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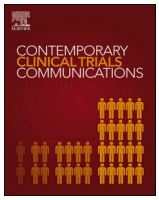

A primary care delivered, technology supported lifestyle program for Type 2 Diabetes Management: An evaluation of changes in metabolic health, feasibility, and acceptability – A pilot interventional study protocol

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ABSTRACT

Background: Type 2 Diabetes (T2D) is associated with significant health complications and socioeconomic costs. Previous research conducted through an outpatient research facility demonstrated use of a low carbohydrate (LC) diet and exercise plan delivered in the format of an education book combined with use of real-time continuous glucose monitoring (RT-CGM) is an effective self-management intervention to improve weight and blood glucose management in patients with T2D. Primary health care remains the central access point for patient management of T2D, but General Practitioners (GPs) lack access to effective evidenced-based, self-management programs that can be prescribed to improve patient outcomes.

Methods: A single-arm, within-participant pilot intervention study will be conducted to evaluate the changes in metabolic health, acceptability and feasibility of a prescriptive LC diet and lifestyle program combined with RT-CGM (LC-RTC) delivered via GP practices. Forty adults with T2D will be recruited from GP practices and prescribed the LC-RTC intervention for 12 weeks. Outcomes will be assessed at baseline and 12-weeks post intervention. Changes in metabolic health will be assessed by changes in glycosylated hemoglobin (primary outcome), body weight, blood pressure, blood lipids, and medication usage. Post-intervention, participants will complete questionnaires and participate in focus groups to explore their experience of the LC-RTC program including acceptance, perceived benefits/barriers, limitations, financial feasibility, intervention drop-out rates, participant and GP engagement with the program (clinic attendance and contacts made to clinic for program support) and RT-CGM use and wear time acceptance. GPs and clinical staff involved will participate focus groups to evaluate the perceived value and feasibility of the LC-RTC program.

Discussion: This trial will provide a powered evaluation of the changes in metabolic health, acceptability, and feasibility of the LC-RTC program for patients with T2D delivered via GP practices.

Trial registration: ANZCTR: 12622000635763 (Website Link to full registration: ANZCTR - Registration). Registered 29th April 2022. Overall trial status: Commenced; Recruitment Status: Commenced 1st May 2022, with 40 participants recruited as of 2nd May 2023 using a rolling recruitment approach.

1. Background

In parallel with the global obesity epidemic there has been a dramatic rise in the prevalence of Type 2 Diabetes (T2D) [1]. Diabetes related health complications and costs are underpinned by poor blood glucose control that remains a primary therapeutic target for diabetes management [2–4].

Governing health bodies recommend lifestyle changes of dietary energy restriction for weight loss combined with increased physical activity as the first-line treatment for people with T2D. Research consistently shows diet and exercise induced sustained weight loss can improve glycaemic control, reduce cardiovascular disease risk factors

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[5,6], and may achieve diabetes remission [6]. A separate body of evidence has also shown that dietary macronutrient composition can play an important role. Compared to a traditional high carbohydrate, low fat diet, a low carbohydrate diet has favourable benefits for lowering HbA1c in a dose response manner, reduces diurnal glycaemic variability (GV: Amplitude, frequency and duration of diurnal glucose fluctuations – an independent risk factor for diabetes related complications including cardiovascular disease [CVD]), diabetes pharmacotherapy, improve blood lipid profile and achieves greater T2DM remission without adverse consequences [7–12]. This growing evidence base demonstrating the effectiveness and safety of LC diets for the management of T2D has advanced dietary practice guidelines of global health authorities [13].

In a 2-year randomised controlled trial (RCT), we previously showed that compared to a lifestyle modification program incorporating a structured exercise regime with a traditional high unrefined carbohydrate, low fat weight loss diet, a program incorporating the same exercise regime with an energy-matched diet lower in carbohydrate, higher in protein and unsaturated fat (LC) elicited greater improvements in blood glucose control and reductions in diabetes medication requirements and CVD risk factors in adults with T2D [14]. The LC diet and exercise plan also achieved clinically relevant improvements in mood and quality of life [15], maintained cognitive and kidney function [14,15], and was nutritionally replete [16]. This study showed that incorporating a LC diet within a comprehensive lifestyle modification program magnifies the therapeutic benefits of weight loss and lifestyle modification for improving acute and chronic glycaemic control and CVD risk management in adults with T2D. This highlights the urgent need to translate this evidence-based diet and exercise approach from the research milieu into the community health care environment that will facilitate improved T2D management for the wider population.

The aforementioned evidence-based LC diet and exercise plan has been previously translated into an easy to follow, self-management education guide for T2D management in the form of the 'The CSIRO Low Carb Diet' book series [17,18], for public uptake and use by diabetes health care specialists with their patients. Despite availability of this resource, adherence remains a key challenge and strategies to promote sustained adherence and maximise lifestyle changes that engender metabolic benefits is critical. Research suggests a mechanism of effective adherence to lifestyle interventions relies on providing patients with immediate feedback based on results of their behaviours [19]. In this way, self-monitoring of objective health markers and behaviours beyond the clinical setting has been used effectively to monitor treatment response and improve adherence for a variety of health outcomes including body weight, blood pressure and physical activity [19]. In a 12-week RCT study conducted in adults with T2D, we examined the effects of the prescription of the CSIRO Low Carb Diet book program with limited professional support, combined with wearing a real-time continuous glucose monitor with and without access to the real-time data [20,21]. Both groups experienced clinically and statistically significant reductions in body weight (7%), HbA1c (0.7%), fasting blood glucose (1.1 mmol/L) and triglycerides levels (0.34 mmol/L) with good tolerance and compliance to continuous glucose monitor wearing [20]. Moreover, patients with access to the continuous glucose monitor with real-time data (RT-CGM) experienced a 6-fold greater lowering in diurnal GV, ~40% greater reduction in diabetes medication requirements and improved blood glucose and self-management behaviours [21]. These data suggest prescription of an evidence-based self-management tool with minimal support that combines a self-directed lifestyle program (CSIRO Low Carb Diet book) with RT-CGM that provides biofeedback to create a technology-integrated solution (Low Carb Real-Time Coaching Program; LC-RTC) is a well-accepted, effective treatment strategy to improve weight and glycaemic control in adults with T2D. However, to date the LC-RTC program has only been tested within an outpatient clinical research setting.

Primary care remains the centre point for T2D management. Primary health care providers deliver clinical care to ~90% of individuals with T2D, with this proportion projected to increase over time [22]. With the increasing prevalence of T2D and complexity of patient care in the primary care setting [23], a primary health care providers' access to effective evidence-based, self-management programs that can be prescribed to improve a patient's lifestyle behavior is critical. Lack of delivery of such programs through primary health care providers has been identified as a barrier limiting wide-scale uptake and adoption by the general population [24].

This paper presents a study protocol that will evaluate the changes in metabolic health, feasibility and acceptability of the LC-RTC intervention program delivered via General Practitioner (GP) led practices. This will assist to understand the viability and barriers of administering this evidence-based self-management T2D treatment through primary care.

2. Main research question

What changes occurred in glycemic control and cardio-metabolic health markers, and the feasibility and acceptability of the LC-RTC program for the treatment of patients with T2D delivered by GP practices though primary health care?

3. Research objectives

3.1. Primary objectives

1. To assess the changes in glycemic control and cardio-metabolic health markers in adults with T2D with the LC-RTC program delivered through GP practices.

3.2. Secondary objectives

2. To assess the feasibility and acceptability of delivering the LC-RTC program through GP practices to adults with T2D from both the perspective of the patient with T2D and primary health care providers.

4. Methods

4.1. Trial design

A 12-week single-arm, pilot intervention study. This design is appropriate gain insights into the acceptability and feasibility of the intervention design and delivery model and effect sizes of the outcomes being assessed to inform the design of subsequent adequately powered larger randomised controlled trials with a control group.

4.2. Method

Forty adults (≥18 years of age) diagnosed with T2D defined as glycosylated haemoglobin (HbA1c) of 6.5% (48 mmol/mol) and up to 15% (140 mmol/mol) will be recruited into the study to undertake a 12-week LC-RTC program intervention. Outcome assessments will be conducted at baseline (Week 0) and post-intervention (Week 12). The treating GPs and associated practice staff will also present as research participants to understand the feasibility and acceptability of the health care delivery model being assessed and will be invited to participate in structured focus groups, post-intervention.

4.3. Setting

The study will be conducted in multiple centres across three independent GP practices in Australia (1. Health Matters Medical Centre, Paralowie, Adelaide, South Australia, 2. Health Focus, Ingleburn, New South Wales, Australia; 3. Hills Family General Practice, Castle Hill, New South Wales, Australia) deemed suitable to participate in the study and

to administer the intervention program. Established GP practices, in lower socioeconomic regions were engaged and identified as suitable if they were a sole practice or group-based practice with on-site or linked to allied health services (dietitian, exercise physiologist, psychology) that provide chronic disease management plans for patients living with T2D.

4.4. Target population

4.4.1. Inclusion criteria

- Adults aged 18 years and over with a diagnosis of T2D under routine GP review
- Identified as appropriate as per clinical management needs by their treating GP, including but not limited to, good clinic attendance records, ability to adopt self-care strategies with minimal support, clinically stable according to current GP management and intervention identified as beneficial to care needs and health goals.
- Willing to participate and engage with a prescriptive lifestyle plan
- Able to read and write in English
- Willing to wear and self-manage a RT-CGM device and sensor, including sensor insertion and removal
- Willing to be monitored by their GP and attend all trial visits
- Access to a compatible Smart Phone and willing to use a continuous glucose monitor application.

4.4.2. Exclusion criteria

- Have existing Oncological issues
- Have Type 1 Diabetes
- Have an HbA1c >15% (140 mmol/mol) within 3 months prior to study commencement
- Are lactating or pregnant
- Are within the first 2 years of a bariatric surgery procedure

4.4.3. Withdrawal criteria

Patients who become participants of the trial will be withdrawn from the study if there are any concerns regarding their consent. Participants can choose to withdraw from the study at any point, without stating a reason. The research team will be informed if a participant decides to withdraw consent for follow-up. Participants who discontinue treatment but do not withdraw from the study will be followed up by the research team, any barriers and reasons associated with dropouts, will be recorded.

4.4.4. Recruitment and study procedure

Recruitment techniques will include flyers, verbal referral from clinical staff, face to face recruitment from practice appointments and electronic messages sent confidentially via clinic patient management systems. Participants will be recruited and have the intervention program administered through the participating GP practices. GPs will identify and inform potentially eligible patients (who have previously consented to be contacted about future research participation opportunities) of the trial. Without influence, those interested in participating will be provided a participant information sheet with a study specific QR code or direct contact details for the research office (Author - Taylor). Both approaches will direct the prospective patient to an online, Research Electronic Data Capture (REDCap™) database [25], that contains the ethics approved participant medical screening questionnaire, participant information sheet, and consent forms for participants to complete. This information will be used by the research office to determine patient suitability for study participation. The research team, via REDCap™ will screen the participants medical screening questionnaire to check eligibility, and if the participant satisfies the eligibility criteria, the research office will contact the participant to attend a structured, clinical interview by phone. This interview will ensure participant is informed of the study requirements, have an opportunity to seek further information about the study and its requirements and for the research team to provide verbal and written study information if any is requested. At this structured interview and when explaining and obtaining written informed consent, the research team will provide a detailed verbal and written instruction on what to expect during the 12-week intervention including RT-CGM wear and use, appointments schedules, support help lines, diet and exercise strategies and REDCap™ use for survey completion and data collection. To formally enrol, participants will be asked to provide verbal and written informed consent.

Subsequently, the research team will provide details to the participant's treating GP who will complete baseline outcome assessments and initiate commencement of the 12-week intervention at the participant's next routine clinical management visit. Outcomes will then be re-assessed at 12-week, post-intervention. The treating GP will continue routine patient care for the participant throughout the duration of the intervention and thereafter.

4.5. Planned intervention: low carb diet - real-time coach (LC-RTC) program

The intervention will consist of participants using the LC-RTC program prescribed by their treating GP as an adjunct therapy to routine clinical practice treatment for 12 weeks. At intervention commencement (Baseline) as part of a routine care visit, the GP will provide and introduce participants to the LC-RTC program and associated materials. This will include the CSIRO Low Carb Diabetes Diet and Lifestyle Solution Book [17], a RT-CGM device (Medtronic, Guardian™ Connect system (MMT-7821L) and sensors (Guardian™ Sensor 3) including guides on connecting to the Guardian™ Connect (CSS7201) application (app) with specific instructions for Android™ or iOS™ platform use, with clear instructional guides. At this visit, the GP will provide the patient with an overview of the lifestyle program and the RT-CGM device and how to interpret glucose 'curves' and changes in response to diet and exercise. GP staff will also initiate the RT-CGM device including instructing the patient how to download the mobile app, perform sensor insertion and device initialisation and patients will perform their first-time sensor insertion under their supervision. GPs and associated staff will receive training prior to delivering the LC-RTC program intervention to participants and be provided access to technical and mobile app support via a free telephone hotline, throughout the intervention.

During the training GPs and associated staff were informed of the therapeutic benefits of lowering dietary carbohydrate on blood sugar and HbA1c management and subsequent need to monitor diabetes related medications in the first 2–4 weeks and adjust according to usual clinical practice. After intervention commencement, treating GPs will manage participants as per routine practice following introduction of any new lifestyle therapy and patients will continue to follow their routine GP care process, including routine blood tests, health reviews and the prescribing/deprescribing of medication as required.

4.5.1. CSIRO low carb diabetes diet and lifestyle solution

The CSIRO Low Carb Diabetes Diet and Lifestyle Solution Book [17], is an evidence-based, prescriptive energy-controlled eating and exercise plan. The book is presented in a simple, self-help guide format that utilises commonly available nutrient dense whole foods widely available from local supermarkets. Recipes and meal builders are provided to enable participants to select meals based on preferred cooking styles. Participants are instructed to engage with the eating and exercise instructions to help adapt their diet and exercise patterns in alignment with the principles described in the book.

The primary anticipated change between the participants anticipated habitual dietary intake to the prescribed CSIRO Low Carb Diet plan is a reduction (not elimination) of carbohydrate containing foods (breads, cereals, rice, pasta, potato, sweet potato and some fruits), and discretionary foods (chocolate, crisps, cakes, pastries, sugar sweetened

beverages and alcohol) with increases in the intake of low-moderate carbohydrate vegetables and monounsaturated fats (avocado, olive oil, olive oil based margarines, nuts). The plan will also instruct participants to calculate their body mass index (BMI) and if determined to be classified as overweight or obese using established WHO criteria (BMI >25 kg/m^2) will be recommended to restrict their energy intake by 2000–4000 kJ/day to achieve a weight loss of between 0.5 and 1.0 kg per week.

The plan also provides a prescriptive, self-guided, home-based exercise plan incorporating both aerobic and strength training-based exercises, in alignment with best-practice exercise principles for the management of T2D [26]. Specifically, participants will be recommended to achieve at least 150 min of moderate intensity or 75 min of vigorous intensity aerobic exercise per week or an equivalent combination. Participants will also be recommended to complete at 2–3 resistance training exercise sessions each week consisting of 5–10 exercises involving major muscle groups.

Apart from the introductory overview of the CSIRO Low Carb Diabetes Diet and Exercise plan provided at baseline (Week 0) by the GP, no formal professional counselling of the diet and exercise plan will be provided by the research team. Participants will remain under the guidance and recommendations of their treating GP and associated health care team throughout the entire 12-week intervention period.

4.5.2. Real time continuous glucose monitoring device

The Guardian™ Connect RT-CGM system (Guardian™ Connect, Medtronic Diabetes Global Headquarters, California, USA), is a commercially available, wearable health device consisting of a CGM recorder, transmitter, and sensor which determines blood glucose from interstitial fluids every 5 min. The transmitter receives blood glucose data from the sensor and transmits this data to the Guardian™ Connect app, which is a Bluetooth enabled, smart system (phone or device). Participants will wear the system daily for the 12-week intervention, during which they will be trained and supported to replace the sensor every 10 days. Participants will be provided guides and instructions to download the free, Guardian™ connect smart phone app that when linked to the data, will provide a 'live' visual display of their glucose readings (the "Glucose Curve"). This will allow participants to visually observe how their blood glucose levels are responding to the diet and exercise changes. It is expected that reviewing this "Glucose Curve" feedback will assist participants to adapt their lifestyle changes to improve their blood glucose control. With the participant's consent, participants will have the option to share and discuss these results with their treating GP.

Instructional materials, commercially available by Medtronic, describing how to insert the sensor and calibrate the glucose monitor will be provided (https://www.medtronic-diabetes.com.au/support/my-learning/guardian-connect). Continuous glucose monitor device calibration will require participants to take up to 2 daily finger prick blood glucose tests, using a glucometer. For the entire 12-week intervention, participants will be provided with all necessary medical consumables and free access to a telephone hotline for technical RT-CGM product support. They will also be able to contact the research office via a dedicated email, for reporting and management of adverse events and consumable replacement requirements.

4.6. Data collection and outcomes

Outcome measures will be collected at baseline (pre-intervention) and at 12 weeks (post-intervention). At each timepoint, as part of routine GP care review, body weight and blood pressure will be measured, medication usage recorded and a fasting blood sample taken to assess blood glucose, HbA1c and blood lipid levels. Height will be measured at baseline only.

To explore the GP's patient management decisions in response to the participants engagement, and to investigate participant engagement within the program, data collected through case notes will be used to assess objective feasibility outcomes including intervention dropout rates, the mode and number of GP consultations, number of nurse or allied health contacts with participants, RTCGM use and wear time.

At Week 12, participants will also be asked to independently complete an online questionnaire designed to assess their experience with and acceptance/tolerance of the glucose sensor use and wear time protocols as previously used and described [21]. This purpose designed questionnaire consists of 16 items, each scored using a 5-point Likert scale to explore participant experience of using the device and how it may have impacted lifestyle choices. This will include questions such as "The sensor and recorder caused me problems with regards to showering", "Installation of the sensor caused me pain" to address intolerance of the device wear protocols (9-items), and "Installing the sensor was easy for me", "I was easily able to calibrate the sensor", "I was satisfied with the look and feel of the sensor and recorder" to address acceptability of the device wear protocols (7-items). In total this questionnaire is expected to take 30 min to complete.

Following the completion of the 12-week intervention, participants and GP clinic staff will be invited by their treating GP to participate in a focus group interview, conducted face to face or via teleconference attendance, to understand their experiences and interactions associated with the LC-RTC program. The 1-h focus group will be conducted by investigator PT, up to 1 week after study completion. Participants will be asked to respond to questions, only if they feel comfortable and willing to do so. The focus groups will be delivered in two separate discussion groups:

- Group 1: GPs and associated staff prescribing and delivering the LC-RTC intervention
- Group 2: Participants using the LC-RTC intervention

Focus group questions will consist of semi-structured questions, generally starting with an opening question and several follow-ups and prompting questions. Questions will be designed to explore with participants the following various topic areas regarding the.

LC-RTC program intervention delivery, barriers and benefits and financial feasibility to understand the acceptance and feasibility of the intervention model. The example sample discussion guide provided below will be further developed by the primary investigators during the program intervention. Topic themes and question samples include:

4.7. Topic: program delivery

- ***Opening Question**: When you first heard about the first program, can you tell me about how you expected it to be delivered (to or by) you?*
- ***Follow-up Question**: How did you measure whether the program was being delivered in a successful or effective way for (you or your GP practice)?*
- ***Probing Question/s**: How could this product be delivered better to access more individuals) living with Type 2 Diabetes? Tell us what you found most useful about the product.*
- ***Opening**: when you first used the program, please tell me about what you expected, or hoped to have achieved.*
- ***Follow-up Question**: How did you measure whether the program was being successful or effective in helping you achieve goals (or your patients)?*
- ***Probing Question**: How acceptable do you feel the program was for improving the management of (you or your patients) living with Type 2 Diabetes?*
- ***Other**: What may have limited your success (on or delivering) the program?*

4.8. Topic: financial feasibility

- o***Opening Question, a:*** *In clinical practice we understand Medicare and Private health insurances have mandatory reporting and coding activities to support health care provision. As a treating GP and Practice Manager, do you feel the payment structure was suitable for this type of program?*
- o***Opening Question b:*** *In Australia, we are lucky to have a health care system that supports payment for Type 2 diabetes health care services under Medicare and in some cases those with private health insurances can access more extensive care. In regards the program you were using, who do you feel should pay for this and what would you expect the payment to be?*

4.9. Topic: perceived benefits and barriers

- o***Follow-up Question a:*** *Do you feel that this program would be cost effective if delivered by your GP practice, please explain?*
- o***Probing Question, a:*** *What would you need for the program to be most feasible, strategically and financially for you and your practice, please explain:*
- o***Follow-up Question b:*** *What is your opinion on paying for programs like this, yourself and not using Medicare? What strategies do you think could be used to reduce the overall cost?*
- o***Probing Questions b:*** *What was the value to you from using the program?*

4.10. Data management and confidentiality

After consenting, a unique participant identifier will be created and appended to the REDCap™ data base which will be used to collate and manage the study data with all data being coded to this identifier. Investigator (PT) will collate and manage the participant baseline data including the participant medical screening questionnaire and health biomarkers in the GP practice setting and offline using the Research Electronic Data Capture REDCap™ database [25,27], a secure web-based software system and password protected server. All data will be protected using secure data extraction methods and password protected computers with only Investigator (PT) responsible for this process throughout the intervention.

Focus group interviews will be audio recorded and transcribed verbatim, with no personal identifiers. All transcripts will be organised and coded thematically into Microsoft Excel and Word documents (Microsoft, New York, USA) under password protection and saved by Investigator (PT) in REDCap™ for data management.

To avoid potential bias within the intervention delivery across settings, Investigator (PT) will not deliver the 12-week program or provide RT-CGM education to participants but will actively monitor the delivery protocols and program governance across the GP practice sites.

4.11. Proposed sample size

The primary outcome will be HbA1c. Based on data from a previous study, a clinically relevant reduction in HbA1c of 0.67% is expected to be observed with the proposed intervention [20]. Based on the known levels of variation for the planned target population, using a paired *t*-test, an estimated sample size of at least 15 participants would be required to detect a mean difference in HbA1c of 0.67% between the pre- and post-intervention scores with a power of 80% at the 5% level of significance.

4.12. Statistical analysis plan

Data will be analysed using standard statistical procedures and statistical analysis will be conducted using SPSS Statistics 25 (IBM Corp, 2017). Data will be expressed as mean ± standard deviation (SD) and range for continuous data; and as frequencies for ordinal/categorial data. Statistical significance will be determined as having a P-value <0.05, two-tailed.

Outcome data will be assessed by paired and independent t-tests. Correlation and multiple regression analyses will determine relationships between variables. Feasibility and acceptability outcomes will be reported using a combination of descriptive (e.g. such as number, frequency and/or duration) qualitative text and quantitative statistics (e.g. mean, SD, range).

Qualitative focus group discussions will be dictated and converted to free text, with no link back to participant identifiers. A reflexive thematic analysis method based on the principles established by Braun and Clarke [28] will be used to examine the free text. This analysis approach will follow the six phases of reflexive analysis including: data familiarization, generation of codes using a deductive method, construction of themes, revising themes, defining themes and naming themes. The thematic analysis will be conducted by author P.T. who is the lead investigator of the study with experience in conducting qualitative analysis research involving individuals with chronic disease including T2D participating in lifestyle interventions including interventions using device technologies to improve health outcomes.

4.13. Trial oversight

The trial will be overseen by the Trial Management Group consisting of the authors and a GP representative from one of the GP practices who will be responsible for ensuring the study is conducted in accordance with the International Conference for Harmonisation of Good Clinical Practice (ICH-GCP) guidelines and will monitor the overall progress of the trial to ensure the study protocol is being adhered to.

4.13.1. Procedures for recording and reporting serious adverse events

All investigators and GP practice support staff involved in the delivery of the study will be advised on identifying and reporting of any adverse events (AE) received by the participant to their GP clinic who will inform the research office (Investigator - Taylor). All serious AEs will be subsequently reported to the trial steering committee and the CSIRO Human Research Ethics Committee. All AEs will be treated and monitored by the treating GP and lead investigator (Taylor).

4.14. Ethics and dissemination

4.14.1. Research ethics approval

Ethical approval has been granted by the Human Research Ethics Committee of the Commonwealth Scientific and Industrial Research Organisation (CSIRO HREC 059–2020).

4.14.2. Insurance/indemnity

Standard procedures for insurance of the Commonwealth, Scientific and Industrial Research Organisation, University of Adelaide, University of South Australia and employees and patients of the GP practices will apply.

4.14.3. Dissemination approach

The results will be presented to healthcare professionals nationally and internationally and published in peer reviewed journals. If the program intervention appears to be successful for improving metabolic health, we expect to use the feasibility and acceptability information to refine the delivery model and to work with the broader primary health care network and industry partners to conduct larger clinical studies and to integrate this health program within existing primary care health services.

5. Discussion

T2D is a global health issue associated with substantial health and socioeconomic costs. Access to timely care management to optimise

glycaemic control is a major barrier to effective diabetes management and prevention of disease progression. This paper outlines a protocol for an interventional study to evaluate the changes in metabolic health, acceptability, and feasibility of translating for wider adoption, an evidence based, wearable technology integrated lifestyle program through primary health care environments and within Australian GP practices. If shown to be efficacious, this study will provide important information to support further development and adoption of this treatment approach which could provide an effective tool for GPs and primary allied health care providers to prescribe to their patients living with T2D to improve their management and health outcomes.

There are several limitations that need to be considered when assessing the potential impact and implications of our findings. First, we do not have a control group, so any change that occur cannot be specifically attributed to the intervention. Second, the LC-RTC program and its related products will be provided free-of-charge. This may limit understanding of its potential as a public health intervention in the 'real-world' when participants have to pay. Although the study aims to evaluate the feasibility of Medicare item number use for delivery of such a program, the current context of health care in Australia is commonly perceived by clinicians and patients to be "free" or "bulk-billed". This may limit engagement with a program which may be termed to have "out of pocket" costs -paid by the patient. Finally, the use of leading statements in some focus group questions (e.g. In Australia, we are lucky to have a health care system that supports payment …), may lead to some response bias. However, context was considered important to obtaining the specific information sought from these questions.

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Role of sponsor

This funding sources will have no role in the design of this study and will not have any role during its execution, analyses, interpretation of data, or decision to submit results.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: PT and GDB are authors of the CSIRO Low Carb Diet Book series that aims to translate clinical research outcomes of low carbohydrate diet studies for the general public in Australia, but he does not personally receive any financial royalties or funds either directly or indirectly from this publication, and any royalties received by his employment institution (CSIRO) do not contribute to his salary, nor have they been used to execute this work. No other relationships or activities that could potentially influence the study are declared.

References

[1] S.J. Han, E.J. Boyko, The evidence for an obesity paradox in type 2 diabetes mellitus, Diabetes Metab. J 42 (3) (2018) 179–187.
[2] S. Ramzan, P. Timmins, S.S. Hasan, Z.U. Babar, Cost analysis of type 2 diabetes mellitus treatment in economically developed countries, Expert Rev. Pharmacoecon. Outcomes Res. 19 (1) (2019) 5–14.
[3] N.H. Cho, J.E. Shaw, S. Karuranga, Y. Huang, J.D. da Rocha Fernandes, A. W. Ohlrogge, B. Malanda, IDF Diabetes Atlas: global estimates of diabetes prevalence for 2017 and projections for 2045, Diabetes Res. Clin. Pract. 138 (2018) 271–281.
[4] A. American Diabetes, Standards of medical care in diabetes - 2020, Diabetes Care 43 (Suppl 1) (2020) s1–s212.
[5] M. Lee, L.J. Aronne, Weight management for type 2 diabetes mellitus: global cardiovascular risk reduction, Am. J. Cardiol. 99 (4A) (2007) 68B–79B.
[6] M.E.J. Lean, W.S. Leslie, A.C. Barnes, N. Brosnahan, G. Thom, L. McCombie, C. Peters, S. Zhyzhneuskaya, A. Al-Mrabeh, K.G. Hollingsworth, et al., Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial, Lancet Diabetes Endocrinol. 7 (5) (2019) 344–355.
[7] E. Sainsbury, N.V. Kizirian, S.R. Partridge, T. Gill, S. Colagiuri, A.A. Gibson, Effect of dietary carbohydrate restriction on glycemic control in adults with diabetes: a systematic review and meta-analysis, Diabetes Res. Clin. Pract. 139 (2018) 239–252.
[8] R. Huntriss, M. Campbell, C. Bedwell, The interpretation and effect of a low-carbohydrate diet in the management of type 2 diabetes: a systematic review and meta-analysis of randomised controlled trials, Eur. J. Clin. Nutr. 72 (3) (2018) 311–325.
[9] Y. Meng, H. Bai, S. Wang, Z. Li, Q. Wang, L. Chen, Efficacy of low carbohydrate diet for type 2 diabetes mellitus management: a systematic review and meta-analysis of randomized controlled trials, Diabetes Res. Clin. Pract. 131 (2017) 124–131.
[10] O. Snorgaard, G.M. Poulsen, H.K. Andersen, A. Astrup, Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes, BMJ Open Diab. Res. Care 5 (1) (2017), e000354.
[11] S. Li, L. Ding, X. Xiao, Comparing the efficacy and safety of low-carbohydrate diets with low-fat diets for type 2 diabetes mellitus patients: a systematic review and meta-analysis of randomized clinical trials, Int. J. Endocrinol. 2021 (2021).
[12] J.Z. Goldenberg, B.C. Johnston, Low and very low carbohydrate diets for diabetes remission, BMJ 373 (2021) n262.
[13] A.B. Evert, J.L. Boucher, M. Cypress, S.A. Dunbar, M.J. Franz, E.J. Mayer-Davis, J. J. Neumiller, R. Nwankwo, C.L. Verdi, P. Urbanski, et al., Nutrition therapy recommendations for the management of adults with diabetes, Diabetes Care 36 (11) (2013) 3821–3842.
[14] J. Tay, C.H. Thompson, N.D. Luscombe-Marsh, T.P. Wycherley, M. Noakes, J. D. Buckley, G.A. Wittert, W.S. Yancy Jr., G.D. Brinkworth, Effects of an energy-restricted low-carbohydrate, high unsaturated fat/low saturated fat diet versus a high-carbohydrate, low-fat diet in type 2 diabetes: a 2-year randomized clinical trial, Diabetes Obes. Metabol. 20 (4) (2018) 858–871.
[15] N. Kakoschke, I.T. Zajac, J. Tay, N.D. Luscombe-Marsh, C.H. Thompson, M. Noakes, J.D. Buckley, G. Wittert, G.D. Brinkworth, Effects of very low-carbohydrate vs. high-carbohydrate weight loss diets on psychological health in adults with obesity and type 2 diabetes: a 2-year randomized controlled trial, Eur. J. Nutr. 60 (8) (2021) 4251–4262.
[16] J. Tay, C.H. Thompson, N.D. Luscombe-Marsh, M. Noakes, J.D. Buckley, G. A. Wittert, G.D. Brinkworth, Nutritional adequacy of very low- and high-carbohydrate, low saturated fat diets in adults with type 2 diabetes: a secondary analysis of a 2-year randomised controlled trial, Diabetes Res. Clin. Pract. 170 (2020), 108501.
[17] G. Brinkworth, P. Taylor, The CSIRO Low Carb Diabetes Diet & Lifestyle Solution, Pan Macmillian, Sydney, 2020.
[18] G. Brinkworth, P. Taylor, The CSIRO Low Carb Diet, Pan Macmillian, Sydney, 2017.
[19] S. Michie, C. Abraham, C. Whittington, J. McAteer, S. Gupta, Effective techniques in healthy eating and physical activity interventions: a meta-regression, Health Psychol. 28 (6) (2009) 690–701.
[20] P.J. Taylor, C.H. Thompson, N.D. Luscombe-Marsh, T.P. Wycherley, G. Wittert, G. D. Brinkworth, Efficacy of real-time continuous glucose monitoring to improve effects of a prescriptive lifestyle intervention in type 2 diabetes: a pilot study, Diabetes Ther 10 (2) (2019) 509–522.
[21] P.J. Taylor, C.H. Thompson, N.D. Luscombe-Marsh, T.P. Wycherley, G. Wittert, G. D. Brinkworth, I. Zajac, Tolerability and acceptability of real-time continuous glucose monitoring and its impact on diabetes management behaviours in individuals with Type 2 Diabetes - a pilot study, Diabetes Res. Clin. Pract. 155 (2019), 107814.
[22] J.A. Davidson, The increasing role of primary care physicians in caring for patients with type 2 diabetes mellitus, Mayo Clin. Proc. 85 (12 Suppl) (2010) S3–S4.
[23] M. Shrivastav, W. Gibson Jr., R. Shrivastav, K. Elzea, C. Khambatta, R. Sonawane, J.A. Sierra, R. Vigersky, Type 2 diabetes management in primary care: the role of retrospective, professional continuous glucose monitoring, Diabetes Spectr. 31 (3) (2018) 279–287.
[24] R. Voelker, Study identifies primary care knowledge gaps and barriers in type 2 diabetes prevention, JAMA 322 (2019) 1945–1946, 20.
[25] P.A. Harris, R. Taylor, R. Thielke, J. Payne, N. Gonzalez, J.G. Conde, Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support, J. Biomed. Inf. 42 (2) (2009) 377–381.
[26] S.R. Colberg, R.J. Sigal, J.E. Yardley, M.C. Riddell, D.W. Dunstan, P.C. Dempsey, E. S. Horton, K. Castorino, D.F. Tate, Physical activity/exercise and diabetes: a position statement of the American diabetes association, Diabetes Care 39 (11) (2016) 2065–2079.
[27] P.A. Harris, R. Taylor, B.L. Minor, V. Elliott, M. Fernandez, L. O'Neal, L. McLeod, G. Delacqua, F. Delacqua, J. Kirby, et al., The REDCap consortium: building an international community of software platform partners, J. Biomed. Inf. 95 (2019), 103208.
[28] V. Braun, V. Clarke, Thematic Analysis: A Practical Guide, SAGE Publications, 2021.