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# **QATAR DIABETES AND CARDIOVASCULAR DISEASE RISK FACTORS RESEARCH AGENDA**

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## 2. FOREWORD

Diabetes is one of the fastest growing health problems of our time and without careful management, it is also one of the most devastating. It imposes a significant burden on the individual patient, his or her family, the society, the entire healthcare system, and the national economy. Qatar has one of the highest prevalence of diabetes worldwide. This has been largely attributed to highly prevalent risk factors such as obesity, and unhealthy diet and physical inactivity. The prevalence of diabetes and pre-diabetes among the adult population is estimated to be in the range of 35-40% of all adults.

The complications of diabetes are numerous and can dramatically reduce the quality of life of the individuals and their families. Diabetes is a major cause of mortality and morbidity, leading to multiple complications such as vision loss, kidney failure needing dialysis and transplantation, limb amputations, nerve pain, heart attacks, strokes and ultimately deaths. In 2017, Diabetes was the 6<sup>th</sup> leading cause of premature deaths and the 5<sup>th</sup> leading cause of disability in Qatar.

Research into diabetes is essential as a guide to clinical interventions for primary prevention of diabetes and for best management approach. While many of these issues have been addressed by research performed in the Western countries, in Japan and China, little has been done in the Middle Eastern countries that share with Qatar similar cultural and environmental factors. Over the past 10 years multiple research projects have been initiated in Qatar by individual researchers based on their own individual scientific interests. However, there has been no systematic approach on priorities that guide and direct diabetes research in Qatar toward areas of high impact for the Qatari population.

The objective of this document is to describe the current status of research being performed in Qatar and to uncover untouched priorities and knowledge gaps where research should be performed to support the implementation of Qatar National Diabetes Strategy, 2016-2022, in terms of primary prevention and the optimisation of clinical management to reduce the risk of diabetes complications and improve quality of life. Therefore, research is central to the national ambition to reduce the burden of diabetes in the coming decades. This document has been developed to guide scientific investigators and funding bodies alike to help them focus research on areas of high priority which are highly likely to have a major impact for the care and prevention of people with diabetes in Qatar. The annual cost of diabetes and its complications has been estimated to be about 1.8 billion in 2015. That cost will increase drastically if Qatar does not take radical action to implement a co-ordinated National Diabetes Strategy. Investing a small fraction of the cost of dealing with diabetes in the future into diabetes research now is a key element of the National Diabetes Strategy which has the potential to reduce the future clinical, financial and societal burden of diabetes for future generations in Qatar.

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## 3. INTRODUCTION

### 3.1 The Challenge of Diabetes and Cardiovascular Disease

Type 2 Diabetes (T2D) and Cardiovascular Disease (CVD) are the greatest contemporary health challenges for Qatar. Qatar is ranked in the top ten countries in the world for T2D prevalence with an estimated prevalence of 17%. A similar percentage of the adult population are likely to have pre-diabetes, which places them at risk for diabetes and CVD. In the future, the prevalence of T2D in Qatar is likely to increase, placing an even greater burden on affected individuals and their families, healthcare services and society.<sup>1</sup>

Type 2 diabetes is associated with serious macrovascular (ischaemic heart disease, stroke, peripheral vascular disease) and microvascular (nephropathy, retinopathy, neuropathy) complications. Because of the insidious nature of diabetes, these complications may be present at the time of diabetes diagnosis.<sup>2</sup> In Qatar, T2D is responsible for about 50% of end-stage renal disease requiring dialysis, about 50% of all acute coronary syndrome cases, and about 70% of stroke and Transient Ischemic Attack (TIA) cases.

Globally, the International Diabetes Federation (IDF) estimates that 14% of all the deliveries are affected by gestational diabetes.<sup>3</sup> A major concern is that nearly one quarter (23.5%) of all young pregnant women in Qatar have gestational diabetes, which has short and long term consequences for both the mother and her offspring.<sup>4</sup> During pregnancy, gestational diabetes is associated with increased risk of pre-eclampsia, pre-term labour, Caesarean-section, macrosomia, shoulder dystocia, stillbirth, polyhydramnios, congenital anomalies and neonatal hypoglycaemia; together with a substantial increase in healthcare costs.<sup>5-8</sup>

The high prevalence of T2D is strongly linked with the nutrition transition, and lifestyle factors leading to excess adiposity (overweight or obesity).<sup>9-11</sup> Excess adiposity is a key driver of T2D development and progression. Excess adiposity and T2D occur at younger age in Qatar compared to other countries. T2D and overweight and obesity are associated with hypertension, Non-alcoholic Fatty Liver Disease (NAFLD), Obstructive Sleep Apnoea (OSA), arrhythmias, and hypercoagulability, all of which confer an increased risk of cardio-metabolic disease.<sup>12-15</sup> Obesity and diabetes are also associated with several cancers,<sup>14</sup> an increased psychological and psychiatric burden,<sup>16</sup> and reduced quality of life.

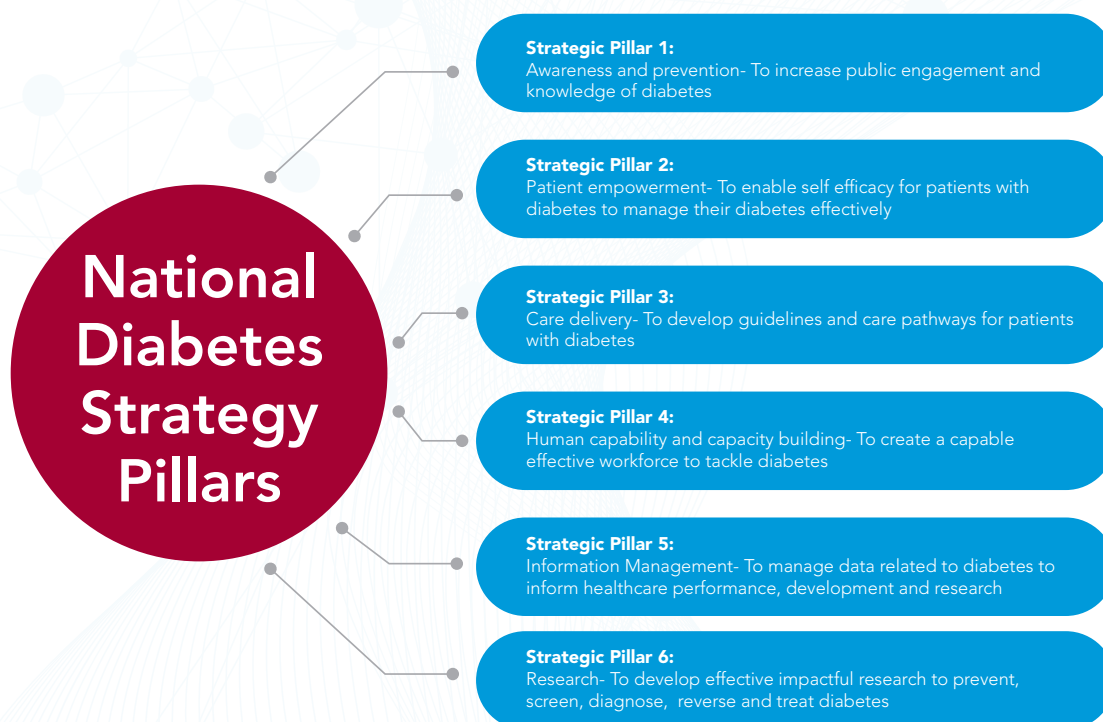
Given the high prevalence of obesity in children in Qatar, a greater number of children and adolescents will progress to developing T2D. Several regional studies have suggested that the prevalence of Type 1 Diabetes (T1D) is also increasing. While, T2D is a major challenge in both children and adults, there is also a need to address T1D and childhood diabetes. This includes efforts to understand the aetiology, prevention, and progression of T1D in Qatar and improve associated clinical services.

The annual cost of diabetes in Qatar has been projected to increase from QR 1.8 bn in 2015, to QR 5 bn in 2035, and QR 8.4 bn by 2055. There is, therefore, an urgent need to develop strategies to prevent diabetes and to improve the care of those affected. The National Diabetes Strategy has been implemented to ensure that key areas related to diabetes are addressed effectively.

## 3.2 The Qatar National Diabetes Strategy

The Qatar National Diabetes Strategy, 2016-2022, is a significant step towards ensuring that diabetes, the major healthcare challenge in Qatar, is addressed effectively to ensure the future health and wealth of the Qatari population. The six strategic pillars of the National Diabetes Strategy are shown in Figure 1.

**Figure 1.** Qatar National Diabetes Strategy Pillars.



## 3.3 The National Diabetes & Cardiovascular Disease Risk Factors Research Agenda

The National Diabetes and Cardiovascular Disease Research Agenda has been developed as part of Pillar 6 of the National Diabetes Strategy. The agenda will provide a roadmap for future research into diabetes and cardiovascular disease (CVD) risk factors. The agenda will be central to the appropriate direction of research resources and funding to ensure that there is maximal benefit for Qatar.

The agenda was developed through the work of the National Diabetes Strategy Research Subcommittee and the National Diabetes Strategy Committee. Workshops, individual meetings and consultations were conducted with researchers and leaders at key research and healthcare institutions in Qatar to ensure that there was adequate input into the development of the strongest research agenda.

The research agenda includes recommendations for key research areas to be addressed, and processes, pathways and infrastructures for diabetes and CVD risk factor research.

## 4. PREVIOUS AND CURRENT RESEARCH

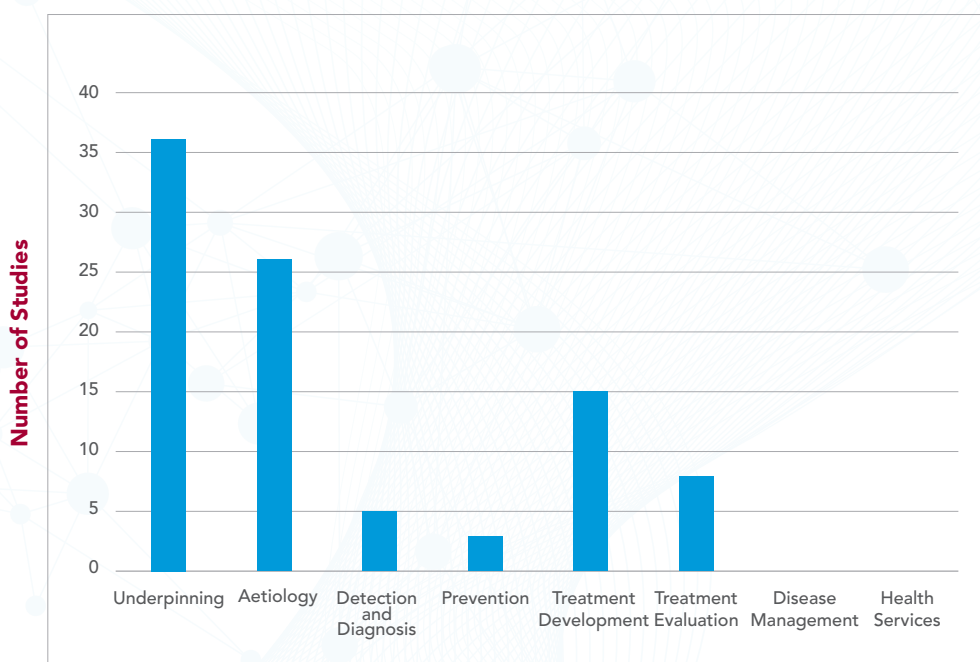
To date, diabetes and CVD risk factor research in Qatar has largely been driven by individual investigators, with few institutions having a dedicated research agenda to inform prioritisation of the diabetes and CVD risk factor research. With the advent of the Qatar National Research Strategy (QNRS) in 2012, and QNRS 2014 thereafter, Qatar's goals and objectives addressing the national health priorities became better defined. The development of research in Qatar was initially focused on basic science through establishment of laboratories and technologies related to individual research endeavours. Over the years, more emphasis has been placed on clinical research, but this continues to be less well supported financially, tends to be fragmented, and has not always been directed at priority issues for diabetes prevention and care in Qatar.

The sources of funding for diabetes research have included the Qatar National Research Fund (QNRF), intramural funding within research institutes and higher education establishments, and funding through the health service. While QNRF funding (mainly through the National Priorities Research Program, (NPRP)) is subject to a rigorous peer review system with considerable oversight of research outcomes and impact, this

has not been fully extended to other funding sources available in Qatar. This has meant that research funding has not always been targeted at the highest quality most impactful research.

A review of funding allocation in Qatar over the years demonstrates that the majority of research funding has been directed towards underpinning and aetiology research (Figure 2). This is similar to other countries in the development of their research endeavours. For example, in the United Kingdom, the National Institute of Health Research (NIHR) was established using a combination of existing and new investment to fund and support clinical research, while other government supported funders continued to focus on aetiology and underpinning research. As Qatar's research capabilities increase, there is a need to extend research beyond underpinning basic and aetiological research and expand research into disease prevention and treatment and applied and public health research. Achieving this enhanced balanced portfolio of research requires collaboration amongst key stakeholders to create appropriate mechanisms for funding research into diabetes and CVD risk factors. These mechanisms should support competitive and impactful research in both basic and clinical research into diabetes and CVD risk factors.

**Figure 2.** Funded Research Areas for Diabetes.

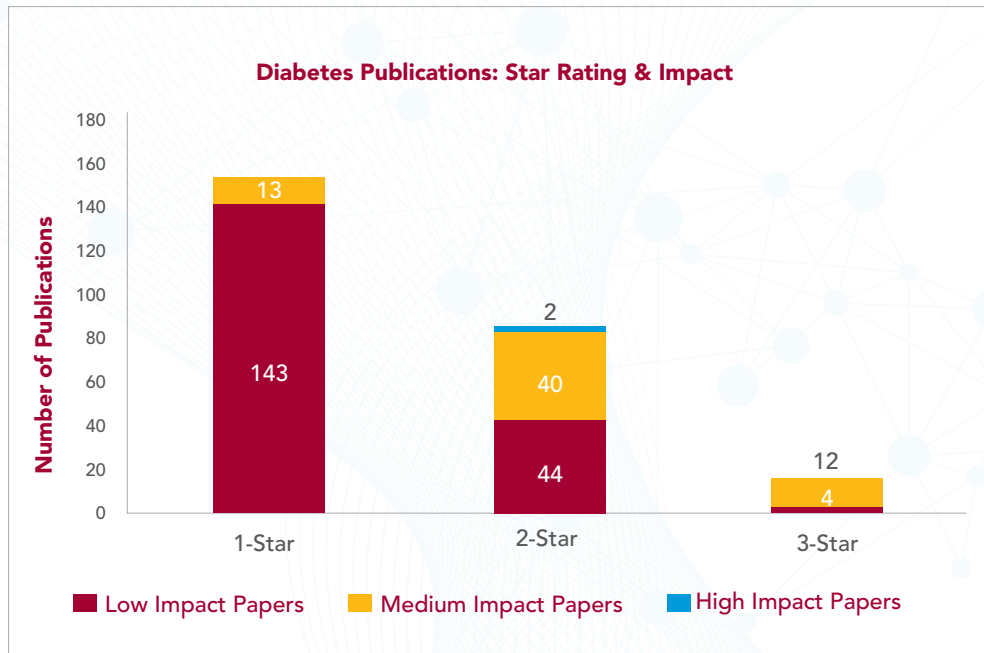


As part of the process of formulating this research agenda, publications reporting research into diabetes conducted in Qatar were examined and independently ranked by two reviewers in terms of star rating (quality of publication) and impact. Table 1 and Figure 3 show that the majority of publications were in lower quality journals and had low impact. Figure 4 shows that for the majority of publications of low rating, no funding was declared, suggesting that there are pools of funding that may not have been used to their maximum efficiency.

**Table 1.** Star Rating (quality of publication, 3-star highest) and Impact of Publications on Diabetes from Qatar.

Impact	Star Rating		
	1-Star	2-Star	3-Star
High		2	
Medium	13	40	12
Low	143	44	4
Total	156	86	16

**Figure 3.** Star Rating (quality of publication, 3-star highest) and Impact of Publications on Diabetes from Qatar.



**Figure 4.** Star Rating (quality of publication, 3-star highest) of Publications on Diabetes from Qatar and their Funding Source.

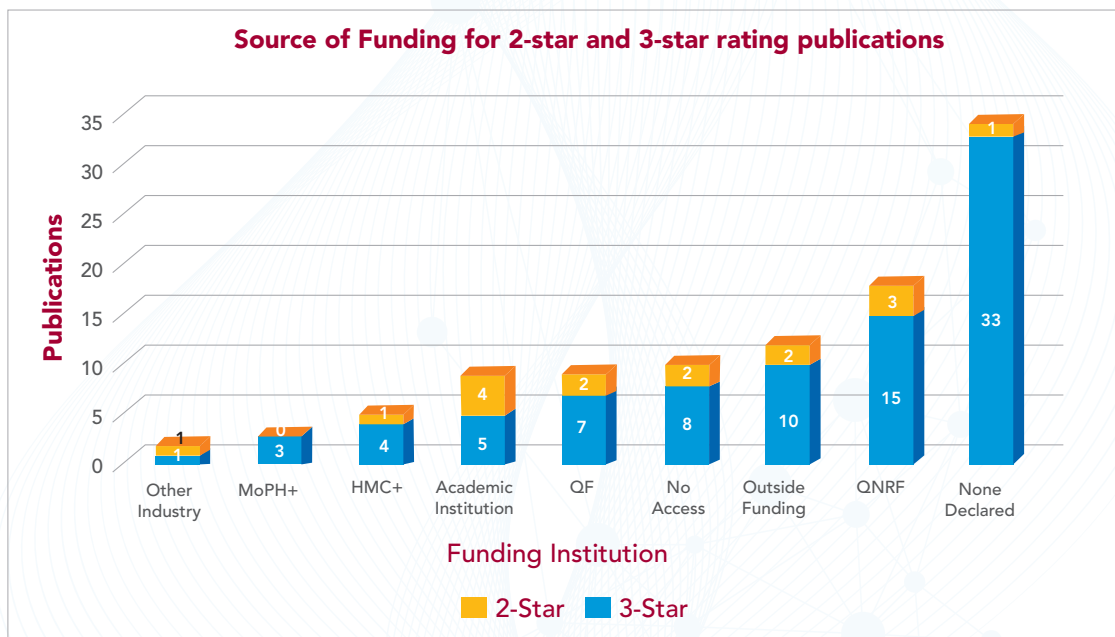
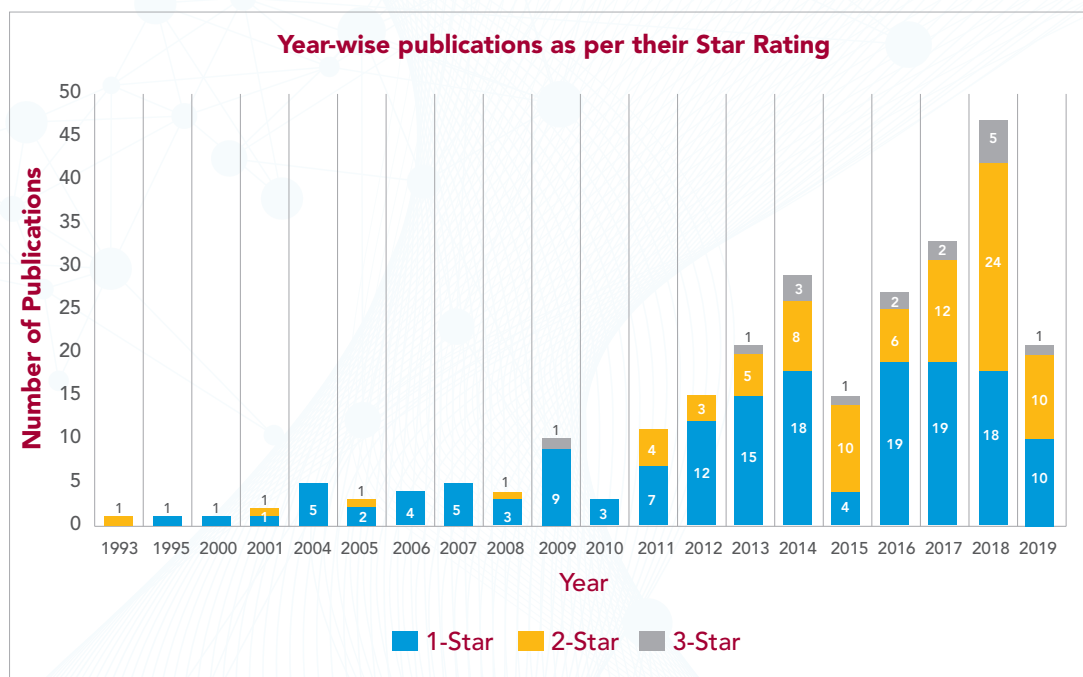
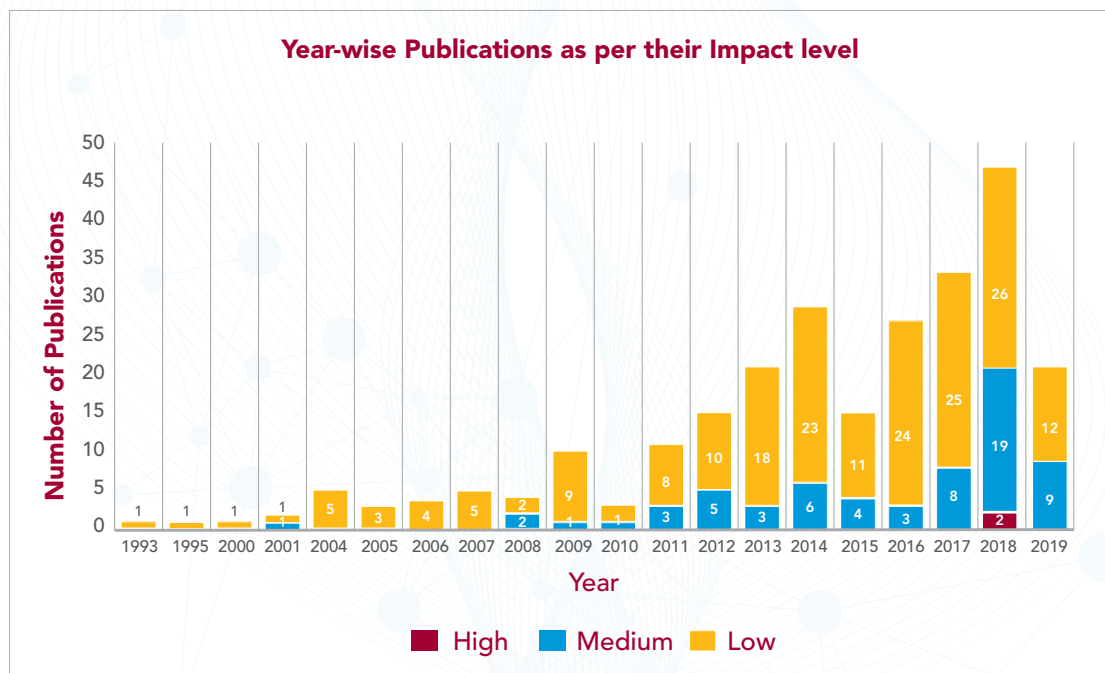


Figure 5 shows that the quality of research into diabetes in Qatar has improved over the years and more impactful work is being conducted (Figure 6). It is essential that this trend continues, and that the Diabetes and CVD Research Agenda aims to ensure that future research in Qatar continues to advance science, improve efforts towards tackling diabetes and has a major beneficial impact in Qatar. The literature search for this review was completed in June 2019.

**Figure 5.** The Quality of Publication on Diabetes from Qatar from 1993 Onwards.



**Figure 6.** The Impact of Publication on Diabetes from Qatar from 1993 Onwards.



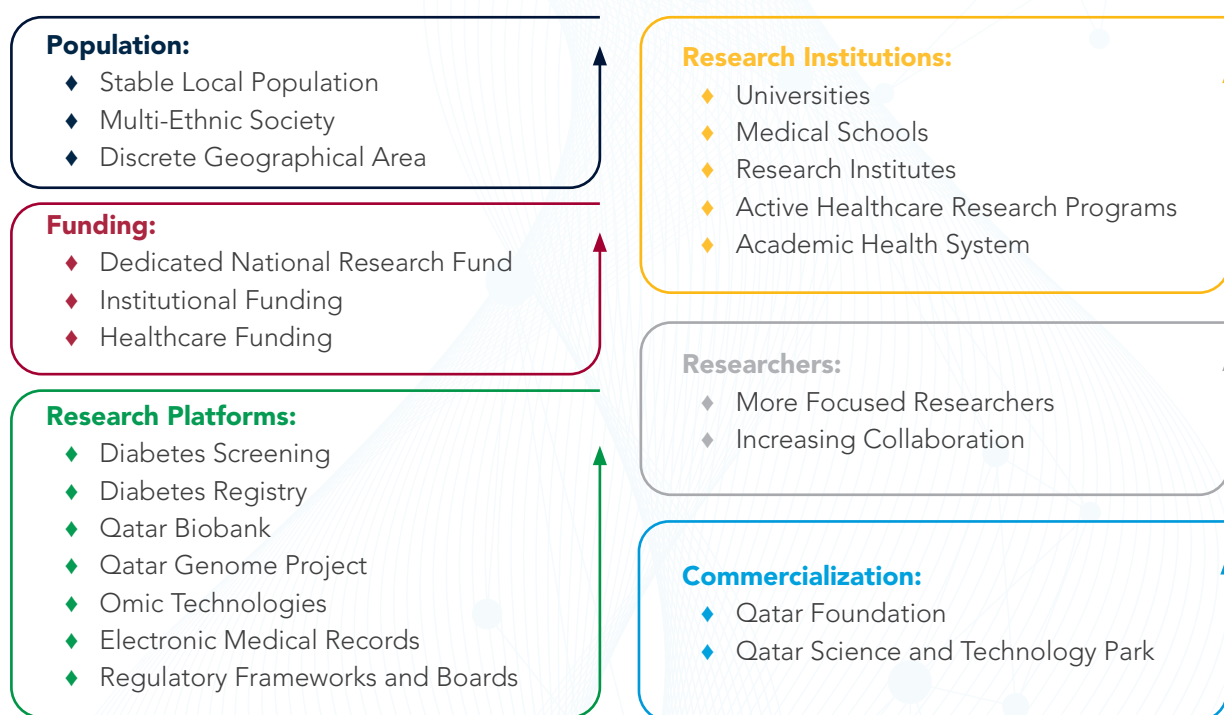
## 5. RESEARCH STRENGTHS

The public health challenge of the high prevalence of obesity, T2D and CVD in Qatar creates an imperative to support research that advances science in key fields including metabolism and precision medicine in order to positively impact wellbeing of the Qatari population.

The economic costs of treating the complications of diabetes are very high and investment in upstream research that has an impact on prevention strategies is very likely to have a high economic return on investment. As obesity, T2D and CVD are global health and societal challenges, high quality research in Qatar will also have an impact on science at the international level and will contribute to advances in global health.

There are several features of the national research environment that put Qatar in a strong position to drive a world leading focused research programme into diabetes and CVD risk factors (Figure 7).

**Figure 7.** Qatar's Research Environment: Qatar enjoys a strong developing research environment.



### 5.1 Population

The Qatari population is stable, has a uniform socio-cultural background, and is located within a discrete accessible geographical area, making it relatively easy to consider including the whole population in research. Since there are a significant number of expatriates living and working in Qatar, research that is inclusive of the social and ethnic heterogeneity of these multi-ethnic population groups creates an opportunity to conduct research that is much more generalisable to countries within the Middle East and North Africa (MENA) region and beyond.

## 5.2 Research and Clinical Structures and Platforms

A key recommendation of the National Diabetes Strategy is the establishment of a diabetes and atherosclerotic CVD risk factors screening programme. Screening will identify those with early diabetes and those at high risk for development of diabetes. This creates an opportunity to enrol people at risk into future clinical trials of different approaches to diabetes prevention and to recruit people with previously untreated diabetes into early intervention programmes aimed at increasing the likelihood of diabetes remission. The establishment of a national diabetes registry, whose primary purpose is to enhance the management of people with diabetes within a system of care, also creates a strong platform for research aimed at quantifying the incidence, prevalence, and progression of diabetes and its complications in Qatar.

Qatar has invested significantly in developing key institutions, research structures, platforms, and regulatory structures and processes. These include national research institutes incorporating focused research into diabetes and universities and medical schools with dedicated basic and clinical research infrastructures. Importantly, there has been particular attention to the development of “omic” based technology and platforms. There is increasing work conducted with inducible pluripotent stem cells. The successful establishment of the Qatar Biobank (QBB) is key to future research into obesity, T2D and CVD. The plan to extend QBB to include disease specific cohorts in collaboration with the healthcare system will enhance the work of QBB further. QBB has been the enabler of the ambitious Qatar Genome Project (QGP) which will extend the understanding of the genetic contribution to diabetes and cardio-metabolic disease in Qatar. Sidra Medicine has developed a strong research environment including key platforms to support QGP. Sidra Medicine has also established a centre for the study of paediatric diabetes including monogenic diabetes, which is a key

exemplar of how modern genetic approaches can be translated into patient stratification and care.

A multi-institutional Academic Health System (AHS) has been established to foster collaboration and joint efforts in clinical and basic research. The Qatar Metabolic Institute (QMI) has been established within the AHS, with QMI already making a demonstrable impact in driving clinical research into obesity, diabetes and other metabolic disorders. The establishment of a diabetes registry in Qatar will be a strong enabler of population research in Qatar. Community engagement and research in diabetes in Qatar is facilitated by the Qatar Diabetes Association (QDA). Hamad Medical Corporation (HMC) has developed new patient care and research centres and Wellness Centres have been established within the Primary Health Care Corporation (PHCC) to support the delivery of lifestyle interventions and research into their effectiveness. In 2020, PHCC completed its first clinical trial of a lifestyle intervention in early diabetes with promising early results.<sup>17</sup>

Unlike many regional countries, research in Qatar has been strongly enhanced by the establishment of a strong research funding organisation, the Qatar National Research Fund (QNRF), which provides significant funding for collaborative and individual research, capacity building, and scientific workshops. QNRF has been for over a decade and will be an important enabler for future research into diabetes and CVD risk factors. Beyond QNRF, research funding is also available through sizeable intramural research funding systems within research institutes, universities, the AHS, and the health service. The development of Qatar’s research infrastructure has required the recruitment of researchers from within and outside Qatar. Initially, the researchers recruited were focused on multiple scientific areas. Over the years, the research environment has matured to include researchers who are more focused on areas that are of importance to Qatar.

The Ministry of Public Health (MoPH) has established regulatory policies and frameworks. In addition, institutional review boards have also been developed. This has allowed the conduct of ethical clinical and scientific research. Clinical research efforts have increased over the last decade and robust regulatory structures are essential. A registry of clinical trials has been established by MOPH to inform on-going clinical trials and track clinical trial activity more accurately.

### 5.3 Capacity Building

There are currently two medical schools in Qatar with an increasing number of medical graduates. The creation of this local capacity building initiative is crucial to the development of a cohort of graduates who can become the academic clinical leaders of the future. There is an absence as yet of a systematic programme that can support the development of clinical academics. Investment in training programmes that combine post-graduate training in medical specialties with the development of academic expertise and interest through protected time will allow academic medicine to flourish in Qatar.

There are also greater research opportunities in other healthcare and allied healthcare professionals. There are increasing opportunities for postgraduate training and research with ongoing and novel doctoral programmes. For example, the Qatar National Research Fund (QNRF) has developed a number of post-graduate and training programmes focused on building capacity and delivering valuable postgraduate degrees in line with Qatar's National Health priorities. These include the Graduate Sponsorship Research Award (GSRA), the Postdoctoral Research Award (PDRA) and the Early Career Researcher Award (ECRA), which help enhance research quality while encouraging the development of novel research concepts.

### 5.4 Innovation and Commercialization

Qatar's ambition is to develop a strong knowledge-based economy. Commercialisation of scientific discoveries and innovations is encouraged and facilitated. Commercialization is supported by several research institutions and universities with dedicated funding from Qatar Foundation (QF) and the Qatar Science and Technology Park (QSTP).

## 6. CHALLENGES TO DIABETES & CVD RESEARCH

There are several challenges to diabetes and CVD research that are common to other research areas. Addressing these challenges will strongly facilitate and accelerate research.

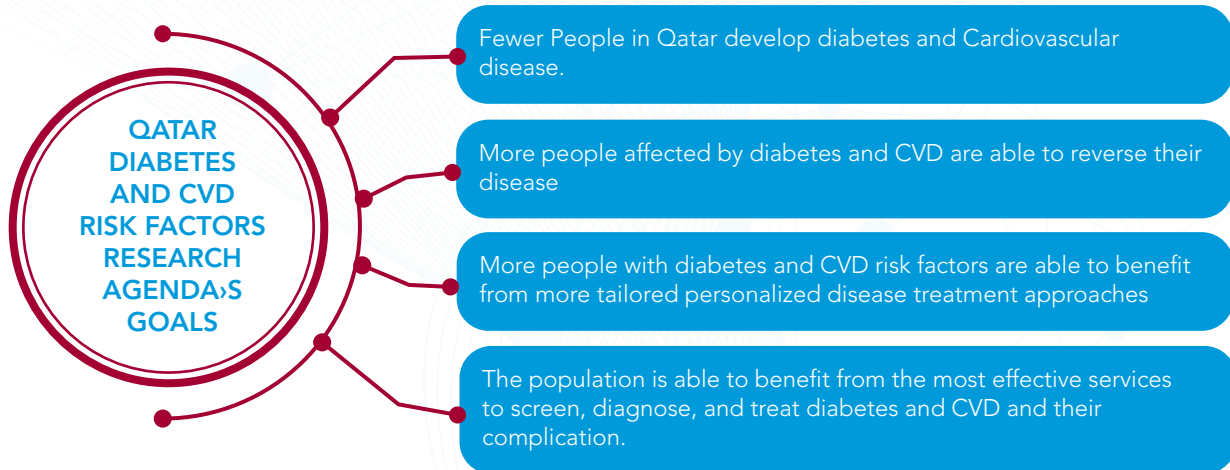
**Figure 8.** Challenges to Research and Potential Solutions

CHALLENGE	POTENTIAL SOLUTION
Research funding has been mainly directed at underpinning and aetiology research	<ul style="list-style-type: none"> <li>• Additional and dedicated funding to support translational and applied health research.</li> </ul>
	<ul style="list-style-type: none"> <li>• Streamlining of funding streams and greater collaboration amongst funders.</li> </ul>
	<ul style="list-style-type: none"> <li>• Better co-ordination of intramural funding.</li> </ul>
There are insufficient ongoing clinical trials and there are no dedicated clinical trial units to help design, support, and facilitate clinical research	<ul style="list-style-type: none"> <li>• Incentivisation of clinical research and clinical trials through dedicated funding</li> </ul>
	<ul style="list-style-type: none"> <li>• Establishment of a national clinical trials unit to help design, support, and facilitate clinical research</li> </ul>
There are many regulatory barriers that delay and hamper clinical research in Qatar. This includes navigation of multiple institutional review boards.	<ul style="list-style-type: none"> <li>• Streamlining of processes across institutions</li> </ul>
There are insufficient trained researchers for efficient progress of research studies	<ul style="list-style-type: none"> <li>• Targeted recruitment and training</li> </ul>
	<ul style="list-style-type: none"> <li>• Development of Clinician Scientist funded academic tracks</li> </ul>
Insufficient utilization of Qatar Biobank (QBB) Resource. While the QBB is a key resource, the use of data and samples are provided at a price, albeit subsidized. This discourages the wider use of QBB and delays key research.	<ul style="list-style-type: none"> <li>• Streamlining of data sharing and access processes</li> <li>• Providing dedicated funding for research using QBB data and samples</li> </ul>
Extensive duplication of research platforms and equipment with insufficient cross use	<ul style="list-style-type: none"> <li>• Improved institutional coordination, collaboration and cross-use</li> </ul>
Many institutions operate on an annual funding model which significantly affects long term planning.	<ul style="list-style-type: none"> <li>• Longer-term funding based on specific institutional programme</li> </ul>
Population participation	<ul style="list-style-type: none"> <li>• Greater public and patient education and involvement in research</li> </ul>

## 7. RESEARCH VISION

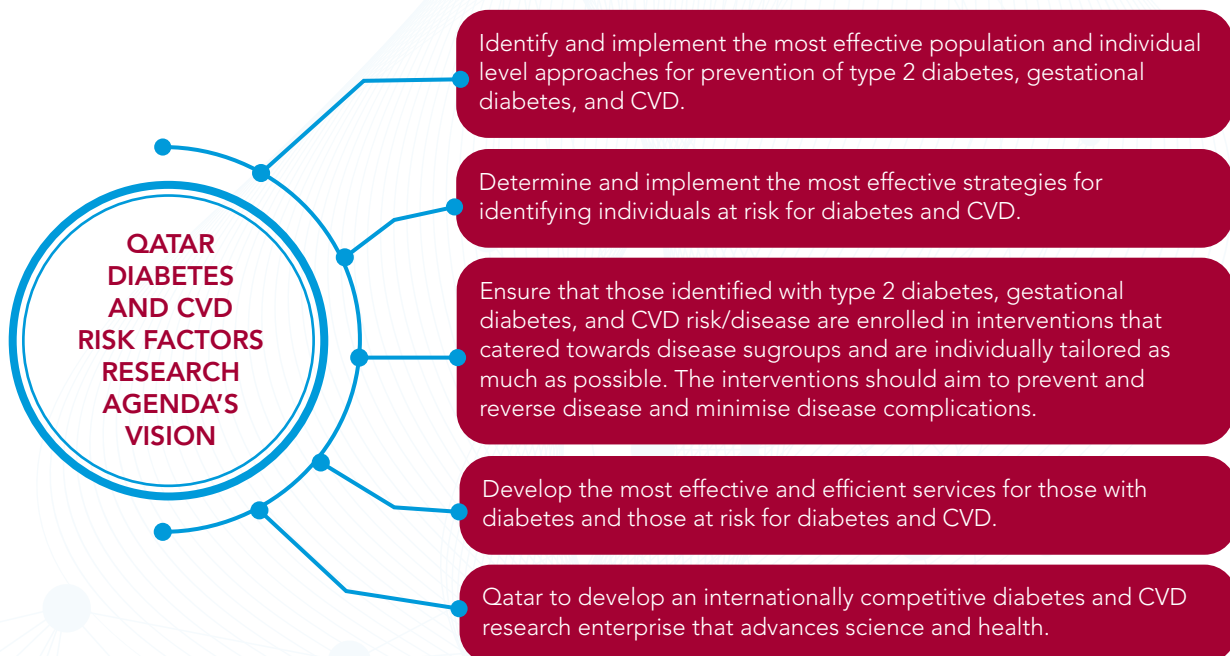
The Qatar Diabetes Research Agenda's goals are shown in Figure 9.

**Figure 9.** Qatar Diabetes and CVD Risk Factors Research Agenda's Goals.



In line with Qatar's National Vision 2030, the diabetes and CVD risk factors research agenda aims to provide the research roadmap to achieve key outcomes by 2030. Figure 10 shows the vision that aims to have the greatest impact on Qatar's health and future wealth.

**Figure 10.** Qatar Diabetes and CVD Risk Factors Research Agenda's Vision.



## 8. RESEARCH AGENDA

The research agenda will address the following research areas:

- Prevention
- Early detection
- Disease reversal
- Treatment
- Systems and outcomes

### 8.1 Prevention

The rising prevalence of T2D is a major clinical, public health and societal challenge in Qatar. The future public health burden linked to the long-term complications of diabetes is sizeable. Even within the context of a well-funded health care system, the future cost of treating those complications is unaffordable, creating a strong imperative for a long-term strategy of investment in prevention founded on a strong research base. That strategy needs to be long-term because the costs of investment in prevention need to be met now but the benefits will accrue over a 30-year time horizon.<sup>18</sup> Qatar is in the fortunate and unique position to be able to take such a long-term time perspective about research and evidence-informed action.

There is no singular approach to the prevention of T2D. Most of the global research literature is dominated by studies of individual level approaches to prevention, because of the relative ease with which the efficacy of such approaches can be evaluated in classical randomised controlled designs. However, the greatest potential for prevention in terms of population impact comes from whole population-approaches<sup>19</sup> which, by necessity, need to be supported by a different form of evidence base.<sup>20</sup> In formulating a forward research agenda it would be important to create an integrated strategy for prevention which brings together individual level

prevention approaches in people at high risk, with approaches delivered at communities and those that operate at the wider societal level and impact on the whole population. The research agenda that is established to provide the evidence base to inform the prevention strategy needs to mirror the approach of intervening at multiple levels.

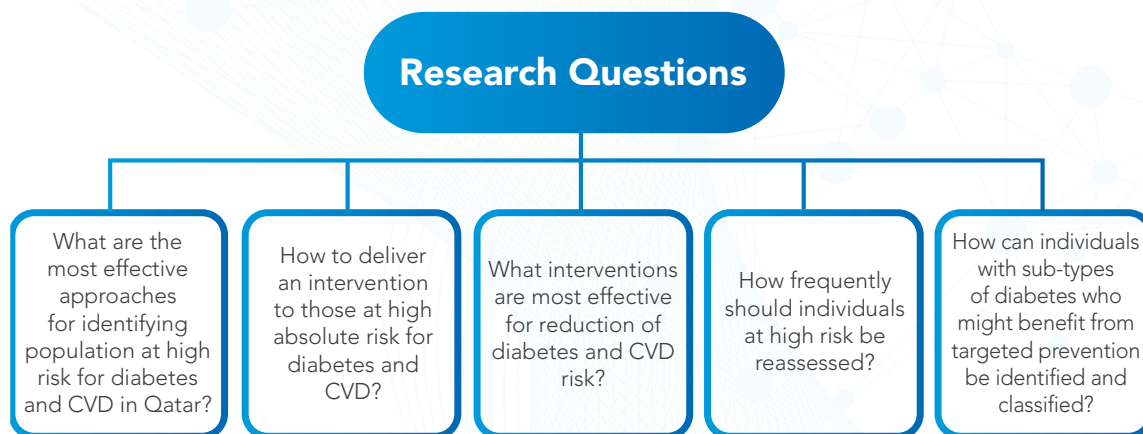
#### 8.1.1 Individual level prevention of Type 2 Diabetes

It is well established from studies in European and Asian populations that individual-level approaches to the prevention of T2D are efficacious in reducing risk of progression from pre-diabetes to diabetes by 50%.<sup>21</sup> There are, to date, no efficacy studies of individual-level prevention in Middle Eastern populations. There is a major research gap in identifying how to implement interventions in the real world and how to close the gap between what is demonstrably efficacious in the ideal setting of a randomised controlled trial and what can be achieved in the real world.<sup>22</sup> This is a particular concern since that gap can be large and can result in unrealistic expectations about the benefits of individual level prevention, both for the participants involved and for the population as a whole. Most individual level diabetes prevention programmes struggle with implementation and with key issues that are researchable, such as how to efficiently identify an at-risk population who are at sufficiently high absolute risk to make individual-level intervention effective or how to deliver effective individual-level intervention programmes in a sustainable way.

Many individual-level prevention programmes treat people at risk as a homogeneous and uniform group and, therefore, provide a similar standardised intervention to everyone who, for example, is categorised as having pre-diabetes.

This one size fits all approach is easy to implement but is potentially at odds with the pathophysiological reality that pathways to T2D vary between individuals, and also with the participant or patient perspective that recommendations need to be more tailored to individual circumstances. The investment in population-based studies in Qatar and particularly the Qatar Biobank, creates a strong environment for research into personalised or stratified prevention. Examples of key researchable questions are shown in Figure 11.

**Figure 11.** Examples of Research Questions for Individual Level Prevention.



**Research priorities and milestones:**

- To have developed a plan for a co-ordinated diabetes prevention in high risk individuals research programme that could underpin the delivery of a national initiative to deliver an integrated screening and high-risk prevention programme.
- To have a plan to build on the investments in technology platforms and the Qatar Biobank to create an established programme of research into greater stratification and personalisation of prevention with a view to this being implemented into the national integrated screening and high-risk prevention programme by end 2024.

**8.1.2 Diabetes prevention in population sub-groups**

To differing degrees, everyone lives their lives in connection with others; people with whom we share attitudes, beliefs and behaviours affect our health risks. These social networks or communities not only influence our health but can be an important vehicle for interventions aimed at changing health behaviours in a positive

direction. The nature of those communities is very particular to specific socio-cultural settings and cannot easily be generalised. Local research in Qatar would be crucial to the identification of the influence of communities on health behaviours and health risks and on the development and evaluation of interventions that capitalise on those networks.

**Examples of key researchable questions:**

- What is the role of social networks or communities such as work, school, army, faith-based groups or families in determining health risks?
- What is the effectiveness of community interventions aimed at determinants of diabetes?

**Research priorities and milestones:**

To have a plan for a community and population-level diabetes prevention research programme to complement the research programme in high risk individuals with the aim of identifying community-level determinants of key health behaviours and to develop and evaluate community-level interventions.

### 8.1.3 Whole population approaches to prevention

The wider environment in which we lead our lives has a major influence on health behaviours. Whilst we might wish to believe that we all make rational decisions about our physical activity and food intake influenced by our knowledge about health impacts, we operate in a wider world that may or may not aid those healthy choices. Factors beyond the control of individuals in the built environment and the food system, for example, have been shown to be important determinants of population-level risk of obesity and diabetes. Interventions that impact on those risk factors have the potential to favourably influence health behaviours and to reduce the incidence of diabetes. However, this type of prevention research needs to be conducted in a different paradigm than that for individual-level since whole population approaches to prevention are rarely amenable to evaluation through randomised controlled trials. Examples of key researchable questions are shown in Figure 12.

**Figure 12.** Examples of Research Questions for Population Level Prevention.



#### Research priorities and milestones:

- To have a plan for a community and population-level diabetes prevention research programme to complement the research programme in high risk individuals with the aim of identifying the population-level determinants of key health behaviours and to develop and evaluate population-level interventions.

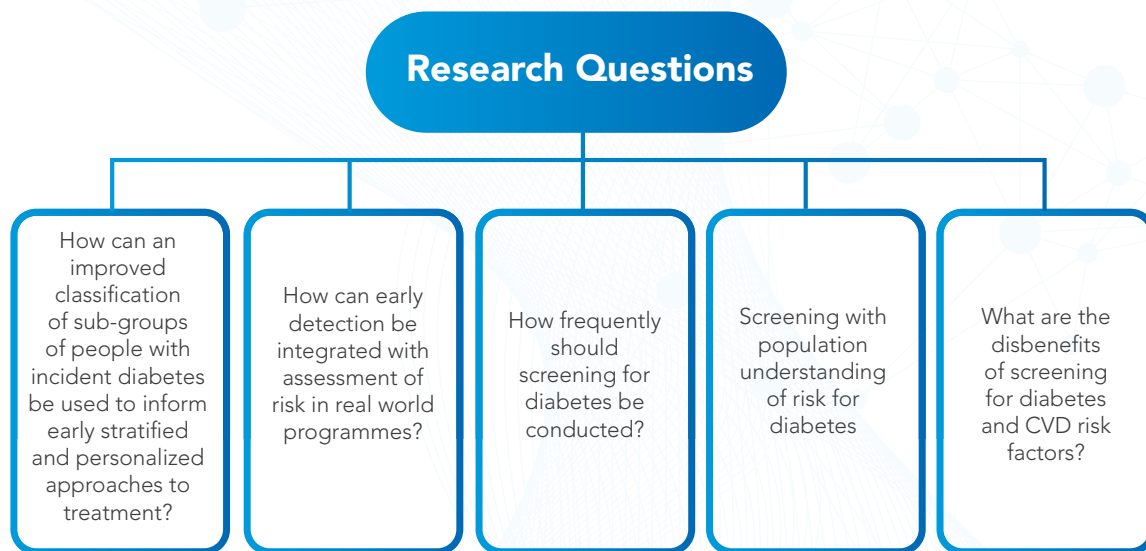
### 8.2 Early Detection

As a slowly progressive disease that typically originates without symptoms, T2D can exist for many years without being recognised by patients or by their physicians. In many previous studies, prevalent but undiagnosed diabetes is common and can account for up to 50% of all cases at any one time.<sup>23</sup> The prevalence of undiagnosed T2D in Qatar is unknown. Many

people with T2D that is found by screening have evidently had the disease biochemically for several years and previous studies suggest that the true biochemical onset may be 3-5 years before the point of clinical recognition.<sup>24</sup> As many of these individuals already have evidence of the complications of diabetes at the point of diagnosis, this suggests that there is a window of opportunity in which diabetes is detectable by screening which may bring forward the point at which clinical management and therapy are commenced. Research in formulating quantifying these benefits is difficult since it is not generally considered ethical to randomise people with screen-detected diabetes to a group receiving no care or management. In general, the benefits of screening in other populations outweigh the disbenefits<sup>25</sup> and the critical questions in Qatar relate to how a screening programme could be implemented rather than whether it

should be in the first place. Within Qatar there is very clear opportunity to link the implementation of a screening programme and diagnosing diabetes with an enhanced national system for improved phenotypic sub-categorisation at the point of diagnosis or in the early phases of disease. This would be a realisable proposition in Qatar which would be internationally unique and would link together efforts at early detection with investments in personalised medicine which are dependent on enhanced early phenotyping. Examples of key researchable questions are shown in Figure 13.

**Figure 13.** Examples of Research Questions in Early Disease Detection.



**Research priorities and milestones:**

- To have a plan for a research programme into strategies for early detection of diabetes that could underpin the delivery of a national initiative to deliver an integrated screening and high-risk prevention programme.
- To have built on the investments in technology platforms and the Qatar Biobank to have a plan for a co-ordinated research programme of detailed phenotyping of individuals with newly diagnosed (incident) diabetes research to create the basis for a personalised diabetes treatment initiative to be integrated with the national integrated screening and high-risk prevention programme by end 2024.

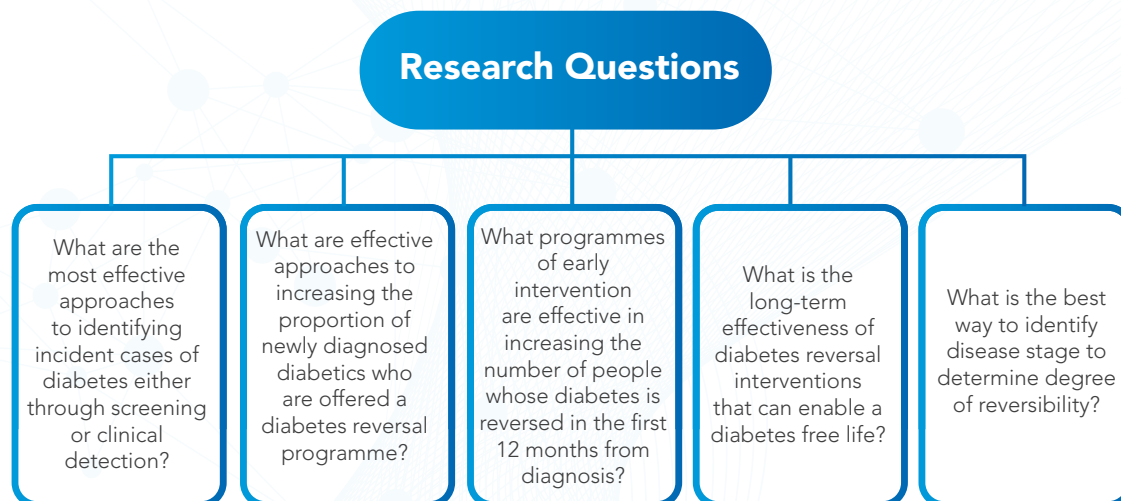
**8.3 Reversal**

T2D is driven by insulin resistance and relative insulin deficiency. Previously it was generally held that this insulin deficiency inevitably worsened,

necessitating the addition of incrementally more glucose lowering therapy including insulin as a consequence of the underlying pathophysiology.<sup>26</sup> Whilst this may have been a description of a frequent trajectory, the sense that this was an inevitability was disempowering for patients. The demonstration in studies like DIADEM-I (in Qatar) and DiRECT (in UK), that early intensive intervention aimed at weight loss can bring about reversal of T2D is a very powerful message for patients and clinicians alike.<sup>17,27</sup> For patients, it is empowering because it gives them the opportunity, if they take and sustain purposeful action, to put their diabetes into remission. For clinicians, it provides an imperative to promote early detection and intensive action, which is a positive alternative to the standard more reactive approach whereby therapies are sequentially added to deal with worsening hyperglycaemia, instead of dealing radically with the underlying root problem. A national screening programme for cardio-metabolic disease in Qatar

coupled with an investment in phenotyping at the point of diagnosis creates an opportunity for a linked programme of research into different approaches to early intensive therapy and management aimed at diabetes reversal. Examples of key researchable questions are shown in Figure 14.

**Figure 14.** Examples of Research Questions in Disease Reversal.



**Research priorities and milestones:**

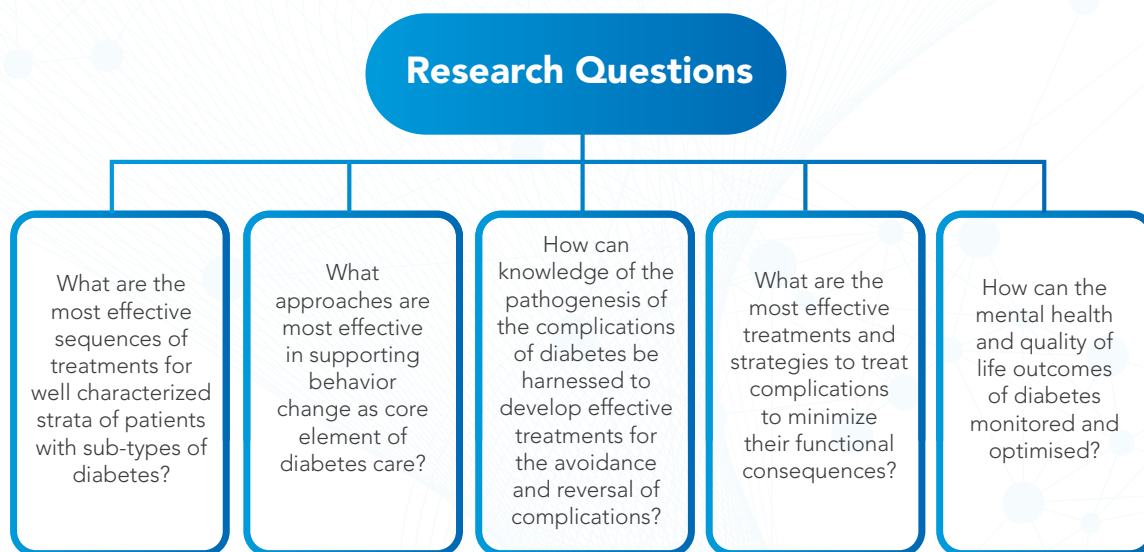
- To have a plan for established systems for rapid identification and phenotyping of people with newly diagnosed diabetes to create a programme of research into strategies for intensive early therapy aimed at diabetes reversal.

**8.4 Treatment**

The management of people with diabetes focuses less on the amelioration of current symptoms, which are fortunately rare, but rather on the optimisation of risk factors (hyperglycaemia, hypertension, dyslipidaemia etc) that are linked to the long term complications of the disease and on the early identification of those complications and their effective treatment. The range of possible glucose lowering therapies has widened over the past decade and whilst research has demonstrated the individual effectiveness of these treatments,<sup>28</sup> trials that have included hard clinical endpoints have often focused (for regulatory reasons) on demonstration of non-inferiority to placebo rather than on the estimation of benefits.<sup>29</sup> Quite how different treatments should be combined, what order they should be commenced in and

whether all therapies are equally effective in all individuals are major areas of clinical uncertainty. The potential for disease sub-classification through early phenotyping and proposed investments in personalised medicine in Qatar creates an opportunity to evaluate stratified approaches to care in T2D in a way that would be world leading. In other areas of medicine, most particularly in leukaemia as an example, uncertainties about what constitutes the most effective therapeutic approach for a given disease sub-type have been tackled through sequential evaluations of different treatment protocols. This has created a culture whereby the majority of patients are enrolled in clinical trials and they and their clinicians embrace the idea that the effectiveness of therapy is improved by incremental acquisition of knowledge about what works best and for whom. The investments that have been made in platforms and technologies in Qatar are most likely to deliver on their potential to change personalised medicine, if they are deployed in diabetes care not only to stratify patients into sub-groups, but also to evaluate the effectiveness of targeted therapeutic approaches in an integrated evaluative system embedded with clinical care. Examples of key researchable questions are shown in Figure 15.

**Figure 15.** Examples of Research Questions in Disease Treatment.



**Research priorities and milestones:**

- To have set up a diabetes clinical research network aimed at providing a co-ordinated infrastructure in which all patients with diabetes are offered the chance to participate in on-going behavioural, pharmacological and health system trials.
- To aim to recruit 50% of all patients with newly diagnosed diabetes into observational studies or trials.

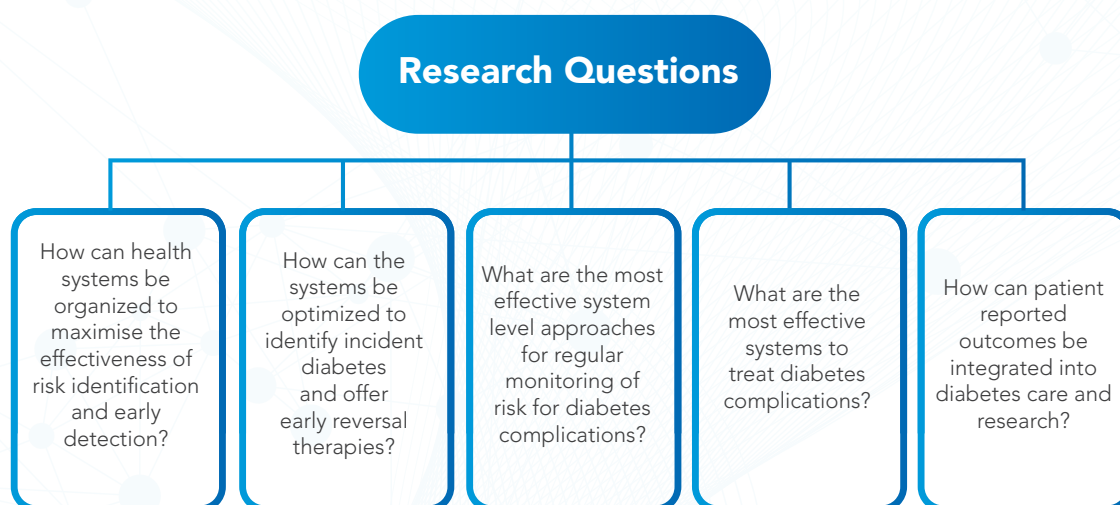
**8.5 Systems and outcomes**

Diabetes is a classic example of a medical condition for which the overall effectiveness in reducing the risk of complications at the population-level is as affected by the organisation and delivery of the system of care as much as by the efficacy of any of the individual treatments that make up an overall care package. Multiple trials have demonstrated improvements in HbA1c, lipid and blood pressure control with interventions aimed at implementing integrated multi-component team-based care.<sup>30</sup> Within Qatar, the establishment of a population-based diabetes register would create the denominator

for research into system-level factors that could optimise the proportion of patients receiving optimal risk factor control. It also acts as the starting point for the implementation of the key elements of the organisation of diabetes care that have been demonstrated previously to be effective.<sup>31</sup>

Internationally, there is an increasing appreciation of the importance of measuring Patient Reported Outcomes (PROs) in clinical care and in research, particularly for diabetes. Patient Reported Outcomes have been defined as “any report of the status of a patient’s health condition that comes directly from the patient, without interpretation of the patient’s response by a clinician or anyone else”. These PROs complement more traditional biomedical assessments of outcomes and many authorities have called for their wider incorporation in care and research.<sup>32</sup> PROs are contextual and are affected by socio-cultural factors and thus research into their definition and utility in Qatar needs to be conducted with the participation of Qatari patients. Examples of key researchable questions are shown in Figure 16.

**Figure 16.** Examples of research questions on systems and outcomes.



**Research priorities and milestones:**

- To have established a programme of health systems research aimed to investigating the system level determinants of effectiveness of risk identification and early detection.

## 9. BASIC LABORATORY SCIENCE AND TECHNOLOGY

There are several international diabetes research strategies that have highlighted current gaps in our understanding of the mechanisms underlying diabetes and CVD. Many of these gaps can be addressed through collaboration between basic scientists and clinical researchers. The areas of research highlighted within the research agenda will be key to ensuring that basic laboratory science research also focuses on areas where there may be great impact for the Qatari population. The research agenda

supports translational research and the testing of key hypotheses that advance our understanding of diabetes and CVD pathophysiology. There are also many technological solutions that can be tested within the research framework. Through this national research agenda, there is great scope to advance novel ways to screen disease, assess its severity, monitor disease and treatment responses, and determine disease prognosis. For example, there is increasing interest in the use of Artificial Intelligence (AI) and machine learning.

## 10. GOVERNANCE AND REVIEW

The National Diabetes Strategy Research Sub-Committee will be responsible for progress of the diabetes and CVD risk factors research agenda. The Sub-Committee will provide an on-going review of the progress of the diabetes research agenda and on-going research and examine their impact of the health and wellbeing on Qatar's population. The Sub-Committee will make recommendations to key stakeholders regarding diabetes and CVD risk factor research. The Sub-Committee will collaborate with funding agencies

to develop requests for research applications to ensure that the goals of the research agenda are met.

### **The Sub-Committee will annually review the following:**

- Grants awarded
- Publications
- Collaborations
- Research quality and impact
- Data sharing and collaboration

## 11. APPENDIX

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### 11.2 Acknowledgements

We are grateful to Her Excellency Dr Hanan Mohamed Al Kuwari, Minister of Public Health, for her leadership and support of the National Diabetes Strategy.

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## 11.4 Research Agenda – Contributing Institutions

The following institutions and groups contributed to the development of the research agenda:

Academic Health System (AHS), Hamad Bin Khalifa University (HBKU), Hamad Medical Corporation (HMC), Ministry of Public Health (MOPH), Primary Health Care Corporation (PHCC), Qatar Biobank (QBB), Qatar Biomedical Research Institute (QBRI), Qatar Computing Research Institute (QCRI), Qatar Diabetes Association (QDA), Qatar Foundation (QF), Qatar National Research Fund (QNRF), Qatar Metabolic Institute (QMI), Qatar University (QU), Sidra Medicine, and Weill Cornell Medicine Qatar (WCMQ).

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## 12. ABBREVIATIONS

AHS: Academic Health System  
AI: Artificial Intelligence  
CVD: Cardiovascular Disease  
ECRA: Early Career Researcher Award  
GSRA: Graduate Sponsorship Research Award  
HbA1C: Glycated haemoglobin  
HBKU: Hamad Bin Khalifa University  
HMC: Hamad Medical Corporation  
IDF: International Diabetes Federation  
MENA; Middle East and North Africa  
MOPH: Ministry of Public Health  
NAFLD: Non-alcoholic Fatty Liver Disease  
NIHR: National Institute of Health Research  
NPRP: National Priorities Research Program  
OSA: Obstructive Sleep Apnoea  
PHCC: Primary Health Care Corporation  
PDRA: Postdoctoral Research Award  
PRO: Patient reported outcome  
QBB: Qatar Biobank  
QBRI: Qatar Biomedical Research Institute  
QCRI: Qatar Computing Research Institute  
QDA: Qatar Diabetes Association  
QF: Qatar Foundation  
QGP: Qatar Genome Project  
QMI: Qatar Metabolic Institute  
QNRF: Qatar National Research Fund  
QNRS: Qatar National Research Strategy  
QR: Qatari Riyal  
QSTP: Qatar Science and Technology Park  
QU: Qatar University  
TIA: Transient Ischemic Attack  
WCMQ: Weill Cornell Medicine Qatar

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