

Study Title: Type-2 diabetes: risk perceptions and self-management behaviour.

Ethics Ref:

Date and Version No: 7 April 17 – Version No 1.0

Chief Investigator: Thomas Rouyard
DPhil student
HERC, Nuffield Department of Population Health
Old Road Campus
Headington, Oxford, OX3 7LF
e: thomas.rouyard@gtc.ox.ac.uk | t: 01865 289221

Investigators: Pr Alastair Gray
HERC, Nuffield Department of Population Health
Old Road Campus
Headington, Oxford, OX3 7LF
e: alastair.gray@ndph.ox.ac.uk | t: 01865 289279

Dr Jose Leal
HERC, Nuffield Department of Population Health
Old Road Campus
Headington, Oxford, OX3 7LF
e: jose.leal@ndph.ox.ac.uk | t: 01865 289263

Dr Richard Baskerville
27 Beaumont St Practice
Oxford, OX1 2NR
e: richard.baskerville@nhs.net | t: 01865 311500

Sponsor: University of Oxford

Funder: The research is supported by the University of Oxford ('Oxford-Health Economics Research Centre Graduate Scholarship').

Chief Investigator Signature:

X

Thomas Rouyard

Conflicts of interest: None.

Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, host organisation, and members of the Research Ethics Committee, unless authorised to do so.

TABLE OF CONTENTS

1.	SYNOPSIS	5
2.	ABBREVIATIONS.....	5
3.	BACKGROUND AND RATIONALE.....	5
4.	OBJECTIVES AND OUTCOME MEASURES.....	6
5.	STUDY DESIGN	7
6.	PARTICIPANT IDENTIFICATION	7
6.1.	Study Participants.....	7
6.2.	Inclusion Criteria.....	7
6.3.	Exclusion Criteria	7
7.	STUDY PROCEDURES	7
7.1.	Recruitment.....	7
7.1.	Screening and Eligibility Assessment.....	8
7.2.	Informed Consent.....	8
7.3.	Procedure	8
7.4.	Intervention.....	9
7.5.	Intervention Effects	9
7.6.	Discontinuation/Withdrawal of Participants from Study.....	9
7.7.	Definition of End of Study	9
8.	STATISTICS AND ANALYSIS.....	9
8.1.	Description of Statistical Methods	9
8.2.	The Number of Participants	10
8.3.	Analysis of Outcome Measures	10
9.	DATA MANAGEMENT	10
9.1.	Access to Data	10
9.2.	Data Recording and Record Keeping.....	10
10.	QUALITY ASSURANCE PROCEDURES	11
11.	ETHICAL AND REGULATORY CONSIDERATIONS.....	11
11.1.	Declaration of Helsinki.....	11
11.2.	Guidelines for Good Clinical Practice	11
11.3.	Approvals.....	11
11.4.	Reporting.....	11
11.5.	Participant Confidentiality.....	11
11.6.	Expenses and Benefits.....	12

11.7.	Other Ethical Considerations	12
12.	FINANCE AND INSURANCE	12
12.1.	Funding	12
12.2.	Insurance	12
13.	PUBLICATION POLICY.....	12
14.	REFERENCES	13

1. SYNOPSIS

Study Title	Type-2 diabetes: risk perceptions and self-management behaviour	
Internal ref. no. / short title		
Study Design	Pilot study, Questionnaires	
Study Participants	People with Type 2 diabetes, aged 30 to 75	
Planned Sample Size	40	
Planned Study Period	01/06/2017 – 01/10/2017	
	Objectives	Outcome Measures
Primary	To assess the feasibility of a larger study.	Feasibility of study protocol, consent rate, acceptability of intervention, retention rate, rates of missing data.
Secondary	To assess the effectiveness of the intervention in patient's awareness of risks for complications associated with Type 2 diabetes.	Change in risk perception scores.
	To assess whether the intervention encourages the adoption of recommended self-care behaviours.	Change in self-management behaviour scores.

2. ABBREVIATIONS

CI	Chief Investigator
CRF	Case Report Form
CTRG	Clinical Trials & Research Governance, University of Oxford
GCP	Good Clinical Practice
GP	General Practitioner
NHS	National Health Service
REC	Research Ethics Committee
T2DM	Type-2 Diabetes Mellitus

3. BACKGROUND AND RATIONALE

For the past twenty years, evidence has accumulated about the harmful effects caused by type 2 diabetes. Overall, people with type-2 diabetes (T2DM) have age-specific death rates about twice those of the general population. In particular, they have a higher risk of experiencing cardiovascular diseases.

In the recent literature, there is a consensus that consistent self-management behaviour can delay the onset of complications associated with type 2 diabetes. Several studies have shown that diabetes self-management education - i.e. interventions aiming at improving (multidimensional) self-management in patients – are associated with improved intermediate outcomes (especially glycaemic control) and thus, indirectly, clinical outcomes. [1-6] This might explain why self-management has become the cornerstone for treating T2DM. [7, 8] However, in spite of this consensus, the most effective method to provide diabetes self-management education (SME) is still unclear.

Although many factors are known to influence health behaviours, risk perceptions are thought to play a key role in the behavioural process. People who underestimate their risks may be less likely to adopt recommended behaviours, while overestimating their risks may cause so much anxiety that it hampers people from taking precautionary measures [9]. There is strong evidence supporting the causality of the association between perceived risks and precautionary behaviours; empirical data have shown a highly significant, albeit small-to-moderate, positive association [10-12]. In addition, perceived risks are significant predictors of behavioural intentions [13, 14]. Although behavioural processes are complex, wrong risk perceptions are a major impediment to the adoption of self-care behaviours and, as a result, an additional risk for the occurrence of adverse outcomes.

Recent studies have shown that people with T2DM largely underestimate their risks of developing complications. [15] Existing risk communication interventions have shown mixed results, with many participants barely understanding the explanations of health professionals about risks and having poor recall of risk information [16-18]. In this context, there is a need for better risk communication interventions. [15] Rather than increasing the quantity of information to be communicated ('less is often more' [19]), it is necessary to improve its quality. New interventions that make use of patients' decision-making biases are considered to be very promising in the risk communication field [20-22]. We believe that such interventions, through which personalised risks are communicated, will help to correct erroneous risk perceptions, and, in turn, have a greater impact on self-care behaviours.

Based on the results of recent studies investigating the risk perceptions and risk attitudes of people with T2DM, we have developed a new, tailored risk communication intervention. This intervention aims to increase patients' awareness of their risks for complications associated with T2DM and, in turn, to encourage the adoption of recommended self-care behaviours. The objectives of the full trial are to assess the feasibility and measure the expected impact of such an intervention, in order to inform the design of a larger study (RCT to be conducted in the future).

4. OBJECTIVES AND OUTCOME MEASURES

Objectives	Outcome Measures	Timepoint(s) of evaluation of this outcome measure (if applicable)
To assess the feasibility of a larger study.	Feasibility of study protocol, consent rate, acceptability of	After the study.

	intervention, retention rate, rates of missing data.	
To assess the effectiveness of the intervention in patient's awareness of risks for complications associated with Type 2 diabetes.	Change in risk perception scores.	<ul style="list-style-type: none"> • Baseline (right before the intervention). • Baseline (right after the intervention). • After 12 weeks.
To assess whether the intervention encourages the adoption of recommended self-care behaviours.	Change in self-management behaviour scores.	<ul style="list-style-type: none"> • Baseline (right before the intervention). • After 12 weeks.

5. STUDY DESIGN

We have designed a pilot study to assess the feasibility and measure the impact of a risk communication intervention for people with T2DM on risk perceptions and self-management behaviour. The intervention has been developed in collaboration with both health professionals and patients.

6. PARTICIPANT IDENTIFICATION

6.1. Study Participants

40 participants will be recruited (20 in the intervention group, 20 in the control group).

6.2. Inclusion Criteria

- Participant is willing and able to give informed consent for participation in the study.
- Aged between 30 and 75.
- Diagnosed with Type-2 diabetes.

The rationale for the lower age limit (30) is that the disease is rarely diagnosed before that age. The rationale for the upper age limit (75) is to be in line with similar existing studies.

6.3. Exclusion Criteria

- If unable to provide informed consent.
- If non-English speaker.
- If not suitable for the study according to GP.

7. STUDY PROCEDURES

7.1. Recruitment

Potential participants will be identified by their GP at 27 Beaumont St practice, Oxford.

Patients willing to participate in the study will be notified during their regular clinical appointments and research visits will be set up to coincide with patients' appointments.

7.1. Screening and Eligibility Assessment

The GP will screen his records in order to identify eligible patients.

7.2. Informed Consent

A patient information sheet; detailing no less than the exact nature of the study, what it will involve for the participant, the implications and constraints of the protocol, and any risks in taking part; will be given to eligible patients during their regular clinical appointment. It will be clearly stated that the study is optional and that the participant is free to withdraw without a reason at any time without prejudice to future care or affecting their rights. The GP will also explain the study and answer potential questions.

Patients willing to participate in the study after reading the patient information sheet will let their GP know and research visits will be set up to coincide with the patients' next appointments, approximately 6 weeks after approach. The CI will meet with the patient to discuss the study, answer any questions they have and receive written informed consent, in the form of a participant dated signature and the dated signature of the CI, to take part.

7.3. Procedure

• Visit 1

For participants who gave their informed consent, the CI will administer the study questionnaires that measures risk perceptions and assesses self-management behaviour (~10 minutes). [23, 33]

After the first set of questionnaires are completed, all participants will attend their routine clinical consultation with their GP. During the consultation, half of the participants will receive the risk communication intervention from the GP (intervention group, ~5 minutes) and half of the participants will not (control group). Participants will be randomised into the intervention or the control group by means of a list drawn up by a computerised randomisation program. They will be attributed with an order number and this number will be randomly allocated into one of the two groups. The participant will be blind to their allocation but the CI will not be.

Right after the consultation, risk perceptions of all participants (i.e. in both groups) will be measured by the CI once again (~5 minutes), to account for potential effect of the consultation on the control group.

• Visit 2

At participants' next consultation visit, which will be approximately 12 weeks after the intervention, the same questions about risk perceptions and self-management behaviour will be asked by the CI right before the consultation (~10 minutes).

The interest of face-to-face appointments is that it ensures reliability in participants' answers, as compared to email or telephone interviews.

This methodology has been used in most recent studies that aimed at measuring the impact of risk communication interventions. [17, 24, 25]

7.4. Intervention

The GP will discuss participants' personalised risk estimates for diabetes-related complications and life expectancies associated with different self-management behaviours (~5 minutes). These personalised risk estimates will be calculated by the GP through a validated simulation model (UKPDS-OM [32]). According to personal characteristics (age, gender, ethnicity...) and risk factors (duration of diabetes, history of complications, blood glucose level...), the UKPDS-OM allows to compute, for each individual, their own (personalised) risk estimates of developing diabetes-related complications and life expectancies.

7.5. Intervention Effects

In the unlikely event of a negative effect of the intervention on risk perceptions and/or self-management behaviour found after data analysis, the CI will inform the GP. Personal details of participants will be kept separate from research data, and the CI will use ID numbers to refer to a given participant. The use of ID numbers will be limited for the purpose of giving feedback to the GP after data analysis.

In case a positive effect on risk perceptions and self-management behaviour is found in the intervention group, the intervention will also be offered to participants in the control group at their next consultation visit.

7.6. Discontinuation/Withdrawal of Participants from Study

Each participant has the right to withdraw from the study at any time. In addition, the Investigator may discontinue a participant from the study at any time if the Investigator considers it necessary for any reason including withdrawal of consent. Data collected up to the withdrawal will be used.

7.7. Definition of End of Study

The end of study is the date when the questionnaire of the last participant will have been filled out.

8. STATISTICS AND ANALYSIS

8.1. Description of Statistical Methods

Frequencies and percentages will be used to describe categorical variables, and means \pm SD to describe continuous variables.

Pre-post intervention differences between groups in terms of study outcome variables will be tested using Chi-square and Student t-tests, whereas pre-post intervention differences within groups will be tested using McNemar and paired t-tests.

The Kappa test will be used for detecting the degree of agreement between pre- and post-perceived risk with baseline objective risk.

In the intervention group, correlation between appropriateness of risk perceptions and self-management scores (post-intervention) will be tested by means of point biserial correlation. Finally, Pearson and Spearman correlations will be used to test for correlations between observable characteristics and outcome variables.

8.2. The Number of Participants

40 participants will be recruited (20 in the intervention group, 20 in the control group).

According to Connelly (2008), extant literature suggests that a pilot study sample should be 10% of the sample projected for the larger parent study. [26] Isaac and Michael (1995) suggested 10 - 30 participants [27]; Hill (1998) suggested 10 to 30 participants for pilots in survey research [28]; Julious (2005) in the medical field [29] and van Belle (2002) suggested 12 [30]; Treece and Treece (1982) suggested 10% of the project sample size. [31]

Existing studies of reference used the following sample sizes:

Welschen et al (2012) [17]: 261

Asimakopoulou et al (2008) [24]: 95

Tawfik & Mohamed (2016) [25]: 180

Based on these observations, we decided to take the size of the bigger sample as reference (n=261) and to apply the 10% rule. However, in order to allow for drop-outs and facilitate comparison between the two arms, we decided to add a margin and target 40 participants in total.

8.3. Analysis of Outcome Measures

We will analyse the following outcome variables:

- Feasibility of a larger study: in order to inform the design of a larger study, we will assess the following criteria: integrity of study protocol, consent rate, acceptability of intervention, expected impact of intervention.
- Appropriateness of risk perceptions: we will compare participants' perceived risks to their personalised risk estimates computed via a validated simulation model (UKPDS-OM [32]).
- Self-management scores: we will assess participants' adherence to self-care activities using two validated questionnaires: 1) The Summary of Diabetes Self-Care Activities Measure (SDSCA) [23]; 2) The 8-Item Morisky Medication Adherence Scale (MMAS-8) [33]

9. DATA MANAGEMENT

9.1. Access to Data

Direct access will be granted to authorised representatives from the Sponsor and host institution for monitoring and/or audit of the study to ensure compliance with regulations.

9.2. Data Recording and Record Keeping

Data will be anonymised and no participant will be identifiable from the data in the possession of the researchers, outside of the CI and the direct care team. Participants will be linked to an ID number that will be used by the CI to give feedback to the GP after study.

Anonymised research data will be recorded and stored numerically (University password-protected computers), managed by Thomas Rouyard, for the duration of the project. Only the researchers involved in the project will have access to the data. Data may be kept up to 5 years following the publication of research findings in University locked up cupboards. Data may also be used to inform the design of a larger trial before publication of research findings and be included in the analysis of this larger trial.

10. QUALITY ASSURANCE PROCEDURES

The study may be monitored, or audited in accordance with the current approved protocol, GCP, relevant regulations and standard operating procedures.

The CI administering the questionnaires will continually be present with the participants, which will ensure reliable, high quality data to be collected.

11. ETHICAL AND REGULATORY CONSIDERATIONS

11.1. Declaration of Helsinki

The Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

11.2. Guidelines for Good Clinical Practice

The Investigator will ensure that this study is conducted in accordance with relevant regulations and with Good Clinical Practice.

11.3. Approvals

The protocol and participant information sheet will be submitted to an appropriate Research Ethics Committee (REC), HRA, and host institution(s) for written approval.

The Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

11.4. Reporting

The CI shall submit once a year throughout the study, or on request, an Annual Progress report to the REC Committee, host organisation and Sponsor. In addition, an End of Study notification and final report will be submitted to the same parties.

11.5. Participant Confidentiality

The study staff will ensure that the participants' anonymity is maintained. The participants will be identified only by a participant ID number on all study documents and any electronic database, with the exception of the CRF, where participant initials may be added. All documents will be stored securely and

only accessible by study staff and authorised personnel. The study will comply with the Data Protection Act, which requires data to be anonymised as soon as it is practical to do so.

11.6. Expenses and Benefits

Each participant will receive £10 for their time taking part in the study, upon completion of the last questionnaire (visit 2). This has been determined on the basis of previous studies published in the literature.

11.7. Other Ethical Considerations

The intervention has been developed in collaboration with both health professionals and patients. Although some patients might find risk communication distressing, the intervention has been designed to be as patient-friendly as possible and will be conducted by patients' personal GP. Patients will be encouraged to share any concern with their GP.

12. FINANCE AND INSURANCE

12.1. Funding

The research is supported by the University of Oxford ('Oxford-Health Economics Research Centre Graduate Scholarship').

12.2. Insurance

The University has a specialist insurance policy in place which would operate in the event of any participant suffering harm as a result of their involvement in the research (Newline Underwriting Management Ltd, at Lloyd's of London). NHS indemnity operates in respect of the clinical treatment that is provided.

13. PUBLICATION POLICY

The Investigators will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge that the study was funded by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care Oxford at Oxford Health NHS Foundation Trust. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged.

Amendment table				
Amendment number	Protocol number	Date	Author	Description

14. REFERENCES

1. Ellis, S. E., T. Speroff, R. S. Dittus, A. Brown, J. W. Pichert and T. A. Elasy (2004). "Diabetes patient education: a meta-analysis and meta-regression." *Patient education and counseling* 52(1): 97-105.
2. Gary, T. L., J. M. Genkinger, E. Guallar, M. Peyrot and F. L. Brancati (2003). "Meta-analysis of randomized educational and behavioral interventions in type 2 diabetes." *The Diabetes Educator* 29(3): 488-501.
3. Norris, S. L., M. M. Engelgau and K. V. Narayan (2001). "Effectiveness of self-management training in type 2 diabetes: a systematic review of randomized controlled trials." *Diabetes care* 24(3): 561-587.
4. Norris, S. L., J. Lau, S. J. Smith, C. H. Schmid and M. M. Engelgau (2002). "Self-Management education for adults with type 2 Diabetes A meta-analysis of the effect on glycemic control." *Diabetes care* 25(7): 1159-1171.
5. Tang, T. S., M. M. Funnell, S. Noorulla, M. Oh and M. B. Brown (2012). "Sustaining short-term improvements over the long-term: results from a 2-year diabetes self-management support (DSMS) intervention." *Diabetes research and clinical practice* 95(1): 85-92.
6. Yuan, C., C. W. Lai, L. W. Chan, M. Chow, H. K. Law and M. Ying (2014). "The Effect of Diabetes Self-Management Education on Body Weight, Glycemic Control, and Other Metabolic Markers in Patients with Type 2 Diabetes Mellitus." *Journal of diabetes research* 2014.
7. ADA (2013). "Standards of medical care in diabetes—2013." *Diabetes care* 36(Suppl 1): S11.
8. NICE (2009). *Type 2 diabetes: the management of type 2 diabetes*, National Institute for Health and Clinical Excellence.
9. Cameron L. Conceptualizing and assessing risk perceptions: a self-regulatory perspective. National Cancer Institute workshop on conceptualizing and measuring risk perception. Washington, DC, 2003. Available at http://cancercontrol.cancer.gov/brp/research/theories_project/cameron.pdf Last accessed 1 March 2016.
10. Sheeran P, Harris P, Epton T. Does heightening risk appraisals change people's intentions and behavior? A meta-analysis of experimental studies. *Psychol Bull* 2014; 140: 511.
11. Harrison J, Mullen P, Green L. A meta-analysis of studies of the health belief model with adults. *Health Educ Res* 1992; 7: 107–116.
12. Janz N, Becker M. The health belief model: a decade later. *Health Educ Behav* 1984; 11:1–47.
13. Floyd D, Prentice-Dunn S, Rogers R. A meta-analysis of research on protection motivation theory. *J App Soc Psychol* 2000; 30: 407–429.

14. Milne S, Sheeran P, Orbell S. Prediction and intervention in health-related behavior: a meta-analytic review of protection motivation theory. *J Appl Soc Psychol* 2000; 30: 106–143.
15. Rouyard, T., Kent, S., Baskerville, R., Leal, J., & Gray, A. (2016). Perceptions of risks for diabetes-related complications in Type 2 diabetes populations: a systematic review. *Diabetic Medicine*.
16. Saver B, Mazor K, Hargraves J, Hayes M. Inaccurate risk perceptions and individualized risk estimates by patients with type 2 diabetes. *J Am Board Fam Med* 2014; 27: 510–519.
17. Welschen L, Bot S, Kostense P, Dekker J, Timmermans D, van der Weijden T et al. Effects of cardiovascular disease risk communication for patients with type 2 diabetes on risk perception in a randomized controlled trial: the @RISK study. *Diabetes Care* 2012;35: 2485–2492
18. Sultan S, Hartemann-Heurtier A, Grimaldi A. Understanding patients to promote self-regulation in Type 2 diabetes: how to live with an illness beginning before its onset? *Diabetes Metab* 2003;29: S21–S30
19. Peters E, Hibbard J, Slovic P, Dieckmann N. Numeracy skill and the communication, comprehension, and use of risk-benefit information. *Health Aff* 2007; 26: 741–748.
20. Waters E, McQueen A, Cameron L. Perceived risk and its relationship to health-related decisions and behavior. In: DiMatteo R, Martin L eds. *Handbook of Health Communication, Behavior Change, and Treatment Adherence*. Oxford: Oxford University Press, 2013: 193–213.
21. Arvai J. Rethinking of risk communication: lessons from the decision sciences. *Tree Genet Genomes* 2007; 3: 173–185.
22. Roach P, Klindukhova O, Saha C, Hudson B, Cantrell M, Marrero D. Project Red Car: Cardiovascular disease risk communication for people with type 2 diabetes combining the power of electronic health records and computer-based multimedia technology. *Diabetes Spectr* 2010; 23: 155–160.
23. Toobert, D. J., Hampson, S. E., & Glasgow, R. E. (2000). The summary of diabetes self-care activities measure: results from 7 studies and a revised scale. *Diabetes care*, 23(7), 943-950.
24. Asimakopoulou K, Fox C, Spimpolo J, Marsh S, Skinner T. The impact of different time frames of risk communication on type 2 diabetes patients' understanding and memory for risk of coronary heart disease and stroke. *Diabet Med* 2008; 25 : 811–817
25. Tawfik, M. Y., & Mohamed, R. A. (2016). The impact of communicating cardiovascular risk in type 2 diabetics on patient risk perception, diabetes self-care, glycosylated hemoglobin, and cardiovascular risk. *Journal of Public Health*, 24(2), 153-164.
26. Connelly, L. M. (2008). Pilot studies. *Med surg Nursing*, 17(6), 411-2.

27. Isaac, S., & Michael, W. B. (1995). Handbook in research and evaluation. San Diego, CA: Educational and Industrial Testing Services.
28. Hill, R. (1998). What sample size is “enough” in internet survey research? *Interpersonal Computing and Technology: An Electronic Journal for the 21st Century*, 6(3-4).
29. Julious, S. A. (2005). Sample size of 12 per group rule of thumb for a pilot study. *Pharmaceutical Statistics*, 4, 287-291.
30. van Belle, G. (2002). Statistical rules of thumb. New York: John Wiley.
31. Treece, E. W., & Treece, J. W. (1982). Elements of research in nursing (3rd ed.). St. Louis, MO: Mosby.
32. Clarke, P. M., Gray, A. M., Briggs, A., Farmer, A. J., Fenn, P., Stevens, R. & UK Prospective Diabetes Study (UKPDS) Group. (2004). A model to estimate the lifetime health outcomes of patients with type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model (UKPDS no. 68). *Diabetologia*, 47(10), 1747-1759.
33. Morisky, D. E., Ang, A., Krousel-Wood, M., & Ward, H. J. (2008). Predictive validity of a medication adherence measure in an outpatient setting. *The Journal of Clinical Hypertension*, 10(5), 348-354.