

Patient information sheet – Non-Randomised Participants

TITLE/ACRONYM

Beyond education: A **H**ypoglycaemia **A**wareness **R**estoration **P**rogramme for people with type 1 diabetes and problematic hypoglycaemia persisting **d**espite **o**ptimised self-**c**are (HARPdoc)

PART 1

We'd like to invite you to take part in our research study.

Joining the study is entirely up to you, before you decide we would like you to understand why the research is being done and what it would involve for you.

One of our team will go through this information sheet with you, to help you decide whether or not you would like to take part and answer any questions you may have. We suggest this should take about 20 minutes. Please feel free to talk to others about the study if you wish.

Part 1 of this information sheet tells you the purpose of the study and what will happen to you if you take part.

Part 2 will give you more detailed information about the conduct of the study. Please ask if anything is unclear.

What is the purpose of the study?

The aim of the study is to find an effective way to help people with type 1 diabetes reduce their risk of hypoglycaemia (low blood sugar episodes), particularly those who continue to have problems with hypoglycaemia, despite their best efforts at insulin self-management. Specifically, we want to help people who can't always tell when their blood sugar is dropping to regain awareness of hypoglycaemia and most importantly reduce the number of times they have hypoglycaemia so severe that it has to be treated by someone else. In the study, we will compare two interventions, both new to the NHS and both short courses, run over six weeks. One course, called Blood Glucose Awareness Training or BGAT for short) teaches new ways for people with diabetes to predict and feel what their blood sugar levels will be. This course has been successful in reducing severe hypoglycaemia in America, where it was designed and in some European countries. The other course, HARPdoc, is a completely new approach. As well as revising learning about hypoglycaemia and how to avoid it, HARPdoc explores thoughts and beliefs around hypoglycaemia that we have identified as possible barriers to regaining awareness of hypoglycaemia and reducing risk of severe episodes. It uses "talking therapies" to find new ways of thinking and worked very well in an early small test.

The study will try to find out how important such thoughts and beliefs really are in increasing risk of severe hypoglycaemia and whether addressing them helps people lower their risk and stop having hypoglycaemia that affects their quality of life.

Why have I been invited?

You have been invited to take part in the study because you have type 1 diabetes and your insulin treatment is complicated by hypoglycaemia problems that have persisted despite best efforts at diabetes self-management. Those efforts will have included structured education in flexible insulin therapy (such as DAFNE, or BERTIE or the Joslin courses) and may have included trying insulin pump therapy or glucose sensing. The study will take place in King's College Hospital and Guy's and St Thomas' Hospital in London; Sheffield Teaching Hospitals and the Royal Bournemouth General Hospital and we also have a centre in America at the Joslin Diabetes Clinic in Harvard. We expect approximately 96 patients will take part in a randomised controlled trial (RCT) comparing the two interventions. Because you do not fulfil all the criteria we have set for the trial, we are inviting you to participate outside the main trial, although the experience you receive should be the same as for the trial itself. The usual reason for participating in this study outside the RCT is that you have problems recognising your hypoglycaemia, so-called impaired awareness of hypoglycaemia, but have happily managed to avoid experiencing severe episodes of hypoglycaemia, perhaps through using continuous glucose monitoring. We plan to compare the two interventions for their ability to stop severe hypoglycaemia, so if you don't have any, while you may benefit from the course, we can't show that that benefit has included a reduction in severe episodes!

Do I have to take part?

It is up to you to decide. We will describe the study and go through this information sheet, which we will then give to you. You will be able to keep this information sheet and think about taking part. You are free to discuss the information with anyone you wish including your family and friends, your GP or your usual diabetes care team if your care is not based at one of the participating hospitals. If you agree, we will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason. This will not affect the standard of care you receive.

What will happen to me if I take part?

If you agree to take part, we will want to make a record of how you are, how you manage your diabetes, how much hypoglycaemia you are having and what impact that is having on your life. We will take a medical history and do a physical examination to check for possible complications of diabetes. We will ask you about your hypoglycaemia (hypo) experience – for example, how often you have hypos, how well you feel when your blood sugar is falling and how many severe episodes (ones in which your blood sugar fell so low you could not treat yourself and someone else had to give you treatment). We will take blood to check that you have no medical reason, apart from diabetes, increasing your personal risk of hypoglycaemia and to measure your diabetes control and we will ask you to fill in a questionnaire booklet that will tell us about how you think about your hypoglycaemia, how much you worry about it and how you try to avoid it. There are also questions about how much your diabetes and your hypoglycaemia affect your mood and your quality of life. The questionnaires have been reviewed by people with type 1 diabetes and they take about 30 minutes to complete. You will notice that the blood sugar values used to define hypoglycaemia may differ between questionnaires in the booklet, and sometimes even within one questionnaire. This reflects either differences in international definitions for hypoglycaemia or the context of each question, which may be exploring the clinical effects of different degrees of hypoglycaemia. For the

interventions, this will be much clearer as there will be only one blood sugar threshold defined as hypoglycaemia. We will download your glucose meter and look at the results together.

We will then invite you to attend one of our two six-week courses. You will be offered a space on either of the courses that has space, after slots have been allocated randomly to people on the full RCT. Each course includes four days (one a week on weeks one, two, three and six) spent with one or more senior diabetes educators (nurses and dietitians) and about five other people with type 1 diabetes and problems with hypoglycaemia. There will be formal one-to-one contact with the educators using telephone or face to face visits (your choice) in weeks four and five for one of the courses. In this way we can be sure that any difference we may find in the number of severe hypos people have in the two years after the courses is due to the difference in the course content. We will let you know of space availability as soon as we can, but this will be confirmed absolutely only a day or two before the course starts.

It is important for us to know how accurately the diabetes educators deliver each intervention, and in particular we need to assess how well the techniques that are novel to the HARPdoc intervention are used in either course. This is called assessing the fidelity with which each intervention is given. We will therefore be asking all participants on a course to allow us to make audio-recordings of sessions. The recordings will be reviewed only by the researchers for the purpose of assessing the accuracy with which each intervention is being delivered and for no other purpose.

After your course, you will return to your usual diabetes care, but you can keep in touch with your course educator to get on-going support for your diabetes self-management. We will invite you to formal review and update with the other people who were in your group at the hospital at 3, 6, 12, 18 and 24 months after your group was first run. Your involvement in the study ends with your last visit, 24 months (2 years) after you had your course.

We will check your blood HbA1c (glycated haemoglobin, the blood test that tells you about your sugar control over the last couple of months) as a marker of your diabetes control at each visit. Three times in the study, at the start of the course, year 1 and year 2) we will ask you to re-do all the questionnaires.

During the study, you will be discussing your diabetes self-management with your course educators. We will send clinical information, including the HbA1c measurements, to your GP and your usual diabetes care team. You may be able to reduce the frequency with which you visit your usual care team during the study, as you can get advice about your insulin management from your educators.

What are the alternatives for treatment?

Participation in the trial does not alter your diabetes treatment. You will continue to take your usual insulins and do your usual glucose monitoring. You should be testing your blood at least four times a day – before each meal and at bedtime and you should continue to adjust your doses as you usually would. Changes in your insulin regimen may be made as in usual practice, in discussion between you and your diabetes health care team, although we do ask that you continue the same insulins and glucose monitoring techniques throughout the study if possible. We will record any changes made at each study visit.

Assuming you have tried everything available to you to reduce your hypoglycaemia risk already, we have no other alternatives to offer. Neither of the treatments in this trial are currently offered as standard practice in the UK. We need to do the trial in order to establish how well each treatment works – both have been shown to reduce severe hypoglycaemia, HARPdoc in a very small pilot study of 24 people and BGAT in several formal trials in the US and Europe – BGAT however has not yet been tested in people who have already completed a structured education course in flexible intensive insulin therapy. As such courses also reduce severe hypoglycaemia risk, this study will tell us how much more BGAT can do.

You are being asked to participate in this trial because you have continued to experience severe hypoglycaemia despite having attended a structured education programme in flexible insulin self-management (such as DAFNE or BERTIE) which do minimise bad hypoglycaemia experience. If you have not yet tried them, insulin pump therapy and/or glucose sensing can help reduce severe hypoglycaemia although they do not work for everyone and they do not seem to restore natural protection from severe hypoglycaemia – ie. awareness of hypoglycaemia. The only other treatment currently available would therefore be either islet or pancreas transplantation.

What are the possible benefits of taking part?

We cannot promise the study will help you but we do expect both of the interventions to help you reduce your risk of severe hypoglycaemia and perhaps regain some awareness of hypoglycaemia. One intervention may be more powerful in its effects than the other and if this proves to be the case, and people do not get benefit from one course, we would expect to be able to offer you the more effective intervention at the end of the study. We will have external monitoring of the rates of severe hypoglycaemia during the study so if we find one intervention is much better than the other early in the trial, we can stop the trial and offer everyone the more effective intervention.

What are the possible disadvantages and risks of taking part?

We do not think doing this study exposes you to new risks. There is the inconvenience of the time the courses take to do, but this is no longer than undertaking an existing structured education programme in flexible intensive insulin therapy. As one of the courses explores your thoughts and beliefs around diabetes control and hypoglycaemia, strong feelings may be provoked. Your educators are trained to help you deal with such feelings. Indeed, there is evidence that exploring such feelings and beliefs in a sensitive and constructive way is likely to help you achieve your goal of reducing your hypoglycaemia risk.

Because this is a research study, and you may provide us with information that you would not otherwise have given, such information will be treated in confidence. The study protocol provides for anonymised reporting of your hypoglycaemia experience, in parallel with open reporting. The anonymised data will be recorded directly into the study database, in which individual participants cannot be identified. Any information you give us otherwise, through open questionnaires or during interactions with your educators or the researchers, will be treated as confidential, as would be usual for any clinical interaction. If you describe to us a greater problem with your hypoglycaemia than you have previously reported, we will discuss with you the risks that this may create for you and for others, discuss with you what you can do to reduce those risks and advise you of your legal

responsibilities, which may include the need to inform other authorities such as Driving and Vehicle Licencing Agency (DVLA).

Who is organising and funding this study?

The doctor in charge of this study is Prof Stephanie Amiel, diabetes consultant at King's. The study is funded by the JDRF (Juvenile Diabetes Research Foundation) and is being jointly sponsored by King's College London and King's College Hospital NHS Foundation Trust.

The research team are not receiving any financial reward for undertaking this study.

How have patients and the public been involved in this study?

Reducing the risk of severe hypoglycaemia and tackling impaired awareness of hypoglycaemia were topics listed as priorities for research in type 1 diabetes by a national exercise involving people with diabetes, their families and their health care professionals in 2012. People with type 1 diabetes helped develop the HARPdoc intervention, both by participating in the original design of its curriculum and by providing feedback that has led to its present form. People with type 1 diabetes have also reviewed the questionnaire packs and this patient information sheet. One of them will continue to be involved in the study as part of the research team and will chair a group of people with type 1 diabetes who will assist in monitoring the progress of the study and the analysis of the data.

Who has reviewed this study?

The study protocol was reviewed by a research review committee of the JDRF and was developed with them. All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by London-Dulwich Research Ethics Committee. It has also been approved by the Health Research Authority and each local hospital will also give confirmation that the study can go ahead. The American site will have been reviewed and approved by its own local Investigation Review Board, the US equivalent of the Research Ethics Committee.

Expenses and Payments

There are funds available for you to claim back travel expenses for attending study visits.

What happens when the research study stops?

The study ends two years after your course. At the end of that time, you will return fully to your usual diabetes care team. We hope that any improvement in your hypoglycaemia experience gained from your course will persist but we cannot be sure that this will be the case.

This completes Part 1 of the Information Sheet.

If the Information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

PART 2

What if new information becomes available?

Sometimes we get new information about the treatment being studied. If this happens, your study doctor will tell you and discuss whether you should continue in the study. If you decide not to carry on, your study doctor will make arrangements for you to leave the study and return to your usual diabetes care team. If you decide to continue in the study he/she may ask you to sign an agreement outlining the discussion.

This new information that becomes available might specifically affect you and your health. If this happens, your study doctor might consider that you should withdraw from the study. He/she will explain the reasons for withdrawing from the study and arrange for your care to continue with your usual diabetes care team.

If the study is stopped for any other reason, we will tell you and you will continue your care with your usual diabetes care team.

What will happen if I don't want to carry on with the study?

You are free to withdraw from the study at any time; and if you would like to do so; please speak to your study nurse or doctor.

Your decision to withdraw from the study will not affect the usual health care you receive.

If you withdraw your consent to continuing in the study, we would ask you to allow us to use information we have already collected from you. We would also like to keep in contact with you through your doctor or GP so that we can know about your progress. Specifically, we will ask if we may collect information about your awareness of hypoglycaemia, the number of severe hypoglycaemic episodes you are having and your HbA1c. NICE recommends that this information is collected routinely for every person with diabetes, at least once a year, so allowing us to collect this information will not need to involve you in any extra effort. We would ask that we may collect these data at 12 and 24 months after your course. You may withhold your permission for this if you wish and you can ask that your entire data collection be deleted from the study files.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to your study doctor (Prof Amiel, Dr Jacob or Dr Choudhary, 0207 848 5639) who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints procedure by contacting your local Patient Advice Liaison Service (PALS) office. Details of your local office can be obtained by asking your study doctor, GP, telephoning your local hospital or looking on the NHS choices website. <http://www.nhs.uk/pages/home.aspx>

Every care will be taken in the course of this study. However in the unlikely event that you are injured by taking part, compensation may be available.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against King's College Hospital NHS Foundation Trust. but you may have to pay your legal costs.

Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects (adverse events) you may have experienced due to your participation in the study the normal National Health Service complaints mechanisms are available to you. Please ask your study doctor if you would like more information on this.

Will my taking part be kept confidential?

King's College London and King's College Hospital are the sponsors for this study based in the United Kingdom. We will be using information from you and/or your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. King's College London and King's College Hospital will keep identifiable information about you for 10 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. [NHS/other site] will collect information from [you and/or your medical records] for this research study in accordance with our instructions.

You can find out more about how we use your information on <https://www.guysandstthomas.nhs.uk/research/patients/about.aspx>

HARPDoc sites will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from HARPDoc sites and regulatory organisations may look at your medical and research records to check the accuracy of the research study. HARPDoc sites will pass these details to Sponsor organisations, King's College London and King's College Hospital along with the information collected from you and/or your medical records. The only people in King's College London and King's College Hospital who will have access to information that identifies you will be people who need to contact you to discuss study related matters or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

Information collected by us as part of the study protocol is confidential. In the research records, your data will be identified only by a number that you will be given when you start the study. The list linking that number to you will be kept separately in an NHS data system. You will not be identifiable in the publications of the results of the study. Only anonymised data will be kept in the research data base.

Because we are interested in how long the benefits of each intervention last, we will want to keep your data for about 10 years after the study is finished. We ask that you allow us to review your records for hypoglycaemia experience and diabetes control at any time during this period but we will

let you know if we are doing this and give you the opportunity to withdraw your consent. If we want to do any other research around your experiences of the study, we will ask you separately for your consent. We will ask for ethical committee approval before asking you about any new use of your data.

It is common practice now to allow other researchers access to study information. We will not keep the blood samples you give during the study. Data sharing with other researchers is useful to ensure that research is open to peer scrutiny, to optimise the use of good quality research data and to support policy and other decision-making. Only the anonymised data will be open to other researchers.

Prof Amiel will be the custodian of the data collected in this study.

Because we have an American centre in the study, your data will be merged with the US data and our US collaborators will be able to work with the data base. This data base will only contain the anonymised data set, so you will not be identifiable to the US researchers.

If you consent to take part in the research, any of the information collected about you may be inspected by the sponsor (including representatives of the sponsor). These inspections are solely for the purposes of the research and analysing the results. Your records may also be looked at by the regulatory authorities or ethics committees to check that the study is being carried out correctly.

The organisations listed above will keep information about you confidential and secure. Your name will not be used in any reports about the study and all data is stored in accordance with the principle of the Data Protection Act 1998. However, your study doctor may tell your GP about your participation if you agree to enter the trial.

Involvement of the General Practitioner/Family Doctor (GP)

With your consent, your GP and your usual diabetes care team will be informed of your involvement in the trial.

What will happen to any samples that I give?

The only samples you give are blood samples for measurement in a laboratory of your diabetes control, and at the start of the study, for measuring things such as liver, kidney and thyroid function that might be increasing your risk of hypoglycaemia. These samples will be destroyed using the usual procedures of the measuring laboratory once the data are obtained.

Will any genetic tests be done?

We are not including any genetic studies in this proposal

What will happen to the results of the research study?

We will let you know the results of the study when we have completed the analysis. We will do this with a written report drafted specifically for study participants as well as offering you copies of the scientific papers we write. We hope the participants in the study will also publicise it and its

results using social media. Individuals will not be identifiable from any report or publication placed in the public domain.

Thank you

Thank you for considering taking part and taking the time to read this information sheet. If you decide to take part in the study, we will give you a copy of the information sheet and a signed consent form to keep.

Further information and contact details

If you would like more information about research participation you may wish to contact the organisation that advises on patient and public involvement in research listed below:

INVOLVE, Alpha House, University of Southampton Science Park, Chilworth, Southampton, SO16 7NS. Telephone: 023 8059 5628 Email: involve@nihr.ac.uk

If you would like more information about other research in type 1 diabetes funded by the JDRF, you may wish to visit their website: www.jdrf.org

In the UK, research into diabetes is also supported by the charity Diabetes UK (www.diabetes.org.uk)

If you have questions about this study in particular, please contact your local research team. For you, that will be

Local Contact:

Your nurse:
E mail:
Tel:

Your doctor:
E mail:
Tel:

Trial Manager:
Email: HARPdoc@kcl.ac.uk
Tel:

Please remember your e mail and e mails that do not end "nhs.net" are not secure against hacking and should not be used for sensitive personal information.