Cadence Study

A feasibility study and pilot RCT to establish methods for assessing the acceptability, and clinical & cost effectiveness of Enhanced Psychological Care (EPC) in cardiac rehabilitation (CR) services

Adverse Event Reporting:

Standard Operating Procedure for Cardiac Rehabilitation Teams and Researchers

Adverse Event (AE)

An **Adverse Event (AE)** is any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in participants, users or other persons **whether or not related to any research procedures or to the intervention.**

Non-serious adverse events which are not related to study procedures or to the study intervention will **not** be reported in this study.

Adverse Reaction (AR)

An adverse event judged by the reporting cardiac rehabilitation nurse or researcher as having a reasonable causal relationship to study procedures and/or to the intervention will be considered an **Adverse Reaction (AR).** The expression 'reasonable causal relationship' means to convey, in general, that there is evidence or argument to suggest a causal relationship. In this study, we define this as an adverse reaction that is 'possibly', 'probably' or 'definitely' related to study participation or the study intervention.

The reporting nurse or researcher will assess the causal relationship between reported events and study participation or the study intervention according to the standardised guidance given below:

Relationship	***Description***
Unrelated	*There is no evidence of any causal relationship*
Unlikely	*There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the study treatment/procedure). There is another reasonable explanation for the event (e.g. the participant's clinical condition, other concomitant treatment).*
Possible	*There is some evidence to suggest a causal relationship (e.g. because the event occurs within a reasonable time after administration of the trial treatment/procedure). However, the influence of other factors may have contributed to the event (e.g. the participant's clinical condition, other concomitant treatments).*
Probable	*There is evidence to suggest a causal relationship and the influence of other factors is unlikely.*
Definitely	*There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out.*

If there is any uncertainty about the relationship of the event to study participation or the study intervention, the nurse or researcher should seek guidance from the Chief Investigator or a Responsible Clinician.
If you are alerted to an **Adverse Event which meets the criteria for an Adverse Reaction,** please contact the Responsible Clinician for your site immediately to discuss the event and seek advice about any further action that may be required. The Responsible Clinician could be the Chief Investigator (Professor John Campbell) or a clinician from the Research Team delegated on the Site Delegation Log to manage adverse events on behalf of the site Principal Investigator. You may be asked to complete an **Adverse Reaction & Potentially Serious Adverse Event or Reaction Recording Form** (see Supplementary material) to record details of the event.

Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR)

An adverse event can be further classified as a **Serious Adverse Event (SAE) or a Serious Adverse Reaction (SAR)** if the event:

- Results in death
- Is life threatening
- Requires hospitalisation or prolongs existing hospitalisation
- Results in significant or persistent disability or incapacity
- Relates to imminent suicidal intentions (defined as being 'Actively Suicidal' (Level C) when considering the participant's responses to further questions outlined the study self-harm/suicide protocol or actual self-harm/suicidal actions by a study participant
- Leads to any other condition, judged significant by a clinician.

An adverse event meeting any one of these criteria will be a **Serious Adverse Event (SAE).** An adverse reaction meeting any one of these criteria will be a **Serious Adverse Reaction (SAR).**

In this study, all serious events (SAEs and SARs) will be reported, regardless of their relatedness to study participation or the study intervention. Any non-serious adverse events (regardless of relatedness) will not be reported.

****Immediate Action is required for reporting an SAE or an SAR****

If you are alerted to an **AE or an AR which you suspect might be an SAE or an SAR,** please make immediate contact with the Chief Investigator (Professor John Campbell) or the Responsible Clinician for your site. The Responsible Clinician could be the local Principal Investigator or a clinician from the Research Team delegated to manage adverse events by the site Principal Investigator.

An immediate report (within 24 hours of a SAE or SAR coming to light) must be made by the Chief Investigator orally or in writing to the research sponsor (Royal Devon & Exeter NHS Foundation Trust). Therefore, you should telephone the Chief Investigator (Professor John Campbell) or the Responsible Clinician nominated on your Site Delegation Log to manage adverse events on behalf of the Principal Investigator. If you are unable to speak to either the Chief Investigator or the Responsible Clinician, and have left answer phone messages, it is important that you also telephone or e-mail the Cadence study team (Dr Christine Wright, Dr Suzanne Richards, or Ms Julie Chudley).

Please complete an 'Adverse Reaction & Potentially Serious Adverse Event or Reaction Recording Form' and fax a copy to the Exeter site immediately (XXX). Please telephone or e-mail the Cadence study team (Dr Christine Wright, Dr Suzanne Richards, or Ms

Julie Chudley) to alert them to the fact that you are sending the fax. The immediate report must be followed by a detailed written report of the event.

The Chief Investigator must complete a 'Serious Adverse Event or Reaction (SAE/SAR) Report Form' (see Appendix 2) and send a copy of the form with a detailed written report to the main Research Ethics Committee (South West REC) and to the Cadence Trial Steering Committee (TSC) and the Data Monitoring Committee (DMC; (if convened) **within 15 days** of the Chief Investigator becoming aware of the event. This will be handled by the lead site (Exeter).

At 5 month (feasibility and pilot trial phases) and 8 month (pilot trial only) study follow-up assessments, information about AE/ARs and SAE/SARs that might have occurred since the previous visit should be elicited from the participant by the researcher. If a participant (or their cardiac rehabilitation nurse, GP, or next of kin) discloses an AR or an SAE/SAR, please document it using the **'Adverse Reaction & Potentially Serious Adverse Event or Reaction Recording Form'**.

As Cadence is a non-CTIMP, we are not required to log all non-serious AE's, however the **'Adverse Reaction & Potentially Serious Adverse Event or Reaction Recording Form'** will allow the research team to monitor and record all AR's and those when it is not immediately clear if the adverse event or reaction falls into the SAE or SAR category.

General completion guidelines

Ask the participant the start and end date/time of the event. If they cannot remember then enter as accurate an estimate as possible. Document the outcome of the event and any actions taken. Confirm it with the Responsible Clinician for your site and ask them to countersign it.

Please note that ALL instances where the self-harm/suicide risk protocol is enacted must be recorded in the usual manner on the Risk Assessment Form and countersigned by the site lead or a nominated deputy.

Cadence study team contact details

Chief Investigator	Professor John Campbell	*<Contact details removed>*
Responsible Clinicians	Professor John Campbell Professor Chris Dickens	*<Contact details removed>* *<Contact details removed>*
Project Manager/Academic Lead	Dr Suzanne Richards	*<Contact details removed>*
Trial Researcher	Dr Christine Wright	*<Contact details removed>*
Study Administrator	Ms Julie Chudley	*<Contact details removed>*
Confidential study fax number	*<Contact details removed>*	

Supplementary material

Adverse Reaction & Potentially Serious Adverse Event or Reaction Recording Form

Date of incident:	Participant ID:
Details of incident: Outcome:	

To determine whether this is a 'serious' adverse event/reaction, please tick below all that apply:

Fatality	☐
Life-threatening	☐
Hospitalisation or prolongation of current hospitalisation	☐
Persistent or significant disability or incapacity	☐
Imminent suicidal intentions or actual self-harm/suicidal action	☐
Other (please describe)	☐
None of the above	☐

Additional relevant information:

Action taken by rehabilitation specialist or researcher (if any):

Name of Rehabilitation Specialist or Researcher (BLOCK CAPITALS)**:**	**Date:**	**Signature:**
Name of Chief Investigator or Responsible Clinician* (BLOCK CAPITALS)**:**	**Date:**	**Signature:**

* The Responsible Clinician could be the local Principal Investigator or a clinician from the research team delegated to manage adverse events on the Site Delegation Log.

Please fax completed Reporting Forms to the study team on XXX – if possible, within 24 hours of the event coming to light.

If the event clearly meets any of the criteria listed above for a 'Serious Adverse Event' or 'Serious Adverse Reaction', please e-mail or telephone Dr Christine Wright, Dr Suzanne Richards or Ms Julie Chudley to inform the study team that the Reporting Form is being faxed.

Serious Adverse Event or Serious Adverse Reaction (SAE or SAR) Report Form

The Chief Investigator should report any SAE or SAR to the sponsor **within 24 hours**, orally or in writing.

The immediate report must be followed by a detailed written report on the event, using the form below.

A copy of this form must also be sent to the main Research Ethics Committee and TSC/DMEC **within 15 days** of the Chief Investigator becoming aware of the event.

1. Details of Chief Investigator

Name:	Professor John Campbell
Address:	XXX
Telephone:	XXX
Email:	XXX
Fax:	XXX

2. Details of Study

Full title of study:	Cadence: A feasibility study and pilot RCT to establish methods for assessing the acceptability, and clinical & cost effectiveness of Enhanced Psychological Care (EPC) in cardiac rehabilitation (CR) services
Name of main REC:	NRES Committee South West – Exeter
REC reference:	14/SW/0139
Research sponsor:	Royal Devon & Exeter NHS Foundation Trust
ISRCTN	34701576
Sponsor's reference for this report (if applicable):	HTA Outline Bid (12/189CB)

3. Details of Participant affected by the Event

Participant's Study ID:	
Initials:	
Date of birth:	
Gender:	

4. Circumstances of the Event

Date and time of event onset:	
Location of event:	
Date and time of event end (or duration)	
Details of the event (attach further details if required): *Include full description of the event or reaction, including body site affected, reported signs and symptoms and diagnosis where appropriate.*	
What is your assessment of the implications, if any, for the safety of study participants and how will these be addressed?	

5. Assessment and Categorisation of the Event

Please categorise this event, ticking all appropriate options in each section (intensity, causality, expectedness, seriousness):

Intensity: *Maximum intensity up until time of this report*	☐ Mild ☐ Moderate ☐ Severe		
Causality: *Relationship to study participation or the study intervention*	☐ Not likely ☐ Unlikely to be related ☐ Possibly related ☐ Probably related ☐ Definitely related		
Expectedness:	☐ Expected ☐ Unexpected (i.e. not described in protocol, or scientific literature)		
Seriousness:	☐ Not serious ☐ Results in death* ☐ Life threatening* ☐ Results in hospitalisation or prolongation of existing hospitalisation* ☐ Results in persistent or significant disability or incapacity* ☐ Imminent suicidal intentions or actual self-harm/suicidal action* ☐ Other (please specify)*		
Assessed by:	**(Print name)**	**Signed by:**	**Signature**

6. Declaration of Cadence Chief Investigator or Deputy

I confirm that the contents of this form are accurate and complete.

Name of Chief Investigator or Deputy: (BLOCK CAPITALS)	
Signature:	
Date of report submission:	

7. Record of notifications

	Notified by (print name)	Signature	Date of notification
Sponsor notified:			
Main REC notified:			
TSC/DMEC notified:			

8. Acknowledgement of Receipt by Research Ethics Committee (REC)

The NRES Committee South West – Exeter acknowledges receipt of the above.

Name: (BLOCK CAPITALS)	
Position on REC:	
Date:	
Signature:	

Signed original to be sent back to the Chief Investigator; copy to be kept for information by main REC.