UNED **YMCHWIL DIABETES** CYMRU
DIABETES RESEARCH UNIT CYMRU

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

Ariennir gan **Lywodraeth Cymru**
Funded by **Welsh Government**

2019-20 Annual Report

Contents

Foreword

This is the fifth and final annual report from the Diabetes Research Unit Cymru (DRU Cymru) which was established in April 2015 with funding from Health and Care Research Wales. The aim of DRU Cymru has been to develop and deliver research to address the important health and social care needs faced by people living with diabetes. Diabetes remains a serious health issue and the number of people living with the condition continues to rise with over 200,000 people diagnosed with diabetes in Wales (nearly 8% of the population) and a further 580,000 people estimated to be at risk of developing Type 2 diabetes. Diabetes costs the NHS in Wales approximately £500m a year, 10% of its annual budget.

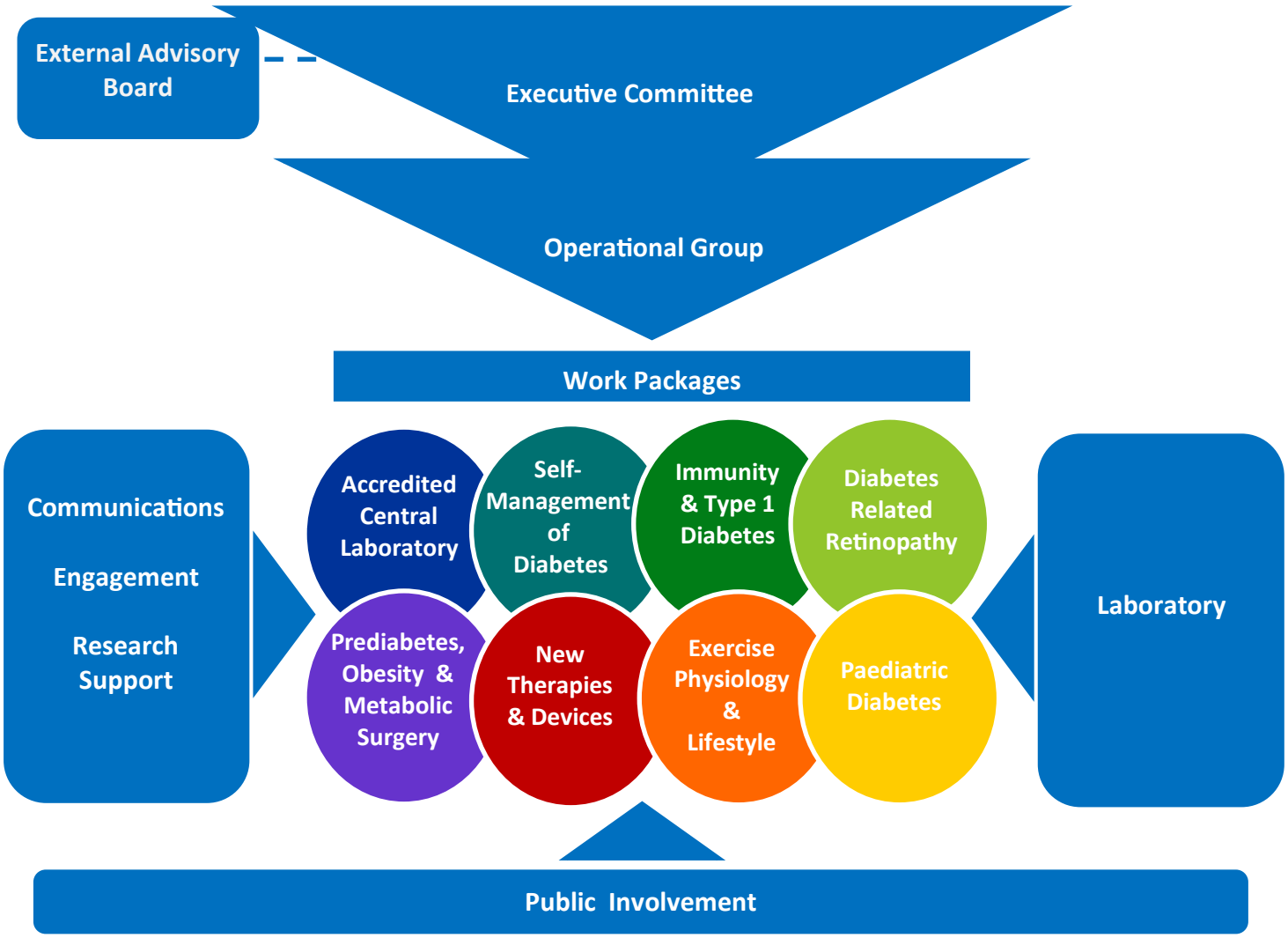
In this report we will highlight some of the research that we have carried out over the last five years to demonstrate the strength of our collaborative working and to acknowledge the support of doctors, nurses and other professions involved in diabetes care who have helped make these research activities possible. We have been involved in over 170 research studies across Wales, actively recruiting over 3000 people. We have also been successful in generating nearly £10 million of external research income with over £8 million accruing to Wales. To help develop future strategy we strengthened our governance arrangements with the addition of an External Advisory Board who brought experience from clinical diabetes, the pharmaceutical industry, the major diabetes charities (Diabetes UK and the Juvenile Diabetes Research Foundation), and the Welsh Diabetes and Endocrine Society. We are extremely grateful to all of them for their support.

In addition, in this report we will celebrate the work of the DRU Cymru Public Reference Panel. One of our key objectives from inception was to involve members of the public in all aspects of our work. The formulation of the panel facilitated this and working with them has helped to ensure that our research reflects the issues faced by those living with or at risk of developing diabetes. Throughout the report you will see examples of how they have been integral to our work and I would like to thank all our public contributors for the work they've done over the last 5 years.

I hope you enjoy this final report. Once again I would like to express my gratitude to all those people and institutions with whom we have collaborated and who have made the achievements of DRU Cymru possible.

Professor Steve Bain
Unit Director

Our Governance Structure



External Advisory Board

Our governance structure is enhanced by having an independent advisory board to overview our current activities and advise on new directions.

- **Professor Mike Baxter (Chair)**
  Diabetologist / Medical Director, Sanofi UK
- **Professor Donald Fraser**
  Director, Wales Kidney Research Unit (WKRU)
- **Dr Richard Greville**
  Director, Association of the British Pharmaceutical Industry (ABPI)
- **Dr Gillian Hood**
  Diabetes Research Manager, Queen Mary University of London / Barts Health NHS Trust
- **Dr David Millar-Jones**
  Chair, Primary Care Diabetes Society (PCDS)
- **Professor John Petrie**
  Founding Chairperson, Scottish Diabetes Research Network
- **Dr Julia Platts**
  National Clinical Lead for Diabetes, Wales
- **Dr Aled Rees**
  Chair, Welsh Endocrine and Diabetes Society (WEDS)
- **Caroline Schmutz**
  Senior Grants & Research Officer, Juvenile Diabetes Research Foundation (JDRF)
- **Professor Fiona Verity**
  Director, Wales School for Social Care Research
- **Dai Williams**
  National Director Wales, Diabetes UK

Executive Board

All our activities are overseen by an Executive Board which is responsible for providing high level oversight and is the ultimate decision making body of the Unit. The Executive Board determine the long term strategy and vision for the Unit and contribute to the planning and development of the DRU Cymru infrastructure. The Executive Board is also responsible for ensuring members of the public and people living with diabetes are involved in all aspects of our work; working in partnership to plan, manage, deliver and disseminate our research.

Members of the Executive Board 2019/20

Professor Steve Bain

Unit Director
Work Package Lead
New Therapies & Devices

Professor Steve Luzio

Operational Manager
Work Package Lead
Accredited Central Lab

Dr Sharon Parsons

Operational Manager

Professor Jeff Stephens

Work Package Lead
Prediabetes, Obesity & Metabolic Surgery

Professor David Owens

Work Package Lead
Diabetes Related Retinopathy

Professor Colin Dayan

Work Package Lead
Immunity & Type 1 Diabetes

Professor John Gregory

Work Package Lead
Paediatric Diabetes

Dr Sam Rice

Work Package Lead
Self-Management of Diabetes

Dr Richard Bracken

Work Package Lead
Exercise Physiology & Lifestyle

Professor Fiona Verity

Director
Wales School for Social Care Research

Barbara Harrington

Public Contributor
DRU Cymru Public Reference Panel

Jan Davies

Public Contributor
DRU Cymru Public Reference Panel

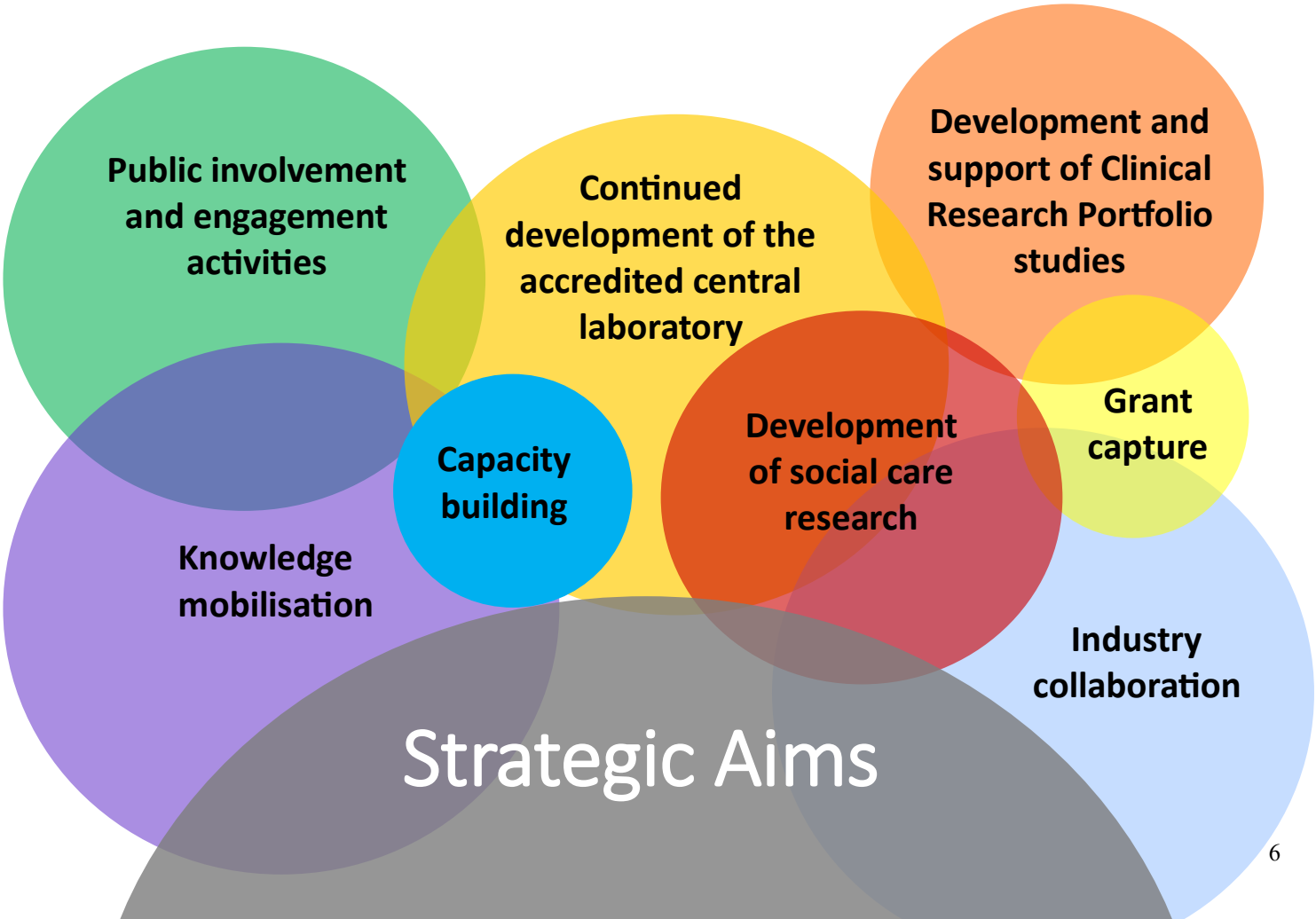
Introduction

DRU Cymru is active in areas of basic, clinical, epidemiological, social care and health services research across Wales. The core DRU Cymru team link basic scientists, clinicians, patients and the third sector, to facilitate multi-disciplinary collaborations as part of the wider Health and Care Research Wales Infrastructure.

Our Mission

The overarching aim of DRU Cymru is to address the important social and health care needs of people living with and at risk of developing diabetes. We will achieve this by undertaking and supporting a comprehensive, integrated translational research programme, designed to advance development and implementation of therapeutic strategies for prevention, treatment and self-management of diabetes.

Our strategic aims focus on 8 core activities that help fulfil our mission and deliver research impact.



Core Team

We have a core team part funded through Health and Care Research Wales with additional funding from research grants and commercial research. The team provide specialist diabetes research support to researchers, health care professionals, industry and third sector organisations. They also play a key role in engaging and involving members of the public in diabetes research.

Professor Steve Bain

Unit Director.

Management

Professor Steve Luzio, Manager	*Responsible for the day-to-day management of activities and staff.*
Dr Sharon Parsons, Manager	

Laboratory

Dr Gareth Dunseath, Lab Manager	*Day-to-day responsibility for the central lab*
Evie Bain, Lab Technician	*Development and performance of lab projects*
Dominic Bright, Lab Technician	*Development and performance of lab projects*
Dr Charlotte Jones, Quality Facilitator	*Laboratory quality management*

Engagement

Moira Morgan, Engagement Officer	*Facilitates delivery of public involvement, engagement and communications.*
Teena Seby, Administrator	*Organises and services meetings and clinical studies groups*

Research Support Team

Sarah Dowrick, Clinical Trials Officer	*Specialist advice and support for study setup and delivery.*
Dr Rebecca Thomas, Researcher	*Supports development of diabetes related retinopathy projects.*
Dr Ivy Cheung, Statistician	*Statistical input into grant applications and publications.*
Dr Jim Rafferty, Data Analyst	*Data analysis of linked datasets.*

Executive Summary

This is the fifth year since the inception of Diabetes Research Unit Cymru. In the 5 years we have directly led or supported **104 research studies**, recruiting over **3,000 participants**. We have also submitted **136 grant applications,** published **239 journal articles** and generated over **£8 million of grant income into Wales.** Public involvement and engagement is important to us and in addition to the creation of our Public Reference Panel we have organised and supported a variety of events to inform both public and health and social care professionals about the latest research and opportunities to get involved.

Performance Highlights 2015-2020

Grants

136

Grant applications

Over £8.2 Million

Grant income brought into Wales

Publications

239

Journal articles published

Research Participants

Over 3,000

Participants recruited to new studies across all Health Boards in Wales

Website

72,855

Website page views

14,161

Website visitors

Research Studies

171

Active studies

104

Directly led or supported by DRU Cymru

58%

Involving an intervention

52%

Involving commercial collaboration

Public Involvement

25

Events open to the public

723

Public attendees

463

Public involvement opportunities offered

Twitter

435,004

Twitter impressions

838

Followers on Twitter

Lay Summary

The Diabetes Research Unit Cymru develops, supports and delivers research relevant to the health and social care needs of people living with or at risk of developing diabetes. The Unit receives funding from Welsh Government through Health and Care Research Wales which has enabled us to support researchers develop diabetes research across Wales. The funding has also allowed us to facilitate public involvement and engagement in diabetes research, which is key to undertaking meaningful research, relevant to those living with or at risk of developing the condition.

What We Do

- Ensure the views of people living with or at risk of developing diabetes are taken into account in all that we do.
- Develop research proposals and apply for grants, both inside and outside of Wales, to fund the research.
- Run events, speak at meetings and publish articles so people can learn from what we are doing.
- Help people become good researchers and support researchers to do good research that makes a positive difference to peoples' lives.
- Work with industry for the benefit of people living with diabetes.
- Provide lab facilities for research studies.

The Impact of the Public Reference Panel

Our public contributors have played a vital role in ensuring the work we do is relevant to people living with or at risk of developing diabetes.

They have helped shape our strategic direction through membership of the Unit Executive Group, have worked with researchers to develop research proposals, reviewed grant applications and helped to design research information for participants. They have also been involved in making research findings more accessible by producing lay summaries of research publications.

In their role as Research Ambassadors they have raised awareness of diabetes research and supported Unit engagement activities.

The Difference We Have Made

Our research has focused on ways to both prevent diabetes and manage the condition and has had local, national and international impact. We have been involved in over 170 research studies, involving more than 3,000 participants from Wales. We have worked on clinical studies with the pharmaceutical industry to help develop new ways of treating and managing diabetes, giving people in Wales the opportunity to access new medicines and innovations.

The work undertaken by the DRU Cymru Lab has helped to develop and test new innovative technologies making diagnosing diabetes, taking part in research and living with diabetes easier. The high quality service they provide has made them the 'lab of choice' for a number of high profile, multi-centre studies.

Working with large datasets and routinely collected data, we have been able to understand some of the longer term health outcomes for people diagnosed with Type 1 diabetes in childhood. We have also been part of the international team mapping diabetes progression worldwide.

Through our partnership with Diabetes UK we have helped improve the lives of people living with Type 1 diabetes by sharing the latest knowledge on 'Type 1 and Technology' at our public event in November.

Our Work Packages

We organise our research into "work packages" with an expert in the field leading the research activities. Our current work packages are:

Accredited Central Laboratory

Lead - Professor Steve Luzio

The DRU Cymru accredited laboratory based at Swansea University provides support to clinical studies and works with the pharmaceutical, devices and diagnostic industries to develop new products.

Self-Management of Diabetes

Lead - Dr Sam Rice

This work package explores the tools for successful self-management including alternative methods for supporting education and learning in diabetes.

Immunity and Type 1 Diabetes

Lead - Professor Colin Dayan

The Immunity and Type 1 Diabetes work package leads on clinical trials in diabetes immunotherapy across the UK in close collaboration with the Type 1 Diabetes UK Immunotherapy Consortium.

Diabetes Related Retinopathy

Lead - Professor David Owens

This work package develops research into diabetes related retinopathy including looking at the risk factors that affect the incidence and progression of the disease.

Prediabetes, Obesity and Metabolic Surgery

Lead - Professor Jeff Stephens

This work package encompasses translational research from basic to clinical science, clinical trials and population health to explore the predictors of Type 2 diabetes, aspects of obesity and the effects of weight loss surgery.

New Therapies and Devices

Lead - Professor Steve Bain

In collaboration with industry partners, this work package investigates new therapies and devices for the treatment and management of diabetes by advising on, developing and delivering new studies.

Exercise Physiology and Lifestyle

Lead - Dr Richard Bracken

The Exercise Physiology and Lifestyle work package focuses on the impact and relevance of physical activity and nutrition in Type 1 and Type 2 diabetes.

Paediatric Diabetes

Lead - Professor John Gregory

This work package investigates the impact of childhood-onset diabetes on long-term health and educational outcomes. It also examines new interventions in Type 1 diabetes and the support given to children and their families.

Key Achievements:
Public Involvement

DRU Cymru Public Reference Panel

When DRU Cymru was funded in 2015, one of the first things we achieved was to establish a Reference Panel of public contributors who had experience of living with diabetes. All public contributors responded to public advertisements that were widely shared amongst the diabetes community and were selected on the basis of their relationship to diabetes and the area they lived. The DRU Cymru Public Reference Panel currently consists of 11 people from across Wales who work alongside the DRU Cymru team, developing and supporting diabetes research. We are very proud of this partnership and highly value the involvement of our public contributors.

Our public contributors are not only members of the Reference Panel but also active members of other groups within DRU Cymru including the Executive Group and the Research Development Groups. In addition, panel members also provide lay representation on trial specific steering and management groups.

Reference Panel activities range from reviewing grant applications, helping to set research priorities, supporting engagement activities and acting as diabetes research ambassadors by raising awareness of diabetes in general and more specifically, diabetes research. Panel members are also co-applicants of grant applications and have produced lay summaries of research publications that are shared on the DRU Cymru website.

The Panel attended:
13 Public Reference Panel meetings
12 Executive Group meetings
6 Trial Management Group meetings
2 Trial Steering Committee meetings

The Panel reviewed:
28 Grant applications
6 Participant information sheets
2 Questionnaires
1 Service delivery evaluation

Best Practice

To ensure the Reference Panel functions well and meets the expectation of all stakeholders, we evaluate the way we work together annually. Our annual review gives everyone the opportunity to have their say and we gather feedback from panel members, work package leads, researchers who have worked with the panel and members of the DRU Cymru core team.

Everyone's views count. We have a role description, terms of reference and code of conduct documents in place that are also reviewed annually as part of the evaluation. As a consequence of the feedback received, we adapt the way we work to ensure we continue with the productive partnership we have developed.

"I was listened to and my contributions were valued." **Reference Panel member**

As one example of this, panel members highlighted the need for additional training to be provided on reviewing research documents. Additional training was provided by our Public Engagement Officer Moira Morgan, and access given to NIHR online materials.

Our public contributors have developed their skills over time and are experienced at reviewing research documents effectively. Their comments have been very helpful to researchers and due to their personal experience and knowledge of diabetes, they have been able to highlight issues that may not have been considered.

"I have found that participating as a member of the public by reviewing academic proposals for research, has been extremely worthwhile." **Reference Panel member**

At the beginning of 2019, members of the Executive Group, including two public members, conducted an audit of public involvement across DRU Cymru using the National Standards for Public Involvement. As a result of the audit, a nine point action plan was developed to improve areas where the national standards were only partially met, for example co-production of the DRU Cymru public website.

Since the review, panel members have contributed to making changes to the publications section of the website by producing lay person summaries of current publications. This innovative idea received a commendation at the Health and Care Research Wales 2019 Conference.

Panel members have also been working together in smaller working groups, an example being a recent grant application where two panel members contributed to the bid, with one being involved as co-applicant on the application. Feedback from researchers is very important to the panel and we encourage researchers to feedback to the panel to demonstrate how their comments have been incorporated, for example, in the grant application.

"The response from researchers to comments from the panel are also enlightening and it is very much appreciated by both researchers and panel members alike." **Reference Panel member**

The Public Reference Panel meet quarterly, with our end of year meeting a celebration of what we have achieved together throughout the year.

Impact:

Working with our Public Reference Panel who have experience of diabetes and the issues faced by people living with diabetes has improved the quality and relevance of our research.

Key Achievements:
DRU Cymru Laboratory

Laboratory Accreditation

In February 2019, the DRU Cymru Lab successfully retained its Good Clinical and Laboratory Practice (GCLP) accreditation following a day long external audit. To ensure this success the Lab employs a member of staff in a quality role, responsible for audits, documentation and maintenance of the Lab's quality system. This is the second time the DRU Cymru Lab has been successful with accreditation during the period of HCRW funding. Since the latest successful re-accreditation, the lab has continued to evolve its quality management system, moving from the previous, largely paper-based system to an online management software system.

Maintenance of the GCLP accreditation has enabled the Lab to continue being the 'lab of choice' for a number of high profile, multi-centre studies.

Central Lab for CLOuD and Ustekid Studies

Over a number of years, the DRU Cymru Lab has been the central laboratory for 2 prestigious NIHR EME funded, UK-wide multicentre trials in young people with Type 1 diabetes; the CLOuD and Ustekid trials. CLOuD is a study to find out if Closed Loop technology can preserve the function of beta cells, and Ustekid is a study of a new medication (see page 20).

Health and Care Research Wales support for the DRU Cymru Lab team for the next 2 years will allow the Lab to continue to provide central laboratory support for the duration of these studies.

Alternative Sampling Methods

The DRU Cymru Lab has long had an interest in investigating sampling methods and technology that provide greater convenience and comfort for study participants.

Microsampling - Dried Blood Spots (DBS) and Volumetric Absorptive Microsampling (VAMS®) involve collecting a small amount of blood from a'fingerprick' sample onto a collection card or device which is then posted to the Lab. DRU Cymru successfully developed and validated a method for collection and measurement of C-peptide (a marker of insulin secretion) from DBS and VAMS collected samples, publishing the results in the Journal of Diabetes Science and Technology (JDST) (https://doi.org/10.1177/1932296818763464). The Lab team continues to look at other potential biomarkers that can be measured from samples collected using these novel methods.

Continuing on from this, the DRU Cymru Lab has been measuring C-peptide in the Ustekid trial, enabling study participants to collect and send in samples directly to the Lab to allow the monitoring of trends in insulin secretion over time, without the need to attend hospital.

Microsampling has also been a feature of the CLOuD study, with small volume, 'fingerprick' blood samples being collected between the main study visits for measurement of HbA1c by the DRU Cymru Lab, allowing the monitoring of longer term glucose control.

Novel Technologies and Techniques

Over a number of years, the DRU Cymru Lab has been involved with the development and validation of a novel device that enables an 'at home' oral glucose tolerance test (OGTT), a diagnostic test for diabetes. DRU Cymru staff were involved from the early stages of development, running pre-clinical lab testing, prior to designing and running a comparison trial in 100 volunteers. The findings of this validation study led to a publication and numerous conference abstracts. The recently commercialised product has now gained much interest globally during the current Covid-19 pandemic as a potential alternative to in-hospital OGTT, especially for pregnant women.

DRU Cymru Lab has been involved in a number of industrial collaborations resulting in trials testing and validating a variety of technologies for minimal or non-invasive methods of detecting changes in glucose levels, offering potential alternatives to monitoring glycaemic control or diagnosis of diabetes. These measurement technologies include use of microwaves, microneedles and most recently, the analysis of biomarkers taken from breath samples.

Another project being run in conjunction with a long-term industrial collaborator of the DRU Cymru Lab is looking to develop rapid, point of care tests that could help identify those at risk of developing prediabetes or diabetes or to monitor the beta-cell function of those with diabetes. These tests allow results to be available in approximately 5 minutes, from a small fingerprick sample, rather than the usual 2-3 hour laboratory test that would also require a sample collected from a vein.

Members of the DRU Cymru Lab team have contributed to the design of a novel study looking at whether the gut microbiota from a lean individual without diabetes, transplanted into the gut of a participant with glucose intolerance, can lead to an improvement of their glucose control. The study is being carried out in the Joint Clinical Research Facility, with the samples being analysed by the DRU Cymru Lab.

Cardiovascular Health in a Prison Population

The DRU Cymru Lab team have been involved in the design and analysis of a trial run by colleagues in Public Health Wales, aiming to identify the cardiometabolic risk in the population of a long stay UK prison, a population known to have poorer health outcomes.

The lab team were able to advise on the most appropriate methods of sample collection, limiting the logistical challenge of collecting samples from this population and provided the materials that were needed. After collection, approximately 300 anonymised samples were then posted directly to the lab, where they were logged, analysed for HbA1c and the results reported to the study team.

Continued Collaborations:

Industry

EKF
Invitron
Digostics
Neoteryx
NanoNose

Academic

Swansea University
Cardiff University
Cambridge University
Leeds Beckett University
University of South Wales
Aberystwyth University

Key Achievements:
Generating Insights

Diabetes Related Retinopathy

Screening Intervals

Research by the Diabetes Related Retinopathy group explored the impact of extending diabetic retinopathy screening beyond the current annual interval, using data from the Diabetic Eye Screening Wales (DESW) service and Primary Care data held in the SAIL (Secure Anonymised Information Linkage) databank.

Initial research indicated that for people with Type 2 diabetes of less than 10 years duration and not requiring insulin therapy, screening every 2 years (biennial) was safe. This work contributed to the findings of the UK National Screening Committee that biennial screening presented a low risk of developing sight-threatening diabetic retinopathy in those without evidence of any diabetic retinopathy at 2 consecutive annual screening events.

Further analysis of the data from Wales (DESW, SAIL) revealed that for people with Type 2 diabetes without evidence of diabetic retinopathy, screening every 2 years was also cost effective. However, for people with Type 1 diabetes, unless diabetes control was good (HbA1c<6.5%) or duration of diabetes was below 6 years, annual screening should be retained.

Retinal Image Analysis

We have collaborated with researchers in Lyon, France in assessing methods for improving retinal image quality.

Over recent years there has been an explosion in research using large datasets (big data) and artificial intelligence (AI) especially in ophthalmology i.e. occulomics. We are conducting a study to validate an automated retinal image analysis algorithm to detect changes in the blood vessels of the retina that predict events of cardiovascular disease and stroke.

Plans are underway to further explore using retinal images to predict the risk of stroke and other complications of diabetes.

2 Reference Panel members are working with this group

Impact:

The group has successfully completed and initiated many new research projects whilst establishing national and international collaborations as a basis for our future activities involving AI and 'Big data' to explore the retina as a window to other diabetes related complications.

Screening Attendance

Work to explore and understand the obstacles and enablers to attendance at diabetes related retinopathy screening in Wales has recently been completed and the findings are due to be published shortly.

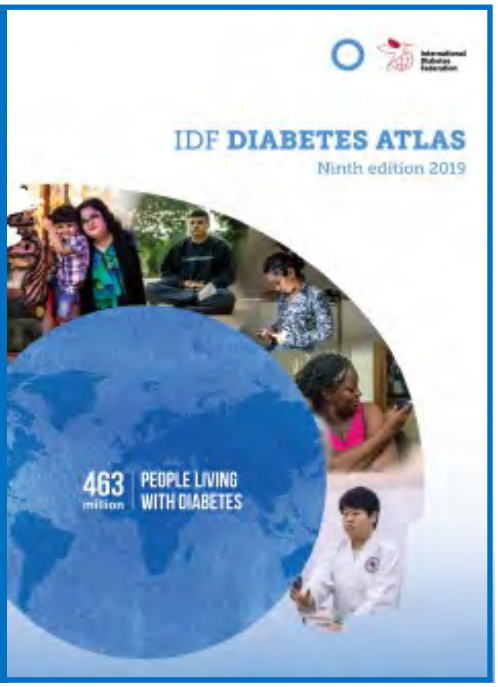
The IDF Diabetes Atlas

Members of DRU Cymru have been involved in the production and launch of the latest version of the International Diabetes Federation (IDF) Diabetes Atlas. Professor Rhys Williams from Swansea University was overall editor of the Atlas. Since the first edition published in 2000, the IDF Diabetes Atlas has provided robust estimates of the prevalence of diabetes by country, IDF Region and globally. It also projects these estimates into the future, serving as an advocacy tool, not only for the quantification of the impact of diabetes worldwide, but also for reducing that impact through preventive measures.

The Atlas had its global launch on 14th November 2019, World Diabetes Day, and an event was held in Swansea on the 15th November to highlight sections of the Atlas that members of DRU Cymru had contributed to.

The speakers at the event were:

- Professor Rhys Williams: 'Overview of the IDF Diabetes Atlas - methods used to estimate the global prevalence of diabetes'.
- Dominic Bright: 'Putting together the Atlas – reflections on the experience and the process'
- Dr Rebecca Thomas: 'Global prevalence of diabetes-related retinopathy – what do we have and what do we need?'
- Professor David Owens: 'The eyes – window of opportunity'.
- Professor Rhys Williams: 'Some of the challenges of the 9th Atlas edition and thoughts for the future'



Professor Rhys Williams was overall editor of the IDF Atlas, Dominic Bright contributed to the chapter on 'Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045'. Professor David Owens and Dr Rebecca Thomas contributed to the chapter on 'A review of studies utilising retinal photography on the global prevalence of diabetes related retinopathy between 2015 and 2018'.

In 2000, the global estimate of diabetes prevalence in the 20–79 year age group was 151 million. Since then estimates have since shown alarming increases, tripling to the 2019 estimate of 463 million.

Projections for the future have clearly indicated that the global impact of the diabetes is likely to continue increasing considerably

Key Achievements:
Generating Insights

1 Reference Panel member is working with this group

The Brecon Cohort

The Brecon Group was originally set up in 1994 and subsequently a database of children living with diabetes in Wales was established in 1996. This is now a high quality clinical dataset (the Brecon Cohort) of all children and young people known to be diagnosed with diabetes in Wales since 1996. The database has been merged within the Secure Anonymised Information Linkage (SAIL) Databank in Swansea University, and provides a unique opportunity to investigate outcomes by linking data in an anonymised manner to a variety of other health and government databases.

This initiative has resulted in a number of research questions being answered with the results disseminated via publications and presentations:

Hospital Admissions

By linking the Brecon Cohort data anonymously to multiple Welsh national health databases we have been able to demonstrate there is a 480% increase in the rate of all cause hospital admissions in children diagnosed with Type 1 diabetes compared to those without diabetes. This increase represents a clear burden to families with diabetes and to the health system.

Mortality

Long term outcomes in young people with Type 1 diabetes continue to be of interest, and may help evaluate the effects of changes to the clinical care of children that have occurred in recent decades. We have studied mortality and its causes in people who developed Type 1 diabetes and shown that, despite the developments in clinical care in recent years, by the age of 30, the mortality risk remains high in young adult life.

Educational Outcomes

Members of DRU Cymru in Cardiff University are investigating whether children with diabetes experience adverse outcomes with respect to their education and to what extent these outcomes may be influenced by the quality of their diabetes management. This is an important question not just because of the direct medical effects of diabetes on the brain caused by low or high glucose levels, but also because management of Type 1 diabetes can be a time consuming and isolating process.

Furthermore, concerns have been expressed that, due to the practical difficulties of diabetes care, some children are excluded from educational experiences. These data have been anonymously linked to the educational records of children with diabetes collected by schools and other healthcare databases available in the SAIL Databank. Linking this data will help establish if health and educational outcomes are different in children with Type 1 diabetes and those without diabetes.

Pregnancy Outcomes

The characteristics and outcomes of pregnancies have also been studied using the Brecon Cohort Dataset. Teenage girls with childhood-onset Type 1 diabetes in Wales are less likely to have children than teenage girls without diabetes. Within the Cohort, glycaemic control was poor in both teenage and young adult mothers with Type 1 diabetes. Pregnancy outcomes were comparable between teenage and young adult mothers with Type 1 diabetes, but hospital admissions during the first year of life were five times more common among babies of teenage mothers with Type 1 diabetes than those of young adult mothers with diabetes.

Early Diagnosis

Type 1 diabetes is a fairly rare condition, and about 25% of children first present for medical attention in the life threatening condition of diabetic ketoacidosis. Unfortunately the symptoms of Type 1 diabetes can be attributed to other illnesses or key developmental periods in a child's life. Using the Brecon Cohort database we have shown that children with Type 1 diabetes are more likely than children who have not got diabetes to visit their GP for a number of specific conditions (such as respiratory tract infections, vomiting and weight concerns) in the year before their diagnosis. To aid the early detection of Type 1 diabetes we aim to build on this work, using machine learning to create an algorithm, with the potential to flag children at risk of diabetic ketoacidosis in primary care.

Biological Sampling

A small study has been carried out to determine the best way of collecting biological samples from children and young adults who are part of the Brecon Cohort. This included determining whether the children and young adults preferred clinic, home sampling or a combination of the two. Information gained from this small pilot study will now be used in a much larger grant application to support the collection of biological samples from the whole of the Brecon Cohort throughout Wales.

Transition from Paediatric to Adult Care

A new study is being developed to look at the effect of diabetes management through the period of transition from paediatric to adult services, on the long-term complications of Type 1 diabetes. The overall aim is to identify people most likely to have a difficult time managing their diabetes during this period and identify the barriers and enablers which may improve management. The study will also identify ways in which care can be improved during this transition period.

Key Achievements: Supporting Research Development

Ustekid Study

DRU Cymru work package leads, Professors Colin Dayan and John Gregory successfully secured five years of funding from the National Institute of Health Research Efficacy and Mechanism Evaluation (NIHR EME) programme to undertake the Ustekid Study. This was the first successful bid from Wales to this particular NIHR research programme. The study has been developed to evaluate the effectiveness of a monoclonal antibody (ustekinumab), already licensed for use in the treatment of psoriasis and Crohn's disease, as a means to preserve insulin producing cells in young people with recent onset Type 1 diabetes.

The trial is open to children and young people aged 12-18 who are within 100 days of diagnosis of Type 1 diabetes. There are 15 assigned research sites across England, Scotland and Wales. The first site recruited the first participant in December 2018 and so far recruitment is ahead of schedule with 35 participants out of the required total of 72 having been recruited.

How Did We Help?

Public Involvement

The DRU Cymru public involvement team, Sharon Parsons and Moira Morgan, were instrumental in making sure that the views of people living with diabetes were taken into account. They arranged a focus group for young people living with diabetes and their parents, to find out more about the research and help with the study design. Those taking part in the group had the opportunity to discuss the proposed procedures with the study Chief Investigator and explore how acceptable and practical these would be to potential participants. The points raised by the young people and their parents were incorporated into the final study design and subsequently a study specific information film was developed. Prior to review by the ethics committee the engagement team also arranged for participant information sheets to be reviewed by young people of the same age as the proposed study participants (12-18 years). The engagement team also arranged for a parent contributor from the DRU Cymru Public Reference Panel to attend the Ethics Committee meeting alongside the study team to provide a public perspective on the study. That Reference Panel member now sits on the Trial Steering Committee along with another member of the panel to provide ongoing public input.

Information film produced for the USTEKID Trial

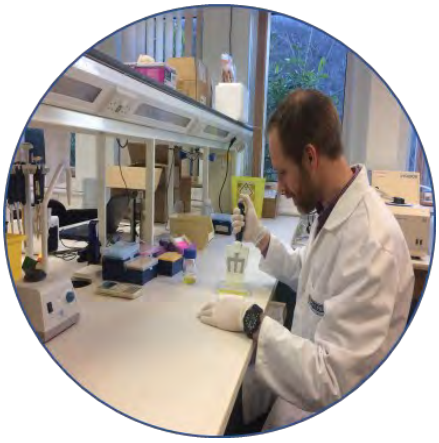
2 Reference Panel members are working with this group

Study Design and Documentation

DRU Cymru core team members, Dr Ivy Cheung and Sarah Dowrick, worked with the USTEKID study team to provide support on the study design and documentation. Ivy is the designated statistician for the study and is instrumental to determine the safety and effectiveness of the study drug. Sarah was involved in writing the Patient Information Leaflets for the study, which were designed to be age appropriate. To make sure that they conveyed the study information to the potential participants and their parents in an accurate and understandable way, the leaflets were reviewed by children and young people before being finalised. Input from the DRU Cymru lab team has also been integral to the design of the study protocol and site sampling manual.

Laboratory Analysis

The lab team have advised on the sample collection, storage and analysis processes as well as the logistics of transport of 'sample collection kits' and subsequent temperature controlled transport of study samples between the multiple study sites across the UK and the lab. The DRU Cymru lab carries out laboratory analysis of study samples, including both rapid testing and reporting to determine a participant's eligibility for the trial, and longer-term analysis of samples from enrolled participants to see how effective the study treatment is at preserving the insulin producing cells in these young people with recent onset Type 1 diabetes.



Impact:

This study could show that interrupting the destruction of insulin producing cells at the time of diagnosis may preserve and maintain some insulin secreting capacity in people with newly diagnosed Type 1 diabetes.

"Having the opportunity to be a public representative on the TMG for an immunotherapy trial, 'Ustekid', has been a benefit resulting from my time on the Reference Panel: seeing how a research trial works from the outset, and also having my views and opinions taken into account have been both informative and enriching." **Reference Panel Member**

Trial Delivery

The DRU Cymru team have worked together with the Type 1 Diabetes UK Immunotherapy Consortium and the Swansea Trials Unit to deliver the trial. Members of the core team take part in weekly study team meetings and also serve on the Safety and Trial Management committees.

Key Achievements:
Industry Collaboration

DRU Cymru has focussed its research on ways of both preventing and managing the epidemic of diabetes and has contributed to local, national and international healthcare impact, performing clinical studies essential to the development of diabetes therapies. These therapies have now become part of standard diabetes treatment guidelines in the UK and worldwide. The Unit has developed to become a leading UK collaborator for conducting clinical trials in the area of diabetes making more new therapies and devices available to patients in Wales through participation in research. The Unit has also provided senior investigators at local, national and international levels for clinical trials relating to diabetes therapies and as a consequence the Diabetes Research Group in Swansea was selected by the Sanofi Global Investigator Network as their UK Diabetes Centre of Excellence.

In this section we will highlight two diabetes therapies in which the Unit has worked closely with industry, supporting the conduct of clinical trials, and which have led to international healthcare impact.

Liraglutide

Liraglutide is an injectable glucagon-like peptide-1 receptor agonist (GLP-1 receptor agonist) which improves glucose control by increasing insulin release from the pancreas and decreasing excessive glucagon release. Members of the Unit have actively participated in the global LEADER cardiovascular outcomes trial involving over 9000 patients worldwide. This study showed that Liraglutide safely and effectively lowers the overall risk of heart attack, stroke or cardiovascular death among people with Type 2 diabetes at high risk for cardiovascular disease. Professor Steve Bain was the UK Chief Investigator for the trial and co-chair of the LEADER global expert panel which guided the trial.

Semaglutide

Professor Bain was also the UK Chief Investigator for the SUSTAIN 4 and 6 studies of semaglutide, a new once-weekly GLP-1 analogue injection for the treatment of Type 2 diabetes. These studies evaluated cardiovascular and other long-term outcomes in people taking semaglutide and the studies showed that in people with Type 2 diabetes who were at high cardiovascular risk, the rate of cardiovascular death was significantly lower among those receiving semaglutide than among those receiving placebo. These results were used in the UK licensing application which was granted in January 2019, and as patients only need to take semaglutide once a week, is an important step in helping to manage diabetes and reducing cardiovascular risk.

Oral Semaglutide

Although widely recognised as being safe and effective treatments, the GLP-1 analogues have not had a wide uptake in the UK as patients prefer to avoid injectable therapies. An oral treatment option would make this class of medicine much more likely to be used, however, the molecules are rapidly destroyed by stomach acid, meaning regular injections are needed.

A new synthetic formulation of Semaglutide enables it to survive digestion in the stomach and be given as a once daily tablet. A series of global studies (the Pioneer studies), in which the Unit was involved, compared oral semaglitide with established anti-diabetes treatment and showed that it has a favourable cardiovascular safety profile and significant reduction in cardiovascular death and all-cause mortality in people with Type 2 diabetes. This was a major milestone in the development of oral semaglutide.

Awards

Members of the Unit (Professors Bain, Luzio and Stephens) won the 'Outstanding Impact on Industry, Commerce and Innovation' Award at the Swansea University Research and Innovation Awards 2016, the Wales wide 2017 MediWales 'NHS Industry Collaboration Award and were also shortlisted for the 2018 NHS Wales Awards 'Promoting Clinical Research and Application to Practice'.

Key Achievements:
Knowledge Transfer

Public Engagement

Diabetes and Exercise Conference

DRU Cymru in collaboration with Diabetes UK Cymru have hosted three successful events around Diabetes and Exercise. The events were designed to be of interest to people living with Type 1 or Type 2 diabetes and featured parallel sessions to cover relevant topics for each group. The events also provided information stands and a separate area displaying research posters as a way of sharing the latest diabetes research findings.

The oral presentations included personal perspectives from people living with Type 1 and Type 2 diabetes, and presentations from healthcare professionals and researchers. Topics were varied and included presentations around physical activity, exercise and nutrition, the effects of diabetes medications and exercise, diabetes complications and research evidence around blood glucose management and aerobic or strength exercise.

Highlights from our conferences and speakers presentations are available to view on our website www.diabeteswales.org.uk

Type 1 and Technology Conference

The Unit also partnered Diabetes UK to deliver a series of Type 1 and Technology events, with the second event held in November 2019 at Swansea University Bay Campus. As with the event in 2018, this was once again webcast live, which has proved to be a huge success with **4,081** people viewing the presentations. Feedback from those who attended indicate that **100%** of attendees would recommend the event to other people and **over 90%** said their knowledge and confidence with diabetes technology had increased.

We had some really positive comments following the event which shows it had a real impact:

"Very good speakers and relevant up to date topics. Ability to communicate with speakers during and since event has been huge. Potentially a life changing event for me."

"I was live streaming from Uganda! It was great to be part of the day from such a distance."

"Thank you. I think it might have changed my life."

Celebrating World Diabetes Day

DRU Cymru have celebrated World Diabetes Day in various ways over the past few years including hosting seminars and information days, being interviewed by BBC Wales news and lighting our building at Swansea University blue!

All our events have been highlighted by the International Diabetes Federation on their World Diabetes Map.

For 2019, we held a public seminar for researchers, clinicians, students and members of the public at Swansea University. The seminar included presentations from Professor Rhys Williams, Professor David Owens, Dr Rebecca Thomas and Dominic Bright and focused on the 9th Edition of the International Diabetes Federation Diabetes Atlas which was launched on World Diabetes Day. All the presenters were involved in producing the Atlas and shared some of the research underpinning the publication and their experiences of being part of the international team. Reviews of the global prevalence of diabetes and diabetes related retinopathy were also published to coincide with World Diabetes Day and the launch of the Atlas.

Professional Engagement

DRU Cymru 2019 Conference 'Diabetes Research in Wales'

More than 50 delegates attended the DRU Cymru Conference 'Diabetes Research in Wales', which took place on 14th May, 2019. The conference provided a platform for researchers, clinicians, industry representatives, and people living with diabetes to come together to network and learn about the latest diabetes research taking place across Wales.

DRU Cymru work package leads showcased research being undertaken within their research themes and Dr Gareth Dunseath, DRU Cymru Lab Manager, highlighted some of the recent clinical trials supported by the lab. DRU Cymru Public Reference Panel member Barbara Harrington and Unit Manager Sharon Parsons, gave an overview of Public Involvement and Engagement within the Unit and highlighted some of the achievements.

Impact: DRU Cymru researchers engage with both public and professionals to inform them about diabetes research and disseminate research findings.

Conclusion:

As we hope we have shown in this report, the last five years of the Diabetes Research Unit Cymru has produced many achievements. We have conducted research into new treatments and therapies for diabetes and much of this work has gained national and international recognition. We have also submitted 136 grant applications, published 239 journal articles and generated over £8 million of grant income into Wales. Numerous events have been held over the past 5 years to raise awareness of our research to both healthcare professionals and the public.

During this period, the ethos of collaboration has been strong and we have worked closely with our key partners, healthcare professionals and academics across Wales and the UK, partners from the pharmaceutical, devices and diagnostic industries, and our Public Reference Panel who have enhanced our research providing advice and input to grant applications and on-going research studies. We are grateful to all those who have been involved in our research.

Key Partners

- Swansea University (Host organisation)
- Cardiff University
- NHS Health Boards across Wales
- Patients and members of the Public
- Diabetic Eye Screening Wales (DESW)
- Welsh Institute of Metabolic and Obesity Surgery (WIMOS)
- Primary Care Diabetes Society (PCDS)
- Children and Young People's Wales Diabetes Network and Brecon Group
- Diabetes UK Cymru
- Juvenile Diabetes Research Foundation (JDRF)
- MediWales
- Welsh Endocrine and Diabetes Society (WEDS)
- Association of the British Pharmaceutical Industry
- Swansea Trials Unit (STU)
- Welsh Health Economics Support Service (WHESS)
- The Wales School for Social Care Research
- Secure Anonymised Information Linkage (SAIL) databank
- NHS R&D offices

Contact us

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