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

NEWSLETTER

Nr. 3 - Summer-Autumn 2018

Welcome to the third edition of our Newsletter.

The Reference Panel [DRP] and the Online Group [DORG] met on the 12th of June 2018 for the 3rd 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.

PLEASE HELP! Let us find the best time to meet! Finally, I would like to ask you to complete a short survey HERE (***https://goo.gl/forms/KFxbZbsS0NThNcYX2***) designed to understand which time of the day is more suitable for you to attend PPI meetings.

Dr. Marco Pontecorvi

Research Design Day *[Teresa FInlay]*

Dr. Finlay reporting on the very successful Research Design Day.

Dr. Finlay presented a summary of the Research Design Day that considered patients' expectations of a data sharing platform. The day was organised and hosted by the Oxford Biomedical Research Centre's Partnerships for Health Wealth and Innovation theme. The background to how this patient, clinician, researcher and Informatics staff "hack day" came about was covered before going into the content of the day and the important summary of features that any such platform should have as agreed by all at the day. A very positive evaluation was summarised and the next steps for the project outlined.

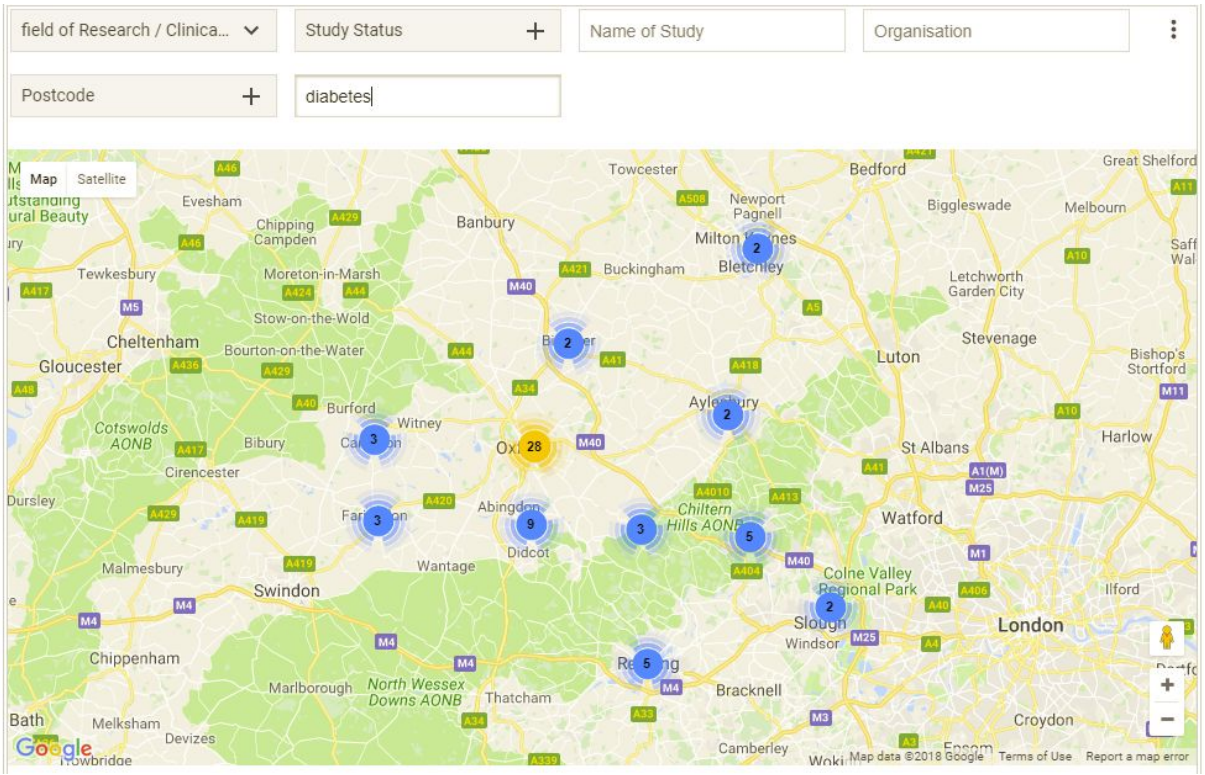
How many chefs are stirring the broth? *[Dr. Christopher Hille]*

Dr. Hille has been actively involved in preclinical and clinical research since he joined University of Manchester as a research technician over 30 years ago. He worked as a senior manager in the Thames Valley and South Midlands Clinical Research Network as a research delivery manager, covering amongst other disease areas. He also worked with the Oxford Academic Health Science Network. Prior to this he managed the research networks that predated the current network structure, covering both Diabetes and Stroke Local Research Networks. Drawing from his background and knowledge on the matter, and following some interest expressed by members of our panel of patients, he presented a concerted overview of the many organisations which contribute to the administration and provision of health care in UK, particularly in Oxfordshire.

Dr. Hille is talking about how many different organizations come together to provide healthcare and input into research.

An additional note: CAN YOU HELP?

The Thames Valley & South Midlands Local Clinical Research Network is developing a Google map based platform for highlighting the available clinical research studies in the region. The map could be searched by keyword, research area/clinical condition, postcode, organisation and will provide hyperlinks through to study information. The project is at the development stage and would benefit from patient and public input to improve the functionality, language and general format. Eventually this will be publically available but in the development stage **we are looking for reviewers that use Google Chrome or would be happy to use Google Chrome to provide feedback**.



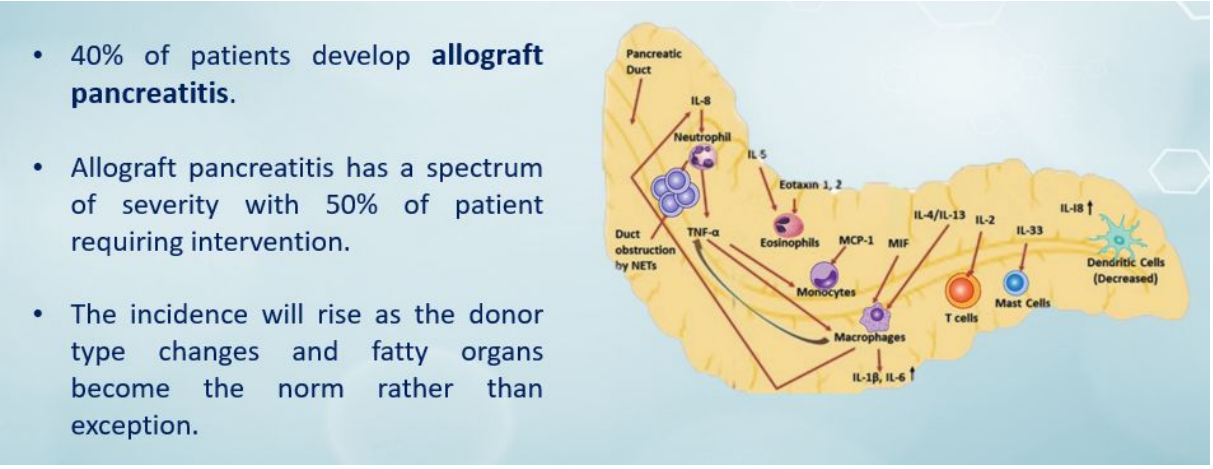
If interested please contact Dr. Christopher Hille at Christopher.Hille@ouh.nhs.uk

The JAK kinase trial *[Dr. Sham Dholakia]*

Pancreas transplantation is a life transforming treatment for some patients with type 1 diabetes, halting and even reverses some of the complications seen. It is used for those patients who despite insulin cannot control their blood sugar but despite its clear advantages has been hindered by complications that happen frequently following surgery.

Pancreatitis describes inflammation of the pancreas, and when a donated pancreas is taken out of one body and put into another, this inflammation occurs frequently affecting approximately 40% of patients. The result of inflammation are longer stays in hospital and more surgical complications and so developing a solution for this problem is critical.

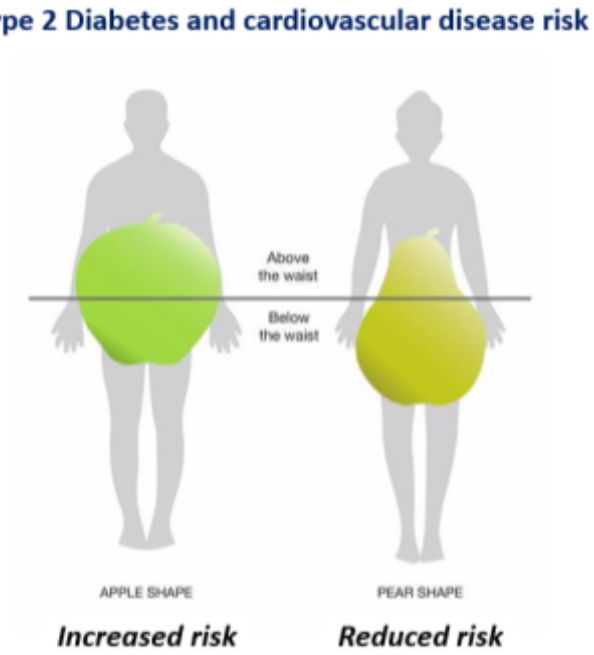
The BRC have funded a clinical trial to look at a new medication, designed to combat this inflammation and prevent patients from developing pancreatitis following surgery, in hope that it will eliminate the problems seen following surgery. Providing better outcomes for patients and also allow more people to benefit from pancreas transplant. The trial is ongoing with results expected next year.



Fat distribution and diabetes: LRP5 gene *[Dr. Nellie Loh]*

Dr. Loh is a scientist working on fat cell metabolism and physiology. Fat cells (adipocytes) are to our body, what a fuel tank is to a car. They are important for the safe storage of excess energy and its release from fat stores when our body needs it. The storage capacity of fat tissue depends on the number and size of fat cells available. If we overfill a car with a 45 litre fuel tank we'd end up accumulating fuel in undesirable places, so too if we exceed the storage capacity of our fat tissue, our body starts storing dietary fat in other organs such as muscle, liver and pancreas, which ultimately leads to metabolic complications.

However, it's not just their size and number; the location of our fat cells is also important. Population studies have shown that individuals who have more tummy fat have a greater risk of developing type-2 diabetes and cardiovascular disease, whereas those with more bum fat are protected. One reason is that fat cells from different locations are formed from different types of stem cells. Just as cars of different make and model have fuel tanks of different size and complexities, the different stem cells develop into mature fat cells with distinct characteristics. Moreover, our body fat distribution is hereditary. The aim of our research is to in identify and understand how some genes determine our body fat distribution.



Fat distribution is a key issue in Diabetes and Cardiovascular disease risk

One such gene encodes LRP5, a protein present on the cell surface of some types of stem cells. LRP5 (and associated proteins) is important for the maintenance and regeneration of adult tissue throughout life. It does this by signalling stem cells to divide and form more specialised cells when a tissue/ an organ needs it. There are individuals with rare genetic variants in LRP5 who were identified because they have higher bone mineral density than the general population. We found that these individuals also have more lower-body (bottom and leg) fat and are more insulin-sensitive compared with matched controls.

To understand how changes in LRP5 signalling affect insulin sensitivity in these individuals, we've taken fat biopsies from the abdomen and bottom area of volunteers, isolated their fat stem cells, and grew them in culture. In some cases we genetically engineered the stem cells to express either control or high bone mineral density variants of LRP5, to study how well the different stem cell types divide and form fat cells in culture, and how well these fat cells respond to insulin. Using these cells we hope to better understand what makes individuals with LRP5 high-bone-mass variants more insulin sensitive, and ultimately bring us one or two steps closer to improving treatment for increasing insulin sensitivity in patients with type-2 diabetes.

Transplant pancreatectomy study *[Dr. Richard Dumbill]*

Dr. R. Dumbill

Patients with type 1 diabetes have lost the ability to produce insulin, due to an autoimmune reaction to insulin-producing cells in the pancreas. This can be treated by replacing the insulin (with injections), or by replacing the pancreas with a transplant. This is most commonly done with a kidney transplant, to treat kidney failure resulting from diabetes. Transplants such as these commonly last between 7 and 14 years, although there is some risk of graft loss in the first year due to technical complications. The factors that lead to transplant failure in the longer term are not well understood.

We sought to study this by examining changes in pancreas grafts that have had to be removed due to complications early after the operation. We studied the cells that make up the pancreas to determine how much insulin was being produced, and looked at the relationship between this and factors related to the transplant. A grant from the Biomedical Research Centre allowed us to extend this work to find and study grafts that were removed after a long time in place, to inform us about the long-term effect of these changes. It also contributed to the development of image analysis software to more accurately measure our microscope images of the pancreatic tissue. Work is ongoing, and we hope to publish our results in the not-too-distant future.

Final remarks *[Prof. K. Owen]*

Prof. Owen discussing some of the outcome of the Research Design Day

It's been great to work with groups of patients recently to get input into some of the Digital developments that are occurring at the OUH Trust. When the current projects come to fruition we should see a great improvement in both clinical care and our ability to do research.

Recently some of our researchers, volunteers and PPI enthusiasts have been involved in filming about diabetes research in Oxford, this should be up on the website soon and provide a great overview and introduction to our projects. Finally there have been a few

requests for your help - thanks to all those who can offer comments, feedback and further help. We really appreciate it.

More News

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

Tuesday 9th October 2018 - Meeting #4

Tuesday 29th of January 2019 - Meeting #5

Tuesday 18th of June 2019 Meeting #6

All Panel meetings are still planned to run from **1:00pm to about 3:30pm**, but as you can read on page 1, we are also investigating other possible times during the day (i.e., late afternoon/evening) in order to facilitate member still in full time employment, as well as video-conference for members with limited mobility or availability to travel during the day. **If you want to have your say on this matter** please complete the short survey HERE (***https://goo.gl/forms/KFxbZbsS0NThNcYX2***) designed to understand which time of the day is more suitable for you to attend our meetings

You will be kept informed on any development on the matter.

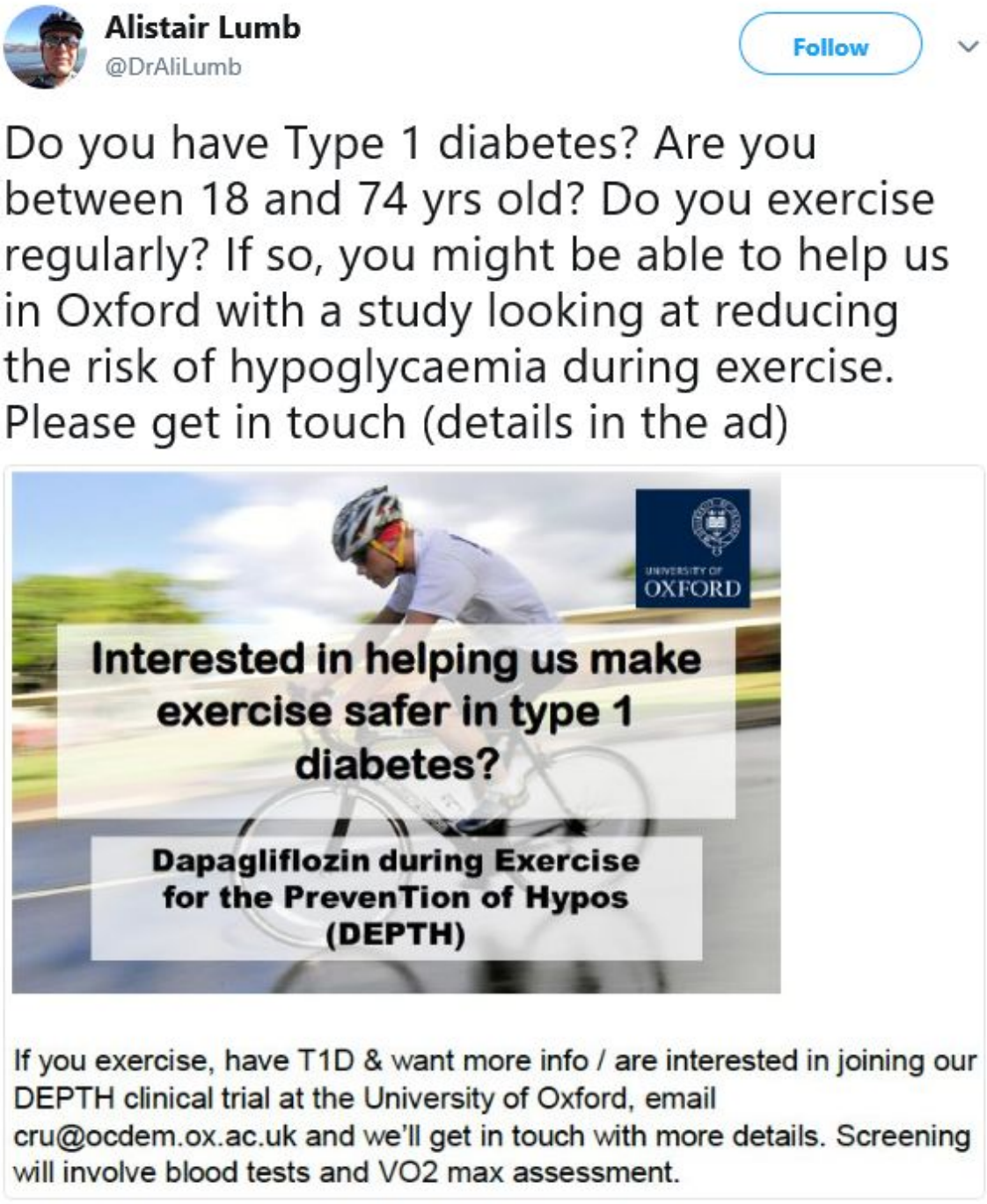
Further you will find information about the following trials:

DEPTH Clinical Trial

TICSI Trial (JT/Nantia)

Option-DM Trial

TriMaster Trial



For more information please contact cru@ocdem.ox.ac.uk

TICSI TRIAL

Tackling Iatrogenic Cushing's Syndrome through 11β-HSD1 Inhibition (TICSI)
Poster v1.03_23022018
IRAS ID no. reference: 212634
Chief Investigator: Prof J Tomlinson

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NHS
National Institute for Health Research

Want to know your body fat percentage? Join our study into limiting the impact of steroids.

We are running a clinical study to trial a new medication to block the unwanted side effects of steroid medication.

If you are a healthy man aged between 18-60 and interested in taking part - please contact:

Dr Nadia Othonos
Oxford Centre for Diabetes, Endocrinology and Metabolism,
Churchill Hospital,
Headington.
01865 857359
Nantia.Othonos@ocdem.ox.ac.uk

Prof Jeremy Tomlinson
Oxford Centre for Diabetes, Endocrinology and Metabolism,
Churchill Hospital,
Headington.
01865 857359
Jeremy.tomlinson@ocdem.ox.ac.uk

We will reimburse any travel costs and offer compensation for your time and inconvenience

For more information please contact Nantia.Othonos@ocdem.ox.ac.uk or Jeremy.tomlinson@ocdem.ox.ac.uk

Oxford University Hospitals NHS
NHS Foundation Trust

OPTION-DM

Do you have diabetes?

Do you suffer from painful nerve damage as a result of your diabetes?

If you answered YES to these questions, you may be interested in our research study, OPTION-DM.

This study will look at three commonly used medications to try to find the most effective treatment for painful nerve damage as a result of diabetes.

At the moment we don't know which is the best initial treatment, or combination of treatments. This study will provide important information which will inform the treatment of future patients, and may help to find a better treatment for your own pain.

The study will look at amitriptyline, duloxetine and pregabalin, both as single medications, and also in combination with each other, to see which single treatment, and which combination treatment is the most effective. All three of these drugs are currently recommended for use in treating patients with painful diabetic neuropathy in the NHS, but until now, there have been no comparisons between the drugs.

All participants who join the study will receive all three treatment pathways that are compared in this trial, but the order in which these are received, will be randomly allocated. Each treatment pathway will last approximately 13 weeks, so participation in the study will last around a year. The research is entirely voluntary, confidential and will not affect your usual care and treatment. Participation in the study will last around a year with regular contact with the research team.

You may be eligible to take part if you:

- **Have diabetes**
- **Suffer from painful nerve damage as a result of your diabetes**
- **Are aged 18 or over**

The research study has been reviewed by an NHS research ethics committee. The study is funded by the National Institute for Health Research Health Technology Assessment (NIHR HTA) programme.

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

TriMaster

A research study to help improve treatment of type 2 diabetes, by learning how individuals respond to different blood sugar-lowering drugs

Would you be willing to try three regularly prescribed diabetes medicines over a year, to see which one works best for you and to help us improve diabetes care for others?

- **Before you decide whether to take part, it is important to understand why the research is being done and what it will involve.**
- **Please take the time to read the following information carefully.**
- **You are free to decide if you want to take part in this research study.**
- **You can decide to stop taking part in the study at any time without giving a reason.**
- **Please ask us if anything is not clear or if you would like more information.**

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

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.

If interested, please contact Marco Pontecorvi (marco.pontecorvi@ocdem.ox.ac.uk), thanks.

Feedback Request *[Dr. M. Pontecorvi]*

If you have any feedback on the meeting (if you attended), this newsletter or the NIHR/BRC website, please do feel free to contact me at marco.pontecorvi@ocdem.ox.ac.uk and discuss any suggestion you may have. Also, if you wish to participate to the next edition of the Newsletter you are very welcome to contact me as well. Thanks!