Submission from SPHERE[1] to the House of Representatives Standing Committee on Health, Aged Care and Sport regarding the Committee's Inquiry into Diabetes

New evidence-based advances in the prevention, diagnosis and management of diabetes, in Australia and internationally.

Executive summary

Maridulu Budyari Gumal (SPHERE) is a Research Translation Centre that puts evidence into practice. Through consultation with our network of consumers, clinicians, health service managers, researchers, and industry contacts, we have highlighted in this submission significant gaps in service access for diabetes management within key communities in Australia. We present our evidence-informed proposals to address these gaps:

- Ensure that health services for Indigenous communities are culturally-proficient:
  - Proactive approach in Aboriginal Medical Services
  - Ensure Aboriginal Liaisons Officers are present in metabolic clinics
  - Promote and implement programs including GP Management Plan, Team Care Arrangement and Aboriginal and Torres Strait Islander 715 health check
- Scale the Diabetes Contraception and Pre-Pregnancy Program (DCAPP) and implement learnings from the Treatment of Booking Gestational Diabetes Mellitus (TOBOGM) trial
- Scale peer support intervention programs to support young adults with diabetes e.g. APHLID-M, Diabetes Contraception and Pre-Pregnancy Programs
- Expand integrated healthcare initiatives in rural areas e.g. Joint Specialist-GP based case conferencing, with consumer-focused education for healthcare providers
- Implement intervention programs for more CALD communities (e.g. SPHERE's Le Taeao Afua)
- Implement more integrated healthcare programs (e.g. KBIM) with specialist clinicians to address clinical and social needs for those with severe mental health conditions
- Increase access to subcutaneous insulin pumps, Continuous and Flash Glucose Monitoring devices
- Support further research into the following areas:
  - Risk reduction for those at risk of developing T2DM due to overweight and obesity
  - Digital technologies to assist in metabolic and lifestyle screening

It is crucial that we address the gaps in these aspects of the management of diabetes in order to reduce the burden of disease, and to ultimately achieve better health outcomes for our whole community.

[1] Maridulu Budyari Gumal is an academic health partnership – the Sydney Partnership for Health, Education, Research and Enterprise (SPHERE). SPHERE combines 15 thought-leading organisations (including Local Health Districts, Specialty Health Networks, Universities, and Medical Research Institutes) in the Sydney region.

Background

SPHERE is responding to the Standing Committee's request for submissions on its inquiry into diabetes in Australia - a growing concern for the Australian population - and we thank the Standing Committee for this opportunity. In June 2019, there were 1,309,070 people with diabetes registered on the Australian National Diabetes Service Scheme (NDSS). Of those registered, 87% were diagnosed with type 2 diabetes (T2DM) and an additional 500,000 people are estimated to have undiagnosed T2DM. [1, 2] In 2019-20, an estimated $3.1 billion of expenditure in Australian health was attributed to diabetes, representing 2.2% of total disease expenditure. T2DM represented 63%, whilst type 1 diabetes (T1DM) represented 10%. [3] When we consider the current burden of disease, we must consider equity of access to adequate treatment, and to preventative measures that would reduce future complications and future burden of disease.

Maridulu Budyari Gumal is an NHMRC accredited Research Translation Centre with an ambitious purpose: to change the future of healthcare. We put evidence into practice. We have combined 15 thought-leading organisations (universities, hospitals, research institutes, community members and primary care centres) to create the Sydney Partnership for Health, Education, Research and Enterprise, also known as SPHERE. With over 50,000 staff and over $5 billion in annual revenue, our unique combination of staff, facilities, and resources underpins our commitment to addressing health problems our community needs us to solve, such as diabetes. We are committed to working towards a world-leading health system in Australia.

Professor David Simmons co-leads SPHERE's Diabetes, Obesity and Metabolic (DOM) Clinical Academic Group (CAG) and has coordinated this submission on behalf of SPHERE. Professor Simmons is a Distinguished Professor at Western Sydney University, Head of the Campbelltown Hospital Endocrinology Department and Director of the Diabetes, Obesity, Metabolism Translational Research Unit. The DOM CAG's overarching goal is to target under-serviced and under-researched groups with projects that seek to:

- Prevent/reduce diabetes, obesity and metabolic disease,
- Prevent diabetes and obesity adverse effects during pregnancy,
- Prevnt or reduce long term complications from DOM diseases,
- Reduce the impact of T1DM and identify other rare forms of diabetes, and
- Create new integrated cost-effective ways of working across healthcare/community.

SPHERE's Aboriginal Health and Wellbeing CAG (AHW CAG) comprises Indigenous Elders, community organisations, Aboriginal community health advocates, researchers, and clinicians. Diabetes prevention and management are core priorities of the AHW CAG. Aunty Kerrie Doyle (co-leader of the AHW CAG) has coordinated the Indigenous engagement in this submission.

SPHERE's consultation with its wide network of consumers, clinicians, health service managers, and researchers has highlighted some case-based and evidence-informed gaps in service access and equity for diabetes management within the following priority populations:

1. Indigenous health
2. Contraception, pre-pregnancy and young adults
3. Communities in rural areas
4. CALD communities (Pasifika)
5. Overweight and obesity
6. Severe mental health conditions
7. Gastrointestinal cancers
8. Chronic respiratory diseases

SPHERE acknowledges the Elders past, the Elders present, and the Elders yet to come. SPHERE respectfully interprets the term 'Indigenous' to include Australian Aboriginal and Torres Strait Islander peoples.

1. Indigenous health

Denise is a proud grandmother and a Dharawal woman who struggles every day living with diabetes. Denise says that as an Indigenous person she does not have any positive example of ageing. Denise has grown up seeing people that she loves decline due to diabetes. Denise remembers caring for her grandmother with diabetes and is scared that one day it will be her daughters who are left to look after her. Denise describes the importance of integrating health services into Aboriginal Medical Services to undertake a holistic approach to care.*

A culturally proficient health system values Indigenous culture and provides equitable access to healthcare services. [4] Australia's current health system follows a Western framework of healthcare that is not always inclusive of Indigenous needs. [5] The NSW Diabetes Framework 2016 identifies Indigenous people as a key demographic for prevention initiatives due to their poorer health outcomes. The framework highlights the important role that Aboriginal Medical Services (AMS) play in T2DM screening in general practice (GP) and community based care. [6] The NSW Aboriginal Health Partnership agreement aims to ensure that the expertise and experience of the Aboriginal Community Controlled Health Sector is brought to healthcare processes. [7]

The adaptation and embedding of mainstream services within AMS and the infusion of indigenist cultural values within mainstream services encourages ongoing community engagement and guidance from local Elders, community stakeholders, and clinicans. [8, 9] SPHERE are already experienced in this, and are piloting an indigenist adaption of a mainstream metabolic program to be placed within an AMS. This program will be delivered in a familiar and safe environment, integrating Indigenous cultural beliefs and behaviours.

Although T2DM is often preventable, a qualitative evaluation of Indigenous people living with diabetes highlighted a sense of fatalism. It is important to evaluate how diabetes prevention education is implemented, to overcome the perception of inevitability. [10] The 715 health check provides the opportunity for Indigenous Australians to regularly check their health status and make lifestyle changes. Across NSW, of the 128 programs implemented with AMS focused on chronic disease prevention, there is only a minimal focus on promoting the 715 health check. [11]

<u>Key proposals:</u>

- Support and promote the 715 health check and similar indigenist health programs
- More proactive approaches in AMS and other health services

2. Contraception, pre-pregnancy and young adults with diabetes and hyperglycaemia in pregnancy

Unmet needs for young adults with diabetes include mental health management, peer and community support, and glucose monitoring, especially before and when pregnant.

*Sarah** was diagnosed with T1DM at the age of 5. When Sarah moved into the transitional care services on starting university, they began to experience diabetes burnout. This condition was triggered by several factors, including anxiety and depression, low self-esteem, low efficacy in diabetes management, stigma*

from obesity, and an abusive relationship (with several pregnancy scares) that encouraged them to skip insulin and meals to lose weight. Sarah also felt they experienced stigma and judgement attending diabetes clinical services from work and their partner, and began to miss appointments. After being referred to a psychologist specialising in diabetes, Sarah's mental health improved to the point of being able to continue their university studies and end the abusive relationship. Now in a healthy relationship and eager to explore preconception planning, Sarah has been referred to a new treating team established by recent health district funding. Sarah is now being supported by a diabetes team that helps them feel empowered in their health, continuing to manage diabetes with confidence and without judgement.
**Sarah uses the pronouns they/them

Diabetes distress and burnout is common in people transitioning from pediatric clinical care to transitional/adult care services. Young adults are experiencing a transitional life stage full of new experiences first jobs, moving out of home, university, relationships, alcohol and drugs. It makes this stage in their lives discordant in the context of independence and responsibility. People with diabetes in a transitional stage of care have more frequent hospitalisation due to suboptimal glucose levels and increased risk of complications, as well as increased risk for mental health conditions such as depression, anxiety and eating disorders. [12] Up to 63% of patients with T1DM have depressive symptoms and 32% experience anxiety. [13] Not surprisingly, 80% of young adults with diabetes aged 19–24 years do not achieve the glycaemic target (HbA1c of 7.0%). [14] There is also a 50-70% increase in risk of malformations and perinatal mortality if a pregnancy is unplanned and has no engagement with pre-pregnancy care. [15] The lifetime costs per major malformation is estimated at AUD$1 million. [16]

An audit of South Western Sydney Local Health District Services found the overall rate of congenital malformations was identified to range from 6.8% to 12.4% compared to a background population of 1.7%. In response, an integrated Diabetes Contraception and Pre-Pregnancy Program (DCAPP) was developed. [17] The DCAPP program consisted of a multifaceted educational program for women and healthcare professionals to increase awareness, contraception uptake, and referrals to diabetes pre-pregnancy clinics. DCAPP has obtained proof-of-concept within South Western Sydney and can now be scaled nationally.

The Treatment of Booking Gestational Diabetes Mellitus (TOBOGM) randomised controlled trial led by DOM CAG Leader Professor Simmons, compared pregnancy outcomes among 802 women with booking gestational diabetes (GDM) receiving immediate or deferred treatment. [18, 19] Treatment of gestational diabetes before 20 weeks' gestation without waiting for confirmation of a repeat oral glucose-tolerance test (OGTT) led to significantly reduced adverse neonatal outcomes including preterm birth, birth trauma, high birth weight, respiratory distress, phototherapy, stillbirth, or neonatal death. The outcome of TOBOGM highlights the need to support women with gestational diabetes with early treatment.

Effective programs to support young adults have included community engagement and peer support. [15, 12] In the context of pre-pregnancy care peer support, programs to improve pre-pregnancy care have seen a 71% reduction in malformations, lower HbA1c, and a 54% decrease in pre-term delivery within pre-pregnancy clinics. [20] Collaboration between primary and secondary care with effective referrals to peer support, has been identified as a cornerstone of a district-wide diabetes contraception and pre-pregnancy support program for women with diabetes between the ages of 15 and 50. [20]

Effective interventions that support young people with diabetes need to be developed in partnership. For example, our Apps and Peer Support for a Healthy Future and Living Well with Diabetes – Mental Health (APHLID-M) project has been developed in partnership with consumers, clinicians, academics and industry. APHLID-M is a health app adapted to create a one stop shop for people with diabetes between the ages of

16 to 25. The study assists participants in managing their diabetes and reduces their risk of diabetes-related complications. [21]

Blood Glucose Monitoring is an integral component of hyperglycaemia management. This is particularly important for pregnant women with any type of diabetes to achieve better glycaemic control. [22] This testing allows a woman's self-management of her diabetes. [23] Blood Glucose Monitoring throughout the pregnancy process is an effective tool to reduce the risk of malformations for women with diabetes. [24] In Australia, access to Continuous Glucose Monitoring (CGM) and Flash Glucose Monitoring are subsidised for women with T1DM who are actively planning pregnancy, pregnant or immediate post-pregnancy. The utilisation of these CGM devices needs to also be supported and promoted across other communities.

Key proposals:

- Scale the Diabetes Contraception and Pre-Pregnancy Program (DCAPP) and implement learnings from Treatment of Booking Gestational Diabetes Mellitus (TOBOGM) for treatments
- It is vitally important to be able to monitor and address variation and outcomes over time. A Diabetes in Pregnancy Benchmarking program/Clinical Quality Register (a nation-wide database relating to T1 and T2 diabetes and pregnancy outcomes) should be funded.This would include a national office and support for the local data collection. The data repository and transfer methods (which need to be secure and follow contemporary standards of information governance) could be shared with other diabetes organisations.
- Scale peer support intervention programs to be embedded into primary and secondary health systems e.g. the APHLID-M Project, to support young adults with diabetes
- Support and promote CGM and Flash Glucose Monitoring devices across all communities

3. Communities in rural areas

Donna, a Darug woman living in Bathurst was diagnosed with T2DM in 2018. Donna has spent the last 9 months struggling to obtain a referral to a public endocrinologist at a close-by clinic. Donna describes the need for culturally proficient healthcare that welcomes Indigenous people.*

The fifth goal of the Australian National Diabetes Strategy 2021–2030 focuses on reducing the impact of diabetes among Indigenous people, many of whom reside in rural areas. There is a requirement described in the strategy to promote models of care that provide necessary specialist support through regional networks, by optimising telehealth services and linked facilities for treatment of serious complications of diabetes – particularly heart, kidney, eye and foot disease. [25] An indigenist approach to care draws on the principles, core values, knowledge and ideals of Indigenous culture to design a program for the community that is strength-based and solutions-focused. [26]

A successful education strategy implemented in South Western Sydney has focused on diabetes case conferencing in primary care. Diabetes case conferencing involves an endocrinologist and diabetes educator co-consulting with a GP to advise on the care of the patients with diabetes. SPHERE recently evaluated a patient-free model of diabetes case conferencing where the patient consents for a joint review of their case followed by joint development of a management plan. SPHERE's evaluation highlighted that blood glucose (HbA1c), blood pressure, weight, and other cardiovascular risk factors all improved over a 3 year period following case conferencing across 645 patients from 40 general practices. [27] The SPHERE Integrated

Action Group brought together diabetes leads, policy makers and consumers across NSW in 2018, to identify a series of recommendations for Integrated Diabetes Care. The number 1 recommendation was to support and facilitate the uptake of diabetes case conferencing. [28]

An integrated approach will be required to support people with diabetes in rural regions. Wollondilly Shire is an inner regional Local Government Area in South Western Sydney. Wollondilly has approximately 2519 people with diabetes, and 11 GPs. [29] Our Wollondilly Diabetes Program offers clinical and prevention services for people with or at risk of diabetes. The program includes diabetes case conferences, a monthly specialist and allied health clinic supported by a dietitian and podiatrist, a weekly diabetes education session coordinated by a Credentialled Diabetes Educator, and monthly Clinician Reference Groups. This program has been highly successful, with resulting improvements in glycaemia, blood pressure, total and LDL cholesterol, and weight. [30]

Key proposal:

- Expand integrated approach (similar to the Wollondilly Diabetes Program) in rural areas that links primary and secondary care services through diabetes case conferencing, outreach specialist consultancy (as opposed to ongoing) clinics and consumer-focused education.

4. CALD communities (Pasifika)

"Talofa lava, my name is L Lelei. I am a Peer Support Facilitator within the Le Taeao Afua (LTA Program). When I volunteered to be a Peer Support Facilitator, I was worried about diabetes but I was interested to learn more. As we were trained by our coach, I learned that the messages were very clear to understand. I was able to also speak my own Samoan language to deliver the program. In the workshop, I saw how much sugar was in a bottle of 1.5L Coke – I could not help but realise what I was giving my family. With our Sabbath community meals, we enjoyed very large meals. We cooked so that there was always plenty of food. Through the LTA we learned new cooking techniques and started having lighter meals with our church. We split our church into 3 walking groups so that everyone had the chance to walk together at a park close to their homes. Without participating in the LTA, we would have continued living with habits that were making us unhealthy, with increased risk of diabetes."

Greater Western Sydney has a significant Pacific Islander (Pasifika) migrant population. [31] Pasifika communities have some of the highest rates of obesity and T2DM globally, along with high rates of diabetes complications. [32] Insufficient physical activity and poor nutrition, as well as inherited predisposition factors amplify the obesity and diabetes rates. [33] While progression from impaired glucose tolerance (a form of pre-diabetes) to diabetes can be prevented or delayed, there is limited evidence of successful interventions that help to do this. [34]

Our Le Taeao Afua (The New Dawn; LTA) program is a pilot theory-based lifestyle program. Based on similar programs in New Zealand, it was introduced at the request of the local Samoan community in South Western Sydney. The program was implemented over 6 months across 4 South Western Sydney Samoan Churches. [35] The project was governed at all stages by a Samoan community reference group. As the prevention projects developed, the group has expanded to include representation from other Pacific communities from across Sydney. The LTA intervention had a train-the-trainer approach, using Peer Support Facilitators (PSFs) to deliver support to the wider community. A Community Activator (CA) trained and

supported the PSFs. GP attendance was promoted in parallel to the community approach through referral letters for those who received abnormal results. [36]

The LTA program confirmed that recruitment and delivery of the intervention via churches is feasible. During the 12-month period, over 110 intervention activities were delivered across the three churches. Churches are well attended by Pacific communities in Australia. Pre-post evaluation showed an overall reduction in HbA1c and diastolic blood pressure, with near doubling of self- reported total physical activity, and an increase in low fat choices (such as removing fat from chicken during food preparation). [36] The program greatly benefited the local Samoan community of South Western Sydney. The Pacific Reference Group who manages the program would like to extend the program across GWS. Through an NHMRC Partnership Grant the project is current being expanded across the Sydney Pasifika Community to include 48 more churches.

Key proposal:

- More intervention programs (of a type similar to SPHERE's LTA program) need to be supported and implemented in other CALD communities.

5. Overweight and obesity

Dan is a 40-year-old Indigenous Australian man and is overweight. He was recently told by his GP that he has pre-diabetes. Dan believes his diagnosis with diabetes was inevitable; he has watched his mum and grandparents struggle with T2DM. Dan describes feeling judged by the health system and feeling a sense of shame when ringing up to access free services. He wishes that the health service was responsive and would reach out to him instead.*

The prevalence and severity of obesity in Australia is increasing. Overweight and obesity was responsible for 7% of the total health burden in Australia in 2011. Alarmingly, 63% of this was fatal burden. Indigenous Australians are 1.2 times more likely to be either overweight or obese compared to non-Indigenous Australians. The associated burden of obesity-related diseases - such as T2DM - poses considerable long term health challenges. [37] Some of this burden can reduced by improvement to service access.

Many Indigenous people struggle to attend metabolic clinics due to limited public transport, lack of trust in mainstream health, not feeling safe with non-Indigenous people and service providers, and most importantly, the sense of shame that comes with having obesity. This leaves Indigenous people at a higher risk of obesogenic conditions. Placing services in community control and appointing Aboriginal Liaison Officers (ALOs) will have a crucial role in supporting Indigenous people in the health system, improving continuity of care, and in reducing incidence of patient discharge against medical advice. [38]

The National Obesity Strategy recommends improved integration and uptake of existing healthcare resources, including the GP Management Plan, Team Care Arrangement and the Aboriginal and Torres Strait Islander 715 health check. [39, 40] Upskilling the primary care workforce was also recommended to prevent and reduce the incidence of diabetes within Indigenous people. Having a significant number of adults with clinically severe obesity leads to an increased health burden for Indigenous Australian families and the community. Integrated resources therefore need to be culturally proficient and strengths based.

The National Association of Diabetes Centres (NADC) has produced and collated a best-practice toolkit and QI tools and resources. Others have done similar, for example, QI Toolkit Diabetes 2020 (bsphn.org.au). These resources provide successfully implemented examples of diabetes-related

complications and Models of Care. We are now lacking a strategic framework for best practice supported by implementation science to drive change and create a virtuous improvement cycle. A team at Nepean Hospital recently published a study on the impact of specialised obesity management services on the reduction in the use of acute hospital services. [41] Further research will be needed to assess broader risk reduction through changes in body weight for those at risk of developing T2DM.

Key proposals:

- Upskill the primary care workforce with uptake of integrated and culturally-proficient healthcare resources e.g. GP Management Plan, Team Care Arrangement and Aboriginal and Torres Strait Island 715 health check
- Ensure ALO staff are supporting Indigenous people accessing health programs
- Provide dedicated support for further research into risk reduction for those at risk of developing T2DM due to overweight and obesity.

6. Severe mental health conditions

Greg is a 50-year-old man with schizophrenia who has been under the care of the SESLHD Mental Health Service since 2016. Since being prescribed clozapine 4 years ago, Greg has gained 28kg and has faced challenges in adhering to crucial fasting blood tests necessary for monitoring his health due to difficulties with organisation, night-time cravings, and a lack of motivation. During this period, he was consuming 3L of soft drinks daily and smoking 50 cigarettes a week. He developed T2DM. However, Greg's journey took a positive turn a year ago when he became a part of Keeping the Body in Mind (KBIM). KBIM is a lifestyle program, unique to SESLHD, where clients of the mental health service can access physical health support from dedicated mental health practitioners including dietitians, exercise physiologists, nurses, and peer workers. Greg attributes KBIM with playing a pivotal role in enhancing his physical well-being and mobility, offering valuable education, improving his sleep quality, and subsequently improving his overall health condition while he strives towards effective diabetes management.*

Comorbidities such as diabetes are significantly more common among people with serious mental illness compared to the general population. People with serious mental illness often die 15 years younger than the general population due to treatable physical illnesses. Fatal comorbidities in people with severe mental illness cost Australia an estimated $15.0 billion in 2014. In the same year, comorbidities contributed to a societal cost of $743 million – this figure was calculated based on excess GP consultations, inpatient admissions, and productivity losses. [42]

Several significant barriers prevent health service consumers from accessing necessary treatment for physical health issues. Current health services are fragmented; mental health care is not adequately connected with primary and acute healthcare providers. Literature indicates a need for integrated healthcare and suggests mental health consumers receiving diabetes care may benefit from such integration. [43] There are also several interconnected social determinants - such as unemployment, unstable housing, and stigma - that perpetuate poor physical health, prevent access to healthcare, and contribute to poorer overall standards of care. Current care models do not address these structural disadvantages and fail to acknowledge the necessity of consumer and carer collaboration when developing care plans. [44] More programs similar to KBIM at hospitals would be highly beneficial to holistic healthcare.

Further research is needed to establish holistic, integrated, person-centred models of care that address both clinical and social needs for people at risk. [3, 44, 45] Health assessments (including metabolic and lifestyle

screening) should be integrated into physical and mental health care plans. These plans should be developed alongside the consumer, family, carers and multi-disciplinary teams. Future research could then investigate the integration of digital technologies into these assessments, to increase engagement, and to reduce cost.

Key proposals:

- Implement integrated healthcare programs (similar to KBIM) in more locations in Sydney, with upskilled specialist clinicians.
- Support further research into digital technologies to assist in metabolic and lifestyle screening assessments.

Summary

SPHERE is a research translation centre that puts evidence into practice. Our consumer stories have identified critical gaps in equity, access and delivery of diabetes care. We have provided our evidence-based proposals for implementation, as well as areas that require further research. On behalf of the community we serve, we present to the Standing Committee our highest priority proposals to address the consumer identified gaps in effective diabetes management and prevention:

- Ensure that health services for Indigenous communities are more culturally-proficient:
    - Proactive approach in Aboriginal Medical Services
    - Ensure Aboriginal Liaisons Officers are appointed in metabolic clinics
    - Promote and implement programs including GP Management Plan, Team Care Arrangement and Aboriginal and Torres Strait Islander 715 health check
- Scale the Diabetes Contraception and Pre-Pregnancy Program (DCAPP) and implement learnings from Treatment of Booking Gestational Diabetes Mellitus (TOBOGM) trial
- Scale peer support intervention programs to support young adults with diabetes e.g. APHLID-M, Diabetes Contraception and Pre-Pregnancy Programs
- Expand integrated healthcare initiatives in rural areas e.g. Joint Specialist-GP based case conferencing, with consumer-focused education for healthcare providers
- Implement more intervention programs for CALD communities (e.g. SPHERE's Le Taeao Afua)
- Implement more integrated healthcare programs (e.g. KBIM) with specialist clinicians to address clinical and social needs for those with severe mental health conditions
- Increase access to subcutaneous insulin pumps, Continuous and Flash Glucose Monitoring devices
- Support further research into the following areas:
    - Risk reduction for those at risk of developing T2DM due to overweight and obesity
    - Digital technologies to assist in metabolic and lifestyle screening

To improve management and prevention of diabetes in Australia, it is crucial that we address the identified gaps in service access and equity. With dedicated support, our network in SPHERE have the experience and capacity to implement many of these evidence-based proposals to help reduce the burden of disease, and to ultimately achieve better health outcomes for our whole community.

* Names of consumers have been changed to protect identity.

Two further reports on cases of secondary diabetes, as well as references for all information can be found in the document entitled 'SPHERE Supplementary Information and References.'