

- Aged ≥18 years
- Completes <150 minutes per week of MVPA as assessed by the Physical Activity Vital Sign (PAVS) Questionnaire
- Owns a mobile phone capable of hosting apps (e.g. Apple iOS 13.0+ and Android 4.3+)
- Able to provide informed consent
- Agreement for their HCP to be notified of their involvement in the trial

## 4.2. Exclusion criteria

- Unable to understand English sufficiently to complete the trial assessments
- Women known to be pregnant or breastfeeding
- Inpatient, bedbound or unable to complete physical activity

## 4.3. Co-enrolment

Requests to co-enrol participants in other trials will be considered by the Trial Management Group (TMG) on a case-by-case basis. Where co-enrolment is permitted, the agreement of vested parties will be documented. A log of co-enrolled participants will be maintained by the trial team at BCTU.

# 5. CONSENT

## 5.1 Consent procedure

### 5.1.1. Consent to screening

There is a brief outline of the trial at the beginning of the screening form as well as links to the participant information sheet (PIS) and a video summarising the trial that potential participants can click on before completing the form (if the screening form is completed online). Potential participants will need to confirm at the start of the screening form (which can be completed electronically or on paper) that they are happy for their answers to the screening questions to be saved and retained on the trial database. If the participant answers 'yes', this will be considered as providing consent for screening and they will be allowed to answer the subsequent screening questions. If the participant answers 'no' to their answers being retained on the database, they will not be able to answer any further questions on the screening form and they will be deemed as ineligible for the trial.

### 5.1.2. Consent to the main trial

Consent for trial related processes (collection of accelerometery data and randomisation (if the criteria for accelerometery data return is met)) will be obtained before any participant joins the main trial and it will be taken and recorded electronically via an online method known as eConsent, either completed by the participant themselves remotely or on their behalf by the trial team at BCTU over the telephone or video call.

Potential participants who following screening are considered eligible for the trial will be invited/approached to take part in the trial. Prior to completing the eConsent form, potential participants will need to read the PIS (either electronically or on paper) and confirm that they have read it on the eConsent form. If the potential participant indicates that they have not read the PIS, a prompt with a link to read an electronic copy of the PIS will appear.

Potential participants will have the opportunity to contact the trial team at BCTU via telephone or email to clarify any points they do not understand or to ask any questions about the trial:

- The trial team will talk through the PIS with the potential participant if requested, ensuring that they fully explain the aims, trial interventions, anticipated benefits and potential hazards of taking part in the trial.
- They will also highlight that participation is voluntary and that the potential participant is free to refuse to take part and may withdraw from the trial at any time.

Consent for the trial will be completed online at a time and location convenient to the participant, using a smartphone, computer or tablet. The eConsent form will consist of checkboxes to indicate consent for each aspect of the trial. Participants will also need to sign (finger drawn signature) the consent form confirming that they are happy to take part in the trial. If the researcher completes the consent form on behalf of the participant, the participant will need to agree to a declaration which will be the equivalent of signing a physical document.

The participant must give explicit consent for the data collected during the trial to be looked at by responsible individuals from the Snacktivity™ trial office at the University of Birmingham (UoB), the Programme Coordinating Centre at Loughborough University (LU), the University of Leicester (UoL), Birmingham Community Healthcare NHS Foundation Trust (the co-sponsor), regulatory authorities

and from the NHS Trust, where it is relevant to them taking part in the trial. They will be made aware that all information collected will be used for research purposes only.

When the participant completes the eConsent form, it will automatically record the participant's internet protocol (IP) address and time stamp when the form was submitted. Participants will have the option of either receiving a completed copy of the consent form via email or have a printed copy posted to them.

If a participant is recruited via an NHS service/setting, a copy of the completed eConsent form will be sent to the participants HCP along with a copy of the PIS in the post or via NHSmail. The eConsent form and PIS will be placed in the participant's records and Investigator Site File (ISF).

A copy of the eConsent form, PIS and GP letter will be sent to the participant's GP (if they were not recruited via this pathway) to inform them of their patient's involvement in the study.

### 5.2 Ongoing consent

Prior to completing the three- and twelve-month follow-up questionnaires, participants will be asked to confirm their willingness to continue in the trial. Throughout the trial, the participant will have the opportunity to ask questions about the trial and any new information that may be relevant to the participant's continued participation will be provided. Where new information becomes available which may affect the participant's decision to continue, participants will be given time to consider and if happy to continue will be re-consented. The participant's right to withdraw from the trial will remain.

## 6. ENROLMENT, RANDOMISATION and BLINDING

### 6.1. Identification

Recruitment will take place from NHS Trusts/settings and non-NHS settings. NHS settings are defined as any service that is delivered to members of the public by an HCP employed/funded by the NHS, and includes community health services, primary care and general practices, secondary care and mental health organisations. Non-NHS settings will include recruiting via social media platforms (including via NIHR Be Part of Research), third sector organisations, public health organisations, community support groups and workplaces.

#### 6.1.1. NHS Trusts/settings

We anticipate NHS Trusts/settings will search their databases using search protocols developed by the lead Clinical Research Network (CRN) and invite potential participants by letter based on eligibility at the pre-screening stage. Potential participants who are aged 18 years or more and have a healthcare consultation booked during the recruitment phase of the trial will be invited to take part. For those recruited via an NHS Trust/setting the date of the consultation should be at least three weeks prior to the date of invitation to allow enough time for screening, consent and baseline data collection to be completed before the participant sees the HCP . Alternatively, HCP's can raise the topic of the Snacktivity™ trial in consultations and ask the patient if they would be interested in participating in the trial and offer the invitation pack which includes the invitation letter, PIS, screening form and a prepaid envelope to return the screening form to BCTU (if the patient has an additional consultation booked at least three weeks away).

If an NHS Trust/setting uses, or wishes to use, short messaging service (SMS) text messages to send patients details of their scheduled appointments and/or to notify them about this trial, a trial invite link will be added to these text messages (as detailed in section 6.2.1).

Identifiable information will not be reviewed by people outside of the clinical care team without consent. We also plan to provide posters for NHS Trusts/settings to exhibit in appropriate areas so that patients may self-refer. These advertisements will also be customised for web-based display via the trial's unit, patient support groups and other relevant social media, containing contact details for the trial's unit.

In Scotland, the NRS Primary Care Network will support practices by facilitating patient identification and offering Research Nursing Support to participating sites.

NHS Research Scotland (NRS) Primary Care Network is funded by the Scottish Government, Chief Scientist Office (CSO) and facilitates research in primary care across Scotland.

NRS Primary Care Network provides an expert service, recruiting Practices, undertaking searches of their electronic Patient Management Systems, identifying potentially eligible patients and preparing the ethically approved invitations to be sent out to patients on behalf of the practice. The Network may also offer specialist research nursing support.

Network staff work on behalf of the healthcare team with the permission of the Practice. Network staff must have a current substantive or honorary NHS contract to allow them to carry out these duties. Memorandum of Agreements between the Network and GP practices are signed to set out responsibilities regarding Data Protection and GDPR.

Searches are undertaken at each GP practice and the list generated by the search is screened by a clinician before invitations are sent out on behalf of the practice. Patients are asked to contact the research team if they are interested in participating in the study. Patient details are not disclosed to the research team during the invitation process.

Further information is available at Working with us | NHS Research Scotland | NHS Research Scotland.

#### 6.1.2. non-NHS settings

Potential participants can be identified in any way that works best for the non-NHS setting or they could self-select to take part. This could include via posters, flyers or sending SMS text messages to members of the public who use their services (e.g. community support groups).

## 6.2. Screening and enrolment

### 6.2.1. Potential participants identified and invited to participate using the electronic trial link

The electronic trial link, when clicked, will direct the potential participant to an online survey, hosted on the study REDCap™ database. Embedded within the survey will be a link to the full PIS, a summary PIS and a short video explaining the trial for potential participants to view before deciding if they would like to take part in the trial or not. If interested, the potential participant will then be directed to complete the eScreening form, which includes the Physical Activity Vital Sign (PAVS) questionnaire. Consent to screening is described in section 5.1.1.

Based on the answers provided, the screening CRF will indicate to the participant if they are eligible or ineligible for the trial. If eligible, and the potential participant is still willing to participate, they will be asked to complete the eConsent form for the trial as described in section 5.1.2. If ineligible, the only data recorded by the database will be the reason for ineligibility.

#### 6.2.2. Potential participants identified and invited to participate using paper invitation packs

Paper invitation packs can be sent with the consultation appointment letter (or reminder of their upcoming appointment) or handed to them by the HCP if they are seen in clinic before their upcoming appointment.

The invitation packs will contain the trial invitation letter, PIS, screening form, and a prepaid return envelope. The trial invitation letter will include the electronic trial link (as a web address, as described in section 6.2.1, in case the potential participant would like to complete the screening form online), otherwise they can complete the paper form and post it back to the trial office.

Paper screening forms received in the post will be entered into the REDCap™ database by the trial office. All potential participants who return the paper screening forms will be contacted and informed whether they are eligible or ineligible for the trial.

Eligible participants will, depending on how they indicated they would like to provide consent on the screening form, either be sent a link (via email or text message) to complete the eConsent form online or the trial team will call the participant and complete it online on their behalf over the telephone or video call.

The paper screening form will collect identifiable data such as name, email address and telephone number to allow the trial team to contact the potential participant to inform them if they are eligible or ineligible for the trial. If the potential participant is deemed as ineligible, the paper forms will be destroyed once their eligibility status has been confirmed with them, and the only data recorded by the database will be the reason for ineligibility.

### 6.3. Randomisation

Randomisation will be provided by BCTU using a secure online system (available at https://snacktivity.bctu.bham.ac.uk), thereby ensuring allocation concealment. Randomisation may only occur once the baseline questionnaires have been completed and the accelerometer data has been checked for completeness. Participants will not be randomised into the trial, until they have provided valid accelerometer data (at least 4 valid days).

The trial team at BCTU will be responsible for randomising participants. Unique log-in usernames and passwords will be provided to those who have been delegated the role of randomising participants into the trial as detailed on the Snacktivity™ BCTU Site Signature and Delegation Log. These unique log-in details must not be shared with other members of the trial team. The online system will be available 24 hours a day, 7 days a week, apart from short periods of scheduled maintenance.

### 6.4. Randomisation process

After participant eligibility has been confirmed by the database, eConsent has been provided, the baseline questionnaires have been completed and valid accelerometer data has been confirmed as received (minimum of 4 days), eligibility will be reconfirmed by the trial team at BCTU before participants are randomised into the trial using the online system. All questions and data items on the randomisation electronic case report form (eCRF) must be answered by the BCTU trial team prior to a participant being randomised. Following randomisation, participants will be informed which group they have been allocated to (by text, email or phone call) and a confirmatory e-mail will be sent to the randomiser and the participants HCP (if recruited via an NHS Trust/setting).

The local research team should add the participant to the Snacktivity™ Participant Recruitment and Identification Log which links participants with their Trial Number. PIs must maintain this document

securely and it must not be submitted to the trial office. The Snacktivity™ Participant Recruitment and Identification Log should be held in strict confidence.

### 6.5. Randomisation method

Participants will be randomised at the level of the individual in a 1:1 ratio to receive either the Snacktivity™ intervention or usual care. A minimisation algorithm will be used within the randomisation system to ensure balance in the intervention allocations over the following variables:

- Route of recruitment (NHS, Non-NHS)
- Total minutes per week of physical activity (at baseline assessed using the PAVS) (0-49, 50-99, 100-149 minutes)
- Age group (18-45, 46+ years old)
- Gender (male, female, prefer not to say)

To avoid the possibility of the intervention allocation becoming predictable, a random element will be included in the minimisation algorithm. Full details of the randomisation specification will be stored in a confidential document at BCTU.

### 6.6. Blinding

This is an open trial; participants will not be blinded.

### 6.7. Informing the participant's GP and other parties

As agreed on the eConsent form, a copy of the participants completed eConsent form, alongside the GP letter will be sent to their GP, and to the HCP who invited them to take part in the study if they were not recruited via their GP, to inform them of their participation in the Snacktivity™ study.

## 7. TRIAL INTERVENTION

### 7.1. Trial intervention

Participants will be randomised to receive:

- The Snacktivity™ intervention, which involves a brief Snacktivity™ consultation, a Fitbit™ watch linked to the SnackApp and an infographic detailing the current guidance for physical activity.

OR

- Usual care (an infographic detailing the current guidance for physical activity with no other support offered).

### 7.2. Snacktivity™ intervention

#### 7.2.1. Outline and overview

The Snacktivity™ intervention aims to promote the importance of regular physical activity through participation in Snacktivity™, the usefulness of Snacktivity™, encouraging regular self-monitoring of Snacktivity™ to achieve sustained Snacktivity™, goal setting for daily Snacktivity™, as well as action planning and implementation strategies for Snacktivity™. There are two main components within the Snacktivity™ intervention: HCPs (for participants recruited via NHS Trust/setting) or researchers (for participants recruited via non-NHS setting) raising and encouraging Snacktivity™ with participants in their consultations/telephone calls; and the promotion of technology to support behaviour change and sustained engagement in Snacktivity™ (via the SnackApp phone app and the Fitbit™). The role of the HCP/researcher is to simply raise the topic of Snacktivity™/ physical activity, to signpost participants to the SnackApp for further advice and support, and to encourage

participants to use their physical activity tracker device to facilitate their engagement with Snacktivity™ and to obtain feedback. The intervention components are outlined in more detail below.

The Snacktivity™ intervention is based on self-regulation theory and the habit formation model (36-37). Our own work and other studies have shown self-regulation/self-monitoring to be an effective foundation strategy for health behaviour change (38-39). Self-monitoring of Snacktivity™ may act as a reward for individuals who control their physical activity behaviour, who are then provided with positive feedback from the monitoring process, thereby enhancing their motivation and reducing the potential for relapse. Frequent monitoring and reflection of Snacktivity™ progress may also improve self-efficacy for participation in both short and longer bouts of physical activity, which, in turn, could improve other health outcomes, such as weight and mental health (5, 37-38). Encouragement of self-monitoring and recording of Snacktivity™ is a simple concept for an HCP to advocate as a public health communication. It is also simple for people to understand and implement. Trials have shown that participants can adhere to daily self-monitoring of physical activity (40). The behavioural goal is for participants to work towards achieving 150 minutes of MVPA per week. Snacktivity™ participants will be granted access to the SnackApp and sent a physical activity tracker (FitBit™) once the trial office have received confirmation that the HCP or researcher has introduced the idea and the benefits of the Snacktivity™ intervention to the participant.

### 7.2.2. Snacktivity™ Consultation

The intervention will start with delivery of the Snacktivity™ message within the participant's consultation with an NHS HCP (for participants recruited via NHS services) or during a telephone or video call with a researcher (for participants recruited via non-NHS services). The HCP/researcher will discuss with the participant the purpose of Snacktivity™, the hypothesis underpinning its principals, how it differs from standard physical activity advice, and provide examples of Snacktivity™. Participants will receive standard guidance about the importance of physical activity and advised to accumulate their physical activity through Snacktivity™. A Snacktivity™ picture board will be used to support these conversations (the picture board has previously received favourable approval: REC reference: 20/WM/0315).

The role of the HCP/researcher is to simply raise the topic of Snacktivity™/physical activity, to signpost participants to the SnackApp for further advice and support, and to encourage participants to use the physical activity tracker device that they will receive to facilitate their engagement with Snacktivity™ and to obtain feedback.

See below for more information on the practicalities and processes for the HCPs (section 7.2.6) and researchers (section 7.2.7) delivering the Snacktivity intervention.

### 7.2.3. SnackApp and physical activity tracker

To facilitate habit formation of participation in Snacktivity™, a mobile phone application called the SnackApp (ethically approved - REC reference 20/PR/0323) will generate regular reminders and notifications to engage in Snacktivity™. Self-monitoring may be particularly relevant for developing Snacktivity™ habits because it may be more difficult for people to easily recall how many activity snacks they have achieved each day. The design and content of the SnackApp is based on previous work packages within this NIHR programme grant, some of the principals of existing apps and our previous experiences of developing Apps for promoting physical activity and lifestyle behaviours (20, 41). Participants will receive a free Fitbit™ and access to the SnackApp which, within its functions, contains features common in digital health interventions. For example, the SnackApp:

- Automatically captures/tracks daily physical activity and inactive time via a wrist worn tracker (e.g. Fitbit™).
- Classifies participants into an activity profile according to their physical activity and inactive time.
- Provides physical activity prompts after user-defined inactive periods, encouraging regular active snacks throughout the day.
- Generates individualised motivational push notifications to participants mobile phones based on prior behaviour.
- Supports goal setting (both automatic and user-defined).
- Provides individualised feedback related to goal achievement to encourage adherence and facilitate self-efficacy. Individualised feedback will be provided on the accumulated number of physical activity snacks completed and total minutes 'activity snacking' per day, progress towards meeting the recommended level of physical activity for health benefits (at least 150 minutes of MVPA per week) and the total number of minutes of physical activity, MVPA and the number of steps each day.
- Enables access to educational content (text, static images, video and audio content) regarding Snacktivity™, both externally hosted and supplied by the research team, including examples of Activity Snacks (with instructive photos and gifs) and information on the management of chronic disease.
- Encourages social support via a forum to facilitate a Snacktivity™ social community.
- To promote habit formation, users will be able to plan when to perform activity snacks.

The participant's first name, surname, email address, date of birth (DOB), height and weight will be used to configure and personalise the SnackApp and these details will be loaded into the SnackApp.

User testing of the SnackApp suggested that physically inactive adults will engage with the SnackApp, indicating its applicability of use in the Snacktivity physical activity intervention (20).

#### 7.2.4. Commercial development of the SnackApp and MHRA

The SnackApp has been developed by a commercial software company (Cuttlefish Multimedia Ltd) based on a commercial agreement with LU. The decision to engage with Cuttlefish was based on an open procurement process. There are no conflicts of interest to declare.

A number of physical activity tracker devices are available, but we currently plan to use the Fitbit™ Versa tracker device. However, this may be subject to change as the commercial devices change frequently. The Fitbit™ Versa tracker device is a wireless physical activity tracker, worn on the wrist, which is able to track daily activity levels. A proprietary algorithm translates raw acceleration signals into steps and activity level. It provides measures of steps, activity level, inactivity and energy expenditure each minute. A companion SnackApp will be downloaded onto the clock face of the Versa to allow instantaneous feedback on Snacktivity™ progress throughout the trial. The Fitbit™ Versa will be procured from Fitbit™ Inc.

The Medicines and Healthcare products Regulatory Agency (MHRA) do not consider the SnackApp to have a medical purpose as defined in the device regulations. The MHRA considered it to be a health and wellbeing product (email confirmation received on 12 February 2020 and email correspondence to this effect is filed in the trial master file (TMF)).

#### 7.2.5. Training of HCPs/Researchers to deliver the Snacktivity™ intervention

Intervenors (HCPs and researchers) will be trained by the trial office and/or research team to deliver the Snacktivity™ intervention following a standard protocol. A media-based training module that can be delivered face-to-face or remotely has been developed. The training will either be delivered online using video conferencing software or face to face. All components of the intervention will be

explained during the training. The training tools will include information on the importance of adhering to the trial protocol, the research trial procedures, trial design and ways of delivering the Snacktivity™ intervention. The training for intervenors aims to demonstrate different ways in which Snacktivity™ can be promoted by HCPs within consultation. Intervenors will be trained to promote the rationale for Snacktivity™ and the benefits of physical activity for health, give examples of Snacktivity™, and explain implementation plans and action planning. Intervenors will be asked to highlight to participants that Snacktivity™ will work best if they develop habits or routines and 'what needs to change' to achieve this. The purpose of the physical activity tracker and SnackApp for facilitating self-monitoring of snacks will be discussed; use of this technology by participants will be specifically encouraged. Video clips are included in the training that show the Snacktivity™ intervention being delivered in GP practices, so that intervenors understand how the intervention might be delivered by them. An intervention checklist will be completed by intervenors to aid delivery and provide a reminder prompt of areas that must be covered.

### 7.2.6. HCP Snacktivity™ consultations (intervention group)

All HCPs will receive in the post or via secure NHSmail, a copy of the participants completed eConsent form confirming their involvement in the trial for the HCP's records, as well as the HCP letter. In addition to sending the eConsent form and HCP letter, the following three methods can be used to remind HCPs of the need to discuss the Snacktivity™ intervention with their patient during the consultation:

1. Participants will be asked to remind their HCP that they are taking part in the trial at the start of their consultation either verbally or through presenting the HCP with the email/text message from the trial team confirming the group they have been randomised to.
2. The administration team at the participating health service may add an electronic prompt to the participant's notes ahead of the consultation
3. The trial team will email the HCP to inform them of their participants' involvement in the trial and which group they have been randomised to.

In some instances, one of these three methods may be preferred over the other or it may be that all three methods are used depending on the preference of individual NHS services/sites.

HCPs can decide when the best time is to raise the topic of Snacktivity™ within the consultation, and they can discuss any behavioural change strategies usually adopted by HCPs, but the participant will be advised to accumulate their physical activity through Snacktivity™. An intervention checklist will be completed by the HCP to aid delivery of the intervention and to provide a reminder prompt of areas that must be covered. See also section 7.2.2.

We anticipate in NHS settings, that HCPs will deliver the Snacktivity™ intervention to participants during face-to-face consultations. However, if this is not possible, then it may be the case that the HCP delivers the Snacktivity™ intervention as part of an online consultation with the participant. Each NHS service will use their preferred and approved online conferencing tools. If online consultations take place, a copy of the Snacktivity picture board and infographic detailing the current guidance for physical activity will be emailed or posted to the participant prior to the consultation taking place.

Following the consultation, the HCP should inform the trial team at BCTU that the participant has received the Snacktivity™ intervention information, so that the study intervention technology can be sent to the participant. BCTU will then notify the LU research team/study administrator that a Snacktivity™ intervention participant has received their consultation, and the team at LU will arrange for the Fitbit™ to be sent to the participant and for the SnackApp to be made available to the participant (see also sections 7.2.9 and 7.2.10).

As detailed below (in section 7.2.8), 10-20% of consultations will be audio recorded (if the participant has consented to this).

### 7.2.7. Researcher Snacktivity™ appointments (intervention group)

If a participant is recruited via a non NHS setting, such as third sector organisations, workplaces or social media, a researcher will schedule a telephone/video call with the participant to deliver the Snacktivity intervention information. The researcher will mimic the role of an HCP and will deliver the information as described in section 7.2.2. A copy of the Snacktivity™ picture board and infographic detailing the current guidance for physical activity will be emailed or posted to the participant before the researcher contacts the participant to deliver the intervention. During the appointment, an intervention checklist will be completed by the researcher to aid delivery of the intervention and to provide a reminder prompt of areas that must be covered.

Following the appointment, the researcher should inform the trial team at BCTU that the participant has received the Snacktivity™ intervention information, so that the study intervention technology can be sent to the participant. BCTU will then notify the LU research team/study administrator that a Snacktivity™ intervention participant has received their consultation, and the team at LU will arrange for the Fitbit™ to be sent to the participant and for the SnackApp to be made available to the participant (see also sections 7.2.9 and 7.2.10).

As detailed below (in section 7.2.8), 10-20% of appointments will be audio recorded (if the participant has consented to this).

### 7.2.8. Intervention fidelity

With the consent of participants, 10-20% of the Snacktivity™ interventions will be audio-recorded to assess for fidelity using an encrypted Dictaphone or a secure and GDPR compliant online conferencing tool (where consultations take place online), to assess whether the intervention is being delivered according to the intervention checklist.

An intervention checklist will be completed by the intervenors to aid their delivery of the intervention and provide a reminder prompt of areas that must be covered during intervention consultations. Additionally, a range of strategies to reinforce intervention fidelity will be used and will include: training HCPs/researchers to deliver the intervention as per protocol; explaining the intervention logic model; development and use of a standardised training resource; checks for intervention 'receipt' and enactment by checking whether participants attended their consultation; and whether the physical activity tracker/SnackApp is activated by participants.

### 7.2.9. Delivery of the Fitbit™ and access to the SnackApp (Intervention group only)

As detailed above, once the HCP or researcher confirms that they have successfully delivered the Snacktivity™ intervention to the participant, LU will set up the participant's Fitbit™ and post it to them. A letter within the parcel will explain to the participant that a member of the research team based at LU will call them to help set up and link the Fitbit™ and SnackApp to their mobile phone. If the HCP or researcher does not inform the trial team within 24 hours after the participant's scheduled consultation or telephone call, the trial team will contact the HCP/researcher or the participant directly to gain confirmation that the consultation/telephone/video call took place.

### 7.2.10. Additional support for participants using the Fitbit™ and SnackApp

The Fitbit™ and SnackApp need to be connected to the internet in order to function and synchronise data. Participants will be advised to connect to Wi-Fi when at home or updates are required. If a participant is having to use and purchase additional mobile phone data in order to take part in the

Snacktivity™ study, supplementary monetary support is available as we do not want this to be a barrier to participation. Each request will be reviewed on a case by case bases by the Chief Investigator (CI) and the trial team.

### 7.3. Usual care

#### 7.3.1. HCPs discussing the current guidance for physical activity (usual care group)

All HCPs will receive in the post or via secure NHSmail, a copy of the participants completed eConsent form confirming their involvement in the trial for the HCP's records, as well as the HCP letter.

At the consultation with the participant, HCPs will only discuss the current guidance for physical activity (large changes, non-habit-based information only), which advises to work towards the accumulation of at least 150-minutes of MVPA per week. HCPs will only deliver the normal physical activity advice and any typical behavioural change strategies adopted by HCPs within standard consultations. A standard physical activity factsheet/infographic will be given to the participant with no other support offered.

We anticipate in NHS settings, that HCPs will discuss the current guidance for physical activity to participants during face-to-face consultations. However, if this is not possible, then it may be the case that the HCP delivers the guidance as part of an online consultation with the participant. Each NHS service will use their preferred and approved online conferencing tools. If online consultations take place, a copy of the infographic detailing the current guidance for physical activity leaflet will be emailed or posted to the participant prior to the consultation taking place.

With the consent of participants, the delivery of the usual care information will be audio-recorded to assess fidelity and intervention contamination (the aim is for around 25% of consultations to be audio-recorded).

Following the consultation, the HCP should inform the trial team at BCTU that the participant has received the Snacktivity™ usual care information.

#### 7.3.2. Researchers discussing the current guidance for physical activity (usual care group)

If a participant is recruited via a non NHS settings, such as third sector organisations, workplaces or social media, a researcher will schedule a telephone/video call with the participant to deliver the usual care information. The researcher will mimic the role of an HCP and will deliver information as described in section 7.3.1. A standard physical activity factsheet/infographic will be emailed or posted to the participant ahead of the scheduled telephone call. With the consent of participants, the delivery of the usual care information will be audio-recorded to assess fidelity and intervention contamination (the aim is for around 25% of consultations to be audio-recorded).

Following the appointment, the researcher should inform the trial team at BCTU that the participant has received the Snacktivity™ usual care information.

### 7.4. Continuation of intervention after the trial

There would be no issue with a participant in the intervention group continuing with Snacktivity™ until the trial ends as they will be given the Fitbit to keep and allowed continued access to the SnackApp until the last participant completes follow-up. The SnackApp will be taken offline once follow-up has been completed.

### 7.5. Intervention supplies

Prior to site activation, the Snacktivity™ trial office will arrange for copies of the Snacktivity™ picture board, infographics detailing the current guidance for physical activity and the intervention fidelity checklists to be sent to sites.

## 8. OUTCOME MEASURES

### 8.1. Pilot trial outcomes

The success of the internal pilot phase will be based upon:

- Recruitment
- Activity adherence

In the internal pilot, we are aiming to recruit 218 participants (30% of the total sample size of the trial). At the end of the internal pilot phase, the TMG and Trial Steering Committee (TSC) will review the pilot data against a set of pre-specified criteria and a traffic light system (see Table 1).

**Table 1 – Internal pilot traffic light criteria**

| | |
|---|---|
| **Green** | ≥100% of the internal pilot target sample size is recruited |
| | ≥80% of the intervention group are achieving Snacktivity adherence* |
| If the two criteria are met, we will proceed to recruitment of the required sample size with the protocol unchanged. | |
| **Amber** | 99-70% of the internal pilot target sample size is recruited |
| | 60-79% of the intervention group are achieving Snacktivity adherence* |
| If one or more of our amber criteria are met, we will plan to adapt the protocol to improve which ever criteria is not at the 'green light' level before proceeding to completion of the required sample size. | |
| **Red** | ≤69% of the pilot target sample size is recruited |
| | ≤59% of the intervention group are achieving Snacktivity adherence* |
| If one or more of these criteria are met, we would consider the current protocol not feasible and consider discontinuing the trial | |

*Snacktivity™ adherence is defined as participants achieving a minimum of four bouts of MVPA lasting ≥2-minutes on average each day over 12 weeks. This criterion will be based on those who would be expected to have reached 12 weeks follow-up after the trial has been open for 6 months, which we estimate to be approximately 100-120 participants (i.e. 50-60 participants in the Snacktivity™ group).

## 8.2. Main trial outcomes

### 8.2.1. Primary outcome(s)

The primary outcome is average weekly MVPA at 12 months measured using the Axivity (AX3) device

### 8.2.2. Secondary outcomes

We will assess the following using the Axivity (AX3) device at 3 and 12 months post-randomisation:

- proportion of participants meeting the guidance amount of 150 minutes of MVPA per week
- average total minutes (sum of light, moderate and vigorous) of physical activity per day
- average number of minutes of light, moderate and vigorous physical activity per day
- average minutes of MVPA accumulated in bouts lasting ≥2, ≥5 and ≥10-minutes per day
- average number of MVPA bouts lasting ≥2, ≥5 and ≥10-minutes per day
- average magnitude of dynamic wrist acceleration per day (as a proxy for total volume of activity)
- average intensity gradient per day (no unit for this variable)
- average minutes of sedentary time per day
- average time (minutes) spent in prolonged sedentary behaviour per day
- average number of prolonged sedentary bouts per day
- average sleep duration (mins/day) and average efficiency (quality) (%/day)

We will also assess at 3 and 12 months post-randomisation:

- weight (objective (or self-reported if participant is unable to provide objective weight))
- depression/anxiety (using the Hospital Anxiety and Depression Scale (HADS))
- quality of life (using the EQ-5D-5L questionnaire)
- self-reported sedentary behaviours (using the Workforce Sitting Questionnaire (WSQ) and International Physical Activity Questionnaire (IPAQ) (sitting question only))
- self-efficacy for physical activity (using the Self-Efficacy for Exercise questionnaire)
- enjoyment of physical activity (using the Physical Activity Enjoyment Scale (PACES))
- habitual physical activity (using the Self-Report Habit Index (intervention group only))
- participation in Snacktivity™ using Fitbit™ data (to assess adherence to Snacktivity™ ) (intervention group only)
- serious adverse events (SAEs) related to participation in physical activity

Participant's experiences of the trial will be captured using single item exit questions at three and twelve months follow-up.

### 8.2.3. Cost-effectiveness outcomes

We will assess the following at 3 and 12 months post-randomisation:

- The ICECAP-A and health care resource use will be assessed by questionnaire at three months (for resource use in the past three months) and twelve months (for resource use in the past six months)

### 8.2.4. Snacktivity™ intervention outcomes

Feedback on the Snacktivity™ intervention will be collected from participants randomised to the Snacktivity arm, focusing on the use of the SnackApp and the suggested activity snacks.

With consent from participants, the Fitbit™ will provide the data on the following:

- steps
- distance

- calories
- bouted active minutes*
- inactive time
- sleep and awake time
- wear time (through body sensor)
- minutes of light physical activity
- minutes of moderate physical activity
- minutes of vigorous physical activity

*The Snacktivity™ Active Minutes will be computed from Fitbit™ measured METs and Activity Snacks.

# 9. TRIAL PROCEDURES

## 9.1. Baseline Data Collection

### 9.1.1. Questionnaires

Participants will be asked to provide full informed consent (section 5.1) before being sent a link to their email address and/or mobile phone asking them to complete the baseline questionnaires directly into the trial database. If specifically requested, a paper copy of the questionnaires can be posted to the participant with a freepost envelope for participants to return the booklet to BCTU.

The Baseline Measures Case Report Form (CRF) asks for the participant's weight. Participants will be asked to upload a picture of themselves standing on their home weighing scales with their weight clearly visible. If the participant has difficulty uploading a photograph of their weight (objective), we will accept the participant entering their weight into the questionnaire without a photo (self-reported).

If the participant does not complete the questionnaires within 7 days from the original date sent, the trial team will either resend the link, send a paper copy of the questionnaires in the post or call the participant to complete the questionnaires over the telephone.

### 9.1.2 Accelerometer

Following consent, an accelerometer will be set up by the UoL and mailed directly to the participant. Participants will be asked to wear the accelerometer for up to nine days (seven full days plus a partial day, the day before and day after the seven full days) and to complete the accompanying diary (which records the time the participant went to sleep and the time they woke up) every day. Instructions on how to wear the accelerometer and complete the diary will be included in the parcel. Following up to nine days of wear, the participant will post (free of charge) the accelerometer and diary back to the UoL, where researchers will check the accelerometer data for completeness.

To ensure data completeness, UoL will contact the participants (by phone or email) to chase up return of the accelerometer, if it is not returned in a timely manner. If the accelerometer is lost in the post, UoL will post a new accelerometer to the participant and ask them to wear it and complete the diary again. If the accelerometer is received back at UoL and the accelerometer data is incomplete (less than 4 valid days), a new accelerometer will be posted to the participant to allow them to provide the required data. The UoL will follow a SOP for the collection of this data.

## 9.2 Participants not progressing to randomisation

If the baseline questionnaires are not completed and/or valid accelerometer data (at least 4 valid days) is not recorded for the participant (after the participant is given an opportunity to re-wear the

accelerometer) within an appropriate time period (60 days from consent) they will be considered ineligible and will not be randomised into the trial.

If the accelerometer is not received back from the participant after they have received several reminders to return the device (via email, text message, telephone call or letter), a final letter will be sent to them. This final letter will offer the participant a £10 voucher in exchange for returning the device safely to the UoL. This is because the devices are expensive at £135 each and we need to minimise the loss of these devices.

### 9.3 Intervention

Participants recruited from an NHS setting will receive the Snacktivity™ intervention during their next consultation with an HCP. Participants recruited from a non NHS setting will receive a telephone call from a researcher who will deliver the intervention over the telephone. Details of the intervention can be found in section 7.2.

### 9.4 Usual care

Participants recruited from an NHS setting will receive the usual care information during their next consultation with an HCP. Participants recruited from a non NHS setting will receive a telephone call from a researcher who will deliver the information over the telephone. Details of usual care can be found in section 7.3.

### 9.5 Three month follow-up

#### 9.4.1. Questionnaires

A link to complete the three month follow-up questionnaires will be sent via email or SMS message to the participant up to 14 days before their follow-up date. If the questionnaires have not been completed within 7 days, the link will be resent up to two further times (7 and 14 days from the date originally sent). If the questionnaires have not been completed within 21 days of the original date sent, the trial office will call the participant to complete the questionnaires over the phone with them (if they agree). Three telephone call attempts will be made. A paper copy of the questionnaires can also be sent in the post. If the questionnaires have not been completed within 28 days of the follow-up due date, no further chasing of this data will take place. If data is completed online or returned after 28 days it will be entered onto the database but will be considered late.

#### 9.4.2. Accelerometer

An accelerometer will be set up by the UoL and posted to the participant between 7 and 14 days before their follow-up date. Participants will be asked to wear the accelerometer for up to 9 days (7 full days plus a partial day, the day before and day after the 7 full days) and to complete the accompanying diary (which records the time the participant went to sleep and the time they woke up). Once the participant has worn the accelerometer for the appropriate amount of time, they will post the accelerometer and the diary back to the UoL.

When received back, researchers at the UoL will check the accelerometer for completeness. If the accelerometer has not been worn for at least 4 valid days, the UoL will post a new accelerometer to the participant and request them to re-wear it and complete the diary again. The UoL will follow a SOP for the collection of this data.

Only once the follow-up questionnaires have been partially completed (at minimum) and at least 4 valid days of accelerometer have been recorded, will LU send the participant a £30 voucher as a thank you.

## 9.6 Twelve month follow-up

### 9.5.1. Questionnaires

A link to complete the twelve month follow-up questionnaires will be sent via email or SMS message to the participant up to 14 days before their follow-up date. If the questionnaires have not been completed within 7 days, the link will be resent up to two further times (7 and 14 days from the date originally sent). If the questionnaires have not been completed within 21 days of the original date sent, the trial office will call the participant to complete the questionnaires over the phone with them (if they agree). Three telephone call attempts will be made. A paper copy of the questionnaires can also be sent in the post If the questionnaires have not been completed within 28 days of the follow-up due date, no further chasing of this data will take place. If data is completed online or returned after 28 days it will be entered onto the database but will be considered late.

### 9.5.2. Accelerometer

All participants will be asked to wear an accelerometer at 12 months and will receive a £30 voucher as a thank you as detailed in section 9.4.2.

## 9.7 Schedule of Assessments

**Table 2:** Schedule of Assessments

| | | | From randomisation date | |
|---|---|---|---|---|
| **Visit** | **Screening** | **Baseline** | **3 months -14 /+ 28 days** | **12 months -14 /+28 days** |
| Eligibility screening form | x | | | |
| Physical Activity Vital Sign (to measure MVPA) | x | | | |
| Personal identifiers and demographics | | x | | |
| Height | | x | | |
| Weight | | x | x | x |
| Body Mass Index (BMI; calculated from height and weight) | | x | x | x |
| Current medications | | x | x | x |
| Smoking history | | x | | |
| Medical history | | x | | |
| Household income/composition | | x | | |
| Quality of life (EQ-5D-5L, ICECAP-A) | | x | x | x |
| Anxiety & depression (HADS (42)) | | x | x | x |
| Sedentary behaviours (WSQ (43), IPAQ sitting question only (44)) | | x | x | x |
| Enjoyment of physical activity (PACES) (45) | | x | x | x |

| | | | | |
|---|---|---|---|---|
| Confidence to engage in physical activity (Self-efficacy for Exercise) (46) | | x | x | x |
| Healthcare utilisation (resource use questionnaire) | | x | x | x |
| Habit strength (Self-report Habit Index; Snacktivity™ group) (47) | | | x | x |
| SnackApp use (intervention group) | | | x | x |
| Checklist of popular snacks (Snacktivity™ group only) | | | x | x |
| Feedback on Snacktivity™ consultation with HCP or researcher | | | x | |
| Single item exit questions (e.g. thoughts about Snacktivity™ trial) | | | x | x |
| Axivity (AX3) device | | x | x | x |

### 9.8 Withdrawal and changes in levels of participation

Informed consent is defined as the process of learning the key facts about a clinical trial before deciding whether or not to participate. It is a continuous and dynamic process and participants should be asked about their ongoing willingness to continue participation. Participants should be made aware at the beginning that they can freely withdraw (discontinue participation) from the trial (or part of) at any time. A participant may wish to cease to participate in a particular aspect of the trial. Participants found to be ineligible post randomisation should be followed up according to all trial processes and will still have their data analysed unless they explicitly change their level of participation.

The changes in levels of participation within the trial are categorised in the following ways:

**No trial intervention:** The participant would no longer like to receive the trial intervention but is willing to be followed up in accordance with the schedule of assessments and if applicable using any central UK NHS bodies for long-term outcomes (i.e., the participant has agreed that data can be collected and used in the trial analysis).

**No further data collection:** The participant is not willing to be followed up in any way for the purposes of the trial AND does not wish for any further data to be collected (i.e., only data collected prior to any changes of levels in participation can be used in the trial analysis).

The details of changes of levels in participation within trial (date, reason and category of status change) should be clearly documented in the source documents.

# 10. ADVERSE EVENT REPORTING

## 10.1. Definitions

**Table 3**: Adverse event reporting definitions

| | | |
|---|---|---|
| Severity Definitions | Mild | Awareness of signs or symptoms that do not interfere with the participant's usual activity or are transient and resolved without treatment and with no sequelae. |
| | Moderate | A sign or symptom, which interferes with the participant's usual activity. |
| | Severe | Incapacity with inability to do work or perform usual activities. |
| Adverse Event | AE | Any untoward medical occurrence in a participant participating in the trial which does not necessarily have a causal relationship with the intervention received. |
| Related Event | RE | An event which resulted from the administration of any of the research procedures. |
| Serious Adverse Event | SAE | An untoward occurrence that:<br>Results in death<br>Is life-threatening*<br>Requires hospitalisation or prolongation of existing hospitalisation<br>Results in persistent or significant disability or incapacity<br>Consists of a congenital anomaly/ birth defect<br>Or is otherwise considered medically significant by the Investigator** |
| Unexpected Event | UE | The type of event that is not listed in the protocol as an expected occurrence. |
| Related and Unexpected Serious Adverse Event | N/A | A SAE that meets both the definition of a Related and Unexpected Event. |

* The term life-threatening is defined as diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted.

** Medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the participant or may require intervention to prevent one of the other outcomes listed in the definitions above.

## 10.2. Adverse event reporting in Snacktivity

There is no reason to assume that this trial will lead to an excess of adverse events (AEs). The intervention consists of HCPs/researchers promoting short bouts of MVPA within everyday life and use of a commercially available physical activity tracker to monitor activity, along with a mobile app to log movement, none of which are likely to create harm. Furthermore, the promotion of physical activity by health professionals is already part of standard care and has been demonstrated as being low risk for all citizens in England as per the NHS Making Every Contact Count Campaign (48). Therefore, no AEs will be collected for this trial, however, the reporting HCP should still record any relevant events in the participant's medical records in accordance with normal Good Clinical Practice (GCP) policy (NHS Trusts/settings only).

## 10.3. Serious Adverse Advents reporting in Snacktivity™

**SAEs identified by an NHS Trust/setting**

For all SAEs identified by the recruiting site, the principal investigator (PI) or delegate must do one of the following:

1. **Record safety reporting-exempt SAEs** in the medical notes but **not report** them to the trial's office on an SAE form as per Section 10.3.1 Serious Adverse Events not requiring reporting to the trial office.

2. **Report SAEs to the trial office in a non-expedited manner**. This can only be done for the pre-defined subset of SAEs as per Section 10.3.2 Serious Adverse Events requiring non-expedited reporting to the trial office.

3. **Report SAEs to the trial office in an expedited manner** (within 24 hours of the site research team becoming aware of the event). All SAEs not covered by the above 2 categories must be reported as per Section 10.4 SAE Reporting process.

**SAEs identified by the trial team**

Participants will have no further trial contact with the recruiting site once the intervention/usual care information has been provided. In addition, participants recruited from non-NHS settings (e.g. social media) will not be under the care of a HCP, meaning the reporting method described above will not be possible. Therefore, the trial team will identify any potential SAEs from the three and twelve month questionnaires and complete an SAE form. If a participant contacts the trial team directly to inform them of a potential event, this will also be reported on an SAE form.

### 10.3.1. Serious Adverse Events not requiring reporting to the trial office

At whatever time they occur during an individual's participation, from the date that the intervention is started (date the participant has their consultation with the HCP or researcher) to the end of participant follow-up, the following are not considered to be critical to evaluations of the safety of the trial:

- Events related to any pre-existing conditions that the participant may have (pre-existing conditions are medical conditions that existed before the participant entered the trial, or for which they have already consulted medical advice, as identified on the baseline questionnaire (as per the diseases/conditions specified below†))
- Hospital visits for any elective procedures

**Table 4: Pre-existing conditions**

| | | |
|---|---|---|
| † | ➢ Cancer | ➢ Sarcopenia (loss of muscle strength) |
| | ➢ Type 1 diabetes | ➢ COPD/emphysema (Chronic obstructive pulmonary disease) |
| | ➢ Type 2 diabetes | ➢ Asthma |
| | ➢ High cholesterol | ➢ Kidney disease |
| | ➢ High blood pressure (hypertension) | ➢ Back pain resulting in time off work |
| | ➢ Heart disease, heart attack, angina, aneurysm (cardiovascular disease) | ➢ Rheumatoid arthritis |
| | ➢ Stroke | ➢ Osteoarthritis |
| | ➢ Depression or anxiety | ➢ Neurological condition (e.g. epilepsy, ME or MS) |
| | ➢ Dementia or Alzheimer's disease | ➢ Long COVID |
| | ➢ Osteoporosis (thinning of the bones) | ➢ Foot/ankle problem affecting patient's mobility |
| | ➢ Obesity | |

All events which meet the definition of serious must be recorded in the participant notes (except if the participant is recruited from a non-NHS setting), including the causality and severity, throughout the participant's time on trial, including follow-up, but for trial purposes these events do not require reporting on the SAE Form. Such events are "safety reporting exempt".

### 10.3.2. Serious Adverse Events requiring non-expedited reporting to the trial office

Where the safety profile is well established, the causal relationship between the intervention (or the participant's underlying condition), and the SAE, may be known. That is, such events are protocol-defined as "expected" and are listed in Table 5 as expected SAEs and will be collected on follow-up CRFs.

**Table 5: Non-expedited events**

| Event | CRF |
|---|---|
| Musculoskeletal and bone injuries/fractures | 3- and 12-month follow-up form |
| Trips and fall injuries | 3- and 12-month follow-up form |

### 10.3.3. Serious Adverse Events requiring expedited reporting to the trial office

All SAEs not listed in Sections 10.3.1 and 10.3.2 must be reported to the trial office on a trial specific SAE form within 24 hours of the site HCP becoming aware of the event.

As participants recruited via a non-NHS setting will not be under the care of an HCP the above reporting process to the trial office cannot be followed. The process for reporting SAEs for participants recruited via a non-NHS setting is detailed in section 10.4.

## 10.4. SAE Reporting process

**SAEs identified by an NHS Trust/setting**

If an NHS Trust/setting becomes aware that a participant has experienced an SAE which requires reporting on an SAE form, the PI or delegate should report the SAE to their own Trust in accordance with local practice and to the trial office. To report an SAE to the trial office, the PI or delegate must complete, date and sign the paper SAE form. Any other relevant, appropriately anonymised, data

should be submitted to the trial office using the information below in accordance with the timelines given in Section 10.3.2 and 10.3.3.

**To report an SAE or to submit any other relevant, appropriately anonymised, data, please send it to:**

Snacktivity@trials.bham.ac.uk

Where an SAE Form has been completed by someone other than the PI initially, the original SAE form must be countersigned by the PI to confirm agreement with the causality and severity assessments.

SAE forms will be completed on paper (and then entered into the database by the trial team) and a unique reference number will be assigned to each SAE by the trial team at BCTU. The site and the trial office should ensure that the SAE reference number is quoted on all correspondence and follow-up reports regarding the SAE and filed with the SAE in the ISF.

**SAEs identified by the trial team for participants recruited via an NHS Trust/setting**

If a potential SAE is identified on one of the follow up questionnaires or if the participant reports a potential SAE to the trial team directly, the trial team will complete as much of the SAE form as possible. This will then be sent to the recruiting site for additional information and review/assessment by the PI.

**SAEs identified by the trial team for participants recruited via a non-NHS setting**

If a potential SAE is identified on one of the follow up questionnaires or if the participant reports a potential SAE to the trial team directly, the trial team will complete an SAE form and send it to the trials central PI for review and assessment.

### 10.4.1. Assessment of causality of an SAE

**SAE identified by sites**

When completing the SAE form, the PI (or, throughout this section, a medically qualified delegate) will be asked to define the nature of the seriousness and causality (relatedness; see Table 6: Categories of causality) of the event.

In defining the causality, the PI must consider if any concomitant events or medications may have contributed to the event and, where this is so, these events or medications should be reported on the SAE form. It is not necessary to report concomitant events or medications which did not contribute to the event.

As per Table 6, all events considered to be ‘possibly’, ‘probably’, or ‘definitely’ related to the intervention will be reported by the trial office as ‘related’; all events considered at site to be ‘unlikely’ or ‘unrelated’ to the intervention will be reported by the trial office as ‘unrelated’. The same categorisation should be used when describing AEs and protocol-exempt SAEs in the source data.

**SAE identified by the trial team**

The trial team will complete the SAE form as much as possible from the information provided. If further information is required, the trial team will contact the participant directly. The SAE form will then be sent to the designated member of the investigator team for assessment as per Table 6.

**Table 6**: Categories of causality

| Category | Definition | Causality |
|---|---|---|
| Definitely | There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. | Related |
| Probably | There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. | |
| Possibly | There is some evidence to suggest a causal relationship. However, the influence of other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events or medication) | |
| Unlikely | There is little evidence to suggest there is a causal relationship. There is another reasonable explanation for the event (e.g., the participant's clinical condition, other concomitant events or medication). | Unrelated |
| Not related | There is no evidence of any causal relationship. | |

On receipt of an SAE form, the trial office will notify the clinical member of the co-investigator group or delegate(s) who will independently review the causality of the SAE. An SAE judged by the PI or clinical member of the co-investigator group or delegate(s) to have a reasonable causal relationship ("Related" as per Table 6: Categories of causality) with the intervention will be regarded as a related SAE. The severity and causality assessment given by the PI/investigator will not be downgraded by the clinical member of the co-investigator group or delegate(s). If the clinical member of the co-investigator group "or delegate(s)" disagrees with the PI or investigator's causality assessment, the opinion of both parties will be documented, and where the event requires further reporting, the opinion will be provided with the report.

#### 10.4.2. Assessment of expectedness of an SAE by the clinical member of the co-investigator group

The clinical member of the co-investigator group or delegate(s) will also assess all related SAEs for expectedness with reference to the criteria in Table 7: Categories of expectedness.

**Table 7**: Categories of expectedness

| Category | Definition |
|---|---|
| Expected | An adverse event that is consistent with known information about the trial related procedures or that is clearly defined in the relevant safety information. |
| Unexpected | An adverse event that is <u>not</u> consistent with known information about the trial related procedures. |

If the event is unexpected (i.e., it is not defined in the protocol as an expected event) it will be classified as a related and unexpected SAE.

The clinical member of the co-investigator group will undertake review of all SAEs and may request further information from the clinical team at site for any given event(s) to assist in this.

#### 10.4.3. Provision of SAE follow-up information

Following reporting of an SAE for a participant, the participant should be followed up until resolution or stabilisation of the event. Follow-up information should be provided using the SAE reference number provided by the trial office. Once the SAE has been resolved, all critical follow-up information has been received and the paperwork is complete, the electronic SAE form should be updated.

### 10.5. Reporting SAEs to third parties

The joint TSC and Data Monitoring Committee (DMC) may review any SAEs at their meetings.

The trial office will submit a progress report to the Research Ethics Committee (REC) and the Sponsor annually starting 12 months after the date of the favourable opinion was given. An electronic copy should be emailed to the REC within 30 days of the end of the reporting period.

The trial office will report all events categorised as Unexpected and Related SAEs to the REC and the Sponsor within 15 days of being notified.

Details of all unexpected and related SAEs and any other safety issue which arises during the course of the trial will be reported to the PIs. A copy of any such correspondence should be filed in the ISF and TMF.

### 10.6 Mortality

If mortality is related to a pre-existing condition (as per the diseases/conditions specified in Table 4), this should be documented on the SAE form and the Withdrawal & Change of Status Form. If mortality is deemed to have a possible causal relationship with the intervention, this should be documented on an SAE form.

## 11. DATA HANDLING AND RECORD KEEPING

### 11.1.Source data

Source data is defined as all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. In order to allow for the accurate reconstruction of the trial and clinical management of participants, source data will be accessible and maintained.

**Table 8**: Source data in Snacktivity™

| Data | Source |
|---|---|
| Participant Reported Outcome - Screening | Participants will be asked to answer the questionnaires directly into the trial database. The electronic record will be the source. If the participant requests to complete the questionnaires on paper, the paper questionnaires will be the source. The paper forms will be transcribed into the database by trial office staff. |
| Participant Reported Outcomes | Participants will be asked to answer the questionnaires directly into the trial database and upload a picture of their weight. The electronic |

| | |
|---|---|
| (Questionnaires and weight) - baseline, 3 and 12 month follow-up | record will be the source. If the participant requests to complete the questionnaires on paper, the paper questionnaires will be the source. The paper forms will be transcribed into the database by trial office staff. |
| Recruitment | The original record of the randomisation is the source. It is held on BCTU servers as part of the randomisation and data entry system. |
| Accelerometer data | Data is downloaded from the accelerometers and stored on the secure servers at UoL. The downloaded data is the source. |
| Snacktivity™ consultation or telephone/video call | 15-20% of intervention and 25% of usual care consultations or telephone/video calls will be audio recorded by the HCP/Researcher. The audio recording will be the source. |
| Fitbit™ and SnackApp data | Data is downloaded from the Fitbit™ and SnackApp and stored on the secure servers at LU. The downloaded data is the source. |
| Withdrawal | Where a participant expresses a wish to withdraw, the conversation detail will be recorded on the electronic Withdrawal & Change of Status CRF which is the source. |

### 11.2. Case Report Form (CRF) completion

The CRFs will include (but will NOT be limited to) the following Forms (see Table 9: Case report forms in ).

**Table 9**: Case report forms in Snacktivity™

| Form Name | Schedule for submission |
|---|---|
| Screening Form | At the point of screening |
| Informed Consent Form | At the point of consent |
| Baseline CRF | As soon as possible after consent |
| Accelerometer CRF | As soon as possible after consent |
| Fitbit™ and SnackApp details | As soon as the Fitbit has been issued |
| Randomisation CRF | At the point of randomisation |
| Snacktivity™/usual care consultation/researcher call details CRF | As soon as possible after randomisation |
| Three month follow-up CRF | As close to the three month follow-up time point as possible |
| Twelve month follow-up CRF | As close to the twelve month follow-up time point as possible |
| Completion of accelerometer follow-up CRF | As soon as the accelerometer data has been confirmed as complete |

| | |
|---|---|
| Withdrawal and change of status CRF | At the point of change of status, withdrawal or death |
| Serious adverse event form | At the point of being aware of an SAE |

A CRF should be completed for each individual participant.

### 11.3. Participant completed questionnaires

Participants will be sent the baseline, three- and twelve-month follow-up questionnaires electronically via a link sent to their email address or mobile phone. If paper copies are requested, they will be posted to the participant with a freepost envelope included to allow the participant to return them to BCTU. If a paper copy of the questionnaires is completed, once returned to BCTU, a member of the trial team will enter the data into the database and store the paper forms securely in locked filing cabinets.

### 11.4. Data management

Processes will be employed to facilitate the accuracy and completeness of the data included in the final report. These processes will be detailed in the trial specific Data Management Plan and include the processes of data entry and self-evident corrections on the trial data.

Data entry will be completed by the trial office and participants via a bespoke trial database developed by BCTU. The data capture system will conduct automatic range checks for specific data values to ensure high levels of data quality.

The trial office will endeavour to obtain any missing data on the questionnaires by contacting the participant directly (via telephone or email). Overdue and missing data will be reviewed on a fortnightly basis.

### 11.5.Self-evident corrections

Self-evident corrections will be permitted by the trial office on paper questionnaires only. For example:

- Contingent fields: When a response to a question determines, to a degree, the response required by a second question, then conflicts in the responses can be resolved by the data entry clerk e.g. Has the person had procedure “x”? If yes, state type. If the response to the first question is “no”, yet the type of procedure is stated, it is self-evidently true that the initial response was incorrect.

### 11.6.Data security

#### 11.6.1 University of Birmingham

UoB has policies in place, which are designed to protect the security, accuracy, integrity and confidentiality of Personal Data. The trial will be registered with the Data Protection Officer at UoB and will hold data in accordance with the Data Protection Act (2018 and subsequent amendments). The trial office has arrangements in place for the secure storage and processing of the trial data which comply with UoB policies.

The Trial Database System incorporates the following security countermeasures:

**Physical security measures:** restricted access to the building, supervised onsite repairs and storages of back-up tapes/disks are stored in a fire-proof safe.

**Logical measures for access control and privilege management:** including restricted accessibility, access controlled servers, separate controls of non-identifiable data.

**Network security measures:** including site firewalls, antivirus software and separate secure network protected hosting.

**System management:** the system will be developed by the Programming Team at the Trial Office and will be implemented and maintained by the Programming Team.

**System design:** the system will comprise of a database and a data entry application with firewalls, restricted access, encryption and role based security controls.

**Operational processes:** the data will be processed and stored within BCTU.

**System audit:** The system will benefit from the following internal/external audit arrangements:

- Internal audit of the system
- Periodic IT risk assessment

**Data Protection Registration:** UoB's Data Protection Registration number is Z6195856.

The audio recordings will be kept by BCTU as they are the source data. All audio recordings will be transcribed by a commercial company who will have a confidentiality agreement in place with LU. The commercial company will remove and destroy all personal identifiable data from the transcripts and participants will be coded and referred to in study documents using a unique identification number.

#### 11.6.2 Loughborough University

Data from the physical activity tracker (e.g. Fitbit™) is stored on the device until it can be wirelessly transferred to the Fitbit™ App via a Bluetooth Low Energy (BLE) connection which is installed on the participant's mobile phone. Data transferred to the app is stored there until it can be wirelessly transferred to Fitbit's servers. Upon initial set up, the participant will grant permission to the SnackApp to access the metrics measured by the Fitbit™ via a request made to the Companion Application Programming Interface (API) within the Fitbit™ App. The requested metrics along with any computed metrics and the SnackApp engagement analytics will be stored on a dedicated encrypted server. The servers are based in the UK (London) and are Google servers and the data is encrypted at rest (further details can be found at https://cloud.google.com/security/encryption-at-rest/default-encryption last accessed 24/01/2024) and in transit over https. Cuttlefish Multimedia (who developed the SnackApp) have their own in-house infrastructure team who will manage the servers. All data will be stored centrally in a secure PostgreSQL database. The user account information (including personal identifying information, passwords, etc.) will be stored in a distinct data table from the app analytic activity. Anonymised Fitbit™ and SnackApp analytics will be downloaded from a password protected bespoke built Customer Relationship Management (CRM) reporting system, accessed online and hosted on a dedicated encrypted server. Anonymised data will be downloaded to a password protected timestamped excel spreadsheet and stored on the University's secure server for 10 years after the completion of the programme grant.

#### 11.6.3 University of Leicester

Accelerometer data will be held in a trial specific folder on UoL secure servers. Access to the folder will be restricted to Snacktivity™ researchers only. All trial data will be kept for 10 years or the minimum determined time by the funder, whichever is longer.

### 11.7. Archiving

It is the responsibility of the PI to ensure all essential trial documentation and source documents at their site are securely retained for the contractual period. Archiving will be authorised by BCTU on

behalf of Birmingham Community Healthcare NHS Foundation Trust (BCHC) following submission of the end of trial report. No documents should be destroyed without prior approval from the BCTU Director or their delegate.

The TMF will be stored at BCTU for at least 3 years after the end of the trial. Long-term offsite data archiving facilities will be considered for storage after this time; data will be stored securely and confidentially for at least 25 years. BCTU has standard processes for both hard copy and computer database legacy archiving.

# 12. QUALITY CONTROL AND QUALITY ASSURANCE

## 12.1. Site set-up and initiation

All PIs will be asked to sign the necessary agreements including a Site Signature and Delegation log between the PI and the Trial Office and supply a current Curriculum vitae (CV) and GCP certificate. All members of the site research team are required to sign the Site Signature and Delegation Log, which details which tasks have been delegated to them by the PI. The Site Signature and Delegation Log should be kept up to date by the PI. It is the PI's responsibility to inform the trial office of any changes in the site research team.

Prior to commencing recruitment, each recruiting site will undergo a process of site initiation, either a meeting or a teleconference, at which key members of the site research team are required to attend, covering aspects of the trial design, protocol procedures, safety reporting, principles of GCP, collection and reporting of data and record keeping. Sites will be provided with an ISF containing essential documentation, instructions, and other documentation required for the conduct of the trial.

## 12.2. Monitoring

The central and on-site monitoring requirements for this trial have been developed in conjunction with the trial specific risk assessment and are documented in the trial specific monitoring plan.

### 12.2.1. On-site monitoring

For this trial, all sites will be monitored in accordance with the trial risk assessment and monitoring plan. Any monitoring activities will be reported to the trial office and any issues noted will be followed up to resolution. PIs and site research teams will allow the Snacktivity™ trial staff access to the ISF. The monitoring will be conducted by BCTU/UoB staff.

### 12.2.2. Central monitoring

The trial office will check eConsent forms and CRFs for compliance with the protocol, data consistency, missing data and timing at a frequency and intensity determined by the Data Management Plan (DMP).

## 12.3. Audit and inspection

The Investigator will permit trial-related monitoring, audits, ethical review, and regulatory inspection(s) at their site and provide direct access to the ISF. The investigator will comply with these visits and any required follow-up. Sites are also requested to notify the trial office of any relevant inspections or local audits.

### 12.4. Notification of Serious Breaches

The sponsor is responsible for notifying the REC of any serious breach of the conditions and principles of GCP in connection with that trial or of the protocol relating to that trial. Sites are therefore requested to notify the trial office of any suspected trial-related serious breach of GCP and/or the trial protocol as soon as they become aware of them. Where the trial office is investigating whether or not a serious breach has occurred, sites are also requested to co-operate with the trial office in providing sufficient information to report the breach to the REC where required and in undertaking any corrective and/or preventive action.

Sites may be suspended from further recruitment in the event of serious and persistent non-compliance with the protocol and/or GCP, and/or poor recruitment.

## 13. END OF TRIAL DEFINITION

The end of trial will be the date of the last data query resolution. This will allow sufficient time for the completion of protocol procedures, data collection and input and data cleaning. The trial office will notify the REC and the Sponsor within 90 days of the end of trial. Where the trial has terminated early, the trial office will notify the REC within 15 days of the end of trial. The trial office will provide the REC and the Sponsor with a summary of the clinical trial report within 12 months of the end of trial.

## 14. STATISTICAL CONSIDERATIONS

### 14.1. Sample size

The sample size is based on detecting a difference of 30 minutes in weekly MVPA between the two treatment groups (Snacktivity™ and usual care) with a standard deviation of 120 minutes. We have purposefully proposed a relatively small standardised effect size (0.25) to ensure it is consistent with the intervention we are proposing. To detect this difference with 80% power (alpha=0.05) and allowing for 30% attrition (composed of 20% loss to follow-up/ withdrawal and 10% incomplete/ unusable accelerometer data), we require 724 participants (362 per group). We aim to recruit 36-37 participants per month during the 6-month internal pilot and 50-51 participants per month over the remaining 10 months (total recruitment time 16 months). If our recruitment rates exceed our target rates, we will consider increasing our sample size to 966 participants to achieve 90% power.

### 14.2. Analysis of outcomes

A separate Statistical Analysis Plan (SAP) will be produced and will provide a more comprehensive description of the planned statistical analyses. A brief outline of these analyses is given below.

The primary comparison groups will be composed of those randomised to the Snacktivity™ intervention versus those randomised to the usual care group. In the first instance, all analyses will be based on the intention to treat principle, i.e. participants will be analysed in the treatment group to which they were randomised irrespective of adherence to randomised intervention or other protocol deviation. For all outcomes, appropriate summary statistics and differences between groups e.g., mean differences, risks ratios, will be presented, along with confidence intervals. Where possible intervention effects will be adjusted for the minimisation variables listed in Section 6.5, and baseline values (where appropriate and available).

#### 14.2.1. Primary outcome

In participants who have at least 4 days of valid axivity (AX3) wear time, the primary outcome of MVPA will be expressed as a weekly average time (scaled as appropriated based on number of valid wear days) and reported by group using means and standard deviations. A mixed-effects repeated measures model will be fitted and results presented as adjusted mean differences and 95% confidence intervals at each time point (3 and 12 months), with 12 months being the primary time point. Time will be included as a categorical (fixed) variable in the model. To allow for a varying treatment effect over time, a time by treatment interaction parameter will be included in the model as standard. A general 'unstructured' covariance structure will be assumed. Longitudinal plots of the mean values over time by treatment group will be produced for visual inspection of the data.

#### 14.2.2. Secondary outcomes

Secondary outcomes of a continuous nature (measured at 3 and 12 months) will be analysed as per the primary outcome. Secondary outcomes which are considered binary (e.g. the proportion of participants meeting the guidance amount of 150 minutes of MVPA per week) will be summarised using frequencies and percentages. A regression model will be fitted and results presented as adjusted risk ratios, risk differences and 95% confidence intervals. Secondary outcomes which are collected in the Snacktivity™ group only will be presented using summary statistics only.

#### 14.2.3. Planned subgroup analyses

Subgroup analyses will be limited to the same variables used in the minimisation algorithm (section 6.5) and performed on the primary outcome only. The effects of these subgroups will be examined by including an intervention group by subgroup interaction parameter in the regression model, which will be presented alongside the effect estimate and 95% confidence interval within subgroups. The results of subgroup analyses will be treated with caution and will be used for the purposes of hypothesis generation only.

#### 14.2.4. Missing data and sensitivity analyses

Every attempt will be made to collect full follow-up data on all participants; it is thus anticipated that missing data will be minimal. Participants with missing primary outcome data will not be included in the primary analysis in the first instance. This presents a risk of bias, and sensitivity analyses will be undertaken to assess the possible impact of the risk. Full details will be included in the SAP.

### 14.3. Planned final analyses

The primary analysis for the trial will occur once all participants have completed the 12-month follow-up assessment and corresponding outcome data has been entered onto the trial database and validated as being ready for analysis.

## 15. HEALTH ECONOMICS

A separate Health Economics Analysis Plan will be produced and will provide a more comprehensive description of the planned analyses. A brief outline of these analyses is given below.

### 15.1. Within-trial economic evaluation

All economic analyses will be conducted on an intention to treat basis comparing the intervention with the control group as randomised. The costs related to Snacktivity™ will be collected by the study team. Staff time (and staff grade) will be recorded in both arms to estimate the incremental difference in staff cost from delivering the physical activity advice. The study team will record any

costs associated with maintaining the App-tracker device throughout the 12-month follow-up period. Participants will report any health care resource use during the past 3 months at baseline and 3 months, and during the past 6 months in the 12 month follow-up questionnaire. This resource use will be combined with the Unit costs of Health and Social Care (for primary care) (49), and with NHS reference costs (for secondary care) (50). Any prescribed medication will be costed using the British National Formulary. Productivity will be self-assessed and self-reported. Participants will be asked to report productivity based on the extent to which health problems affected productivity in the past 3 months (at baseline and at 3 months) and in the past 6 months at 12 months measured on a 10-point scale. This will be converted to wages using median weekly earnings, assuming a 1-point decrement on the scale equates to a 10% loss in earnings (51). Self-reported number of days off work in the last 3 months will be converted to wages using median weekly earnings.

Wellbeing and HRQOL effects will be measured at baseline, 3 and 12 months using the ICECAP-A, and the EQ-5D-5L, respectively. The responses to these questionnaires will be combined with the respective tariff scores to estimate the incremental wellbeing effects and quality-adjusted life year (QALY) effects at 12 months, for the intervention versus the control arm.

The costs will then be combined with the outcomes to form a cost-effectiveness analysis (CEA), where the result will be expressed as 'cost per recommended MVPA per week' achieved. This will be conducted from a health care perspective. A cost-utility analysis will combine the costs with outcome to estimate the 'cost per QALY', conducted from a health care perspective. In addition, a 'cost per capability' achieved will be estimated by combining the costs from a broader perspective (including productivity costs) offset against improvements in wellbeing, measured using the ICECAP-A. The above analyses will be conducted as a within-trial economic evaluation, therefore only using data collected over the 12-month period. All incremental costs and outcomes will be presented as adjusted difference in means with a 95% confidence interval and p-value. Discounting will not be relevant as the trial is within 1 year. Missing data will be explored and imputed using the most appropriate imputation technique. Sensitivity analysis will be conducted to explore how sensitive the results are to assumptions made during the analyses.

### 15.2. Model-based economic evaluation

If the intervention demonstrates superiority in terms of the primary outcome (difference of 30 minutes of MVPA achieved per week) in comparison to usual care, Markov decision modelling will be used to extrapolate beyond trial findings and will be populated using both data on costs and outcomes within the trial and reviews of previously published studies. This will allow linkage of intermediate activity outcomes to mortality and morbidity, from a health and social services perspective. The exact nature of the modelling and the health states will be determined using information from a review of previously published modelling studies of interventions to promote physical activity and expert opinion. Model parameters will be sought from the trial and review of previously published studies.

## 16. SUB-STUDIES

There are no sub-studies within this trial.

# 17. TRIAL ORGANISATIONAL STRUCTURE

## 17.1. Sponsor

The Birmingham Community Healthcare NHS Foundation Trust (BCHC) and Loughborough University are the co-sponsors for this trial.

## 17.2. Coordinating centre

The School for Sport, Exercise and Health Sciences, Loughborough University is the lead institution. As CI for the study, Professor Amanda Daley will have overall responsibility for the scientific and strategic oversight. Loughborough University are responsible for the distribution and management of the Fitbits and the SnackApp used in the Snacktivity™ intervention. The day-to-day management of the trial will be coordinated by the trial office at BCTU based at the UoB. The University of Leicester researchers are responsible for all tasks relating to the accelerometer devices.

## 17.3. Trial Management Group (TMG)

The TMG includes those individuals responsible for the day-to-day management of the trial, including the CI, Programme Manager, Trial Statistician(s), Trial Programmer, Trial Manager, Data Manager, Research Associate (RA), Public Advisory Group (PAG) lead and PAG representatives. The role of the group is to monitor all aspects of the conduct and progress of the trial, ensure that the protocol is adhered to and take appropriate action to safeguard participants and the quality of the trial itself.

The TMG will meet regularly (approximately every month) to ensure successful implementation of the trial. They will monitor participant recruitment; any departure from the expected recruitment rate will be dealt with according to the specific issues that arise.

## 17.4. Co-investigator group

The Co-investigator group, an extended TMG, will comprise all members of the co-applicant group and the members of the TMG to review progress, troubleshoot and plan strategically.

## 17.5. Joint Trial Steering Committee and Data Monitoring Committee

A joint independent TSC/DMC has been created for the Snacktivity™ trial. The TSC/DMC will meet via teleconference/face-to-face at least twice a year or as required depending on the needs of the trial. This is a general population study, the intervention is considered low risk, and no serious adverse events are expected as a result of the intervention.

Membership and duties/responsibilities are outlined in the DMC/TSC Terms of Reference. In summary, the joint TSC/DMC will provide overall oversight of the trial, including the practical aspects of the trial, as well as ensuring that the trial is run in a way which is both safe for the participants and provides appropriate data to the sponsor and investigators.

Additional meetings may be called if recruitment is much faster than anticipated and the joint TSC/DMC may, at their discretion, request to meet more frequently or continue to meet following completion of recruitment. An emergency meeting may also be convened if a safety issue is identified. The joint TSC/DMC may consider recommending the discontinuation of the trial if the recruitment rate or data quality are unacceptable, or if any issues are identified which may compromise participant safety.

### 17.6. Public and patient involvement

This trial is supported by a PAG that consists of members of the public from a range of backgrounds with different attitudes towards physical activity. The PAG is facilitated by a public involvement Lead and PAG members contributed to the development of the Snacktivity™ intervention through attending quarterly meetings or completing tasks remotely (e.g. providing feedback on documentation) in earlier work packages on this programme grant. PAG member(s) will be part of the TMG and joint TSC/DMC groups. All PAG members will be offered an honorarium for involvement, which aligns to the NIHR Centre for Engagement and Dissemination recommendations.

### 17.7. Finance

The research costs of the trial are funded by the NIHR (Programme Grants for Applied Research, reference number: RP-PG-0618-20008) awarded to Professor Amanda Daley employed by Loughborough University.

## 18. ETHICAL CONSIDERATIONS

The trial will be conducted in accordance with the UK Policy Framework for Health and Social Care Research and applicable UK Acts of Parliament and Statutory Instruments (and relevant subsequent amendments), which includes the Data Protection Act 2018 and the Principles of GCP as set out in the UK Statutory Instrument (2004/1031; and subsequent amendments). The protocol will be submitted to and approved by the REC prior to the start of the trial.

Before any participants are enrolled into the trial, the PI at each site is required to obtain the necessary local approval.

It is the responsibility of the PI to ensure that all subsequent amendments gain the necessary local approval. This does not affect the individual clinicians' responsibility to take immediate action if thought necessary to protect the health and interest of individual participants.

## 19. DATA PROTECTION AND CONFIDENTIALITY

Personal data and sensitive personal data recorded on all documents will be regarded as strictly confidential and will be handled and stored in accordance with the Data Protection Act 2018 (and subsequent amendments). Personal data categories that will be collected include: name, DOB, email address, postal address, health information and medical history.

Participants will only be identified by their unique trial identification number on CRFs and on any correspondence with the trial office.

Invitation/screening data including sex and age will be collected on all participants invited to take part in the study to help with analysis. This data will be anonymous and not linked to any other personal information.

In the case of specific issues and/or queries from the regulatory authorities, it will be necessary to have access to the complete trial records. Representatives of the Snacktivity™ trial team and sponsor may be required to have access to participants' notes for quality assurance purposes, but participants should be reassured that their confidentiality will be respected at all times. The trial office will maintain the confidentiality of all participant data and will not disclose information by which participants may be identified to any third party.

Participants will acknowledge that researchers at UoB, LU and UoL will have access to their personal data to allow them to perform their delegated tasks.

## 20. FINANCIAL AND OTHER COMPETING INTERESTS

There are no financial or other competing interests related to the results of this trial. Members of the joint TSC/DMC are required to provide declarations on potential competing interests as part of their membership of the committee. Authors are similarly required to provide declarations at the time of submission to publishers.

## 21. INSURANCE AND INDEMNITY

### 21.1 University of Birmingham

The UoB has in place clinical trials indemnity coverage for this trial which provides cover to the University for harm which comes about through the University's, or its staff's, negligence in relation to the design or management of the trial and may alternatively, and at the University's discretion provide cover for non-negligent harm to participants.

With respect to the conduct of the trial at participating clinical sites and other clinical care of the participants, responsibility for the care of the participants remains with the NHS organisation responsible for the clinical site and is therefore indemnified through the NHS Litigation Authority.

### 21.2 Loughborough University

LU maintains Public Liability insurance which covers the activities which its researchers have responsibility for during this trial.

### 21.3 University of Leicester

The UoL provides insurance for staff whilst undertaking research.

## 22. ACCESS TO FINAL DATASET

The final dataset will be available to members of the Trial Management and co-applicant group who need access to the data to undertake the final analyses.

Requests for data generated during this trial will be considered by BCTU. Data will typically be available six months after the primary publication unless it is not possible to share the data (for example: the trial results are to be used as part of a regulatory submission, the release of the data is subject to the approval of a third party who withholds their consent, or BCTU is not the controller of the data).

Only scientifically sound proposals from appropriately qualified Research Groups will be considered for data sharing. The request will be reviewed by the BCTU Data Sharing Committee in discussion with the CI and, where appropriate (or in absence of the CI) any of the following: the trial Sponsor, the TMG, or independent TSC/DMC.

A formal Data Sharing Agreement (DSA) may be required between respective organisations once release of the data is approved and before data can be released. Data will be fully de-identified (anonymised) unless the DSA covers transfer of participant identifiable information. Any data transfer will use a secure and encrypted method.

## 23. PUBLICATION PLAN

Outputs from this trial will be submitted for publication in peer reviewed journals and the findings of the trial will be made public. Manuscripts will be prepared by the writing group as defined in the trial publication plan. Manuscripts should be submitted to the TMG in a timely fashion and in advance of being submitted for publication to allow time for review. In all publications, authors should acknowledge that the trial was performed with the support of NIHR, BCHC and BCTU. Intellectual property rights will be addressed in the Clinical Trial Site Agreement between Sponsor and site.

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