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LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

Prevention of type 2 diabetes and poor mental health amongst immigrants from the Middle-East to Sweden

FAIZA SIDDIQUI
DEPARTMENT OF CLINICAL SCIENCES | FACULTY OF MEDICINE | LUND UNIVERSITY

Prevention of type 2 diabetes and poor mental health amongst immigrants from the Middle-East to Sweden

Faiza Siddiqui

LUND UNIVERSITY

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Mai-Lis Hellénius, Professor, Department of Medicine,
Karolinska Institute, Stockholm

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Title and subtitle: Prevention of type 2 diabetes and poor mental health amongst immigrants from the Middle-East to Sweden

Background: Type 2 diabetes (T2D) and poor mental health are two major public health concerns in Europe. Ethnicity is identified as a risk marker for both conditions. Middle-Eastern immigrants represent the largest group of non-European immigrants in Sweden and are at increased risk for T2D. In clinical trials, lifestyle interventions focusing on physical activity and healthy diet have been shown to delay/prevent the onset of T2D. Physical activity also has therapeutic effects on anxiety and depression. However, the evidence related to the efficacy of such interventions in non-European immigrants is scarce. **Aims:** In residents of Malmö born in Iraq or Sweden, to study the prevalence and risk factors associated with poor mental health (*Paper I*). In a Middle-Eastern immigrant population at high risk for T2D, to elaborate on the effects of a culturally adapted lifestyle intervention on lifestyle habits & cardio-metabolic profile *(Paper II)*, on objectively measured physical activity *(Paper III)*, on dietary habits *(Paper IV)* as well as on mental health *(Paper V)*.

Methods: *Paper I*: The **MEDIM study**, a population-based cross-sectional study, conducted between 2010 and 2012. Iraqi-born and Swedish-born residents of Malmö (30-75 years) were randomly selected from the census register and invited to participate. Physical examinations were performed and fasting blood samples were collected. Information on lifestyle, socio-demography and mental health was provided through questionnaires. Logistic regression was used to study the associations. *Paper II-V*: The **MEDIM intervention study,** a randomised controlled trial, recruiting Iraqi immigrants at high risk of T2D, was conducted from January to June 2015. High risk for T2D was defined as having a body mass index (≥ 28 kg/m^2) and/or waist circumference (≥80 cm in women, and ≥94 cm in men) and/or pre-diabetes. The participants were randomised to the control group (CG) or the intervention group (IG). Anthropometric measurements, blood tests and oral glucose tolerance test were performed at the start, mid-term and end of the study. Information on socio-demography and lifestyle habits was collected. Physical activity data was collected using accelerometers. Linear mixed models and proportional odds model were assessed. The intervention was adapted to match Middle-Eastern culture and comprised of seven group sessions including one cooking class.

Results: *Paper I*: Compared to Swedes (n=634), anxiety was three times and depression five times as prevalent in Iraqi immigrants (n=1255). Iraqis had three times higher odds of anxiety/depression. Physical inactivity, economic insecurity, inability to trust people and smoking were associated with anxiety and depression in the Iraqis. *Paper II*: A reduction in body weight (0.4% per month), LDL-cholesterol levels (2.1% per month), as well as improvement in insulin sensitivity index (10.9% per month), was observed in the IG (n=50) compared to the CG (n=46). *Paper III*: An increase in number of hours/day spent in light-intensity activities and in least sedentary activities within the sedentary behaviour range was observed in the IG compared to the CG. *Paper IV*: No significant changes in dietary intake were observed in the IG compared to the CG, however the IG exhibited favourable trends in intake of energy, sucrose, fats & carbohydrates. *Paper V*: The odds of scoring lower on Montgomery Åsberg Depression Rating Scale (MADRS-S) and Hospital Anxiety & Depression Scale (HADS) for depression at follow-up vs. baseline were higher in the IG compared to the CG. P-values <0.05 were considered significant.

Conclusion: Middle-Eastern immigrants exhibit high levels of anxiety and depression which is strongly associated with physical inactivity. Adopting a culturally sensitive lifestyle intervention approach in primary health care settings could be potentially beneficial for improving lifestyle habits and reducing the risk of T2D and poor mental health in this vulnerable immigrant population.

Keywords Clinical trial, immigrants, lifestyle intervention, mental health, prevention, type 2 diabetes

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Faculty of Medicine
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As you start to walk on the way, the way appears

Rumi

To Umair, Naba & Ibrahim

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II. **Siddiqui F**, Kurbasic A, Lindblad U, Nilsson PM, Bennet L. Effects of a culturally adapted lifestyle intervention on cardio-metabolic outcomes: a randomized controlled trial in Iraqi immigrants to Sweden at high risk of type 2 diabetes. *Metabolism, Clinical and Experimental*, 2016; 66: 1-13.

III. **Siddiqui F**, Koivula R, Kurbasic A, Lindblad U, Nilsson PM, Bennet L. Physical activity in a randomized culturally-adapted lifestyle intervention. *American Journal of Preventive Medicine*, 2018; 55(2): 187-196.

IV. **Siddiqui F**, Winther V, Kurbasic A, Sonestedt E, Lundgren KB, Lindberg S, Nilsson PM, Bennet L. Changes in dietary intake following a culturally adapted lifestyle intervention among Iraqi immigrants to Sweden at high risk of type 2 diabetes: a randomised trial. *Public Health Nutrition*, 2017; 20(15), 2827-2838.

V. **Siddiqui F**, Lindblad U, Nilsson PM, Bennet L. Effects of a randomised, culturally-adapted, lifestyle intervention on mental health among Middle-Eastern immigrants. *European Journal of Public Health (under review).*

List of Abbreviations

ADA	American Diabetes Association
BMI	Body Mass Index
CVD	Cardiovascular Disease
DPP	Diabetes Prevention Program
DPS	Diabetes Prevention Study
FINDRISC	Finnish Diabetes Risk Score
FPG	Fasting Plasma Glucose
HADS	Hospital Anxiety and Depression Scale
HbA_{1c}	Glycosylated Haemoglobin
HPA	Hypothalamic Pituitary Axis
ISI	Insulin Sensitivity Index
LTPA	Leisure Time Physical Activity
MADRS-S	Montgomery Åsberg Depression Rating Scale
MEDIM	Impact of Migration and Ethnicity on Diabetes In Malmö
NEFA	Non-Esterified Fatty Acids
NNR	Nordic Nutrition Recommendations
RCT	Randomised Controlled Trial
UK	United Kingdom
US	United States
VM-HPF	Vector Magnitude High Pass Filtered
WHO	World Health Organization

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Introduction

Diabetes and Depression: Global Challenges

Type 2 Diabetes, which represents 90% of the global burden of diabetes [1], and poor mental health are two major public health concerns today. The World Health Organization (WHO) has estimated that in 2014, 422 million people had diabetes corresponding to a global prevalence of 8.5% [2]. At the same time, poor mental health continues to plague well-being and quality of life for millions of people around the globe. Mental health encompasses a wide range of conditions, ranging from generalised anxiety disorders to schizophrenia and psychosis. However, within this spectrum of poor mental health, anxiety disorders and depression are the most prevalent and co-occurring conditions [3]. Around 300 million people suffer from depression globally equating to a global prevalence of 4.4%, whereas the global prevalence of anxiety disorders is estimated to be around 3.6% [4]. From a European perspective, around 60 million Europeans (10%) suffer from diabetes [5] whereas around 27% are affected by anxiety and depression every year [6].

Diabetes and poor mental health also exhibit a bidirectional association. Poor mental health, in particular depression, has been placed on causal pathway for diabetes suggested by an increased risk for developing diabetes among individuals with depression [7]. The underlying mechanisms are hypothesised to be elevated Hypothalamic Pituitary Adrenal (HPA) axis activity [8] as well as a pro-inflammatory state in the body [9] with subsequent insulin resistance and b-cell destruction [10]. In addition, depression predisposes to unhealthy lifestyle habits such as physical inactivity and poor diet [11] as well as weight gain [8, 12], which are all established risk factors for type 2 diabetes. Similarly, another body of evidence suggests that patients with diabetes tend to develop depression under the daily stress exposure of living with a chronic disease [13].

Migration - A Public Health Perspective

Migration is a historical but ongoing phenomenon rooted in political instability and war, economic disadvantage and social causes to mention but a few contributing factors [14]. We live in a world where around 260 million people are immigrants, living outside their country of birth. From the year 2000 to 2015, positive rates of migration contributed to around 40% of population growth in America and Oceania. During the same time period, Europe experienced a population growth of 2% that would have fallen by 1% if there was no migration [15]. This clearly indicates the increasing proportion of immigrants in western populations. As per statistics from the European Union, 35 million people born outside Europe were living in one of the 28 member states in 2015 [16]. In Sweden, around 18.5% of the population is foreign-born and half of them are from non-European countries with some of the largest groups originating from Middle-Eastern countries, namely Syria, Iraq and Lebanon as well as Iran and Afghanistan [17].

The relationship between health and migration is multidimensional and an important contributing factor in determining global health. On the one hand, only the healthy members of the source population tend to migrate owing to the medical examinations at the time of immigration as well as the fact that higher education and better physical and mental health facilitates the process of migration [18]. Consequently, immigrants in earlier years of migration exhibit better health compared to the natives in the host country, the so called ‘healthy migrant effect’ as observed in some epidemiological studies [19, 20]. On the other hand, migrants are considered to be a vulnerable group with regards to worse health outcomes [21]. Migrants are exposed to a variety of adverse factors in the pre-migration, migratory and post migration phases, leading to an increased risk for both poor physical and mental health. Pre-migratory factors that influence health include exposure to war/stressful events, and to the risk factors as well as the socio-economic status and lifestyle of the individual in the country of origin. The nature of migration such as for economic reasons, family reunification, refuge, asylum or illegal immigration status, determine access to healthcare in the host country. Acculturation, social support and ethnic discrimination, language skills, access to healthcare, economic insecurity and the social situation in the host country, together with lifestyle changes, are some of the factors that operate at the post-migratory phase and serve as determinants of health among immigrant groups [22]. Even in healthy voluntary immigrants, obesity rates [23] and risk for diseases like diabetes [24] and cancers [25] tend to approximate those of the host population over the period of time accompanied by changes in lifestyle and socioeconomic situation [26, 27].

Studies have reported an increased risk of communicable diseases as well as non-communicable diseases like cardiovascular diseases (CVD), diabetes, schizophrenia and psychosis among immigrants compared to the native populations [28]. However, the data on health status of immigrant groups in Europe is patchy [29]. Studies conducted in countries like Sweden, Denmark, Norway, UK and the Netherlands have compared immigrant groups to the native populations for a variety of health outcomes. However, Middle-Eastern immigrants constitute a comparatively less explored group in spite of their large proportion and increasing numbers in Europe.

Diabetes Risk in Immigrants

In the studies conducted in Sweden in the late 1990s and early 2000s, the prevalence of diabetes among non-European immigrants was found to be 2-3 times higher as compared to Swedes [30 31 32]. In one study conducted in the year 2000, age and sex adjusted prevalence rate was reported to be 5.82% in non-Europeans vs. 1.80 in the native Swedes [33]. In a systematic literature review in 2010, Wändell et al. reported a much higher risk of diabetes among non-European immigrants, particularly among Middle-Eastern immigrants than in native Nordic populations, with the highest risk being observed in women [34]. Carlsson et al. reported standardised prevalence rate ratio of 6.0 (95% CI: 1.3-28.9) and 2.4 (95% CI: 0.6-14.6) for Iraqi-born women and men, respectively [35]. It appears that the risk is highest among immigrant women indicating that gender differences exist in diabetes risk. Moreover, the increased risk was associated with overweight and obesity [30, 36].

The increased risk of diabetes observed in immigrant groups has been attributed to various factors such as sedentary lifestyle, increased prevalence of risk factors such as obesity, abdominal obesity and family history of diabetes, as well as socio-economic factors like low education and unemployment [30, 37, 38]. Moreover, lack of acculturation was reported as a risk factor in one study among Arab immigrants in the US [39], although studies among other immigrant groups have shown conflicting results [40] . A high genetic susceptibility to diabetes has been reported in some immigrant groups. However, it appears that environmental factors like physical inactivity, poor dietary habits and obesity serve as a trigger for this increased genetic risk [14, 34].

Mental Health in Immigrants

The process of migration is inevitably associated with *change and loss* in a person's life as the immigrants lose their social support in the form of family and friends, and experience a lot of changes in lifestyle, culture, language and socio-economic situation [41]. In addition, factors like racial discrimination, marginalisation, length of stay in the host country and socioeconomic situation [42] play an important role in determining mental health among immigrants. Cultural factors such as stigma associated with mental ill-health, differences in response to stressors, limited access to healthcare due to language barriers, somatization of mental ill-health and difficulties in diagnosis have an effect on mental health among immigrants [43-45]. Epidemiological studies conducted in Europe report higher prevalence and incidence rates as well as risk of mental disorders in immigrant groups compared to native European populations [46-50]. In Sweden, studies have highlighted much higher risk of mental disorders in non-European immigrants compared to native Swedes [51]. In one such study the odds of depression and low subjective wellbeing assessed using Major Depression Inventory and WHO wellbeing Index were much higher in non-European immigrants (3.69, 95%CI: 2.91-4.69) and (2.26, 95%CI: 1.81-2.81) respectively, compared to Swedes. A considerable part of this risk was explained by socioeconomic risk factors like education, income, labour market position and economic insecurity [52]; however, a casual inference could not be drawn due to the cross-sectional study design. In another study Bayerd-Burfield et al demonstrated that the Polish, Chilean, Turkish and Iranian immigrants in Sweden were more prone to long standing self-reported psychiatric illness and intake of psychotropic drugs compared to Swedes [53]. Being married, having knowledge of Swedish language, being employed and having a sense of coherence had a protective effect in these groups. In one Swedish study among Iraqi immigrants, factors not related to migration such as female gender, being single, lack of social network and economic insecurity as well as immigrant-specific factors like poor socio-cultural adaptation accounted almost completely for the excessive risk [54].

Although these socioeconomic factors have been studied in relation to mental health among immigrants, research on the effect of lifestyle related factors like physical activity on mental health among immigrant groups is scarce.

Lifestyle and Migration

Dietary transition is part and parcel of the process of migration. Individuals moving to a new country are not only exposed to different types of foods but also experience differences in availability and access to the food depending upon dietary patterns in the host society as well as their own socio-economic situation. These differences therefore lead to changes in dietary intake among immigrants [55]. At the same time, beliefs and religious restrictions relating to food play an important role in shaping the dietary intake among immigrant groups [56].

In a systematic review, which highlighted dietary changes in South Asian immigrants in Europe, an increased intake of energy and fat was reported together with a shift from whole grains to refined carbohydrates resulting in decreased fibre intake [57]. In another systematic literature review focusing on changes in dietary habits among immigrant groups in Europe, the authors reported that these groups tend to adopt less healthy food habits characterised by consumption of westernized fast foods with high caloric content as well as high levels of sugars and fats. In this review, different immigrant groups were discussed specifically, however Middle-

Eastern immigrants were not addressed which indicates a need for further research on this group[58].

With regards to physical activity habits, immigrant groups, particularly non-western immigrants in western countries often exhibit low levels of physical activity owing to cultural practices and religious beliefs as well as lack of social support and differences in perception of health and disease [59]. In the Canadian community health survey, prevalence of physical activity in recent immigrants (≤10 years since migration, 16%) and immigrants (> 10 years, 20%) was lower compared to natives (24%). Although the probability of engaging in leisure time physical activity (LTPA) in immigrant groups increases with longer time since migration, the concomitant increase in overweight and obesity indicates that increased caloric intake or reduction in occupation-related activities most likely offset the benefits of LTPA in immigrant groups [60-62].

Middle-Eastern Immigrants

In Sweden, Middle-Eastern immigrants constitute the largest group of non-European immigrants. Epidemiological studies have highlighted the increased risk of type 2 diabetes in this group in Sweden [31]. This together with the fact that they originate from an area of high diabetes prevalence[63] and have been exposed to urbanisation and westernisation as a result of migration, makes it highly relevant to study this group with regards to type 2 diabetes risk. The risk factors, as well as the underlying mechanisms predisposing Middle-eastern immigrants in Sweden, to type 2 diabetes have not been explored in the earlier studies although some studies have reported high levels of physical inactivity and obesity in this group as potential contributors [30, 64].

The MEDIM study

The MEDIM (impact of Migration and Ethnicity on Diabetes In Malmö) study, which was conducted between 2010 and 2012 in Malmö, provided a comparison of type 2 diabetes risk factors in a population-based sample of Iraqi-born residents of Malmö with that of native Swedes. It also provided a detailed description of the socio-economic situation and lifestyle habits of residents of Malmö born in Iraq or Sweden. In addition, conduction of blood tests and oral glucose tolerance tests on around 2000 participants in this study enabled metabolic profiling of study participants as well as facilitated understanding of mechanisms that underlie the increased risk of type 2 diabetes in the Iraqi-born group compared to the Swedes.

The study revealed, that the prevalence of type 2 diabetes (11.6% vs. 5.8%) was twice higher among Iraqi-born immigrants as compared to the native Swedes [65]. Iraqi ethnicity was identified as a risk factor, independent of other risk factors. This was accompanied by a clustering of diabetes related risk factors like obesity, abdominal obesity, physical inactivity and a positive family history of diabetes. Moreover, 45% of Iraqis were found to be at moderate-very high risk of developing diabetes in the next decade as per FINDRISC scores [65]. With regards to the lifestyle habits, 83% did not achieve recommended levels of physical activity as per objectively measured physical activity levels. In addition, an over-estimation of self-reported physical activity time by 71% was observed [66]. Almost 50% reported less than daily intake of vegetables and fruits. Characteristics of the Iraqi-born participants vs. Swedish participants in the MEDIM population-based study are summarised in Table 1.

Table 1:

Risk factor profile of Iraqi-born and Swedish born participants in the MEDIM study.

Characteristics	Iraqis (%)	Swedes (%)	P-value
Obesity (BMI > 30 kg/m^2)	38	23	< 0.001
Physical Inactivity (< 150min/week)	83	73	< 0.001
Type 2 diabetes (new and previously diagnosed cases)	11.6	5.8	< 0.001
Low self-rated health	43.9	21.9	< 0.001
Family history of diabetes (1st degree relatives)	51.7	27.6	< 0.001
Abdominal obesity (waist circumference > 88 cm in women, > 102 cm in men)	48.2	38.4	< 0.001

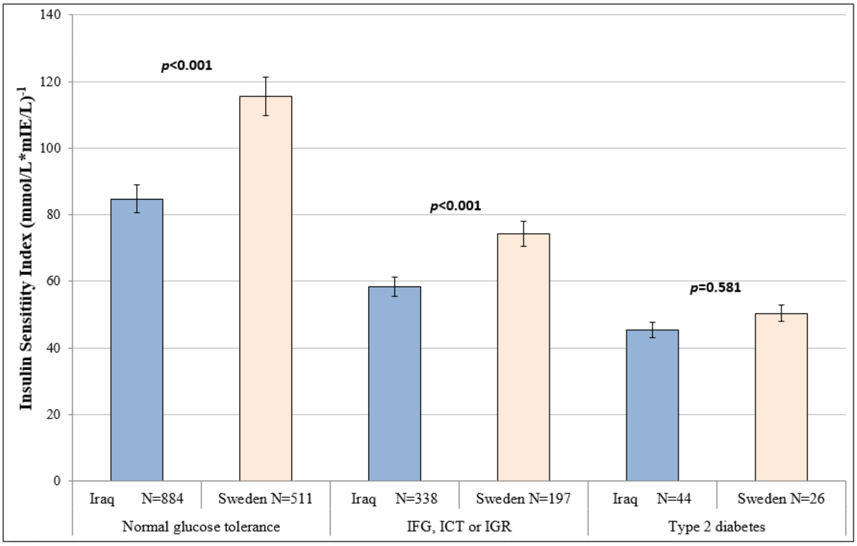

Figure 1: Insulin sensitivity index in Iraqis vs. Swedes at three levels of glucose tolerance.
From Bennet et al [67]

One of the most important finding in the MEDIM population-based study was the lower insulin sensitivity among Iraqis vs. Swedes even in normoglycaemic individuals (Figure 1) [67], and in those with normal body mass index (BMI) (Figure 2) and waist circumference [68].

The contribution of impaired insulin action to the risk of type 2 diabetes was much greater for Iraqis vs. Swedes and insulin resistance appeared to be the primary driver of type 2 diabetes in this population. Similarly, disposition index, a measure of insulin secretion which takes into account the degree of insulin resistance, was generally lower in Iraqis compared to Swedes [67]. This indicated that insulin secretion from beta-cells could not match the profound insulin resistance as also indicated by higher glycosylated haemoglobin (HbA_{1C}) levels in the Iraqi group [69].

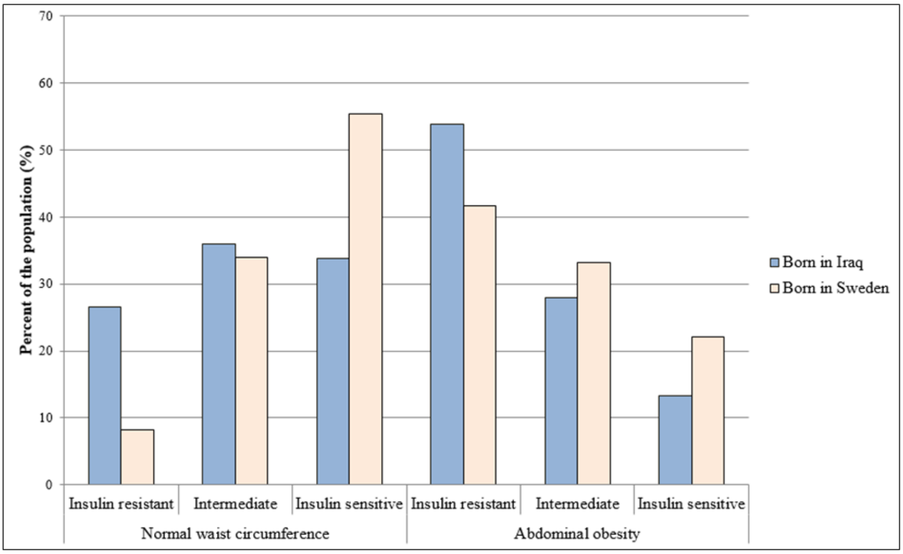

Figure 2: Distribution of tertiles of insulin sensitivity in Iraqis vs. Swedes with and without abdominal obesity.
From Bennet et al [68]. (licensed under Creative Common Attribution 4.0 international Public License)

The findings from the MEDIM study had multiple implications for diabetes prevention in this high-risk group. Firstly, it highlighted the need for greater awareness among health practitioners of type 2 diabetes risk in this immigrant population. Secondly, the earlier onset of type 2 diabetes [69], a stronger association with CVD [70] and worse metabolic profile indicated not only a greater risk of complications but also future burden of disease and healthcare costs associated with treatment of diabetes and its complications. This, together with the prevalence of a sedentary lifestyle conducive to diabetes, indicated the need to intervene actively for diabetes prevention in this risk group rather than passive observation. Moreover, it appeared that the major defect was in insulin action rather than insulin secretion, hence why improvement in insulin sensitivity should be targeted to achieve diabetes prevention among Middle-Eastern immigrants such as through increased physical activity. Insulin sensitivity at a BMI of 30 kg/m2 in Swedes corresponded to the insulin sensitivity at BMI of 28.5 kg/m2 and 27.5 kg/m2 in Iraqi men and women respectively, indicating that Middle-Eastern immigrants should be targeted for prevention at an even lower BMI levels than the commonly prevalent cut-offs for diabetes prevention [68].

Pathophysiology of Diabetes

Diabetes is broadly classified into two main types; type 1 diabetes and type 2 diabetes. The characteristic phenotype associated with diabetes is elevated blood glucose levels. Insulin, a hormone secreted by beta-cells in the pancreas, plays an important role in the pathophysiology of diabetes. Insulin regulates blood glucose levels by promoting glucose uptake in the muscle tissue and by decreasing glucose production in liver. As per WHO, diabetes is defined as Fasting Plasma Glucose (FPG) of ≥ 7.0 mmol/l, and/or a 2-h post-load plasma glucose ≥ 11.1 mmol/l [71].

Type 1 diabetes accounts for approximately 10% of diabetes cases. It is characterised by auto-immune destruction of beta-cells which could either be triggered by environmental factors such as viral infections or could be idiopathic. The primary defect in type 1 diabetes is therefore absolute insulin deficiency, where genetic predisposition seems to play an important role [72].

This thesis is focused on type 2 diabetes, which is a multifactorial disease resulting from an interplay of genetic, epigenetic, lifestyle and socio-economic factors. A combination of impaired insulin action, i.e. insulin resistance in liver and muscle as well as impaired insulin secretion from beta-cells, plays a role in pathogenesis of type 2 diabetes. In a recent research report, up to five different sub-groups of type 2 diabetes have been identified with *severe insulin deficiency* and *severe insulin resistance* as two prominent subgroups [73]. In the predominantly insulin resistant form of type 2 diabetes, the initial defect is impaired insulin action characterized by impaired glucose uptake in skeletal muscles and excessive glucose production in the liver. This in turn leads to a compensatory increase in insulin production from pancreatic beta-cells to maintain blood glucose levels. Over the period of time, this over-stimulation leads to beta-cell failure and gradual decrease in insulin production from the pancreas finally leading to the onset of type 2 diabetes [74]. On the other hand, in the insulin deficient form, the primary defect is insufficient insulin production as a result of beta-cell dysfunction.

Although both impaired insulin sensitivity and impaired insulin secretion play a role in pathogenesis of type 2 diabetes [75], the relative contribution of these two conditions in the development of diabetes varies in different ethnic groups [76]. A comparison between African, Caucasian and East Asian populations revealed that Africans were most insulin resistant whereas East-Asians were worst-off regarding insulin secretion [76]. Similarly, in the MEDIM study, Middle Eastern immigrants without type 2 diabetes had marked peripheral insulin resistance, but the corresponding beta-cell response was not sufficient to compensate for the high insulin resistance [67] reflected by a relative insulin deficiency and higher HbA_{1c} values in the Middle Eastern compared to the native Caucasian population [69].

Type 2 diabetes is preceded by a phase of abnormal blood glucose levels that are not yet within the diabetic range. This phase, termed pre-diabetes, provides a therapeutic window where reversal to normoglycaemia is possible based on lifestyle interventions. The prevalence of pre-diabetes in developed countries is estimated to be 15%-20% with conversion to diabetes rates of around 5%-10% annually [77, 78].

Lifestyle and Type 2 Diabetes

The rapid rise in diabetes prevalence in recent decades has been accompanied by a corresponding increase in overweight and obesity. The Middle-East region exhibits the second highest rate of increase in diabetes [79] together with the fact that obesity rates in the region have tripled since 1980 [80]. In countries like Saudi Arabia and Iraq, age-adjusted obesity prevalence has gone up from 13-14 % in 1980 to above 30% in 2016 [80]. Similarly, age-adjusted diabetes prevalence rate has risen from 6-7% to as high as 17-18% as per WHO estimates [81]. One study in the Swedish general population reported an increase in obesity rates from 7.2% and 6.4% in 1985 to 11% and 14.8% in 2002, in women and men, respectively [82]. The association between an increase in obesity and diabetes rates in the Swedish population was not as prominent as in the Middle-East population, yet it was estimated that every three out of four cases of diabetes in the obese native Swedes could be attributed to obesity [82].

BMI is one of the strongest predictors of type 2 diabetes [83]. In a prospective cohort study of 7000 men, weight gain of 10% over a period of 12 years was associated with an increased risk of type 2 diabetes (OR 1.61) and the risk increased with increasing period of overweight and obesity [84]. The increased risk associated with weight gain has also been observed in a cohort of women followed-up for 14 years [85]. The main culprit behind obesity, and therefore diabetes risk, is believed to be energy imbalance characterised by excessive energy intake from diets with high caloric content and less energy expenditure in the form of sedentary lifestyle. Large epidemiological studies have provided evidence in favour of this association. In one such study that included 85,000 nurses, it was found that unhealthy dietary and physical activity habits accounted for around 91% of new cases of diabetes that occurred in this cohort over a period of 16 years [86]. In another cohort of 700,000 Korean men, overweight and obesity as well as low physical activity levels (<150 min/week) were associated with higher incidence of type 2 diabetes over a follow-up of 7.5 years. In addition, higher BMI was associated with a higher diabetes incidence in all sub-categories of physical activity (PA), and meeting PA guidelines had a protective effect at all levels of BMI indicating that the association of obesity and physical inactivity with type 2 diabetes incidence was mutually independent [87].

Physical activity, weight loss and prevention of diabetes

The term *physical activity* refers to the skeletal muscle movement that leads to energy expenditure above basal metabolic rate. Epidemiological studies have indicated 30-50% lower risk of type 2 diabetes in physically active individuals. There is a general agreement that 30 minutes of moderate intensity physical activity per day is beneficial for health [88]. Apart from moderate to vigorous intensity physical activity, the paradigm of sedentary behaviour has also gained attention in relation to prevention of chronic non-communicable diseases, in particular diabetes. In the Health Professional Follow-up Study where 38,000 men were followed-up for a duration of 10 years, higher number of hours per week spent watching television, which is a marker of sedentary lifestyle, was associated with increased risk of type 2 diabetes even after adjustment for physical activity [89].

Physical activity plays an important role in determining insulin sensitivity, a key factor in the pathogenesis of type 2 diabetes. Although the beneficial effects of 30 minutes of moderate intensity physical activity performed 3-5 times/week on insulin sensitivity are well-established [90-92]; physical activity tends to improve insulin sensitivity at all intensity levels [93]. In one study, Balkau *et al* demonstrated an association between total physical activity and insulin sensitivity even in the most sedentary group of participants [94].

Apart from physical activity, weight loss is an important contributor to the reduction in diabetes risk. In the European Diabetes Prevention randomised controlled trial (RCT), a 65% lower incidence of diabetes was reported in participants with weight loss of ≥5% at one year and the protective effect was much higher (89% lower incidence) if the weight loss was maintained after three years [95]. Similarly, in the Finnish National Diabetes Prevention Program (FIN-D2D), in the participants who lost ≥ 5% weight, the relative risk of diabetes was much lower (0.31: 95%CI 0.16-0.59) than in those who maintained their weight.

However, the protective effect of physical activity on diabetes risk has been reported both with and without concomitant weight loss. Physical activity imparts type 2 diabetes risk reduction in the range of 20-30% even after adjustment for BMI [96]. In large clinical trials, meeting physical activity goals has been associated with a reduced risk of type 2 diabetes even in the participants who did not meet weight loss goals [97, 98]. In the Da Qing study, reduction in diabetes incidence was comparable in over-weight and lean participants [99].

One plausible biological mechanism that leads to improved glycaemic control and insulin sensitivity as a result of physical activity is increased concentration and translocation of glucose transporter 4 (GLUT4) through activation of AMP-activated protein kinase (AMPK) and Ca/Calmodulin dependent protein kinases and deactivation of BDC1D4 leading to increased glucose uptake in skeletal muscles. In addition, improvement in skeletal muscles mitochondrial function and capillarisation, as well as reduction in body weight and lipids resulting from physical activity, has been associated with improved insulin sensitivity [93, 100].

Weight gain leads to an increase in adipose tissue in the body. The adipose tissue releases non-esterified fatty acids (NEFA) as well as a number of pro-inflammatory cytokines and hormones like leptin and adiponectin [101]. NEFA levels are important determinants of insulin sensitivity as it worsens acutely in response to a rise in NEFA levels [102]. NEFA are believed to effect insulin receptor signalling and cellular events following that through inhibition/activation of certain enzymatic pathways [103]. In addition, chronic elevation of NEFA levels leads to impaired glucose-stimulated insulin release and insulin synthesis [104]. Adipocyte-derived pro-inflammatory cytokines like IL-6 and TNF promote inflammation, which can contribute to insulin resistance. Weight loss as a result of lifestyle modification leads to reversal of these metabolic pathways, thereby resulting in improved insulin sensitivity.

Diet and prevention of diabetes

The interest in the association between lifestyle and type 2 diabetes has also prompted research on the role of dietary intake concerning prevention of type 2 diabetes. The main focus in this regard has been the quantity and quality of dietary fats and fibre intake, in addition to total energy intake.

Epidemiological studies suggest that high intake of saturated fats is associated with high FPG and insulin levels [105-107]. In intervention studies, replacing saturated fats in diets with poly-unsaturated fats has shown improvement in glucose tolerance and insulin sensitivity [108, 109]. The underlying mechanisms could be changes in insulin receptor concentration, impaired glucose transport and post receptor changes in liver, muscle and adipose tissue, all leading to impaired glucose tolerance and insulin resistance in association with a high intake of saturated fat. Moreover, diets rich in fats promote weight gain and adiposity, which then mediates increased risk for type 2 diabetes.

Dietary fibre content has also been linked to risk of type 2 diabetes. In large cohort studies like the Health Professional Follow up study and the Nurses study, low fibre intake has been associated with increased risk for developing type 2 diabetes [110, 111]. In a meta-analysis, reviewing prospective studies on dietary fibre intake and type 2 diabetes, a risk reduction of 6% was reported for an increment of 2g/day in cereal fibre intake [112]. Fibre intake effects gastric emptying and intestinal tract transit time thereby reducing absorption of carbohydrates. Reduction in post-prandial glucose and insulin levels and improvement in insulin sensitivity has been reported with increased fiber intake [113]. In addition, it modifies gut microbiota [114] and regulates the release of appetite-stimulating peptides [115], inflammatory cytokines and hormones like adiponectin [116].

Reviewing the current existing scientific evidence on the role of diet in causing lifestyle related diseases, a working group in Nordic countries updated the Nordic Nutrition Recommendations (NNR) in 2012 [117]. These recommendations aim at identifying daily reference values for various nutrients for prevention of type 2 diabetes, obesity, CVD and cancers. The recommended intake of fats, saturated fats and fibre in NNR 2012 was 25-40 E%, <10 E% and 25-35 g/day, respectively. Dietary recommendations from the American Diabetes Association (ADA) for diabetes prevention focus on reduction in fat intake and an increase in fibre intake [118]. As per WHO, the role of dietary factors in causation of chronic diseases is mainly mediated through their *obesity-promoting effect.* However, the evidence for the association between increased consumption of saturated fatty acids and decreased consumption of non-starch polysaccharides with increased diabetes risk is more convincing than for the other nutrients [119].

Lifestyle and Mental Health

Research has highlighted the therapeutic potential of physical activity in improving mental health. Exercise tends to reduce symptoms of anxiety and depression and improves sleep patterns as well as cognitive functioning [120, 121]. In a systematic review of RCTs, analysing the effect of exercise on clinical depression, the authors reported a moderate to high anti-depressant effect [122]. In other studies, the antidepressant effect of physical activity is reported to be comparable to that of psychotherapy and cognitive therapy [123]. In spite of convincing evidence regarding the role of physical activity in prevention and treatment of mental health issues [120], the effects of culturally adapted lifestyle interventions on mental health are relatively unexplored.

Several biological mechanisms are hypothesised to explain the positive effect of physical activity on mental health. The effects are believed to be mediated through increased release of neurotransmitters in the brain, reduction in elevated sympathetic nervous system activity and decreased production of stress hormones such as cortisol in response to psycho-social stressors [124-126]. Further engaging in physical activities provides a platform for social interactions, as well as a distraction from stressful situations and improves self-esteem.

Few studies have also explored the relationship between dietary intake and mental health. Reduced caloric intake, a high intake of omega 3 from sea-food and a lower intake of animal fats is reported to have a neuroprotective effect [127, 128].

Lifestyle Intervention Trials

One of the first landmark studies highlighting the role of lifestyle modification in type 2 diabetes prevention was conducted in the city of Malmö. This study, the Malmö Feasibility Study, enrolled approximately 200 middle-aged male individuals with newly diagnosed type 2 diabetes or impaired glucose tolerance into a lifestyle intervention comprising of dietary advice and supervised physical activity. The participants were identified from a population-based screening survey of Malmö men aged 47-49 years in the year 1974. The active intervention lasted for 12 months during which time the intervention group participants received six months of supervised physical activity training followed by six months of dietary advice or vice versa. The control group was comprised of individuals with normal or impaired glucose tolerance and did not receive any treatment with regards to diabetes prevention; they were however referred to their own physician or hypertension clinic depending upon their condition. At the end of the six-year follow-up period, the study demonstrated a lower incidence of diabetes in the intervention group (10.6% vs. 28.6%) than in the control group comprising of individuals with impaired glucose tolerance. In addition, around 50% of subjects with diabetes in the intervention group went into remission. Concurrent improvement was observed in metabolic outcomes such as lipid profile, glycaemia and insulin sensitivity. In spite of its limitations, i.e. its non-randomised design and recruitment of only male participants, the study demonstrated not only the potential of long-term intervention effects but also its feasibility on a large scale with a low drop-out of only around 10% [129]. However, ethnicity was not considered in this study. Later on, the Da Qing trial in China [99], Diabetes Prevention Study (DPS) in Finland [130] and Diabetes Prevention Program (DPP) in the US [131] established convincing evidence in favour of lifestyle interventions for diabetes prevention.

In the Da Qing trial, which was conducted in China over a period of six years, healthcare clinics were randomised to one of the four study arms namely; control, exercise only, diet only or diet plus exercise. A total of 577 individuals with impaired glucose tolerance, as per WHO 1985 criteria, were recruited at these clinics. The intervention comprised of individual dietary or physical activity counselling followed by group sessions weekly for one month, monthly for three months, and then every three months for the rest of the study duration [99]. The Da Qing study was the first RCT that demonstrated a reduction in diabetes incidence following lifestyle modification in high-risk individuals. However, the authors highlighted the need to test the efficacy of such interventions in ethnic sub-groups.

The DPS in Finland randomised 522 overweight individuals with impaired glucose tolerance (FPG < 7.8 mmol/l and 2 h glucose 7.8-11.0 mmol/l) to the control or the intervention groups. The aim was to study the efficacy of lifestyle modification in type 2 diabetes prevention. The intervention addressed both diet and physical activity with focus on decreasing fat intake and increasing the intake of whole grains and physical activity levels. This trial also reported a comparable diabetes risk reduction of 58% in the intervention group as in DPP after a mean follow-up of three years [130]. The incidence of diabetes strongly and inversely correlated to the achievement of study goals pertaining to intake of calories and fat as well as physical activity [130].

DPP (n=3234) recruited individuals with impaired FPG (5.3-6.9 mmol/l) and 2 h glucose levels (7.8-11.0 mmol/l), with the aim to study if onset of type 2 diabetes can be delayed with lifestyle intervention or pharmacotherapy. The participants were randomised to the lifestyle intervention, metformin or placebo arms. The active lifestyle intervention lasted for 24 weeks followed by the maintenance phase. DPP was a large resource-intensive trial that used an individual-based approach [132]. By the end of three years, subjects in the lifestyle intervention arm had 58% reduced risk of diabetes compared to the placebo group [131]. It was reported that 45% participants in DPP belonged to ethnic minorities; a mix of African, Hispanic, Indian and Asian origins. The tailoring of intervention for these participants relied mainly on the "case managers" who delivered the intervention and were recruited from the same ethnic population. In addition, information materials were available in Spanish and English, and foods and cooking methods specific to certain ethnic groups were incorporated in the information provided to the participants [132]. The effect of the intervention was comparable in all ethnicities.

Lifestyle interventions in primary health care settings

Translation of these large clinical trials discussed earlier into real-life settings is essential if the aspiration of halting the diabetes epidemic is to be realised at a population level. In general, studies on efficacy of lifestyle interventions in primary care have shown mixed effects [133-135]. The GOAL trial in Finland, which included 352 participants at increased risk for type 2 diabetes and conducted in primary health care settings, reported improvement in diabetes risk factors such as BMI and waist circumference. The intervention comprised of six group sessions delivered over one year and was based on the five lifestyle changes advocated by DPS. However, the weight loss goal (5% weight loss) was achieved less frequently compared to DPS [136]. A systematic review and meta-analysis of studies translating lifestyle intervention trials into clinical settings reported modest but consistent positive effect on weight loss [137]. Two studies in Poland and Greece, conducted under the *"Diabetes in Europe- Prevention using Lifestyle, Physical activity and Nutritional intervention (DE-PLAN)"* project, reported weight loss of 2.3 kg and 1.0 kg respectively at one year [138, 139]. A RCT of a physical activity intervention conducted in primary health care settings in Sweden in 2014 and recruiting 96 individuals with impaired glucose tolerance demonstrated a 32% reduction in diabetes risk over a period of three years in the intervention group. The intervention in this study comprised of eight group sessions, physical activity on prescription, a step counter and access to a nurse for support [140].

In spite of the convincing evidence from large clinical trials it still remains a concern if we can expect these lifestyle interventions to be equally effective in immigrant groups or in ethnic minorities, particularly when such interventions are implemented in primary health care settings. These interventions cannot be expected to deliver equivalent results in immigrant groups who have different dietary and physical activity habits depending upon their country of origin, religion and culture. Dietary advice suited to a native population might be irrelevant for an immigrant residing in the same geographical location. Physical activity patterns differ in various ethnic groups shaped by the influence of gender [141 142], religious restrictions and cultural norms as well as acculturation to the host culture [143] . Understanding of disease and health and its association with lifestyle habits may not be the same in immigrant groups as in native populations and can lead to a *Knowledge Gap,* which can limit the efficacy of lifestyle interventions unless this gap is appropriately addressed. Similarly, barriers and facilitators to a lifestyle change experienced by an immigrant group might be different from other populations. Studies have highlighted that among women, in some immigrant groups, sharing a physical activity facility with men, physical distance to the activity centre, safety concerns in the neighbourhood, dress code for being physically active, unsupportive social environment, and unpleasant feeling of increased hear rate during exercise are perceived as barriers to physical activity [141, 144]. Language barriers limit the efficacy of interventions in immigrant groups that are otherwise proven effective in native populations.

Culturally Adapted Lifestyle Interventions addressing Immigrant Populations

Few culturally adapted lifestyle interventions have been conducted in Europe and mainly in South-East Asian immigrants. The Podosa trial in UK [145], Innva-Diab Deplan study among Pakistani women in Norway [146], the Physical activity and minority health study on Pakistani men in Norway [147] and SAHELI study on Surinamese immigrants in Netherlands [148] are examples of such studies.

In a primary health care based trial of a lifestyle intervention tailored for South-Asian Surinames immigrants in Netherlands, no effect on metabolic profile was observed after one year. In this 1-year intervention, lifestyle counselling was offered as 6-8 individual sessions. In spite of components like family session, cooking class and supervised physical activity sessions, the intervention had no effect on body weight, lipid profile or glucose metabolism in the intervention group [148]. This indicates that diabetes prevention in primary health care settings could be challenging in certain groups and might require additional strategies to tackle the issue. In a systematic review of physical activity interventions among ethnic minorities and population with disabilities, the authors highlighted the need to appreciate diversity within these groups and to design interventions that address challenges and barriers specific to the target group in a particular community [149].

Aims

The overall aim of this thesis was both to highlight the alarming levels of poor mental health in the diabetes-prone Middle-Eastern immigrants in Sweden, and to study if a culturally adapted lifestyle intervention approach could be utilised to address the risk of both type 2 diabetes and poor mental health in this group.

We hypothesised that a lifestyle intervention based on culturally appropriate advice will lead to improvements in cardio-metabolic profile and lifestyle habits, as well as anxiety and depression levels in this group. The study specific aims were as follows.

Paper I: To study and compare the prevalence of anxiety and depression among residents of Malmö born in Iraq with that of residents born in Sweden. The aim was also to study socio-economic and lifestyle related risk factors associated with anxiety and depression in these two groups and to elaborate if these risk factors differ between Iraqis and Swedes.

In a Middle-Eastern immigrant population at high risk for T2D, to elaborate on the effects of a culturally adapted lifestyle intervention on

Paper I: Lifestyle habits and cardio-metabolic outcomes, in the intervention group compared with that in the control group.

Paper III: Objectively measured physical activity levels in the intervention and the control groups. As a secondary aim, to study associations between objectively measured physical activity and ISI.

Paper IV: Changes in dietary intake in particular energy, fat and fibre intake, in the intervention group compared with that in the control group.

Paper V: Self-reported mental health in the intervention group compared to the control group.

Subjects and Methods

The work presented in this thesis is based on two studies namely the MEDIM population-based study and the MEDIM intervention study.

Table 2: Outline of the papers included in the the thesis.

	MEDIM study (n= 2155)	**MEDIM intervention study (n=96)**			
Papers	**I**	**II**	**III**	**IV**	**V**
Design	Cross-sectional	RCT*	RCT*	RCT*	RCT*
Year	2010-2012	2015	2015	2015	2015
Eligible Participants	Born in Iraq (n**=1255) Born in Sweden (n**=634)	Born in Iraq (n**=82)	Born in Iraq (n**=69)	Born in Iraq (n**=71)	Born in Iraq (n**=82)
Outcomes	Prevalence and odds of anxiety and depression. Factors associated with anxiety and depression	Changes in Body weight, self-reported physical activity, caloric intake glycaemia, HbA_{1C}, insulin sensitivity, disposition index, BP, lipid profile	Changes in objectively assessed physical activity such as VM-HPF⁺ and number of hours spent in sedentary, light, moderate and vigorous intensity activities	Changes in dietary intake such as total energy as well as absolute and relative intake (energy percentage) of, carbohydrates, total fats, saturated fats, proteins, sugar and fibre	Changes in mental health. Odds of scoring lower on HADS⁺⁺ and MADRS-S⁻ at followup vs. baseline
Statistical Analysis	General linear model, logistic regression	Independent sample t-test, Mann-Whitney U test, chi-square test, linear mixed model	Independent sample t-test, Mann-Whitney U test, chi-square test, linear mixed model	Independent sample t-test, paired sample t-test, Mann-Whitney U test, chi-square test, linear mixed model	Independent sample t-test, chi-square test, proportional odds model

* Randomised Controlled Trial

** n represents number of participants included in analysis

⁺ Vector Magnitude High Pass Filtered

⁺⁺Hospital Anxiety and Depression Scale

⁻ Montgomery Åsberg Depression Rating Scale

Paper I: The MEDIM population-based study

The MEDIM population-based study, a cross-sectional study by design, was carried out between 2010 and 2012. The study was conducted in Malmö, a city in southern Sweden which has 30% of its population born abroad. In Malmö, Iraqi immigrants consist of a population of around 11000 [17]. The study recruited a random sample of residents of Malmö, aged 30-75 years, born in Iraq (n=1398) or born in Sweden (n=757). Individuals with mental and physical illnesses that incapacitated them from participation in the study were excluded. The flow of participants through the study is presented in Figure 4. The study achieved a response rate of 49% and 32% in Iraqis and Swedes, respectively. The study involved a health examination as well as collection of information regarding participants' socio-economic situation, lifestyle habits and mental health using validated questionnaires. In addition, an oral glucose tolerance test (OGTT; 75g glucose) was performed and fasting blood samples were collected.

Assessment of Mental Health

In Paper I, mental health was assessed using the Hospital Anxiety and Depression Scale (HADS) questionnaire. The HADS questionnaire has two parts; one pertaining to anxiety and the other pertaining to depression, each of which contains 14 questions. In this self-reported questionnaire, participants were asked to respond to these questions based on how they have been feeling for the last week. Participants responded with one of the four possible responses provided in the questionnaire which were scored from 0-3. The responses to these questions were added to obtain anxiety and depression scores separately. Scores in the range of 0-7 indicated no anxiety or depression whereas those from 8-10 and 11-21 indicated doubtful and moderate/severe cases of depression and anxiety respectively.

Based on anxiety or depression scores in the range of 11-21 and/or the use of anti-depressants, participants were categorised as anxious and/or depressed. Participants with HADS scores below 11 and not receiving anti-depressants were considered as non-anxious/non-depressed.

HADS questionnaire has been shown to possess good sensitivity and specificity with regards to identifying cases of anxiety and depression [150]. In a Swedish study, total HADS score showed strong correlation with Becks Depression Inventory (BDI) and Spielberger's State Trait Anxiety Inventory (STAI) indicating its usefulness as an indicator of anxiety and depression [151]. In addition, HADS has also been validated in Middle-Eastern populations [152].

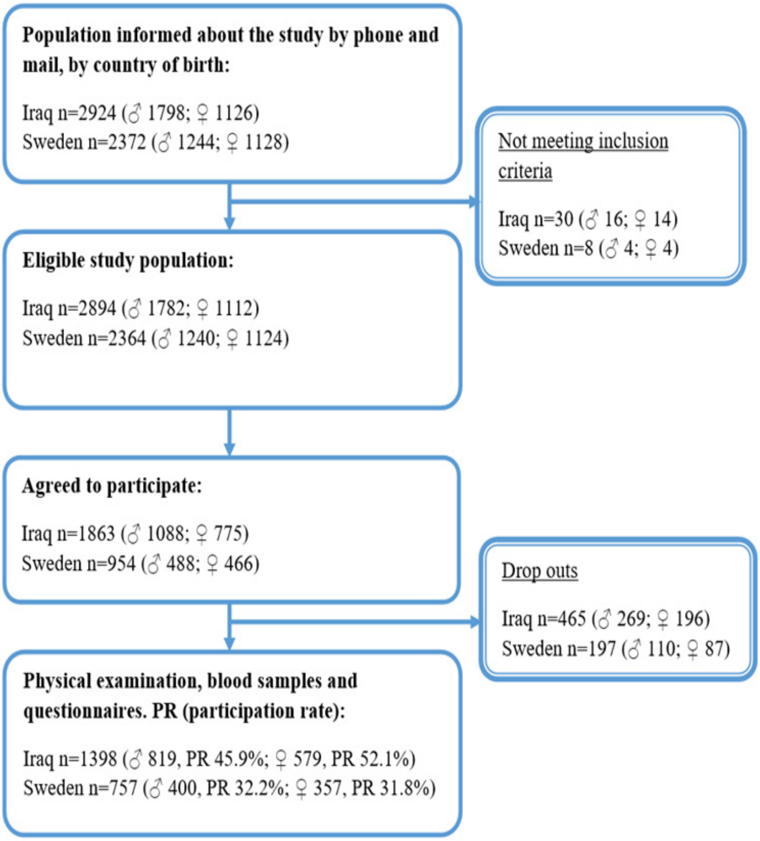

Figure 3: Flowchart representing recruitment of participants in the MEDIM study.
From Siddiqui et al [161].

Assessment of Physical Activity

In Paper I, physical activity was self-reported by the participants using the questionnaire developed by the Swedish National board of health and welfare [153]. The participants were asked to report the time they spent in physical activities of strenuous and non-strenuous nature during a usual week. The two types of activities were clarified using examples such as swimming and playing football for strenuous and walking and gardening as non-strenuous activities. The time spent in strenuous activities was doubled and added to the time spent in non-strenuous activities to obtain total amount of time spent in being physically active during a week.

Participants were then categorised into those achieving <150 min/week or ≥150 min/week of physical activity.

Statistical Analysis

In the descriptive analysis, characteristics of anxious and/depressed participants were compared with that of non-anxious/non-depressed participants in the Iraqi-born and Swedish-born group separately. For advanced analysis, anxiety and depression were considered together and not as separate entities in this study. Logistic regression was used to study the odds of anxiety and depression in the Iraqis compared to the Swedes, while adjusting for the confounding effect of anthropometrics, lifestyle and socioeconomic factors.

A separate analysis was carried out for Iraqis and Swedes to study socio-economic and lifestyle related factors associated with anxiety and depression in these two groups. In Iraqis, acculturation-related factors namely Swedish reading and writing skills and time since migration were included in a separate model.

Ethical Considerations

Ethical permissions for the MEDIM population based study were obtained from the Lund university ethical review board (2009/36 and 2010/561). Written informed consent was obtained from all participants.

Paper II, III, IV, V: The MEDIM intervention study

The MEDIM intervention study was an RCT of a culturally adapted lifestyle intervention, which was conducted in 2015 over a period of four months. The study recruited Iraqi-born residents of Malmö at increased risk for developing type 2 diabetes within the next decade.

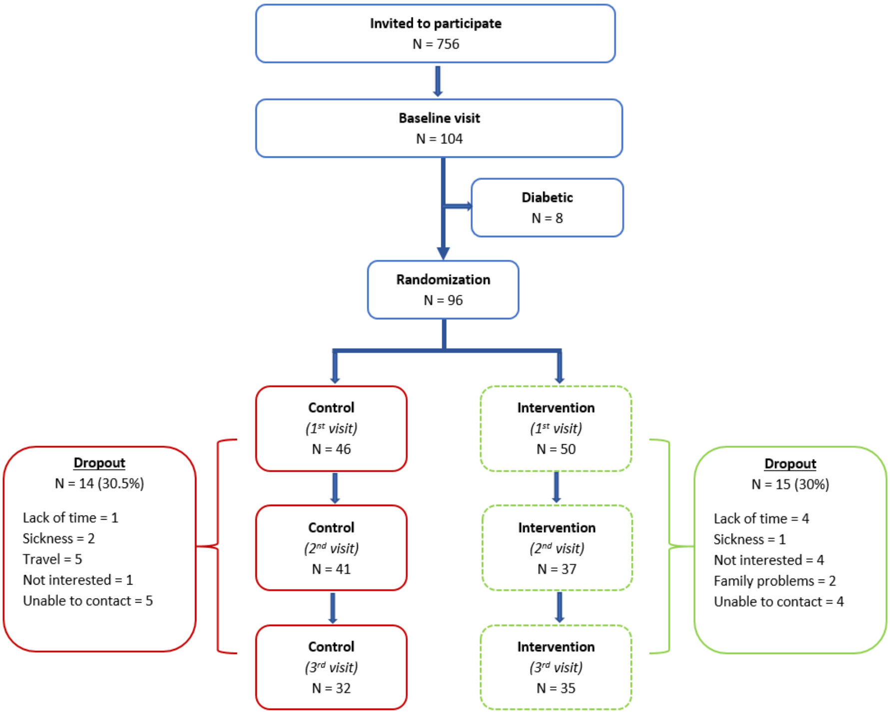

Figure 4: Flowchart representing recruitment and flow of participants in the MEDIM intervention study.
From Siddiqui et al [154].

The increased risk was defined as being overweight (BMI ≥28 kg/m2), having abdominal obesity (waist circumference ≥80 cm in women and ≥94 cm in men) or having prediabetes (FPG): 6.1- 6.9mmol/l, and/or 2-h glucose < 7.8 mmol/l), impaired glucose tolerance (FPG <6.1 mmol/l. and/or 2-h glucose: 7.8-11 mmol/l) or impaired glucose regulation (FPG: 6.1- 6.9 mmol/l, and 2-h glucose: 7.8-11 mmol/l). The participants were identified from the population-based study and fulfilled one of the above-mentioned criteria. A total of 636 individuals in the population-based study met the inclusion criteria and were invited to participate. In all, 96 participants were recruited in the study corresponding to a participation rate of 15.1% [154] (Figure 4).

The Lifestyle intervention

The intervention comprised of seven group sessions including a cooking class. These sessions were spaced out at intervals of 1-4 weeks over a period of four months. The intervention components were based on the similar intervention offered in DPP in the US, with a focus on diet and physical activity and with cultural adaptation for Middle-Eastern immigrants. The *cultural adaptation* included gender-specific group sessions, engagement of a diabetes nurse and health coach familiar with Middle-Eastern culture as well as a professional Arabic translator at all meetings. In addition, economic support for admission to physical activity centres and to buy sports clothes was offered. Of importance, *socio-cultural barriers* to physical activity relevant to this group were addressed e.g. women in the groups were introduced to a females-only activity centres in the city as performing outdoor physical activity was a barrier among female participants. Last but not the least, *knowledge gaps* in understanding of type 2 diabetes and its association with lifestyle were addressed. The educational content used in the group sessions reflected Middle-Eastern dietary habits, e.g. excessive use of carbonated drinks as highlighted in the MEDIM study in this group, was discussed. Similarly, traditional fat-rich foods like Baklava, and cooking methods like deep frying were brought under discussion. Considering that eating together and sharing food is often at the very centre of social interactions, healthy eating at social events was addressed. The study goals defined for the intervention group were i) weight loss ≥ 5% ii) moderate intensity physical activity of at least 30 min/day iii) fat intake < 30 E% iv) saturated fat intake < 10 E% v) fibre intake ≥15g/1000 kcal.

The tool that we used to deliver the intervention included *action plan work sheet,* a one-page document on which participants indicated their Specific, Measureable, Achievable, Realistic and Time bound (SMART) goals with regards to physical activity and dietary modification. E.g. to increase daily physical activity, the SMART goal identified by the participants was for instance to take the stairs instead of the elevator every day. We also used Physical Activity on Prescription (FaR) as well as discussed keyhole products and plate model from *Swedish National Food Agency (Livsmedelsverket)*. In the cooking classes, participants were asked to bring their favorite recipe which was then prepared and cooked in a healthier way by a professional chef familiar with cooking diabetes-friendly diets. Dietary recommendations from *Livsmedelsverket* were used which are in turn based on NNR 2012. The participants actively participated in the cooking. The main focus during the group sessions was to enhance self-empowerment and self-efficacy and to make participants realise their potential for a lifestyle change.

Figure 5: Participants preparing food in the cooking class.

Health Examinations

Three health examinations were performed during the study, i.e. at the start, mid (2 months), and end of the study (4 months). Height (m) and weight (kg) were recorded together with abdominal height (cm), waist (cm) and hip (cm) circumference, blood pressure (mmHg) and pulse rate (beats/min). At the time of the health examinations, participants also filled out questionnaires pertaining to their sociodemographic profile including education and employment status, history of CVD, diabetes, cancers and lung disease, family history of diabetes, medication, mental health, lifestyle, health-related quality of life, and self-efficacy with regards to diet and physical activity.

Assessment of Cardio-metabolic outcomes

In Paper II, cardio-metabolic variables were assessed as follows for fasting and 2-h glucose levels, HbA_{1C}, Insulin Sensitivity Index (ISI), disposition index, LDL, HDL and triglyceride levels. Participants were advised to fast for 10 hours prior to the health examination. Fasting blood samples were collected and an oral glucose tolerance test (75g) was performed with blood samples collected at 0, 30, 60 and 120 min. ISI was estimated using Matsuda indices **[155]**.

$$ISI = 10{,}000/\sqrt{[(FPG\ (mmol/l) * fasting\ insulin\ (mIE/l)\ ) * (mean\ OGTT\ glucose\ conc\ (mmol/l) * mean\ OGTT\ insulin\ conc\ (mIE/l))]}$$

Disposition index, representing insulin secretion adjusted for insulin resistance, was calculated as a product of corrected insulin response (CIR) and ISI. CIR was calculated using the formula

$$CIR = (100 * insulin\ at\ 30\min(\frac{mIE}{l})) /(glucose\ at\ 30\min\left(\frac{mmol}{l}\right) * (glucose\ at\ 30\min(\frac{mmol}{l}) - 3.89))$$

For estimation of plasma HDL (mmo/l) and trigylerides (mmo/l), enzymatic methods were used whereas LDL cholesterol (mmo/l) levels were estimated using Friedewald's equation [156, 157]. Plasma glucose (mmol/l), plasma insulin (mIE/L), and HbA_{1C} (mmol/mol) were measured using a HemoCue photometer, radioimmunoassay and high pressure liquid chromatography, respectively [158].

Assessment of Physical Activity

In the MEDIM intervention study, both subjective and objective measures of physical activity were gathered. Subjective measures were used in Paper II and IV and objective measures were used in Paper III and Paper V.

Subjective measure was based on the International Physical Activity Questionnaire short form (IPAQ). Participants reported the number of days/week as well as the amount of time per day spent in performing moderate and vigorous intensity physical activities and walking. The time spent in performing these activities per week was multiplied with corresponding energy expenditure (metabolic equivalent of tasks, METs) for these activities i.e. 8.0 METs for vigorous physical activity, 4.0 METs for moderate intensity physical activities and 3.0 METs for walking. MET hours/week were thus obtained, which summarised total physical activity during the week. Furthermore, individuals accumulating 10 MET-hours/week were considered moderately active, i.e. achieving 30 minutes of moderate intensity physical activity per week.

Objective measurements of physical activity were made using Actigraph GT3X+ accelerometers, which were worn by the participants three times during the study for 10 days each. The accelerometers recorded any acceleration that occurred across three planes of movement namely x, y and z axes. The accelerometers started to record data at 9.00 a.m. following the day of health examination and stopped after 10 days. The accelerometers recorded 30 observations per second. The accelerometers were wrist-worn and participants were instructed to wear them continuously including during sleep. The devices were water resistant up to a depth of 30m.

The data collected through accelerometers was processed using an open source software called PAMPRO (version uploaded 21st, 2015) to obtain vector magnitude high pass filtered (VM-HPF). VM-HPF, an inferred measure of PA, summarised the intensity of acceleration across three axes of movement namely x, y and z axes. The software removed acceleration signals arising from gravity and noise using low and high frequency filters respectively. The software was developed at MRC Epidemiology Unit, University of Cambridge, UK and is accessible under the public license (https://github.com/thomite/pampro) [159].

Assessment of Dietary Intake

Dietary intake (Paper IV) was recorded using 4-day food records which were handed out to the participants at each health examination. The participants were requested to fill in the time, quantity and type and cooking method of the food they would consume over the next four days. The records were returned by the participants by post in pre-paid envelopes. Dietary records were analysed using the Dietist XP software version 3.2. The software program contains information on around 1600 food items and covers 52 nutrients. The Arabic dishes were manually added to the program to capture their energy content and nutritional value. The information retrieved from the software included daily mean energy intake (kcal/day), absolute intake of macronutrients (g/day) and relative contribution of macronutrients to the total energy intake (E%) for each individual. The energy conversion factors for carbohydrates, fats and proteins were 4 kcal/g, 9 kcal/g, and 4 kcal/g respectively [160].

Assessment of Mental Health

In Paper V, mental health was assessed using HADS and Montgomery Åsberg Depression Rating Scale self-reported version (MADRS-S) questionnaires. These questionnaires were filled out by the participants at each health examination, i.e. at the start, mid and end of the study. HADS has been discussed under the "Methods" section for Paper I.

MADRS-S is a nine-item scale, each of which has six responses scored from 0-6. The total score range is 0-54 with scores of 13-19, 20-34 and >34 corresponding to mild, moderate and severe depression, respectively.

Ethical Consideration

Ethical permission for the intervention study (2011/88) was obtained from the Lund University ethical review board. The participants diagnosed with diabetes were referred to their own physicians for appropriate management, and all participants were informed of their blood test results. Moreover, the control group received *usual care* advice on healthy lifestyle as is given to the patients at primary health care in general. The study was compliant to the Helsinki declaration. Written informed consent was obtained from all participants prior to the participation.

Statistical Analysis

The overall statistical approach in Papers II, III and IV was similar. The intervention and control group participants were compared for baseline differences using independent sample t-test and Mann-Whitney U test depending upon normal or non-normal distribution, respectively. Chi-square test or Fishers exact test was used for categorical variables.

For advanced analysis, linear mixed models were used to compare change in outcomes in the intervention group with that in the control group. Participants for whom information on outcome variables was available on at least two out of the three visits were included in the analysis. The independent variables in the simple model were group status, time since baseline visit, as well as a group x time interaction, which indicated the intervention effect. Outcome variables were log-transformed and β-coefficient for the interaction term indicated percentage change in the outcomes $100^{*}(\exp\beta - 1)$ in the intervention group compared to the control group.

In Paper V, a proportional odds model was used to study the odds of scoring lower on MADR-S and HADS at follow-up vs. baseline in the intervention group vs. control group.

Results

Paper I

Out of the 2155 participants recruited in the MEDIM population based study, information on mental health was available for 1255 Iraqi-born and 634 Swedish-born participants [161]. The prevalence of moderate-severe anxiety (HADS anxiety score ≥ 11) was 52.6% in the Iraqi-born group vs. 16.3% in the Swedish-born group (p-value< 0.001). Similarly, the prevalence of moderate-severe depression (HADS depression score ≥ 11) was 16.3% in the Iraqi-born group compared to 3.1% in the Swedish group (p-value< 0.001).

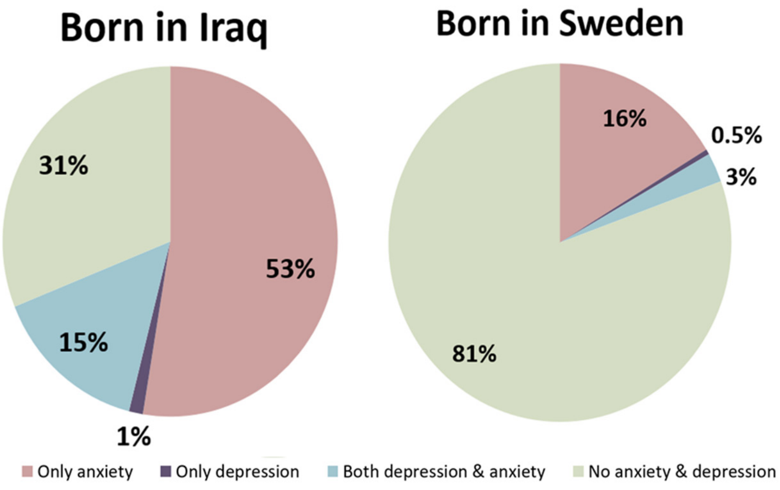

Figure 6: Prevalence of Anxiety and/ Depression in the participants born in Iraq and Sweden.
From Siddiqui et al [161].

In both Swedes and Iraqis, anxious and/or depressed participants were younger and with a higher percentage of women compared to non-anxious non-depressed participants. They also reported higher levels of physical inactivity and economic insecurity, as well as lower social participation (Table 3).

Table 3: Characteristics of the study participants stratified by country of birth.

Variables	Born in Iraq n=1255			Born in Sweden n=634		
	Not anxious or depressed n=383 (30.5%)	Anxious and/or depressed n=872 (69.5%)	p-value	Not anxious or depressed n=488 (77.0%)	Anxious and/or depressed n=146 (23.0%)	p-value
Age, (yrs)	46.5 (10.3)	45.1 (19.0)	0.014	48.9 (11.2)	46 (10.3)	0.007
Female sex, n (%)	116 (30.3)	393 (45.1)	<0.001	219 (44.9)	81 (55.5)	<0.001
Living alone, n (%)	32 (8.9)	60 (7.7)	0.73	108 (23.9)	54 (42.2)	<0.001
Education < HS	82 (21.4)	263 (30.2)	0.014	78 (16.0)	18 (12.3)	0.754
Economic insecurity, n (%)	265 (69.2)	738 (84.6)	<0.001	62 (12.7)	48 (32.9)	<0.001
Inability to trust people, n (%)	277 (72.3)	698 (80.1)	0.003	95 (19.5)	40 (27.4)	0.069
Low social participation*, n (%)	306 (79.9)	760 (87.2)	0.004	158 (32.4)	70 (47.9)	<0.001
Physical activity <150min/week n (%)	230 (62.2)	661 (78.5)	<0.001	152 (31.1)	57 (39.0)	0.054
Smoking, n(%)	81 (21.2)	215 (24.7)	0.016	112 (23.0)	37 (25.3)	0.641

*Fewer than four social activities in last 12 months
From Siddiqui et al [161].

Being born in Iraq contributed with three times higher odds of anxiety and depression, odds ratio (OR) 3.02 (95% confidence interval (95% CI): 2.06-4.41). The risk persisted even after adjustment for potential confounders namely age, sex, BMI, education, economic insecurity, employment, physical inactivity, smoking, alcohol consumption, mutual trust, and social participation. In Iraqis only, physical inactivity contributed with twice higher odds of anxiety and depression. An interaction was observed between country of birth and physical inactivity (<150 min/week) (p=0.058). In addition, economic insecurity was an important factor associated with poor mental health in both Swedes and Iraqis.

Paper II

A total of 104 individuals were examined at the first visit out of which eight (7.7%) were found to be diabetic and were therefore excluded from the study. The remaining participants (n=96) were randomised into two groups namely; the intervention group and the control group. The drop-out rate in the study was around 30% (n=29). With regards to the baseline characteristics, the intervention and the control groups did not differ in terms of age, sex and employment and the outcomes studied in this paper, i.e. body weight, waist circumference, abdominal height, self-reported physical activity, mean daily caloric intake, glycaemia, HbA_{1C}, BP, ISI, disposition index and blood lipid profile. The only differences noted at baseline were lower level of education in the control group (p=0.03), lower triglyceride levels in the intervention group (p=0.01), and a higher proportion of moderately active individuals (p=0.05) in the control group.

Table 4: Characteristics of the participants in the MEDIM intervention study at baseline.

Variables	Intervention n=50	Control n=46	p-value
Age (years)	47.9 (10.4)	48.9 (9.05)	0.63
Male sex, n (%)	23 (46)	22 (47.8)	1.00
Family history of diabetes in first degree relatives, n (%)	34 (68)	24 (52.2)	0.14
Education < HS⁺, n (%)	7 (14)	16 (34.8)	0.03
Unemployment, n (%)	26 (52)	24 (52.2)	1.00
Smoking, n (%)	8 (16)	8 (17.4)	0.86
Physical activity (MET⁺⁺-hours/week), median (IQR⁺⁺⁺)	8.5 (0-47.6)	12.4 (0-66.3)	0.32*
Moderately active, n (%)**	18 (36)	26 (56.5)	0.05
Mean caloric intake (kcal)	1886.3 (619)	2052.3 (616)	0.21
Body weight (kg)	85.5 (15.2)	80.0 (13.1)	0.06
Body mass index(kg/m²)	31.0 (4.4)	29.6 (3.6)	0.09
Waist circumference men (cm)	108.2 (9.6)	106.1 (8.9)	0.45
Waist circumference women (cm)	100.7 (8.1)	97.2 (8.1)	0.13
Abdominal height (cm)	22.7 (3)	22.5 (2.3)	0.75
Systolic blood pressure (mmHg)	121.6 (13.3)	126.9 (16.1)	0.08
Diastolic blood pressure (mm Hg)	77.6 (8.4)	79.7 (11.2)	0.30
Anti-hypertensive drugs, n (%)	8 (16)	6 (13)	0.68
Fasting glucose (mmol/L)	5.6 (0.5)	5.4 (0.7)	0.25
2-h glucose (mmol/L)	6.6 (1.8)	6.5 (1.8)	0.87
HbA_{1C} (mmol/mol) **HbA_{1C} in %**	34 (4.7) 5.3% (0.4)	35(4.4) 5.4% (0.4)	0.33
0-h insulin (mIE/L)	11.6 (6.4)	9.9 (5.7)	0.20
2-h insulin (mIE/L)	77.6 (54.8)	70.7 (52.1)	0.55
Insulin sensitivity index* (mmol/L mIE/L)$^{-1}$, median (IQR)	62.4 (44.1-102.3)	73.3 (55.8-121.5)	0.13*
Disposition Index (mmol/L mmol/L mmol/L), median (IQR)	11128.0 (6248.3-19080.9)	11113.0 (7000.0-19263.5)	0.90*
Triglycerides (mmol/L)	1.3 (0.5)	1.7 (0.8)	0.01
Lipid-lowering drugs, n (%)	1 (2)	0 (0)	1.00∞
LDL cholesterol (mmol/L)	3.4 (0.7)	3.3 (0.9)	0.51
HDL-cholesterol (mmol/L)	1.3 (0.3)	1.3 (0.4)	0.97
Follow-up time (months)***	3.9 (0.3)	3.5 (0.4)	< 0.001

Data presented as mean (standard deviation), numbers (percentages) or median (interquartile range). Differences between groups were compared using independent sample t-test for continuous variables and chi-square test for categorical variables.
⁺High school; ⁺⁺ Metabolic Equivalent of Task; ⁺⁺⁺Interquartile range; *Mann-Whitney U-test; ∞ Fisher's exact test; ** Individuals accumulating 10 MET-hours/week; ***n=32 for control, n=35 for intervention
From Siddiqui et al [154].

Significant reduction in *body weight* (β -0.004, 95% CI: -0.007 to -0.001) and *LDL cholesterol* (β -0.021, 95% CI: -0.042 to -0.001) and improvement in *ISI* (β 0.104, 95% CI: 0.032 to 0.175) was observed in the intervention group compared to the control group. A plot of predicted values from the simple linear model representing change over time in $\log_e$-transformed ISI in the intervention and control groups is presented in Figure 7.

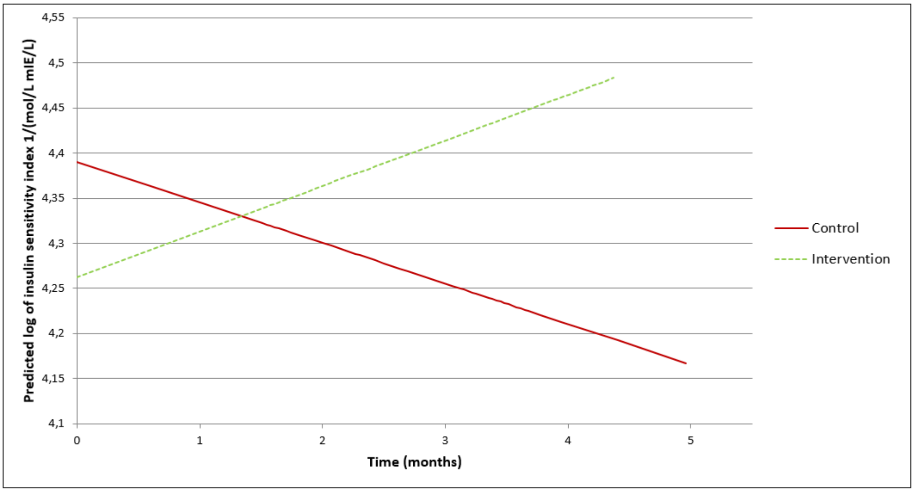

Figure 7: Predicted lines representing change over time in insulin sensitivity index (loge-transformed) in the participants in the intervention and control groups.
From Siddiqui et al [154].

The percentage of participants who lost ≥ 5% body weight by the end of the study was 14.3% in the intervention group vs. none in the control group (p=0.05). Similarly, the proportion of moderately active individuals at last visit was 85.7% in the intervention group vs. 64.5% in the control group (p=0.04). However, no significant change over time in physical activity (β 0.092, 95% CI: -0.178 to 0.362), measured as MET-hours/week, was observed in the intervention group compared to the control group. Similarly, change over time in caloric intake in the intervention group was not significantly different from the control group.

Paper III

A total of 69 participants (intervention group n=32, control group n=37) were included in the analysis of objectively measured physical activity data collected using accelerometers. No significant between-group differences were observed at baseline. Both groups spent almost 80% of the time in sedentary activities, i.e. 19.7 and 19.4 hours/day in the intervention and control group, respectively. In a descriptive analysis, the intervention group increased the amount of time spent in light intensity activities from 2.8 hours/day at visit 1 to 3.1 hours/day at visit 3. This and the change over time spent in performing different activities in the two groups is presented in Figure 8.

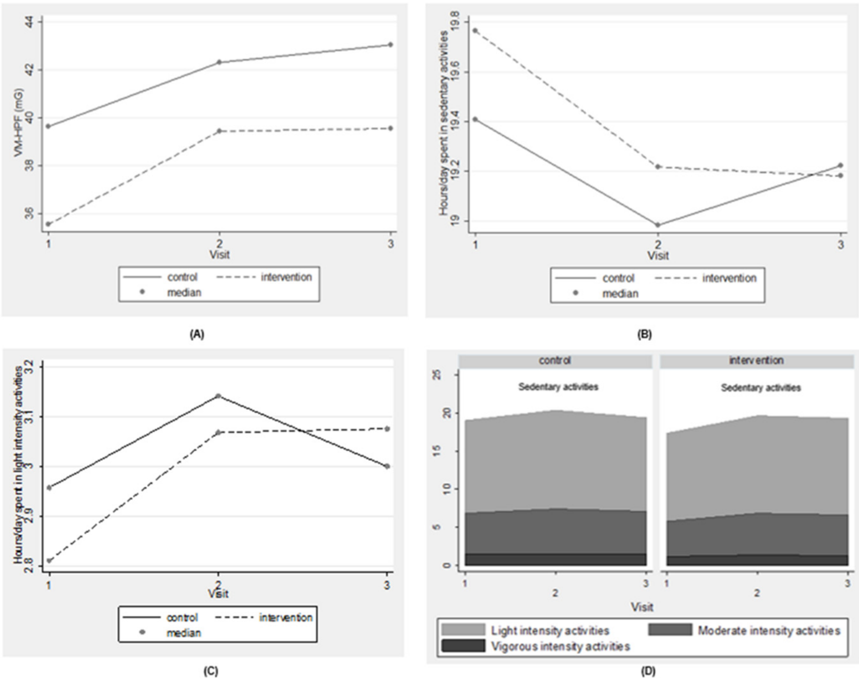

Figure 8: Changes in VM-HPF (A), number of hours (B & C) and percentage of time (D) spent in different activities in the two groups during the intervention.
From Siddiqui et al [159].

In the advanced analysis, change over time in the number of hours spent in sedentary activities was not significantly different in the intervention group compared to the control group. Considering that sedentary activities constitute a large part of daily activities, we further explored the time spent in sedentary activities by categorising it into four categories. Sedentary behaviour corresponded to a VM-HPF of 0 - <48 mGs and these categories corresponded to increasing VM-HPF intensity within sedentary behaviour i.e. *Category 1: 0– <12 mGs, Category 2: 12– <24 mGs, Category 3: 24– <36 mGs, and Category 4: 36– <48 mGs).* We observed a significant increase in number of hours spent in Category 4 of sedentary activities (β=0.022, 95% C: 0.002 to 0.042, p=0.03) in the intervention group compared to the control group. The Intervention group also increased the time spent in light intensity activities compared to the control group, even after adjustment for covariates.

Daily mean physical activity intensity (VM-HPF) was significantly and positively associated with mean ISI in the study participants. The association persisted after adjustment for covariates, namely age, sex, BMI, and time since baseline visit.

Paper IV

A total of 71 participants were included in the analysis for changes in dietary intake. At baseline, study participants reported high fat intake reaching up to 40% of total energy intake. Similarly, saturated fat intake was also high constituting 13E%. Fibre intake averaged at 17.6 g/day and 18.1 g/day in the intervention and control group, respectively. None of the participants met the recommended fibre intake of 25g/day and 35g/day in women and men, respectively.

No significant differences in change over time in intake of energy or in absolute intake of total and saturated fats, carbohydrates, proteins, fibre or sugars was observed in the intervention group compared to the control group. Similarly, between-group differences for change over time in E% of macronutrients were also statistically non-significant.

Favourable trends were observed in the intervention group towards a decrease in absolute intake of total energy (p=0.03), carbohydrates (p=0.06), sugars (p=0.02) and total fats (p=0.02).

With regards to the dietary goals specified in the study, few individuals met the goal of obtaining <30E% from dietary fats at visit 3. The analysis was therefore repeated setting the limits at 40E%. An increase was observed in the proportion of individuals obtaining <40E% from dietary fats in both the intervention and the control groups. However, between-group differences or within-group changes were non-significant. Similarly, the proportion of individuals obtaining <10E% from saturated fats appear to rise in the intervention group and decrease in the control group from visit 1 to visit 3. The original goal for fibre intake (15g/1000 kcal) was also modified to 10 g/1000 kcal because of very few individuals meeting the original goal. A larger proportion met the modified fibre intake-related goal at visit 3 vs. visit 1 in the intervention group, but no significant within or between-group changes were noted.

Table 5: Proportion of individuals meeting dietary goals in the intervention and the control groups.

Dietary Goals	Intervention			Control			p-value†
	V1 (n=31)	V3 (n=31)	p-value*	V1 (n=26)	V3 (n=26)	p-value*	
Sat fat < 10 E%~, n (%)	5.0 (16.1%)	10.0 (32.3%)	0.18	5.0 (19.2%)	3.0 (11.5%)	0.69	0.14
Total fat < 40 E%~, n (%)	8.0 (25.8%)	15.0 (48.4%)	0.09	6.0 (23.1%)	9.0 (34.6%)	0.51	0.65
Fibre 10 grams/1000 kcal, n (%)	10.0 (32.3%)	14.0 (45.2%)	0.48	9.0 (34.6%)	7.0 (26.9%)	0.77	0.46
Fibre 15 grams/1000 kcal, n (%)	0.0	1.0 (3.2%)		0.0	1.0 (3.8%)		
Total fat < 30 E%, n (%)	1.0 (2.7%)	2.0 (6.5%)		1.0 (3.8%)	3.0 (11.5%)		

~E%, percentage of energy intake.
* McNemar test for within group changes
† McNemar test for between group changes
From Siddiqui et al [160].

Paper V

In Paper V, 82 participants (n= 40 from the intervention, n= 42 from the control group) were analysed with regards to changes in MADRS-S and HADS scores, based on availability of mental health-related information on at least two out of the total three visits. The median changes in MADRS-S and HADS anxiety and depression scores from visit 3 to visit 1 in the intervention group was -2 (interquartile range (IQR): -6.0 to 1.0), -1 (IQR: -2.0 to 1.0), and -1 (IQR: -2.0 to 1.0), respectively. Significant within-group change was observed in MADR-S (p=0.01) and HADS depression scores (p=0.04) in the intervention group, however such within-group changes were non-significant in the control group.

Table 6: Odds of scoring lower on MADRS-S[+], HADS[++] anxiety and HADS[++] depression scales at visit 3 vs. visit 1 in the intervention group compared to the control group.

Scales	Simple Model[~]	Adjusted Model[≈]
	OR[+++] (95% confidence interval) (p-value)	OR[+++] (95% confidence interval) (p-value)
MADRS-S, Interaction term (group*visit)		
Visit 2 vs. visit 1	1.6 (0.5-5.7)(0.42)	1.4 (0.3-5.5)(0.62)
Visit 3 vs. visit 1	5.9 (1.6-22.5) (0.01)	7.3 (1.6—33.0) (0.01)
HADS anxiety, Interaction term (group*visit)		
Visit 2 vs. visit 1	6.3 (1.3-29.8) (0.02)	3.6 (0.7-19.2) (0.14)
Visit 3 vs. visit 1	2.7 (0.5-13.5) (0.21)	1.9 (0.3-11.3) (0.49)
HADS depression, Interaction term (group*visit)		
Visit 2 vs. visit 1	1.4 (0.3-5.9) (0.62)	1.9 (0.4-8.8) (0.41)
Visit 3 vs. visit 1	4.4 (0.9-20.3) (0.05)	7.9 (1.4-43.3) (0.02)

[+] Montgomery Åsberg Depression Rating Scale
[++] Hospital Anxiety and Depression Scale
[+++] Proportional odds model
[~] Adjusted for group, visit and group*visit
[≈] Adjusted for age, sex, BMI, time since migration, number of hours spent in sedentary activities per day and language spoken at home in addition to the simple model

In the proportional odds model, the odds of scoring lower vs. higher on MADR-S and HADS depression at visit 3 vs. visit 1 was higher in the intervention group compared to the control group. Adjustments were made for age, sex, BMI, time since migration, number of hours spent in sedentary activities, and language spoken at home, but the group differences persisted. These group differences were non-significant at visit 2 vs. visit 1.

Discussion

The target population described in this thesis were Iraqi-born citizens of Sweden residing in Malmö. We consider this group to be representative of Middle-Eastern immigrants in Sweden not only because of their shared geographical origin, culture, Arabic language, religion and lifestyle habits but also because prevalence and risk of diabetes observed in the Iraqi-born group is similar to that observed in Middle-Eastern immigrants in Northern Europe [31, 65].

The MEDIM population-based study enabled comparisons between Iraqi-born residents of Malmö and native Swedes for a variety of outcomes with particular focus on the prevalence rate and risk of type 2 diabetes. Moreover, the study also captured poor mental health in this diabetes-prone target group. The findings from this observational study motivated the planning and conduct of the MEDIM intervention study to address increasing burden of (primarily) type 2 diabetes and (secondarily) of poor mental health, observed in the Middle-Eastern immigrants in Sweden, using a culturally adapted intervention approach.

The MEDIM intervention study was unique in being the first randomised controlled culturally-adapted lifestyle intervention addressing Middle-Eastern immigrants in Europe. It therefore highlights not only the effects but also the challenges associated with lifestyle modification in the largest non-European immigrant group in Sweden. The study was designed to match the resources available in primary health care (PHC) in Sweden. Nutritionists, diabetes nurses and health coaches are accessible in PHC, therefore our program has the potential to be implemented in primary health care settings in terms of resources.

Symptoms of Anxiety and Depression among Middle-East Immigrants

The first article (Paper I) included in this thesis, reported three times higher prevalence rates of self-reported anxiety and five times higher prevalence of depression among Iraqi-born residents of Malmö compared to the native Swedes. Iraqi ethnicity contributed with three times higher odds of anxiety and/depression. Physical inactivity was strongly associated with anxiety and/depression in the Iraqi-born group whereas the association between physical inactivity and anxiety/depression was not significant for the Swedish-born group. This indicates that physical activity might be especially beneficial in combating anxiety and depression in the Iraqi-born group.

The prevalence of anxiety/depression in the Iraqi-born group (69.5%) observed in our study was comparable to that observed in the Iraqi immigrant group (60.6%) in a previous study in Sweden [54]. In addition, the increased risk for poor mental health observed in this group was in-line with an earlier study reporting comparable risk estimates for non-European immigrants in Sweden [52]. In our study, female sex and economic insecurity were associated with increased risk of anxiety and/depression in the Iraqi-born group as observed previously [54]. However, in these studies, lifestyle factors like physical activity were not considered [52 54].

In our study, Iraqi-born participants who did not meet the physical activity recommendations (150 min/week) were more likely to be self-reported anxious or depressed. However, owing to the cross-sectional design of our study, we could not draw a causal association between physical activity and levels of anxiety and/depression. The therapeutic potential of physical activity for mental health has been reported in earlier studies including clinical trials [122, 162]. Considering our findings in relation to these studies, which indicate that physical activity improves mental health, support the idea that physical activity interventions might have beneficial effects on mental health in the Middle-Eastern immigrants. This hypothesis however needs to be confirmed in intervention studies.

In the last manuscript (Paper V), we explored the effect of a culturally adapted lifestyle intervention on mental health among Middle-Eastern immigrants, considering the finding in Paper I of a stronger association between mental health and physical inactivity in Iraqis than in native Swedes. In Paper V, we observed beneficial effects on mental health as depicted by lower odds of scoring higher on HADS and MADRS-S questionnaires at follow-up vs. baseline in the intervention group compared to the control group. This study highlighted the effects of a culturally adapted intervention on symptoms of mental health, which to the best of our knowledge has not been reported from culturally adapted lifestyle interventions conducted among other immigrant groups in Europe.

It was beyond the scope of this study to explain mechanisms behind the beneficial impact on mental health as observed in the intervention group. However, considering our finding in relation to what has been reported earlier, we hypothesise that it might be the product of increased physical activity and weight loss [163], as well as the opportunities for social interaction/support provided by the group sessions [164].

One important consideration here is the effect size, as the change in MADRS-S and HADS scores from baseline to follow-up in the intervention group was rather small.

A possible explanation could be that the participants in the study were not selected based on poor mental health and consequently HADS and MADRS-S scores at baseline were not in the range of overt anxiety or depression, thereby leaving little room for improvement. This could also be a potential limitation as the effects of the intervention in those with more severe forms of anxiety and depression could be different.

The therapeutic value of physical activity is underutilised with regards to treatment and prevention of poor mental health [165]. In primary health care in Sweden, pharmacotherapy and cognitive behaviour therapy are often used for the treatment of clinical anxiety and depression. In spite of the possibility to prescribe physical activity, physical activity on prescription (Sw. FAR) is not used commonly for mental health issues. Considering that both type 2 diabetes and poor mental health are major concerns among Middle-Eastern immigrants, lifestyle modification appears to be an effective strategy for combating both adverse health conditions. Considering the evidence produced by our study, a culturally adapted approach to promote physical activity among Middle-Eastern immigrants could be used more extensively in primary health care settings.

Changes in Cardio-metabolic Outcomes

One of the main findings in the second article (Paper II) was a reduction in body weight in the intervention group compared to the control group. This is important with regards to reduction in diabetes risk as in large clinical trials, such as DPP, weight loss has been reported as the primary driver of diabetes prevention [97].

The reduction in body weight in the intervention group (-2.5 kg) in our study was modest compared to an earlier non-randomised intervention conducted among Arab-Americans in the US which reported a weight loss of 3.5 and 5.2 kg at 12 and 24 weeks, respectively [166]. In that study, 59% of participants reported a weight loss of ≥ 5% at 24 weeks compared to 14.3% in our study. Since the study lacked a control group, it is difficult to attribute the observed weight changes solely to the intervention. Furthermore, the longer study duration (24 vs. 16 weeks in our study) might explain the greater weight loss in the US study. Studies show that maximum weight loss following an intervention is often achieved at around six months (24 weeks). The participants in the US study were heavier at baseline compared to our participants, which represents a greater potential for improvement. The difference might have resulted from differences in intervention design. In the US intervention, group sessions were more frequent, a supervised physical activity session was offered and there was a greater focus on family involvement as the family members were invited to attend all activities. In a systematic review of weight loss interventions in pre-diabetes, intervention contacts were correlated with greater weight loss [167].

The amount of weight loss observed in lifestyle intervention studies in real life settings is around one third of that observed in large clinical trials such as DPP [168] . That, however, is still clinically relevant as one unit decrease in weight loss was shown to be associated with a 16% reduction in diabetes incidence in the lifestyle intervention arm of DPP trial [97, 168]. Moreover, among participants of these pragmatic intervention studies, progression rates from pre-diabetes to diabetes were found to be much lower than in the general population [168].

The reduction in body weight was accompanied by improvement in insulin sensitivity in the intervention group. This is important in terms of diabetes prevention as in the MEDIM population-based study, insulin resistance appeared to be the major determinant of high diabetes risk in this group [67] . This finding is in-line with that observed in a previous Swedish RCT addressing individuals with impaired glucose tolerance, where a physical activity intervention comprising of group sessions and physical activity on prescription, prevented deterioration of insulin sensitivity in the intervention group compared to the control group [140]. Improvement in insulin sensitivity is one of the most important markers of reduction in diabetes risk. The DPP study showed that the lifestyle intervention was superior to metformin in reducing type 2 diabetes risk which was accompanied by the most prominent improvement in insulin sensitivity in the lifestyle intervention arm compared to the metformin and the placebo arms [169].

Age, sex, BMI, physical activity levels and visceral adiposity are various factors associated with insulin sensitivity. Our analysis was adjusted for age and sex, BMI, education, physical activity and family history of diabetes; in a separate model BMI was replaced by waist circumference. The improvement in insulin sensitivity was significant after adjustment for these variables. The positive associations between mean ISI and physical activity and negative associations with BMI and waist circumference, as observed in our study, are in line with previous studies [94, 170, 171].

Furthermore, we also observed a reduction in LDL cholesterol levels in the intervention group compared to the control group. We speculate that this might have resulted from changes in dietary intake and physical activity levels [172]. In addition, weight loss has been linked to reduction in LDL cholesterol through mechanisms such as increased LDL receptor activity in liver [173, 174]. Elevated LDL cholesterol is an established risk factor for CVD [175, 176]. Reduction in LDL cholesterol through pharmacotherapy has been shown to reduce the risk of CVD in men with hypercholesterolemia [177] as well as mortality rates in CVD patients [178]. Similar benefits are believed to result from reduction in LDL cholesterol achieved through lifestyle modification such as dietary changes [179]. Physical activity is more strongly related to HDL levels, however, the amount and intensity of physical activity needed to improve HDL levels might be greater than what was achieved by the participants in our study [180].

Diabetes, abnormal blood lipid and overweight/obesity are three major risk factors for CVD [181, 182] and clustering of these risk factors imparts greater risk compared to the risk imparted individually [183]. The improvement in multiple cardio-metabolic risk factors, namely body weight, insulin sensitivity and LDL cholesterol in our study, indicates the efficacy of this intervention approach, not only in diabetes prevention but also in CVD prevention. This is of particular importance considering the strong association between diabetes and CVD risk observed in this target group in the MEDIM study.

We did not observe any significant changes in glycaemia. This could be because of the short study duration as glycaemic changes might take up to 12 months to appear [184]. In addition, our study participants had glucose levels within the normal range at baseline with little potential for improvement. No significant changes in disposition index, a product of insulin secretion and insulin sensitivity, might represent compensatory reduction in insulin secretion as a result of improved insulin sensitivity.

Changes in Lifestyle

Physical activity

Paper III: On the spectrum of objectively measured physical activity intensity, which ranges from 0 mGs for no activity to > 420 mGs for vigorous intensity activities, the intervention group increased the amount of time spent in light intensity activities as well as in the sedentary activities which are closest to light intensity activities in intensity (i.e. increased activity in the range 36 - <163mGs). This represents a shift from spending time in very sedentary activities to engaging in relatively less sedentary activities. Sedentary time has been associated with risk of metabolic syndrome, type 2 diabetes and CVD irrespective of exercise or LTPA [185-187]. Correspondingly, breaks in sedentary time have been associated with improvement in metabolic risk factors [188].

In daily lives, individuals spent most of their time in sedentary behavior or in performing non-exercise light intensity activities such as household work and ambulatory activities, which therefore determine a major part of daily energy expenditure [189, 190]. In one study, Healy et al, demonstrated an inverse relationship between light intensity activities and postprandial glucose concentrations independent of moderate-vigorous intensity activities [191]. Although the evidence on the effect of daily low-intensity physical activity on insulin sensitivity is not as strong as for moderate-vigorous intensity activities; it is nevertheless important for type 2 diabetes prevention. In already sedentary populations and non-exercisers, a considerable part of the day is spent in standing and conducting light intensity ambulatory activities (6-12 hours/day). In these groups, the existing risk of metabolic syndrome, type 2 diabetes and CVD is more likely to increase with further increase in sedentary activities like prolonged sitting rather than any further decrease in exercise. Conversely, maintaining or increasing the duration of light intensity activities in their daily routines might be helpful in reducing the risk of CVD and diabetes as shown in some studies [89, 191]. Moreover, the adverse metabolic consequences of sedentary behaviour cannot be compensated by performing moderate –vigorous intensity physical activity for a small part of the day [192]. It is also important to consider that most of the existing evidence depends on questionnaire-based estimation of physical activity, which might have under-estimated the role of light intensity activities in type 2 diabetes prevention [96].

A five month RCT targeting physical activity among Pakistani men in Norway, reported improvements in all objectively measured physical activity related variables which were maintained at six months follow-up [147]. However, longer duration of intervention and recruitment of Norwegian speaking immigrant group might explain the difference in our findings as both intervention duration and level of acculturation can affect lifestyle modification. Moreover, the Norwegian intervention focused on physical activity only, whereas our intervention targeted both diet and physical activity which could be more challenging for the participants.

One might argue that in the absence of any significant reduction in sedentary time, increase in the time spent in light intensity activities might originate from reduction in moderate or vigorous intensity activities. However, considering the reduction in sedentary time as observed in the descriptive data, we deduce that the increase in time spent in light intensity activities came from reduction in sedentary time.

In addition to the above-mentioned changes, daily mean physical activity intensity (VM-HPF) was significantly associated with ISI, which is in-line with the earlier studies [94, 193].

Dietary composition

In **Paper IV**, with regards to change over time in dietary intake, no significant differences were observed between the intervention and the control group at the end of the intervention period. At baseline, intake of dietary fats in the study participants was very high; constituting 40% of total energy intake. The study goals relating to dietary fat intake (<30 E%) and fibre intake (>15 g/1000 kcal) were met by very few individuals at the end of the study, indicating not only the patterns of dietary intake in this group but also that changing dietary habits in this group is a challenging task.

The encouraging finding in this study was the within-group trends for reduction in absolute intake of dietary fats, carbohydrates and sucrose observed in the intervention group. This indicated that the culturally-adapted intervention approach has the potential to modify dietary intake in Middle-Eastern immigrants. Although no *post-hoc* power calculations were made, the absence of statistically significant changes might have resulted from the small sample size.

Although small in magnitude, the dietary changes observed in the intervention group correspond well with our previous findings of reduction in body weight and LDL cholesterol, as well as the improvement in insulin sensitivity in the intervention group.

General Discussion

In Paper I, physical inactivity was found to be associated with anxiety and depression. Acculturation is an important factor effecting physical activity patterns as well as mental health in immigrant groups [194, 195]. We adjusted for three acculturation related variables namely Swedish reading and writing skills and time since migration. These variables did not show any significant association with mental health and did not affect the association between physical activity and mental health. Considering that physical inactivity and economic insecurity exhibited a strong association with anxiety and depression in the Iraqi-born group, it appears that in our study participants who had lived in Sweden for approximately 20 years, socio-economic and lifestyle related factors become more important as determinants of mental health compared to the acculturation related factors. However, acculturation is a broad concept and also connected to factors like employment status and economic security as well as social capital [196]. In our study, inability to trust people, an aspect of social capital, was associated with poor mental health in the Iraqi-born group, which might represent an indirect effect of acculturation. In the MEDIM study, the Iraqi-born group reported poor self-rated heath compared to the Swedes which was associated with poor social capital as well as with depression suggesting association between acculturation and mental health [197]. In Paper V, favourable effects of the intervention on mental health in the intervention group compared to the control group persisted after adjustment for two acculturation related variables namely, time since migration and language spoken at home, in addition to the other variables.

One can argue if the Middle-Eastern immigrant group, with its high diabetes risk and clustering of risk factors, qualifies for pharmacological interventions with or without lifestyle modification. Pharmacological agents like metformin, orlistat targeting weight loss, troglitazone and alpha glucosidase inhibitors like acarbose have shown positive effects on diabetes risk reduction [198]. However, considering that in the DPP study, the risk reduction in the lifestyle modification group was greater than in metformin group as well as the costs and side effects associated with pharmacotherapy, lifestyle modification appears to represent an implementable intervention approach in primary health care settings. It is important to appreciate that DPP primarily addressed a Caucasian population with western lifestyle, and the findings cannot be generalized to the Middle-Eastern populations due to marked cultural differences and a very sedentary life style. Our findings favour lifestyle modification for diabetes prevention and also highlight that it will provide extra beneficial effects in the form of improved mental health in this group. However, the role of lifestyle modification in comparison to pharmacotherapy needs to be explored further in Middle-Eastern immigrants.

Considering our modest sample size, we could not study gender differences. However, some lifestyle intervention trials have pointed to gender differences in the effects of intervention. In the DPP trial, a greater reduction in diabetes risk factors was observed for men who lost >3% body weight compared to women with a similar amount of weight loss [199]. Similarly, in the GOAL trial effects were more pronounced in men [136]. Although the participation rates for women were higher compared to men in these studies, relatively meagre intervention effects might indicate some gender-determined biological mechanisms.

An important consideration with regards to the lifestyle interventions is its effects on quality of life. While adoption of a healthier lifestyle often leads to improvement in cardio-metabolic markers, the process of change itself could be a stressful experience for the participant/patient. A detailed discussion on the effects of this culturally-adapted lifestyle intervention on quality of life is beyond the scope of this thesis. The improvement in mental health, however, as observed in Paper V, suggests that the intervention had no negative effects on quality of life, or was not regarded as a stressful experience by the participants.

Methodological considerations

As discussed earlier in the Methods section, this thesis is based on two study designs, namely a cross-sectional population-based study and an intervention study.

In the cross-sectional study (Paper I), the major concern was lack of causal inference or reverse causality. We demonstrated an association between physical inactivity and poor mental health, however, it could be that lack of physical activity is a cause or consequence of poor mental health.

In Paper I, we used self-reported physical activity estimated through a questionnaire developed by the Swedish National board of Health and Welfare. Self-reported physical activity is liable to over-estimation as was previously observed in the MEDIM study, where questionnaire-based physical activity was over-estimated by 71% and 115% in Iraqis and Swedes respectively compared to objectively measured physical activity using accelerometers [66]. However, it is unlikely that this over-estimation would affect anxious/depressed participants differently from non-anxious/non-depressed participants thereby minimizing concerns regarding its impact on our estimates.

The strengths of this study were its population-based design together with the use of well-validated HADS questionnaire to measure self-reported anxiety and depression levels. HADS was originally designed to be used in non-psychiatric hospital settings. However its sensitivity and specificity is comparable to that of mental questionnaires commonly used in primary care settings such as General Health Questionnaire [200]. Moreover, it has been validated in both Middle-Eastern and Swedish populations [151, 152]. The participation rate in the study was low in both Iraqis and Swedes; 49% and 32%, respectively. It can lead to under-estimation of prevalence rates as individuals with poor mental health are less likely to participate in the study. [201]

In Paper III, objectively measured physical activity data obtained from accelerometers was analysed using a novel approach and physical activity intensity was summarized in units of accelerations (mGs) rather than the traditional "counts/min" approach [202]. Since counts/min are arbitrary units and calculations are based on data processing within the accelerometer, between monitor comparisons are difficult [203]. Our data was processed using an open source code that can be replicated in future studies therefore, making it easy to compare data from different studies. Moreover, it led to a more accurate assessment of physical activity as we adjusted for diurnal variation in physical activity levels.

Another important consideration was the dietary data collection tool. We used 4-day food records, an approach considered to be one of the best methods for dietary data collection [204, 205]. However, due to cultural differences in food preparation methods and hidden sources of fats and sugars in the diet, there is a potential for under-reporting of nutritional intake. Combining food records with personal interviews could be a better approach in this group [206]

One potential limitation for the RCT (Paper II-V) was the short study duration. The study was originally planned to be of six months duration. However, it was decided to finish the study before the month of fasting, Ramadan, to avoid bias resulting from the changes in dietary and physical activity levels during this month. The study duration was therefore four months. This might have affected the various outcomes studied. As per Prochaska's stages of change theory, participants might take quite some time moving from pre-contemplation and contemplation to action stage with regards to changing dietary and physical activity habits. Similarly, metabolic changes might take some time to appear depending upon the magnitude of the lifestyle change and duration of follow-up [137, 184]. We could not study long-term effects of the intervention. However, we speculate that the effects could have been greater with longer intervention duration, as longer intervention duration has been linked to greater effects on behaviour change and clinical outcomes [207, 208]. Interventions with longer duration such as the Da Qing study in China where active intervention lasted for six years, reduction in diabetes risk in the intervention group in comparison to the control group persisted at 20-years follow-up [99, 209]. Another important consideration with regards to study duration is that lifestyle modification often results in a period of initial weight loss (usually peaking around six months) followed by a period of weight regain. However, weight loss can be sustained with longer duration of intervention [210].

We experienced low participation rates (15%) as well as high drop-out rates (30%) in the intervention study. From the scientific perspective, it raises concerns on the representativeness of the study sample as well as compromises the power for observing statistically significant differences. From a societal perspective, it represents a real-life challenge, where motivating individuals for a lifestyle change is a daunting task. With a larger sample size, we might have been able to observe statistically differences in the outcomes such as dietary changes and some of the cardio-metabolic outcomes. However, significant impact on some important outcomes such as insulin sensitivity, physical activity and mental health in spite of the small sample size are encouraging findings in our study. In the non-participant survey, we found that non-participants were heavier and with even lower levels of physical activity compared to those who participated in the study. This indicated that those in greater need of intervention were not motivated enough to participate in the study. There is therefore a need to better identify strategies that will motivate high-risk individuals in this group for a lifestyle change. One potential strategy could be to conduct an educational intervention prior to the lifestyle intervention as was done in the US study on Arab-Americans [166]. Another strategy could be to recruit families into the intervention rather than individuals, since families play an important role in shaping diet and physical activity patterns in the Middle-Eastern culture. It can be speculated that positive effects of the intervention would be more pronounced if these high-risk individuals were recruited as there would have been greater potential for improvement. Based on feedback from the participants and the finding of a higher dropout rate among couples, it seems like the drop-out could have been lower if the health examinations were more spaced out in time with a longer study duration and greater involvement of family members. Moreover, monetary compensation for time taken off from work, although not feasible in all situations, could perhaps have contributed to retention of participants. Other studies which were conducted in real-life settings, have also reported the need for considerable efforts in recruiting and retaining participants in these studies with "lack of time" being the most common reason for dropouts [138, 139]. Being a pilot project, our study provides important insights into the study duration as well as the challenges associated with recruitment and retention in Middle-Eastern immigrants which is valuable information for future studies.

In some real-life implementation studies of lifestyle interventions like the De-plan and GOAL projects [136, 139], no control group was used considering that the efficacy of lifestyle intervention for diabetes prevention has already been established. We decided to adopt a randomised design and therefore include a control group as efficacy of culturally adapted lifestyle interventions in Middle-Eastern immigrants has not been established before. Having a control group enabled us to establish that the intervention had an effect greater than the "usual care" in the form of written advice on healthy lifestyle habits.

In the study protocol published in 2013 [211], FPG was identified as the primary outcome. Later on, the primary outcome was modified to weight changes and changes in physical activity and dietary habits while cardio-metabolic outcomes including glycaemic changes and insulin sensitivity and secretion were studied as secondary outcomes. This was done not only to match the goals for the intervention group participants in the study (weight loss ≥5%, moderate intensity physical activity of at least 30 min/day, fat intake <30 E%, saturated fat intake <10 E% and fibre intake ≥15g/1000 kcal) but also because lifestyle changes precede metabolic changes following the lifestyle interventions. Moreover, in the DPP as well as the DPS studies, meeting the weight loss, physical activity and fat intake related goals predicted the reduction in type 2 diabetes risk [97].

In order to get a comprehensive understanding of the impact of this culturally-adapted RCT intervention, we studied all relevant outcomes ranging from changes in body weight and cardio-metabolic outcomes, subjective and objective measures of physical activity and dietary intake to its effects on mental health. Since this trial addressed lifestyle change from a public health perspective, analysing its effect on risk factors for type 2 diabetes was important if such a program is to be advocated and implemented in primary healthcare settings for prevention of type 2 diabetes and poor mental health.

Conclusions

The key findings in this thesis are a) the high prevalence of anxiety and depression in the Iraqi-born residents of Malmö which showed a stronger association with physical inactivity in the Iraqi-born than in the native Swedish population; and b) that a culturally adapted randomized controlled lifestyle intervention had beneficial effects on cardio-metabolic profile, physical activity levels and mental health among Middle-Eastern immigrants at high risk for type 2 diabetes.

The alarmingly high levels of anxiety and depression observed in the Middle-Eastern immigrants in this thesis, call for attention on mental health in this group in primary healthcare settings. Apart from the socio-economic factors, the worse mental health in Middle-Eastern immigrants compared to the native Swedes, appeared to be associated with lifestyle related risk factors like physical inactivity. While little can be done to modify socio-economic risk factors in primary healthcare, lifestyle factors provide a window of opportunity, where physicians can engage this group at high risk to prevent the increasing burden of mental ill-health. In particular, increasing physical activity might have beneficial effects on mental health in this group.

However, for engaging an immigrant group in a lifestyle change, healthcare providers require a different approach than is commonly used for the native Swedes. The second part of this thesis focussed on utilizing a culturally adapted intervention approach for lifestyle modification among Middle-Eastern immigrants at high-risk for type 2 diabetes and elaborated its effects with regards to prevention of type 2 diabetes as well as poor mental health. Considering that the intervention group reduced body weight and LDL-cholesterol levels and exhibited improvement in insulin sensitivity, we conclude that the intervention led to reduction in type 2 diabetes risk as well as CVD risk. Also, the increase in amount of time spent in light intensity activities in the intervention group following the intervention, leads us to the conclusion that in this highly sedentary group, replacing sedentary time with light intensity activities could be a more realistic and potentially beneficial goal in early stages of lifestyle modification. The intervention did not result in prominent changes in dietary intake in the intervention group in comparison to the control group, albeit favourable trends were observed in the intervention group indicating that modifying dietary intake is a challenging task. Finally, the intervention had favourable effects on mental health in the intervention group compared to the control group.

We conclude that a group-based culturally adapted lifestyle intervention addressing components like gender differences, language barriers, knowledge gaps, self-empowerment, cultural barriers and ways to overcome them, has the potential to reduce risk of type 2 diabetes as well as of poor mental health in the Middle-Eastern immigrant population in Sweden. Since the intervention utilized minimal resources easily accessible in Swedish primary healthcare, it is implementable in primary healthcare settings of today.

Future research

The association between physical inactivity and poor mental health, as highlighted in this thesis, needs to be explored further. It would be interesting to study if the objectively measured physical activity exhibits even stronger association with poor mental health among Middle-Eastern immigrants.

Our intervention study has provided a stepping stone for further research into culturally adapted lifestyle intervention among Middle-Eastern immigrants, particularly in the European context. Future research should focus on gender differences, not only in terms of participation and compliance to the intervention, but also if the metabolic effects differ in the two genders. In the MEDIM population-based study, some gender differences have already been highlighted as Iraqi men were found to be most insulin resistant with a differential effect of BMI, waist circumference and plasma triglycerides on insulin resistance. This might represent disturbed fat metabolism particularly in Iraqi men [68]. It would be valuable to explore if the intervention had greater benefits for a particular gender. Moreover, future studies should explore the effect of lifestyle interventions on mental health among Middle-Eastern immigrants with clinical anxiety or depression.

With our modest sample size, we could not explore relative contribution of dietary or physical activity changes to the improvement in cardio-metabolic outcomes. Future studies with larger sample sizes can eventually provide this information which can lead to more effective intervention design and advice for the patients in primary care. There is a need to study the optimal duration and the long-term effects of lifestyle intervention for this group.

This thesis did not focus on the role of genetics in type 2 diabetes prevention among Middle-Eastern immigrants. However, it would be interesting and relevant to study if genetic variations among individuals could explain some of the differences in outcomes following an intervention, i.e. why some individuals fail to lose weight in spite of lifestyle modification. This information could help to identify those individuals who will benefit most from such interventions.

Popular Science Summary

Currently around 18.5% of the Swedish population is foreign-born and Middle-Eastern immigrants are one of the largest immigrant groups in Sweden. The MEDIM (impact of Migration and Ethnicity on Diabetes In Malmö) population study, which was conducted by our research group in Malmö between 2010-2012, highlighted that type 2 diabetes was almost twice as common in Middle-Eastern immigrants compared to native Swedes. In addition, Middle-Eastern immigrants exhibited high rates of obesity, physical inactivity and positive family history of diabetes, all of which are known risk factors for type 2 diabetes. The study also revealed that if nothing was done to prevent the disease, a large proportion of Middle-Eastern immigrants would develop type 2 diabetes during the next decade, eventually leading to worse health in this group as well as increasing health care costs to treat diabetes and its complications. Large clinical trials across the globe have shown that in individuals at high risk for developing type 2 diabetes, lifestyle changes such as increasing physical activity and reducing caloric and fat intake together with weight loss leads to marked reduction in the diabetes risk. However, these trials were conducted mainly in Caucasian populations and there are studies showing that these studies are not effective in non-Western populations if they are not aligned with the current cultural and social norms, lifting the importance of culturally adapted lifestyle interventions.

Apart from the increased risk for type 2 diabetes, few earlier studies in Sweden, also indicated that non-European immigrants have poor mental health as compared to Swedes. There is also scientific evidence for an association between type 2 diabetes and mental ill-health such as anxiety and depression. It has been shown in western populations that physical activity reduces symptoms of depression and can be used in treatment and prevention of poor mental health. With this background information on the state of mental health and risk of type 2 diabetes among Middle-Eastern immigrants, this thesis had two main aims. Firstly, to highlight the burden of and risk factors for anxiety and depression among residents of Malmö born in Iraq (the largest immigrant group from Middle-East at the time of study conduction) and to compare with a background population of Sweden. Secondly to test if a randomised controlled culturally adapted intervention aimed at changes in lifestyle can be used to delay the risk of primarily type 2 diabetes and secondarily poor mental health in this group.

In Paper I (MEDIM population study), we studied a cohort of around 1400 Iraqi-born and 750 Swedish-born residents of Malmö. Analysis of this data revealed that anxiety and depression were three to five times more common in Iraqi-born participants compared to the Swedish-born. In addition, the study showed a stronger link between physical inactivity and mental ill-health in the Iraqi-born than in the Swedish-born group, indicating that physical activity has a bearing on mental health, especially in the Iraqi-born population and that mental health could be improved by increasing physical activity.

Due to the fact that MEDIM population study showed that a high proportion (> 40%) first-generation immigrants from Iraq had a high risk of developing type 2 diabetes in the close decade, we developed a lifestyle intervention based on previous Western intervention studies but adapted to the Middle East culture (MEDIM intervention study). The study aimed at first-generation immigrants from Iraq with high risk of type 2 diabetes. was completed in 2015 and includes Article II through Article V. Of nearly 700 invited participants, 100 chose to participate and randomized to intervention and control group (customary advice on healthy living habits given in primary care today). The intervention group was invited to attend regular group meetings during the 4-month study period, which also included a cooking class. In the sessions led by a diabetes nurse together with a health coach, the impact of living habits was discussed at the risk of developing type 2 diabetes and CVD. Cultural adaptation addressed components such as language barriers, knowledge barriers, financial difficulties, gender differences, but also focused on supporting their own self-empowerment ability. Participants were motivated to discuss socio-cultural barriers to lifestyle change and ways to overcome these barriers. Dietary advice given was tailored to the Middle East culture and involved traditional foods as well as cooking methods. The cooking class gave participants the opportunity to bring traditional favourite recipes and, with the help of diabetes-trained chef, made it healthier. The study is unique as it is the first randomized, culturally-adapted lifestyle intervention targeting Middle Eastern immigrants in Europe.

In Paper II, we demonstrated that compared to the control group, our intervention group participants reduced their body weight and the less healthy cholesterol (low density lipoprotein, LDL) and improved their insulin sensitivity/insulin action. Impaired insulin action in the liver and muscles is an important contributor to the development of type 2 diabetes and improvement in insulin sensitivity, hence a marker of reduced diabetes risk.

In Paper III and IV, we studied changes in lifestyle namely physical activity and dietary intake. As compared to the control group, the intervention group started to spend more time in performing light intensity activities by the end of the intervention. We concluded that replacing the time spent in sedentary activities with light intensity activities could be an achievable target in this group and will be beneficial as there is now scientific evidence indicating benefits of even light intensity activity with regards to type 2 diabetes prevention. Although the dietary intake in the intervention group did not change in comparison to the control group, we observed that the intervention group, tend to decrease their intake of calories, fats and carbohydrates following the intervention.

Last but not least, we noted in Paper V that the culturally adapted lifestyle intervention program had more pronounced beneficial effects on mental health in the intervention group than the control group, which means that lifestyle change has an effect on mental well-being in immigrant groups from the Middle East.

In summary, this thesis shows that immigrants from the Middle East have a high load of type 2 diabetes and mental health risk factors where we could demonstrate that a culturally adapted lifestyle intervention -based on available healthcare resources- could be a model that can reduce diabetes risk and improve mental health in this vulnerable and growing population of non-European immigrants.

Populärvetenskaplig Sammanfattning

För närvarande är cirka 18,5 procent av den svenska befolkningen utrikesfödd varav Mellanöstern-invandrare är en av de största invandrargrupperna. MEDIM populations-studie (betydelsen av Migration och Etnicitet för Diabetesutvecklingen I Malmö), som genomfördes av vår forskningsgrupp i Malmö mellan 2010-2012, visade att typ 2-diabetes var nästan dubbelt så vanlig bland malmöbor födda i Mellanöstern jämfört med Malmöbor födda i Sverige. Dessutom visade studien en anhopning av riskfaktorer för typ 2 diabetes i den invandrade populationen från Mellanöstern såsom fetma, fysisk inaktivitet och ärftlighet för diabetes. Studien visade också att en mycket hög andel hade en hög risk att utveckla diabetes inom de närmsta 10 åren, dvs att om inget gjordes för att förebygga sjukdomen skulle en stor del av Mellanöstern-invandrare utveckla typ 2-diabetes vilket skulle leda till sämre hälsa i denna grupp men även öka diabetesrelaterade hälso- och sjukvårdskostnader.

Stora kliniska prövningar över hela världen har visat att hos individer med hög risk för att utveckla typ 2-diabetes kommer livsstilsförändringar som ökad fysisk aktivitet och minskad kalori- och fettintag tillsammans med viktminskning leda till en markant minskning av diabetesrisken. Dessa studier har emellertid huvudsakligen genomförts i västerländska populationer och det finns studier som visar att dessa studier inte är effektiva i icke västerländska populationer om de inte anpassas till rådande kulturella och sociala normer vilket lyfter betydelsen av att kulturellt anpassade livsstilinterventioner.

Tidigare studier genomförda i Sverige har visat att icke-europeiska invandrare har ökad förekomst av typ 2 diabetes men också ökad förekomst av mental ohälsa jämfört med icke invandrade svenskar. Det finns också vetenskapliga bevis för en koppling mellan typ 2-diabetes och psykisk ohälsa, såsom ångest och depression. I studier av västerländska populationer har man sett att fysisk aktivitet minskar symptomen på depression och därmed kan användas vid behandling och förebyggande av psykisk ohälsa. Med bakgrund av detta hade denna avhandling två huvudmål; För det första att belysa förekomsten och riskfaktorerna för ångest och depression bland invånare i Malmö född i Irak (den största icke europeiska invandrargruppen i Sverige vid tidpunkt för studiens genomförande) jämfört med en bakgrundsbefolkning född i Sverige. För det andra att studera och utvärdera om en randomiserad kontrollerad kulturellt anpassad intervention som syftar till förändring av levnadsvanor kan användas för att fördröja risken för typ 2-diabetes och psykisk ohälsa i denna invandrargrupp med hög risk för typ 2 diabetes.

I Artikel I (MEDIM populationsstudie) studerades en kohort på cirka 1400 irakisk födda och 750 svensk födda Malmöbor. I studien var förekomst av ångest och depression tre till fem gånger mer vanliga hos irakisk födda jämfört med svensk födda deltagare. Dessutom visade studien starkare samband mellan fysisk inaktivitet och psykisk ohälsa i den irakiskfödda än i den svenskfödda gruppen vilket indikerar att fysisk aktivitet har betydelse på psykisk hälsa framför allt i den Irakiskfödda populationen och att psykisk hälsa skulle kunna förbättras genom ökad fysisk aktivitetsnivå.

Med anledning av att MEDIM populationsstudie kunde påvisa att en hög andel (>40%) första generationens invandrare från Irak hade hög risk att utveckla typ 2 diabetes inom det närmtsa decenniet, utvecklade vi en livsstilsintervention baserad på tidigare västerländska interventionsstudier men anpassad efter Mellanösternkulturen (MEDIM interventionsstudie). Studien vände sig till första generationens invandrare från Irak med hög risk för typ 2 diabetes. genomfördes 2015 och omfattar Artikel II till och med Artikel V. Av nästan 700 inbjudna deltagare, valde 100 att delta och randomiserades till intervention respektive kontrollgrupp (sedvanliga råd om hälsosamma levnadsvanor som ges i primärvården idag). Interventionsgruppen uppmanades att under den 4 månader långa studieperioden delta i regelbundna gruppmöten som också inkluderade en matlagningskurs. I sessionerna som leddes av en diabetessjuksköterska tillsammans med en hälsocoach diskuterades levnadsvanornas inverkan på risken att utveckla typ 2-diabetes och hjärt-kärlsjukdom. Den kulturella anpassningen behandlade komponenter som språkbarriärer, kunskapsbarriärer, ekonomiska svårigheter, könsskillnader men fokuserade även på stötta sin egna förmåga till livsstilsförändring (self-empowerment). Deltagarna motiverades för att diskutera socio-kulturella hinder för livsstilsförändring samt sätt att övervinna dessa hinder. Kostråd som gavs var anpassade till Mellanöstern-kulturen och involverade traditionella livsmedel samt matlagnings metoder. Matlagningskursen gav deltagarna möjlighet att ta med traditionella favoritrecept och med hjälp av diabetesutbildade kocken tillaga det på ett hälsosammare sätt. Studien är unik då det är den första randomiserade kulturellt anpassade livsstilsinterventionen som riktar sig till Mellanöstern-invandrare i Europa.

I Artikel II visades att i jämförelse med kontrollgruppen minskade interventionsgruppen kroppsvikten och nivåerna av det mindre hälsosamma kolesterolet (low density lipoprotein, LDL), samtidigt som deras insulinkänslighet förbättrades vilket är en markör för minskad diabetesrisk.

I Artikel III och Artikel IV studerade vi förändringar i livsstil över tid, nämligen fysisk aktivitet och kostintag. I jämförelse med kontrollgruppen ökade interventionsgruppen tiden som de spenderade att utföra aktiviteter av lätt intensitet. Vi drar slutsatsen att ersätta stillasittande aktiviteter med aktiviteter av lätt intensitet i denna riskgrupp kan vara ett uppnåeligt mål som kan vara fördelaktigt då det nu också finns vetenskapliga bevis för att aktiviteter av lätt intensitet förebygger typ 2-diabetes. Trots att kostintaget i interventionsgruppen inte förändrades jämfört med kontrollgruppen såg vi tendens till att interventionsgruppen i högre utsträckning minskade intaget av kalorier, fetter och kolhydrater jämfört med kontrollgruppen.

Sist men inte minst noterade vi i Artikel V att det kulturellt anpassade livsstilsinterventionsprogrammet hade mer uttalade gynnsamma effekter på psykisk ohälsa hos interventionsgruppen än kontrollgruppen vilket betyder att livsstilsförändring har effekt på psykiska välbefinnandet i invandrargrupper från Mellanöstern.

Sammanfattningsvis visar denna avhandling att invandrare från Mellanöstern har en hög belastning av riskfaktorer för typ 2 diabetes och psykisk ohälsa där vi kunnat visa på att en kulturellt anpassad livsstilintervention -baserad på tillgängliga resurser inom hälso- och sjukvården- kan utgöra en modell för att minska diabetesrisken och förbättra den psykiska hälsan i denna utsatta och växande population av icke-europeiska invandrare.

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Faiza Siddiqui completed her medical graduation (MBBS) from Allama Iqbal Medical College in Pakistan and her Master's in Public Health (MPH) from Malmo University, Sweden. She conducted her doctoral research in Public Health at the Faculty of Medicine, Lund University, Sweden. Her PhD thesis focusses on prevention of type 2 diabetes and poor mental health amongst immigrants from the Middle-East to Sweden.

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