The Diabetes Reference Panel [DRP] & Diabetes Online Review Group [DORG]

NEWSLETTER

Nr. 6 - Summer 2019

Welcome to the sixth edition of our Newsletter.

The Reference Panel [DRP] and the Online Group [DORG] met on the 18th of June 2019 for the 6th BRC-sponsored meeting, with researchers and clinicians to hear more about the research taking place in Oxford and get a glimpse of the scientific world behind the closed door of a lab.

This newsletter aims to recap the main points of the talks, connecting our scientists and managers with patients and providing an important communication channel between them. At the end you will also find some active calls for participation to trials and other opportunities to get involved in research.

An important communication: the meeting scheduled for Tuesday the 8th of October 2019 (Meeting #7) has been CANCELLED for technical reasons. The dates and times for the next few meetings are at the end of this Newsletter.

On a final note, I will be leaving my post as Project Manager for the Diabetes Theme at the end of September, and I would take this occasion to thank all the panel members and all the brilliant speakers for the exceptionally positive experience in collaboration, cooperation and dissemination of science that we have had over the last couple of years. I wish all panel members many more successful, interesting and enjoyable meetings in the future.

Dr. Marco Pontecorvi

Sleep improvement for metabolic health: Feasibility trial of a digital sleep treatment in people who are at high risk of type 2 diabetes and have insomnia

[Prof. S. Kyle]

Sleep is important for maintaining good health and well-being. Sleep restriction has been shown to reduce insulin sensitivity and glucose tolerance. Because of this, insomnia has been recognised as a risk factor for the development of type 2 diabetes. Insomnia is also associated with poorer glycaemic control in people with type 2 diabetes. Because of these associations, we would like to test whether improving sleep can help improve metabolic health in people at high-risk of type 2 diabetes. This hypothesis would be best tested in a randomised controlled trial (RCT).

Before undertaking a RCT we will conduct a small feasibility study (SleepTMH) to test the intervention and the recruitment process. The SleepTMH study will allow us to gather data to inform the design of a future RCT. It will also allow for patient and public input on the recruitment process and the intervention. The SleepTMH study will use a digital cognitive behavioural therapy (dCBT) as an intervention. Several RCTs have shown that dCBT improves sleep but the effect on metabolism has not yet been tested. Patients will be identified and recruited from primary care by searching patient records. Participants will then be invited to a secondary care setting. Here they will undergo detailed metabolic measurement testing and answer several questionnaires.

Diabetes and pregnancy: Finding out the important questions for research to address

[Dr. G. Ayman]

Diabetes affects over one in 20 (5%) of all women giving birth in the UK. Compared to the population of women without diabetes, it increases the risk of complications during pregnancy and birth for the mother and her baby, and can also affect them in the long-term. More research is needed to help provide the best health care for women, with or at risk of diabetes who are planning a pregnancy or are pregnant.

The research that is being done by commercial organisations e.g. drugs companies and non-commercial organisations e.g. universities, does not match up well with the areas considered most important of those who would benefit from the research. For example, the majority of

commercial research is focussed on developing drugs as treatments. However, patients and their families would like more research on non-drug treatments.

A Priority Setting Partnership has been established by the NPEU, University of Oxford, in partnership with the James Lind Alliance, Diabetes UK, JDRF, DRWF, healthcare professionals (HCPs), and people who have lived experience of diabetes and pregnancy.

Our aim is to produce a top ten list of research questions that women, their support networks, and HCPs agree are the most important for research to address in diabetes and pregnancy.

The top ten list will be shared with the public, research funders, national policy makers and clinical studies groups to inform their priorities and strategies for funding research. Thereby, this project will enable funders to support research for which there is great need and that is aligned with the priorities of those impacted by it.

The project's initial survey is now open. The team invite women, their families and friends and healthcare professionals with any interest, worries or experiences in pregnancy with diabetes of any type, to put forward their questions. This can be anything about the time before, during or after pregnancy with diabetes of any type e.g. type 1, type 2, MODY, gestational diabetes and others.

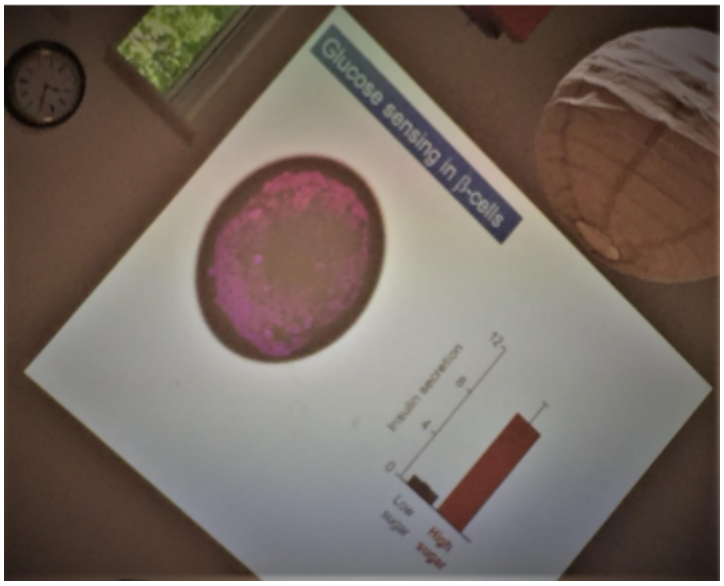
For further information and to take part in the project, please visit our website: www.npeu.ox.ac.uk/jla-psp

Exciting islet cells - Ca2+ and electrical activity

[Dr. Q. Zhang]

Pancreatic islets, the endocrine micro-organs embedded in the parenchyma of the pancreas, play a central role in maintaining the whole body blood sugar within a narrow range (glucose homeostasis). They do so by secreting sugar-lowering insulin (from beta cells) and glucose-elevating glucagon (from alpha cells). In addition to beta and alpha cells, pancreatic islets also contain somatostatin-producing delta cells, which function as intra-islet paracrine regulators of insulin and glucagon secretion. Appropriate function/activity of the islet cells prevents

hyperglycemia (too high blood sugar) and hypoglycaemia (too low blood sugar); abnormal secretory pattern of insulin and/or glucagon leads to diabetes, a disease that is characterised by uncontrolled blood sugar levels. All the islet cells are electrically excitable and are able to use electrical signals (action potentials) to control hormone secretion. In beta cells, the glucose sensing is mainly attributable to their fuel sensors – the ATP-sensitive potassium channels (KATP-channels). High intracellular ATP levels (from glucose metabolism) act at the KATP-channels and trigger beta cell electrical activity which allows influx of Ca2+ through voltage-gated Ca2+ channels. Subsequent increase in intracellular Ca2+ triggers release of insulin through exocytosis (a process that the hormone-containing granule fuses to cell membrane to release its contents). In contrast to this 'on/off' electrical control of insulin secretion, regulation of glucagon secretion is more complex. Alpha cells are able to generate high amplitude electrical signals at low glucose and thus provide enough Ca2+ to trigger glucagon secretion; high glucose reduces the amplitude of alpha cell electrical signals and thus lowers glucagon secretion due to insufficient Ca2+ influx into the alpha cells. Understanding the electrophysiology of the islet cells provides insights of the regulatory mechanisms of islet hormone release, the foundation for developing drugs for modulation of islet cell activity.



Do 5a-reductase inhibitors worsen the metabolic effects of steroids?

[Dr. N. Othonos]

Obesity is associated with metabolic conditions such as insulin resistance, type 2 diabetes and fatty liver. These conditions are similar to the metabolic side-effects of steroids such as Prednisolone. 5a-reductases are important enzymes in the metabolism of steroids, therefore their

inhibitors can theoretically prolong the action of steroids. These enzymes also convert

testosterone to its more biologically potent form, dihydrotestosterone and therefore, 5a-reductase inhibitors are commonly used for prostate problems. The aim of our clinical study was to investigate if co-administration of prednisolone and a 5a-reductase inhibitor worsens the metabolic side-effects of steroids, such as insulin resistance. By confirming this theory, it will indicate a possible pathway by which steroids cause these metabolic problems, which are similar to obesity effects.

Six healthy volunteers were given prednisolone 10mg daily for a week and 13 were given prednisolone 10mg daily and a 5a-reductase inhibitor (finasteride 5mg daily or dutasteride 0.5mg daily) for a week. The volunteers underwent a variety of metabolic assessments which included blood sample analysis, insulin clamp, analysis of the fluid around the abdominal fat and fat tissue biopsy. The assessments were performed twice, once before the medication and the second time on the 7th day the medication was taken.

The results showed that there was evidence of increase in insulin resistance in participants taking both prednisolone and a 5a-reductase inhibitor. We know that insulin inhibits fat breakdown, therefore during the insulin clamp we expect to see less products of fat breakdown as time progresses. However, after taking both prednisolone and a 5a-reductase inhibitor for a week there were more products of fat breakdown in this group compared to the group taking only prednisolone, by the end of the clamp. This indicates that the combination of the two medications exacerbates the action of steroids on fat breakdown. We also looked at and compared all the active

genes, via RNA sequencing, in the fat tissue before and after treatment. This is a helpful method to help us understand at a molecular level how steroids can affect the function of fat cells. However, we did not find any significant changes pre and post treatment.

In conclusion, metabolic side-effects of steroids, similar to those developed due to obesity, are exacerbated when co-administered with a 5aR inhibitor. It is therefore important to consider a steroid dosage adjustment in cases where a patient is also required to take a 5aR inhibitor.

How to communicate a diagnosis of type 2 diabetes in primary care

[Dr. O. Kozlowska]

Introduction The way a diagnosis is broken to patients have been evidenced as having a variety of consequences on both patients and healthcare professionals. Communication about the illness at its early stages, including diagnosis, is a first step in building patient-healthcare professional rapport and determining the patients' attitude towards their illness and treatment, and health services.

Primary care healthcare professionals are tasked with informing patients about their condition even if they do not have the skills to do it. Building on the evidence from the literature, observations of clinical practice and conversations with patients and practitioners, this study will address this gap in diabetes care.

Key goals The aim of this study is to promote the significance of patient-healthcare professional communication in diabetes care and inform the clinical practice by assisting those communicating diagnosis in doing it in a way that supports understanding of the condition and patient's engagement with treatment.

The study goals include:

1. To determine what, when and how is communicated to patients at the time of diagnosis of type 2 diabetes.

2. To understand how different ways of communicating a diagnosis of type 2 diabetes shape healthcare professionals and patients' construction of the illness and engagement in treatment

3. To identify effective ways of communicating a diagnosis of type 2 diabetes

Stages of the project and methodologies to be used

1. A review of the ways of communicating diagnosis of chronic conditions (type 2 diabetes in particular) and their effectiveness in terms of patient understanding of their condition, adherence to treatment and engagement with health services

2. Twenty consultations with giving a diagnosis to be video-recorded. Adult patients with type 2 diabetes, GPs and practice nurses will be interviewed about their experiences of receiving/giving diagnosis of diabetes after the first consultation.

3. The participating patients to be interviewed again after six months of diagnosis to explore their understanding of their condition, adherence to treatment and engagement with health services.

We will explore the interactions during the consultation and how different ways of interacting impact on the overall experience of communicating about the diagnosis. We will then explore the participants' understanding of the diagnosis of diabetes and their perceptions of the consultation.

Acknowledgement

I would like to thank the group for their questions and encouragement. Your advice about the ethical and practical issues benefited this proposal. We are going to seek funding to proceed with the study

Final remarks *[Prof. K. Owen]*

Thanks to all for attending the meeting again and for the helpful comments and input. We are now in the process of organising speakers and topics for our 2020 meetings, so please let us know if you have any suggestions.

I have some sad news - after 3 years working for the Diabetes Theme, Marco is going to moving onto a new post at the beginning of October. He's been appointed as General Manager for the Oxford Health BRC so will be involving himself in research into Brain Health - mental health, dementia and neuroscience among other topics. This another very important set of long term health conditions, with some overlapping research with with diabetes, so I'm sure we will continue to be in touch with Marco. I'm tremendously grateful to him for the time he has devoted to PPI within the Diabetes theme and in particular for making the patient panel meetings such a success. I'm sure you'll all join me in thanking him for all his efforts and wish him well in the future.

Remember that the next Panel meeting scheduled on October 8th has been cancelled: please refer to the dates below for our next appointments.

FROM PATIENTS' EYES *[Dr. M. Pontecorvi]*

All patients in the group are welcome to submit a short comment they may want to share about their experience in the group, the meeting, other involvements they may have across the numerous and different PPI bodies and organizations. Thanks to the comments already received.

If interested, please contact Prof. Katharine Owen (katharine.owen@drl.ox.ac.uk), thanks.

More News

SAVE THE DATES! Calendar and dates for 2018-2019 meetings

NEW DATES 2019-2020

Tuesday 8th of October 2019 Meeting - MEETING CANCELLED!

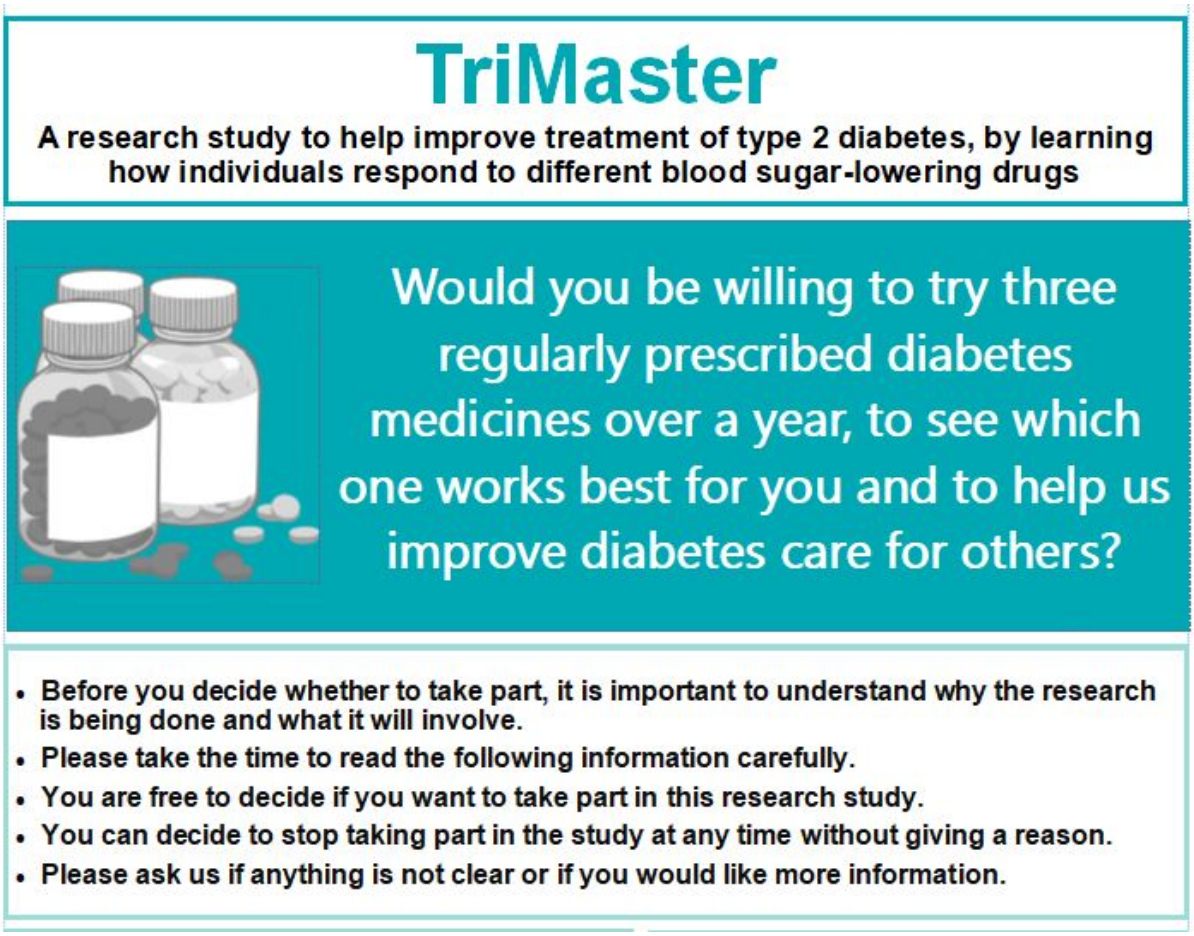
Tuesday 28th of January 2020 Meeting #7

Tuesday 26rd of June 2020 Meeting #8

Tuesday 13th October 2020 Meeting #9

Please be aware that panel meetings are now planned to run from **1:30pm to about 4:00pm** instead of 1:00 to 3:30pm!

We are still open to evaluate different needs and we aim to propose again a similar poll in a few months time. However, for the next couple of dates we will keep our norm. If you have any feedback or suggestion as to the meeting dates or times please do send an email to Prof. Katharine Owen (katharine.owen@drl.ox.ac.uk) to discuss.



Important things you need to know

The study will involve taking three standard diabetes drugs alongside your current medication: sitagliptin, canagliflozin and pioglitazone. They will be prescribed randomly, one drug at a time, for 16 weeks. There will be an appointment before starting each drug. Participation in this study will involve six visits over a year (2 x 30 minute visits, 3 x 60 minute visits and 1 x 3 hour visit) The 30 and 60 minute visits may be able to be conducted at your home if you are unable to attend the hospital. We will ask you to provide blood samples to ensure you are safe and eligible to participate in the study. All the drugs will be made to look identical, so that you and the study team will not know which drug you are taking. A dedicated team will be available to help if you suffer any side-effects and your doctor needs to find out what you are taking.

If you would like to find out more information about the OPTION-DM TRIAL, please contact Viv Thornton-Jones Vivien.thornton-jones@ouh.nhs.uk or Nicky McRobert nicky.mcrobert@ouh.nhs.uk OR telephone 01865 857511