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# Pharmaceutical care in management of type-2 diabetes and primary prevention of cardiovascular disease with risk analysis of developing cardiovascular events

By

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‘This thesis is the result of the author's original research. It has been composed by the author and has not been previously submitted for examination which has led to the award of a degree.’



Signed: Date:

**Dedicated to Professor Steve Hudson**

***(1952-2010)***

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**Abstract**

**Aim**:

To identify the needs for improved levels of care provided to patients with type-2 diabetes in Qatar with a special focus on cardiovascular disease (CVD) prevention.

**Subjects and Settings**:

305 patients attending the diabetes clinic in Hamad General Hospital, Qatar, from 2010-2011, all having type-2 diabetes and no history of CVD. Patients' medical records accessed from medical files manually and electronically.

**Methods**:

a) 38 criteria medication assessment tool (MAT) designed from recommendations on the management of type-2 diabetes and combined with recommendations relevant to primary prevention of CVD. The MAT was validated by a group of researchers and practitioners and field tested. Levels of applicability and adherence to each criterion and for each patient were calculated individually and the overall adherence determined. Areas needing improvement were identified and patients' clinical factors associated with prescribing adherence were studied b) Patients' 10 year risk estimates of developing any coronary heart disease (CHD), fatal CHD, any stroke and fatal stroke obtained using the type-2 specific CVD risk calculator from the UK Prospective Diabetes Study (UKPDS risk engine). Patients were defined to be at 'high' risk if estimates were ≥15%. The association between each risk factor within the risk calculator and being at a higher risk of developing CVD was studied and used to target patients for a designed pharmaceutical care plan. Levels of care provided to patients at higher risk of developing CVD were also assessed and used to address care issues to achieve effective CVD risk reduction in clinical practice.

**Results**

a)- The MAT was applied to the whole study sample (11590 assessed criteria in 305 patients). Application of the MAT identified 18/38 criteria with high levels of adherence (≥80%), 10/38 criteria with intermediate levels of adherence (≥50%; <80%) and 10/38 criteria with low levels of adherence (<50%)**.** The overall adherence in 305 patients was 68.1% (95% CI: 67, 69; n= 6657 applicable criteria). Insufficient documentation to assess care was found in 1.1% (95% CI: 0.9, 1.4; n=74) of the

applicable criteria. Total non-adherences were found in 30.7% (95% CI: 30, 32; n=2049) of the applicable criteria in which only 5.8% (95% CI: 5, 7; n=118) had a documented justification. Consequently 94.2% (95% CI: 93, 95; n=1931) had unjustified non-adherence and indicated a need for inclusion in a treatment review through an appropriate pharmaceutical care plan. Adherence using the individual patient as the unit of analysis (MAT adherence per patient) revealed that prescribers adhered to < 70% of the applicable criteria in 50.5% (95% CI: 45, 56; n=154) of patients. Only blood pressure status and total cholesterol levels were found to be associated with prescribing adherence levels.

( b) Overall, in the following patient groups: any CHD (n= 282 eligible), fatal CHD (n=278 eligible), any stroke (n=274 eligible) and fatal stroke (n=305 eligible) there were 46.1% (95% CI: 40.3, 51.9, n=130), 29.5% (95% CI: 24.4, 35.1, n=82), 12.8% (95% CI: 9.3, 17.3, n=35) and 0% (95% CI: 0, 0) high risk patients identified respectively. A high risk of developing any CHD was significantly associated with increased means ± [standard deviation (SD)] of age (60.0±[8.7] vs 47.0±[9.7], p<0.0001), diabetes duration in years (13.6±[6.9] vs 7.5±[4.5], p<0.0001), systolic blood pressure, SBP (144±[16.9] vs 136±[17.5], p<0.0001), HbA1c level (9.0±[1.7] vs 8.1±[1.9], p<0.0001), and reduced high density lipoprotein (1.07±[0.3] vs 1.2±[0.42], p=0.002). Significantly more males than females were at high risk of developing CHD (64.6% vs. 35.4%, respectively, p<0.0001). In addition to total cholesterol (4.9±[1.1] vs 4.6±[1.0], p=0.04), similar associations and trends were also observed when these above variables were compared with the risk of developing fatal CHD. High risk of developing any stroke was significantly associated with increased means of age (69.4±[5.4] vs 49.5±[9.2], p<0.0001), diabetes duration in years (18.4±[7.2] vs 8.6±[5.0], p<0.0001) and SBP (145±[19.8] vs 138±[17.4], p=0.04). Targeted HbA1c and blood pressure values were not achieved in the majority of patients (84% and 75%, respectively) who are at higher risk of developing CVD.

**Conclusion**:

The study identified levels of adherence to guideline recommendations, the need for additional documentation and criteria with low adherence that might be a focus for a possible change at individual or organisational levels (changes in policies or structures) as well as educational interventions and a starting point for targeted

pharmaceutical care. The risk of developing any CHD in patients with type-2 diabetes was significantly higher than the risk of developing fatal CHD, any stroke or fatal stroke. Risk calculators can be used to target patients for pharmaceutical care according to their CVD risk factors.

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**Glossary**

| Abbreviation | Text in full |
|---|---|
| AACE/ACE | American Association of Clinical Endocrinologist/ American College of Endocrinology |
| ACEI | Angiotensin Converting Enzyme Inhibitors |
| ACOVE | Assessing Care of Vulnerable Elders |
| ACR | Albumin to Creatinine Ration |
| AF | Atrial Fibrillation |
| AHCPR | Agency for Health Care Policy and Research |
| ANOVA | One-way Analysis of Variance |
| ARB | Angiotensin Receptor Blockers |
| BMI | Body Mass Index |
| BNF | British National Formulary |
| BP | Blood Pressure |
| CCM | Chronic Care Model |
| CG | Clinical Guidance |
| CHD | Coronary Heart Disease |
| CHP | Community Health Partnerships |
| CI | Confident Interval |
| CKD | Chronic Kidney Disease |
| COPD | Chronic Obstructive Pulmonary Disease |
| CVD | Cardiovascular Disease |
| DDP-4 | Dipeptidylpeptidase-4 inhibitors |
| DESMOND | Diabetes Education and Self-Management for On-going and Newly Diagnosed |
| DM | Diabetes Mellitus |
| EBM | Evidence-Based Medicine |
| eGFR | Estimated Glomerular Filtration Rate |
| EMC | Electronic Medicine Compodium |
| GCC | Gulf |
| GDG | Gulf Cooperation Council |
| GFR | Glomerular Filtration Rate |

| Abbreviation | Text in full |
|---|---|
| GMS | General Medical Services |
| GPs | General Practitioners |
| HbA1c | Glycosylated Hemoglobin |
| HDL-C | High Density Lipoprotein Cholesterol |
| HGH | Hamad General Hospital |
| HMC | Hamad Medical Corporation |
| HTN | Hypertension |
| IDF | International Diabetes Federation |
| IDQ | Insufficient Data Qualifier |
| IDS | Insufficient Data Standard |
| IFG | Impaired Fasting Glucose |
| IGT | Impaired Glucose Tolerance |
| IQR | Inter-quartile range |
| IT | Information Technology |
| J/U | Justified |
| JBS | Joint British Societies |
| LDL-C | Low-Density Lipoprotein Cholesterol |
| LES | Local Enhanced Services |
| MAT | Medication Assessment Tool |
| MENA | Medill-east and North-Africa |
| MODY | Maturity Onset Diabetes of Youth |
| N/A | Not Applicable |
| NEHI | New England Healthcare Institute |
| NHS | National Health System |
| NICE | National Institute for Clinical Excellence |
| NOJ | Justified non-adherence |
| NOU | Not Justified non-adherence |
| NSAID | Non Steroidal Anti-inflammatory Drugs |
| OGTT | Oral Glucose Tolerance Test |
| OR | Odd Ratio |
| Qat | Qatar |

| Abbreviation | Text in full |
|---|---|
| QDA | Qatar Diabetes Association |
| QOF | Quality and Outcome Framework |
| RCT | Randomised Controlled Trials |
| SBP | Systolic Blood Pressure |
| SD | Standard Deviation |
| SDM | Steroid-Induced Diabetes |
| SE | Standard Error |
| SIGN | Scottish Intercollegiate Guidelines Network |
| START | Screening Tool to Alert doctors to the Right Treatment |
| STOP | Screening Tool of Older Persons' Potentially inappropriate Prescriptions |
| TC | Total Cholesterol |
| TCAS | Tri-cyclic Anti-depressants |
| TG | Triglyceride |
| TIA | Transient Ischaemic Attack |
| TQM | Total Quality Measurement |
| UAE | United Arab Emirates |
| UK | United-Kingdom |
| USD | United Stated Dollars |
| UTI | Urinary Tract Infection |
| WHO | World Health Organisation |

**List of publications and presentations from this project**

**Full-Papers**

- Diab M, Johnson BJ, Hudson S. Adherence to clinical guidelines in management of diabetes and prevention of cardiovascular disease in Qatar. Int J Clin Pharm. 2013; 35: 101-112.

- Diab M, Johnson BJ. Targeting diabetic patients in Qatar for pharmaceutical care using cardiovascular risk analysis. Int J Clin Pharm (in press).

- Diab M, Johnson BJ, Hudson S. Design and validation of medication assessment tool for the management of type-2 diabetes and primary prevention of cardiovascular disease. Int J Clin Pharm (in press).

**Abstracts**

- Diab M, Johnson BJ. Adherence to prescribing guidelines in the primary prevention of cardiovascular disease and in the management of patients with type 2 diabetes in Qatar. Oral Communication to 40th European Society of Clinical Pharmacy Symposium, Dublin 2011. Int J Clin Pharm (2012) 34: 173.

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**Oral and poster presentations**

- Adherence to prescribing guidelines in the primary prevention of cardiovascular disease and in the management of patients with type-2 diabetes in Qatar. Oral Communication and poster to 40th European Society of Clinical Pharmacy Symposium, Dublin, October 2011.

- Adherence to prescribing guidelines in the primary prevention of cardiovascular disease and in the management of patients with type-2 diabetes in Qatar. Oral presentation to Medicine Use and Health (MUH) research group seminars, Strathclyde Institute of Pharmacy and Biomedical Sciences University of Strathclyde, Glasgow, February 2012.

- Targeting diabetic patients in Qatar for pharmaceutical care using cardiovascular risk analysis. Oral and poster presentation to Annual research symposium, Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, September 2012.

- Targeting diabetic patients in Qatar for pharmaceutical care using cardiovascular risk analysis. Poster to 41st European Society of Clinical Pharmacy Symposium, Barcelona, October 2012.

# Chapter 1

# Type-2 diabetes mellitus

## 1.1 General introduction and background to diabetes mellitus

This chapter aimed to give general background information about the disease terminology, prevalence and aetiology in the first section. The second section will be mainly focusing on type 2 diabetes.

### 1.1.1 Definition and classification of diabetes mellitus

Diabetes Mellitus (DM) is a major and increasing health problem and is one of the most familiar chronic endocrine diseases. The condition is defined according to the World Health Organization (WHO) as a metabolic disorder of multiple aetiology characterised by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in pancreatic insulin secretion, insulin action, or both [(1)]. It is classified into two major classes:

Type 1 diabetes: also known as early-onset diabetes as it frequently develops at the teenage years and usually before the age of 40 years [(2)]. This type of diabetes is associated with deficiency of insulin secretion and is found to have a strong genetic constituent (hereditary), but the aspects that activate the commencement of clinical illness continue to be unidentified [(3)].

Type-2 diabetes: in which there is inadequate insulin formed by the body for normal function or when the body's cells do not respond to insulin resulting in what is usually called insulin resistance. It usually occurs in those over the age of 40 years with a peak incidence at 50-70 years [(4)].

Other specific types of diabetes involve: drug or chemical induced diabetes, immune-mediated diabetes and gestational diabetes in which glucose intolerance develops during pregnancy [(5)].

### 1.1.2 Epidemiology of DM

Diabetes is an increasing health problem affecting approximately 285 million people around the world in 2010. This number is estimated to reach 438 million people by 2030 according to International Diabetes Federation atlas (IDF) [6]. In the UK there is a large increase in the number of individuals diagnosed with diabetes. The prevalence of diabetes increased from 2.8% to 4.3% in the period from 1996 to 2005 with an incidence increased from 2.71 (2.58-2.85)/1000 person-years in 1996 to 4.42 (4.32-4.53)/1000 person-years in 2005 [7, 8]. The number of diabetes cases are expected to reach more than 4 million by 2025 [9]. Furthermore, there is another half million people expected to have undiagnosed diabetes in the UK [10].The increase in diabetes prevalence was mainly due to type 2 diabetes which is the commonest type of diabetes representing around 85-90% of the cases in the UK. Type-1 diabetes affects only 10% of people with diabetes [11].

The prevalence of diabetes is higher in Asian and African-Caribbean people. It is estimated that approximately 20% of Asians and 17% of African-Caribbean people aged over 40 years have type 2 diabetes [12]. The IDF reported that Nauru, United Arab Emirates, Saudi Arabia, Mauritius and Bahrain showed the highest prevalence of diabetes in 2010. In Qatar, the prevalence of diabetes among the adult Qatari population was 16.7%, which is around four times higher than the prevalence in the UK [13].

### 1.1.3 Aetiology and diagnosis of DM

Diabetes develops as a result of many pathogenic reactions. This could include autoimmune destruction of the beta cells of the pancreas leading to insulin insufficiency or other abnormalities in carbohydrate, fat, and protein metabolism that reduce normal insulin secretion or action on its target tissues leading to a reduced tissue response to insulin or insulin resistance. Commonly both insulin insufficiency and insulin resistance coexist in the same patient with diabetes [14].

In 2006, the WHO incorporation with IDF published an updated guideline for the definition, diagnosis and classification of DM and its complications. This guideline

recommended the oral glucose tolerance test (OGTT) as the diagnostic test for diabetes and did not consider HbA1c as a suitable diagnostic test. Furthermore, the guideline recommended the use of venous plasma glucose to measure and report glucose concentrations in the blood [15]. WHO recommendations for the diagnosis of DM and intermediate hyperglycaemia are summarised in the following table:

**Table 1 : Criteria for the diagnosis of diabetes mellitus**

| | |
|---|---|
| **Diabetes** | |
| Fasting plasma glucose | ≥7.0mmol/l (126mg/dl) |
| Or | |
| 2–h plasma glucose* | ≥11.1mmol/l (200mg/dl) |
| **Impaired Glucose Tolerance (IGT)** | |
| Fasting plasma glucose | <7.0mmol/l (126mg/dl) |
| and | |
| 2–h plasma glucose* | ≥7.8 and <11.1mmol/l |
| (140mg/dl and 200mg/dl) | |
| **Impaired Fasting Glucose (IFG)** | |
| Fasting plasma glucose | 6.1 to 6.9mmol/l |
| (110mg/dl to 125mg/dl) | |
| and (if measured) | |
| 2–h plasma glucose* | <7.8mmol/l (140mg/dl) |
| * Venous plasma glucose 2 hours (2-h) after ingestion of 75g oral glucose load | |
| * If 2–h plasma glucose is not measured, status is uncertain as diabetes or IGT cannot be excluded | |

The symptoms of both type-1 and type-2 diabetes are similar but they usually differ in magnitude. Those relating to type-1 diabetes are more strong and faster in onset. The most common symptoms include polyuria, nocturia and polydipsia (increased thirst). These occur as a consequence of osmotic diuresis secondary to hyperglycaemia. These symptoms usually present with fatigue (due to failure to use glucose) and obvious weight losses (due to degradation of body protein and fat as a substitute

energy source to glucose). Blurred vision (caused by change in lens refraction) may take place and patients should be advised that as glucose levels are normalised, vision should improve. Patients may also have a higher susceptability to infections, particularly Candida, and urinary tract infections due to increased circulating glucose levels. If the symptoms of hyperglycaemia are not predictable in type-1 diabetes, life threatening diabetic ketoacidosis may develop. About one-third of those who develop type-1 diabetes present with diabetic ketoacidosis [16].

The next section will focus more on type-2 DM as this is more prevalent and is the main focus of this thesis.

## 1.2 Type-2 DM

Type-2 diabetes is the most familiar type of diabetes responsible for more than 90% of diabetes cases in the UK and around 88% of cases in Scotland [17]. It is also known as non-insulin dependant diabetes in which high blood glucose level results from insulin resistance and relative insulin deficiency. It usually occurs in those over the age of 40 years with a peak incidence at 50-70 years, however, it can still be diagnosed in younger age and in children who are obese or have a family history of type-2 DM. The disorder can lead to a serious long-term microvascular (retinopathy with potential loss of vision; nephropathy leading to renal failure), macrovascular (cardiovascular and peripheral vascular disease), and neuropathic (peripheral neuropathy with risk of foot ulcers, amputations, and autonomic neuropathy causing gastrointestinal, genitourinary symptoms as well as sexual dysfunction) complications.

### 1.2.1 Pathophysiology and aetiology of type-2 DM

In type-2 diabetes, both insulin resistance and insufficient insulin secretion are present. Insulin resistance is usually the result of high levels of plasma free fatty acids which reduce tissue response to insulin, increase hepatic glycogenolysis and increase fat degradation [18]. Pancreatic beta cell dysfunction which leads to insufficient insulin secretion is another important factor in the disease pathophysiology and may happen at an earlier stage irrespective of insulin resistance [19].

There are many factors that contribute to type-2 diabetes. These include:

- Being over 45 years of age
- Excess body weight especially around the waist
- Family history: a first degree relative with type 2 diabetes (parent or sibling)
- Ethnicity: people from black, Asian, African-Caribbean, Pacific Islands and minority ethnic groups
- Known to have previous impaired glucose tolerance or impaired fasting glucose glycaemia
- Women who have had gestational diabetes or of delivering a baby with a birth weight of >9 lb or with polycystic ovary syndrome
- Medical conditions such as hypertension (HTN), dyslipidaemia, Cushing's syndrome and thyrotoxicosis.

Lifestyle factors (modifiable risk factors) play an essential role in the development of type-2 diabetes. Physical activity, healthy diet (rich with fibres and with low level of saturated fats), not smoking and lower alcohol consumption can reduce the risk of developing type 2 diabetes by 82% [(20)].

Obesity is another modifiable risk factor for developing type-2 diabetes. Recent statistics in Scotland showed that 33% of diabetic patients with a recorded body mass index (BMI) were overweight (BMI 25-29.9 $kg/m^2$) and 50.3% were obese (BMI $\geq$ 30 $kg/m^2$). Obesity reduces tissue response to insulin causing insulin resistance which can lead to type-2 diabetes. Adipose tissue surrounding the internal organs in the abdomen can produce chemical signals, hormones and cytokines that can result in insulin resistance. An example of such a mechanism is the inflammatory cytokines which may initiate the NF-kB pathway contributing to insulin resistance [(21)].

Some medications can initiate or exacerbate type 2 diabetes (secondary diabetes). Corticosteroids are a good example of such treatments. Diabetes was reported to be four times more frequent in a corticosteroid-treated group when compared to placebo

in one meta-analysis [22]. Glucocorticoids (example: dexamethasone and prednisolone) oppose insulin action and stimulate gluconeogenesis in the liver resulting in a net increase in hepatic glucose output. They also increase insulin resistance and can lead to steroid-induced diabetes (SDM).

The contribution of genetic factors in the development of type-2 diabetes is complicated and not fully understood. Regardless of clinical risk factors, evidence suggests eleven genes (TCF7L2, PPARG, FTO, KCNJ11, NOTCH2, WFS1, CDKAL1, IGF2BP2, SLC30A8, JAZF1, and HHEX) are significantly associated with the risk of developing type 2 diabetes. The majority of these genes are involved with pancreatic beta-cell dysfunction [23]. The other obvious example on the involvement of genetic factors in type 2 diabetes is a syndrome called maturity onset diabetes of youth (MODY). This syndrome is responsible for 1-5% of patients with type 2 diabetes and is associated with mutations in the autosomal dominant gene leading to defects in beta-cell dysfunction [24].

### 1.2.2 Complications of DM

Patients with diabetes are at high risk of developing long-term complications, which are the responsible cause of the disease morbidity, hospitalisation and mortality. This risk increases with time, especially as most patients with type 2 diabetes may have the disease for a long time before diagnosis. Diabetic complications are frequently divided into microvascular and macrovascular complications. The frequency of these complications among type 2 diabetic patients was assessed in the Cost of Diabetes in Europe - Type II (CODE-2) study. It showed that 72% of the total patients within the study had at least one diabetes complication, in which microvascular complications were more frequent than macrovascular ones (19% vs 10%, respectively). Both microvascular and macrovascular complications co-existed in 24% of the total patient sample [25].

There is good evidence on how the onset of the complications associated with the disease can be prevented, delayed or their progression slowed, if the disease is managed appropriately and from an earlier stage. Hyperglycaemia and hypertension are the two major controllable risk factors for developing diabetes complications.

Other risk factors include: duration of diabetes, smoking, hyperlipidaemia and albuminuria [26]. Multi-centre studies, such as the Diabetic Control and Complications Trial (DCCT) and the UK Prospective Diabetes Study (UKPDS) contribute evidence for best practice in an effort to reduce mortality and improve the quality of life in diabetics. The UKPDS 33 showed that there was 12% reduction in the risk of diabetes-related endpoint (sudden death, death from hyperglycaemia or hypoglycaemia, fatal or non-fatal myocardial infarction, angina, heart failure, stroke, renal failure, amputation, vitreous haemorrhage, retinopathy requiring photocoagulation, blindness in one eye, or cataract extraction) associated with intensive blood glucose control over 10 years [27]. This was also associated with 6% reduction in over-all mortality from diabetes [27]. Furthermore, the UKPDS 35 showed that for every 1% reduction in HbA1c there was 37% reduction in the risk of microvascular complications from type 2 diabetes [28]. The effect of tight blood pressure control on the risk of developing diabetes complications was assessed in the UKPDS 38 [29]. The study showed that tight blood pressure control around 144/ 82 mmHg, was associated with 24%, 32%, 44% and 37% reduction in diabetes related end-points, deaths from diabetes, strokes and microvascular end-points respectively [29].

#### 1.2.2.1 Microvascular complications

*Diabetic retinopathy*

Ocular complications associated with diabetes include transient visual disturbances secondary to osmotic changes, retinopathy, cataract and glaucoma. Diabetic retinopathy is one of the most commonly seen microvascular complications of diabetes and is the main reason behind new cases of blindness among people of working age in the UK. It is responsible for 4200 (0.21%) cases of blindness in England and is increasing by 1280 (0.064%) new cases every year [30], [31]. This kind of microvascular complication is highly dependent on the duration of diabetes, severity of hyperglycaemia and the presence of hypertension. It is believed that 60% of patients with type 2 diabetes will develop a degree of retinopathy within 20 years of diagnosis. However, in patients with type 2 diabetes, diabetic retinopathy can start developing as early as seven years before diagnosis [32], [33].

Formation of microaneurysms in the retina and loss of pericytes (the connective tissue that protect the endothelial cells of retinal capillaries and their damage can lead to eyes swelling from edema and the end results is vision loss or reduction) are signs of diabetic retinopathy. Aldose reductase may have a role in the development of diabetic retinopathy through the conversion of glucose, present in high levels, into sorbitol. Accumulated cellular sorbitol causes osmotic stress which can lead to microvascular complications of diabetes including diabetic retinopathy. However, using reductase inhibitors in patients with diabetes did not give the expected results [(34)]. It is also thought that glycoproteins may cause cell injury. Advanced glycosylated end products can form as a result of increased glucose levels, which are associated according to animal study, with the formation of microaneurysms and loss of pericytes. Other mechanisms for the development of diabetes retinopathy involve oxidative stress and growth factors.

The DCCT showed that intensive blood glucose control delayed the development and progression of retinopathy in patients with diabetes. Consequently, good glycaemic control aiming for an HbA1c of around 7% should be maintained. Pan-retinal and focal retinal laser photocoagulation are other treatments that reduce the risk of visual loss. However, annual screening for diabetic retinal disease is recommended for people with type-2 diabetes from the time of diagnosis and annually after that[(35)].

*Diabetic nephropathy*

Kidney disease represents 11% of deaths in type-2 diabetic patients and end stage renal failure is commonly happening as a consequence of diabetes [(36)]. Diabetic kidney disease can be classified as microalbuminuria or nephropathy according to the level of urinary protein excretion. If urinary albumin loss is between 30 and 300 mg in 24 hours, this is known as microalbuminuria. However, because timed urine collections are not always accurate, urinary albumin/creatinine ratio (ACR) >2.5 mg/mmol in men and >3.5 mg/mmol in women is used instead to describe microalbuminuria, which is considered as an earliest sign of diabetic kidney disease and mortality, cardiovascular mortality and morbidity, and end-stage renal failure. Diabetic nephropathy (which indicates clinical proteinuria) is characterised by an elevated urinary albumin excretion to >300 mg in 24 hours or an ACR > 30 mg/mmol in a spot urine sample regardless of serum creatinine level. Proteinuria is associated

with more severe renal (including end stage renal failure) and cardiovascular disease mortality and morbidity if compared to microalbuminuria [37].

Around 7% of patients with type 2 diabetes may already have microalbuminuria at the time of diabetes diagnosis. The incidence of microalbuminuria among type 2 diabetic patients was around 2% per year with 25% prevalence in 10 years after diagnosis [38, 39]. Some pathological changes associated with the development of diabetic nephropathy are: increased glomerular basement membrane thickness, microaneurysm formation and mesangial nodule formation (Kimmelsteil-Wilson bodies). Although the underlying cause of these changes is still unknown, it is believed that it may include some or all of the mechanisms mentioned in diabetic retinopathy involving hyperglycaemia (causing hyperfiltration and renal injury), advanced glycosylation products, and activation of cytokines [40].

*Diabetic neuropathy*

Diabetic neuropathy (involving peripheral neuropathy and autonomic neuropathy) is another common type of microvascular complication of diabetes affecting around 20-30% of patients with type 2 diabetes [41]. The disorder involves a progressive loss of nerve fiber function affecting sensory, autonomic and motor neurones of the peripheral nervous system. It can be presented in many different types, including sensory, focal/multifocal, and autonomic neuropathies that all together can significantly decrease patients' quality of life and increase morbidity and mortality. For example, foot ulceration or injury can lead to amputations in more than 80% of patients with diabetic neuropathy. One out of twenty patients with diabetes develops foot ulceration every year and amputation of a foot or a leg affects more than one out of ten of these patients. Diabetes also increases the rate of leg amputations to over 15 times and these amputations (resulting from diabetes) are associated with 70% death rate within five years [36]. As a result, it is important for the health care providers to deal seriously with this disorder through appropriate screening, prevention and treatment [40].

Sensorimotor neuropathy is the most common form of diabetic neuropathy. It affects large afferent nerves (responsible for cold and vibration sensation) and small afferent nerves (responsible for sensation of touch and warmth) to varying degrees resulting in

mixed symptoms and sensory loss. The symptoms of this disorder include: burning, tingling, paraesthesia or pain on normal touch. Other symptoms include an inability to feel, identify or manipulate small objects.

Autonomic neuropathy plays an important role in the increased morbidity and mortality from diabetes. It can affect the sympathetic and parasympathetic innervations of the heart (cardiovascular autonomic neuropathy) which can lead to silent or asymptomatic myocardial infarction and increased risk of sudden death. Autonomic neuropathy can also affect the gastrointestinal system (gastrointestinal autonomic neuropathy) which most commonly leads to gastroparesis (delayed gastric emptying and gastric retention can cause nausea, vomiting, early satiety and loss of appetite). Gastroparesis can also interfere with pharmacotherapy by delaying the time of absorption of glucose, complicating attempts to manage glycaemic control. Furthermore, genitourinary autonomic neuropathy can lead to erectile dysfunction and bladder complications manifested as an inability to sense bladder fullness, urinary retention or overflow incontinence [40, 42].

#### 1.2.2.2 Macrovascular complications

The risk of macrovascular complications, including morbidity and mortality from cardiovascular disease (coronary heart disease and stroke) and peripheral vascular disease, is 2-5 times higher in patients with diabetes[43]. Cardiovascular risk in patients with diabetes is equal to non-diabetic individuals with a previous heart attack and the risk of stroke was found to be two-folds higher in patients with type 2 diabetes within the first five years of diagnosis when compared with general population[44, 45]. Cardiovascular disease is the main cause of death in patients with diabetes, responsible for 52% of deaths in patients with type 2 diabetes. Women with type 2 diabetes showed 50% higher risk of death from coronary heart disease than men [36, 46]. However, life expectancy of both men and women who had type 2 diabetes at the age of 40 years is reduced by eight years compared to individuals without diabetes[37].

Atherosclerosis which leads to narrowing of blood vessels within the body is the main component of diabetes macrovascular disease. The pathway by which atherosclerosis develops, involves the accumulation of the oxidised lipids in the endothelial wall of

peripheral or coronary arteries as a result of chronic inflammation and injury to these vascular system. Angiotensin II may play a role in the oxidation of low-density lipoprotein cholesterol (LDL-C) particles and the formation of these oxidised lipids. The accumulated oxidised lipids then make foam cells promoted by the penetration of monocytes through arterial walls and they differentiate into macrophages. These foam cells intensify macrophage proliferation which attracts T-lymphocytes and results in collagen build-up. All these changes lead to development of atherosclerotic lesions which are rich with lipid and have a fibrous cap, that can cause vascular infarction if they are ruptured or moved from position[47]. Other mechanisms that can lead to macrovascular complications in type 2 diabetic patients include: increased platelet adhesion (resulting from insufficient nitric oxide production and increased free radical formation in platelets, as well as changed calcium regulation, that may facilitate platelet aggregation) and hypercoagulability due to high levels of plasminogen activator inhibitor which impair fibrinolysis[48].

Risk factors for the development of cardiovascular disease in diabetic patients involve: age, gender, duration of diabetes, dyslipidaemia, high blood pressure, hyperglycaemia, smoking status, ethnicity and atrial fibrillation.

### 1.2.3 Management of type-2 DM

When treating patients with diabetes, the targets of therapy should focus on symptom alleviation as well as achieving appropriate blood glucose control with a minimum interruption to the patients' normal life. Preventing or limiting morbidity and mortality associated with the disease and its long term complications should be also an important part of diabetes management. Risk of long-term microvascular complications in type 2 diabetic patients is significantly reduced if tight blood pressure and optimal glycaemic control was achieved. Treatment should start usually (unless the patient is acutely ill) with life style management and then drug therapy can be added when appropriate.

#### 1.2.3.1 Life style management

Changing inappropriate life style habits as part of diabetes management have an important effect on macrovascular and microvascular complications. Some of these interventions include: advice on nutrition, moderate alcohol consumption, physical activity, weight loss and smoking cessation if applicable.

*Diet*

Diagnosis and assessment of type 2 diabetes should be undertaken by GP, and once confirmed; management usually starts with dietary modification unless the patient is very unwell or has a very high blood glucose level. Dietary interventions have beneficial effects on weight loss, glycaemic control and general well-being. It should be tailored to meet each patient's needs which differ according to personal choices, cultural preferences and ability to change. Consequently, a registered dietician should be offered to all newly diagnosed diabetics as a part of the multidisciplinary diabetes management team to provide the appropriate nutritional / lifestyle advice and to make sure that all team members are informed about the nutritional therapy. Some of the dietary advice which can be given to patients include: high-fibre intake, choosing low glycaemic index sources of carbohydrate in the diet, such as fruit, vegetables, wholegrains and pulses; consumption of low-fat dairy products and oily fish; and to control the intake of foods containing saturated and trans fatty acids.

*Alcohol*

Alcohol has a high calorific value and contains carbohydrates, so that it can affect body weight if consumed in high amounts, in addition to its effect on blood glucose level. Moreover, high alcohol consumption reduces hypoglycaemia awareness due to its additive adverse effect on the cognitive functions. However, moderate alcohol consumption (2-3 units) considered safe in diabetic patients and they should be advised on the importance of restricting alcohol consumption to the same maximum weekly quantities as for the general population (14 units and 21 units per week for women and men respectively with 1-2 alcohol-free days per week).

*Smoking cessation*

Smoking is an established risk factor for cardiovascular diseases in the general population as well as in type 2 diabetic patients and is associated with an increased mortality among both men and women. Smoking cessation reduces cardiovascular complications of diabetes and all patients who smoke should be offered smoking cessation advice through intensive motivational interviews which can be combined with pharmacological interventions when necessary. Nicotine replacement therapy should be offered as a first pharmacological intervention; however, bupropion is another option and could be used alone or together with nicotine replacement when applicable.

*Excise and physical activity*

Physical activity is known as any bodily movement formed by skeletal muscles (occupational, sports, conditioning, household, or other activities) that results in energy expenditure (measured in kilocalories). Exercise is a subset of physical activity that is planned, structured, and repetitive and has the improvement or maintenance of physical fitness as a final or an intermediate objective[49]. Physical activity and exercise are both recommended for all patients with type-2 diabetes as they are associated with improved glycaemic control and reduced cardiovascular risk factors. In a meta-analysis, eight weeks to 12 months exercise in patients with type 2 diabetes was associated with 0.6%, 45.5 $cm^2$ and 0.25 mmoml/l reduction in HbA1c, visceral adipose tissue and plasma triglycerides respectively[50].

*Weight loss*

There is a direct correlation between overweight/obesity and the risk of developing type-2 diabetes. Individuals with body mass index (BMI) over 35 $kg/m^2$ are up to 80 times more likely to develop type 2 diabetes[51]. In 2008, diabetes affected 4.3% of people in Scotland. Among these patients, 33% were overweight (BMI 25-29.9 $kg/m^2$) and 50.3% were obese (BMI $\geq$ 30 $kg/m^2$). Weight loss has benefits for glycaemic control and is significantly associated with HbA1c reduction. As a result, it should be considered as an important part of diabetes management.

### 1.2.3.2 Oral antidiabetic agents (Pharmacological management)

Oral antidiabetics are a group of drugs that are used to treat type-2 diabetes. They should only be commenced if lifestyle interventions have failed to control symptoms and to reduce blood glucose level. Furthermore, their use should be as an enhancement to lifestyle interventions, but not to replace them. If life-style interventions together with oral hypoglycaemic drugs are still not enough in the management of blood glucose levels, insulin can be added initially and may substitute for the use of some oral hypoglycaemic agents at a later stage.

*Biguanides* (Metformin)

Metformin is a biguanide with antihyperglycaemic properties which is used as monotherapy or in combination with other oral antidiabetic agents or with insulin for the treatment of type 2 diabetes especially in overweight and obese patients. It reduces basal and postprandial blood glucose without affecting insulin secretion from the pancreas, which eliminates the risk of hypoglycaemia with this drug. Metformin performs its action by inhibiting gluconeogenesis and glycogenolysis in the liver resulting in reduced hepatic glucose production. It also improves peripheral glucose uptake and consumption in muscles leading to increased insulin sensitivity. Other mechanisms for metformin involve: delaying glucose absorption in the intestine, enhancing intracellular glycogen production and increasing the transport capacity of membrane glucose transporters. Metformin also has a beneficial effect on lipid metabolism (by reducing total cholesterol, LDL cholesterol and triglyceride levels) beside its effect on glycaemia[52, 53].

Gastrointestinal undesirable effects (nausea, vomiting, diarrhoea, abdominal pain) are most likely to happen when metformin is first introduced. This may carry on in some patients, especially, when very high doses such as three grams/day are prescribed. Metformin treatment should be avoided in those at increased risk of lactic acidosis such as those with renal impairment, as metformin clearance is reduced. It should also be stopped temporarily in the case of acute illness, prior to surgery or radiocontrast investigations. Metformin treatment could be also associated with vitamin $B_{12}$ deficiency anaemia.

*Sulphonylureas*

Sulfonylureas are commonly used to treat patients with type 2 diabetes. These drugs exert their hypoglycaemic effects by stimulating insulin secretion from the pancreatic β-cells and can cause hypoglycaemia (usually with massive dose). Their primary mechanism of action is to bind to receptors on the surface of pancreatic beta-cells leading to the closure of voltage-dependent KATP channels. This promotes calcium entry into the cell and insulin secretion. Therefore, they improve the sensitivity of the pancreatic beta-cells to glucose resulting in increased insulin release for the existing levels of glycaemia. As a result, sulfonylureas are effective only when some residual pancreatic beta-cell activity is present [(54)].

Sulphonylureas are considered for patients who are not overweight, or when metformin is contra-indicated or not tolerated. A number of sulphonylureas are available and choice is determined by side-effects and the duration of action as well as patients' age and renal function. The long-acting sulphonylureas, chlorpropamide and glibenclamide are associated with a greater risk of hypoglycaemia; for this reason they should be avoided in the elderly and shorter-acting alternatives, such as gliclazide or tolbutamide, should be used instead. They can be used alone or in combination with metformin, thiazolidinediones or insulin. As the sulphonylureas primarily undergo metabolism by the liver and excretion by the kidney, they should be used with caution in patients with advanced forms of hepatic or renal impairment [(52), (35)].

*Meglitanides*

The melitanides (repaglanide and nataglanide) are amino acid derivatives which have a mechanism of action similar to sulphonylureas, but with different structures, binding sites, duration of action (a rapid onset of action and short duration of activity) and method of elimination. The effect of repaglinide in lowering HbA1c level is similar to sulfonylureas, however it is characterised by its effect on lowering postprandial glucose levels and decreased risk of hypoglycaemias. Furthermore, some experimental data advised that over time glinides might maintain β cell function better than sulfonylureas and protect against cardiovascular long-term complications. Unlike repaglinide which can be given as monotherapy or in combination with metformin,

neteglinide is licensed only for use with metformin as it has no effect on fasting plasma glucose level and due to its shorter duration of action [55], [56].

*Acarbose*

Acarbose is another agent used in the treatment of type-2 diabetes, which can reduce postprandial hyperglycaemia and regulate unstable daily blood glucose profile. This agent has nothing to do with the pancreas and is considered to be a competitive inhibitor of intestinal alpha-glucosidase enzymes (in the brush border of the small intestines) which results in delayed digestion and absorption of starch and sucrose. It reduces fasting blood glucose levels and can reduce HbA1c levels (with an average of 0.7%) as a long-term effect [57], [58]. Acarbose can be used alone or in combination with other anti-diabetic agents, however, it should be considered only when the other anti-diabetic agents are contraindicated or not tolerated [59].

*Thiazolidinediones*

Thiazolidinediones are another group of medications used as monotherapy or in combination with metformin or sulphonylureas to treat type 2 diabetes. It can also be added as a third-line agent to the dual therapy with metformin and sulphonylureas. This group of medications are not associated with insulin secretion from the pancreas. They increase insulin sensitivity as they bind to and activate peroxisome-proliferator–activated receptors (PPARs) which are found on the liver, heart, skeletal muscle, adipose tissue and vascular endothelium leading to increased glucose utilisation and reduced hepatic glucose output. Thiazolidinediones can also decrease triglycerides and increase high-density lipoprotein cholesterol (HDL-C), however, their effect on LDL-C needs more investigation [60]. Pioglitazone is the only licensed glitazone in the UK after the withdrawal of rosiglitazone (European Medicines Agency, September 2010) due to its cardiovascular risk. Pioglitazone improves both fasting and postprandial glycaemic control in patients with type 2 diabetes mellitus. It can also reduce total plasma triglycerides, and increase HDL cholesterol levels without any statistically significant increases in LDL cholesterol levels compared with placebo [61], [62].

*Dipeptidylpeptidase-4 inhibitors (Gliptins)*

This group of medications (linagliptin, saxagliptin, sitagliptin, and vildagliptin) are used in the treatment of type 2 DM increase insulin levels and reduce glucagon secretion. They block the DDP-4 enzyme which increases incretin levels (a group of gastrointestinal hormones, GLP-1 and GIP, responsible for increasing insulin secretion after having food) and leads to inhibition of glucagon release, raised insulin levels and delayed gastric emptying.

Linagliptin and sitagliptin can be use for mono, dual or third-line therapy with both metformin and a sulfonylurea. Sitagliptin can be also added to pioglitazone or insulin when appropriate. Saxagliptin and vildagliptin can only be used in combination with metformin or a sulfonylurea (if metformin inappropriate) or pioglitazone, when treatment with either metformin or a sulfonylurea or pioglitazone fails to achieve adequate glycaemic control [(63)].

*Exenatide and liraglutide*

These two non-oral medications stimulate GLP-1 through binding directly to its receptor leading to an increase in insulin secretion, inhibition in glucagon release and slow gastric emptying. They are given as a subcutaneous injection in combination with other oral agents (metformin, sulfonylurea, or pioglitazone) as part of the dual or third-line therapy, particularly in obese patients (BMI $\geq$35 kg/m$^2$ according to NICE and $\geq$30 kg/m$^2$ according to SIGN) to encourage weight loss [(59), (37)].

*Insulin*

Insulin subcutaneous injection is another treatment option for patients with type 2 DM. Its use has become more common due to the progressive nature of the disease and the presence of other circumstances (acutely ill patients, rapid onset of symptoms, before operations and pregnant women) which indicate its use as the first treatment option. Other than those circumstances, insulin can be added to or substitute for diet and oral hypoglycaemic drugs if they are not adequately controlling hyperglycaemia.

There are different types of insulin according to its duration and onset of action. Those with short duration have a relatively rapid onset of action. However, those with long duration have a slower onset of action. Isophane insulin is a third type of insulin

with an intermediate action. The choice of insulin type according to duration of action or the use of mixtures of these types should be determined for each patient individually according to his/her needs and goals of therapy. Furthermore, it is recommended to continue the current oral hypoglycaemic agents (metformin, sulfonylurea or acarbose) when insulin is added to the therapy and to review and discontinue the sulfonylurea only if hypoglycaemia occurs. Increased body weight and hypoglycaemia are two important complications associated with insulin therapy and all patients should be closely educated on how to prevent them [(52)].

## 1.3 Introduction to thesis

The author of this thesis is employed as a clinical pharmacist in the Department of Pharmacy at Hamad General Hospital which is part of Hamad Medical Corporation in Doha, Qatar. The incentive for this study came from the increased prevalence of diabetes in Qatar which reached to 16.7% among the adult Qatari population in 2009. Diabetes can lead to a serious long-term microvascular (retinopathy with potential loss of vision; nephropathy leading to renal failure) and macrovascular (cardiovascular and peripheral vascular disease) complications which are responsible for the disease morbidity, hospitalisation and mortality. However, there is good evidence on how the onset of the complications associated with the disease can be prevented, delayed or their progression slowed, if it is managed appropriately and from an earlier stage. Furthermore, pharmacists can play an important role in the management of diabetes and its complications through an appropriate pharmaceutical care plan, but they are not yet involved as part of the multidisciplinary team for the management of diabetes in Qatar.

This highlighted the importance of measuring the current level of care provided to patients with diabetes and in exploring how their illness or disease complications are managed to avoid or delay its development with a special focus on the cardiovascular disease complications (as it is the responsible cause of death in the majority of patients with type-2 diabetes). Knowing the current level of care provided to diabetic patients will help to identify the specific clinical areas (those lacking the appropriate care) where the pharmacist may contribute and will allow them to be included in the delivery of an appropriately designed pharmaceutical care plan designed to deliver targeted patient care.

# Chapter 2

## Design and validation of a medication assessment tool for management of type 2 DM and the primary prevention of CVD

## 2.1 Introduction

### 2.1.1 Need for quality evaluation

The quality of health services provided to patients receiving care within primary or secondary health settings has been a subject of health care authorities' research for many years. Measuring this quality of care is of great importance, not only for health care authorities in order to guarantee that services provided to people are meeting the expected level of performance, but also for clinicians, managers, other health care providers as well as for patients or the public. Its value for physicians, managers or other health care providers originates from its ability to identify areas, policies or services that need more attention or are appropriate for re-design and change to achieve optimum levels of performance. For the public, it contributes to their debates on service quality, performance and accountability. Quality assessment is also essential for other applications such as accreditation, pay for performance, new services evaluation and targeting or prioritising vulnerable patient groups lacking the appropriate level of care [(64)].

The Quality and Outcomes Framework (QOF) in the UK is a good example of data generation and analysis for the purpose of service quality and assessment. The programme was launched in April 2004 as part of the new General Medical Services (GMS) contract to be the major source of potential income (detailing practice achievement results for all general practices or surgeries across the UK) for annual resourcing and rewarding good practice. Overall achievement of a surgery is measured through a points system (can reach up to 1000 points). The award of these points is based on 134 indicators in four major components as follows:

*1. Clinical care components*

These include a total of 86 indicators in 20 clinical areas categorised by disease and the GPs only have to complete the information by coding and registering chronic diseases. These components can yield up to 697 points and the clinical areas are: coronary heart disease, heart failure, hypertension, diabetes, asthma, cancer, chronic obstructive pulmonary disease (COPD), epilepsy, mental health, smoking indicators,

stroke and transient ischaemic attack, atrial fibrillation, chronic kidney disease (CKD), dementia, depression, learning disabilities, obesity and palliative care.

*2. Organisational components*

These include 36 indicators in 5 areas and can yield up to 167.5 points. These areas are:

- Records and information
- Information for patients
- Education and training
- Practice management and medicines management

*3. Patient experience components*

These include 3 indicators and can yield up to 91.5 points. Areas include:

- Length of consultations
- Patient experience of access to GPs

*4. Additional services components*

These include 9 indicators in 4 areas and can yield up to 44 points. These areas are:

- Cervical screening
- Child health surveillance
- Maternity services
- Contraceptive services

READ codes (specific codes for each disease which are used to enter data onto the computer system easily) play an important role in fulfilling the data collection according to the criteria of QOF. All READ codes are based on NHS standards to be able to produce the achievement report and are used to put the data onto the computer system easily. The GPs can decide whether they want to participate in all, some or none of these components.

Higher quality of care provided in these areas leads to higher points score and more financial reward for the practice. Surgery workload and the prevalence of chronic conditions in the practice's local area are other parameters considered for payment

adjustment. Furthermore, patients' regulators, health and social care professionals and policy makers are allowed to access this database to identify the performance of their GP practice for the purpose of improvement in knowledge and efficacy [65], [66], [67], [68].

### 2.1.2 Clinical audit and medication assessment tool

Clinical audit is the process which involves a systematic review of care or a service against explicit criteria and implements change in order to improve the quality of patient care and outcomes. The explicit criteria within the clinical audit assess the structure, processes and outcomes of care when conducting the systematic review. Based on findings, modifications are implemented at an individual, team, or service level and further monitoring is used to assure improvement in healthcare delivery [69]. Adding clinical audit as a key element within the health service could yield many benefits including:

- Developing a mechanism for reviewing the quality of care provided to patients with chronic diseases or co-morbidities such as asthma, diabetes or CVD.

- Using the long history of data collected within the case notes to confirm the quality of clinical services and to provide physicians and other healthcare professionals with areas needing improvement to achieve better patient care.

- Addressing quality issues systematically and explicitly, providing reliable information.

Clinical audit needs certain conditions in order to be effective. It needs to be fully supported by the national health authorities and provided with the required time, facilities and expertise. Providing a central clinical audit facility can organise audit activity by giving the necessary advice and support for the audit process and make use of the collected data and results for further action [70].

Clinical audit can be expressed as a cycle of steps that follow orderly processes (assessment of care, implementation of changes and observation of changes) to

achieve its aim and maintain it (figure 1). The cycle indicates that the process is contentious until reaching the optimum level of quality. The processes involve a wide range of methods and organisational, statistical and technological management skills. It can be conducted by an individual health care worker or a group of professionals in single or multidisciplinary teams in coordination with the central audit centre within the primary or secondary health care authority. The audit project can assess a single service or a number of services within a local region or across the country. Effective systems for audit management and providing the essential environment are important elements at the start of the audit project [71].


**Figure 1: The clinical audit cycle [71]**

The need for an organisational environment that supports effective clinical audit and better understanding of clinical audit are important to achieve audit aims. If the organisational environment is supportive, staff involved are well prepared and methods are fully understood, clinical audit has more chance of succeeding. The two major elements for an appropriate environment are structure (provide the necessary structure, for example facilities like time, technical support, or library services) and

culture (creativity and openness are encouraged, and errors and failures are reported and investigated without fear of blame) [70].

#### 2.1.2.1 Stages of clinical audit

An audit project usually involves five stages (shown in figure 2). These stages need to be combined with the supportive environment and the use of effective system and methods [72].

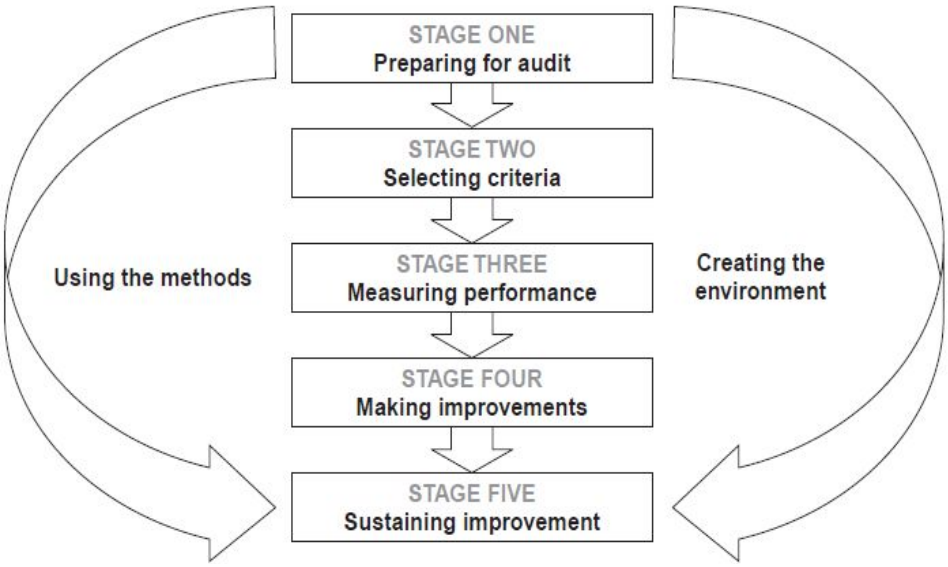


**Figure 2: stages of clinical audit**

**Stage one: preparing for audit**

This stage concerns audit project management and methodology which includes: topic selection, aims identification, appropriate structure presentation and determination of the skills and people needed to carry out the work.

*Topic selection*

The subject of clinical audit needs to be carefully selected and planned in order to obtain a valuable quality improvement and investment of resources. Clinical topics for audit projects could be decided by the clinical members and the following points can help in decision making while selecting a topic:

- Topic's cost, volume, or risk to staff or users (including patients, other service users and carers).
- Presence of indications for serious quality problems (patients' complaints, increased disease prevalence, increased rates of disease complications).
- Presence of high-quality evidence to inform standards (systematic reviews or national clinical guidelines).
- Subject's ability to change.
- Subject's potential for the involvement in a national audit project.
- Importance of the subject for the health authority or organisation.

*Aims identification*

Audit projects, as with any other projects, should have a clear aims and objectives. Keywords for good aims include: to improve, to identify, to ensure and to modify. For example, the audit project aim could be to improve adherence to guidelines recommendations in the management of type-2 DM or to identify patients at higher need of pharmaceutical care attention. At this stage, project management, data requirements and collection should also be considered to create a proposal which will be then updated and widened to produce the final report of the audit findings and recommendations [73].

*Structure presentation and determination of the skills*

This includes identifying the research group members (well-qualified audit team with enough experience and skills), feedback mechanisms, funding and regular audit meetings. When selecting group members it is important to include members who deliver care (doctors, specialists or consultants) and all team members should be aware of the project aims and objectives and about the involvement of other members of the team. Effective communication between team members should be also maintained. The member of the team who will carry on the audit should have sufficient knowledge about the selected topic, information technology within the organisation, other projects on the same field, data management (collection, entry, analysis and presentation) and the appropriate skills to communicate with the other members of the audit team (enable the group to work together effectively) and to guide the project from planning to reporting [73].

**Stage two: Selecting criteria**

*Defining criteria*

Identifying and defining criteria are the major part of a clinical audit project. It is the explicit statement which is used to measure the quality of care provided to patients against standards through an organisation. Criteria within clinical audit are usually designed to measure a wide range of aspects of care quality objectively and is defined as: A systematically developed statement that enables the achievement of a standard (broad objective of care) and the evaluation of whether it has been achieved or not, so that it can be used to assess the appropriateness of specific healthcare decisions, services, and outcomes [71]. The standard is the level of care to be achieved for any particular criterion or the percentage of events that should comply with the criterion [71].

*Developing valid criteria*

For criteria to be valid and lead to improvement in care, they need to be based on evidence, related to important aspects of care and easily measured. Such criteria are not easy to develop and require a considerable amount of time, effort and expertise. Using already existing criteria which were previously developed by individuals, who are trained in the procedures of evaluating evidence from the literature and grading criteria by strength of evidence would be an easier alternative. Below are examples on methods which can be used in order to develop appropriate criteria:

*Implicit criteria*

This method depends on the use of experts (senior clinicians or health care providers) to carry on the care review based on their own experience in judging care. However, the use of this method should be avoided or restricted because of its limited reliability in the interpretation of information. [74]

*Using guidelines*

This method uses guidelines recommendations in order to develop explicit criteria. Criteria based on this method can be considered valid criteria as long as the guideline selected is updated and is a high-quality guideline which relies on a careful review of

the related research evidence. Criteria can also be generated from a literature search of certain journal article or from high-quality systematic reviews. [74]

*Other methods of developing criteria*

If appropriate guidelines are not available for the selected audit subject, other methods for developing criteria can be used. These methods include:

- Prioritising the evidence method: systematic review of the high-quality evidence available on the selected topic and the use of it to develop criteria. The developed criteria can be then identified, prioritised, peer reviewed and included in the final audit according to its evidence strength, ability to be measured and its importance on outcomes.

- RAND/UCLA appropriateness method: Criteria developed from a literature review rated on 9-point scale ranging from 1 (extremely inappropriate) to 9 (extremely appropriate) by a board of professionals who are expert in the topic field. [75]

- Agency for Health Care Policy and Research (AHCPR) method. [76], [77]

- Criteria based on professional consensus method. [78]

**Stage three: measuring levels of performance**

The main concern of this stage of an audit is the data (which will be used to assess the level of care) source and collection. The collection of data should be specific and the population to be involved has to be clearly defined (inclusion criteria) to collect just the necessary data. To achieve this limitation in data collection, the person who will carry out the audit should know the range and reliability of information about the identified population on the electronic systems or within patients' case notes and consult other members within the audit team (or other teams when necessary) to determine the exact data which are directly related to the care processes.

Determination of the time needed for data collection can also be done at this stage depending on the number of patients needed for assessment. [79]

**Stage four: Making improvement**

Making improvement may involve a change in behaviour and this change can take place at organisational, group or individual levels.

*Organisational change*

Changes at organisational level could face difficulties when implemented which can limit its final effect. For example, workload, national policies, culture or rigid structures within the organisation are some factors which may limit the implementation of new services or a re-design of the existing ones to improve overall care. These factors should be identified in order to be reduced or removed.

*Group change*

Group change is smaller than a change in the whole organisation, in which a minority within a group stresses its members to carry out the change and improve trust among group views and decisions. The influence of this minority can be supported by forces from the group itself or from outside the group.

*Individual change*

Changing individuals' routine behaviours may involve five stages from precontemplation (individual has no intention of changing) to contemplation (change is planned for the near future), preparation (explicit plans are made), action (the change occurs) until reaching maintenance (the changed behaviour is preserved). Each of these stages may involve one or more strategies to be completed. [80]

**Stage five: Sustaining improvement**

When the clinical audit achieves its aim in care improvement, maintaining this improvement is an important final step. This step includes monitoring, evaluating, maintaining and reinforcing the change. For change, monitoring and evaluation a second time of data collection should be done after change implementation using the

same strategies in the sample selection, collection and analysis. The importance of using the same methods is to get valid and comparable results. If the expected level of improvement was not achieved after change implementation, then plan modification or additional interventions should be critically considered. [81]

Information technology may become a good option at this stage. It can be constructed (linked to specific patient records or clinical performance indicators) to electronically and frequently record level of care long-term. It is also important to provide enough time for the change to achieve its goals before a re-audit to evaluate and monitor its effect on the level of care [71].

#### 2.1.2.2 Medication Assessment Tool (MAT)

MAT is an example of practising clinical audit in clinical settings which is designed to assess the adherence of current health facilities to the expected clinical performance according to specific criteria assessing quality of care within the clinical audit. It was developed within the University of Strathclyde in the UK (methodology described by JJ McAnaw in his PhD thesis in 2002) [82] to enable researchers to identify gaps in management of specific diseases and evaluate the appropriate medication use to improve clinical outcome of treatment. Its development was a result of the increased importance of clinical guidelines in the delivery of health care as well as the need to demonstrate clinical effectiveness. It is one of the most important tools which can be used for clinical auditing and has been shown to be a valid instrument for use in a variety of care settings.

This instrument is capable of detecting change in the adherence of medication to the evidence base, not only for treatment but also prevention of specific disease published in the clinical guidelines so that the recommendations of the updated clinical guidelines can be turned into measurable criteria and applied in the clinical settings. Each criterion in a MAT follows a basic algorithmic structure which evaluates the data and patients' information according to the criteria of the MAT. Common structural elements for each criterion are a qualifying statement and a standard, where 6 different answer categories are possible. Furthermore, the tool is suitable for manual and computer-based applications [82), (83)].

The currently existing MAT criteria within the University of Strathclyde which assess the appropriate medication use in the management of type 2 DM were checked and it was found that they only cover those medications related to CVD prevention and management in diabetic patients. However, criteria assessing the appropriate use of anti-diabetic medications were lacking and so it was decided to revise the MAT using the most recently published guidelines and use these to generate some of these criteria.

### 2.1.3 Aim and Objectives

#### 2.1.3.1 Aim

To design and to validate a medication assessment tool (MAT) for evaluation of the quality of medication use, according to international guideline recommendations in the management of type 2 DM and in the primary prevention of CVD in adults.

#### 2.1.3.2 Objectives

1. To review sources of evidence-based guideline recommendations for the management of type 2 diabetic patients.

2. To identify a list of recommendations from the recently updated guidelines for the management of diabetic patients, and to produce the corresponding medication use criteria.

3. To design a MAT based on objective 2 in order to address the appropriate disease management and complications.

4. To include the primary prevention of CVD criteria from the currently existing CVD tool after being updated according to the relevant guideline to the MAT developed above.

5. To validate the new MAT to fit its use in the clinical settings in Qatar and in the UK using experienced academic staff and diabetic clinic doctors/consultants.

6. To recommend further application of the tool and report on its field-testing and implementation.

## 2.2 Methods

### 2.2.1 Literature review of the evidence-based guidelines

To identify the existing and the most updated evidence-based recommendations on the management of type-2 DM and its CVD complications, four clinical guidelines were reviewed in depth as the starting point for this project. These internationally accepted guidelines were:

- National Institute of Clinical Excellence (NICE): type 2 diabetes: national clinical guideline for management in primary and secondary care (update, CG66) [35].

- NICE: type 2 diabetes: newer agents for blood glucose control in type 2 diabetes (CG87) [59].

- NICE: type 2 diabetes: prevention and management of foot problems (CG10) [84].

- Scottish Intercollegiate Guidelines Network (SIGN): management of diabetes: a national clinical guideline (SIGN 116) [37].

Recommendations within each guideline were developed according to their evidence source (table 2). However, only SIGN offers recommendation grading which facilitated the selection of recommendations from this guideline (priority given to recommendations with grade A & B) for inclusion within the MAT draft (table 3).

For background information of this thesis, other literature sources, particularly journal papers were accessed to describe the importance of evaluating the current management of diabetes and its complications with special focus on CVD as well as the important role of the pharmacist in diabetes management. This review utilised databases MEDLINE and EMBASE, British Medical Journal (www.bmj.com) as well as The Pharmaceutical Journal's web site (http://www.pharmj.com) using a variety of

search key words (appendix 11). The search was limited to publication data from 1980 to date. Results of the database search were filtered when needed using key words combination options or filtration according to the journal's date (last five years). Moreover, Electronic Medicines Compendium (EMC) website was also used (http://www.emc.medicines.org.uk), which provides continuously updated information on licensed medicines available in the UK.

**Table 2: Grading the evidence statements**

| Level of evidence | Type of evidence |
|---|---|
| 1++ | High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias. |
| 1+ | Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias. |
| 1– | Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.* |
| 2++ | High-quality systematic reviews of case-control or cohort studies.<br>High-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal. |
| 2+ | Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal. |
| 2– | Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal.* |
| 3 | Non-analytic studies (for example case reports, case series). |
| 4 | Expert opinion, formal consensus**.** |

*Studies with a level of evidence '–' are not used as a basis for making a recommendation. RCT, randomised controlled trial.

**Table 3: Grades of recommendation***

| | |
|---|---|
| **A** | At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results |
| **B** | A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+ |
| **C** | A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++ |
| **D** | Evidence level 3 or 4; or extrapolated evidence from studies rated as 2+ |

*Recommendations are graded A B C D to indicate the strength of the supporting evidence

### 2.2.2 MAT development

#### 2.2.2.1 Development of the new criteria

After the in depth review of NICE and SIGN guidelines, recommendations related to type-2 DM diagnosis, non-pharmacological and pharmacological management of the disease itself and its complications were identified and selected. Selected recommendations from these clinical guidelines were also checked against the American Association of Clinical Endocrinologist/ American College of Endocrinology algorithm (AACE/ACE diabetes algorithm) [85] for glycaemic control before its final inclusion (an algorithm used in Qatar, which use international guidelines as it dose not have its own guideline for management of DM). Each of the selected recommendations was then re-arranged to generate a MAT criterion using methodology developed by JJ McAnaw, 2002 (table 4).

The generated criteria (a total of 39 criteria) were collected into one table containing the standard MAT format to produce the first draft of the tool (MAT 1st draft) with three sub-headings including: General criteria, Disease management and Management of disease complications. Every new criterion was built up systematically and divided into two statements: a qualifier and standard. The qualifying statement (qualifier) which is the bold part of the criterion assesses the applicability of each patient to each criterion (eligible for inclusion in the assessment). Consequently, the standard is only considered if the qualifier applied to the patient and expresses the expectation of the criteria (table 4).

**Table 4: Examples of a MAT criterion structure and development**

| Guideline recommendation | Final criteria generated after validation stage |
|---|---|
| **A** An HbA1c target of 7.0% *(53 mmol/mol)* among people with type 2 diabetes is reasonable to reduce risk of microvascular disease and macrovascular disease. A target of 6.5% *(48 mmol/mol)* may be appropriate at diagnosis. Targets should be set for individuals in order to balance benefits with harms, in particular hypoglycaemia and weight gain. | **Patients with type 2 diabetes** should have an $HbA_{1c}$ recorded at ≤7 % as their most recent value<br><br>**Patient with type 2 diabetes** should have a recorded target $HbA_{1c}$ |

| | |
|---|---|
| **A** Metformin should be considered as the first line oral treatment option for overweight patients with type-2 diabetes. | **Patient with type-2 diabetes on glucose lowering agent(s)** is on metformin or sulphonylurea |
| **A** Sulphonylureas should be considered as first line oral agents in patients who are not overweight, who are intolerant of, or have contraindications to, metformin. | |

For each criterion there were six possible answers: “Not applicable (N/A)” [if the patient did not meet the qualifier], “yes” [if the patient met both the qualifier and standard], “No” [if the patient met the qualifier but not the standard], “No, but justified (J/U) [if the patient met the qualifier but not the standard and there is a plausible justification recorded in the patient’s notes], “Insufficient data qualifier (IDQ)” [when there is a lack of information to assess whether a criterion was applicable or not ]and “Insufficient data standard (IDS)” [when there is lack of information to assess whether the applicable criterion met the standard statement or not ]. Figure 3 explains the steps of MAT criterion application.

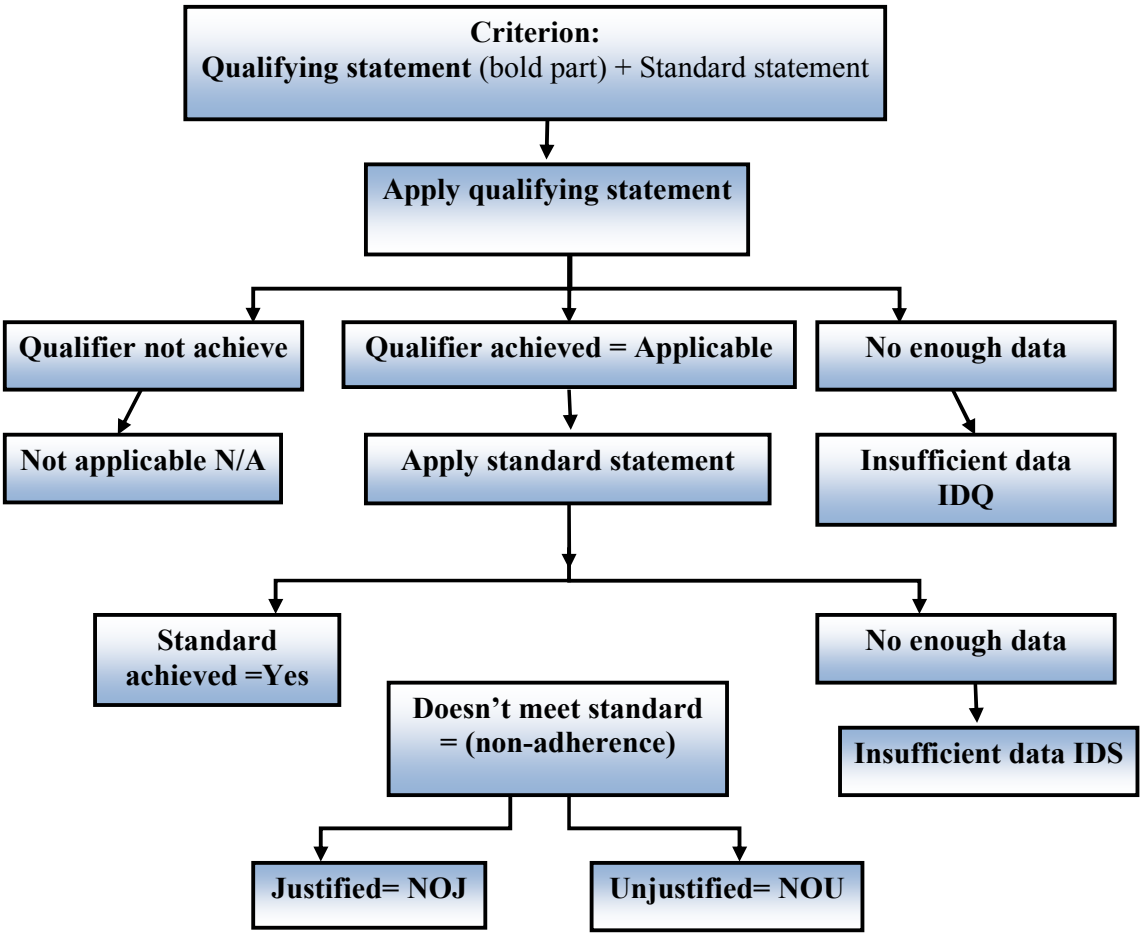


**Figure 3: steps of MAT criterion application**

#### 2.2.2.2 MAT validation by the research group

An expert research group consisted of two academic tutors (a senior lecturer and a Professor of Pharmaceutical care) and two post-graduate researchers (who have been involved in previous MAT designs and validations) reviewed all the identified recommendations and decided on which ones would be suitable for audit and which ones to remove. Factors taken into consideration to determine criterion auditability were: availability of data to answer question, time needed to collect data, avoidance of searching historical data. Furthermore, the research group also reviewed criteria wording and structure (combining criteria and separating other complex criteria into more than one criterion) in order to make them more precise and easier to read and use (to define the qualifying and standard statements for each criterion in a clear way). This stage involved a considerable time and number of meetings. A hard copy of the guideline recommendations were referred to when needed.

Total agreement among the review groups was achieved and draft 2 of the MAT (MAT 2nd draft) was generated. Criteria formed within this draft were organised into groups according to the following headings: Control of blood glucose, management of diabetes complications (blood pressure control, kidney disease, retinopathy and neuropathy/ foot disease) and primary prevention of CVD.

#### 2.2.2.3 Addition of CVD prevention criteria

To assess the appropriate use of CVD prevention procedures in diabetic patients, the DM criteria obtained from the above literature review was added to the MAT previously developed, evaluated, peer-reviewed and applied by previous authors for the primary prevention of CVD and hypertension management (appendix 1)[86), (87)]. The existing MAT contains 31 and 56 criteria for the primary and secondary prevention of CVD respectively. Only those criteria which are involved in the primary prevention of CVD were selected, updated against the recent guidelines (SIGN 97 & NICE 34) [(88), (89)] and added to the 2nd draft of the MAT (a total of 6 criteria). Furthermore, all criteria relating to the use of aspirin for the primary prevention of CVD in patients with diabetes were not considered as recommended by SIGN 116. Another two criteria were generated to include management of triglyceride levels in

diabetic patients that were imported from NICE guideline (CG 66). The overall criteria were agreed within the research group and added to the 2nd draft of the MAT (table 7).

#### 2.2.2.4 Clinical MAT validation in Qatar

To apply the above designed MAT within the clinical settings in Qatar, the head of diabetes clinic (Dr. Ziri, diabetes consultant, Hamad General Hospital, Qatar) was previously contacted and requested to give information about the current guidelines used there. Dr. Ziri informed that the currently used algorithm for management of type-2 DM in Qatar is the American Association of Clinical Endocrinologist/ American College of Endocrinology (AACE/ACE diabetes algorithm) for glycaemic control [85] as well as NICE guidelines. As this algorithm was previously checked at the design stage and found to meet the NICE and SIGN recommendations related to the use of anti-diabetic medications, draft 2 MAT directly entered the clinical validation stage in Qatar by the diabetes consultants.

In coordination with the head of the diabetes clinic, the researcher set an appointment with three diabetes consultants to carry-out a clinical expert group meeting in order to validate the 2nd draft of the MAT before its application. During meeting, a detailed explanation about the aims of the project and about the MAT methodology was given. A hard copy of the MAT containing the original structure was also provided. Consultants were asked to review each criterion within the MAT and decide whether they agreed or disagreed with its measurement, giving a reason if they disagreed or if they made any modification. Based on discussion with diabetes consultants, an updated $MAT_{Qat}$ was developed after this meeting.

#### 2.2.2.5 Clinical Validation in the UK

To use the above developed MAT ($MAT_{Qat}$) in the clinical settings within the UK, another expert group meeting was performed in Gartnavel Royal Hospital, Glasgow, UK. This group involved project supervisor, researcher, postgraduate researcher, lead for prescribing and clinical pharmacy- North West Sector of Glasgow city Community Health Partnerships (CHP) and prescribing support pharmacist- North West Sector of Glasgow CHP. Three weeks prior to the group meeting, the draft $MAT_{Qat}$ was sent to all the attendees in order to ensure familiarity with it. The group meeting lasted 2 hours and notes were taken. Recommendations for the final version of the MAT (to form $MAT_{UK}$) and future conduct of an audit were made. Figure 4 summaries stages of MAT drafting.

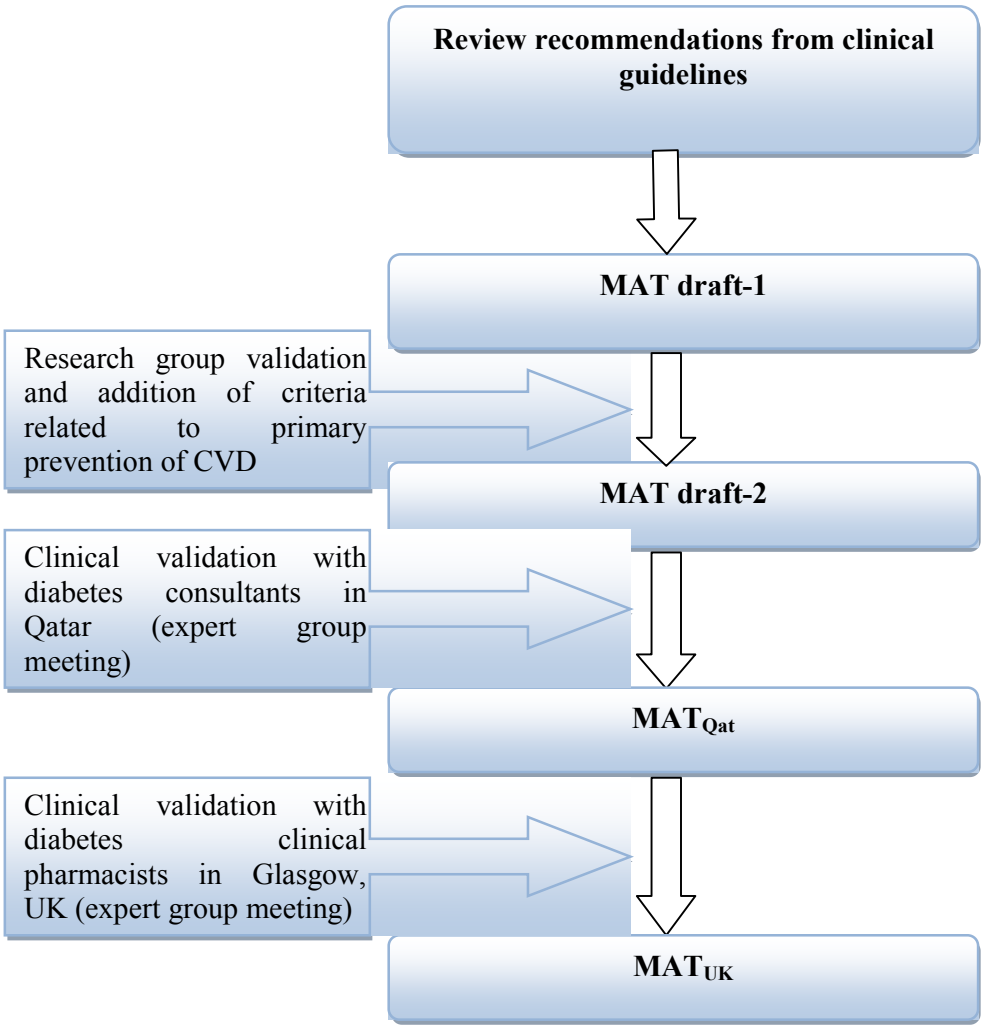


**Figure 4: Stages of MAT development**

## 2.3 Results

### 2.3.1 Drafting of the MAT

#### 2.3.1.1 MAT 1st draft

Table 5 lists the selected guideline recommendations after being adapted to meet the standard MAT structure as follows:

**Table 5: Adapted guideline recommendations (MAT draft-1)**

| **Indicators of appropriate drug treatment in diabetic patients as recommended in NICE (CG 66, 87 & 10) and SIGN (116) guidelines** | | | | | | | |
|---|---|---|---|---|---|---|---|
| *General criteria* | | | | | | | |
| **Patient diagnosed with DM** | **N/A** | **Yes** | **NO** | **J/U** | **ID(Q)** | **ID(S)** |
| **1** has the diagnosis supported by the presence of diabetes symptoms[1] plus one of the following:<br>❑ random venous plasma glucose concentration ≥11.1 mmol/l<br>❑ fasting plasma glucose concentration ≥ 7.0 mmol/l<br>❑ plasma glucose concentration ≥ 11.1 mmol/l two hours after 75g anhydrous glucose in an oral glucose tolerance test (OGTT)<br>❑ has at least one additional glucose test result on another day with a value in the diabetic range (either fasting, from a random sample or from the two hour post glucose load) in the absence of diabetes symptoms. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **2** offered a structured diabetes education programme with annual reinforcement and review as part of diabetes care | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **3** reached a good glycaemic control (HbA1c ideally around 6.5% [48 mmol/mol] at time of diagnosis or 7% [53 mmol/mol]). | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **4** **Patient with Impaired Fasting Glycaemia (IFG)[2]** has an OGTT to exclude the diagnosis of DM, and is actively managed with lifestyle advice [3] | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| *Disease management* | | | | | | | |
| **Patient on glucose lowering therapy** | | | | | | | |
| **5** has been involved in setting a target glycated haemoglobin $HbA_{1c}$ which should be measured<br>❑ every 6 month intervals — once the blood glucose level and blood glucose lowering therapy are stable)<br>❑ every 2-3 month intervals — when blood glucose lowering therapy need to be changed | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

**Table 5: Adapted guideline recommendations (MAT draft-1) continued**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **6** | has been started with non-pharmacological treatment (life-style measures)[3] | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **7** | has been started on metformin if he/she is overweight. | | | | | | |
| **8** | has been started with pharmacological treatment (if $HbA_{1c} \geq 6.5\%$ after trial of life-style measures) as follow | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| | First-line therapy<br>❑ Metformin — person who is overweight or obese[4]<br>❑ Sulfonylurea — ❑ person is not overweight; ❑ person does not tolerate or is contraindicated to metformin; ❑ if rapid response to therapy is required to mange the symptoms | | | | | | |
| **9** | has been started on second line therapy when blood glucose control remains or become inadequate ($HbA_{1c} \geq 6.5\%$) with the first-line therapy as follow: | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| | ❑ Metformin + Sulfonylurea — Inadequate control with metformin and life-style mesures.<br>❑ Metformin + DDP-4 inhibitor — If sulfonylurea are intolerated/ contraindicated or in person with significant risk of hypoglycaemia[5]<br>❑ Metformin + thiazolidinedione — If sulfonylurea are intolerated/ contraindicated or in person with significant risk of hypoglycaemia[5]<br>❑ Sulfonylurea + DDP-4 inhibitor or thiazolidinedione — Metformin was not tolerated/contraindicated<br>❑ Rapid acting insulin secretagogue — person with erratic (non-routine daily) life-style pattern<br>❑ Acarbos — If unable to use other oral glucose-lowering medication | | | | | | |

**Table 5: Adapted guideline recommendations (MAT draft-1) continued**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **10** | **Patient on second-line blood glucose lowering therapy and still have $HbA_{1c} \geq 7.5\%$** has been started on third-line therapy as follow:<br><br>❑ *thiazolidinedione* to combination of :<br>❑ metformin and sulfonylurea (when insulin is likely to be unacceptable or of reduced effectiveness)<br>❑ Metformin + DDP-4 inhibitor<br>❑ Sulfonylurea + DDP-4 inhibitor<br>or<br>❑ *gliptin* to combination of:<br>❑ metformin and sulfonylurea<br>❑ Metformin + thiazolidinedione<br>or<br>❑ *Exenatide* (to metformin and sulfonylurea ) when body weight is of concern (BMI >35 $kg/m^2$)<br>or<br>❑ *insulin* | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **Patients on metformin therapy** | | | | | | | |
| **11** | have the dose stepped-up gradually according to blood glucose measurements over 10-15 days to minimise risk of gastrointestinal side effects. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **12** | Have their renal function been checked before initiating the treatment and regularly thereafter at least<br><br>❑ annually in patients with normal renal function<br>❑ 2-4 times a year in patients with serum creatinine levels at upper limit of normal and in elderly | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **13** | have their treatment stopped if serum creatinine >150 micromol/l or the eGFR is <30 ml/min/1.73 $m^2$ | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **14** | **Patient on Sulfonylurea therapy** has been educated about the risk of hypoglycaemia | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **Patient prescribed a thiazolidinedione** | | | | | | | |
| **15** | has no evidence of heart failure or at high risk of fracture. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **16** | has been warned about the possibility of significant oedema and advised on the action to take if develops | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **17** | has continued the therapy only if a metabolic response (reduction of at least 0.5 percentage points in $HbA_{1c}$ in 6 months) | | | | | | |
| **18** | **Patient started on insulin therapy** has continued with metformin and sulfonylurea (if used) and has reviewed the use of sulfonylurea if hypoglycaemia occurs | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **19** | **Patient with type 2 diabetes on insulin** has previously received oral glucose lowering therapy. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **20** | **Patient on exenatide or liraglutide** has a BMI>30 $kg/m^2$. (SIGN 116) | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

**Table 5: Adapted guideline recommendations (MAT draft-1) continued**

*Management of disease complications*

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Blood pressure control** | | | | | | | | |
| **21** | **Patient diagnosed with diabetes** had blood pressure measured<br>❑ annually — in person without previously diagnosed hypertension or renal disease.<br>In person on antihypertensive therapy<br>❑ monthly — with BP>150/90 mmHg<br>❑ in 2 months — with BP>140/80 mmHg or if BP>130/80 and there is kidney, eye, or cerebrovascular damage<br>❑ 4-6 months — in person who has attained and consistently remained at the pressure target | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **22** | **Patient diagnosed with diabetes and have a high blood pressure** offered angiotensin converting enzyme inhibitors (ACEI) or angiotensin II-receptor antagonist (ARB) as first-line[6] blood pressure lowering therapy | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **23** | reached blood pressure target (<140/80 mmHg or <130/80 mmHg if there is kidney, eye, or cerebrovascular damage) | | | | | | |
| **24** | had a calcium channel blocker or a diuretic added to therapy if blood pressure is not reduced to target with first-line therapy (or both if the target is not reached with dual therapy) | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **25** | had an alpha-blocker, a beta-blocker or potassium-sparing diuretic added to therapy if blood pressure is not reduced to target with triple therapy | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **Kidney damage control** | | | | | | | | |
| **26** | **Diabetic patient with or without detected nephropathy** had a first-pass urine specimen checked annually for albumin:creatinine ratio (in the absence of proteinuria/UTI) | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **27** | had serum creatinine and estimated glomerular filtration rate checked annually | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **28** | **Patient with microalbuminuria** had the condition confirmed after three repeated albumin:creatinine ratio tests (>2.5 mg/mmol for men, >3.5 mg/mmol for women) | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **29** | started on ACE-inhibitors (or on angiotensin II-receptor antagonist if ACE-inhibitors are not tolerated) | | | | | | |
| **Eye damage control** | | | | | | | | |
| **30** | **Patient with diabetes** performed eye screening at or around the time of diagnosis and has arranged repeat of structured eye surveillance annually. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **31** | Maintained on $HbA_{1c}$ around 7% and blood pressure <130/80 mm Hg to prevent onset and progression of diabetic eye disease. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

**Table 5: Adapted guideline recommendations (MAT draft-1) continued**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Nerve damage control** | | | | | | | |
| **32** | **Patient without neuropathic symptoms** has been checked for neuropathic symptoms and its severity[7] annually | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **33** | **Patient with neuropathic symptoms** has been offered a trial of tricyclic medication and advised to maintain blood glucose control. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **34** | has been offered a trial of duloxetine, gabapentin or pregabalin if the symptoms are not controlled with tricyclic medication | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **35** | reviewed for opiate analgesia, pain clinic referral and psychological support if a trial of another duloxetine, gabapentin or pregabalin failed to control the symptoms | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **Diabetic foot control** | | | | | | | |
| **36** | **Patient with diabetes** has been assessed and screened for the risk of developing foot ulcer and had the results analysed using an online screening tool | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **37** | **Diabetic patient with low current risk of foot ulcers (normal sensation, palpable pulses)** has been offered an appropriate foot care education and minimise self-harm | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **38** | **Diabetic patient with increased risk of foot ulcers (neuropathy or absence of pulses)** has been referred to a foot protection team and arranged regular review, 3-6 monthly. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **39** | **Diabetic patient with high risk of foot ulcer (neuropathy or absence of pulses+deformity or skin changes or previous ulcer** has been referred to a foot protection team and arranged frequent review, 1-3 monthly. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

**N/A**: not applicable; **No**: unjustified deviation from the guideline, **No (j):** justified deviation from the guideline; **ID (s):** insufficient data to assess the applicable criterion; **ID (q):** Insufficient data to assess criterion applicability; **CI**: confidence interval.

Bold qualifier statements indicate patient's applicability to the relevant standard statement criterion.

[1] Diabetes symptoms: polyuria, polydipsia, weakness or fatigue and unexplained weight loss.

[2] Impaired Fasting Glycaemia: fasting glucose values above the normal range, but below those diagnostic of diabetes (Fasting plasma glucose ≥ 6.1 mmol/l but < 7.0 mmol/l).

[3] Advice on healthy balanced eating (encourage high-fibre, low glycaemic index sources of carbohydrate in the diet, such as fruit, vegetables, wholegrains and pulses; include low-fat dairy products and oily fish; and control the intake of foods containing saturated fatty acids. Lifestyle modification, such as increasing physical activity and losing weight (target, for people who are overweight, an initial body weight loss of 5–10%, lesser degrees of weight loss may still be of benefit). Individualise recommendations for carbohydrate and alcohol intake, and meal patterns.

[4] Metformin can still be considered as an option for first-line therapy for a person who is not overweight.

[5] Older people and people in certain jobs (those working at heights or with heavy machinery) or in certain social circumstances (living alone).

[6] The first-line blood pressure-lowering therapy for a person of African-Caribbean descent should be an ACE-inhibitor plus either a diuretic or generic calcium channel blocker. Furthermore, calcium channel blocker should be the first-line blood pressure lowering

therapy for a woman agreed becoming pregnant.

[7] neuropathic symptoms include paraesthesia, burning or tingling sensation and shooting pain. Symptoms severity can be assessed if sleep disturbances, depression, and interference with normal activities are present.

#### 2.3.1.2 Research group validation of MAT draft-1

The first draft of the MAT included a total of 39 criteria focusing on type 2 DM diagnosis, non-pharmacological and pharmacological management of the disease itself and its complications. This draft was first validated by the research group and had many changes following a considerable amount of time and number of meetings.

The modifications of this draft involved the decision to remove 13 criteria. Of these criteria, 7/13 were thought to be more related to diagnostic purposes and did not meet the rationale of the MAT in measuring appropriate medication use (criterion 1, 4, 28, 36, 37, 38 & 39). Another 2/13 criteria were thought to be difficult to apply as the data items needed to determine the applicability (qualifying statement) or the standards of these criteria may not be documented or would require going back to very old records to obtain them (criterion 6 & 11). The remaining 4/13 criteria were found to be too detailed and more related to patient educational needs during sulfonylurea or thiazolidinedione therapy and the use of hypertension treatment algorithm for the management of hypertensive patients (criterion 14, 16, 24 & 25). The research group has also modified the remaining 26 criteria to achieve the standards mentioned in part 2.4.3 above.

The last meeting of the research group involved the selection of the primary prevention of CVD criteria and the approval of the two new added criteria related to management of triglyceride level in diabetic patients. While selecting the primary prevention of CVD criteria, any criterion related to the one following subjects were not included in the drafted MAT:

- Criteria related to secondary prevention of CVD as it deviated from the study aims.

- Criteria related to the use of aspirin or clopidogrel for the primary prevention of CVD in diabetic patients as it was not recommended any more by SIGN guidelines. Although the use of aspirin is still recommended by NICE guidelines to manage the high CV risk, it was not considered for audit based

on the research group decision that SIGN guidelines would overwrite NICE guidelines on the recommendations from NICE guidelines conflicting with others from SIGN guidelines as it was the most recent guideline.

- Criteria related to the use of statin based on CVD risk calculators as patients with diabetes are considered at a high risk of developing CVD and a statin should be prescribed for those aged > 40 years regardless their CVD risk score.

During this meeting MAT-draft 2 comprising a total of 38 measurable criteria was achieved. Moreover, the research group decided to separate the MAT into three tables with three new sub-headings ranked alphabetically from A to C as follows:

- **A**: assessing the appropriate control of blood glucose.
- **B:** assessing the appropriate management of diabetes complications.
- **C:** assessing the appropriate use of primary prevention of CVD.

Table 6 summarises the changes to MAT draft-1 made by the research group to generate MAT draft-2.

**Table 6: Modifications made to the first MAT draft**

| | Draft criterion | Modified criterion | comment |
|---|---|---|---|
| **Patient diagnosed with DM:** | | | |
| **1** | has the diagnosis supported by the presence of diabetes symptoms plus one of the following<br>❑ random venous plasma glucose concentration ≥11.1 mmol/l<br>❑ fasting plasma glucose concentration ≥ 7.0 mmol/l<br>❑ plasma glucose concentration ≥ 11.1 mmol/l two hours after 75g anhydrous glucose in an oral glucose tolerance test (OGTT)<br>❑ has at least one additional glucose test result on another day with a value in the diabetic range (either fasting, from a random sample or from the two hour post glucose load) in the absence of diabetes symptoms. | **Removed** | The research group decided to remove this criterion as it was related more to diagnostic purposes |
| **2** | offered a structured diabetes education programme with annual reinforcement and review as part of diabetes care | **Patient with type 2 diabetes** should have been invited to join a structured diabetes education programme | Rephrased |
| **3** | reached a good glycaemic control (HbA1c ideally around 6.5% [48 mmol/mol] at time of diagnosis or 7% [53 mmol/mol]). | **Patient with type 2 diabetes** should have an $HbA_{1c}$ recorded at ≤ 6.5% as their most recent value.<br>[Exceptions are patients who have had a change in glucose lowering therapy within the past 3 months or where a reason (*justification)* is provided in the case notes] | Rephrased to define the exact HbA1c value |
| **4** | **Patient with Impaired Fasting Glycaemia (IFG)[2]** has an OGTT to exclude the diagnosis of DM, and is actively managed with lifestyle advice [3] | **Removed** | The research group decided to remove this criterion as it was related more to diagnostic purposes |
| | *Disease management* | | |
| **Patient on glucose lowering therapy** | | | |
| **5** | has been involved in setting a target glycated haemoglobin $HbA_{1c}$ which should be measured :<br>❑ every 6 month intervals (once the blood glucose level and blood glucose lowering therapy are stable)<br>❑ every 2-3 month intervals (when blood glucose lowering therapy need to be changed | **Patient with type 2 diabetes should have** a recorded target Hb $A_{1c}$.<br>a record of at least two $HbA_{1c}$ measurements in the previous 15 months | Rephrased to simplify application. 15 months used to avoid missed results from very recent tests. |

**Table 6: Modifications made to the first MAT draft-continued**

| | | | |
|---|---|---|---|
| **6** | has been started with non-pharmacological treatment (life-style measures) | **Removed** | The research group decided to remove this criterion as it may not be auditable (not documented or needs to go back to very old records) |
| **7** | has been started on metformin if he/she is overweight. | **Patient with type 2 diabetes with BMI ≥25 kg/m$^2$** is on metformin | Rephrased to define overweight. |
| **8** | has been started with pharmacological treatment (if $HbA_{1c} \geq 6.5\%$ after trial of life-style measures) as follow:<br><br>First-line therapy:<br>❑ Metformin — person who is overweight or obese<br>❑ Sulfonylurea — ❑ person is not overweight; ❑ person does not tolerate or is contraindicated to metformin; ❑ if rapid response to therapy is required to mange the symptoms | **Patient with type 2 diabetes on glucose lowering agent(s)** is on metformin or sulphonylurea. | Rephrased to simplify application |
| **9** | has been started on second line therapy when blood glucose control remains or become inadequate ($HbA_{1c} \geq 6.5\%$) with the first-line therapy as follow:<br><br>❑ Metformin + Sulfonylurea — Inadequate control with metformin and life-style mesures.<br>❑ Metformin + DDP-4 inhibitor — If sulfonylurea are intolerated/ contraindicated or in person with significant risk of hypoglycaemia<br>❑ Metformin + thiazolidinedione — If sulfonylurea are intolerated/ contraindicated or in person with significant risk of hypoglycaemia[5]<br>❑ Sulfonylurea + DDP-4 inhibitor or thiazolidinedione — Metformin was not tolerated/contraindicated<br>❑ Rapid acting insulin secretagogue — person with erratic (non-routine daily) life-style pattern<br>❑ Acarbos — If unable to use other oral glucose-lowering medication | **Patient with type 2 diabetes on glucose lowering agent (s) and with a stable $HbA_{1c}$ measurement ≥6.5%** is on more than one agent.<br><br>**Patients on a gliptin, pioglitazone or a glinide** is co-prescribed metformin or a sulphonylurea. (*Exception is a patient for whom both metformin/sulphonylurea are contra-indicated or not tolerated)* | .Rephrased to promote, simplify analysis and to define applicability |

**Table 6: Modifications made to the first MAT draft-continued**

| | | | |
|---|---|---|---|
| **10** | **Patient on second-line blood glucose lowering therapy and still have $HbA_{1c}$ ≥7.5%** has been started on third-line therapy as follow:<br><br>❑ *thiazolidinedione* to combination of :<br>❑ metformin and sulfonylurea (when insulin is likely to be unacceptable or of reduced effectiveness)<br>❑ Metformin + DDP-4 inhibitor<br>❑ Sulfonylurea + DDP-4 inhibitor<br>or<br>❑ *gliptin* to combination of:<br>❑ metformin and sulfonylurea<br>❑ Metformin + thiazolidinedione<br>or<br>❑ *Exenatide* (to metformin and sulfonylurea ) when body weight is of concern (BMI >35 kg/$m^2$)<br>or<br>❑ *insulin* | **Patient with a stable $HbA_{1c}$ measurement ≥7.5%** should be on a third oral agent - a gliptin, glinide or pioglitazone, or prescribed exenatide.<br><br>**Patient on two or a three oral glucose lowering agents** is co-prescribed metformin and/or a sulphonylurea<br><br>**Patient with a stable $HbA_{1c}$ measurement ≥7.5 despite oral glucose lowering therapy** has been started on Insulin<br><br>**Patients on agents added to metformin and/or sulphonylurea-gliptin, acarbose, pioglitazone or a glinide-** are not on more than three oral agents. | Rephrased to promote, simplify analysis and to define applicability |
| **Patients on metformin therapy** | | | |
| **11** | have the dose stepped-up gradually according to blood glucose measurements over 10-15 days to minimise risk of gastrointestinal side effects. | **Removed** | The research group decided to remove this criterion as it may be difficult to audit (requires going back to very old records) |
| **12** | Have their renal function been checked before initiating the treatment and regularly thereafter at least<br><br>❑ annually in patients with normal renal function<br>❑ 2-4 times a year in patients with serum creatinine levels at upper limit of normal and in elderly | **Patients on metformin therapy** have an estimated GFR is >45 ml/min/1.73 $m^2$<br><br>**Patients on metformin therapy and an estimated GFR ≤45 ml/min/1.73 $m^2$** have had their renal function measured within the past 12 months | Rephrased to simplify analysis and to define GFR values. |
| **13** | have their treatment stopped if serum creatinine >150 micromol/l or the eGFR is <30 ml/min/1.73 $m^2$ | **Patients on metformin therapy** do not have a current estimated GFR <30 ml/min/1.73 $m^2$ | Rephrased to simplify analysis |
| **14** | **Patient on Sulfonylurea therapy** has been educated about the risk of hypoglycaemia | **Removed** | Detailed criterion and related more to patient educational needs |
| **Patient prescribed a thiazolidinedione** | | | |
| **15** | Has no evidence of heart failure or at high risk of fracture. | does not have heart failure.<br><br>does not have osteoporosis | Rephrased to simplify analysis, determine standard, and to define high risk of fracture |
| **16** | has been warned about the possibility of significant oedema and advised on the action to take if develops | **Removed** | Detailed criterion and related to patient educational needs |

**Table 6: Modifications made to the first MAT draft-continued**

| | | | |
|---|---|---|---|
| **17** | Has continued the therapy only if a metabolic response (reduction of at least 0.5 percentage points in $HbA_{1c}$ in 6 months) | **Patient on a thiazolidinedione (pioglitazone) and receiving it for >6 months** has evidence that it has reduced $HbA_{1c}$ by $\geq 0.5\%$. | Rephrased to simplify analysis |
| **18** | **Patient started on insulin therapy** has continued with metformin and sulfonylurea (if used) and has reviewed the use of sulfonylurea if hypoglycaemia occurs | **Patient with type 2 diabetes previously on oral glucose lowering agent(s) and now on insulin therapy** continues to be prescribed the previous oral therapy (metformin/ sulphonylurea). | Rephrased to simplify analysis |
| **19** | **Patient with type 2 diabetes on insulin** has previously received oral glucose lowering therapy. | **Patient with type 2 diabetes on insulin** has previously received oral glucose lowering therapy | Not changed |
| **20** | **Patient on exenatide or liraglutide** has a BMI>30 kg/m$^2$. | **Patient on exenatide or liraglutide** has a BMI>30 kg/m$^2$ | Not changed |
| | *Management of disease complications* | | |
| **Blood pressure control** | | | |
| **21** | **Patient diagnosed with diabetes** had blood pressure measured<br>❑ annually in person without previously diagnosed hypertension or renal disease.<br>In person on antihypertensive therapy<br>❑ monthly with BP>150/90 mmHg<br>❑ in 2 months with BP>140/80 mmHg or if BP>130/80 and there is kidney, eye, or cerebrovascular damage<br>❑ 4-6 months in person who has attained and consistently remained at the pressure target | **Patient with diabetes** has had their blood pressure measured within the past 15 months. | Rephrased to simplify analysis |
| **22** | **Patient diagnosed with diabetes and have a high blood pressure** offered ACE-inhibitors (or angiotensin II-receptor antagonist) as first-line[6] blood pressure lowering therapy | **Patient diagnosed with hypertension** is prescribed an ACE Inhibitor or angiotensin II-receptor antagonist (ARB). | Rephrased to simplify analysis |
| **23** | reached blood pressure target (<140/80 mmHg or <130/80 mmHg if there is kidney, eye, or cerebrovascular damage) | **Patient who is diagnosed as hypertensive and is prescribed antihypertensive drug therapy** has achieved BP < 140/80 mmHg.<br>**Patient with treated hypertension and with co-existing kidney, eye or cerebrovascular damage** has achieved a blood pressure level < 130/80 mmHg. | Rephrased to simplify analysis and to allow measurement of the standard statement |
| **24** | had a calcium channel blocker or a diuretic added to therapy if blood pressure is not reduced to target with first-line therapy (or both if the target is not reached with dual therapy) | **removed** | Detailed criterion and related more to management of hypertension |

**Table 6: Modifications made to the first MAT draft-continued**

| | | | |
|---|---|---|---|
| **25** | had an alpha-blocker, a beta-blocker or potassium-sparing diuretic added to therapy if blood pressure is not reduced to target with triple therapy | **removed** | Detailed criterion and related more to management of hypertension |
| **Kidney damage control** | | | |
| **26** | **Diabetic patient with or without detected nephropathy** had a first-pass urine specimen checked annually for albumin:creatinine ratio (in the absence of proteinuria/UTI) | **Patient with diabetes** has had renal function (serum creatinine/ eGFR) or microalbuminuria checked within the past 15 months. | Rephrased to simplify analysis |
| **27** | had serum creatinine and estimated glomerular filtration rate checked annually | | |
| **28** | **Patient with microalbuminuria** had the condition confirmed after three repeated albumin:creatinine ratio tests (>2.5 mg/mmol for men, >3.5 mg/mmol for women) | **removed** | The research group decided to remove this criterion as it was related more to diagnostic purposes |
| **29** | started on ACE-inhibitors (or on angiotensin II-receptor antagonist if ACE-inhibitors are not tolerated) | **Patient with microalbuminuria or proteinuria** is prescribed an ACE inhibitor or an ARB. | Rephrased to promote, simplify analysis and to define applicability |
| **Eye damage control** | | | |
| **30** | **Patient with diabetes** performed eye screening at or around the time of diagnosis and has arranged repeat of structured eye surveillance annually. | **Patient with diabetes** has had retinal examination within the past 15 months | Rephrased to simplify analysis |
| **31** | Maintained on $HbA_{1c}$ around 7% and blood pressure <130/80 mm Hg to prevent onset and progression of diabetic eye disease. | **removed** | Repetition |
| **Nerve damage control** | | | |
| **32** | **Patient without neuropathic symptoms** has been checked for neuropathic symptoms and its severity[7] annually | **Patient with diabetes** has had neuropathy/ foot check in the past 15 months. | Rephrased to promote, simplify analysis |
| **33** | **Patient with neuropathic symptoms** has been offered a trial of tricyclic medication and advised to maintain blood glucose control. | **Patient diagnosed with diabetic neuropathy** is prescribed a tricyclic antidepressant, gabapentin, pregabalin or duloxetine. | |
| **34** | has been offered a trial of duloxetine, gabapentin or pregabalin if the symptoms are not controlled with tricyclic medication | | |
| **35** | reviewed for opiate analgesia, pain clinic referral and psychological support if a trial of another duloxetine, gabapentin or pregabalin failed to control the symptoms | | |

**Table 6: Modifications made to the first MAT draft-continued**

| | | | |
|---|---|---|---|
| **Diabetic foot control** | | | |
| **36** | **Patient with diabetes** has been assessed and screened for the risk of developing foot ulcer and had the results analysed using an online screening tool | **removed** | The research group decided to remove these criteria as they were detailed and related more to diagnostic purposes |
| **37** | **Diabetic patient with low current risk of foot ulcers (normal sensation, palpable pulses)** has been offered an appropriate foot care education and minimise self-harm | **removed** | |
| **38** | **Diabetic patient with increased risk of foot ulcers (neuropathy or absence of pulses)** has been referred to a foot protection team and arranged regular review, 3-6 monthly. | **removed** | |
| **39** | **Diabetic patient with high risk of foot ulcer (neuropathy or absence of pulses+deformity or skin changes or previous ulcer** has been referred to a foot protection team and arranged frequent review, 1-3 monthly. | **removed** | |

**MAT**: medication assessment tool, **DM**: diabetes mellitus, **TC**: total cholesterol, **BP**: blood pressure

Bold qualifier statements indicate patient's applicability to the relevant standard statement criterion

## Table 7: Primary prevention of CVD criteria

| | | | |
|---|---|---|---|
| **1** | **Patient who is diagnosed with hypertension and is prescribed antihypertensive drug therapy** is not prescribed a combination of thiazide diuretic and beta-blocker | **Taken from existing MAT** | Checked against updated guidelines |
| **2** | **Patient with hypertension** has a treatment plan that excludes the following drugs<br>Corticosteroids (except inhaled or topical) / Sympathomimetics (except inhaled beta 2- agonists)<br>Oral contraceptives / Monoamine-oxidase inhibitor<br>NSAIDS (except aspirin as anti-platelet) / Carbenoxolone<br>High sodium-containing products (effervescent formulations) | **Taken from existing MAT** | Checked against updated guidelines |
| **3** | **Patient with diabetes aged >40** is prescribed a statin | **Taken from existing MAT** | Checked against updated guidelines |
| **4** | **Patient maintained on the same dose of a statin for >6 weeks** has achieved a re-test total cholesterol level of < 5 mmol/l | **Taken from existing MAT** | Checked against updated guidelines |
| **5** | **Patient prescribed a simvastatin or atorvastatin** not co-prescribed macrolide antibiotics (erythromycin, clarithromycin) or ketoconazole or itraconazole | **Taken from existing MAT** | Checked against updated guidelines |
| **6** | **Patient with a triglyceride level > 4.5mmol/L (whether on a statin or not)** is prescribed a fibrate | **Newly added criterion (NICE, CG 66)** | Approved by research group |
| **7** | **Patient with triglyceride level of 2.3-4.5 mmol/L despite statin therapy** is prescribed a fibrate | **Newly added criterion (NICE, CG 66)** | Approved by research group |
| **8** | **Patient who continues to smoke** has been offered smoking cessation advice which either involves structured behavioural support and nicotine replacement therapy or bupropion | **Taken from existing MAT** | Checked against updated guidelines |

**MAT**: medication assessment tool, **CVD**: cardiovascular disease

Bold qualifier statements indicate patient's applicability to the relevant standard statement criterion

### 2.3.1.3 MAT draft-2

The above modified criteria were collected into one table (table 8) and re-arranged under the new sub-headings and the modified format as follows:

**Table 8: MAT draft-2**

| **Indicators of appropriate drug treatment in Diabetic patients as recommended in NICE (CG 66, 87 & 10) and SIGN (116) guidelines** | | | | | | | |
|---|---|---|---|---|---|---|---|
| **A** | **Control of Blood Glucose** | | | | | | |
| **Patient with type 2 diabetes** should have | | | | | | | |
| | | **N/A** | **Yes** | **NO** | **NOJ/U** | **ID(Q)** | **ID(S)** |
| **1** | been invited to join a structured diabetes education programme. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **2** | a recorded target Hb $A_{1c}$. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **3** | a record of at least two $HbA_{1c}$ measurements in the previous 15 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **4** | an $HbA_{1c}$ recorded at ≤6.5 % as their most recent value[1]. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **5** | **Patient with type 2 diabetes on glucose lowering agent(s)** is on metformin or sulphonylurea[2]. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **6** | **Patient with type 2 diabetes on glucose lowering agent (s) and with a stable $HbA_{1c}$ measurement ≥6.5%** is on more than one agent. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **7** | **Patients on glucose lowering agents added to metformin and/or sulphonylurea - a gliptin, acarbose, pioglitazone or a glinide-** are not on more than three oral agents. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **8** | **Patients on a gliptin, pioglitazone or a glinide** is co-prescribed metformin or a sulphonylurea[2]. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **9** | **Patient with a stable $HbA_{1c}$ measurement ≥7.5%** should be on a third oral agent - a gliptin, pioglitazone, a glinide, or prescribed exenatide | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **10** | **Patient with type 2 diabetes with BMI ≥25 $kg/m^2$** is on metformin. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **11** | **Patients on metformin therapy** have an estimated GFR is >45 ml/min/1.73 $m^2$ | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **12** | **Patients on metformin therapy and an estimated GFR ≤45 ml/min/1.73 $m^2$** have had their renal function measured within the past 12 months | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **13** | **Patients on metformin therapy** do not have a current estimated GFR <30 ml/min/1.73 $m^2$ | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **14** | **Patient on two or a three oral glucose lowering agents** is co-prescribed metformin and/or a sulphonylurea[2]. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

**Table 8: MAT draft-2 -continued**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **15** | **Patient with type 2 diabetes on insulin** has previously received oral glucose lowering therapy. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **16** | **Patient with a stable $HbA_{1c}$ measurement ≥7.5 despite oral glucose lowering therapy[3]** has been started on Insulin | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **17** | **Patient on exenatide or liraglutide** has a BMI>30 $kg/m^2$. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **Patient on a thiazolidinedione (pioglitazone)** | | | | | | | |
| **18** | does not have heart failure. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **19** | does not have osteoporosis. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **20** | **Patient on a thiazolidinedione (pioglitazone) and receiving it for >6 months** has evidence that it has reduced $HbA_{1c}$ by ≥ 0.5%. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **21** | **Patient with type 2 diabetes previously on oral glucose lowering agent(s) and now on insulin therapy** continues to be prescribed the previous oral therapy (metformin/ sulphonylurea). | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **B** | **Management of Diabetes Complications** | | | | | | |
| **Kidney Disease** | | | | | | | |
| **22** | **Patient with microalbuminuria or proteinuria** is prescribed an ACE inhibitor or an ARB. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **23** | **Patient with diabetes** has had renal function (serum creatinine/eGFR) or microalbuminuria checked within the past 15 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **Retinopathy** | | | | | | | |
| **24** | **Patient with diabetes** has had retinal examination within the past 15 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **Neuropathy/foot disease** | | | | | | | |
| **25** | **Patient with diabetes** has had neuropathy/ foot check in the past 15 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **26** | **Patient diagnosed with diabetic neuropathy** is prescribed a tricyclic antidepressant, gabapentin, pregabalin or duloxetine. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **C** | **Primary prevention of CVD** | | | | | | |
| **27** | **Patient with diabetes** has had their blood pressure measured within the past 15 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **28** | **Patient diagnosed with hypertension** is prescribed an ACE Inhibitor or angiotensin II-receptor antagonist (ARB). | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **29** | **Patient who is diagnosed as hypertensive and is prescribed antihypertensive drug therapy** has achieved BP < 140/80 mmHg. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **30** | **Patient with treated hypertension and with co-existing kidney, eye or cerebrovascular damage** has achieved a blood pressure level < 130/80 mmHg. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **31** | **Patient who is diagnosed with hypertension and is prescribed antihypertensive drug therapy** is not prescribed a combination of thiazide diuretic and beta-blocker | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

**Table 8: MAT draft-2 -continued**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **32** | **Patient with hypertension** has a treatment plan that excludes the following drugs<br>Corticosteroids (except inhaled or topical) — Sympathomimetics (except inhaled beta 2- agonists)<br>Oral contraceptives — Monoamine-oxidase inhibitor<br>NSAIDS (except aspirin as anti-platelet) — Carbenoxolone<br>High sodium-containing products (effervescent formulations) | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **33** | **Patient with diabetes aged >40** is prescribed a statin | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **34** | **Patient maintained on the same dose of a statin for >6 weeks** has achieved a re-test total cholesterol level of < 5 mmol/l | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **35** | **Patient prescribed a simvastatin or atorvastatin** not co-prescribed macrolide antibiotics (erythromycin, clarithromycin) or ketoconazole or itraconazole | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **36** | **Patient with a triglyceride level > 4.5mmol/L (whether on a statin or not)** is prescribed a fibrate | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **37** | **Patient with triglyceride level of 2.3-4.5 mmol/L despite statin therapy** is prescribed a fibrate | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **38** | **Patient who continues to smoke** has been offered smoking cessation advice which either involves structured behavioural support and nicotine replacement therapy or bupropion | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

**N/A**: not applicable; **No**: unjustified deviation from the guideline, **No (j):** justified deviation from the guideline; **ID (s):** insufficient data to assess the applicable criterion; **ID (q):** Insufficient data to assess criterion applicability; **CI**: confidence interval.

Bold qualifier statements indicate patient's applicability to the relevant standard statement criterion.

[1] *Exceptions are patients who have had a change in glucose lowering therapy within the past 3 months or where a reason (justification) is provided in the case notes*

[2] *Exception is a patient for whom both metformin/sulphonylurea are contra-indicated or not tolerated*

[3] *when the use of two or three oral glucose lowering agent not achieved the appropriate HbA1c level*

#### 2.3.1.4 $MAT_{Qat}$ draft

As the aim of this project was to design a MAT to be used within the clinical settings in Qatar, draft-2 of the MAT entered the second validation phase with three diabetes consultants including the head of diabetes clinic at Hamad General Hospital, Qatar. Pharmacists were not involved at this stage as they have no role in the management of diabetic patients and were not part of the multidisplinary team in the management of diabetes. The role of pharmacist was just dispensing patients' medication according to doctors' prescriptions.

During this meeting the expert group approved most of the content of the MAT. However, five criteria (from MAT draft-2 which entered this validation phase) raised discussion during the meeting. These criteria were:

- Criterion 2 (setting and recording a target HbA1c for each patient with type-2 DM): the point raised by doctors during the validation of this criterion was that they do not set an individual target for HbA1c and are using a general target of 7% for all patients. However, as HbA1c targets can range from 6.5% in some patients to 7% or more in other patients, the researcher highlighted the importance of setting and recording an individual HbA1c target as recommended by the guidelines in order to balance benefits with harms, in particular hypoglycaemia and weight gain. Therefore, the expert group agreed to keep this criterion to highlight it and for it to be considered in the future.

- Criterion 4 (achieving an HbA1c value of ≤6.5% in patients with type-2 DM with an exception of *patients who have had a change in glucose lowering therapy within the past 3 months or where a reason (justification) is provided in the case notes*): the HbA1c value in this criterion (≤6.5%) was determined using NICE and SIGN guidelines and met the AACE/ACE recommendation. However, during the validation of this criterion and according to their experience, doctors considered this value too strict and difficult to achieve in all patients. Furthermore, doctors though that a value of 7% would be still acceptable. Consequently and as SIGN guidelines would still consider an HbA1c value of 7% reasonable to reduce risk of microvascular and

macrovascular disease among type-2 diabetes patients, this value was changed to be ≤ 7%.

- Criterion 6 (Patient with type 2 diabetes on glucose lowering agent and with a stable $HbA_{1c}$ measurement ≥6.5% is on more than one agent): as mentioned for criterion 4, doctors accept an HbA1c value of 7% and would not recommend any change in therapy unless HbA1c exceeded 7%. Therefore, criterion 6 modified and accepted.

- Criterion 12 (Patient on metformin therapy and an estimated GFR ≤45 ml/min/1.73 $m^2$ have had renal function measured within the past 12 months): Doctors prefer to avoid metformin and not to prescribe it at all in patients with GFR ≤45 ml/min/1.73 $m^2$. Therefore, it was agreed to keep this criterion without any change in order to identify if there is any patient with a GFR ≤45 ml/min/1.73 $m^2$ and is receiving metformin.

- Criterion 23 (Patient with diabetes has had renal function (serum creatinine/eGFR) or microalbuminuria checked within the past 15 months): Doctors thought that more frequent renal function tests should be performed and prefer its measurement every 6 months. The researcher here explained that 15 months was determined by the research group as follows: 12 months to cover annual check-up (which is the recommended period for check up by guidelines) + 3 months to avoid any missed results from recently requested tests. However, doctors still thought that especially for renal function measurement 15 months is a long period and recommended its change to be 12 months instead.

Only 3 criteria were modified and agreed during the meeting. These criteria were criterion 4, 6 and 23 as follows:

| Criterion # | Criterion from draft-2 | Modified criterion | comments |
|---|---|---|---|
| **4** | **Patient with type 2 diabetes** should have an $HbA_{1c}$ recorded at ≤ 6.5% as their most recent value. | **Patient with type 2 diabetes** should have an $HbA_{1c}$ recorded at ≤7 % as their most recent value. | Doctors consider an HbA1c value of ≤6.5 is very strict and consider a value of 7% would be acceptable. So the cut-off was modified accordingly. |
| **6** | **Patient with type 2 diabetes on glucose lowering agent (s) and with a stable $HbA_{1c}$ measurement ≥6.5%** is on more than one agent. | **Patient with type 2 diabetes on glucose lowering agent (s) and with a stable $HbA_{1c}$ measurement > 7%** is on more than one agent. | Doctors consider an HbA1c value of ≥6.5% is very strict and they changed it to >7%. |
| **23** | **Patient with diabetes** has had renal function (serum creatinine/eGFR) checked within past 15 months | **Patient with diabetes** has had renal function (serum creatinine/eGFR) checked within the past 12 months. | Doctors consider 15 months as a very long period to check renal function and reduced it to 12 months. |

#### 2.3.1.5 $MAT_{UK}$ draft

As another part of the aims of this project was to use the designed MAT within the clinical settings in the UK for comparative reasons between type-2 diabetes management in Qatar and in the UK, the MAT draft achieved for application in Qatar ($MAT_{Qat}$) entered the third validation phase which involved an expert group meeting performed in Gartnavel Royal Hospital, Glasgow, UK with two clinical members: the lead for prescribing and clinical pharmacy- North West Sector of Glasgow city Community Health Partnerships (CHP) and prescribing support pharmacist- North West Sector of Glasgow CHP. The two clinical members received the $MAT_{Qat}$ previously by e-mail and reviewed it in depth against published guidelines. During this meeting the expert group approved the content of $MAT_{Qat.}$ However, the in depth review of the MAT by the clinical team raised the following discussion:

- Criterion 18 (Patient on a thiazolidinedione (pioglitazone) does not have heart failure): the two clinical members asked to add another contraindication with regard to pioglitazone. Patients with current or history of bladder cancer or patients with uninvestigated haematuria should not be prescribed pioglitazone. However, these contraindications were not added to the MAT. The reason for not including them was explained by the researcher during the meeting. Although these contraindications are true about pioglitazone, none of the latest

guidelines (SIGN 116 or NICE CG66 & 78) mentioned these. The MAT has been developed exclusively from guidelines recommendations. Adding in further contraindications would deviate from MAT methodology.

- Criterion 19 (Patient on a thiazolidinedione (pioglitazone) does not have osteoporosis): the two clinical members asked about the reason behind using the term osteoporosis instead of high risk of fractures. It was explained that the term high risk of fractures is a very wide and general and will be difficult to apply, therefore using the term osteoporosis to define patients at high risk of fractures would be easier for application.

- Criterion 32 (Patient with hypertension has a treatment plan that excludes drugs that interfere with blood pressure control for example, NSAIDs): This criterion was commented on by the two clinical members, who asked how it can work in practice. The concern was how the MAT will deal with patients on NSAIDs to manage peripheral neuropathy or rheumatoid arthritis or those on oral contraceptives whose blood pressure is well controlled. The researcher explained that NOJ (no justified) is the correct option to cover such patients providing there is a documented reason and a clear indication to use any of these medication in such patients.

- Criterion 35 (Patient prescribed a simvastatin or atorvastatin not co-prescribed macrolide antibiotics (erythromycin, clarithromycin) or ketoconazole or itraconazole): The discussion raised about this criterion was that many patients prescribed antibiotics are told verbally to stop statin for a week and it probably would not be recorded. Therefore, it was decided to keep this criterion for audit just to highlight the number of patients applicable in order to recommend future documentation.

The expert group meeting also discussed the possibility of adding another 5 criteria recommended by the two clinical members. These criteria were:

- Criterion 17a & 17b: measuring the appropriate continuation of treatment with exenatide and liraglutide.

- Criterion 17c: measuring the appropriate use of liraglutide dose.

- Criterion 17d: measuring the appropriate continuation of treatment with gliptin.

- Criterion 35a: avoiding drug interaction between simvastatin and verapamil. (the risk of serious myopathy is increased when simvastatin is combined with verapamil [cytochrome P450 inhibitor which increases plasma levels of simvastatin and increases the risk of adverse effects, such as rhabdomyolysis]).

The research group agreed the addition of these 5 new criteria to the $MAT_{UK}$ as they were part of NICE guideline recommendations (CG 87) for criterion 17a, 17b, 17c, & 17d and SIGN guideline recommendations (SIGN 97) for criterion 35a. However, these 5 criteria were not added to $MAT_{Qat}$ for the following reasons:

- Although criterion 17c & 35a was recommended by the clinical guidelines, the addition of these criteria was recommended by the clinical team within the UK and was not validated with doctors in Qatar during the second validation stage, so their approval for final inclusion in the $MAT_{Qat}$ was questionable.

- Evidence behind recommendation of criterion 17a, 17b & 17d in the guideline were lacking and based on guideline development group (GDG) agreement in defining a beneficial metabolic response for continuation of these agents only to ensure that people do not remain for long periods on medication that is ineffective at controlling their HbA1c levels. Therefore, these recommendations were not selected for inclusion within the first MAT draft at the earlier stage of this project.

- Criteria 17a, 17b & 17c were expected to have low applicability, so it was not worth looking at them in depth.

The addition of the new 5 criteria was recommended by the clinical pharmacists and agreed within the research group. These 5 new criteria were added to the $MAT_{Qat}$ draft keeping the original numbering of criteria (the newly added criteria were identified using alphabets with numbers and added under the relevant criterion within the relevant sub-heading) as follows:

| Criterion # | Criterion measurement |
|---|---|
| **17**a | **Patient on exenatide or liraglutide for > 6 months** has evidence that it has reduced $HbA_{1c}$ by ≥ 0.5% |
| **17**b | **Patient on exenatide or liraglutide for > 6 months** has evidence that it has reduced body weight by ≥3% of initial body weight |
| **17**c | **Patient on a liraglutide** is prescribed a dose of 1.2 mg daily |
| **17**d | **Patient on a gliptin and receiving it for > 6 months** has evidence that it has reduced $HbA_{1c}$ by ≥ 0.5% |
| **35a** | **Patient prescribed >20mg simvastatin** not co-prescribed verapamil |

The new added criteria are further discussed in the discussion part of this chapter. Final versions of $MAT_{Qat}$ and $MAT_{UK}$ for application in clinical settings are presented in appendix 2 & appendix 3.

## 2.4 Discussion

DM is an increasing health problem with the phenomena of a rapidly growing world population, aging, urbanisation, and increasing incidence of obesity and sedentary life style [(90)]. It is the 8th leading cause of death in most high-income countries and the 9$^{th}$ leading cause of death in middle-income countries with a mortality rate of 2.6% and 2.3% per year respectively [(91)]. Type-2 DM is the major type of diabetes and the burden of this disease is proportionally increasing with its increased prevalence worldwide.

Patients with type-2 diabetes are at high risk of developing long-term microvascular and macrovascular complications which are the responsible cause of the disease morbidity, hospitalisation and mortality. Cardiovascular disease is the most common complication of the disease and is the responsible cause of death in the majority of cases. However, there is good evidence on how the onset of the disease complications can be prevented, delayed or their progression slowed, if it is managed appropriately and from an earlier stage. Hyperglycaemia and hypertension are the two major controllable risk factors for developing diabetes complications.

This highlighted the importance of managing the disease and its complications according to an evidence-base, and clinical guidelines may offer the best advice for the management of type-2 DM based on best published clinical and economic evidence, as well as expert agreement. This has also made diabetes a promising area for audit as it often responds dramatically to treatment and improved diabetes care.

The purpose of the present study was to design a MAT to evaluate the levels of adherence to the internationally recognised guidelines for the management of type 2 diabetes and primary prevention of CVD, in order to identify areas of low adherence and provide a focus to improve these areas in the future using concepts of pharmaceutical care.

### 2.4.1 Development of the MAT

The application of a medication assessment tool within a clinical audit is a novel approach to the assessment of appropriate management of type-2 diabetes and in the primary prevention of CVD. The tool is intended to be valuable for the evaluation of clinical practice and the provision of constructive feedback for prescribers and other health care professionals involved in the care of diabetic patients.

The tool was constructed on the basis of recommendations from NICE/SIGN guidelines and used a criterion-based methodology. The process of building-up the first draft was also an intensive learning process that took a long time, as it involved the full revision of all recommendations from both guidelines and then to select, prioritise and adapt them into the drafted tool. The selection and prioritisation of criteria obtained from SIGN guidelines were made according to recommendation grading. Furthermore, for recommendations from NICE guidelines conflicting with others from SIGN guidelines, the research group decided that SIGN guidelines would supersedes NICE guidelines as it was the most recent guideline.

One of the difficulties that also faced the researcher during the development of the first draft of the MAT was the conversion of the scheme related to use of glucose lowering pharmacotherapy in people with type-2 diabetes from an algorithm into measurable criteria. The researcher made the initial draft and then the research group modified it to reach the final applicable format. Recommendations related to primary prevention of CVD in diabetic patients have been reviewed for updates as it was previously developed and field-tested by previous authors within the University of Strathclyde, Glasgow.

### 2.4.2 Evidence-based medicine systematic review

Systematic review is a literature review performed to identify and to collect all high-quality research evidence (example: high-quality randomised controlled trials: an important and reliable form of scientific evidence in the hierarchy of evidence that have ability to reduce spurious causality and bias and can influence healthcare policy and practice) for the purpose of answering a research question. It provides a comprehensive summary of the available literature related to the research question. This involves searching for related papers using databases (example: EMBASE, PubMED and MEDLINE) or any specific journals. Identified articles are checked against pre-determined criteria for eligibility and relevance. [92]

Systematic reviews sometimes use meta-analysis (an analytical technique designed to summarise findings and combines the results of multiple studies and thus increases the sample size and the power to study effects of interest) to combine results of the eligible studies, which are increasingly being used in the conduct of evidence-based medicine. Each included study may be assigned an objective assessment of methodological quality preferably using a method conforming to PRISMA (the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: a standardised way to ensure a transparent and complete reporting of systematic reviews which has been widely used by medical journals worldwide) or the high quality standards of Cochrane collaboration. A systematic review uses an objective and transparent approach for research synthesis aiming to minimise bias. [93], [94]

Bias is defined as any tendency which prevents unprejudiced consideration of a question. In research, bias occurs when systematic error is introduced into sampling or testing by selecting or encouraging one outcome or answer over others. Bias can occur at any phase of research, including study design, data collection, data analysis and publication. As a result, reviewers of the literature must consider the degree to which bias was prevented through a proper study design and implementation and how bias might influence a study's conclusions. [95]

Recommendations related to the evidence-based use of medication in the management of type-2 diabetes and in the primary prevention of CVD were used to design MAT criteria in this study based on clinical guidelines. The reason behind the decision to select NICE and SIGN clinical and to give the priority to 'A' graded recommendations as a source of criteria generation came from the following facts:

- Both of these clinical guidelines were clear in explaining the methods used in generating recommendations. While grading the level of evidence (table 2 in methods section 2.2.1), both guidelines did not include any evidence with (-) level due to the high risk of bias in making decision.
- 'A' graded recommendations derived using the highest available level of evidence (which is at least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results).

### 2.4.3 Validation of the MAT

Techniques used to develop an instrument to measure quality of medication use such as the MAT, determine the instrument's face and content validity. Achieving face validity means that the developed tool shows that it meets the purpose behind its development and is able to measure what it intends to assess. On the other hand, content validity concerns the clinical significance of the tool based on supporting evidence and benefits behind its application. The development of the MAT was based on published guidelines and involved three validation stages to facilitate its application in the clinical settings (one at academic level and two at clinical level) and is therefore likely to have strong face and content validity[96].

Each stage of validation used focus group interview technique. Focus group interview is a well-established research tool that becoming increasingly prominent in health services research and generally considered as a qualitative research tool. The

important distinguishing feature of this tool is the interaction between participants which provides a stimulus for the generation and discussion of a wider range of ideas. This interaction can be seen as a normal activity in which people discuss issues and form opinions. Focus groups may also be employed for their effectiveness in exploring and identifying relevant questions in a research area [97].

Other useful methods of validation could be also considered in this study. Criteria developed within the drafted MAT could be sent through an e-mail to clinical experts as a questionnaire survey using the five-point Likert scale. The experts can then be asked to fill in the survey telling whether they strongly agree/agree/neutral/disagree/ strongly disagree with each standard. Standards could then be eliminated if, after analysing the survey, they fell into either the disagree/strongly disagree fields. The advantage of using such measure for validation is that level of agreement or disagreement between respondants can be measured and compared (using Fleiss Kappa or Delphi technique). When responding to a Likert questionnaire item, respondents specify their level of agreement or disagreement on a symmetric agree-disagree scale for a series of statements. Thus, the range captures the intensity of their feelings for a given item. [98], [99]

Although focus group interview involves interaction between participants which provides a stimulus for the generation and discussion of a wider range of ideas, its use as the only validation technique in this study was considered as a limitation. This technique was not able to provide the advantages of being able to measure the level of agreement or disagreement between diabetes consultants and thus limited the use of the tool as a generalisable measure to evaluate the level of care provided to diabetic patients in Qatar.

The changes made to the drafted MATs were mainly due to logical reasons including some criteria rearrangement or restructure to simplify and increase the precision of wording. This process involved the removal of any strange, confusing or overly-subjective terms or phrases and defining the qualifying and standard statements in a clearer way. These modifications were essential to make the MAT applicable by other users who were not involved in its development process.

### 2.4.4 Strengths and limitations of the project

*Strengths of the study*

- The newly developed and added criteria within the designed MAT originated from the latest recommendations of well established clinical guidelines on the management of type-2 diabetes and in the primary prevention of CVD.

- The development of the tool involved a multi-stage process to reach the final applicable form with enhanced functionality.

- Each draft of the MAT was peer-reviewed in repeated research group meetings and the final draft was validated by two expert groups from clinical fields. This process increased the precision of the tool.

- The application of the tool was neither labour-intensive nor time-consuming.

- The design of this study allows modification to be made in the MAT in order to make the tool reproducible when guidelines are changed or updated.

*Limitations of the study*

- The process of MAT development including in depth review of guidelines , selection and identification of clinical recommendations and multi-stage validation requires a considerable amount of time and effort making it not easy to design.

- The validation process used only focus group meeting technique which limited the ability to measure agreement and disagreement between diabetes consultants.

- The tool does not cover the diagnostic elements and the detailed management of hypertension, foot ulcers, established CVD and educational needs in patients with type-2 diabetes.

- Untrained persons without a pharmacological background will face difficulties in data collection and application of the tool.

# Chapter 3

## Pilot and application of a medication assessment tool for management of type-2 DM and the primary prevention of CVD

## 3.1 Introduction

### 3.1.1 Diabetes in Qatar

Qatar is an independent sovereign state located in the middle of the west coast of the Arabian Gulf. It has maritime and land borders with Saudi Arabia and it has also maritime boundaries with Bahrain, United Arab Emirates and Iran [100]. It is a small peninsula country with a length of 200 km and width of 100 km. The population of Qatar is 1,699,435 inhabitants according to the final results of the 2010 population census with a small citizen population of less than 300,000 people [101]. The predominant population comprises diverse expatriate populations, of which as many as 700,000 are from South East Asia and possess inherent predisposition towards diabetes.

#### 3.1.1.1 Prevalence and burden of diabetes

In 2009, it was estimated that the overall prevalence of DM among adult Qatari population was as high as 17% [13], and due to the estimated high percentage of Qatari adults considered as pre-diabetics, this prevalence is expected to rise in the next few years. While other risk factors such as hypertension, triglyceride levels, HDL levels, metabolic syndrome and heart disease were found to be significantly higher in adult Qatari diabetic patients; smoking habits, family history of DM and central obesity were considered to be the major contributors to the higher prevalence of DM [102]. According to IDF, Qatar was considered as one of the countries in the Middle East and North Africa (MENA) with the highest diabetes rates. It is the second highest ranked country for diabetes prevalence among the Gulf Cooperation Council (GCC) countries after Kuwait. The IDF estimates that healthcare expenditure to manage diabetes and prevent its complications in Qatar is currently running at USD $2,269 per person in 2010 [103].

### 3.1.1.2 Diabetes Care

*Qatar Diabetes Association*

Qatar Diabetes Association (QDA) is the sector that works with other partners in the Health Care Field in Qatar to combat the diabetes epidemic. It provides useful and up to date information that helps patients understand the nature of diabetes and ways of living with it. It also works on diabetes prevention and produces the necessary leaflets and information related to disease management and prevention aiming to improve the overall quality of life for those who are affected and raising awareness throughout the country. The QDA team consists of:

- Patients' diabetes education and support section (providing education about healthy food, physical activity, self monitoring of blood glucose and insulin pump support and education).

- Community outreach programme section (working with patients, their families, their health care professionals and their schools or work place in order to make their surroundings diabetes safe, healthy and supportive)

- Volunteer centre.
- Scientific committee.
- Events and conferences committees [104].

*Diabetes clinic - Hamad Medical Corporation*

The Diabetes and Endocrinology clinic is situated in the outpatient department of Hamad General Hospital (HGH) at the capital city of Doha. HGH offers highly specialised care to the whole population of Qatar and is managed by Hamad Medical Corporation (HMC), the premier non-profit government sponsored healthcare provider for citizens, residents and visitors of Qatar and the sector managing the whole public hospital services in the State [105].

The diabetes clinic on the second floor of HGH serves both children and adult patients and offers all diabetes-related services including treatment, pharmacy, diabetes educators, dieticians and foot care. As part of the outpatient department, the diabetes

clinic operates as an ambulatory service 8 hours a day, 5 days per week. The service provided is based on a patient appointment booking system and walk-in patients with urgent referrals. The facility is in the process of massive expansion to improve its patient care services. [106]

*Other private clinics and health centres*

Diabetes care can also be provided in some public as well as private health centres across the country. Most private health settings offer services to any insured or cash-paying patient. Furthermore, certain company-based private diabetes care is offered to the local community. Patients are often seen in private settings without initial appointments. However, the diabetes clinic within Hamad Medical Corporation remains the major centre for the management of diabetes, providing comprehensive services, and represents the focal point for all referrals from other sectors. [107]

### 3.1.2 Clinical guidelines

*Concepts and development*

Clinical guidelines are group of recommendations and advice that guide the care process provided by healthcare professionals to individuals within health care facilities. These recommendations are the translation of the best available and updated evidence-based medicine which involves a multi-stage process to form the standards that ensure more efficient use of healthcare resources, improved patient outcomes and provide effective and cost-effective care. The recommendations cover advice on disease diagnosis, screening as well as detailed management.

In the UK, the multidisciplinary expert group known as Guideline Development Group (GDG) performs systematic reviews in order to assess the scientific evidence about the given subject or the clinical question. The GDG achieve a summary of the clinical and economic evidence on the studies reviewed and appraised. High quality sources, such as meta-analyses or systematic reviews of randomised controlled trials (RCTs) are usually selected as a priority. Case-control or cohort studies as well as valuable non-analytic studies and expert opinions can also be considered. From this information the GDG derive the guideline recommendations. The newly developed recommendations form the new or the updated guideline which then enters the

validation stage within the NHS Appraisal Centre for Clinical Guidelines before its final implementation. [108]

*Benefits and importance*

Implementing clinical guidelines offers benefits not only to patients, but also to healthcare professionals and organisations. For patients and healthcare professionals, it guarantees the delivery of the best available evidence of clinical care which builds a confidence on service and ensures equality of care in different health care institutes. For organisations, it helps to reach standards in care requirements, reduce claims, improve cost saving and fulfil its remit to promote the economic and social well-being of its communities. However, adherence to guideline recommendations does not ensure a successful outcome in every single case and all other clinical data available for an individual case should be considered by the appropriate healthcare professional(s) responsible for clinical decisions to determine the standard of care in such cases. [109]

### 3.1.3 Previous studies used MAT methodology

Although MAT methodology was originally developed in the UK, its application has been widely adopted as an audit tool to measure prescribers' adherence to guidelines in Europe and in the Middle East after being adapted. The tool has also showed the ability to measure quality of prescribing and identify areas lacking appropriate care in different therapeutic areas including: asthma, Chronic Obstructive Pulmonary Disease (COPD)[110], CVD[111), (112), (113), (114], heart failure, osteoporosis [115], obesity[116], cancer care [83), (117], long-term use of corticosteroids[110] and palliative care[118]. Furthermore, a specific MAT for type-2 DM has been developed within this project. In the Middle East the MAT methodology was applied in Oman[119], Kuwait[120], United Arab Emirates [86] and Jordan[118].

For diabetic patients as well as health care providers, the greatest benefit that could be achieved by guidelines is to improve health outcomes and quality of care received by patients. Guidelines that promote interventions of proven benefit and discourage ineffective ones have the potential to reduce morbidity and mortality and improve quality of life for some conditions. For type-2 diabetes primary prevention of disease

complications is the recommended way to minimise morbidity and mortality. Improved adherence to clinical guideline recommendations was positively related to better disease prognosis [121]. Although the goal of evidence-based clinical practice has led to an increased interest in the development of tools to measure adherence to national guidelines, an audit to measure quality of prescribing according to internationally recognised guidelines in the management of type-2 diabetes and in the primary prevention of CVD in Qatar is lacking.

### 3.1.4 Aim and objectives

#### 3.1.4.1 Aim

The aim of this project was to pilot and field test a developed medication assessment tool (MAT)in order to conduct an audit to evaluate the quality of prescribing and medication use in patients with type 2-diabetes in Qatar. The audit should address blood glucose management and the primary prevention of CVD by a criterion-based approach ($MAT_{Qat}$ which was previously developed in chapter 2) with reference to internationally recognised diabetes guidelines.

#### 3.1.4.2 Objectives

1. Design a data collection form to collect the required data needed to apply the $MAT_{Qat}$.

2. Pilot the data collection form and $MAT_{Qat}$ application procedures in order to check their practical manageability (feasibility) in obtaining accurate and reliable data that fits the study aim.

3. Conduct the audit by retrieving data onsite in an anonymised form and populating a database of audit criteria to:

    a)- quantify adherence and non-adherence to overall and individual criteria within the care setting in Qatar.

    b)- quantify adherence and non-adherence to overall and individual patients within the study sample and use it to study patients' clinical demographics associated with adherence level.

4. Report on issues concerning implementation and evaluation of best practice in type-2 diabetes management.

5. Combine the analysis with data from a parallel study in the UK for comparison of adherences.

## 3.2 Methods

### 3.2.1 Study design

The study was a cross-sectional retrospective population based survey conducted between February and June 2011. The study was undertaken by the post-graduate researcher under the supervision of academic and clinical staff.

### 3.2.2 Subjects and Settings

#### 3.2.2.1 Patients

A sample of 305 patients with type 2 diabetes and living in Qatar who meet the following inclusion and exclusion criteria:

*Inclusion criteria*:

1. Patients diagnosed with type-2 DM with or without hypertension.
2. Aged ≥ 18 years
3. Currently alive and attended the diabetes clinic at least once during the past 2 years.

*Exclusion criteria*:

1. Patients with type 1 diabetes.
2. Aged < 18 years
3. Patients already diagnosed with CVD (coronary heart disease, TIA or stroke).

#### 3.2.2.2 Study site

Patient sample was drawn from a defined population attending the out-patient diabetes clinic at Hamah General Hospital in Qatar. The project was conducted at the University of Strathclyde, Glasgow.

### 3.2.4 Ethical approval

The researcher received advice from the Medical Research Centre at HMC which confirmed that the proposed study requires ethical approval from their Research Committee. The procedure to get ethical approval involved filling two applications and a letter from the researcher (appendix 4). Ethical approval was finally granted (appendix 5).

### 3.2.5 Sample size calculation

Because clinical audit may lead to hypothesis development and not hypothesis testing, it does not necessarily need a statistically valid sample size calculation [122]. The sample chosen for audit should be small enough to allow for rapid data acquisition but large enough to be representative. In clinical audit, the sample will be time driven as if the data acquisition time is too long interest will be lost and data completeness will often suffer. Furthermore, clinical audit only needs to determine the extent to which practice complies with standards or criteria and smaller sample sizes can often provide the information [122].

However, clinical members need to have confidence in clinical audit data in order to agree to change their practices. Use of a statistical formula to determine what sample size to use for an audit will enable the clinical group to state how sure it is that the true population value falls within a confidence interval. For example, for an audit finding of 70% compliance with clinical audit standards, using a sample size sufficient for a 95% level of confidence and a 5% range of accuracy, could make them 95% sure that the true value is 70%±5%, or that the true value lies between 65% and 75%. In other words, they can be 95% confident that the compliance with the audit standard in the entire population would be between 65% and 75%. [123] As a result, the sample size required for this audit (and because this audit is investigating a proportion of adherence) was determined using standard formula $n = Z^2 [p (1-p)] / d^2$.

The application of this formula to estimate sample size was limited due to the lack of previous similar studies carried out in this field in Qatar to obtain the expected levels of adherence (needed as an important part of the equation that estimates sample

size). Furthermore the use of results from other studies done in different countries within the same region such as Oman, UAE or Kuwait to calculate the expected levels of adherence was limited, as these studies used similar methods but with different parameters (criteria) to assess the adherence to the guidelines within individual MATs designed for assessing different disease states. Therefore, this study can be used in the future to calculate the exact sample size required for any further studies in this field in Qatar.

The selected formula was applied as follow:

n= Sample size
Z = Z value (1.96 for 95% confidence level),
p = expected proportion of adherence (0.77 based on a previous study in Kuwait*),
d = precision of estimate (margin of error [0.05])

* *The Kuwaiti study was selected as it was the most recent and judged to has the most relevant parameters to the current study aims.* [120]

The formula estimated that 272 patients are needed for this study, but the time scale for data collection allowed a larger sample of 305 patients. [120), (124]

### 3.2.6 Piloting of the data collection form and $MAT_{Qat}$

To facilitate the application procedure of $MAT_{Qat,}$ a data collection sheet was designed by the investigator containing all the required data items to fill the MAT. The designed data collection sheet was revised, modified and finally agreed by the research group. Prior to $MAT_{Qat}$ application, the feasibility of the designed audit tool and data collection sheet was tested on a sample of 20 patients' records (details on data collection procedure provided in the next section). The data collected for piloting was undertaken under the supervision of the project supervisors in Qatar: Dr. Mouna Al-Bakri, assistant director of pharmacy, Hamad General Hospital, Doha, Qatar who attended patients' data collection and Dr. Halima Al-Tamimi, the director of pharmacy who facilitated the process. The main aim of this step was to test if the essential information on the data collection sheet is possible to be obtained from patients' records and is sufficient and easily retrieved and transcribed into the audit

tool. This can also determine the auditability of the $MAT_{Qat}$ to reveal the need of any modifications and validate the data collection carried out by the researcher. During this process, the investigator realised that the data collection sheet required some modifications including the need to add some more data items to enhance its practicability. The required fields were then modified/ added and final form of data collection sheet was achieved (appendix 6).

### 3.2.7 Data collection

Data needed to apply the $MAT_{Qat}$ was collected for each patient using the data collection sheet achieved from the previous section (3.2.6). One sheet was filled for each patient individually. Data were obtained manually from patients' medical notes as well as electronically from an electronic Medical Record (eMR viewer). Medical files of all patients attending the diabetes clinic during the period of data collection were reviewed. Therefore, any patient who visited the clinic within this period had the chance to be included in this audit project.

In coordination with the nursing director of the out-patient department, the head nurse of the diabetes clinic was asked to keep all the files of patients who attended the clinic by the end of each day of data collection. The investigator daily checked these files and selected all files that met the inclusion criteria. The selected files were then used to prepare a list of patients' keys (each file contained a unique number known as HC) and a list of anonymised patient keys, which could be cross referenced back to patient information by medical staff. As all medical files should be kept in the medical record department, the researcher gave the daily prepared list to the head of medical records. This list was then submitted on the second day according to patients' keys and files collected and kept ready for the investigator to collect the required data. It was also noticed that some of patients' keys were not included within the files prepared on the next day and that was because these files were taken from the medical records department for other appointments in other out-patient clinics. This resulted in reduced numbers of patients collected per day and lengthened the period of data collection. The investigator was assigned an office within the medical records department for the whole period of data collection.

The data collection sheet was filled from data obtained from these medical files as well as from the e-MR viewer. All data related to pharmacy or laboratory was obtained from the e-MR viewer. However, all other data related to medical information were obtained from patients' medical notes written by doctors (as the e-MR viewer still doesn't allow any medical records not related to pharmacy, radiology and laboratory to be added). The e-MR viewer was able to give all medications prescribed and laboratory test results performed on the patient within the last 10 years upon entry request (figure 5 & 6). The system also allowed asking for a specific laboratory test result (for example: HbA1c) or specific medications (for example: metformin). This electronic medical system has a restricted access and the investigator was granted this access for the period of data collection.

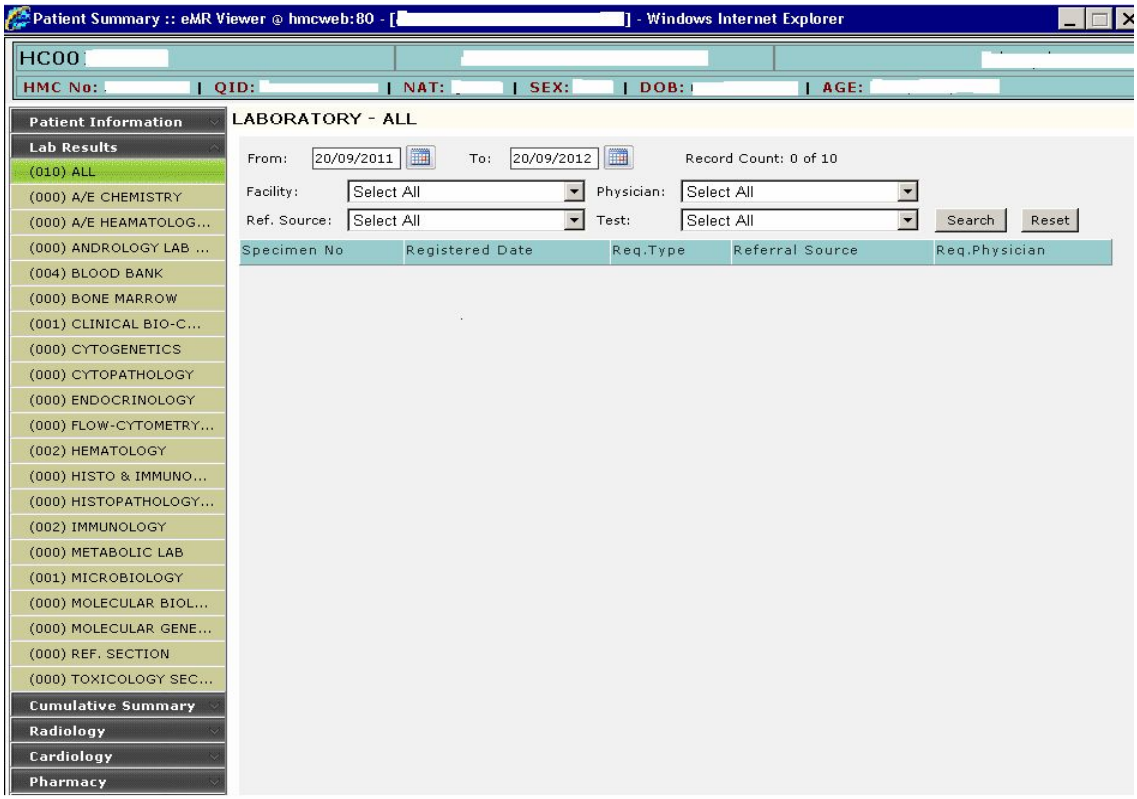


**Figure 5: e-MR viewer software (laboratory information)**

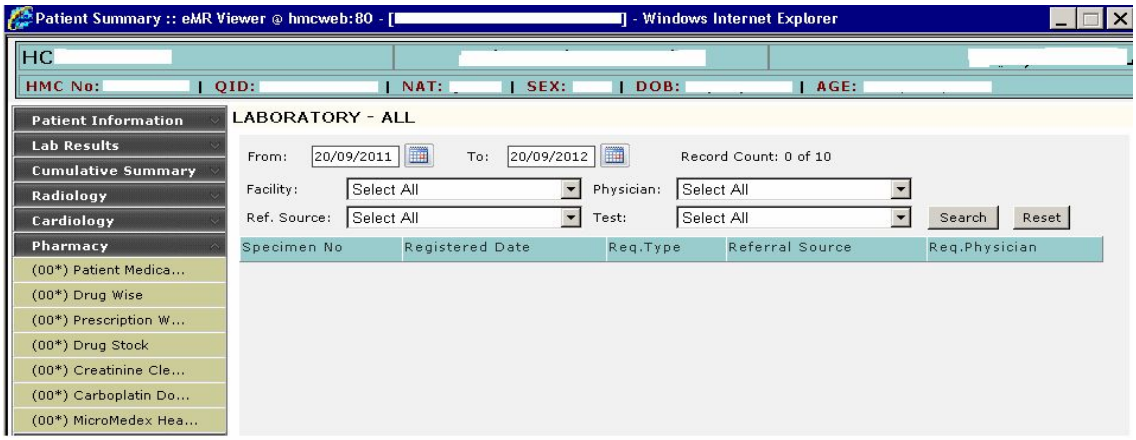


**Figure 6: e-MR viewer software (pharmacy information)**

### 3.2.8 Data analysis

Each of the collected data sheets was used to fill a copy of the $MAT_{Qat}$ for each patient individually. MAT answers for each patient were directly entered into a previously prepared Excel sheet to allow analysis. The prepared Excel sheet contained a total of 49 columns as follows:

Column 1: Patient key
Columns 2-39: Criteria 1-38
Columns 40-49: Patient demographics

The prepared Excel sheet was filled with the 305 patients' information (individual patient information was evaluated and appropriate criteria from the MAT were applied) and was used to determine the level of applicability and adherence to individual criteria within the MAT. The adherence for every single criterion was calculated and expressed as percentage, adjusted percentage and 95% confidence interval (CI). Overall adherence to all criteria for the entire study sample was then determined and expressed as percentage, adjusted percentage and 95% CI. Furthermore, adherence using individual patients as unit of analysis (MAT adherence per patient) was also performed to:

a)- assess individual patient care: to reveal how each individual patient conforms to the recommended care process.
b)- assess patient demographics and clinical characteristics associated with adherence.

#### 3.2.8.1 MAT equations and calculations:

*Adherence for each criterion and individual patient was calculated as follows*:
The total number of each answer (Yes, No, Noj, N/A, IDs and IDq) was calculated for each criterion/patient and was then used to calculate the percentage of adherence to this criterion/patient from the summation of all adhered criteria (criteria recoded "Yes"[numerator]) over the summation of all applicable criteria (criteria recoded "Yes", "No", "Noj" and "IDs" [denominator]). All 95% CI obtained through a calculation formula installed into Excel Windows software® as follows:

Standard error (SE) [square root of (adherence*(1-adherence)/ (applicability)], confident interval minimum (CI min) [adherence- SE*1.96] and confident interval maximum (CI max) [adherence+ SE*1.96] for each criterion [125].

The criteria adherence was initially judged using arbitrary cut-offs used in previous studies to reflect a high level of adherence if ≥80%, intermediate level of adherence if between 79.9% - 50% and low level of adherence if < 50%. However, adherence based on the patient as the unit of analysis used four threshold cut-offs to reflect low (<50%), low intermediate (≥50-<70%), intermediate (≥70-<80%) and high (≥ 80%) adherence. Analysis based on 3 levels of adherence (low, intermediate and high) were not sufficiently discriminating as the majority of the patient sample was found to have intermediate levels of adherence, consequently results for MAT adherence per patient have been re-analysed using four threshold cut-offs to reflect low, low intermediate, intermediate and high adherence to give increased discrimination of results. Patients who would benefit from improving prescribers' adherence to criteria with low levels of adherence through an appropriate pharmaceutical care plan were judged to be those who scored a low and a low-intermediate level of adherence to applicable criteria. Therefore, adherence of <70% was finally used as the cut-off value to target care in patients as well as in the criteria.

*Overall adherence in all criteria and patients*:

The same equation was used to calculate the total adherence for overall criteria in all patients, but in this case depending on the summation of the entire Yes, No, Noj, N/A, IDs, IDq and applicability for the whole criteria. Equations used are summarised as follows:

$$\textit{Applicability} = \Sigma \text{ Yes, No, Noj, IDs}$$

$$\textit{Adherence} = \frac{\Sigma \text{ Yes}}{\Sigma \text{ Yes, No, Noj, IDs}} * 100$$

$$\textit{Adjusted adherence} = \frac{\Sigma \text{ Yes, Noj}}{\Sigma \text{ Yes, No, Noj, IDs}} * 100$$

$$Standard\ error\ (SE) = \sqrt{\frac{\text{Adherence x } (1 - \text{Adherence})}{\text{Applicability}}}$$

*Confident interval (CI min)* = adherence – (SE*1.96)

*Confident interval (CI max)* = adherence + (SE*1.96)

*Patient demographic and clinical characteristics associated with adherence*

For this part of the project, all statistical analyses were carried out using statistical package SPSS 19.0 (SPSS Inc. Chicago, IL) after transferring data from Microsoft Excel. Categorical and continuous values were expressed as frequency (percentage) and mean ± SD. Descriptive statistics were used to summarise all demographic and clinical characteristics of the patients. The primary outcome variable was the percentage of adherence levels to clinical guidelines, which was estimated and presented with their corresponding 95% CI. Quantitative means of variables between the four independent groups (low, low-intermediate, intermediate, and high) and two (low and high) of adherence levels were summarised and analysed using the unpaired Student t test and one-way analysis of variance (ANOVA). Associations between two or more than two qualitative variables were assessed using appropriate Chi-square test.

The effect of individuals' characteristics on the adherence levels was assessed using univariate and multivariate logistic regression analyses considering low and high adherence levels as a dependent variable and age, gender, BMI, diabetes duration, systolic BP, hypertension status, HbA1C levels, HDL and total cholesterol (TC) levels as independent variables. The variable 'smoking' has not been included in the logistic regression analysis due to insufficient documentation in patients' files. Logistic regression results were presented in terms of odds ratio (OR) along with corresponding 95%CI. All p values presented were two-tailed, and p values <0.05 was considered as statistically significant.

### 3.2.9 Investigation of gaps in guidelines implementation

Based on findings from the MAT analysis, criteria showing low and low-intermediate levels of adherence (any criterion which showed a level of adherence of < 70%) were fed-back and discussed with the head of diabetes clinic to find out:

- What would be the reason behind its low adherence?
- How these criteria are prioritised (ranked according to its importance)?
- Reasons behind poor smoking status documentation.

The researcher prepared a report of findings (appendix 7) which was discussed and agreed by the research group and arranged a meeting with the head of diabetes clinic (consultant physician). Comments and opinions were documented during the meeting and reported in the results section.

### 3.2.10 Comparison with the UK study

$MAT_{UK}$ designed in the previous chapter was applied within the clinical settings in Glasgow, UK by an MSc student at the University of Strathclyde in 2012 and aimed to identify areas needed to improve diabetes care in the primary settings within the UK [(126)]. Results obtained from the application of this MAT were compared with findings from Qatar application. The researcher of this project participated in UK study design, preparation, data collection and analysis and to assure consistency between the two studies. Furthermore, the data collection sheet of the current study was also used to collect data from the UK after appropriate adaptation was carried out within the research group [(126)].

Comparing the overall adherence to guidelines for the whole study sample between Qatar and the UK was not performed as the $MAT_{UK}$ contained five additional different criteria. As a result, only common individual criteria were compared and chi-square test to obtain p value performed individually.

## 3.3 Results

### 3.3.1 Patient demographics

The following table (table 9) summarises patients' demographics for the whole study sample:

**Table 9: Patient demographic data for the whole study sample**

| Description | Patients (n= 305) |
|---|---|
| ***Gender*** | |
| Male | 146 (47.9 %) |
| Female | 159 (52.1 %) |
| ***Age* (years)** | |
| Mean (SD) | 53.1 (11.1) |
| Median (IQR 1, 3) | 54.0 (46-60) |
| Range | 21-79 |
| ***Body Mass Index (kg/m$^2$)*** | |
| Mean (SD) | 31.6 (6.9) |
| Median (IQR 1, 3) | 31.0 (26.5-35) |
| Range | 19.5-61 |
| BMI <18.5 (underweight) | 0 (0%) |
| BMI 18.5-24.9 (healthy weight) | 39 (12.8%) |
| BMI ≥ 25 (overweight) | 101(33.1%) |
| BMI ≥ 30 (obese) | 165 (54.1%) |
| BMI 30-34.9 (obese class I) | 86 (28.2%) |
| BMI 35-39.9 (obese class II) | 46 (15.1%) |
| BMI ≥ 40 (obese class III) | 33 (10.8%) |
| ***HbA1c (%)*** | |
| Mean (SD) | 8.6 (1.8) |
| Median (IQR 1, 3) | 8.2 (7.2-9.7) |
| Range | 5.1-16.6 |
| HbA1c < 6.5 | 23 (7.5%) |
| HbA1c 6.5-7 | 45 (14.8%) |
| HbA1c 7.1-7.5 | 38 (12.5%) |
| HbA1c 7.6-9 | 100 (32.8%) |
| HbA1c > 9 | 99 (32.5%) |

**Table 9: Patient demographic data for the whole study sample- continued**

| | |
|---|---|
| ***DM duration in years*** | |
| Mean (SD) | 10.5 (6.5) |
| Median (IQR 1, 3) | 9.0 (6-14) |
| Range | 1-30 |
| | |
| DM duration < 5 years | 55 (18.0%) |
| DM duration 5- <10 years | 99 (32.5%) |
| DM duration 10- <15 years | 78 (25.6%) |
| DM duration 15-< 20 years | 38 (12.5%) |
| DM duration ≥ 20 years | 35 (11.5%) |
| | |
| ***Smoking Status*** | |
| Current smokers | 24 (7.9%) |
| Current non-smokers | 74 (24.3%) |
| Unknown smoking status | 207 (67.9%) |
| | |
| ***Past Medical History*** | |
| With hypertension | 193 (63.3%) |
| Without hypertension | 112 (36.7%) |

**SD:** standard deviation, **IQR**: interquartile range

### 3.3.2 Overall adherence for the total study sample

#### 3.3.2.1 Level of adherence to individual criteria

The total number of assessed criteria in 305 patients was 11590. Number of applicable criteria was 6657 (57.4% of total). Overall adherence to all applicable criteria was 68.1% (CI: 67, 69). Non-adherences were found in 30.8% (CI: 30, 32; in 2049 criteria) of the applicable criteria, with 1.1% (in 74/6657 criteria) criteria having insufficient data (IDs) to assess adherence and 3% (in 346/11590 criteria) criteria having insufficient data (IDq) to assess applicability. Of the non-adherences only 5.8% (CI: 5, 7; in 118 criteria) had a documented justification. Consequently 94.2% of all non-adherences to applicable criteria (CI: 93, 95; in 1931 criteria) had unjustified non-adherence and indicated a need for inclusion in a treatment review through an appropriate pharmaceutical care plan. Table 10 shows details of the percentages of adherence to each individual criterion as well as the adherence of the whole study sample.

**Table 10 : Results for levels of adherence to individual audit tool criteria in 305 patients (n= 11590 criteria)**

| # | Criterion | N/A (%) | Yes (%) | No (%) | No(J) (%) | ID(S) (%) | ID(Q) (%) | Applic-ability (%) | % adherence (95% CI) | % adjusted adherence (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Patient with type 2 DM**: | | | | | | | | | |
| **1** | referred to a structured diabetes education programme | 0 (0) | 87 (28.5) | 218 (71.5) | 0 (0) | 0 (0) | 0 (0) | 305 (100) | 28.5 (23.5-33.6) | 28.5 (23.5-33.6) |
| **2** | had a recorded target $HbA1_c$ | 0 (0) | 0 (0) | 305 (100) | 0 (0) | 0 (0) | 0 (0) | 305 (100) | 0 (0.0-0.0) | 0 (0.0-0.0) |
| **3** | had a record of at least two HbA1c measurements in the previous 15 months | 0 (0) | 226 (74.1) | 75 (24.6) | 4 (1.3) | 0 (0) | 0 (0) | 305 (100) | 74.1 (69.2-79.1) | 75.4 (70.6-80.2) |
| **4** | had an HbA1c recorded at ≤ 7% as their most recent value | 0 (0) | 68 (22.3) | 146 (47.8) | 81 (26.6) | 10 (3.3) | 0 (0) | 305 (100) | 22.3 (17.6-27.0) | 48.9 (43.2-54.5) |
| **5** | **on glucose lowering agent(s)** prescribed metformin or sulphonylurea | 2 (0.66) | 278 (91.1) | 18 (5.9) | 7 (2.3) | 0 (0) | 0 (0) | 303 (99.3) | 91.7 (88.6-94.8) | 94.1 (91.4-96.7) |
| **6** | **on glucose lowering agent with stable $HbA1_c$ >7%** prescribed a dual therapy | 69 (22.6) | 169 (55.4) | 24 (7.9) | 1 (0.33) | 0 (0) | 42 (13.8) | 194 (63.6) | 87.1 (82.4-91.8) | 87.6 (83.0-92.3) |
| **7** | **on oral hypoglycaemic agent(s)** not co-prescribed four of them together | 92 (30.2) | 176 (57.7) | 37 (12.1) | 0 (0) | 0 (0) | 0 (0) | 213 (69.8) | 82.6 (77.5-87.7) | 82.6 (77.5-87.7) |
| **8** | **on a gliptin, pioglitazone or a glinide** co-prescribed metformin or a sulphonylurea | 130 (42.6) | 166 (54.4) | 9 (3.0) | 0 (0) | 0 (0) | 0 (0) | 175 (57.4) | 94.9 (91.6-98.1) | 94.9 (91.6-98.1) |
| **9** | **with stable $HbA1_c$ ≥7.5%** prescribed a third oral agent or exenatide | 124 (40.6) | 88 (28.9) | 53 (17.4) | 0 (0) | 0 (0) | 40 (13.1) | 141 (46.2) | 62.4 (54.4-70.4) | 62.4 (54.4-70.4) |
| **10** | **with BMI ≥ 25 kg/m2** prescribed metformin | 44 (14.4) | 216 (70.8) | 30 (9.8) | 15 (4.9) | 0 (0) | 0 (0) | 261 (85.6) | 82.8 (78.2-87.3) | 88.5 (84.6-92.4) |
| **11** | **on metformin therapy** had an estimated GFR>45ml/min/1.73$m^2$ | 52 (17.0) | 239 (78.4) | 2 (0.66) | 0 (0) | 12 (3.9) | 0 (0) | 253 (83.0) | 94.5 (91.6-97.3) | 94.5 (91.6-97.3) |
| **12** | **on metformin and an estimated GFR ≤45 ml/min/1.73 m2** had renal function measured in the past 12 months | 291 (95.4) | 2 (0.66) | 0 (0) | 0 (0) | 0 (0) | 12 (3.9) | 2 (0.66) | 100 (100-100) | 100 (100-100) |
| **13** | **on metformin** had no current estimated GFR<30ml/min/1.73$m^2$ | 52 (17.0) | 241 (79.0) | 0 (0) | 0 (0) | 12 (3.9) | 0 (0) | 253 (83.0) | 95.3 (92.6-97.9) | 95.3 (92.6-97.9) |

**Table 10: Results for levels of adherence to individual audit tool criteria in 305 patients (n= 11590 criteria)- continued**

| # | Criterion | N/A (%) | Yes (%) | No (%) | No(J) (%) | ID(S) (%) | ID(Q) (%) | Applic-ability (%) | % adherence (95% CI) | % adjusted adherence (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| **14** | **on two or a three oral glucose lowering agents** co-prescribed metformin and/or a sulphonylurea. | 82 (26.9) | 205 (67.2) | 18 (5.9) | 0 (0) | 0 (0) | 0 (0) | 223 (73.1) | 91.9 (88.4-95.5) | 91.9 (88.4-95.5) |
| **15** | **on insulin** had previously received oral glucose lowering therapy | 200 (65.6) | 75 (24.6) | 28 (9.2) | 2 (0.66) | 0 (0) | 0 (0) | 105 (34.4) | 71.4 (62.8-80.1) | 73.3 (64.9-81.8) |
| **16** | use of insulin when indicated | 100 (32.8) | 117 (38.4) | 50 (16.4) | 0 (0) | 0 (0) | 38 (12.5) | 167 (54.8) | 70.1 (36.1-77.0) | 70.1 (36.1-77.0) |
| **17** | **on exenatide or liraglutide** had a BMI>30 kg/$m^2$ | 298 (97.7) | 6 (2.0) | 1 (0.33) | 0 (0) | 0 (0) | 0 (0) | 7 (2.3) | 85.7 (59.8-100) | 85.7 (59.8-100) |
| **18** | **on a thiazolidinedione** have no heart failure | 237 (77.7) | 68 (22.3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 68 (22.3) | 100 (100-100) | 100 (100-100) |
| **19** | **on a thiazolidinedione (pioglitazone**) have no osteoporosis | 237 (77.7) | 61 (20.0) | 7 (2.3) | 0 (0) | 0 (0) | 0 (0) | 68 (22.3) | 89.7 (82.5-96.9) | 89.7 (82.5-96.9) |
| **20** | **on a thiazolidinedione (pioglitazone) for >6 months** had HbA1c reduced by ≥0.5% | 255 (83.6) | 7 (2.3) | 11 (3.61) | 0 (0) | 32 (10.5) | 0 (0) | 50 (16.4) | 14.0 (4.4-23.6) | 14.0 (4.4-23.6) |
| **21** | **on oral agent and had insulin added to therapy** continued to use the oral therapy | 234 (76.7) | 59 (19.3) | 10 (3.28) | 2 (0.66) | 0 (0) | 0 (0) | 71 (23.3) | 83.1 (74.4-91.8) | 85.9 (77.8-94.0) |
| **22** | **with microalbuminuria or proteinuria** prescribed an ACE inhibitor or an angiotensin II-receptor antagonist (ARB*)* | 158 (51.8) | 115 (37.7) | 32 (10.5) | 0 (0) | 0 (0) | 0 (0) | 147 (48.2) | 78.2 (71.6-84.9) | 78.2 (71.6-84.9) |
| **23** | had renal function (serum creatinine/eGFR) checked within the past 12 months | 0 (0) | 287 (94.1) | 18 (5.9) | 0 (0) | 0 (0) | 0 (0) | 305 (100) | 94.1 (91.5-96.7) | 94.1 (91.5-96.7) |
| **24** | had retinal examination within the past 15 months | 0 (0) | 173 (56.7) | 131 (43.0) | 1 (0.33) | 0 (0) | 0 (0) | 305 (100) | 56.7 (51.2-62.3) | 57.0 (51.5-62.6) |
| **25** | had neuropathy/ foot check in the past 15 months | 0 (0) | 75 (24.6) | 230 (75.4) | 0 (0) | 0 (0) | 0 (0) | 305 (100) | 24.6 (19.8-29.4) | 24.6 (19.8-29.4) |
| **26** | **with diabetic neuropathy** prescribed a tricyclic antidepressant, gabapentin, Pregabalin or duloxetine | 258 (84.6) | 37 (12.1) | 10 (3.28) | 0 (0) | 0 (0) | 0 (0) | 47 (15.4) | 78.7 (67.0-90.4) | 78.7 (67.0-90.4) |

**Table 10: Results for levels of adherence to individual audit tool criteria in 305 patients (n= 11590 criteria)- continued**

| # | Criterion | N/A (%) | Yes (%) | No (%) | No(J) (%) | ID(S) (%) | ID(Q) (%) | Applic-ability (%) | % adherence (95% CI) | % adjusted adherence (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| **27** | had blood pressure measured within the past 15 months | 0 (0) | 305 (100) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 305 (100) | 100 (100-100) | 100 (100-100) |
| **28** | **with hypertension** prescribed an ACE Inhibitor or an ARB | 111 (36.4) | 159 (52.1) | 33 (10.8) | 2 (0.66) | 0 (0) | 0 (0) | 194 (63.6) | 82.0 (76.5-87.4) | 83.0 (77.7-88.3) |
| **29** | **with hypertension and prescribed antihypertensive drug** achieved BP < 140/80 mmHg | 111 (36.4) | 65 (21.3) | 129 (42.3) | 0 (0) | 0 (0) | 0 (0) | 194 (63.6) | 33.5 (26.9-40.1) | 33.5 (26.9-40.1) |
| **30** | **with treated hypertension and co-existing kidney, eye or cerebrovascular damage** achieved a blood pressure level < 130/80 mmHg | 263 (86.2) | 7 (2.30) | 35 (11.5) | 0 (0) | 0 (0) | 0 (0) | 42 (13.8) | 16.7 (5.4-27.9) | 16.7 (5.4-27.9) |
| **31** | **with treated hypertension** not prescribed a combination of thiazide diuretic and beta-blocker | 111 (36.4) | 182 (59.7) | 12 (3.93) | 0 (0) | 0 (0) | 0 (0) | 194 (63.6) | 93.8 (90.4-97.2) | 93.8 (90.4-97.2) |
| **32** | **with treated hypertension** not prescribed medication interfere with blood pressure control | 111 (36.4) | 176 (57.7) | 18 (5.9) | 0 (0) | 0 (0) | 0 (0) | 194 (63.6) | 90.7 (86.6-94.8) | 90.7 (86.6-94.8) |
| **33** | **aged >40** prescribed a statin | 27 (8.9) | 170 (55.7) | 105 (34.4) | 3 (1.0) | 0 (0) | 0 (0) | 278 (91.1) | 61.2 (55.4-66.9) | 62.2 (56.5-67.9) |
| **34** | **maintained on the same dose of a statin for >6 weeks** achieved a total cholesterol level of < 5 mmol/l | 132 (43.3) | 105 (34.4) | 60 (19.7) | 0 (0) | 8 (2.62) | 0 (0) | 173 (56.7) | 60.7 (53.4-68.0) | 60.7 (53.4-68.0) |
| **35** | **on simvastatin or atorvastatin** not co-prescribed macrolide antibiotics (erythromycin, clarithromycin) or ketoconazole or itraconazole | 191 (62.6) | 109 (35.7) | 5 (1.64) | 0 (0) | 0 (0) | 0 (0) | 114 (37.4) | 95.6 (91.9-99.4) | 95.6 (91.9-99.4) |
| **36** | **with a triglyceride level > 4.5mmol/L (whether on a statin or not**) prescribed a fibrate | 288 (94.4) | 3 (1.0) | 10 (3.3) | 0 (0) | 0 (0) | 4 (1.31) | 13 (4.3) | 23.1 (1.7-46.0) | 23.1 (1.7-46.0) |
| **37** | **with triglyceride level of 2.3-4.5 mmol/L despite statin therapy** prescribed a fibrate | 254 (83.2) | 6 (2.0) | 42 (13.8) | 0 (0) | 0 (0) | 3 (1.0) | 48 (15.7) | 12.5 (3.1-21.9) | 12.5 (3.1-21.9) |
| **38** | **who continued to smoke** offered smoking cessation advice | 73 (23.9) | 6 (2.0) | 19 (6.2) | 0 (0) | 0 (0) | 207 (67.9) | 25 (8.2) | 24.0 (7.3-40.7) | 24.0 (7.3-40.7) |
| | **Total (%)** | **4587 (39.6)** | **4534 (39.1)** | **1931 (16.7)** | **118 (1.02)** | **74 (0.64)** | **346 (3.0)** | **6657 (57.4)** | **68.1 (67.0-69.2)** | **70.0 (68.8-71.0)** |

**N/A**: not applicable; **No**: unjustified deviation from the guideline, **No (j):** justified deviation from the guideline; **ID (s):** insufficient data to assess the applicable criterion; **ID (q):** Insufficient data to assess criterion applicability; **CI**: confidence interval.

Bold qualifier statements indicate patient's applicability to the relevant standard statement criterion.

Based on the three cut-offs categorising high, intermediate and low adherence ranked as follows (table 11):

**Table 11: Ranking of the level of adherence (38 applicable criteria in 305 patients)**

| Ranking | Level of adherence | Criteria | Adherence (%) | Applicability (n) |
|---|---|---|---|---|
| 1 | High | Criterion 27: blood pressure measurement | 100 | 305 |
| 1 | | Criterion 18: avoid the use of thiazolidinedione in patients with heart failure | 100 | 68 |
| 1 | | Criterion 12: measure renal function for patients on metformin and an estimated GFR ≤45 ml/min/1.73 $m^2$ | 100 | **2** |
| 2 | | Criterion 35: avoid drug interaction with statins | 95.6 | 114 |
| 3 | | Criterion 13: avoid the use of metformin in patients with estimated GFR < 30 ml/min/1.73 $m^2$ | 95.3 | 253 |
| 4 | | Criterion 8: co-prescribe metformin or sulphonylurea with gliptin, pioglitazone or glinide | 94.9 | 175 |
| 5 | | Criterion 11: patient on metformin had an estimated GFR >45 ml/min/1.73 $m^2$ | 94.5 | 253 |
| 6 | | Criterion 23: renal function check | 94.1 | 305 |
| 7 | | Criterion 31: avoid drugs worsen blood glucose control | 93.8 | 194 |
| 8 | | Criterion 14: co-prescribe metformin or sulphonylurea as part of dual or triple therapy | 91.9 | 223 |
| 9 | | Criterion 5: use of metformin or sulphonylurea as first-line therapy | 91.7 | 303 |
| 10 | | Criterion 32: avoid the use of drugs that worsen BP control | 90.7 | 194 |
| 11 | | Criterion 19: avoid the use of thiazolidinedione in patients with osteoporosis | 89.7 | 68 |
| 12 | | Criterion 6: start dual therapy when indicated | 87.1 | 194 |
| 13 | | Criterion 17: on exenatide or liraglutide had a BMI>30 kg/$m^2$ | 85.7 | **7** |
| 14 | | Criterion 21: continuation of oral agent when insulin commenced | 83.1 | 71 |
| 15 | | Criterion 10: with BMI ≥ 25 kg/m2 prescribed metformin | 82.8 | 261 |
| 16 | | Criterion 7: avoid co-prescribing four oral agents | 82.6 | 213 |
| 17 | | Criterion 28: prescribe ACE inhibitor or ARB for hypertension | 82.0 | 194 |

**Table 11: Ranking of the level of adherence (38 applicable criteria in 305 patients)- continued**

| Ranking | Level of adherence | Criteria | Adherence (%) | Applicability (n) |
|---|---|---|---|---|
| 18 | | Criterion 26: prescribe medication to manage neuropathy | 78.7 | 47 |
| 19 | | Criterion 22: prescribe ACE inhibitor or ARB to manage micoabuminuria or proteinuria | 78.2 | 147 |
| 20 | | Criterion 3: had at least two documented HbA1c measurements | 74.1 | 305 |
| 21 | | Criterion 15: try oral therapy before commencing insulin | 71.4 | 105 |
| 22 | **Intermediate** | Criterion 16: prescribe insulin when indicated | 70.1 | 167 |
| 23 | | Criterion 9: prescribe third oral agent or exenatide when indicated | 62.4 | 141 |
| 24 | | Criterion 33: prescribe statin when indicated | 61.2 | 278 |
| 25 | | Criterion 34: achieve targeted TC level with statin therapy | 60.7 | 173 |
| 26 | | Criterion 24: retinal examination | 56.7 | 305 |
| 27 | | Criterion 29: achieve BP target without co-morbidities | 33.5 | 194 |
| 28 | | Criterion 1: referral to a structured diabetes education programme | 28.5 | 305 |
| 29 | | Criterion 25: neuropathy/foot check | 24.6 | 305 |
| 30 | | Criterion 38: smoking cessation advice | 24.0 | 25 |
| 31 | **Low** | Criterion 36: prescribe fibrate when indicated | 23.1 | 13 |
| 32 | | Criterion 4: achieve an HbA1c value of ≤ 7% | 22.3 | 305 |
| 33 | | Criterion 30: achieve BP target with co-morbidities | 16.7 | 42 |
| 34 | | Criterion 20: appropriate continuation of thiazolidinedione therapy | 14.0 | 50 |
| 35 | | Criterion 37: add fibrate to statin therapy when indicated | 12.5 | 48 |
| 36 | | Criterion 2: record a target HbA1c value for each patient | 0.0 | 305 |

The MAT identified 19/38 criteria with high levels of adherence (≥80%), 9/38 criteria with intermediate levels of adherence (≥50%; <80%) and 10/38 criteria with low levels of adherence (<50%).

### 3.3.2.2 Levels of adherence in individual patients

Adherence using individual patients as the unit of analysis (MAT adherence per patient, Table 12) revealed that prescribers adhered to < 50% of the applicable criteria in 9.8% of patients (n=30 patients with low level of adherence). Prescribers also adhered to < 70% of the applicable criteria in 40.7% of patients (n=124 patients with low-intermediate level of adherence). Furthermore, prescribers adhered to ≥70-<80% and ≥80% of the applicable criteria in 33.1% (n=101 patients with intermediate level of adherence) and 16.4% (n=50 patients with high level of adherence) respectively. The levels of adherence ranged between 20.0%- 89.5%. Patients who would benefit from improving prescribers' adherence to criteria through an appropriate pharmaceutical care plan are those who scored low and low-intermediate levels of adherence to applicable criteria (n=154 [50.5%] patients). Detailed levels of adherence and applicability in individual patients to 38 MAT criteria are shown in Appendix 8 and are summarised in the following table.

**Table 12: Overall adherence to the 38 audit tool criteria in individual patients (n=305)**

| Adherence Category | Number of patients (n) | Percentage (%) |
|---|---|---|
| 20 - < 50% (low) | 30 | 9.8 |
| 50 to <70% (low-intermediate) | 124 | 40.7 |
| 70 to <80% (intermediate) | 101 | 33.1 |
| ≥ 80- 89.5% (high) | 50 | 16.4 |
| **Total** | **305** | **100** |

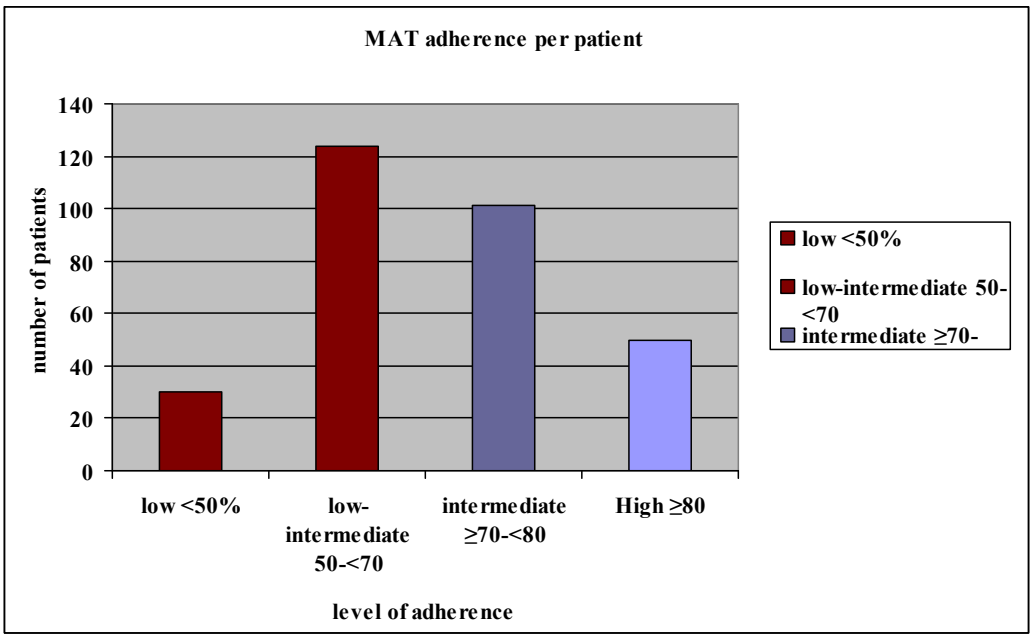


**Figure 7: MAT adherence per patient**

### 3.3.3 Patient demographic and clinical characteristics associated with adherence

A comparison of demographic and clinical characteristics of the study sample across different levels of adherences is shown in Table 13. Mean total cholesterol was found to be significantly lower in the intermediate to high adherence groups compared to low to low-intermediate adherence groups (p=0.001). Among intermediate to high adherence groups the percentage of hypertensive subjects was significantly higher than in the low to low-intermediate adherence groups (p=0.003).

**Table 13: Patients' demographic and clinical characteristics associated with adherence levels (n=305)**

| Variables/adherence category | Low (<50%) n=30 | Low-intermediate (≥50-<70%) n=124 | Intermediate (≥70-<80%) n=101 | High (≥ 80%) n=50 | p-value* |
|---|---|---|---|---|---|
| **Mean age (years)** | 52.1 | 52.6 | 53.5 | 54.2 | 0.780 |
| **(SD)** | (12.0) | (11.0) | 10.9 | 11.4 | |
| **(95% CI)** | (47.7, 56.6) | (50.7, 54.6) | (51.3, 55.6) | (51.9-54.4) | |
| **(Range)** | (32-78) | (21-79) | (27-79) | (21-79) | |
| **Diabetes duration (years)** | 10.7 | 10.1 | 10.3 | 11.7 | 0.514 |
| **Mean (SD)** | (8.2) | (6.2) | (6.2) | (7.0) | |
| **(95% CI)** | (7.6, 13.7) | (9.0, 11.2) | (9.1, 11.5) | (9.8, 13.7) | |
| **(Range)** | (1-30) | (1-29) | (1-30) | (2-30) | |
| **Mean BMI (kg/m$^2$)** | 31.9 | 30.5 | 32.7 | 32.1 | 0.102 |
| **(SD)** | (7.5) | (5.7) | (7.8) | (6.8) | |
| **(95% CI)** | (29.1, 34.7) | (29.5, 31.5) | (31.1-34.3) | (30.2, 34.1) | |
| **(Range)** | (21-49) | (19.5-49.5) | (19.5-61) | (20-49) | |
| **HbA1c level (mmol/l)** | 8.6 | 8.7 | 8.5 | 8.3 | 0.433 |
| **Mean (SD)** | (1.9) | (1.7) | (2.0) | (1.9) | |
| **(95% CI)** | (7.9, 9.3) | (8.4, 9.0) | (8.1, 8.8) | (7.7, 8.8) | |
| **(Range)** | (5.8-12.9) | (5.4-13.3) | (5.8-16.6) | (5.1-12.5) | |
| **Total cholesterol** | 4.9 | 4.8 | 4.7 | 4.2 | 0.001 |
| **Mean (SD)** | (1.1) | (0.9) | (1.0) | (0.7) | |
| **(95% CI)** | (4.5, 5.3) | (4.7, 5.0) | (4.5, 4.9) | (4.0, 4.4) | |
| **(Range)** | (3.0-7.1) | (2.6-6.9) | (2.6-7.7) | (2.9-6.3) | |
| **HDL** | 1.1 | 1.1 | 1.2 | 1.2 | 0.518 |
| **Mean (SD)** | (0.45) | (0.34) | (0.30) | (0.31) | |
| **(95% CI)** | (0.95, 1.29) | (1.09, 1.21) | (1.13, 1.25) | (1.12, 1.30) | |
| **(Range)** | (0.46-2.82) | (0.54-2.37) | 0.60-2.08) | (0.59-2.26) | |
| **Gender: Male (n=146)** | 14 | 65 | 50 | 17 | 0.171 |
| **(%)** | (46.7) | (52.4) | (49.5) | (34.0) | |
| **Female (n=159)** | 16 | 59 | 51 | 33 | |
| **(%)** | (53.3) | (47.6) | (50.5) | (66.0) | |
| **Blood pressure status:** | | | | | |
| **Hypertensive (n=193)** | 22 | 64 | 68 | 39 | 0.003 |
| **(%)** | (73.3) | (51.6) | (67.3) | (78.0) | |
| **Non-hypertensive (n=112)** | 8 | 60 | 33 | 11 | |
| **(%)** | (26.7) | (48.4) | (32.7) | (22.0) | |

* One way ANOVA & Chi-Square tests
**SD**: standard deviation, **CI**: confidence interval

In addition, an exploratory statistical analysis was also carried out in order to assess and examine the association of various parameters with two main categories of adherence levels such as high and low adherence levels (Table 14). Mean BMI was found to be significantly higher in the high adherence group than the low adherence group (32.53±7.57 vs 30.76±6.13; p=0.025). In contrast, mean total cholesterol levels in the high adherence group was observed to be significantly less compared to the low adherence group (4.53±0.95 vs 4.84±0.97vs; p=0.005). Among the high adherence group the percentage of hypertensive subjects was significantly higher than in low adherence groups (p=0.007).

**Table 14: Patients' demographic and clinical characteristics associated with adherence levels**

| Variables/adherence category | Low (<70%) n=154 | High (≥ 70%) n=151 | p-value* |
|---|---|---|---|
| **Mean age (years) (SD)** | 52.5 (11.2) | 53.7 (11.0) | 0.347 |
| **Diabetes duration (years) Mean (SD)** | 10.2 (6.6) | 10.7 (6.5) | 0.476 |
| **Mean BMI (kg/m$^2$) (SD)** | 30.7 (6.1) | 32.5 (7.6) | **0.025** |
| **HbA1c level (mmol/l) Mean (SD)** | 8.7 (1.7) | 8.4 (1.9) | 0.133 |
| **Total cholesterol Mean (SD)** | 4.8 (0.97) | 4.5 (0.95) | **0.005** |
| **HDL Mean (SD)** | 1.1 (0.4) | 1.2 (0.3) | 0.163 |
| **Gender: Male (n=146) (%)** | 79 (51.3) | 67 (44.4) | 0.226 |
| **Female (n=159) (%)** | 75 (48.7) | 84 (55.6) | |
| **Blood pressure status: Hypertensive (n=193) (%)** | 86 (55.8) | 107 (70.9) | **0.007** |
| **Non-hypertensive (n=112) (%)** | 68 (44.2) | 44 (29.1) | |

* Chi-Square tests, **SD**: standard deviation

Univariate logistic regression analysis showed that only blood pressure status and TC levels were significantly associated with high adherence levels. It was observed that odds of high adherence was 1.92 times higher (unadjusted OR= 1.92; 95% CI: 1.20, 3.09) among patients who had hypertension than non-hypertension cases which indicates that patients who do not have hypertension should be target for pharmaceutical care. Odds of high adherence was 1.58 times higher among patients who had a TC level of ≤4.5 mmol/l (unadjusted OR=1.58, 95% CI: 1.01, 2.49) indicating the need to target patients with TC > 4.5 mmol/l for pharmaceutical care review. Similar observations were found when the multivariate regression analysis was performed. This indicates that patients without hypertension or patients with a TC >4.5 mmol/l need to be targeted for pharmaceutical care planning and these two clinical characteristics are independently and even after adjusting other covariates significantly affecting the high adherence levels (tables 15 & 16).

**Table 15: Univariate Logistic Regression Analysis**

| Variable | Regression Coefficient (β) | Standard Error (S. E.) | Unadjusted Odds ratio (OR) | 95% CI for unadjusted OR |
|---|---|---|---|---|
| **Age (Years)** | 0.010 | 0.010 | 1.01 | (0.98, 1.03) |
| **Gender** | | | | |
| Male | -0.278 | 0.230 | 0.76 | (0.48, 1.19) |
| Female | | | 1.00 | |
| **Hypertension** | | | | |
| Yes | 0.654 | 0.242 | **1.92** | **(1.20, 3.09)** |
| No | | | 1.00 | |
| **Body Mass Index (BMI)** | 0.038 | 0.017 | **1.04** | **(1.01, 1.07)** |
| **Diabetes duration (Years)** | 0.013 | 0.018 | 1.01 | (0.98, 1.05) |
| **Systolic BP (SBP)** | 0.006 | 0.007 | 1.01 | (0.99, 1.02) |
| **HbA1C Levels (mmol/l)** | 0.096 | 0.064 | 0.91 | (0.80, 1.03) |
| **HDL** | 0.486 | 0.350 | 1.63 | (0.82, 3.23) |
| **Total cholesterol** | | | | |
| ≤ 4.5 mmol/l | 0.460 | 0.231 | **1.58** | **(1.01, 2.49)** |
| >4.5 mmol/l | | | 1.00 | |

***Reference category- Low adherence***

**Table 16: Effect of Various Quantitative and Qualitative Covariates on Adherence levels (Multivariate Logistic Regession)**

| Variable | Regression Coefficient (β) | Standard Error (S. E.) | Adjusted Odds ratio (OR) | 95% CI for adjusted OR |
|---|---|---|---|---|
| **Hypertension** | | | | |
| Yes | 0.666 | 0.244 | **1.95** | **(1.21, 3.14)** |
| No | | | 1.00 | |
| **Total cholesterol** | 0.475 | 0.234 | **1.61** | **(1.02, 2.54)** |
| ≤ 4.5 | | | 1.00 | |
| >4.5 | | | | |

***Reference category- Low adherence***

### 3.3.4 Investigation of gaps in guidelines implementation

Observations and comments obtained from the head of diabetes clinic about the reasons behind low adherence in some criteria, poor documentation of smoking status and criteria ranking are summarised in the following Table 17.

**Table 17: Investigation of gaps in guidelines implementation**

| Criteria | Expected reason behind low adherence | Ranking* |
|---|---|---|
| Criterion 1: referral to a structured diabetes education programme | It is hard to refer all patients to diabetes education programme and to foot clinic due to the shortage in space and in staff within these two facilities. So we only refer who are at higher need of education or foot check and treatment and some of these referrals may not be documented. We do also some foot checks and education during appointment. Furthermore, we don't know if the referred patients have attended their clinics or not. | 1 |
| Criterion 25: neuropathy/foot check | | 3 |
| Criterion 4: achieve an HbA1c value of ≤ 7% | I believe that 22% is not bad as most of the cases seen within our clinic are complicated and patient compliance play an important role in achieving an HbA1c value of ≤ 7%. We hope to achieve a higher percentage and aiming to increase time given per patient at every visit to reach a higher percentage. | 2 |
| Criterion 38: smoking cessation advice/ smoking status documentation. | I have no reason for not documenting smoking status and I agree that we need to pay more attention toward this criterion. | 4 |
| Criterion 2: record a target HbA1c value for each patient | Documenting a target HbA1c for each patient is not part of our policy within the diabetes clinic. | 5 |
| Criterion 37: add fibrate to statin therapy when indicated | Some times addition prescribing a fibrate or adding it to statin can be missed, especially in the presence of other CVD risk factors that shift our attention. I think this should be taken in consideration for the future. | 6 |
| Criterion 36: prescribe fibrate when indicated | | 7 |
| Criterion 29: achieve BP target without co-morbidities | There could be many reasons for not achieving target BP control which may include for example: in-accurate BP reading due to in-appropriate measurement technique or patient may be stressed from being at clinic and so BP may rise. The reasons behind low adherence in these two criteria may need more investigation. | 8 |
| Criterion 30: achieve BP target with co-morbidities | | 9 |
| Criterion 34: achieve targeted TC level with statin therapy | We concentrate more on LDL-C levels. | 10 |
| Criterion 20: appropriate continuation of thiazolidinedione therapy | The decision to continue or to stop thiozolidinedione is up to the doctor as he/she may still wish to increase the dose before changing of stopping the medication | 11 |
| Criterion 9: prescribe third oral agent or exenatide when indicated | The decision to prescribe a third oral agent or exenatide is up to the doctor as he/she may still wish to increase the dose of current agents before adding a new medication. | 12 |
| Criterion 33: prescribe statin when indicated | We use statin based on patients' blood cholesterol level and not on patients' age. | 13 |
| Criterion 24: retinal examination | I believe that we are doing well in this criterion and there maybe a problem in the accuracy of auditing this criterion. I am sure we are doing better than 56%. | 14 |

* Doctors believe that all these criteria are important and ranking is for prioritisation purposes.

### 3.3.5 Comparison with the UK study

Results obtained from MAT application in Qatar and in the UK are compared and summarised in the following tables (18 & 19).

**Table 18: Comparison between Qatar and UK study**

| Comparison | Qatar | UK |
|---|---|---|
| **Year of study** | 2011 | 2012 |
| **Number of patients** | 305 | 328 |
| **Study site** | Diabetes clinic within secondary health care hospital | 15 GP practices within primary health care settings |
| **Number of criteria investigated** | 11,590 | 14,104 |
| **% Total adherence (95% CI)** | 68.1% (67.0, 69.2) | 74.0% (72.9, 75.0) |
| **Patient demographics** | | |
| **Age (years)** | | |
| Mean (SD) | 53.1 (11.1) | 61.8 (13.8) |
| Median | 54.0 | 61 |
| Range | 21-79 | 23-84 |
| **Gender (n)** | | |
| Male (%) | 146 (47.9 %) | 187 (57%) |
| Female (%) | 159 (52.1 %) | 141 (43%) |
| **Blood pressure status (n)** | | |
| With HTN (%) | 193 (63.3%) | 216 (65.9%) |
| Without HTN (%) | 112 (36.7%) | 112 (34.1) |
| **Smoking status (n)** | | |
| Current smokers (%) | 24 (7.9%) | 64 (19.5%) |
| Current non-smokers (%) | 74 (24.3%) | 175 (53.4%) |
| Ex-smoker (%) | - | 89 (27.1%) |
| Not documented (%) | 207 (67.9%) | - |

**SD**: standard deviation, **CI**: confidence interval , **HTN**: hypertension

Detailed results from the UK study are shown in Appendix 9.

| Table 19: Comparison between individual MAT criteria in Qatar and in the UK | | | | | | |
|---|---|---|---|---|---|---|
| # | Criteria | Qatar (2011) | | UK (2012) | | p-value* |
| | | Applicability n (%) | Adherence % (95% CI) | Applicability n (%) | Adherence % (95% CI) | |
| 1 | referral to a structured diabetes education programme | 305 (100) | 28.5 (23.5-33.6) | 328 (100) | 25.0 (20.3-29.7) | 0.324 |
| 2 | record a target HbA1c value for each patient | 305 (100) | 0.0 (0.0-0.0) | 328 (100) | 0.0 (0.0-0.0) | - |
| 3 | had at least two documented HbA1c measurements | 305 (100) | 74.1 (69.2-79.1) | 328 (100) | 71.0 (66.1-75.9) | 0.423 |
| 4 | Achieve an HbA1c value of ≤ 7% | 305 (100) | 22.3 (17.6-27.0) | 328 (100) | 42.7 (37.3-48.0) | **0.0001** |
| 5 | use of metformin or sulphonylurea as first-line therapy | 303 (99.3) | 91.7 (88.6-94.8) | 248 (75.6) | 96.4 (94.0-98.7) | **0.032** |
| 6 | start dual therapy when indicated | 194 (63.6) | 87.1 (82.4-91.8) | 117 (35.7) | 63.2 (54.5-72.0) | **0.0001** |
| 7 | avoid co-prescribing four oral agents | 213 (69.8) | 82.6 (77.5-87.7) | 108 (32.9) | 98.1 (59.6-100.7) | **0.0001** |
| 8 | co-prescribe metformin or sulphonylurea with gliptin, pioglitazone or glinide | 175 (57.4) | 94.9 (91.6-98.1) | 51 (15.5) | 96.1 (90.8-101.4) | 1.00 |
| 9 | prescribe third oral agent or exenatide when indicated | 141 (46.2) | 62.4 (54.4-70.4) | 36 (11) | 41.7 (25.6-57.8) | **0.036** |
| 10 | with BMI ≥ 25 kg/m2 prescribed metformin | 261 (85.6) | 82.8 (78.2-87.3) | 275 (83.4) | 70.2 (64.8-75.6) | **0.001** |
| 11 | patient on metformin had an estimated GFR >45 ml/min/1.73 $m^2$ | 253 (83.0) | 94.5 (91.6-97.3) | 218 (66.5) | 95.4 (92.6-98.2) | 0.680 |
| 12 | measure renal function for patients on metformin and an estimated GFR ≤45 ml/min/1.73 $m^2$ | 2 (0.66) | 100.0 | 7 (2.2) | 100.0 | - |
| 13 | avoid the use of metformin in patients with estimated GFR < 30 ml/min/1.73 $m^2$ | 253 (83.0) | 95.3 (92.6-97.9) | 217 (66.2) | 97.7 (95.7-99.7) | 0.216 |
| 14 | co-prescribe metformin or sulphonylurea as part of dual or triple therapy | 223 (73.1) | 91.9 (88.4-95.5) | 82 (25) | 89.0 (82.3-95.8) | 0.495 |
| 15 | try oral therapy before commencing insulin | 105 (34.4) | 71.4 (62.8-80.1) | 32 (9.7) | 93.8 (85.4-100.0) | **0.008** |
| 16 | prescribe insulin when indicated | 167 (54.8) | 70.1 (36.1-77.0) | 73 (22.3) | 61.6 (50.5-72.8) | 0.231 |
| 17 | on exenatide or liraglutide had a BMI>30 kg/$m^2$ | 7 (2.3) | 85.7 (59.8-100) | 7 (2.1) | 100.0 | 1.00 |
| 18 | avoid the use of thiazolidinedione in patients with heart failure | 68 (22.3) | 100.0 | 27 (8.2) | 100.0 | - |
| 19 | avoid the use of thiazolidinedione in patients with osteoporosis | 68 (22.3) | 89.7 (82.5-96.9) | 27 (8.2) | 100.0 | 0.186 |
| 20 | appropriate continuation of thiazolidinedione therapy | 50 (16.4) | 14.0 (4.4-23.6) | 27 (8.2) | 44.5 (25.7-63.2) | **0.005** |
| 21 | continuation of oral agent when insulin commenced | 71 (23.3) | 83.1 (74.4-91.8) | 30 (9.2) | 66.7 (49.8-83.5) | 0.111 |
| 22 | prescribe ACE inhibitor or ARB to manage micoabuminuria or proteinuria | 147 (48.2) | 78.2 (71.6-84.9) | 110 (33.5) | 81.8 (74.6-89.0) | 0.532 |

| Table 19: Comparison between individual MAT criteria in Qatar and in the UK-continue | | | | | | |
|---|---|---|---|---|---|---|
| # | Criteria | Qatar 2011 | | UK 2012 | | p-value* |
| | | Applicability n (%) | Adherence % (95% CI) | Applicability n (%) | Adherence % (95% CI) | |
| 23 | renal function check | 305 (100) | 94.1 (91.5-96.7) | 328 (100) | 97.6 (95.9-99.2) | 0.053 |
| 24 | retinal examination | 305 (100) | 56.7 (51.2-62.3) | 328 (100) | 82.0 (77.9-86.2) | **0.0001** |
| 25 | neuropathy/foot check | 305 (100) | 24.6 (19.8-29.4) | 328 (100) | 84.1 (80.2-88.1) | **0.0001** |
| 26 | prescribe medication to manage neuropathy | 47 (15.4) | 78.7 (67.0-90.4) | 11 (3.4) | 81.8 (59.0-100.0) | 1.000 |
| 27 | blood pressure measurement | 305 (100) | 100.0 | 328 (100) | 97.3 (95.5-99.0) | **0.004** |
| 28 | prescribe ACE inhibitor or ARB for hypertension | 194 (63.6) | 82.0 (76.5-87.4) | 216 (65.9) | 80.6 (75.3-85.8) | 0.800 |
| 29 | Achieve BP target without co-morbidities | 194 (63.6) | 33.5 (26.9-40.1) | 213 (64.9) | 70.4 (64.3-76.6) | **0.0001** |
| 30 | Achieve BP target with co-morbidities | 42 (13.8) | 16.7 (5.4-27.9) | 23 (7) | 26.1 (8.1-44.0) | 0.518 |
| 31 | avoid drugs worsen blood glucose control | 194 (63.6) | 93.8 (90.4-97.2) | 211 (64.3) | 87.2 (82.7-91.7) | **0.028** |
| 32 | avoid the use of drugs that worsen BP control | 194 (63.6) | 90.7 (86.6-94.8) | 214 (65.2) | 91.6 (87.9-95.3) | 0.862 |
| 33 | prescribe statin when indicated | 278 (91.1) | 61.2 (55.4-66.9) | 309 (94.2) | 84.8 (80.8-88.8) | **0.0001** |
| 34 | achieve targeted TC level with statin therapy | 173 (56.7) | 60.7 (53.4-68.0) | 266 (81) | 40.6 (34.7-46.5) | **0.0001** |
| 35 | avoid drug interaction with statins | 114 (37.4) | 95.6 (91.9-99.4) | 266 (81) | 99.6 (98.9-100.0) | **0.011** |
| 36 | prescribe fibrate when indicated | 13 (4.3) | 23.1 (1.7-46.0) | 14 (4.3) | 7.1 (0-20.6) | 0.326 |
| 37 | add fibrate to statin therapy when indicated | 48 (15.7) | 12.5 (3.1-21.9) | 28 (8.6) | 0.0 | **0.0001** |
| 38 | smoking cessation advice | 25 (8.2) | 24.0 (7.3-40.7) | 64 (19.5) | 90.6 (83.5-97.8) | **0.0001** |

*Chi-Square tests

**CI**: confidence interval, **MAT**: medication assessment tool, **TC**: total cholesterol, **BP**: blood pressure

A total of 18 criteria showed a statistically significant difference ($p < 0.05$) in guidelines implementation between Qatar and the UK.

## 3.4 Discussion

### 3.4.1 Assessment of the quality of care

There have been significant shifts in society's attitude to quality in healthcare over recent years. Health care organisations are required to have a comprehensive programme of quality improvement activity that may include clinicians participating fully in audit. Clinical audit is the component of clinical systems that offers the greatest potential to assess the quality of care routinely provided for health care users. This can be used to define essential elements for quality improvement programmes.

The aim of this study was to conduct an audit to evaluate the quality of prescribing and medication use in patients with type 2-diabetes in Qatar. The audit addressed blood glucose management and the primary prevention of CVD by a criterion-based approach ($MAT_{Qat}$) with reference to internationally recognised diabetes guidelines. Based on data obtained from patients' medical files, areas with low and low-intermediate adherence were identified and used to provide resources to improve diabetes care in Qatar. This may also give a great chance for pharmacists to deal with these fields and to get involved in diabetes management in Qatar.

In this part of the project the overall adherence to individual audit tool criteria of the whole study sample and patients' characteristics associated with adherence will be discussed. This will also involve some general observations about different parts of the study, comparison with other studies and some consideration of strength and weakness.

### 3.4.2 General observations

#### 3.4.2.1 Missing data

Auditing each criterion within this tool was based on information documented in patients' files, so that any lack of documentation can affect the level of adherence to the related criterion. For example, justified non-adherences (Noj) might count as unjustified non-adherences (No) if prescribers did not document the rationale behind

prescribing decision in patients' records (example 1 below). As a result, this is considered as one limitation of this audit tool.

One of the observations during the process of data collection was the lack of documentation of some patients' important fields which contributed in the evaluation of the study. For example (see example 2 below), insufficient data ID(Q), to decide if the criterion standard is applicable or not, was observed in 346 (3.0%) criteria of the total applied criteria. Insufficient documentation of patient's data was highlighted during the data collection phase and was fed-back to healthcare providers. The main missing information was detected in the following examples:

*Example 1:*

*Referrals to diabetes education programmes and foot screening clinic*

When low adherences of these criteria (criterion 1 and criterion 25) were discussed with physicians, insufficient documentation was found to be one of the reasons (see Table 16). Furthermore, patient compliance may play an important role in the insufficient documentation here. Undocumented doctors' referrals to these clinics and programmes were detected when the patient's file contained diabetes educators and foot clinic staff medical notes. The presence of these notes was judged as an indicator that the patient was referred to these facilities. However, some patients may have undocumented referrals to these clinics and did not attend them. In these patients, undocumented referrals were not detectable and considered as non-justified non-adherences.

*Example 2:*

*Smoking status records*

Patients' current smoking status or smoking history was not documented in the majority of patients' files. Medical notes taken by diabetes consultants were carefully checked and found to miss this information. Of the 305 files reviewed, a total number of 207 (67.9%) files had no smoking status documented. Consequently, only 98 (32.1%) files had the smoking status documented. The majority of the known patients' smoking status was documented by other physicians who manage other

diseases that patients have which are not related to the diabetes clinic. This missing data affected the application of criterion 38.

Poor quality of patients' data documentation can occur as a result of some factors which may include increased patient load and restricted time available for each patient and associated record keeping. More focus should be done to improve patient's data gathering and documentation. Patients should be also involved in this process to understand the importance of keeping records about their treatment progress which may improve their compliance to attend the clinics for gathering and documenting their important data.

#### 3.4.2.2 Type of diabetes documentation

Medical notes in some patients' files mentioned that the patient had type-1 diabetes in some sheets and type-2 diabetes in other sheets. Information from such files was not collected due to the conflicting documented diagnosis.

### 3.4.3 Reliability testing

Reliability testing was not performed for this study as the data required was collected only by the study author using one standard data collection sheet for each patient. Furthermore, ethical approval was only granted for the main author to undertake any data collection individually. If the data needed to apply this study involved more people, then inter- and intra-observer reliability testing should be conducted and agreed using Cohen's kappa (k).

### 3.4.4 Patients' demographics

The majority of data related to patients' demographics were taken from the patient assessment sheet filled by nurses at each appointment as well as the electronic data base (e-MR viewer). The patient assessment sheet contained information about patient's weight, height, BMI and blood pressure measurement taken at clinic. As a result, this information, in addition to patient's age, was documented in the whole study sample. Detailed information about patients' demographics (means of age, BMI, HbA1c, DM duration and percentages of males and females, patients at different BMI categories and hypertensive/ non-hypertensive patients) are shown in table 9 at the results section.

Mean BMI was found to be 31.6 $kg/m^2$ ranging from 19.5-61 $kg/m^2$, indicating obesity within the whole study sample. The majority of patients were found to be overweight (BMI $\geq$ 25 $kg/m^2$ in 33.1% of patients [n= 101]) and obese (BMI $\geq$ 30 $kg/m^2$ in 54.1% of patients [n=165]). This is found to be parallel with findings from other studies in Qatar [13], [102] and in the UK [127].

### 3.4.5 Assessment of adherence to guidelines

#### 3.4.5.1 Overall adherence to the guidelines for the whole study sample

In a total of 6657 applicable criteria (57.4%, out of 11590 assessed criteria in 305 patients), this survey showed an overall 'intermediate' adherence to prescribing guidelines (68.1%, CI: 67.0, 69.2). The survey has also identified areas with poor adherence requiring medical review and attention (generating care issues) and some other areas lacked the appropriate documentation of clinical information in patients' records.

Non-adherences were found in 30.8% (CI: 30, 32; in 2049 criteria) of the applicable criteria, with 1.1% criteria having insufficient data (IDs and IDq) to assess adherence. Of the non-adherences only 5.8% (CI: 5, 7; in 118 criteria) had a documented justification. Consequently 94.2% of all non-adherences to applicable criteria (CI: 93, 95; in 1931 criteria) had unjustified non-adherence and indicated a need for inclusion

in treatment review through an appropriate pharmaceutical care plan. Justified non-adherences in this study were used to calculate adjusted adherence. Adjusted adherence considers the justified non-adherences as an adherence and obtained from the summation of all adherences (criteria recorded yes) plus criteria recorded Noj. However, criterion evaluation in this study was based on explicit adherence to guideline recommendations (established yes answers).

#### 3.4.5.2 Criteria based analysis

*Criteria assessing control of blood glucose*

Of the 21 criteria assessing the appropriate management of blood glucose, 4 criteria showed a low level of adherence as follows:

*Criterion 1*: Patients with type 2 DM should be offered a structured, evidence based and individualised diabetes education programme. Such programmes are associated with better glycaemic control and improved quality of life in type 2 diabetic patients and graded as an 'A' recommendation in the SIGN guidelines. Only 28.5% (CI 23.5, 33.6 [n=305 applicable patients]) of the applicable patients were referred to such a programme. This could be due to shortage of spaces in such programmes or lack of documentation of some referrals. Educational needs in type-2 diabetic patients in Qatar were identified and highlighted by another project [128].

*Criterion 2*:

Recording a target HbA1c for each patient with type 2 DM is another important guideline recommendation (graded A) and this criterion (criterion 2) showed a 0% level of adherence [n=305 applicable patients]. When discussed with prescribers, they explained that this is not a policy yet in the hospital and that they are generally using an HbA1c value of ≤7% as a target for all patients. Setting an individual target for HbA1c is important as it represents the optimum glucose control reference value for both patient and health care provider. Furthermore, treat-to-target studies accomplished greater outcomes compared to studies with less well defined aims. Using a general HbA1c target for all patients is unhelpful as it may vary according to individual patient's needs including quality of life to be sacrificed in order to reach the target, extent of side effects associated (risk of hypoglycaemia or weight gain) and

different resources available for management. A result obtained from this criterion was parallel with the findings from another study in Qatar which identified a poor practice in setting a goal for therapy [128].

*Criterion 4:*

Although physicians used a single target HbA1c of ≤ 7%, this target was achieved only in 22.3% (CI: 17.6, 27.0 [n=305 applicable patients]) of the applicable patients. Prescribers believe that this could be due to the complicated nature of the cases seen within their clinical setting. The importance of this 'A' graded recommendation came from the fact that good glycaemic control (HbA1c <7%) is associated with a reduction in microvascular and macrovascular complications of diabetes and reduced disease mortality and morbidity. This criterion was highly adjusted when justified non adherences were taken in consideration (adjusted adherence 48.9%, CI: 43.2, 54.5). However, the adherence remained low even after adjustment. Justified non-adherences in this criterion included:

- Documented poor patient compliance in taking medication and in the use of other disease control interventions.
- Refusing to starting insulin treatment when it is recommended to be added to patient's therapy
- Any recent change in glucose lowering therapy (within the last 3 months).

Although poor patient compliance in taking their medication and refusing insulin therapy was considered as justified non-adherences, this should not eliminates the importance of intensive educational and reinforcement programmes needs in these patients.

*Criterion 20*:

A thiazolidinedione (pioglitazone) should not be continued for >6 months unless the patient's HbA1c is reduced by ≥0.5%. The importance of this criterion is to ensure that patients do not remain for long periods on medication associated with risk and is ineffective at controlling their $HbA_{1c}$ levels. This criterion showed a level of adherence of 14.0% (CI: 4.4, 23.6 [n=50 applicable patients]). This could be due to

insufficient information available to assess whether the applicable criterion met the standard statement or not. HbA1c levels should be checked within six months after commencing pioglitazone and out of 50 applicable patients to this criterion, 32 (64%) patients had no HbA1c measured during this period. When low adherence of this criterion was communicated to doctors they mentioned that they may still wish to increase the dose before deciding to stop the medication. However, the high percentage of missed HbA1c level check-ups after prescribing this medication highlighted the importance of including this criterion within the list of care issues generated to improve care.

A further 4/21 criteria assessing the appropriate management of blood glucose showed an intermediate level of adherences, which are:

*Criterion 3:*

Appropriate measurement of HbA1c levels, which showed an adherence of 74.1% (CI: 69.2, 79.1 [n=305 applicable patients)]. In this criterion, 4 cases were found to have a justified non-adherence for not having at least two HbA1c measurements within the last 15 months. These 4 cases were patients with recent referrals to the diabetes clinic. Adjusted adherence was not much affected and found to be 75.4% (CI: 70.6, 80.2). According to the Scottish diabetes survey, 89.8% of diabetic patients had a recorded HbA1c value within the past 15 months [(127)].

*Criterion 9:*

Addition of a third oral glucose lowering agent or exenatide when HbA1c remained ≥7.5%. This criterion showed an adherence of 62.4% (CI: 54.4-70.4 [n=141 applicable patients]). The importance of this criterion came from the diabetes treatment algorithm recommended by clinical guidelines. The applicability of this criterion was not detectable in 40 patients (13.1%) due to the insufficient HbA1c measurements.

*Criterion 15:*

Using oral hypoglycaemic agents before starting insulin, had an adherence of 71.4% (CI: 62.8-80.1 [n=105 applicable patients]. Insulin should only be commenced if other measures are no longer achieving adequate blood glucose control to HbA1c and after

discussing and agreeing the benefits and risks of insulin with patients. For this criterion 2 cases were found to have a justified reason for starting insulin before other measures. These two patients were currently pregnant females who developed gestational diabetes and were not able to receive oral glucose lowering therapy. Adjusted adherence for this criterion was 73.3% (CI: 64.9, 81.8).

*Criterion 16:*

When other measures (life-style interventions & oral hypoglycaemic agents) are no longer achieving adequate blood glucose control, insulin should be introduced to patient. This criterion showed an adherence of 70.1% (CI: 36.1, 77.0 [n=167 applicable patients].

The remaining 13/21 criteria assessing the appropriate management of blood glucose showed a high level of adherence of ≥ 80% with two criteria (criterion 12 & 18) achieving 100% level of adherence. Criterion 12 had very low applicability (only 2/305 patients were found to be on metformin with an estimated GFR ≤ 45 ml/min/$m^2$) and this could be the reason behind the 100% adherence. This also indicates that prescribers are giving high concern to renal function before commencing metformin. Criterion 18 was also found to have a 100% adherence as the study sample did not identify any single patient with a history of heart failure. Absence of heart failure cases within the study sample could be due to patient selection criteria. The inclusion criteria used in this study only selected patients with type-2 diabetes who have no history of CVD (as it concerns primary prevention of CVD). If the inclusion criteria involved those with an established CVD, then the frequency of patients diagnosed with heart failure may increase. Low applicability was also detected in another criterion that showed a high level of adherence, criterion 17 (85.7% adherence, CI: 59.8-100, [n=7]). This was because exenatide and liraglutide were not frequently used to treat type-2 diabetic patients in Qatar.

Of criteria which showed a high adherence, criterion 6, 11, 12, 13 & 21 recorded some justified non-adherences which are: one patient refused to be prescribed another medication for criterion 6, patients don't have a recent renal function test for criterion 11, 12, 13 and one patient was not able to continue the current oral therapy when insulin commenced due to detected pregnancy.

*Criteria assessing management of diabetes complications*

Of the 5 criteria assessing management of diabetes complications, one criterion showed a low level of adherence which was:

*Criterion 25:*

Appropriate neuropathy and foot screening, with an adherence of 24.6% (CI: 19.8, 29.4 [n=305 applicable patients]). Neuropathic pain is an upsetting symptom associated with poor glycaemic control. Patients present with these symptoms may not be aware that they are diabetes related. The symptoms are usually distressing and sometimes depressing, especially if they are predominantly nocturnal and disturb sleeping. Moreover, patients with diabetes are at an increased risk of peripheral arterial disease (PAD) which is mainly associated with diabetic foot ulceration and peripheral neuropathy or both. Diabetic neuropathic pain and foot screening is effective in identifying the severity of symptoms associated with neuropathic disease as well as the level of risk of developing foot ulceration in patients with diabetes. The importance of screening is to manage neuropathic pain in order to improve quality of life and to keep patients with low risk of developing foot ulcers or to manage those with high risk. Insufficient documentation may have a role in the low adherence detected for this criterion. However, other factors including shortage of staff and space available for neuropathy and foot screening programmes are of great importance. As it was essential to screen all patients for neuropathic pain and foot disease, improved documentation of referrals to such clinics is of particular importance. In the UK, 77.2% of those with type-2 diabetes had their foot pulses checked in the previous 15 months[127].

A further 3/5 criteria assessing management of diabetes complications showed an intermediate level of adherence as follows:

*Criterion 24:*

Blindness is one of the most common preventable complications of type-2 diabetes in Europe. The main aim of the ongoing eye screening is to detect referable retinopathic abnormality in asymptomatic patient in order to initiate therapy (normally within ophthalmology clinics) when needed to prevent visual impairment. Up to 39% of patients with type 2 diabetes have retinopathy at diagnosis and screening for diabetic

retinal disease was found to be effective at detecting unrecognised sight-threatening retinopathy [129].However, this 'A' graded recommendation was found to have an adherence of 56.7% (95% CI: 51.2, 62.3 [n=305 applicable patients]). Justified non-adherence for this criterion was found in one case, in which the patient had a documentation of having an eye screening test done in a private ophthalmology clinic. Poor documentation may also play a role for the low adherence here; however, this highlights the importance of improving documentation. In the UK, 85.6% of people with diabetes had had eye screening in the previous 15 months [127].

*Criterion 22:*

ACE inhibitors and ARBs play an important role in renal and cardiovascular protection in diabetic patients. These groups of medication dilate the efferent renal arteriole resulting in reduced intraglomerular pressure and reduced proteinuria regardless of systemic blood pressure status. In diabetic patients, these agents were found to be able to reverse microalbuminuria into no albuminuria or reduce the rate of progression of microalbuminuria to macroalbuminuria in the majority of cases. They were also found to reduce proteinurea and the rate of developing end-stage renal disease or doubling of serum creatinine. This 'A' graded recommendation (use of ACE inhibitors or angiotensin II-receptor antagonist in patients with microalbuminuria or proteinuria) showed an adherence of 78.2% (95% CI: 71.6, 84.9 [n=147 applicable patients]).

*Criterion 26*:

There are many agents which have showed their ability to control painful neuropathic symptoms in diabetic patients and to improve patients' quality of life. Older generation tricyclic antidepressants (TCAs) [amitriptyline, imipramine and desipramine] and newer antidepressants (duloxetine & venlafaxine) are a few examples of such medications. Other agents shown to have more effect on symptoms control involve anticonvulsants such as carbamazepine, gabapentin and pregabalin and opiate analgesia. This 'A' graded recommendation (use of tricyclic antidepressants, gabapentin or duloxetine when indicated) showed an adherence of 78.7% (95% CI: 67.0, 90.4 [n=47 applicable patients]).

The remaining criterion (criterion 23, appropriate screening of renal function) showed high levels of adherence of 94.1% (95% CI: 91.5, 96.7 [n=305 applicable patients]).

*Criteria assessing appropriate primary prevention of CVD*

Of the 12 criteria assessing the appropriate primary prevention of CVD, 5 criteria showed a low level of adherence. These criteria are:

*Criteria 29 and 30:*

Achieving targeted blood pressure levels, with an adherence of 33.5% (CI: 26.9, 40.1 [n=194 applicable patients]) and 16.7% (CI: 5.4, 27.9 [n=42 applicable patients]) respectively. The fact that patients with type-2 diabetes are at higher risk of developing CVD, retinopathy, neuropathy and renal disease gave a great importance to this criterion. Evidence strongly showed that the risk of development of all these diabetes complications (including risk of developing stroke, myocardial infarction, blindness and end-stage renal failure) can be reduced if appropriate blood pressure control has been achieved. Appropriate blood pressure control in patients with type-2 diabetes was defined by NICE guidelines as a target of <140/80 mmHg for most of patients, and <130/80 mmHg for those at more particular risk (co-existing kidney disease [microalbuminuria or patients with eGFR <60 ml/min/1.73 $m^2$], those with retinopathy, and those with previous stroke or transient ischaemic attack). In Scotland, 94.1% of patients with type 2 diabetes had their blood pressure recorded in the previous 15 months in 2011. Of these, 31.7% had a systolic BP measurement of ≤ 130/80 mmHg. Moreover, 36.4 % of type-2 diabetic patients in England had blood pressure control within broadly similar targets [127].

*Criteria 36 and 37:*

Use of fibrate when indicated with an adherence of 23.1% (CI: 1.7, 46.0 [n=13 applicable patients] for criterion 36 and 12.5% (3.1, 21.9 [n=48 applicable patients]) for criterion 37. Hypertriglyceridaemia is considered as an important modifiable biomarker of CVD risk. It is a complex condition which could be genetic related or frequently being secondary to other medical conditions including type-2 diabetes (associated with poor glycaemic control or renal and liver disease) [130]. Although the use of statins was supported by stronger evidence, the effectiveness of fibrates in CVD prevention among type-2 diabetic patients had a convincing evidence. Based on

that, NICE guidelines recommended the use of a fibrate (fenofibrate as first-line) in patients with triglyceride levels above 4.5 mmol/litre (could be more favourable than statin in some cases) or to add it to statin therapy if triglyceride levels remain in the range of 2.3–4.5 mmol/litre during statin use. The application of these criteria identified a total of 7 patients in whom applicability was not detectable due to the insufficient documentation of a recent triglyceride value and a low applicability in criterion 36 (n=13/305, 4.3%).

*Criterion 38:*

Offering smoking cessation advice for current smokers with a level of adherence of 24.0% (CI: 7.3, 40.7 [n=25 applicable patients]). Insufficient documentation of smoking status was highlighted during the application of this criterion. Furthermore, of the low numbers of applicable patients (due to insufficient documentation), only 6/25 (24.0%) patients were offered smoking cessation advice. Consequently, 19/25 (76.0%) patients did not receive the appropriate advice on smoking cessation.

Only 2/12 criteria assessing the appropriate primary prevention of CVD showed an intermediate level of adherences which are:

*Criterion 33:*

Use of statin when indicated, with an adherence of 61.2% (CI: 55.4, 66.9 [n=278 applicable patients]). Dyslipidaemia is an established and independent modifiable factor that increases the risk of developing CVD in patients with type-2 diabetes. Blood lipid profile management based on the appropriate control of LDL-C, TC, HDL-C and triglyceride levels. Statins have shown a great efficacy in controlling blood lipids level and have shown efficacy in reducing CV risk associated with type-2 diabetes with no additional side effects when compared to people without diabetes. Their efficacy in the primary prevention of CVD risk in type-2 diabetic patients was illustrated in three large randomised controlled studies (CARDS, ASCOT, HPS) [(131), (132), (133)]. Consequently, both SIGN and NICE guidelines recommended the addition of statin for primary prevention of CVD in patients with type 2 diabetes aged >40 years regardless of baseline cholesterol. During the application of this criterion, 3 cases were found to have documented justified non-adherences. One case was due to

pregnancy and the other two cases were due to the presence of active liver disease. This makes the adjusted adherence 62.2% (CI: 56.5, 67.9).

*Criterion 34*

Achieving a total cholesterol level of <5 mmol/l during statin therapy, with a 60.7% adherence (95% CI: 53.4, 68.0 [n=173 applicable patients]). When TC is not sufficiently controlled with the current statin dose or type, this could be an indication for the need to increase the current statin dose or to replace it with a more effective statin. NICE guidelines recommended a TC level target of < 4 mmol/l, however, SIGN recommended a TC level target of < 5 mmol/l. Targets used in this study were based on SIGN guidelines recommendations. In Scotland, cholesterol was recorded in 89.2% of patients within the previous 15 months, and the target of ≤5 mmol/l was achieved in 80.7% of those with type 2 diabetes compared to 77.6% in England [(127)]. Both percentages are notably higher than the percentage achieved in Qatar.

The remaining 5/12 criteria assessing the appropriate primary prevention of CVD (criteria 27, 28, 31, 32 and 35) showed high levels of adherence. Criterion 27 showed a 100% level of adherence and was applicable in the whole patient sample. This was because all patients should have blood glucose levels and blood pressure measured by a nurse before entry to doctor. This is a part of the assessment sheet which was completed for each patient at each appointment.

### 3.4.6 Patient based analysis

The overall criteria based analysis of MATs was able to identify areas which lacked appropriate care in the general population (patients with type-2 diabetes) and was used to identify criteria scoring low or a low-intermediate levels of adherence. Although this method of analysis can improve the overall care process, it does not reveal how each individual patient has received the recommended care process. For clinicians and research as well, it is important to know how many of the 305 patients did not receive the recommended care. This can be then used to study patients' clinical characteristics associated with adherence and be an opportunity for targeting pharmaceutical care to vulnerable patient groups. This could be also of great

importance in a busy clinics or hospitals where prioritised patient care plays an important role.

Adherence using individual patients as the unit of analysis revealed that prescribers adhered to < 50% of the applicable criteria in 9.8% of patients (n=30 patients with low level of adherence). Prescribers also adhered to < 70% of the applicable criteria in 40.7% of patients (n=124 patients with low-intermediate level of adherence). Furthermore, prescribers adhered to ≥70-<80% and ≥80% of the applicable criteria in 33.1% (n=101 patients with intermediate level of adherence) and 16.4% (n=50 patients with high level of adherence) respectively. Patients who would benefit from improving prescribers' adherence to criteria with low levels of adherence through an appropriate pharmaceutical care plan are those who scored a low and a low-intermediate level of adherence to applicable criteria (n=154 [50.5%] patients).

Exploratory statistical analysis was carried out in order to assess and examine the association of various parameters between patients in the low adherence group (n=154) and those in the high adherence group (n= 151). The analysis showed that mean BMI was found to be significantly higher in the high adherence group than the low adherence group (32.53±7.57 vs 30.76±6.13; p=0.025). In contrast, mean total cholesterol levels in the high adherence group was observed to be significantly less compared to the low adherence group (4.53±0.95 vs 4.84±0.97vs; p=0.005). Furthermore, among the high adherence group the percentage of hypertensive subjects was significantly higher than in low adherence groups (p=0.007).

Univariate logistic regression analysis showed that only blood pressure status and TC levels were significantly associated with high adherence levels. It was observed that odds of high adherence was 1.92 times higher (unadjusted OR= 1.92; 95% CI: 1.20, 3.09) among patients who had hypertension than non-hypertension cases which indicates that patients who do not have hypertension should be the target or prioritised for pharmaceutical care. Odds of high adherence was 1.58 times higher among patients who had a TC level of ≤4.5 mmol/l (unadjusted OR=1.58, 95% CI: 1.01, 2.49) indicating the need to target or prioritise patients with TC>4.5 mmol/l for pharmaceutical care review. Similar observations were found when the multivariate regression analysis was performed. This indicates that patients without hypertension

or patients with a TC>4.5 mmol/l need to be targeted or prioritised for pharmaceutical care planning and these two clinical characteristics are independently and even after adjusting other covariates significantly affecting the high adherence levels.

### 3.4.7 Clinical guidelines implementation

It is not unusual to find a gap between the clinical guidelines development and their implementation into practice [(134)]. Generally, the reason for low adherence in some criteria in this study could be related to some cultural, educational, time given per patient, and other practical differences between the countries where the guidelines were developed and where they are applied. A guideline developed in the United Kingdom could face difficulties when applied in Bedouin countries. However, published guidelines represent optimum standards for prescribing practice which provide a basis for improving quality of care.

Other factors identified by the New England Healthcare Institute (NEHI) which may influence physician adherence to clinical guidelines could involve the payment system (payment systems consider procedures rather than outcomes, and may be insufficient to change behaviour, or lack the uniformity in payer policies), lack of information technology systems (insufficient access to guidelines, or doesn't adequately support clinical decision-making, or insufficient resources to support adoption, staff training and maintenance of IT systems), physician culture, beliefs and habits (physicians receive little or no comparative feedback on their performance according to their adherence to evidence-based clinical practice guidelines which make them depend on their own judgment and personal experience to determine whether or not they are optimising treatment for patients) and the development and function of guidelines (some guidelines may lack transparency in guideline development or lack sufficient flexibility and relevance to clinical practice which leads to a lack of trust among doctors) [(135)]. With an exception of the payment system, all these factors could also apply to this study and influence prescriber's adherence to clinical guideline recommendations.

For patients, physicians and health care institutes, the greatest benefit that could be achieved by guidelines is to improve health outcomes and the standard quality of care

received by patients in different clinical settings. Guidelines that promote interventions of proven benefit and discourage ineffective ones have the potential to reduce morbidity and mortality and improve quality of life for some conditions. For type-2 diabetes primary prevention of disease complications is the recommended way to minimise morbidity and mortality and improved adherence to clinical guidelines adherence was positively related to better disease prognosis (although other factors such as patient attitudes and compliance are relevant and should be taken in consideration )[136), (121)]. In order to receive all these benefits, guidelines for treatment certain disease must be carefully selected and well introduced to physicians, who must agree to their content and be willing to integrate them into daily practice.

A number of different approaches have been used to improve the implementation of guidelines, and if used appropriately are effective under some circumstances (137). Systematic reviews of strategies for changing professional behaviour show that relatively passive methods of disseminating and implementing guidelines, by publication in professional journals or mailing to targeted healthcare professionals, rarely lead to changes in professional behaviour [(138)]. Some largely effective interventions to promote implementation of guidelines include interactive educational workshops, educational outreach (for prescribing), reminders and multi-faceted interventions. Others such as audit and feedback, local consensus conferences, opinion leader and patient mediated interventions, have variable effectiveness. Audit and feedback, another type of intervention, can be effective in improving professional practice, and when effective, the effects are generally small to moderate. The relative effectiveness of audit and feedback is likely to be greater when baseline adherence to recommended practice is low and when feedback is delivered more intensively. [(139)]

### 3.4.8 Comparison with the UK study

To find the differences in guideline implementation between the country where the guideline was developed and the country where international guidelines are used and to share expertise between the two countries, $MAT_{UK}$ previously designed in this study was applied within the clinical settings in the UK. Comparison between MAT application in the UK and in Qatar showed that a total of 18/38 (47.4%) criteria had a statistically significant difference in adherence levels to clinical guidelines. Of these

18 criteria, 11 criteria (61.1%) showed a better implementation within the UK. The remaining 7 criteria (38.9%) showed a better implementation in Qatar. Although overall adherence to guidelines for the whole study sample between Qatar and the UK was not compared (as the $MAT_{UK}$ contained five extra different criteria), it was thought that overall adherence (in the compared criteria) was higher in the UK. This could be due to the following reasons:

- In the UK, local guidelines are continuously produced and updated and may be widely available as a source of data for prescribers. However, in Qatar, there is no production of a local guideline and international guidelines represent the only source of information. As a result, international guidelines may not be familiar to some prescribers or may lack the appropriate information.

- In the UK, diabetes is part of the local enhanced services (LES) which are additional services provided by primary care practices to cover the enhanced aspects of clinical care of the patient established in Glasgow in 2004, beyond the scope of essential services and QOF. The purpose of diabetes LES is to enable the delivery of a more comprehensive and structured package of care to diabetic patients in primary care and ensures patients receive an annual review of their condition. There are essential elements that should be reviewed annually and recorded in LES for each diabetic patient, such as BMI, HbA1c, retinal screen, foot examination, blood pressure, micro-albuminuria test, e-GFR, blood lipids and smoking status. In addition, people with diabetes should have an annual care plan recorded in LES which includes discussion and advice around progress with diet and exercise, review medication and compliance, assessment for psychological problems (e.g. depression) and for complications, education and onwards referral to structured education programmes such as Diabetes Education and Self-Management for On-going and Newly Diagnosed (DESMOND). [140), (141), (142)]

- The UK study was performed one year after Qatar study in which the newly developed SIGN 116 guidelines became more familiar.

Areas which showed better adherence in Qatar were judged to be due to the differences in MAT application in the two clinical settings. $MAT_{Qat}$ was applied in a secondary care setting where a higher level of disease specific speciality among doctors is expected. This should be considered as a limitation to this comparison which should be added to the fact that information obtained from the UK study was derived from 15 GP practices in secondary care. Some of these GPs scored higher levels of adherence while others scored lower levels. Sampling strategies within these GP practices may also limit the accuracy of data and results (when grouped together) obtained for this comparison.

### 3.4.9 Impact of findings on practice

Implementing clinical guidelines guarantees the delivery of the best available evidence of clinical care which builds confidence in the service and ensures equality of care in different health care institutes. For diabetic patients, the use of high standard clinical guidelines was associated with an improved quality of care provided to patients and improved health outcomes. It was also associated with a reduction in disease morbidity and mortality.

Clinical audit is the component of a clinical system that offers the greatest potential to assess the quality of care routinely provided for health care users against explicit criteria. This can be used to define essential elements for the contentious quality improvement programmes. Adding clinical audit as a key element within a health service is essential and has the ability to yield many benefits.

The audit tool designed in this study provided a mechanism for reviewing the quality of care provided to patients with type-2 diabetes. Explicit criteria within this audit were derived from high standard clinical guideline recommendations. This tool is capable of the following:

- Using the long history of data within the case notes to confirm the quality of clinical services and to provide physicians and other healthcare professionals

with reliable information related to areas needing improvement to achieve better patient care.

- Detecting adherence of current practice to clinical guidelines recommendations in the management of type-2 diabetes and in the primary prevention of cardiovascular disease.

- Identifying clinical criteria with low, intermediate and high levels of adherence to target patients for improved care.

- This tool containing generalisable criteria may be used in different clinical settings to compare equality of prescribing (if patients are getting the same level of care in different care settings across a country) and identify care issues to initiate a pharmaceutical care plan. It can also be used as an example to generate criteria assessing other chronic diseases.

The application of this tool within the clinical settings in Qatar identified areas which lacked the appropriate care. These areas form the basis for future discussion and the starting point for pharmacists to be involved in diabetes management aiming to improve patient care. Pharmacists could be involved in improving these areas through a structured a pharmaceutical care plan. These areas were identified by criteria based MAT analysis and using an adherence of < 70% as threshold cut-off to involve criteria which scored low and low-intermediate level of adherences (a total of 14/35 criteria). These areas involve the following:

- Ensuring that all patients with type-2 diabetes were referred to a structured diabetes education programme and had these referrals documented in their medical notes and followed-up to ensure attendance.

- Ensuring that all patients with type-2 diabetes have been involved in setting their own target for HbA1c and have this target documented in their notes.

- Ensuring that all patients with type-2 diabetes achieved their own HbA1c target which could be ≤ 7%.

- Prescribing a third oral glucose lowering agent for patients with stable HbA1c ≥ 7.5% despite current therapy.

- Having HbA1c measured six to nine months after commencing pioglitazone and only continuing pioglitazone therapy if HbA1c reduced by 0.5%.

- Ensuring that all patients with type-2 diabetes were referred for retinal examination within the last 15 months and have these referrals documented in their medical notes including those carried out within private ophthalmology clinics.

- Ensuring that all patients with type-2 diabetes had a neuropathy/foot check within the last 15 months and have them documented in medical notes. This should involve foot clinic referrals or checking carried out by doctors during the appointment.

- Ensuring appropriate methods were used when blood pressure was measured and that patients achieved a target of <140/80 mmHg or < 130/80 mmHg in the presence of kidney, eye or cerebrovascular damage.

- Ensuring that all patients with type-2 diabetes aged > 40 years were prescribed a statin regardless of blood cholesterol level.

- Ensuring that all patients with type-2 diabetes maintained on the same dose of statin for > 6 weeks achieved a TC level of <5 mmoml/l.

- Ensuring that all patients with type-2 diabetes and a triglyceride level > 4.5 mmol/l are on a fibrate.

- Ensuring that all patients with type-2 diabetes on a statin but with a triglyceride level of 2.3-4.5 mmol/l are on a fibrate.

- Ensuring that all patients with type-2 diabetes have their smoking status documented in their medical notes and those who are currently smokers have been offered appropriate smoking cessation advice.

Vulnerable patient groups were also identified and found to be patients with elevated blood cholesterol level (TC >4.5 mmoml/l) and those who don't have a diagnosis of hypertension.

### 3.4.10 Strengths and limitations

*Strengths of study*

- The MAT and data collection sheet were field-tested on 20 patients, and allowed the assessment of the practicality and application of the final versions applied in this study.

- Results achieved in this study were obtained based on documented data collected from patients' medical notes and the researcher did not make any clinical judgement on the prescribing decisions.

- The MAT in this study was applied by the researcher under the supervision of the research group who were involved in its design and validation stage and who are expert in this field.

- MAT results obtained were fed-back and discussed with prescribers to achieve the best outcomes related to its future improvement.

*Limitations of study*

- The measurement of unjustified non-adherence in some criteria may principally be due to the lack of documentation of the rationale behind prescribing decisions or the failure in achieving certain clinical outcomes in medical records.

- Results obtained for sample size calculation were limited due to the lack of previous similar studies and lack of a diabetes register (which could give an idea about the number of diabetic patients attending the clinic and help in determining sample size and sampling strategy).

- Patient compliance was considered an important part of diabetic patient care and in achieving certain clinical outcomes. However, the MAT study could not identify levels of patients' compliance.

- Majority of data obtained for MAT application were collected from bulky paper medical records within files. Revising all these bulky patients' files and the difficulties in getting these files ready for inspection were associated with a considerable amount of time and effort making collect data process hard and time consuming.

# Chapter 4

## Cardiovascular Risk Assessment in Type-2 DM: targeting patients for pharmaceutical care

## 4.1 Introduction

### 4.1.1 Diabetes and risk of CVD

#### 4.1.1.1 Epidemiology

Cardiovascular disease is the main cause of death in patients with diabetes responsible for 52% of deaths in patients with type-2 diabetes in the UK. The risk of the disease macrovascular complications, including morbidity and mortality from cardiovascular disease (coronary heart disease and stroke) and peripheral vascular disease, is 2-5 times higher in patients with diabetes. Cardiovascular risk in patients with diabetes is equal to non-diabetic individuals with a previous heart attack and the risk of stroke was two-folds higher in patients with type-2 diabetes within the first five years of diagnosis when compared with the general population.

#### 4.1.1.2 Risk factors for developing CVD

*Non-modifiable risk factors*

Non-modifiable risk factors for developing CVD include: age (CVD risk increase with increased age), gender (men are at higher risk of CV events), diabetes duration (risk of diabetes microvascular and macrovascular complications increase with increased disease duration), family history and ethnicity (Asians are at higher risk of developing CVD). [143), (144)]

*Modifiable risk factors*

*Dyslipidaemia*

Dyslipedaemia (increased levels of LDL-C or TC) is an established and an independent risk factor in developing CVD. Type-2 diabetes is usually associated with increased levels of triglyceride combined with a reduced level of HDL and small, dense LDL particles. In people with diabetes, a reduction of 1 mmol/l in LDL-C can reduce the CVD risk by 21%. [(145)]

*Hypertension*

Increased blood pressure is another potential risk factor of CVD morbidity and mortality. The UKPDS 36 trial showed that risk of death over 10 years in type-2 diabetic patients from CVD was reduced by 15% with each 10 mmHg reduction in systolic blood pressure (SBP). This was also associated with a 12% reduction in any type-2 diabetes related complication risk [146]. Blood pressure target for patients with type-2 diabetes is <140/80 mmHg (or <13/80 mmHg in the presence of co-morbidity).

*Hyperglycaemia*

In patients with type-2 diabetes, elevated levels of blood glucose were associated with increases risk of disease complications including CVD morbidity and mortality. Each 1% reduction in HbA1c was associated with 21%, 14% and 37% reductions in risk of: deaths related to diabetes, myocardial infarction and microvascular complications respectively [147], [28]. SIGN guidelines recommended an HbA1c target level of 7.0% in patients with type-2 diabetes and considered it to be reasonable to reduce risk of microvascular and macrovascular diseases.

*Smoking*

One more important and independent risk factor for CVD in diabetic patients is smoking [148]. Unlike other risk factors smoking was found to have an additional excess risk for CVD among diabetic patients [149]. Smoking cessation significantly reduces CVD risk and SIGN guidelines recommended that all diabetic patients who continued to smoke should be offered a smoking cessation advice. [150]

*Other possible risk factors*

Obesity is not yet recognised as an independent CVD risk factor in diabetic patients due to the lack of evidence. Furthermore, microalbuminuria is an independent marker associated with a doubled CVD risk. However, whether reducing albumin excretion rate specifically reduces cardiovascular morbidity or mortality is undetermined due to insufficient evidence. [151]

### 4.1.2 CVD risk estimation and prevention in type-2 diabetic patients

Cardiovascular disease is defined as coronary heart disease (CHD angina and myocardial infarction) plus stroke, peripheral vascular disease and heart failure. The implementation of educational interventions, lifestyle modification and drug treatment to prevent the development of CVD symptoms in high risk individuals is termed primary prevention. The use of similar measures in patients already presenting with one or more of these diseases is referred to as secondary prevention. The identification of high risk individuals and slowing the progression of CVD is becoming increasingly important as a public health priority. According to the Joint British Societies' (JBS) guidelines on prevention of cardiovascular disease in clinical practice, CVD prevention should be equally targeted in patients who are at higher risk in developing a CVD as follows:

- Patients with established CVD.
- Patients with type-1 or type-2 diabetes.
- Asymptomatic individuals who don't have an established CVD but have a combination of risk factors that makes them at higher total risk (estimated multifactorial CVD risk ≥20% over 10 years) of developing atherosclerotic CVD for the first time.

The aim of targeting these patient groups is to reduce the risk of a non-fatal or fatal cardiovascular event and to improve both quality and length of life. Educational interventions, lifestyle modification and drug treatment to prevent the development of CVD symptoms in high risk individuals are aiming to modify patients' risk factors. These include: lowering blood pressure, adjusting plasma lipids and reducing glycaemia to achieve their clinical guidelines recommended targets. [152]

The risk of macrovascular complications, including morbidity and mortality from cardiovascular disease (coronary heart disease and stroke) and peripheral vascular

disease, is 2-5 times higher in patients with diabetes. Cardiovascular risk in patients with diabetes is equal to non-diabetic individuals with a previous heart attack and the risk of stroke was two-folds higher in patients with type 2 diabetes within the first five years of diagnosis when compared with general population[44, 45]. Cardiovascular disease is the main cause of death in patients with diabetes responsible for 52% of deaths in patients with type-2 diabetes. In Qatar, CVD, hypertension, diabetes and cancer accounted for significant levels of mortality and morbidity. As reported by the national authorities, CVD diseases were found to be the first cause of death among Qatari people accounting for 20% of deaths. This was followed by road traffic injuries and endocrine disorders (diabetes) responsible for 16.2% and 11.9% of deaths respectively. [153]

For type-2 diabetes, primary prevention of disease complications with a special focus on CVD is the recommended way to minimise morbidity and mortality. Although all patients diagnosed with type-2 diabetes are at higher risk of developing CVD, patients at highest absolute risk (based on their risk factors) have the most to gain from interventions. Consequently, CVD risk assessment and modification of risk factors have become essential tools in the prevention of CVD in people with type-2 diabetes in order deliver the appropriate care. [154]

There are many different factors associated with an increased risk for cardiovascular events. One of the most challenging tasks is to identify high-risk populations for proper prevention and management. This has raised the following questions: What is the best approach to assessing patients' risk? What is the level of care provided to these patients? What issues should be addressed to achieve effective CVD risk reduction in clinical practice?

### 4.1.3 Pharmaceutical care

Pharmaceutical care was defined according to Hepler and Strand as the responsible provision of drug therapy for the purpose of achieving definite outcomes (including: disease management, symptoms relief or elimination, preventing or delaying disease progress, or preventing disease development) which all lead to improving patients' quality of life [155]. This was later defined by Cipolle *et al* as the effective and safe medication use through the pharmaceutical care practitioners who should learn each patient's medication experience to identify, resolve, and prevent drug therapy problems. [156]

The aim of pharmaceutical care in practice is to deliver a systematic, comprehensive and consistent quality of service to each individual patient. In the hospital settings, clinical pharmacists have a good chance to deliver structured pharmaceutical care that addresses individual patient's needs. Based on a careful patient's assessment, drug therapy problems can be identified (proper indication, efficacy, safety, adverse drug events, failure to provide prophylactic treatment and inadequate follow-up or monitoring of treatment) by the pharmacist and an individualised pharmaceutical care can be delivered. The delivery of pharmaceutical care should be based on a good coordination with other healthcare professionals and use reliable records. [157], [158]

Pharmaceutical care plans are used to organise and document all the patient's pharmaceutical care issues and any drug-related action that was taken or needs to be taken to optimise patient care. Care plan should be clear enough and measurable in order to achieve the recommended goals of therapy in a feasible time-frame. [158]

### 4.1.4 Pharmaceutical care for diabetic patients

There are clearly important pharmaceutical care issues in the management of patients with diabetes. Pharmacists are in a good position to target their knowledge in the care of patients with diabetes, especially if they are elderly patients or tend to have co-existing morbidity and disability. Improving patient education and optimising chronic medication are two important parts of the pharmaceutical care in diabetes [159], [160]. Several studies demonstrated the benefits of pharmacist involvement in the control of

HbA1c and blood pressure and in the management of CVD risk factors in patient with type-2 diabetes. Randomised controlled trials have shown a significant reduction in HbA1c levels when pharmacists are involved as part of the multidisciplinary team caring for patients with type-2 DM [161], [162], [163]. Moreover, the number of patients with type-2 diabetes who achieved better blood pressure control significantly increased when pharmacists involved in the primary care team [164].

The effectiveness of pharmaceutical care programmes provided to type-2 diabetic patients through pharmacists to manage cardiovascular risk was demonstrated in many trials. The effect of a 12- month pharmaceutical care programme on the vascular risk (changes in 10 year coronary heart disease and stroke risk in patients without a history of cardiovascular disease) in type-2 diabetes was evaluated using the changes in $HbA_{1c}$ as an outcome measure. The mean reduction (95% CI) accompanied by the programme subjects (n=92) was greater than the control group (n=88) for HbA1c (-0.5% vs 0.0%), systolic blood pressure (-14 mmHg vs -7 mmHg) and diastolic BP (-5 mmHg vs -2 mmHg) [$P \leq 0.043$]. The median (interquartile range) 10-year estimated risk of the first CHD event decreased (5%) in the programme group compared with no change in the control group. The results of this study showed the importance of the pharmaceutical care programmes and the important role of the pharmacist in the management of diabetes. [165]

Randomised controlled trials of veterans affairs multi-disciplinary education and diabetes intervention for cardiac risk reduction, a pharmacist-led group medical visit programme, illustrated the efficacy of this programme in reducing CVD risk associated with type-2 diabetes and in achieving HbA1c, blood pressure and LDL targets after 4-6 months follow up. [166], [167]

In the Middle-East, the influence of a 12 month pharmaceutical care programme in type-2 diabetes patients and its effect on disease control and health-related quality of life was studied in the United Arab Emirates. The care programme was found to be associated with a significant reduction in HbA1c, blood pressure and CVD Framingham risk prediction score. [168]

Although pharmaceutical care programmes and pharmacists involvement in type-2 diabetes care have a great impact on diabetes outcomes (including HbA1c, blood pressure control and CVD risk reduction), pharmacists in Qatar are not yet involved as part of the multidisciplinary team who provide care to diabetic patients. Currently pharmacists only play a dispensary role and have no direct input in diabetes care. [107]

### 4.1.5 Aims and Objectives

#### 4.1.5.1 Aims

1. To quantify the risk of developing cardiovascular disease among type-2 diabetic patients to identify and target patients at higher risk.

2. To determine to what extent medication needs in patients with high risk of developing CVD are being met to address issues needed to achieve effective CVD risk reduction in clinical practice.

3. To use the results obtained from the evaluation of adherence to guidelines to design a care plan for use in the delivery of pharmaceutical care in patients with type-2 diabetes with a special focus on CVD risk reduction.

#### 4.1.5.2 Objectives

1. Review the evidence for the impact of type-2 diabetes on the risk of developing cardiovascular disease.

2. Investigate primary risk in a sample of patients with type-2 diabetes (with or without hypertension or hypercholesterolaemia) and who have no history of CVD. The patient sample was drawn from a defined population attending Hamad Medical Corporation in Qatar.

3. Apply an existing risk assessment tool to data obtained from sampled patient records and calculate the respective 10 year risks of acquiring CVD (UKPDS Risk Engine).

4. Study the associations between each risk factor within the risk calculator (age, gender, DM duration in years, systolic blood pressure, HbA1c, TC and HDL) and being at a higher risk of developing CVD and use it to characterise (or target) patients at higher CVD risk.

5. Analyse the level of care provided to patients at higher risk of developing CVD compared to patients at lower CVD risk to determine if their medication and pharmaceutical care needs are different.

6. Derive a profile of care issues and formulate the overall findings from the MAT study in chapter 3 and this study into a pharmaceutical care plan to be used as a starting point for the hospital pharmacists in Qatar to deliver pharmaceutical care to patients attending the diabetes clinic.

7. Validate the designed pharmaceutical care plan before its field-testing for implementation in the real practice.

## 4.2 Methods

### 4.2.1 Study design, Subjects and settings

A cross-sectional population based study conducted on a sample of 305 patients with type-2 diabetes drawn from a defined population attending the out-patient diabetes clinic at Hamad General Hospital in Qatar who meet the inclusion and exclusion criteria from the previous study in chapter 3 of this thesis. The project was performed under the supervision of academic tutors within the University of Strathclyde, Glasgow, UK and the medical research centre in Qatar.

### 4.2.2 CVD risk assessment

As the first aim of this study was to quantify and calculate the risk of developing CVD among type-2 diabetic patients, validated on-line tools providing CVD risk scores were used (risk scores are estimating the probability of developing cardiovascular disease in individuals who have not already diagnosed with a CVD and help in making clinical decisions on the use of CVD prevention measures). A search for an appropriate risk calculator was performed during the literature review. Type-2 diabetes specific CVD risk calculator from the diabetes trial unit at the Oxford centre for diabetes, endocrinology and metabolism (the UK Prospective Diabetes Study, UKPDS risk engine) was found and selected. The use of this risk engine for this study was agreed by the research group and supported by the NICE guideline (as it is a specific CVD risk calculator for diabetic patients).

The calculator software was downloaded from the UKPDS risk engine website. Patients' data needed to apply the risk calculator were obtained from the existing filled data collection sheets used in the MAT study (Appendix 6). Individual patient's information was entered into the calculator and 10 year risk estimates (risk scores) of developing any CHD, fatal CHD, any stroke and fatal stroke (Figure 8) were obtained for each patient.

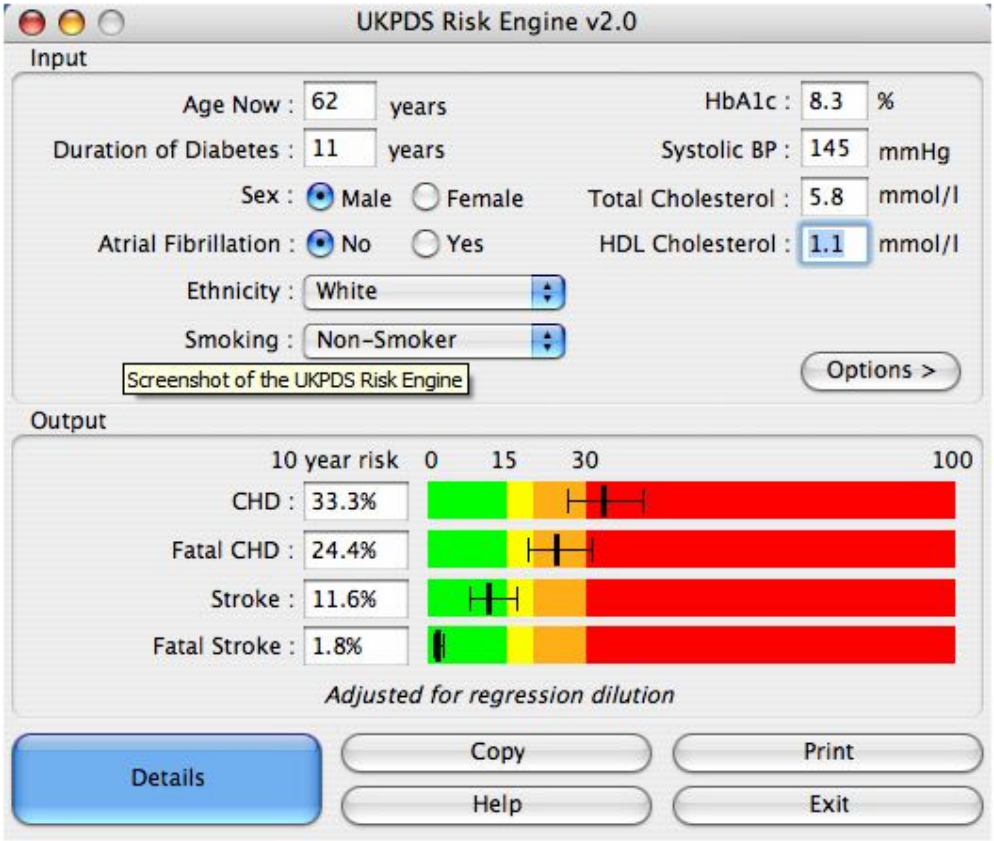


**Figure 8: UKPDS risk engine**

Each patient's four risk scores were recorded on an Excel spread sheet next to patient's key and clinical characteristics. Patients were then categorised according to their CVD risk scores into 3 categories: high risk group, low risk group or undetermined. Patients were defined to be at 'high' risk if an estimate for a particular risk was ≥15% (cut-off value). This cut-off value was determined based on JBS2 guidelines. As the UKPDS risk engine does not provide the combined patient's CVD risk (the tool provides risk of CHD and stroke separately), a CHD risk of ≥ 15% was considered to be equivalent to a CVD risk of ≥ 20% over 10 years. [(152), (169)]

When the calculator was applied to the study sample, three important issues faced the researcher. The first issue was the high number of patients with unknown smoking status. Smoking is an important and an independent risk factor for CVD risk estimation. The second issue concerned ethnicity: under the ethnicity drop-down menu, the UKPDS engine offers a selection of one ethnic background including:

White, Afro-Caribbean or Asian-Indian. Here the following question rose: which ethnic background should be selected for patients from the Middle-East where this study took place? The third issue was about the TC, HDL and systolic blood pressure values that should be entered into the risk calculator if the patient is prescribed medications that lower blood pressure (anti-hypertensive drugs) or lipid lowering therapy. Should the most recently measured values be entered to the risk engine or the original values before starting the treatment? The researcher therefore sent an e-mail inquiry to the UKPDS expert group using the e-mail provided in their website to clarify these issues.

Prof. Rury Holman (Professor of diabetic medicine), the director of diabetes trials unit OCDEM, University of Oxford, responded to the e-mail enquiry and confirmed that good CVD risk estimates can be obtained using the recent blood pressure, TC and HDL values even after treatment. It was also recommended to fix the tool to 'White' ethnic background during the application of the calculator on a sample of patients from the Middle-East. Regarding undocumented smoking status it was advised that the CVD risk for individuals with unknown smoking status cannot be calculated directly. However, it was recommended to calculate the risk for every one in this group (those with unknown smoking status) twice at the same time, firstly, missing smoking status should be set to non-smoker and then secondly as smoker. This will give a range over which the true risk will lie for each patient. This will also give the lower and upper estimates for the whole study sample as it is unlikely that all those with missing smoking status are all smokers or all non-smokers (the true estimate is likely to be somewhere between this range).

The above recommendations from the UKPDS team were discussed among the research group. The research group agreed to perform the CVD risk analysis based on UKPDS team advice. During this meeting, a decision about dealing with unknown smoking status was also achieved as follows:

For each patient with unknown smoking status, the risk calculator should be applied twice at the same time (firstly, missing smoking status should be set to non-smoker and then secondly, as smoker according to UKPDS team recommendation):

- If the two scores were both ≥ 15% for a particular CVD risk category, the patient should join the high risk group (as the patient is already at high risk whether smoker or not and smoking is just adding to risk).

- If the two scores were both < 15% for a particular CVD, the patient should join the low risk group (as the patient is already at low risk whether smoker or not).

- If the score was < 15% for a particular CVD when the calculator was set to non-smoker and become ≥ 15% after changing smoking status to smoker, the patient should be excluded from the analysis and recorded as undetermined (as it will not be possible to decide to which risk group this patient should be assigned without knowing his/her smoking status).

### 4.2.3 Analysis of CVD risk scores and risk factors

Risk groups obtained from the CVD risk calculator were used to study the association between each risk factor within the risk calculator (age, gender, DM duration in years, systolic BP [diagnosis with hypertension was also added], HbA1c, TC and HDL) and being at a higher risk of developing CVD and used to characterise and target patients who are most likely to be at higher risk of developing CVD. Clinical characteristics obtained from this analysis were then used as a measure to identify appropriate candidates needing prioritisation of care. Smoking as a CVD risk factor was not assessed due to insufficient documentation of smoking status in the majority of patients.

*Statistical analysis*

Descriptive statistics were used to summarise all demographic and clinical characteristics of the patients in each CVD risk group. Quantitative variable means between high and low risk groups were compared using Unpaired 't' test. Associations between different categorical variables were assessed using chi-square test. A p-value less than 0.05 was considered as statistically significant. All statistical analyses were carried out using statistical package SPSS version 19 (SPSS, Inc.,

Chicago, IL) after importing the data from Excel. Data were expressed using mean, standard deviation (SD), percentage and 95% CI.

### 4.2.3 Levels of care provided to patients at higher risk of developing CVD

Levels of care provided to patients with type-2 diabetes within the diabetes clinic in HGH, Qatar, have been previously measured in chapter 3 of this thesis. In this study, areas which lacked the appropriate care and needed an inclusion in a clinical review for improvement were identified within the whole study sample. However, whether these measures differ in patients who are at higher risk of developing CVD is unknown.

The Excel sheet contained patients' keys, CVD risk scores and CVD risk categories from a previous section (section 4.2.2) were combined in the Excel sheet which contained MAT results from chapter 3 of this thesis. The final formed Excel sheet contained all the data obtained from the MAT and CVD risk analysis that contains all relevant patient information. This sheet was then imported to SPSS and the adherence for each criterion was compared between the two risk groups (high risk group vs low risk group).

### 4.2.4 Design of pharmaceutical care plan

Overall findings from the MAT study and CVD risk analysis were used to derive a pharmaceutical care plan intended for use used as a starting point for the hospital pharmacists in Qatar to deliver pharmaceutical care to patients attending the diabetes clinic. A previously designed pharmaceutical care plan (produced and validated by E.Ejim within the University of Strathclyde, Glasgow was used and adapted [170]. The author of this thesis was involved in the original design of this exciting care plan which was derived from the findings of several MAT studies in the UK and used to produce a tool (Multi-MAT) for use in the delivery of pharmaceutical care to patients with common long term conditions and co-morbidity (Appendix 10).

Modifications on the original care plan involved the removal of unnecessary data fields and disease specific monitoring data. Standard checks have been also changed

to involve care issues identified from the current study and the study in chapter 3 (criteria which showed low levels of adherence). Care plan adaptation also involved the addition of other relative data items and was used to produce the first-draft of the disease specific care plan.

### 4.2.5 Validation of the designed care plan

The care plan drafted in the previous section was validated by the research group within the University of Strathclyde. The research group included three academic tutors and the researcher. Each member of the group received a copy of the drafted care plan. Modifications on content, format and style were made and documented. These changes were then used to produce the validated form of the care plan.

## 4.3 Results

### 4.3.1 CVD risk assessment

Patients were defined to be at 'high' risk if estimates were ≥15%. There were overall 46.1% (95% CI: 40.3, 51.9, n=130), 29.5% (95% CI: 24.4, 35.1, n=82), 12.8% (95% CI: 9.3, 17.3, n=35) and 0% in the 'high' risk groups for non-fatal and fatal CHD (n= 282 eligible [undetermined cases found in 23 patients]), fatal CHD (n=278 eligible [undetermined cases found in 27 patients]), non-fatal and fatal stroke (n=274 eligible [undetermined cases found in 31 patients]) and fatal stroke (n=305 eligible) respectively (Table 20). Undetermined cases were all due to unknown smoking status. Detailed results obtained from CVD risk analysis are shown in Table 21.

**Table 20: CVD risk assessment in diabetic patient sample (n=305)**

| CVD Risk | Patients at high risk | | 95% CI |
|---|---|---|---|
| | n | % | |
| Any CHD | 130/282 | 46.1 | 40.3, 51.9 |
| Fatal CHD | 82/278 | 29.5 | 24.4, 35.1 |
| Any stroke | 35/274 | 12.8 | 9.3, 17.3 |
| Fatal stroke | 0/305 | 0 | 0 |

**SD**: standard deviation, **CHD**: coronary heart disease

**Table 21: CVD risk analysis**

| Mean of CVD risks<br>Median of CVD risks | Distribution of % risk [95% CI as %] | | | | | |
|---|---|---|---|---|---|---|
| | Any CHD n=282 | | Fatal CHD n=278 | | Any stroke n=274 | |
| | ≥ 15% | < 15% | ≥ 15% | < 15% | ≥ 15% | < 15% |
| All patients (n=305) [95%CI] | 130 (46%) [40, 52] | 152 (54%) [48, 60] | 82 (30%) [24, 35] | 196 (70%) [65, 76] | 35 (13%) [9, 17] | 239 (87%) [83, 91] |
| Mean (SD)<br>Median (IQR 1, 3) | - | | - | | - | |
| Patients with known smoking status (n= 98):<br>Mean (SD)<br>Median (IQR 1, 3)<br>Range | 15.6 (13.3)<br>11.3 (5.9, 21)<br>3.6-58.2 | | 10.8 (11.4)<br>6.4 (2.4, 13.8)<br>1.3-46.2 | | 7.1 (9.4)<br>2.9 (1.3, 7.7)<br>1.5-21.5 | |
| Patients with unknown smoking status (n= 207):<br>Mean (SD)<br>Median (IQR 1, 3) if non-smokers<br>Range | 16.0 (10.9)<br>13.8 (7.4, 22)<br>1.4-68.3 | | 11.5 (9.6)<br>9.9 (4.0, 16.5)<br>0.4-56.5 | | 7.2 (7.3)<br>4.9 (2.4, 9.9)<br>0.4-42.3 | |
| Mean (SD)<br>Median (IQR 1, 3) if smokers<br>Range | 20.6 (13.4)<br>18.2 (10.0, 28.5)<br>1.8-78.8 | | 14.9 (11.9)<br>12.7 (5.3, 21.3)<br>0.5-64.9 | | 10.7 (10.3)<br>7.4 (3.6, 14.9)<br>0.6-57.3 | |

**CVD:** cardiovascular disease**, CHD:** coronary heart disease, **SD**: standard deviation, **IQR**: interquartile range

### 4.3.2 Association between risk factors and CVD risk score

It was observed that the high risk of developing any CHD (n=130 in the high risk group vs. n=152 in the low risk group) was significantly associated with increased means of age (60.0±8.7 vs. 47.0±9.7, p<0.0001), DM duration in years (13.6±6.9 vs. 7.5±4.5, p<0.0001), systolic blood pressure (144±16.9 vs. 136±17.5, p<0.0001), HbA1c level (9.0±1.7 vs. 8.1±1.9, p<0.0001), and reduced HDL-C (1.07±0.3 vs. 1.2±0.42, p=0.002). Also, the percentage of patients who were likely to have had a high risk was significantly higher among males than females and in patients diagnosed with hypertension (64.6% vs. 35.4%, p<0.0001), (76.2% vs. 23.8%, p<0.0001) respectively (Table 22):

**Table 22:**
**Comparison of risk factors in type-2 DM patients with and without a high risk of developing any CHD**

| Variable | Low risk group CHD (n=152) | High risk group CHD (n=130) | p-value* |
|---|---|---|---|
| Age<br>Mean (SD) | 46.9 (9.7) | 60.0 (8.7) | < 0.0001 |
| DM duration (years)<br>Mean (SD) | 7.5 (4.5) | 13.6 (6.9) | < 0.0001 |
| Systolic BP<br>Mean (SD) | 136.0 (17.5) | 144.0 (16.9) | < 0.0001 |
| HbA1c<br>Mean (SD) | 8.1 (1.9) | 9.0 (1.7) | < 0.0001 |
| TC<br>Mean (SD) | 4.7 (0.9) | 4.9 (1.1) | 0.111 |
| HDL<br>Mean (SD) | 1.2 (0.4) | 1.07 (0.28) | 0.002 |
| Gender | | | |
| Male: n=135 | 51 (33.6%) | 84 (64.6%) | < 0.0001 |
| Female: n=147 | 101 (66.4%) | 46 (35.4%) | |
| HTN | | | |
| Hypertensive: n=175 | 76 (50.0%) | 99 (76.2%) | < 0.0001 |
| Non-hypertensive: n=107 | 76 (50.0%) | 31 (23.8%) | |

* chi square test, **SD:** standard deviation, **CHD**: coronary heart disease, **HTN**: hypertension, **TC**: total cholesterol, **DM**: diabetes mellitus, **BP**: blood pressure, **HDL**: high-density lipoprotein

In addition to increased TC (4.9, SD: 1.1 vs. 4.6, SD: 1.0, p=0.042), increased means of age (63±7.9 vs. 48.0±9.6, p<0.0001), DM duration in years (16.0±6.7 vs. 7.8±4.5, p<0.0001), systolic blood pressure (146±17.3 vs. 136±16.9, p<0.0001), HbA1c level (9.2±1.7 vs. 8.3±1.9, p<0.0001), and reduced HDL-C (1.06±0.3 vs. 1.18±0.4, p=0.016) were significantly associated with increased risk of developing fatal CHD (n=82 in the high risk vs. n=196 in the low risk group) as shown in Table 23.

**Table 23:**
**Comparison of risk factors in type-2 DM patients with and without a high risk of developing fatal CHD**

| Variable | Low risk group CHD (n=196) | High risk group CHD (n=82) | p-value* |
|---|---|---|---|
| Age<br>Mean (SD) | 48.4 (9.6) | 62.8 (7.9) | < 0.0001 |
| DM duration (years)<br>Mean (SD) | 7.8 (4.5) | 16.0 (6.7) | < 0.0001 |
| Systolic BP<br>Mean (SD) | 136.3 (16.9) | 146.1 (17.3) | < 0.0001 |
| HbA1c<br>Mean (SD) | 8.3 (1.9) | 9.2 (1.7) | < 0.0001 |
| TC<br>Mean (SD) | 4.6 (0.96) | 4.9 (1.07) | 0.042 |
| HDL<br>Mean (SD) | 1.18 (0.4) | 1.06 (0.28) | 0.016 |
| Gender<br>Male: n=130<br>Female: n=148 | 82 (41.8%)<br>114 (58.2%) | 48 (58.5%)<br>34 (41.5%) | 0.01 |
| HTN<br>Hypertensive: n=174<br>Non-hypertensive: n=104 | 106 (54.1%)<br>90 (45.9%) | 68 (83.0%)<br>14 (17.1%) | < 0.0001 |

* chi square test, **SD:** standard deviation, **CHD**: coronary heart disease**, HTN**: hypertension, **TC**: total cholesterol, **DM**: diabetes mellitus, **BP**: blood pressure, **HDL**: high-density lipoprotein

It was also found that the high risk of developing non-fatal and fatal stroke (n=35 in the high risk group vs. 239 in the low risk group) was significantly associated with increased means of age (69.4±5.4 vs. 49.5±9.3, p<0.0001), DM duration in years (18.4±7.2 vs. 8.6±5.0, p<0.0001), systolic BP (145±19.8 vs. 138±17.4, p=0.04) and in patients diagnosed with hypertension (Table 24).

**Table 24:**
**Comparison of risk factors in type-2 DM patients with and without a high risk of developing any stroke**

| Variable | Low risk group CHD (n=239) | High risk group CHD (n=35) | p-value* |
|---|---|---|---|
| Age<br>Mean (SD) | 49.5 (9.3) | 69.4 (5.4) | < 0.0001 |
| DM duration (years)<br>Mean (SD) | 8.6 (5.0) | 18.4 (7.2) | < 0.0001 |
| Systolic BP<br>Mean (SD) | 138.3 (17.4) | 144.7 (19.8) | 0.047 |
| HbA1c<br>Mean (SD) | 8.6 (1.9) | 8.4 (1.3) | 0.602 |
| TC<br>Mean (SD) | 4.7 (1.0) | 4.7 (0.93) | 0.764 |
| HDL<br>Mean (SD) | 1.15 (0.38) | 1.11 (0.32) | 0.592 |
| Gender | | | |
| Male: n=135 | 113 (47.3%) | 22 (62.9%) | 0.085 |
| Female: n=139 | 126 (52.7%) | 13 (37.1%) | |
| HTN | | | |
| Hypertensive: n=170 | 139 (58.2%) | 31 (88.6%) | 0.001 |
| Non-hypertensive: n=104 | 100 (41.8%) | 4 (11.4%) | |

* chi square test, **SD:** standard deviation, **CHD**: coronary heart disease**, HTN**: hypertension, **TC**: total cholesterol, **DM**: diabetes mellitus, **BP**: blood pressure, **HDL**: high-density lipoprotein

### 4.3.3 Level of care provided to patients at higher risk of developing CVD

Table 25 showed the results obtained from the comparison of adherence in individual MAT criterion in type-2 DM patients with and without a high risk of developing CVD.

**Table 25:**
**Comparison of adherence in individual MAT criterion in type-2 DM patients with and without a high risk of developing CVD (n=282 patients)**

| # | Criteria | High risk group n=130 | | | Low risk group n=152 | | | p value* |
|---|---|---|---|---|---|---|---|---|
| | | Applic-able n (%) | Adher-ence n (%) | Non adherence n (%) | Applic-able n (%) | Adher-ence n (%) | Non-adherence n (%) | |
| 1 | referral to a structured diabetes education programme | 130 (100%) | 39 (30%) | 91 (70%) | 152 (100%) | 44 (29%) | 108 (71%) | 0.847 |
| 2 | record a target HbA1c value for each patient | 130 (100%) | 0 (0%) | 130 (100%) | 152 (100%) | 0 (0%) | 152 (100%) | - |
| 3 | had at least two documented HbA1c measurements | 128 (98%) | 91 (71%) | 37 (29%) | 150 (99%) | 116 (77%) | 34 (23%) | 0.234 |
| 4 | achieve an HbA1c value of ≤ 7% | 90 (69%) | 14 (16%) | 76 (84%) | 107 (70%) | 51 (48%) | 56 (52%) | **<0.0001** |
| 5 | use of metformin or sulphonylurea as first-line therapy | 129 (99%) | 119 (92%) | 10 (8%) | 146 (97%) | 139 (95%) | 7 (5%) | 0.309 |
| 6 | start dual therapy when indicated | 96 (74%) | 83 (87%) | 13 (13%) | 80 (53%) | 71 (89%) | 9 (11%) | 0.647 |
| 7 | avoid co-prescribing four oral agents | 88 (68%) | 69 (78%) | 19 (22%) | 110 (72%) | 96 (87%) | 14 (13%) | 0.096 |
| 8 | co-prescribe metformin or sulphonylurea with gliptin, pioglitazone or glinide | 79 (61%) | 73 (92%) | 6 (8%) | 82 (54%) | 79 (96%) | 3 (4%) | 0.277 |
| 9 | prescribe third oral agent or exenatide when indicated | 70 (54%) | 42 (60%) | 28 (40%) | 58 (38%) | 37 (64%) | 21 (36%) | 0.661 |
| 10 | with BMI ≥ 25 kg/m2 prescribed metformin | 101 (78%) | 89 (88%) | 12 (12%) | 126 (83%) | 110 (87%) | 16 (13%) | 0.852 |
| 11 | patient on metformin had an estimated GFR >45 ml/min/1.73 $m^2$ | 104 (80%) | 103 (99%) | 1 (1%) | 118 (78%) | 117 (99%) | 1 (1%) | 0.928 |
| 12 | measure renal function for patients on metformin and an estimated GFR ≤45 ml/min/1.73 $m^2$ | 1 (0.7%) | 1 (100%) | 0 (0%) | 1 (0.6%) | 1 (100%) | 0 (0%) | - |
| 13 | avoid the use of metformin in patients with estimated GFR < 30 ml/min/1.73 $m^2$ | 105 (81%) | 105 (100%) | 0 (0%) | 118 (78%) | 118 (100%) | 0 (0%) | - |
| 14 | co-prescribe metformin or sulphonylurea as part of dual or triple therapy | 104 (80%) | 93 (89%) | 11 (11%) | 102 (67%) | 96 (94%) | 6 (6%) | 0.221 |
| 15 | try oral therapy before commencing insulin | 53 (41%) | 38 (72%) | 15 (28%) | 41 (27%) | 32 (78) | 9 (22%) | 0.323 |
| 16 | prescribe insulin when indicated | 85 (65%) | 63 (74%) | 22 (26%) | 67 (44%) | 43 (64%) | 24 (36%) | 0.185 |
| 17 | on exenatide or liraglutide had a BMI>30 $kg/m^2$ | 2 (2%) | 1 (50%) | 1 (50%) | 4 (3%) | 4 (100%) | 0 (0%) | 0.121 |
| 18 | avoid the use of thiazolidinedione in patients with heart failure | 32 (26%) | 32 (100%) | 0 (0%) | 30 (20%) | 30 (100%) | 0 (0%) | - |
| 19 | avoid the use of thiazolidinedione in patients with osteoporosis | 32 (26%) | 29 (91%) | 3 (9%) | 30 (20%) | 26 (87%) | 4 (13%) | 0.623 |
| 20 | appropriate continuation of thiazolidinedione therapy | 8 (6%) | 3 (38%) | 5 (63%) | 8 (5%) | 4 (50%) | 4 (50%) | 0.614 |
| 21 | continuation of oral agent when insulin commenced | 34 (26%) | 30 (88%) | 4 (12%) | 30 (20%) | 25 (83%) | 5 (17%) | 0.573 |
| 22 | prescribe ACE inhibitor or ARB to manage micoabuminuria or proteinuria | 72 (55%) | 61 (85%) | 11 (15%) | 59 (39%) | 40 (68%) | 19 (32%) | **0.022** |

**Table 25:**
**Comparison of adherence in individual MAT criterion in type-2 DM patients with and without a high risk of developing any CHD (n=282 patients)-continued**

| # | Criteria | High risk group n=130 | | | Low risk group n=152 | | | p value |
|---|---|---|---|---|---|---|---|---|
| | | Applic-able n (%) | Adher-ence n (%) | Non adherence n (%) | Applic-able n (%) | Adher-ence n (%) | Non-adherence n (%) | |
| 23 | renal function check | 130 (100%) | 125 (96%) | 5 (4%) | 152 (100%) | 139 (91%) | 13 (9%) | 0.107 |
| 24 | retinal examination | 130 (100%) | 73 (56%) | 57 (44%) | 152 (100%) | 87 (57%) | 65 (43%) | 0.855 |
| 25 | neuropathy/foot check | 130 (100%) | 41 (32%) | 89 (69%) | 152 (100%) | 29 (19%) | 123 (81%) | **0.016** |
| 26 | prescribe medication to manage neuropathy | 27 (21%) | 22 (82%) | 5 (19%) | 17 (11%) | 13 (77%) | 4 (24%) | 0.688 |
| 27 | blood pressure measurement | 130 (100%) | 130 (100%) | 0 (0%) | 152 (100%) | 152 (100%) | 0 (0%) | - |
| 28 | prescribe ACE inhibitor or ARB for hypertension | 100 (77%) | 85 (85%) | 15 (15%) | 74 (49%) | 60 (81%) | 14 (19%) | 0.493 |
| 29 | achieve BP target without co-morbidities | 100 (77%) | 25 (25%) | 75 (75%) | 76 (50%) | 33 (43%) | 43 (57%) | **0.010** |
| 30 | achieve BP target with co-morbidities | 21 (16%) | 3 (14%) | 18 (86%) | 14 (9%) | 3 (21%) | 11 (79%) | 0.583 |
| 31 | avoid drugs worsen blood glucose control | 100 (77%) | 97 (97%) | 3 (3%) | 76 (50%) | 71 (93%) | 5 (7%) | 0.259 |
| 32 | avoid the use of drugs that worsen BP control | 100 (77%) | 91 (91%) | 9 (9%) | 76 (50%) | 68 (90%) | 8 (11%) | 0.734 |
| 33 | prescribe statin when indicated | 127 (98%) | 88 (69%) | 39 (31%) | 125 (82%) | 65 (52%) | 60 (48%) | **0.005** |
| 34 | achieve targeted TC level with statin therapy | 80 (62%) | 47 (59%) | 33 (41%) | 69 (45%) | 43 (62%) | 26 (38%) | 0.657 |
| 35 | avoid drug interaction with statins | 52 (40%) | 52 (100%) | 0 (0%) | 53 (35%) | 48 (91%) | 5 (9%) | **0.023** |
| 36 | prescribe fibrate when indicated | 4 (4%) | 1 (25%) | 3 (75%) | 8 (5%) | 2 (25%) | 6 (75%) | 1.000 |
| 37 | add fibrate to statin therapy when indicated | 29 (22%) | 4 (14%) | 25 (86%) | 17 (11%) | 2 (12%) | 15 (88%) | 0.844 |
| 38 | smoking cessation advice | 14 (11%) | 6 (43%) | 8 (57%) | 11 (7%) | 0 (0%) | 11 (100%) | **0.013** |

*chi-square test
**MAT**: medication assessment tool, **CVD**: cardiovascular disease, **DM**: diabetes mellitus, **CHD**: coronary heart disease, **BP**: blood pressure, **TC**: total cholesterol

The comparison showed that the level of care provided to patients at higher or lower CVD risk was not significantly different in the majority of criteria. However, the comparison highlighted the importance of achieving an appropriate blood pressure and HbA1c controls in patients with a higher risk of developing CVD. Achieving an HbA1c level of ≤ 7% and blood pressure of <140/80 mmHg targets were considerably lower in the high risk group compared to lower risk group (criterion 4 and criterion

29). Although not statistically significant, criterion 17 showed lower level of adherence (<70%) in the high risk group.

### 4.3.4 Design of pharmaceutical care plan

#### 4.3.4.1 Pharmaceutical care plan 1st draft

<table>
<tr><td colspan="5">Pharmaceutical Care Plan for Patients with type-2 Diabetes Mellitus with no history of CVD</td><td colspan="3">Date:</td></tr>
<tr><td colspan="3">Patient Information</td><td>Specific Monitoring Data</td><td>Standard Checks</td><td>√</td><td>Care issue</td></tr>
<tr><td colspan="2">HC #:</td><td>Age:</td><td rowspan="4">HbA1c profile:<br>Recent value: ……....<br>Previous values:<br>…….. , ……..</td><td>Referred to structured diabetes education programme</td><td></td><td></td></tr>
<tr><td colspan="2">Name:</td><td>Gender: ❑ Male ❑ Female</td><td>Attended the diabetes education programme</td><td></td><td></td></tr>
<tr><td colspan="2">❑Type 1, ❑Type 2 diabetes</td><td>Known allergies:</td><td rowspan="2">Had a documented HbA1c target</td><td rowspan="2"></td><td rowspan="2"></td></tr>
<tr><td colspan="3">Weight: Height: BMI:</td></tr>
<tr><td colspan="3">Smoking Status: ❑ Smoker ❑ non-smoker ❑ ex-smoker ❑ not documented</td><td>Last check dates:<br>Eye: Foot:</td></tr>
<tr><td colspan="3">Social history: ❑ Lives alone ❑ Housebound ❑ Other: …….</td><td>BP measurement:<br>Recent value: ……...</td><td>Achieved targeted HbA1c (≤ 7% For majority of patients)</td><td></td><td></td></tr>
<tr><td colspan="3">Relevant Medical History</td><td rowspan="2">HbA1c target: ……</td><td rowspan="2">On a third oral glucose lowering agent if HbA1c remained ≥7.5%</td><td rowspan="2"></td><td rowspan="2"></td></tr>
<tr><td>Hypertension</td><td>❑ Yes ❑ No</td><td>Diabetes duration: ……</td></tr>
<tr><td>Pregnancy or breastfeeding</td><td>❑ Yes ❑ No</td><td>Hypoglycaemia attack<br>❑ Yes ❑ No</td><td rowspan="2">Lipid profile:<br>Recent TC: …….<br>Recent HDL: …….<br>Recent triglyceride: ……</td><td></td><td></td><td></td></tr>
<tr><td colspan="3">Other:</td><td>Had HbA1c level measured 6-9 months when pioglitazone initiated</td><td></td><td></td></tr>
<tr><td colspan="3">Current Medication</td><td rowspan="8">CVD risk assessment:<br>CVD risk score: ……<br>Patient likely to be at higher CVD risk if more of the following apply:<br>❑ Aged ≥ 60 years<br>❑ With DM duration ≥14 years<br>❑ Has a systolic blood pressure ≥ 144 mmHg<br>❑ Has an HbA1c ≥9 mmol/l<br>❑ Has a TC level of ≥ 5 mmol/l<br>❑ HDL-C level ≤1.07 mmol/l<br>❑ Male gender</td><td>Continued on pioglitazone only if HbA1c reduced by 0.5% after 6 months from treatment.</td><td></td><td></td></tr>
<tr><td colspan="3" rowspan="7"></td><td>Had retinal examination done and referral documented within the last 15 months</td><td></td><td></td></tr>
<tr><td>Had neuropathy/foot screening done and referral documented within the last 15 months</td><td></td><td></td></tr>
<tr><td>Had blood pressure measured using appropriate technique</td><td></td><td></td></tr>
<tr><td>Achieved BP of <140/80 mmHg (or <130/80 in the presence of kidney, eye or cerebrovascular damage)</td><td></td><td></td></tr>
</table>

**Pharmaceutical care plan 1st draft- continued**

| Standard Checks | √ | Care issue | Individualised care issues | | |
|---|---|---|---|---|---|
| Aged >40 years is on a statin | | | *Care issue* | *Action* | *Output* |
| Maintained on the same dose of statin, achieved a TC level of <5 mmol/l | | | | | |
| Had triglyceride level >4.5 mmol/l, prescribed a fibrate | | | | | |
| On a statin with triglyceride level of 2.3-4.5, prescribed a fibrate | | | | | |
| Had smoking status documented in medical notes | | | | | |
| Currently smoker, offered smoking cessation advice | | | | | |

| Individualised care issues | | | | | |
|---|---|---|---|---|---|
| *Care issue* | *Action* | *Output* | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |

#### 4.3.4.2 Pharmaceutical care plan after validation

<table>
<tr><td colspan="4">Pharmaceutical Care Plan for Patients with Type-2 Diabetes Mellitus with no History of CVD</td><td colspan="3">Date:</td></tr>
<tr><td colspan="4">Patient Information</td><td>Specific Monitoring Data</td><td>Standard Checks</td><td>√</td><td>Care issue</td></tr>
<tr><td colspan="2">HC #:</td><td colspan="2">Age:</td><td rowspan="4"><u>HbA1c profile</u>:<br>HbA1c target: ……<br>Recent value: ……....<br>Previous values:<br>…….. , ……..</td><td>HbA1c target documented</td><td></td><td></td></tr>
<tr><td colspan="2">Name:</td><td colspan="2">Gender: ❑ Male ❑ Female</td><td>HbA1c target achieved</td><td></td><td></td></tr>
<tr><td colspan="2">Diabetes duration:</td><td colspan="2">Known allergies:</td><td>On a third oral glucose lowering agent if HbA1c remains ≥7.5%</td><td></td><td></td></tr>
<tr><td colspan="4">Weight: Height: BMI:</td><td>HbA1c level measured 6-9 months after pioglitazone started</td><td></td><td></td></tr>
<tr><td colspan="4">Smoking Status: ❑ Smoker ❑ non-smoker ❑ ex-smoker ❑ not documented</td><td rowspan="2"><u>Last screening dates</u>:<br>Eye:<br>Foot:</td><td></td><td></td><td></td></tr>
<tr><td colspan="4">Social history: ❑ Lives alone ❑ Housebound ❑ ❑ Other:</td><td>Stop pioglitazone only if HbA1c not reduced by ≥0.5% after 6 months from treatment.</td><td></td><td></td></tr>
<tr><td colspan="4">Relevant Medical History</td><td rowspan="3"><u>BP measurement</u>:<br>Recent value: ……...<br><br><u>Lipid profile:</u><br>Recent TC: …….<br>Recent HDL: …….<br>Recent triglyceride: ……</td><td>Retinal secreening checked/documented in the last 15 months</td><td></td><td></td></tr>
<tr><td>Hypertension</td><td>❑ Yes ❑ No</td><td colspan="2">Any hypoglycaemia episode: ❑ Yes ❑ No</td><td>Neuropathy/foot screening checked/ documented in the last 15 months</td><td></td><td></td></tr>
<tr><td>Pregnancy or breastfeeding</td><td>❑ Yes ❑ No</td><td colspan="2">Other:</td><td>Achieved BP <140/80 mmHg (or <130/80 if kidney, eye or cerebrovascular damage present)</td><td></td><td></td></tr>
<tr><td>Current Medication</td><td colspan="2">Dose/frequency</td><td>Indication</td><td rowspan="9"><u>CVD risk assessment</u>:<br>*CVD risk score: ……%<br><br>CVD risk increases with increasing inclusion criteria below:<br>❑ Age ≥ 60 years<br>❑ with DM duration ≥14 years<br>❑ has a SBP ≥ 144 mmHg<br>❑ Has an HbA1c ≥9 mmol/l<br>❑ has a TC level of ≥ 5 mmol/l<br>❑ HDL level ≤1.07 mmol/l<br>❑ Male gender</td><td>Aged >40 years prescribed a statin</td><td></td><td></td></tr>
<tr><td rowspan="8"></td><td colspan="2" rowspan="8"></td><td rowspan="8"></td><td>Maintained on the same dose of statin for >6 weeks, achieved a TC level of <5 mmol/l</td><td></td><td></td></tr>
<tr><td>Prescribed a fibrate if triglyceride level >4.5 mmol/l.</td><td></td><td></td></tr>
<tr><td>Prescribed a fibrate if on a statin with triglyceride level of 2.3-4.5.</td><td></td><td></td></tr>
<tr><td>Referred to structured diabetes education programme</td><td rowspan="2"></td><td rowspan="2"></td></tr>
<tr><td>Attended a diabetes education programme</td></tr>
<tr><td>Smoking status documented</td><td></td><td></td></tr>
<tr><td>Offer smoking cessation advice to smokers</td><td></td><td></td></tr>
</table>

* UKPDS risk engine, patient considered at high risk if CVD the score was ≥ 15%. For these patients bold parts of standard checks need a high concern.

**Pharmaceutical care plan after validation- continued**

| Individualised care issues | | | |
|---|---|---|---|
| # | *Care issue* | *Action* | *Output* |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |

## 4.4 Discussion

Diabetes is a major factor which places patients at higher risk of vascular events. Cardiovascular disease is the leading cause of morbidity and mortality in type-2 diabetes mellitus. About 52% of mortality from type-2 DM is related to CVD. For type-2 diabetes, primary prevention of disease complications including CVD is the recommended way to minimise morbidity and mortality. Improved adherence to clinical guideline recommendations was positively related to better disease prognosis. As a result, early risk recognition and management of patients with type-2 DM is very important.

The aim of this study was to determine the prevalence and the clinical characteristics of patients diagnosed with type-2 DM who are at higher risk of developing CV events. The study also addressed issues needed to achieve effective CVD risk reduction in clinical practice based on an assessment of care provided to these patients according to clinical guidelines recommendations.

### 4.4.1 CVD risk assessment

As the first aim of this study was to determine the prevalence of type-2 diabetic patients at higher risk of developing CV events, an appropriate technique to evaluate the CVD risk was sought. Direct examination of coronary and peripheral arterial disease using angiographic and intravascular ultrasound techniques represents the "gold standard" for defining the extent of vascular disease for any patient. However, other non-invasive techniques (for example: stress nuclear myocardial perfusion imaging, stress echocardiography, exercise stress test combined with thallium-$^{201}$ scintigraphy) may be useful for the evaluation of high-risk patients with type-2 DM [(171)]. Due to the easier application and data availability, non-invasive techniques based on CVD risk score prediction (from risk factors) through the validated on-line clinical calculator was used in this study.

*CVD risk calculator*

Several calculators to predict CVD risk score in general populations are available. CVD risk calculation differs between these risk calculators according to the CVD definition used and risk factors included within each calculator. Examples of such calculators include:

- Framingham: provides 4 to 12 years risk for CVD, stroke, CHD, myocardial infarction (MI), and death from CVD. [172]

- Joint British Societies (JBS) / British National Formulary (BNF) charts.

- ASSIGN: provides 10-year risk for CVD and chosen for use by the SIGN guidelines. [173]

- QRISK2: provides 10-year risk of heart attack or stroke. [174]

Although some of these calculators consider diabetes as one of the risk factors used to predict the CVD risk, none of them was a diabetes-specific calculator that predicts the absolute CVD risk in patients with type-2 diabetes. Furthermore, the Framingham Heart Study tends to underestimate risks for people with diabetes as this study included relatively few diabetic subjects. As a result, the UKPDS engine (v2.0) was used for the estimation of ten-year percentage risk for this study.

The UKPDS Risk Engine is a type-2 diabetes specific CVD risk calculator based on data from 4, 540 patients. The calculator uses risk factors such as age, sex, duration of diabetes, history of atrial fibrillation, ethnicity, serum cholesterol, blood pressure, HBAIC, smoking status, and HDL to provide risk estimates for non-fatal and fatal coronary heart disease, fatal coronary heart disease, non-fatal and fatal stroke and fatal stroke in individuals with type-2 diabetes who do not have heart disease. The NICE guideline recommended the use of the UKPDS risk engine to estimate CVD risk in diabetic patients annually. The guideline also recommended the use of this

risk engine for educational purposes when discussing cardiovascular complications with patients.

*CVD risk scores*

All patients within the study sample (n=305, patients' demographics described in chapter 3) have had the CVD risk score calculated. The estimated CVD risk score used to define patients at higher risk was ≥15%. The risk of developing any CHD in patients with type 2-diabetes was notably higher (46% of patient scored a high risk, n=130/282) than the risk of developing a fatal CHD (29.5% of patient scored a high risk, n=82/278), non-any stroke (12.8% of patient scored a high risk, n=35/274) or fatal stroke (0% of patient scored a high risk, n=0/305). Average risk score for any CHD was also found to be high at 15.6 (SD: 13.3) for those with known smoking status and ranged from 16 (SD: 10.9) to 20.6 (SD: 13.4) for those with unknown smoking status.

### 4.4.2 Association between risk factors and CVD risk scores

NICE guidelines considered a diabetic patient to be at lower premature cardiovascular risk if the patient is not overweight, is normotensive (<140/80 mmHg in the absence of antihypertensive therapy), does not have microalbuminuria, does not smoke, does not have a high-risk lipid profile, has no history of CVD and, has no family history of CVD. However, in clinical practice it is essential to identify patients at higher risk of developing CVD in order to deliver to these patients the appropriate care that manages their high risks. One of the optimal ways to do this is to apply the UKPDS risk engine for each patient and define patients' risks accordingly.

The other way to target care in these patients is to identify them based on the CVD risk factors they have. Although this way of identifying patients is not very accurate, it provides an easier and quicker way to identify and target patients for care (especially in a very busy clinic or in the presence of a shortage in clinical staff or facilities). The diabetes clinic, where this study took place, is one the busiest clinics

within HGH in Qatar (as it represents the main clinic for management of diabetes in the country). Targeting patients for care in such a clinic using patient's characteristics would be easier and more convenient.

As a result, risk groups obtained from CVD risk analysis were used to study the association between each risk factor within the risk calculator and being at a higher risk of developing CVD. Results obtained (where the risks were intensified) were used to characterise and target patients who are most likely to be at higher risk of developing CVD as follows:

- High risk of developing any CHD was intensified in patients (targeted patient group):

  - Aged ≥ 60 years
  - With diabetes duration ≥ 14 years
  - Patients with hypertension or with SBP≥ 144 mmHg
  - With uncontrolled HbA1c value of ≥ 9%
  - With HDL level of ≤ 1.07 mmol/l
  - Male gender

The risk of developing any CHD was lower among patients aged ≤ 47 years, with diabetes duration ≤ 7.5 years, without hypertension or with controlled SBP of ≤ 136 mmHg, with higher HDL levels ≥ 1.2 mmol/l or females.

- High risk of developing any CHD was intensified in patients:

  - Aged ≥ 63 years
  - With diabetes duration ≥ 16 years
  - Patients with hypertension or with SBP≥ 146 mmHg
  - With uncontrolled HbA1c value of ≥ 9.2 %
  - With TC level ≥ 5 mmol/l
  - With HDL ≤ 1.06 mmol/l

- Male gender

Finally, risk of developing any CHD was intensified only in patients:

- Aged ≥ 69 years
- With DM duration ≥ 18 years
- With hypertension or with SBP ≥ 145 mmHg

There was no analysis performed for the risk of developing fatal stroke, as within the whole study sample there was no patient who scored a risk of ≥ 15% to be considered at high risk for this particular disease.

The above clinical characteristics showed that targeting patients according to any CHD risk would already include patients at higher risk of developing any stroke or fatal CHD. The only variable need to be added to the targeted patients list is TC (≥ 5 mmol/l) which was listed under fatal CHD but did not appear under any stroke. As a result, patients presenting with the highest number of combinations of the following clinical characteristics could be prioritised for care as they are expected to be at higher risk of developing CVD:

- Aged ≥ 60 years
- With diabetes duration ≥ 14 years
- with SBP≥ 144 mmHg
- With uncontrolled HbA1c value of ≥ 9%
- With TC level ≥ 5 mmol/l
- With HDL level of ≤ 1.07 mmol/l
- Male gender

Variables with a statistically significant difference between the low and high CVD risk groups were not evaluated by multiple logistic regression analysis to identify independent risk factors for CVD risk, because patients' categorisation to each group was done based on risk 'estimates' and aiming just to target patients. There was no real CVD group (real cases with an established CVD) to compare these risk factors

against to be able to identify independent risk factors for CVD. Furthermore, when the UKPDS calculator was developed, all variables included in the final UKPDS risk engine model to estimate CVD risk were statistically significant in likelihood ratio testing. The model for example did not include obesity or body size measures (BMI) in the final formula as all available measures of size and obesity were examined and found to be not independently contributing to estimated risk in the presence of the other more informative risk factors included currently in the UKPDS risk engine.

### 4.4.3 Level of care provided to patients at higher risk of developing CVD

After having patients at higher risk of developing CVD identified based on the CVD risk analysis, it was essential to determine what their medication needs were. The study in chapter 3 identified areas of care which needed improvement in the whole study sample. However, it did not show if these areas differ between patients at higher risk of developing CVD and those at lower risk. If the needs are different this should be taken in consideration when delivering care to these patients.

Adherence to the 38 MAT criteria was analysed and compared in the two patient risk groups. When the levels of adherence were compared between the two groups, it showed:

- The majority of criteria showing a level of adherence of < 70% were the same in the two patient groups and should be included in any care plan aiming to improve adherence to clinical guidelines.

- Achieving an HbA1c level of ≤7% (criterion 4) and blood pressure target of <140/80 mmHg (criterion 29) was low in both groups. However, adherence of both criteria was significantly lower among patients at higher risk of developing CVD. As a result achieving appropriate blood glucose and blood pressure controls should be given a high priority to achieve effective CVD risk reduction in clinical practice.

- The use of ACEI or ARB to manage microalbuminurea or proteinuria (criterion 22) showed a significant difference in adherence between the two groups. Adherence to this criterion was significantly lower in the low risk group indicating the importance of targeting this criterion if a generalised care plan to all patients with diabetes is implemented.

- Criterion 17 showed a level of adherence of <70% in the high risk group. However, this criterion was not considered due to the very low number of applicable patients.

### 4.4.4 Design of a pharmaceutical care plan

The benefits of involving pharmacists in the management of diabetes have been demonstrated earlier in this study. As a starting point for the pharmacists to get involved in care of diabetes, the study suggested a pharmaceutical care plan based on MAT and CVD risk analysis findings. Areas needing improvement identified by the MAT study that were found to match the care needs of patients with high CVD risk were grouped into a structured care plan to be applied by pharmacists during the delivery of care. The aim of this care plan was to improve prescribing in patients with type-2 DM according to the evidence base and to reduce the risk of developing CVD among diabetic patients. It represents a part of the service development process which requires long-term follow-up to assess its effectiveness.

The care plan was adapted based on a previous study containing three main headings. The first two headings: patient information and disease specific monitoring data were adapted in a way to help the pharmacist identify any clinical issues or problems related to patient's management. The third heading: standard checks: listed the identified areas (from MAT and CVD risk analysis studies) that needed improvement to be checked in every targeted patient. After completing data fields under these three headings, identified care issues should be used by the pharmacist to complete the individualised care issues table within the care plan. This may include the need of

the addition of a new treatment for the management of blood pressure or blood glucose controls, referrals to other clinics, or the need to have blood tests.

### 4.4.5 Validation of the designed care plan

The suggested care plan was validated by the research group at the University of Strathclyde and the following modifications and suggestions were carried out and discussed:

- Under patient information title: it was suggested to remove type of diabetes row as it was clear from the care plan title that it is intended to be used for type-2 diabetic patients and to use the space left for diabetes duration data field. It was also suggested to replace the word ‘attack’ with ‘any episodes’ and to divide the current medication space into three columns containing: medication name, dose/frequency and indication. This will make improve clarity and should help in identifying more care issues related to drug treatment.

- Under specific monitoring data: it was suggested to move HbA1c target field above, so all that data related to HbA1c are in the same place. It was also suggested to change the word ‘check’ to ‘screening’, add % symbol to CVD risk score (to show that the value to fill this space is a percentage), add information about the risk calculator to be used and the cut-off value to evaluate the risk score obtained, and to change ‘aged’ to ‘age’, systolic blood pressure to SBP and HDL-C to HDL.

- Under standard checks: it was suggested to rearrange the statements to match the relevant item from the next column (specific monitoring data), describe the reason behind typing two statements in bold, restructure the statements to make it easier to read and save space and to remove blood pressure measurement technique (as pharmacist is not expected to monitor blood pressure technique which the nurse used).

- Suggestions on style changes included: improve use of the spaces above and below the table, list all the standard checks in one page, narrow the specific monitoring data column in order to give more space for the standard checks.

All these modifications were carried out and used to produce the care plan after validating the document.

### 4.4.6 Applying developed care plan in clinical settings

The care plan developed above could not be finalised before its field-testing within the diabetes clinic in Qatar. A possible method to apply this care plan is suggested as follows: patients who have an appointment to attend the clinic on a specific day will have their medical files ready to for inspection. The pharmacist will start to screen these files and target his/her patients according to the methods suggested earlier in this chapter. Once patients have been selected, the care plan can be completed by the pharmacist and kept in patient file. Based on the patient's clinical assessment, the pharmacist will identify and document the care issues for this patient and will then suggest actions (under individualised care issues in page 2 of the suggested care plan). Based on a previous arrangement with the clinic doctors, they will be asked to have a look at the pharmaceutical care plan at the time they assess the patient's information written by the nurse. Doctors may then take the appropriate action (example: prescribe the suggested drug or provide a laboratory request for a suggested test) or may take a different action. The pharmacist can then complete the out-put based on the action taken by the doctor. The inclusion of a working pharmaceutical care plan would improve documentation and reduce the number of unjustified non adherences seen in the earlier MAT study.

Providing medication counselling and educational interventions to patients with type-2 diabetes are another important role for pharmacists during the delivery of care to diabetic patients. However, these services were not included in the suggested care plan as the diabetes clinic in Qatar has a special section called diabetes educators.

Diabetes educators provide the essential educational interventions to patient with diabetes. Furthermore, some of the medication counselling is performed by pharmacists with the patients at the time when they get their medication from pharmacy. Therefore, the need of involving pharmacists in providing educational interventions and the type of educational measures which needs to be delivered to patients by pharmacist should be investigated based on the quality of service provided currently by diabetes educators.

### 4.4.5 Study strengths and limitations

*Strengths of study*

- The calculator selected to quantify and assess the CVD risk in this study was a type-2 diabetes specific risk calculator.

- All statistical analyses were done using statistical package SPSS version 19 (SPSS, Inc., Chicago, IL).

- The suggested care plan ensured the involvement of medication needs in patients at higher risk of developing CVD and was validated by academic staff.

*Limitations of study*

- Applying the UKPDS risk engine is more accurate when used with patients similar to those in the UKPDS cohort (aged from 25-65 years and with duration of diabetes < 20 years). However, in this study, age ranged from 21-79 years and diabetes duration ranged from 1-30 years with 11.5% of patients (n=35) had a diabetes duration of ≥20 years.

- Ethnic backgrounds within the UKPDS risk engine offered the selection between White, Afro-Caribbean or Asian-Indian. However, this study was

carried out on patients from the Middle-East fixing the calculator on White background.

- The suggested structure for the pharmaceutical care plan was not field-tested before it can become final.

# Chapter 5

## Overall discussion and future work

## 5.1 Overall discussion

*General Background*

Diabetes is an increasing health problem affecting approximately 285 million people around the world in 2010. This number is estimated to reach 438 million people by 2030 according to the International Diabetes Federation Atlas. The increase in diabetes prevalence was mainly due to an increase of type-2 diabetes which is the most common type of diabetes representing around 85-90% of the cases in the UK.

Patients with diabetes are at high risk of developing long-term complications which are the responsible cause of the disease morbidity, hospitalisation and mortality. This risk increases with time, especially that most patients with type-2 diabetes may have the disease for a long time before the diagnosis. However, there is good evidence on how the onset of the complications associated with the disease can be prevented, delayed or their progression slowed, if it is managed appropriately and from an earlier stage. Hyperglycaemia and hypertension are the two major controllable risk factors for developing diabetes complications. Other risk factors include: duration of diabetes, smoking, hyperlipidaemia and albuminuria.

The risk of macrovascular complications, including morbidity and mortality from cardiovascular disease (coronary heart disease and stroke) and peripheral vascular disease, is 2-5 times higher in patients with diabetes. Cardiovascular risk in patients with diabetes is equal to non-diabetic individuals with a previous heart attack and the risk of stroke was two-folds higher in patients with type-2 diabetes within the first five years of diagnosis when compared with general population. Cardiovascular disease is the main cause of death in patients with diabetes responsible for 52% of deaths in patients with type-2 diabetes.

This highlighted the importance of managing the disease and its complications according to an evidence-base, and clinical guidelines may offer the best advice for the management of type-2 DM based on best published clinical and economic

evidence, as well as expert agreement. The selection of type-2 diabetes as the main subject for this study was due to:

- Increased disease prevalence as well as increased rates of disease complications.
- Its high importance for health care authorities and organisations.
- Availability of high-quality evidence to inform standards in diabetes care.
- Its ability to change (disease complications and morbidity can be reversed or stabilised) as it often responds dramatically to treatment and improved care.

*Improving quality of care*

Health care quality can be defined as the degree to which physicians and health care institutions fulfil their care obligations to individual patients, and the degree to which patients, physicians, and health care institutions enable these obligations to be fulfilled justly across the population [(175)]. Improving quality of health care is the combined and unceasing efforts of everyone (healthcare professionals, patients and their families, researchers, payers, planners and educators) to make the changes that will lead to better patient outcomes (health), better system performance (care) and better professional development [(176)]. As a result, healthcare will not realise its full potential unless change making becomes an intrinsic part of everyone's job, every day, in all parts of the system.

A range of approaches have been introduced into literature, and all of them claim to provide solutions to some of the main problems in patient care. Examples of such approaches (that represent different methods for improving care) include: evidence-based medicine (EBM), total quality management (TQM) assessment, accreditation and accountability, professional development, and patient empowerment (table 26)[(176)]. Some of these approaches focus on professionals and others on

organisations; some emphasise the value of self-regulation, and others believe in external control.

**Table 26: Methods for quality improvement and their theories in improving care**

| Method | Theories |
|---|---|
| Evidence-based medicine<br>Clinical guidelines practice<br>Decision aids | Provision of best evidence and convincing information leads to optimal decision making and optimal care |
| Professional education and development<br>Self-regulation<br>Recertification | Bottom-up learning based on experiences in practice and individual learning needs leads to performance change |
| Assessment and accountability<br>Feedback<br>Accreditation<br>Public reporting | Providing feedback on performance relative to peers, and public reporting of performance data, motivate change in practice routines. |
| Patient-centered care<br>Patient involvement<br>Shared decision making | Patient autonomy and control over disease and care processes lead to better care and outcomes |
| Total quality management and contentious quality improvement<br>Restructuring processes<br>Quality systems<br>Breakthrough projects | Improving care results from changing the system, not from changes the individuals. |

Another method for improving the quality of care in chronic conditions like diabetes is the introduction of chronic care model (CCM). The CCM is a well-established organisational framework (using comprehensive and multisystem approaches) for

chronic care management and practice improvement [177]. The effectiveness and importance of this model in improving chronic illness management has been illustrated in many studies [178]. The model is built on six modifiable components of healthcare delivery which include four concepts to address practice strategies: organisational support, clinical information systems, delivery system design and decision support. The other two concepts are patient centred including self-management support, and community resources. [177]

Pay for performance (equates quality with achievement of several predetermined health targets by populations) as a quality improvement approach has been also used and found to be a limited and unadvisable approach. Comprehensive and valid measures should replace such a method in improving quality of care.[179]

*Clinical audit and feedback*

The quality of health services provided to patients receiving care within primary or secondary health settings has been a subject of health care authorities' research for many years. Measuring this quality of care is of great importance not only for health care authorities, in order to guarantee that services provided to people are meeting the expected levels of performance, but also for clinicians, managers, other health care providers as well as for patients or the public. Its value for physicians, managers or other health care providers originates from its ability to identify areas, policies or services that need more attention or are appropriate for re-design and change to achieve optimum level. For the public it contributes to their debates on service quality, performance and accountability. Quality assessment is also essential for other applications like accreditation, pay for performance, new services evaluation and targeting or prioritising vulnerable patient groups lacking the appropriate level of care.

Clinical audit is the process which involves a systematic review of care or service against explicit criteria and implements change in order to improve quality of patient care and outcomes. The explicit criteria within the clinical audit assess the structure, processes and outcomes of care when conducting the systematic review. Based on

audit findings, modifications are implemented at an individual, team, or service level and further monitoring is used to assure improvement in healthcare delivery.

Use of MAT is an example of practising clinical audit in clinical settings which are designed to assess the adherence of the current health facility to the expected clinical performance according to specific criteria assessing quality of care within the clinical audit. It was developed to enable researchers identify gaps in management of specific diseases and evaluate the appropriate medication use to improve clinical outcome of treatment. Its development was a result of the increased importance of clinical guidelines in the delivery of health care as well as the need to demonstrate clinical effectiveness. It is one of the most important tools which can be used for clinical auditing and shown to be a valid instrument for use in a variety of care settings.

Other tools designed for the purpose of explicit medication use assessment include:

- BEERS set [(180)] which was then updated by McLEOD's set [(181)]. These sets were later extended into STOP/START tools (screening tool of older persons' potentially inappropriate prescriptions/ screening tool to alert doctors to the right treatment). [(182), (183)]
- BASGER set that targets medication screening and reaching therapeutic goals. [(184)]
- ACOVE set (assessing care of vulnerable elders). [(185)]
- Pont and Martirosyan which are disease specific tools for asthma and diabetes. [(186), (187)]

*Key findings*

Developing explicit criteria to measure quality of care provided within a health care facility is the most difficult and time consuming part in terms of clinical audit tool development. The current study provided a total of 33 new criteria for reviewing the quality of care provided to patients with type-2 diabetes. These newly developed criteria were validated at academic and clinical levels and were tested within the clinical settings in Qatar and the UK. As a result, these criteria can be used by other authors for the purpose of quality measurement and improvement. This should only be done after appropriate adaptation against any new or recently updated guidelines.

The designed MAT was applied within the clinical settings in Qatar. The reason behind choosing Qatar was due to the high disease prevalence (four times higher than the prevalence in the UK) which considered as one of the highest in the Middle East and North Africa and the second among Gulf Cooperation Council countries. Although the high disease prevalence in Qatar make it a good place to perform this audit, the country was found to have limited published research about diabetes with which to compare the results obtained from this study. This makes the current study a good starting point for research around diabetes and the quality of care provided to patients.

This study was conducted on a sample of 305 patients attending Hamad General Hospital diabetes clinic from 2010-2011, all having type-2 DM with no history of CVD. The diabetes clinic within this hospital is the main centre for the management of diabetes in the country which provide comprehensive services and represents the focal point for all referrals from other health care sectors.

Results obtained from the MAT application in Qatar highlighted clinical areas which lacked the appropriate care and documentation. Identifying and feeding-back such areas to prescribers could help in improving patients' care and treatment outcomes. For example, referring diabetic patients to structured diabetes education programmes and involving them in setting a their own targets for HbA1c found to be associated with better glycaemic control, improved quality of life and greater percentage of

patients who achieved targeted HbA1c control. Furthermore, early screening and detection of diabetic retinopathy/neuropathy and foot disease can potentially reduce diabetes complications and improve patients' quality of life. Increased CVD risk is another important complication of diabetes that should be highly taken in consideration during the management of diabetes. This study also identified some clinical areas where CVD risk can be managed in a proper way in order to reduce the development of CVD among diabetic patients. Insufficient documentation of smoking status as major contributor to CVD risk was highlighted as an important part in CVD risk management in this clinic.

Association between patients' clinical factors and level of care provided by physicians was also studied. The clinical questions to be answered by this analysis was to determine if prescribers gave special attention to patients' factors (for example: age or diabetes duration) when they provide care. It is important that those patients with longer disease duration or older in age receive appropriate and targeted quality of care. The analysis revealed that the level of care provided to patients did not differ according to such factors and that only blood pressure status as well as total cholesterol levels were associated with the level of care. Patients diagnosed with hypertension received a better quality of care when compared with those who don't have the diagnosis of hypertension. However, those with elevated levels of total cholesterol needed more attention in terms of care.

Analysis of CVD risk associated with type-2 diabetes was performed in this study to identify and describe patients who are at higher absolute risk based on CVD risk factors they have. The other reason to do this analysis was to assess the level of care provided to these patients and to determine their needs. The UKPDS risk engine used in this study was able to identify those patients. As result, this engine can be suggested for use within the clinical settings in Qatar to identify and target patients at higher absolute CVD risk. Although the level of care provided to patients at higher risk of developing a CVD should be superior, the study found that they receive the usual level of care provided to any patient without a higher CVD risk. Not-justified non-adherences to clinical guidelines recommendation in management of diabetes

and prevention of CVD in the high risk group were detect in the majority of the criteria. Furthermore, achieving good glycaemic and blood pressure control (which are important and undependable contributors to CVD risk in diabetic patients) found to be considerably lower in the high risk group. This highlighted the importance of identifying and targeting these patients to reduce the higher CVD risk and the number of patient who will develop a CVD in the future.

### 5.2 Future work

- Field test the designed pharmaceutical care plan within the clinical settings in Qatar to test its practicality and modify it accordingly.

- Explore pharmacists' opinions on their contribution to the delivery of pharmaceutical care to patients with type-2 diabetes in Qatar as well as their educational or training needs.

- Assess the quality of service provided by diabetes educators to diabetic patients and identify any pharmaceutical care issues.

- Assess patients' (type-2 diabetic patients in Qatar) compliance with disease interventions and medications as an important factor affecting diabetes outcomes.

- Re-apply the MAT once the pharmaceutical care plan has been finalised and implemented (this should be carried out after allowing an appropriate time of 6-12 months) to assess its clinical effectiveness (whether it improved areas lacking the appropriate levels of adherence, its effect on CVD risk reduction and diabetes outcomes: HbA1c & BP controls).

- If the care plan showed a good clinical effectiveness, consider the use of MAT to identify areas in secondary prevention of CVD or in other clinics (to

assess prescribing adherence in patients with asthma, COPD, cancer or other long term conditions).

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# Appendices

# Appendix 1

## The previously developed MATs for the primary and secondary prevention of CVD

**Indicators of appropriate drug treatment in patients with type 2 diabetes with or without coronary heart disease as recommended in SIGN guideline 41, 51, 55, and NICE guideline 34.**

*Secondary Prevention of CHD*

If the patient does not have a history of CHD go to criterion 14

| | | N/A | Yes | No | J/U | ID |
|---|---|---|---|---|---|---|
| 1 | **Patient with no apparent contraindication/intolerance to aspirin** is prescribed aspirin | ☐ | ☐ | ☐ | ☐ | ☐ |
| 2 | **Patient with no apparent intolerance/contraindication to aspirin** is prescribed aspirin 75mg as an anti platelet. | ☐ | ☐ | ☐ | ☐ | ☐ |
| 3 | **Patient with hypertriglyceridaemia (>1.7 mmol/L) whose HDL-cholesterol is < 1mmol/l in men or < 1.2 mmol/l in women** is prescribed a fibrate or nicotinic acid unless contraindicated or not tolerated | ☐ | ☐ | ☐ | ☐ | ☐ |
| 4 | **Patient who has no contraindication/intolerance to statin** is prescribed a statin [1] | ☐ | ☐ | ☐ | ☐ | ☐ |
| 5 | **Patient with symptomatic coronary heart disease including post MI** is prescribed a sublingual (SL) glyceryl trinitrate (GTN) or GTN spray | ☐ | ☐ | ☐ | ☐ | ☐ |
| 6 | **Patient with no apparent contraindication/intolerance to a beta-blocker** is prescribed a beta-blocker | ☐ | ☐ | ☐ | ☐ | ☐ |
| 7 | **Patient with apparent contraindication/intolerance to beta-blockers without a documented LVSD** is prescribed either verapamil or diltiazem | ☐ | ☐ | ☐ | ☐ | ☐ |

*Stable angina specific criteria* (8-10)

If patient does not have symptoms of angina go to criterion 11

| | | | | | | |
|---|---|---|---|---|---|---|
| 8 | **Patient with angina and who is prescribed a regular oral nitrate (not SL)** uses a dose regimen that avoids the development of tolerance [2] | ☐ | ☐ | ☐ | ☐ | ☐ |
| 9 | **Patient with apparent contraindication/intolerance to a beta-blocker where diltiazem and verapamil are contraindicated or not tolerated** is prescribed either an oral nitrate or a potassium channel activator | ☐ | ☐ | ☐ | ☐ | ☐ |
| 10 | **Patient who is prescribed a beta-blocker plus a second agent for the control of angina symptoms** [3] is prescribed a long acting dihydropyridine | ☐ | ☐ | ☐ | ☐ | ☐ |

*Post-MI specific criteria (11-13)*

If patient does not have a history of MI go to criterion 16

| | | | | | | |
|---|---|---|---|---|---|---|
| 11 | **Post-MI patient with no apparent contraindication/intolerance to an ACE inhibitor** is prescribed an ACE inhibitor | ☐ | ☐ | ☐ | ☐ | ☐ |
| 12 | **Post-MI patient prescribed an ACE inhibitor who has normal LV function** has achieved target doses or maximum tolerated dose of the ACE inhibitor listed below:<br>› Lisinopril 10mg daily<br>› Captopril 50mg twice daily<br>› Ramipril 10mg daily | ☐ | ☐ | ☐ | ☐ | ☐ |

[1] Assuming all patients already prescribed a statin pervasively have had pre-treatment serum cholesterol ≥ 5mmol/l. therefore all patients on statin should be ticked yes

[2] Either an eccentric conventional twice daily dose (e.g. 8am and 2am) or once daily controlled release formulation or transdermal nitrate patch removed to provide a nitrate free period

[3] Patient will be applicable to this criterion only when indication of a second agent has been recorded as for the control of angina symptoms

**N/A**: not applicable, **J**: justified, **U**: unjustified non-adherence to guidelines.

| | | | | | | |
|---|---|---|---|---|---|---|
| 13 | **Post-MI patient prescribed an ACE inhibitor who has impaired LV function** has achieved target doses or maximum tolerated dose of the ACE inhibitors listed below:<br>• Ramipril 10mg daily<br>• Trandolapril 4mg daily<br>• Captopril 50mg three times daily<br>• Enalapril 20-40mg daily<br>• Lisinopril 30-35mg daily | ☐ | ☐ | ☐ | ☐ | ☐ |
| *Primary Prevention of CHD* | | | | | | |
| If the patient has established CHD go to criterion 15 | | | | | | |
| 14 | **Patient with a 10 year CVD event risk ≥20% and no apparent contraindication/intolerance to aspirin** is prescribed aspirin 75mg [4] | ☐ | ☐ | ☐ | ☐ | ☐ |
| 15 | **Patient prescribed aspirin 75mg** has achieved blood pressure <150/90 mmHg | ☐ | ☐ | ☐ | ☐ | ☐ |
| 16 | **Patient with a 10 year CVD event risk ≥20% aged > 40** [5] is prescribed a statin [6] | ☐ | ☐ | ☐ | ☐ | ☐ |
| *Primary and secondary prevention of CHD* | | | | | | |
| 17 | **Patient with BMI > 26 kg/m$^2$ (female), or > 27kg/m$^2$ (male) and prescribed an oral hypoglycaemic agent** is prescribed metformin unless contraindicated | ☐ | ☐ | ☐ | ☐ | ☐ |
| 18 | **Patient who continues to smoke** has been offered smoking cessation advice which either involves structured behavioural support and nicotine replacement therapy or bupropion | ☐ | ☐ | ☐ | ☐ | ☐ |
| 19 | **Patient maintained on the same dose of a statin for >6 weeks** has achieved a re-test total cholesterol level of < 5 mmol/l | ☐ | ☐ | ☐ | ☐ | ☐ |
| 20 | **Patient with microalbuminuria or protienuria and with no apparent contraindication to an ACE inhibitor** is prescribed an ACE inhibitor | ☐ | ☐ | ☐ | ☐ | ☐ |
| 21 | **Patient with microalbuminurea or protienurea and with documented contraindication to an ACE inhibitor** is prescribed an AIIRB | ☐ | ☐ | ☐ | ☐ | ☐ |
| 22 | **Patient that is diagnosed as hypertensive and/or with blood pressure >140/80 mmHg** is prescribed antihypertensive drug therapy | ☐ | ☐ | ☐ | ☐ | ☐ |
| 23 | **Patient who is diagnosed as antihypertensive and is prescribed antihypertensive drug therapy** has achieved BP ≤ 140/80 mmHg | ☐ | ☐ | ☐ | ☐ | ☐ |
| 24 | **Patient with diagnosis of hypertension prescribed antihypertensive therapy who is ≤ 55 years old and non-black** is prescribed an ACE inhibitor or beta-blocker | ☐ | ☐ | ☐ | ☐ | ☐ |
| 25 | **Patient with a diagnosis of hypertension who is >55 years old OR black prescribed antihypertensive drug therapy** is prescribed a diuretic or calcium channel blocker (LVSD- amlodipine or felodipine; Angina- no short acting dihydropyridines) | ☐ | ☐ | ☐ | ☐ | ☐ |
| 26 | **Patient with a diagnosis of hypertension prescribed a single antihypertensive agent and at least one of the following**<br>**Documented diagnosis of gout**<br>**Poor renal function**<br>**Hypokalaemia or dyslipidaemia**<br>Is not prescribed a thiazide diuretic | ☐ | ☐ | ☐ | ☐ | ☐ |

[4] The calculated CHD event risk can now be used in treated hypertensive events though the calculated risk is an underestimate, see BNF. In the case of specific measurements assume HDL equal 1mmol/l.
[5] Risk calculated using Joint British Societies Coronary Risk Prediction Chart.
[6] Assume all patients already prescribed a statin prevuicely have had pre-treated CHD event risk ≥ 30% and total cholesterol ≥ 5mmol/l. Therefore all patients on statin should be ticked yes.

| | | | | | | |
|---|---|---|---|---|---|---|
| **27** | **Patient with documented sustained systolic BP (140-159) mmHg or diastolic BP (90-99) mmHg and at least one of the following:**<br>**Diagnosis of CVD**<br>**Estimated 10 year CVD risk >20%**<br>**Target organ damage other than CVD**<br>is prescribed antihypertensive drug therapy | | | | | |
| **28** | **Patient with no apparent contraindication/intolerance to an ACE inhibitor, and who falls into any of the following categories**<br>**Post MI**<br>**LVSD**<br>**>55 Years of age with at least one of the risk factors**<br>is prescribed an ACE inhibitor | | | | | |
| **29** | **Patient who is diagnosed with hypertension and is prescribed antihypertensive drug therapy** is not prescribed a combination of thiazide diuretic and beta-blocker | | | | | |
| **30** | **Patient with apparent contraindication/intolerance to aspirin 75mg therapy** is prescribed clopidogrel 75mg | | | | | |
| **31** | **Patient with hypertension** has a treatment plan that excludes the following drugs<br>Corticosteroids<br>Oral contraceptives<br>NSAIDS<br>High sodium-containing products<br>Sympathomimetics<br>Monoamine-oxidase inhibitor<br>Carbenoxolone | | | | | |

# MAT for patients with chronic cardiovascular disease

| | Qualifying criteria | | Standards |
|---|---|---|---|
| 1[1] | Current smoker | MISCELLANEOUS | Invited to join smoking cessation programme |
| 2[2] | Diagnosis of hypertension (HTN) | | Prescribed antihypertensive therapy |
| 3[1,3] | Diagnosis of cardiovascular disease (CVD) | | Prescribed a statin |
| 4[1,3] | Patient without CVD who complies with at least one of the following: Aged >40 and estimated 10 year CVD risk ≥20%, aged >40 and Diabetes Mellitus (DM), familial hypercholesterolaemia | | Prescribed a statin |
| 5[4,5] | Diagnosis of cardiovascular disease (CVD) and prescribed a statin | | Prescribed simvastatin at a dose of at least 40mg or equivalent dose of alternative statin or a documented maximum tolerable statin dose |
| 6[4,5] | Patient without CVD and aged >40 and estimated 10year CVD risk ≥20% and prescribed a statin | | Prescribed simvastatin at a dose of at least 40mg or equivalent dose of alternative statin or a documented maximum tolerable statin dose |
| 7[4,5] | Prescribed a statin and an interacting drug | | Prescribed an acceptable statin or acceptable dose labelled as acceptable on specified list |
| 8[1] | Prescribed a statin | | TC ≤ 4mmol/L |
| 9[1] | Diagnosis of CVD and without history of acute ischaemic stroke or TIA | | Prescribed aspirin 75 mg |
| 10[1] | Patient without CVD and without DM but estimated 10year CVD risk ≥20% | | Prescribed aspirin 75 mg |
| 11[6] | Patient without CVD and WITH DM, who complies with at least one of the following: Aged >50, DM diagnosed ≥10 years ago, prescribed antihypertensive drug therapy, retinopathy, nephropathy | | Prescribed aspirin 75 mg |
| 12[2] | Prescribed aspirin | | Achieved a blood pressure of ≤ 150/90mmHg |
| 13[1] | Patient with a history of acute ischaemic stroke or transient ischaemic attack (TIA) | | Prescribed a combination of aspirin (75-300 mg daily) plus dipyridamole (200 mg twice daily) |
| 14[6] | Patient with CVD who complies with at least one of the following: History of acute ischaemic stroke or TIA while on a combination of aspirin/dipyramidole therapy, contraindication/intolerance to aspirin | | Prescribed clopidogrel at a dose of 75mg instead of aspirin |
| 15[7] | At least one of the following: DM, CHD, diagnosis of heart failure (HF) | | Prescribed an ACE inhibitor |
| 16[8,9] | Diagnosis of DM, overweight and prescribed an oral antihyperglycaemic agent | | Prescribed metformin |
| **DIAGNOSIS OF HYPERTENSION, PRESCRIBED ANTIHYPERTENSIVE THERAPY...** | | HYPERTENSION | |
| 17[2] | ... and at least one of the following: diagnosis of CVD, DM, chronic renal failure | | Achieved a blood pressure of ≤ 130 systolic AND ≤ 80mmHg diastolic |
| 18[2] | ... and NONE of the following: diagnosis of CVD, DM, chronic renal failure | | Achieved a blood pressure of ≤ 140 systolic AND ≤ 85 mmHg diastolic |
| 19[2] | ... and prescribed a single antihypertensive agent and at least one of the following: gout, poor renal function, current hypokalaemia, dyslipidaemia | | Prescribed a calcium channel blocker or ACE- inhibitor |
| **DIAGNOSIS OF HYPERTENSION, PRESCRIBED ANTIHYPERTENSIVE THERAPY AND DOES NOT HAVE A DIAGNOSIS OF CVD OR CHRONIC HEART FAILURE...** | | | |
| 20[2] | ... and ≤ 55 years old and non-black | | Prescribed an ACE inhibitor |
| 21[2] | ... and ≤ 55 years old and non-black and an apparent contraindication or intolerance to an ACE inhibitor | | Prescribed an AII antagonist |
| 22[2] | ... and at least one of the following: >55 years old, black | | Prescribed a thiazide diuretic or calcium channel blocker |
| 23[2] | ... | | NOT prescribed a combination of a thiazide diuretic and a BB |
| **DIAGNOSIS OF HYPERTENSION (with or without CHD or chronic heart failure)...** | | | |
| 24[10] | ... | | Drugs on specified list are avoided * |
| **DIAGNOSIS OF CHD...** | | CHD | |
| 25[7] | ... | | Prescribed a beta-blocker |
| 26[7] | ... and NO heart failure AND apparent contraindication or intolerance to a beta-blocker | | Prescribed a rate limiting calcium channel blocker, long acting nitrates or nicorandil |
| 27[7] | ... and heart failure AND apparent contraindication or intolerance to a beta-blocker | | Prescribed a long acting nitrate or nicorandil |
| 28[7] | ... | | Prescribed sublingual glyceryl trinitrate or glyceryl trinitrate spray |
| 29[7] | ...and NO heart failure and prescribed a beta-blocker AND a second agent for control of angina symptoms | | Prescribed a calcium channel blocker |
| 30[7,9] | ... and heart failure prescribed a beta-blocker AND a second agent for control of angina symptoms | | Prescribed amlodipine or felodipine |
| 31[7] | ... and prescribed regular nitrate | | Uses a dosage regimen which avoids the development of tolerance |
| 32[7] | ... and a history of MI without heart failure and prescribed one of: captopril (C), enalapril (E), lisinopril (L) or ramipril (R) | | Prescribed target dose (C 50mg bd, E 20-40od, L or R 10mg od) or a documented maximum tolerated dose |
| **DIAGNOSIS OF CHRONIC HEART FAILURE...** | | CHRONIC HEART FAILURE | |
| 33[9] | ... and prescribed one of the following: captopril (C), enalapril (E), lisinopril (L), perindopril (P), ramipril, (R) or trandolapril (T) | | Prescribed target dose (C 50 mg tds, E 10-20 mg bd, L 20mg od, R 10 mg od, P 8 mg od or T 4mg od) or a documented maximum tolerated dose |
| 34[9] | ... | | Drugs on specified list are avoided * |
| 35[9] | ... and NOT prescribed an ACE inhibitor | | Prescribed an AII antagonist |
| 36[9] | ... mild to moderate heart failure and prescribed target or maximum tolerable doses (if less) of an ACE-Inhibitor and betablocker and remains symptomatic | | Prescribed candesartan |
| 37[9] | ... and not prescribed an ACE inhibitor or AII Antagonist | | Prescribed a combination of hydralazine and ISDN |
| 38[9] | ... and prescribed Losartan (L), Candesartan (C), Valsartan (V) | | Prescribed target dose (L 50mg od, C 32mg od, V 160mg bd) or a documented maximum tolerated dose |
| 39[9] | ... | | Prescribed a beta blocker (except metoprolol tartrate) |
| 40[9] | ... on Carvedilol (C), Bisoprolol (B) or Nebivolol (N) | | Prescribed target dose (C 25-50mg bd, B or N 10od) or a documented maximum tolerated dose |
| 41[9] | ... and symptoms of heart failure | | Prescribed diuretic treatment |
| 42[9] | ... moderate to severe heart failure and prescribed target or maximum tolerable doses (if less) of an ACE inhibitor and beta blocker and remains symptomatic | | Prescribed spironolactone |
| 43[9] | ... moderate to severe heart failure and prescribed target or maximum tolerable doses (if less) of an ACE inhibitor and beta blocker and remains symptomatic and developed gynaecomastia | | Prescribed eplerenone |
| 44[9] | ... and a history of MI and at least one of: HF symptoms or diabetes | | Prescribed eplerenone |
| 45[9] | ... and on spironolactone (S) or eplerenone (E) | | Prescribed target dose (S 25- 50mg od, E 50mg od) or a documented maximum tolerated dose |
| 46[9] | ... without AF and with current symptoms of heart failure despite optimal therapy | | Prescribed digoxin |
| 47[9] | ... | | Receives an annual influenza vaccination |
| 48[9] | ... | | Received a once-only pneumococcal vaccination |
| 49[11] | ... and well tolerated atrial fibrillation (AF) | | Prescribed a beta-blocker or digoxin |
| **PATIENT WITH ATRIAL FIBRILLATION ...** | | AF | |
| 50[11] | ... and without heart failure and AF is well-tolerated | | Prescribed either a beta-blocker, verapamil, diltiazem or digoxin |
| 51[11] | ... and at least one additional risk factor for thromboembolism | | Prescribed warfarin |
| 52[11] | ... and at least one additional risk factor for thromboembolism and NOT prescribed warfarin | | Is prescribed Antiplatelet therapy |
| **PATIENT PRESCRIBED WARFARIN...** | | WARFARIN | |
| 53[12] | ... | | INR measured at intervals of which none > 12 weeks |
| 54[12] | ... and warfarin dose changed | | INR measured within 1 week after dose change or starting each drug |
| 55[12] | ... prescribed a drug known to potentiate anticoagulant effect for >5 days | | INR measured within 1 week after dose change or starting each drug |
| 56[12] | ... | | INR history with at least 60% of INRs within target range |

* Carbenoxolone, corticosteroids (except inhaled or topical), high sodium-containing products eg. effervescent formulations, liquorice, monoamine-oxidase inhibitors, NSAIDS (except aspirin as an antiplatelet), oral contraceptives, sympathomimetics (except inhaled beta 2- agonists).

\# Antiarrhythmics (class I+III except amiodarone), calcium channel blockers (except amlodipine and felodipine), carbenoxolone, fluconazole, itraconazole, macrolide antibiotics, metformin, minoxidil, NSAIDs (except aspirin as an antiplatelet), oral corticosteroids, terfenadine, thiazolidinediones (glitazones), tricyclic antidepressants, voriconazole.

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1 Risk estimation and the prevention of cardiovascular disease - Guideline No. 97
Edinburgh: Scottish Intercollegiate Guidelines Network (SIGN); 2007 [updated 2007; cited 2008 03/01]; Available from: http://www.sign.ac.uk/pdf/sign97.pdf.

2 British Hypertension Society guidelines for hypertension management 2004 (BHS-IV). BMJ 2004;328; 634-640.

3 British Hypertension Society and National Institute for Health and Clinical Excellence. Clinical Guideline 34: 'Hypertension: management of hypertension of adults in primary care: partial update. June 2006

4 Guidelines for Implementation of Drug of Choice Programme in North Glasgow University Hospitals Division: Cholestereol lowering therapy - Statins. (2004).

5 Committee JF. British National Formulary. 55 ed. London: British Medical Association and Royal Pharmaceutical Society of Great Britain; 2008.

6 Joint British Society's guidelines on prevention of cardiovascular disease in clinical practice: summary 12/2005

7 Management of Stable Angina - Guideline No. 96. Edinburgh: Scottish Intercollegiate Guidelines Network (SIGN); 2007 [updated 2007; cited 2008 03/01]; Available from: http://www.sign.ac.uk/pdf/sign96.pdf.

8 Management of Diabetes - Guideline No. 55. Edinburgh: Scottish Intercollegiate Guidelines Network (SIGN); 2001 [updated 2001; cited 2008 03/01]; Available from: http://www.sign.ac.uk/guidelines/fulltext/55/index.html.

9 Management of Chronic Heart Failure - Guideline 95. Edinburgh: Scottish Intercollegiate Guidelines Network (SIGN); 2007 [updated 2007; cited 2008 03/01]; Available from: http://www.sign.ac.uk/pdf/sign95.pdf.

10 Hypertension in Older People - Guideline No. 49. Edinburgh: Scottish Intercollegiate Guidelines Network (SIGN); 2001 [updated 2001; cited 2008 03/01]; Available from: http://www.sign.ac.uk/guidelines/fulltext/49/index.html.

11 Cardiac Arrythmias in coronary heart disease - Guideline No. 94
Edinburgh: Scottish Intercollegiate Guidelines Network (SIGN); 2007 [updated 2007; cited 2008 03/01]; Available from: http://www.sign.ac.uk/pdf/sign94.pdf.

12 Antithrombotic Therapy - Guideline No. 36 Edinburgh: Scottish Intercollegiate Guidelines Network (SIGN); 1999 [updated 1999; cited 2008/ 03/01]; Available from: http://www.sign.ac.uk/pdf/sign36.pdf.

# Appendix 2

## Final version of MAT applied in Qatar ($MAT_{Qat}$)

| Indicators of appropriate drug treatment in Diabetic patients as recommended in NICE (CG 66, 87 & 10) and SIGN (116) guidelines | | | | | | | |
|---|---|---|---|---|---|---|---|
| **A** | **Control of Blood Glucose** | | | | | | |
| **Patient with type 2 diabetes** should have | | | | | | | |
| | | **N/A** | **Yes** | **NO** | **NOJ/U** | **ID(Q)** | **ID(S)** |
| **1** | been invited to join a structured diabetes education programme. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **2** | a recorded target Hb $A_{1c}$. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **3** | a record of at least two $HbA_{1c}$ measurements in the previous 15 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **4** | an $HbA_{1c}$ recorded at ≤7 % as their most recent value[1]. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **5** | **Patient with type 2 diabetes on glucose lowering agent(s)** is on metformin or sulphonylurea[2]. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **6** | **Patient with type 2 diabetes on glucose lowering agent (s) and with a stable $HbA_{1c}$ measurement > 7%** is on more than one agent. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **7** | **Patients on glucose lowering agents added to metformin and/or sulphonylurea - a gliptin, acarbose, pioglitazone or a glinide-** are not on more than three oral agents. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **8** | **Patients on a gliptin, pioglitazone or a glinide** is co-prescribed metformin or a sulphonylurea[2]. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **9** | **Patient with a stable $HbA_{1c}$ measurement ≥7.5%** should be on a third oral agent - a gliptin, pioglitazone, a glinide, or prescribed exenatide | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **10** | **Patient with type 2 diabetes with BMI ≥25 $kg/m^2$** is on metformin. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **11** | **Patients on metformin therapy** have an estimated GFR is >45 ml/min/1.73 $m^2$ | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **12** | **Patients on metformin therapy and an estimated GFR ≤45 ml/min/1.73 $m^2$** have had their renal function measured within the past 12 months | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **13** | **Patients on metformin therapy** do not have a current estimated GFR <30 ml/min/1.73 $m^2$ | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **14** | **Patient on on two or a three oral glucose lowering agents** is co-prescribed metformin and/or a sulphonylurea[2]. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **15** | **Patient with type 2 diabetes on insulin** has previously received oral glucose lowering therapy. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **16** | **Patient with a stable $HbA_{1c}$ measurement ≥7.5 despite oral glucose lowering therapy[3]** has been started on Insulin | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **17** | **Patient on exenatide or liraglutide** has a BMI>30 kg/$m^2$. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **Patient on a thiazolidinedione (pioglitazone)** | | | | | | | |
| **18** | does not have heart failure. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **19** | does not have osteoporosis. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **20** | **Patient on a thiazolidinedione (pioglitazone) and receiving it for >6 months** has evidence that it has reduced $HbA_{1c}$ by ≥ 0.5%. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **21** | **Patient with type 2 diabetes previously on oral glucose lowering agent(s) and now on insulin therapy** continues to be prescribed the previous oral therapy (metformin/ sulphonylurea). | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

| **B** | **Management of Diabetes Complications** | | | | | | |
|---|---|---|---|---|---|---|---|
| **Kidney Disease** | | | | | | | |
| **22** | **Patient with microalbuminuria or proteinuria** is prescribed an ACE inhibitor or an ARB. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **23** | **Patient with diabetes** has had renal function (serum creatinine/eGFR) or microalbuminuria checked within the past 12 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **Retinopathy** | | | | | | | |
| **24** | **Patient with diabetes** has had retinal examination within the past 15 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **Neuropathy/foot disease** | | | | | | | |
| **25** | **Patient with diabetes** has had neuropathy/ foot check in the past 15 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **26** | **Patient diagnosed with diabetic neuropathy** is prescribed a tricyclic antidepressant, gabapentin, pregabalin or duloxetine. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

| **C** | **Primary prevention of CVD** | | | | | | |
|---|---|---|---|---|---|---|---|
| **27** | **Patient with diabetes** has had their blood pressure measured within the past 15 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **28** | **Patient diagnosed with hypertension** is prescribed an ACE Inhibitor or angiotensin II-receptor antagonist (ARB). | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **29** | **Patient who is diagnosed as hypertensive and is prescribed antihypertensive drug therapy** has achieved BP < 140/80 mmHg. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **30** | **Patient with treated hypertension and with co-existing kidney, eye or cerebrovascular damage** has achieved a blood pressure level < 130/80 mmHg. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **31** | **Patient who is diagnosed with hypertension and is prescribed antihypertensive drug therapy** is not prescribed a combination of thiazide diuretic and beta-blocker | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **32** | **Patient with hypertension** has a treatment plan that excludes the following drugs<br>Corticosteroids (except inhaled or topical) Sympathomimetics (except inhaled beta 2- agonists) | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Oral contraceptives<br>NSAIDS (except aspirin as anti-platelet)<br>High sodium-containing products (effervescent formulations) | Monoamine-oxidase inhibitor<br>Carbenoxolone | | | | | | |
| **33** | **Patient with diabetes aged >40** is prescribed a statin | | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **34** | **Patient maintained on the same dose of a statin for >6 weeks** has achieved a re-test total cholesterol level of < 5 mmol/l | | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **35** | **Patient prescribed a simvastatin or atorvastatin** not co-prescribed macrolide antibiotics (erythromycin, clarithromycin) or ketoconazole or itraconazole | | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **36** | **Patient with a triglyceride level > 4.5mmol/L (whether on a statin or not)** is prescribed a fibrate | | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **37** | **Patient with triglyceride level of 2.3-4.5 mmol/L despite statin therapy** is prescribed a fibrate | | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **38** | **Patient who continues to smoke** has been offered smoking cessation advice which either involves structured behavioural support and nicotine replacement therapy or bupropion | | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

[1] *Exceptions are patients who have had a change in glucose lowering therapy within the past 3 months or where a reason (justification) is provided in the case notes*
[2] *Exception is a patient for whom both metformin/sulphonylurea are contra-indicated or not tolerated*
[3] *when the use of two or three oral glucose lowering agent not achieved the appropriate HbA1c level*

# Appendix 3

## Final MAT version applied in the UK ($MAT_{UK}$)

| Indicators of appropriate drug treatment in Diabetic patients as recommended in NICE (CG 66, 87 & 10) and SIGN (116) guidelines | | | | | | | |
|---|---|---|---|---|---|---|---|
| **A** | **Control of Blood Glucose** | | | | | | |
| **Patient with type 2 diabetes** should have | | | | | | | |
| | | **N/A** | **Yes** | **NO** | **NOJ/U** | **ID(Q)** | **ID(S)** |
| **1** | been invited to join a structured diabetes education programme. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **2** | a recorded target Hb $A_{1c}$. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **3** | a record of at least two $HbA_{1c}$ measurements in the previous 15 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **4** | an $HbA_{1c}$ recorded at ≤7 % as their most recent value[1]. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **5** | **Patient with type 2 diabetes on glucose lowering agent(s)** is on metformin or sulphonylurea[2]. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **6** | **Patient with type 2 diabetes on glucose lowering agent (s) and with a stable $HbA_{1c}$ measurement > 7%** is on more than one agent. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **7** | **Patients on glucose lowering agents added to metformin and/or sulphonylurea - a gliptin, acarbose, pioglitazone or a glinide-** are not on more than three oral agents. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **8** | **Patients on a gliptin, pioglitazone or a glinide** is co-prescribed metformin or a sulphonylurea[2]. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **9** | **Patient with a stable $HbA_{1c}$ measurement ≥7.5%** should be on a third oral agent - a gliptin, pioglitazone, a glinide, or prescribed exenatide. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **10** | **Patient with type 2 diabetes with BMI ≥25 $kg/m^2$** is on metformin. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **11** | **Patients on metformin therapy** have an estimated GFR is >45 ml/min/1.73 $m^2$ | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **12** | **Patients on metformin therapy and an estimated GFR ≤45 ml/min/1.73 $m^2$** have had their renal function measured within the past 12 months | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **13** | **Patients on metformin therapy** do not have a current estimated GFR <30 ml/min/1.73 $m^2$ | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **14** | **Patient on two or a three oral glucose lowering agents** is co-prescribed metformin and/or a sulphonylurea[2]. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **15** | **Patient with type 2 diabetes on insulin** has previously received oral glucose lowering therapy. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **16** | **Patient with a stable $HbA_{1c}$ measurement ≥7.5 despite oral glucose lowering therapy[3]** has been started on Insulin | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **17** | **Patient on exenatide or liraglutide** has a BMI>30 kg/$m^2$. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **17a** | **Patient on exenatide or liraglutide for > 6 months** has evidence that it has reduced $HbA_{1c}$ by ≥ 0.5% | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **17b** | **Patient on exenatide or liraglutide for > 6 months** has evidence that it has reduced body weight by ≥3% of initial body weight | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **17c** | **Patient on a liraglutide** is prescribed a dose of 1.2 mg daily | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **17d** | **Patient on a gliptin and receiving it for > 6 months** has evidence that it has reduced $HbA_{1c}$ by ≥ 0.5% | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **Patient on a thiazolidinedione (pioglitazone)** | | | | | | | |
| **18** | does not have heart failure. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **19** | does not have osteoporosis. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **20** | **Patient on a thiazolidinedione (pioglitazone) and receiving it for >6 months** has evidence that it has reduced $HbA_{1c}$ by ≥ 0.5%. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **21** | **Patient with type 2 diabetes previously on oral glucose lowering agent(s) and now on insulin therapy** continues to be prescribed the previous oral therapy (metformin/ sulphonylurea). | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

| **B** | **Management of Diabetes Complications** | | | | | | |
|---|---|---|---|---|---|---|---|
| **Kidney Disease** | | | | | | | |
| **22** | **Patient with microalbuminuria or proteinuria** is prescribed an ACE inhibitor or an ARB. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **23** | **Patient with diabetes** has had renal function (serum creatinine/eGFR) or microalbuminuria checked within the past 12 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **Retinopathy** | | | | | | | |
| **24** | **Patient with diabetes** has had retinal examination within the past 15 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **Neuropathy/foot disease** | | | | | | | |
| **25** | **Patient with diabetes** has had neuropathy/ foot check in the past 15 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **26** | **Patient diagnosed with diabetic neuropathy** is prescribed a tricyclic antidepressant, gabapentin, pregabalin or duloxetine. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

| **C** | **Primary prevention of CVD** | | | | | | |
|---|---|---|---|---|---|---|---|
| **27** | **Patient with diabetes** has had their blood pressure measured within the past 15 months. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **28** | **Patient diagnosed with hypertension** is prescribed an ACE Inhibitor or angiotensin II-receptor antagonist (ARB). | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **29** | **Patient who is diagnosed as hypertensive and is prescribed antihypertensive drug therapy** has | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | achieved BP < 140/80 mmHg. | | | | | | |
| **30** | **Patient with treated hypertension and with co-existing kidney, eye or cerebrovascular damage** has achieved a blood pressure level < 130/80 mmHg. | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **31** | **Patient who is diagnosed with hypertension and is prescribed antihypertensive drug therapy** is not prescribed a combination of thiazide diuretic and beta-blocker | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **32** | **Patient with hypertension** has a treatment plan that excludes the following drugs<br>Corticosteroids (except inhaled or topical)<br>Sympathomimetics (except inhaled beta 2- agonists)<br>Oral contraceptives<br>Monoamine-oxidase inhibitor<br>NSAIDS (except aspirin as anti-platelet)<br>Carbenoxolone<br>High sodium-containing products (effervescent formulations) | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **33** | **Patient with diabetes aged >40** is prescribed a statin | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **34** | **Patient maintained on the same dose of a statin for >6 weeks** has achieved a re-test total cholesterol level of < 5 mmol/l | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **35** | **Patient prescribed a simvastatin or atorvastatin** not co-prescribed macrolide antibiotics (erythromycin, clarithromycin) or ketoconazole or itraconazole | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **35a** | **Patient prescribed >20mg simvastatin** not co-prescribed verapamil | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **36** | **Patient with a triglyceride level > 4.5mmol/L (whether on a statin or not)** is prescribed a fibrate | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **37** | **Patient with triglyceride level of 2.3-4.5 mmol/L despite statin therapy** is prescribed a fibrate | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |
| **38** | **Patient who continues to smoke** has been offered smoking cessation advice which either involves structured behavioural support and nicotine replacement therapy or bupropion | ❑ | ❑ | ❑ | ❑ | ❑ | ❑ |

[1] *Exceptions are patients who have had a change in glucose lowering therapy within the past 3 months or where a reason (justification) is provided in the case notes*

[2] *Exception is a patient for whom both metformin/sulphonylurea are contra-indicated or not tolerated*

[3] *when the use of two or three oral glucose lowering agent not achieved the appropriate HbA1c level*

# Appendix 4

## Ethical approval application form

# Research proposal submission form

*For Medical Research Centre use ONLY*

| Date of receipt | ID Number | Budget | |
|---|---|---|---|
| | | Amount requested | Amount granted |
| | | | |

**1. Title of the project:**

Pharmaceutical care in the management of blood glucose level and in the prevention of cardiovascular disease in type 2 diabetes mellitus

**2. Principal Investigator(s):**

| Name | Title | Department | Contact details (Tel/Bleep/E-mail) | Signature |
|---|---|---|---|---|
| Mohammad Issam Diab | **Clinical Pharmacist** | **Pharmacy** | **0097455860656** m_issam82@yahoo.com | |
| Dr. Halima Al Tamimi | **Director of pharmacy** | **Pharmacy** | **0097444392090** **0097444397702** | |
| Dr. Mouna Al Bakri | **Assistant director of pharmacy** | **Pharmacy** | **0097444392090** **0097444397702** | |

**3. Address for Correspondence:** *(with Telephone/Bleep/Mobile Nos. and e-mail address)*

Doha-Qatar
PO. Box 7748
0097455860656
m_issam82@yahoo.com

| | |
|---|---|
| **Name of Head of Section(s)**<br><br>**Dr. Muna Albakri** | **Signature** |
| **Name of Chairman/Director of the Department(s)**<br><br>**Dr. Haleema Altamimi** | **Signature** |

## 4. Co-Investigators:

| **Name** | **Title** | **Department** | **Contact details**<br><br>(Tel/Bleep/E-mail) | **Signature** |
|---|---|---|---|---|
| | | | | |
| | | | | |
| | | | | |
| | | | | |

## 5. Details of previous research projects submitted in HMC:

| TITLE | Investigators | AMOUNT GRANTED | Duration | Status |
|---|---|---|---|---|
| | | | | |
| | | | | |

## 6. Background:

*(Description of topic and with justification (rationale) of the study by stating the problem and its public health importance)* ***(Recommended length is around 2 pages)***

Diabetes mellitus (DM) is the most prevalent endocrine disease which has an increasing prevalence all over the world. The Health Improvement Network database showed that diabetes prevalence in the UK increased to 4.3% in 2005 compared with 2.8% in 1996, in which the increase in prevalence was mainly due to type 2 diabetes. The incidence of diabetes is also higher in Asian and African-Caribbean people. It is estimated that approximately 20% of Asians and 17% of African Caribbean people aged above 40 years have type 2 DM. In Qatar, the prevalence of diabetes in 2007-2008 among adult Qatari population was 16.7%, which is around four times higher than the prevalence in the UK.

The effects of the disease include long-term damage, dysfunction and failure of different organs. It is still the most common cause of blindness in the working individuals. Around a quarter of patients having last stage kidney disease replacement programmes are diagnosed with diabetes. Foot disorders are the most common reason of hospital admissions in patients with diabetes; with around twenty fold

more tendency of amputation. The expectancy of life in individuals with type 2 diabetes is decreased by ten years, and atherosclerotic vascular disease, mainly coronary heart disease and stroke, is the popular cause of death in about 70% of diabetics. However diabetic complications can be limited and some times prevented altogether if good management occurs from an early stage.

Hyperglycaemia and hypertension are the two major controllable factors that influence the development of diabetic complications. There is good evidence on how the onset of the complications associated with diabetes can be delayed or their progression slowed. Multi-centre studies, such as the Diabetic Control and Complications Trial (DCCT) and the UK Prospective Diabetes Study (UKPDS) contribute evidence for best practice effort to decrease mortality and improve the quality of life in diabetics.

There are clearly important pharmaceutical care issues in the treatment of individuals with diabetes. Pharmacists are in a good position to target their knowledge in the care of patients with diabetes, especially if they are elderly patients or tend to have co-existing morbidity and disability. Improving patient education and optimising chronic medication are two important parts of the pharmaceutical care in diabetes. Pharmacists can also play a role in the early identification of individuals with diabetes by making appropriate referrals of those with suspicious symptoms as well as participating in local screening programmes. Other roles which can be played by pharmacists in the pharmaceutical care of diabetes include advising diabetic on diet, lifestyle, the use of vitamins or mineral supplements and the identification of defaulters (patients who no longer attend clinic appointments as they believe their diabetes is controlled).

The effect of 12- month pharmaceutical care programme (PCP) on the vascular risk (differences in the estimated 10-year coronary artery disease and stroke risk in individuals having no history of such diseases) in type 2 diabetes was evaluated using the changes in $HbA_{1c}$ as an outcome measure. The mean reduction (95% CI) accompanied by PCP subjects (n=92) were greater than control group (n=88) for HbA1c (-0.5% vs 0.0%), systolic blood pressure (-14 mmHg vs -7 mmHg) and diastolic BP (-5 mmHg vs -2 mmHg) [$p \leq 0.043$]. There was 5% reduction in the median of the 10-year estimated

risk of the first CHD event in the PCP group compared with no change in the control group. The results of this study showed the importance of the pharmaceutical care programmes and the important role of pharmacist in the treatment of diabetes.

I would like to do this study as it will identify the areas of low adherence to the guidelines in the management of diabetes and in the prevention of cardiovascular disease which will give a great chance for the hospital pharmacists to be a part of the medical team in the management of diabetes. The overall findings will also help in improving patient care and well being.

## 7. Objective of the study

**8(a) Goal of the study:** *(State the goal you need to achieve)*

4. To quantify the risk of developing cardiovascular disease among type 2 diabetic patients and identify patients at high risk.

5. To conduct a pharmaceutical care needs assessment in patients with type 2 diabetes which measure the adherence of prescribers to criteria developed from internationally accepted clinical guideline standards regarding the appropriate disease management and the appropriate use of cardio-preventive (in high risk patients) and other disease related complication therapy.

6. To determine to what extent medication needs for cardio-prevention in diabetic patients are being met.

7. Identify the keys needed by hospital pharmacists (as a starting point for HMC pharmacists to be part of DM management team) in order to be able to deliver and improve pharmaceutical care in management of type 2 diabetes and its complication with a special focus on CVD prevention.

**7(b) Specific Objective:** *(State the details of each objective that will finally lead to achievement of the goal)*

1. Review the evidence for the impact of Type 2 diabetes on the risk of developing cardiovascular disease.
2. Design a medication assessment tool (MAT) based on the current updated guidelines in order to address the appropriate disease management and its complications (with a focus on CVD complications)
3. Validating the MAT to fit its use in the clinical settings through experienced academic staff and diabetic clinic doctors.
4. Audit the use of preventative and the appropriate treatment measures in diabetic patients by applying the validated MAT.
5. Design a data collection sheet to collect patient data needed to apply the MAT.

6. Investigate primary risk in a sample of patients with type 2 diabetes through the use of the existing risk assessment tool to data collected from sampled patient records and calculate the respective 10 year risks of acquiring CVD (UKPDS Risk Engine).
7. Determine criteria for patient subgroup analysis for comparison of medication needs in high and less high risk patients (estimated CVD risk of ≥20% and elderly patients)
8. Analyse the level of adherence in patients at high risk of developing CVD subgroup to determine what their pharmaceutical care needs are.

9. Derive a profile of care issues among targeted groups and formulate the overall findings in the study into a pharmaceutical care needs assessment as a starting point for the hospital pharmacists in Qatar to deliver pharmaceutical care to these patient groups.

**7(c) Secondary Objective:** *(There are subsidiary objectives that could be studied during the course of the project but are not the main objective of the study, they are optional and vary according to the type of the study*):

## 8. Materials and Methods: *(Describe the research methods that could best achieve the study objectives. These cover items 9.a to 9.g)*

**8. a. Study area/setting:** *(Describe the area or setting where the study will be conducted.)*

The patient sample will be drawn from a defined population attending the out-patient diabetes clinic at Hamah General Hospital in Qatar. Medical case notes only will be accessed for data collection.

**8. b. Study Subjects:** *(Inclusion and exclusion criteria of the study subjects should be mentioned)*

**Inclusion criteria:**

- Patients diagnosed with type 2 diabetes (with or without hypertension).
- Patients currently alive and have attended the diabetes clinic at least once during the past 2 years.
- Patients >81 years of age and agree to participate in the research.

**Exclusion criteria:**

- Patients with type 1 diabetes.
- Newly diagnosed patients with type 2 DM (within the last 6 months).
- Patients already diagnosed with CVD (coronary heart disease, TIA or stroke).

**8. c. Study Design: (***Mention the type of study design to fulfill aims & objective of the study (eg. retrospective, cross-sectional, case- control, cohort, intervention study, etc.)*

A cross-sectional population based survey

**8. d. Sample Size:** *(Mention the input criteria for sample size estimation like existing prevalence rates, previous study data, pilot study results etc...)*

300 patients attending the diabetes clinic in HGH

**8. e. Sampling Technique:** *(Mention the sampling technique that will be used in order to obtain a representative sample for your target population- this could be probability(random) or non probability techniques )*

Consecutively selected medical files of patients who attended the diabetes clinic at the time of the data collection

**8. f. Data Collection methods, instruments used, measurements:**

**8. f. 1. Describe the instruments used for data collection** *(Questionnaire, Observation recording form, Survey forms, instruments etc. and studied variables included from these instruments with references should be described. Methods used to test for the validity and reliability of used questionnaire, recording forms and survey forms should also be described)*

A data collection form already prepared for this project

**8. f. 2 Procedure of data collection, how the data will be collected?**

**(***Please describe in detail)*

Patient files will be collected from the diabetes clinic or patient HC numbers can be taken from diabetes clinic and the files then can be recalled from medical records. The patient information will be taken from the file and used then to fill in the data collection form as required. Electronic patient's data can be also used when needed. All data will be collected and analysed anonymously to maintain patient confidentiality.

**8. f. 3. Describe the quality control measures and good practices followed during the study implementation** (e.g. Good laboratory practices (GLP), Good Clinical Practices (GCP), methods used to make sure that data collected is accurate, methods used to ensure reliability and validity, methods used to ensure compliance of research with the research protocol, methods in place for ensuring data safety etc .., can be described here)

1. The medication assessment tool used in this research has been already used in other areas and diseases in the UK and the researcher has been already involved in MAT design and applies before.
2. A MAT validation has been already carried out by a group of expert academic staff in the UK (two academic and two PhD researchers) and will be validated as well in Qatar by diabetes clinic doctors before being applied.

3. The data collection form will be piloted using 10 patients first and will be used for the rest of the patient sample depending on the results.
4. Only patients HC numbers will be collected and no names will be taken to take patient's privacy in consideration.

**8. f. 4. Study definitions should be mentioned** *(e.g. Define all the important variables mentioned in the study with their references)*

Variables will be the care of patients before and after identifying the areas of low adherence.

**8. g. Data Management and Analysis plan:**

*(Describe the analysis plan, tests used for data analysis and statistical package(s) used)*

Percentage of adherence will be calculated from the summation of all adhered criteria (criteria recoded "Yes") over the summation of all applicable criteria (criteria recoded "yes", "non-adherence" and "IDS"). All percentages were also expressed as 95% confidence interval (CI) through a calculation formula installed in an excel widows software®. The criteria adherence was judged using arbitrary cut-offs of high level of adherence if ≥70%, intermediate level of adherence if between 69.9% - 50% and low level of adherence if < 50 %.

The applied data will be first entered from the pervious paper work to the Microsoft Office Excel windows software for calculations. The adherence for every single criterion will be also calculated and expressed as 95% confidence interval (CI). The total number of each answer (Yes, NOU, NOJ, N/A, IDS, IDQ) will be calculated for each criterion. These numbers will be used to calculate the applicability (Summation of IDS+ YES+ NOU answers), adherence (total number of YES

answers/ applicability), standard error (SE) [square root of (adherence*(1-adherence)/ (applicability)], confident interval minimum (CI min) [adherence-SE*1.96] and confident interval maximum (CI max) [adherence+ SE*1.96] for each criterion. After that the same equations will be

used to calculate the total adherence for over all criteria, but in this case depending on the summation of the entire YES, NOU, NOJ, N/A, IDS and applicability for the whole criteria

## 9. Implications of study results on disease/public health problem control:

*(Expected results and a description of the diseases or public health problem that the researcher hopes to control or decrease as a result of this study, which might give clues for future research)*

Identified criteria with low level of adherence will be used to generate a questionnaire for pharmacists and doctors to discuss how these fields can be improved and how the pharmacists can help in the management of patients with diabetes. The overall results will be improved patient care in order to minimize the risk of diabetes complications and development of cardiovascular disease as a result of inappropriate disease management.

## 10. Areas of Integration of research activities (If applicable)

*(E.g. integration of research activities related to more than one disease- these might be extrapolated from the secondary objectives or may be the results of the study which revealed areas which could benefit because of collaborative research etc . has to be described,)*

## 11. Bibliographic Reference:

*(Reference all articles relevant to study used in background for review of literature)*


1. SEHD, Diabetes in Scotland: Current challenges and future opportunities- Reviewing the Scottish Diabetes Framework. Edinburgh 2004.

2. Bener A, Zirie M, Janahi IM, Al-Hamaq AO, Musallam M. Prevalence of diagnosed and undiagnosed diabetes mellitus and its risk factors in a population-based study of Qatar. Diabetes Res Clin Pract. 2009; 84: 99-106.

3. Rachel H, Federica B, Mark W. Excess risk of fatal coronary heart disease associated with diabetes in men and women: meta-analysis of 37 prospective cohort studies. BMJ 2006; 332: 7533-73.

4. National Institute for Clinical Excellence (NICE). Type 2 diabetes, national clinical guidance for management in primary and secondary care updated (CG 66). London 2008.

5. UK Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type2 diabetes. UKPDS 33. Lancet 1998; 352: 854-865.

6. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type2 diabetes. UKPDS 38. Br Med J 1998; 317: 703-713

7. Mulnier H, Seaman H, Raleigh V. Risk of stroke in people with type 2 diabetes in the UK: a study using the General Practice Research Database. Diabetologia 2006; 49: 2859-2865.

8. Royal Pharmaceutical Society of Great Britain. Practice guidance on the care of people with diabetes (incorporating Early identification guidance). London 2004.

9. Wermeille J, Bennie M, Brown I, MC Knight J. Pharmaceutical care model for patients with type 2 diabetes: integration of community pharmacist into diabetes team-a pilot study. Pharm World Sci 2004; 26: 18-25.

10. Kamyar M.R., Johnson BJ., McAnaw J., Lemmens-Gruber R. and Hudson S.A. Adherence to clinical guidelines in the prevention of coronary heart disease in type II diabetes mellitus. Pharm World Sci. 2008 Feb;30(1):120-7. Epub 2007 Aug 25

11. Rhonda M, Wendy A, Kevin T, Timothy ME. Effect of a pharmaceutical Care Program on Vascular Risk Factors in Type 2 Diabetes. Diabetes Care 2005; 28: 771-776.

12. Health Education Authority. Black and ethnic minority groups in England: the second health and lifestyles survey. London 2000.

13. National Resource Centre for Ethnic Minority Health in collaboration with Scottish Diabetes Group. Diabetes in Minority Ethnic Groups in Scotland. Scotland 2004.

## 12. Ethical consideration:

**13. a. Informed Consent form**

*(It is a process in which a subject/patient learns key facts about a trial including potential risks and benefits, before deciding whether or not to participate in the study. Informed consent continues throughout the study and used according to research designs. Informed Consent Form is available on the intranet portal of the Medical Research Center and which should be translated into a language understood by the research participant)*

**12. b. From whom and how will consent be obtained? (***Participant or legally authorized representative and Research Committee (in case of retrospective study) should be indicated here)*

The study is a clinical audit and formal ethical approval is usually not required. The investigator can get a local permission in order to access the patient records in the clinical settings and sign a statement of confidentiality if required. The researcher can receive also any advice from Hamad medical corporation Research Ethics Committee.

**12. c. Confidentiality:** (*How and where will the study data can be stored and secured and how will subject's confidentiality be protected, who will have access to confidential research information etc..,)*

The collected data will be anonymised and no patient can be identified. The HC number will be only collected and no one will be able to access the patient information except the researcher.

## 13. Other funding agency:

*Is your study funded by another funding agency? (If yes, specify the agency and available funds)*

**No**

## 14. Required reports:

**14. a. Research Reports:** *(A progress report should be submitted in every 6 months of the project's implementation and a final report at the completion of the project. A list of participants recruited into the clinical trial should be submitted to the MRC at the end of every month where as a progress report should be submitted in every 6 months and final report at the completion of the all types of projects. If the study duration extends beyond a year, an application for extension with progress report must be submitted to the Research Committee to review and renewal of the project. Once research is published, copy of the published article should be submitted to MRC for updating database.)*

**Yes**

**14. b. Strategies to enhance the dissemination and utilization of results.(** *Mention the measures that might be taken to make the research findings generalizable knowledge- could include departmental meetings, journal clubs, articles etc*

Results will help pharmacists to deliver care to diabetic patients through the improvement of the identified areas of low adherence, furthermore, it may be communicated at the next ESCP conference and reported as published findings.

## 15. Timeline:

*(Please indicate the activities to be conducted and mark(X) the corresponding month on the Gantt chart. The research team should be strongly committed to these timelines and to submit the reports on time.*

| Task | Month | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Getting the final approval of the project** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** |
| **Design of the questionnaire** | | X | | | | | | | | | | |
| **Data collection** | | X | | | | | | | | | | |
| **Data analysis** | X | | | | | | | | | | | |
| **Writing up** | | | | X | | | | | | | | |
| **Progress Report** | | | | | | X | | | | | | |
| | | | | | | | | | | | | |
| | | | | | | | | | | | | |
| | | | | | | | | | | | | |
| **Final report** | | | | | | | | | | | X | |

## 16. INVESTIGATORS ASSURANCE FORM

**Title of Proposal:**

Pharmaceutical care in the management of blood glucose level and in the prevention of cardiovascular disease in type 2 diabetes mellitus

**The Investigators named below affirm that they:**

1. Will have a substantial contribution and adhere to the approved proposal.
2. Will abide by the rules and regulations guidelines' of the Research Committee, HMC for intellectual property, conflict of interest, authorship and financial issues.
3. Will submit progress and final reports and correspond with the Research Committee in a timely manner (Principal Investigator).
4. Will accept responsibility to maintain original data and consent forms and submit them for review if requested.
5. Will use scientific rigor and integrity in obtaining, recording and analyzing data; and in reporting and publishing results according to Good Clinical Practice (GCP) and Good Laboratory Practice (GLP) Guidelines.
6. Will be responsible to inform adverse event within one working day, to Research Committee, HMC, at 4392440,4396166, email: research@hmc.org.qa (applicable only for clinical trials)

| Name (s) of PI (s) and Co-PI (s) | Designation | Department | Signature | Date |
|---|---|---|---|---|
| **Mohammad Diab** | | **Pharmacy** | | **12/1/2011** |
| | | | | |
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**Note:** Research Committee (RC) approves a project only for a maximum period of 365 days**.** To renew the approval period of a project, the investigator must submit a progress report to the RC for review and renewal of the approval.

1. *Signature(s) of Principal Investigator(s) (PI(s)) and Co-Investigator (s)*

2. *Head/ Chairman's Signature of PI (s) department/ Section*
3. *Curriculum Vitae of PI.*
4. *Consent Form both in Arabic and English (Signed informed consent/ Informed consent i.e. Verbal or Oral(*
5. *Investigator(s) assurance form.*
6. *Prepared Data sheet/ Questionnaire for data collection.*
7. *Budget details (if required).*
8. *Conflict of interest ( Statement of interest form)*
9. *One copy of the proposal should be sent by email to research@hmc.org.qa and one hard copy of the same should be delivered to The Chairman, Research Committee, Medical Research Center, Building No. 16, 4th Floor, Hamad Medical City, HMC.*
   *Tel. Extn. 439 2440 / Fax: 439 5402. E-mail: research@hmc.org.qa.*

## Procedure for Letter of Endorsement:

Letter of endorsement from Dean of the organization or equivalent in support of the research proposal and the Principal Investigator(s), verifying that the proposal complies with the organization's policies and certain QNRF policies stated in the RFP will be provided to QNRF only to those research proposals submitted to Medical Research Centre. Investigators are also advised to read carefully all the rules and regulations from the website: www.qnrf.org

**Other Information:** (*if needed, please add any further information).*

**Note:** ***Researchers may contact Medical Research Centre for study design, sample size calculations, sample techniques, and terminology used in the Submission Form for clarification. Researchers are also advised to read about intellectual property, conflict of interest, authorship and financial issues from departmental intranet portal http://intranet/deptportal/dept_homepage.asp Medical Research Centre in rules and guidelines for submission of research.***

# Appendix 5

## Ethical approval certificate and author letter

مؤسسة حمد الطبية
Hamad Medical Corporation
HEALTH · EDUCATION · RESEARCH صحة · تعليم · بحوث

مركز البحوث الطبية
Medical Research Center

Ref. No: RC/11083/2011
Date: 25th January 2011

**Mr. Mohammad Issam Diab**
**Clinical Pharmacist**
**Department of Pharmacy**

Dear Mr. Diab,

**Research proposal:-11007/11:"Pharmaceutical care in the management of blood glucose level and in the prevention of cardiovascular disease in type 2 diabetes mellitus"**

Reference is made to the above Research Protocol submitted for review and approval from the Research Committee.

On behalf of Research Committee, this is to inform you that the above Research Proposal meets up with the ethical requirements of the Hamad Medical Corporation and approval is granted for one year from 25th January, 2011.

Progress report of the study should be submitted bi-annually and final report up on completion to Medical Research Centre.

We wish you all success and await the result in due course.

Yours sincerely,

**Dr. Al-Hareth M.Al-Khater**
**Chairman, Medical Research Center**

Cc:
1) Dr. Halima Al-Tamimi, Director of Pharmacy
2) Dr. Muna Al-Bakri, Assistant Director HGH - Pharmacy

Sa/Su

**Tel:** (+974)4439 2440
**Fax:** (+974) 4439 5402
research@hmc.org.qa

**P.O.Box** 3050
Doha, Qatar
www.hmc.org.qa

01 February 2011

To: Dr. Al-Hareth M. Al-Khater
Chairman, Research Committee

Dear Dr. Al-Khater,

**Subject: Research Study # 11007/11**

Thank you for approving my research study No. 11007/11 "Pharmaceutical care in the management of Blood glucose level and in the prevention of cardiovascular disease in type 2 diabetes mellitus."

For the successful completion of the study, it requires to collect data from the medical records of the subject's files from the Medical Records and also from the Diabetic clinic functioning in the 2nd floor of the OPD in HGH.

I would be grateful, if you kindly send a request to Sr. Maytha Al Bouinain, Director of Nursing OPD-HGH and to Mr. Richard Browne, Director of Medical Records to allow me to access patients' files to collect data required for my study.

Yours sincerely,

Mr. Mohammad Issam Diab
Corp. No. 020735
Clinical pharmacist
Department of Pharmacy - HGH

مؤسسة حمد الطبية
Hamad Medical Corporation
HEALTH - EDUCATION - RESEARCH صحة - تعليم - بحوث

مركز البحوث الطبية
Medical Research Center

February 14, 2011

Ms. Maytha Al Bouinain
Director, OPD Nursing

RE: Mr. Mohammed Issam Diab's research involving medical records.

Dear Ms. Al Bouinain,

I would like to inform you that Mr. Mohammed Issam Diab, clinical pharmacist, has applied for a HMC research protocol which was approved. This permits him to conduct this research and authorizes him to request files from the Medical Records department through Mr. Richard Browne. His research protocol reference number is 11007/11, should you need to reference this study in future correspondence.

Please feel free to contact the Medical Research Center if we can assist you further with this issue.

Regards,

Dr. Al-Hareth Al-Khater

**Tel:** (+974) 4439 6166
**Fax:** (+974) 4439 5402
Aalkhater1@hmc.org.qa

**P.O.Box** 3050
Doha, Qatar
www.hmc.org.qa

## Appendix 6

## Data collection form

| ***Patient Details*** | | | |
|---|---|---|---|
| HC number: | Age: | Gender: ❑ M ❑ F | Recorded target Hb $A_{1c}$<br>❑ Yes ❑ No |
| Weight: | Height: | BMI: | |
| Duration of DM in years: | Smoking status: ❑ Smoker ❑ non-smoker ❑ ex-smoker<br>Smoking cessation advice: ❑ Yes ❑ No<br>If yes: ❑ NRT ❑ Bupropion ❑ Others…….. | | Diabetes education programme:<br>❑ Yes ❑ No<br>❑ Leaflets, ❑ recorded advices |

| ***Medical History*** | | | | |
|---|---|---|---|---|
| ❑ Atrial fibrillation | ❑ Hypertension | ❑ Heart failure | ❑ Osteoporosis | ❑ Asthma |
| ❑ COPD | ❑ Rheumatic disorders | ❑ Others (e.g. SLE & Crohn's disease) ……. | | |

History of DM complications:
❑ nephropathy ❑ retinopathy ❑ microalbuminuria or proteinuria ❑ neuropathy ❑ foot ulcers

| ***Medical Screening*** | | | |
|---|---|---|---|
| Hb $A_{1c}$ measurements:<br>Most recent:<br>Date/value<br>……/……..<br>Last 15 months:<br>Date/value:<br>……/……..<br>……/……..<br>……/…….. | Renal function test:<br>Most recent eGFR (or serum creatinine) or microalbuminurea:<br>Date/value<br>……/……<br>Last 12 months:<br>Date/value:<br>……/……<br>……..…..…/……..<br>……...../…… | Retinal examination<br>Last 15 months:<br>❑ Yes ❑ No<br>neuropathy/ foot examination:<br>Last 15 months:<br>❑ Yes ❑ No | BP measurements<br>Most recent:<br>Date/value<br>……..……/……<br>Last 15 months:<br>Date/value:<br>……/……<br>…… …..…./……..<br>……..../…… |

Recent Lipid profile (≤ 6 months):
Total Cholesterol: …….. , HDL Cholesterol: ……, Triglyceride**: ……**

| ***Current drug Therapy*** | | | | | |
|---|---|---|---|---|---|
| **Start date** | **Drug name/ Dose** | **Documented indication** | **Start date** | **Drug name/ Dose** | **Documented indication** |
| | | | | | |
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| | | | | | |

- Glucose lowering agent used before starting insulin: ❑ Yes ❑ No
- Glucose lowering agent used before starting insulin is still used: ❑ Yes ❑ No
- Thiazolidinedione received for >6 months: ❑ Yes ❑ No, if yes:
  Hb $A_{1c}$ when started: ……..…… , Hb $A_{1c}$ after (6-9 months): ……..
- Erythromycin, clarithromycin, ketoconazole or itraconazole prescribed during simvastatin/atorvastatin therapy:
  ❑ Yes ❑ No
- Recent change in statin therapy (within the last 6 months): ❑ Yes ❑ No
- Recent change in glucose lowering therapy within the past 3 months: ❑ Yes ❑ No
- Recorded reason if $HbA_{1c}$ recorded at >7 %, ❑ Yes ❑ No
- Reason to start insulin before trying oral hypoglycaemic agents

| **Miscellaneous** | |
|---|---|
| Contraindicated to:<br>ACEI or ARB: ❑ angioedema ❑ renal artery stenosis ❑ pregnancy& breast-feeding<br>metformin:<br>❑ Renal failure, ❑ Ketoacidosis, ❑ pregnancy & breast-feeding or ❑ not tolerated (side-effects)<br>sulphonylureas:<br>Above or ❑ hepatic failure ❑ prophyria ❑ not tolerated (side-effects) | Contraindicated to statins:<br>❑ active liver disease (excluding fatty liver), ❑ pregnancy & breast-feeding or ❑ not tolerated (side-effects)<br>Contraindicated to fenofibrate:<br>❑ hepatic failure, ❑ gall bladder disease<br>❑pregnancy & breast-feeding<br>Or ❑ not tolerated (side-effects) |

## Appendix 7

## Report of findings

# Findings from MAT application- Levels of adherence to prescribing guidelines

## 1. Study Sample

| Patient demographic data for the whole study sample (n=305) | | | |
|---|---|---|---|
| **Description** | **n (%)** | **Description** | **n (%)** |
| ***Gender*** | | ***Smoking Status*** | |
| Male | 146 (47.9 %) | Current smokers | 24 (7.9%) |
| Female | 159 (52.1 %) | Current non-smokers | 74 (24.3%) |
| | | Not documented | 207 (67.9%) |
| ***Age* (years)** | | ***Past Medical History*** | |
| Mean (SD) | 53.1 (11.1) | With hypertension | 193 (63.3%) |
| Median | 54.0 | Without hypertension | 112 (36.7%) |
| Range | 21-79 | | |
| ***HbA1c (%)*** | | ***HbA1c category*** | |
| Mean (SD) | 8.6 (1.8) | HbA1c < 6.5 | 23 (7.5%) |
| Median | 8.2 (7.2-9.7) | HbA1c 6.5-7 | 45 (14.8%) |
| Range | 5.1-16.6 | HbA1c 7.1-7.5 | 38 (12.5%) |
| | | HbA1c 7.6-9 | 100 (32.8%) |
| | | HbA1c > 9 | 99 (32.5%) |

## 2. Level of adherence

| | |
|---|---|
| Total adherence to 38 MAT criteria in 305 patients | 68.1% |
| Total non-adherence to 38 MAT criteria in 305 patients | 30.8% |

## 3. criteria showed an adherence of ≥70 %

| Criteria | Adherence (%) | Applic-ability (n) |
|---|---|---|
| Criterion 27: blood pressure measurement | 100 | 305 |
| Criterion 18: avoid the use of thiazolidinedione in patients with heart failure | 100 | 68 |
| Criterion 12: measure renal function for patients on metformin and an estimated GFR ≤45 ml/min/1.73 $m^2$ | 100 | **2** |
| Criterion 35: avoid drug interaction with statins | 95.6 | 114 |
| Criterion 13: avoid the use of metformin in patients with estimated GFR < 30 ml/min/1.73 $m^2$ | 95.3 | 253 |

| Criteria showed an adherence of ≥70 %- continued<br><br>Criteria | Adherence (%) | Applic-ability (n) |
|---|---|---|
| Criterion 8: co-prescribe metformin or sulphonylurea with gliptin, pioglitazone or glinide | 94.9 | 175 |
| Criterion 11: patient on metformin had an estimated GFR >45 ml/min/1.73 $m^2$ | 94.5 | 253 |
| Criterion 23: renal function check | 94.1 | 305 |
| Criterion 31: avoid drugs worsen blood glucose control | 93.8 | 194 |
| Criterion 14: co-prescribe metformin or sulphonylurea as part of dual or triple therapy | 91.9 | 223 |
| Criterion 5: use of metformin or sulphonylurea as first-line therapy | 91.7 | 303 |
| Criterion 32: avoid the use of drugs that worsen BP control | 90.7 | 194 |
| Criterion 19: avoid the use of thiazolidinedione in patients with osteoporosis | 89.7 | 68 |
| Criterion 6: start dual therapy when indicated | 87.1 | 194 |
| Criterion 17: on exenatide or liraglutide had a BMI>30 $kg/m^2$ | 85.7 | **7** |
| Criterion 21: continuation of oral agent when insulin commenced | 83.1 | 71 |
| Criterion 10: with BMI ≥ 25 kg/m2 prescribed metformin | 82.8 | 261 |
| Criterion 7: avoid co-prescribing four oral agents | 82.6 | 213 |
| Criterion 28: prescribe ACE inhibitor or ARB for hypertension | 82.0 | 194 |
| Criterion 26: prescribe medication to manage neuropathy | 78.7 | 47 |
| Criterion 22: prescribe ACE inhibitor or ARB to manage micoabuminuria or proteinuria | 78.2 | 147 |
| Criterion 3: had at least two documented HbA1c measurements | 74.1 | 305 |
| Criterion 15: try oral therapy before commencing insulin | 71.4 | 105 |
| Criterion 16: prescribe insulin when indicated | 70.1 | 167 |

## 4. criteria showed an adherence of <70 %

| Criteria | Adherence (%) | Applic-ability (n) |
|---|---|---|
| Criterion 9: prescribe third oral agent or exenatide or insulin when indicated | 62.4 | 141 |
| Criterion 33: prescribe statin when indicated | 61.2 | 278 |
| Criterion 34: achieve targeted TC level with statin therapy | 60.7 | 173 |
| Criterion 24: retinal examination | 56.7 | 305 |
| Criterion 29: achieve BP target without co-morbidities | 33.5 | 194 |
| Criterion 1: referral to a structured diabetes education programme | 28.5 | 305 |
| Criterion 25: neuropathy/foot check | 24.6 | 305 |
| Criterion 38: smoking cessation advice | 24.0 | 25 |
| Criterion 36: prescribe fibrate when indicated | 23.1 | 13 |
| Criterion 4: achieve an HbA1c value of ≤ 7% | 22.3 | 305 |
| Criterion 30: achieve BP target with co-morbidities | 16.7 | 42 |
| Criterion 20: appropriate continuation of thiazolidinedione therapy | 14.0 | 50 |
| Criterion 37: add fibrate to statin therapy when indicated | 12.5 | 48 |
| Criterion 2: record a target HbA1c value for each patient | 0.0 | 305 |

# Appendix 8

# MAT analysis per patient

| Overall adherence in individual patients ranked from patient with highest adherence to lowest | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **#** | **Patient Key** | **N/A** | **Yes** | **NO** | **NOJ** | **IDs** | **IDq** | **applicability** | **Adherence (%)** | **95% CI min** | **95% CI max** |
| 1 | 211 | 18 | 17 | 2 | 0 | 0 | 1 | 19 | 89.5 | 75.7 | 100.0 |
| 2 | 123 | 9 | 25 | 2 | 1 | 0 | 1 | 28 | 89.3 | 77.8 | 100.0 |
| 3 | 133 | 20 | 16 | 2 | 0 | 0 | 0 | 18 | 88.9 | 74.4 | 100.0 |
| 4 | 265 | 12 | 22 | 3 | 0 | 0 | 1 | 25 | 88.0 | 75.3 | 100.0 |
| 5 | 77 | 14 | 21 | 3 | 0 | 0 | 0 | 24 | 87.5 | 74.3 | 100.0 |
| 6 | 193 | 23 | 13 | 2 | 0 | 0 | 0 | 15 | 86.7 | 69.5 | 100.0 |
| 7 | 205 | 7 | 26 | 3 | 1 | 0 | 1 | 30 | 86.7 | 74.5 | 98.8 |
| 8 | 241 | 16 | 18 | 3 | 0 | 0 | 1 | 21 | 85.7 | 70.7 | 100.7 |
| 9 | 162 | 11 | 23 | 4 | 0 | 0 | 0 | 27 | 85.2 | 71.8 | 98.6 |
| 10 | 56 | 17 | 17 | 3 | 0 | 0 | 1 | 20 | 85.0 | 69.4 | 100.6 |
| 11 | 55 | 11 | 22 | 3 | 1 | 0 | 1 | 26 | 84.6 | 70.7 | 98.5 |
| 12 | 60 | 11 | 22 | 4 | 0 | 0 | 1 | 26 | 84.6 | 70.7 | 98.5 |
| 13 | 268 | 11 | 22 | 4 | 0 | 0 | 1 | 26 | 84.6 | 70.7 | 98.5 |
| 14 | 39 | 18 | 16 | 3 | 0 | 0 | 1 | 19 | 84.2 | 67.8 | 100.6 |
| 15 | 192 | 13 | 21 | 3 | 1 | 0 | 0 | 25 | 84.0 | 69.6 | 98.4 |
| 16 | 7 | 13 | 20 | 4 | 0 | 0 | 1 | 24 | 83.3 | 68.4 | 98.2 |
| 17 | 28 | 14 | 20 | 4 | 0 | 0 | 0 | 24 | 83.3 | 68.4 | 98.2 |
| 18 | 95 | 20 | 15 | 3 | 0 | 0 | 0 | 18 | 83.3 | 66.1 | 100.6 |
| 19 | 173 | 7 | 25 | 4 | 1 | 0 | 1 | 30 | 83.3 | 70.0 | 96.7 |
| 20 | 34 | 9 | 24 | 5 | 0 | 0 | 0 | 29 | 82.8 | 69.0 | 96.5 |
| 21 | 100 | 8 | 24 | 5 | 0 | 0 | 1 | 29 | 82.8 | 69.0 | 96.5 |
| 22 | 174 | 9 | 24 | 5 | 0 | 0 | 0 | 29 | 82.8 | 69.0 | 96.5 |
| 23 | 202 | 8 | 24 | 5 | 0 | 0 | 1 | 29 | 82.8 | 69.0 | 96.5 |
| 24 | 149 | 15 | 19 | 4 | 0 | 0 | 0 | 23 | 82.6 | 67.1 | 98.1 |
| 25 | 75 | 21 | 14 | 3 | 0 | 0 | 0 | 17 | 82.4 | 64.2 | 100.5 |
| 26 | 240 | 9 | 23 | 4 | 1 | 0 | 1 | 28 | 82.1 | 68.0 | 96.3 |
| 27 | 282 | 9 | 23 | 5 | 0 | 0 | 1 | 28 | 82.1 | 68.0 | 96.3 |
| 28 | 187 | 15 | 18 | 4 | 0 | 0 | 1 | 22 | 81.8 | 65.7 | 97.9 |
| 29 | 17 | 10 | 22 | 5 | 0 | 0 | 1 | 27 | 81.5 | 66.8 | 96.1 |
| 30 | 177 | 10 | 22 | 4 | 1 | 0 | 1 | 27 | 81.5 | 66.8 | 96.1 |
| 31 | 164 | 21 | 13 | 3 | 0 | 0 | 1 | 16 | 81.3 | 62.1 | 100.4 |
| 32 | 85 | 16 | 17 | 4 | 0 | 0 | 1 | 21 | 81.0 | 64.2 | 97.7 |
| 33 | 86 | 16 | 17 | 4 | 0 | 0 | 1 | 21 | 81.0 | 64.2 | 97.7 |
| 34 | 93 | 17 | 17 | 4 | 0 | 0 | 0 | 21 | 81.0 | 64.2 | 97.7 |
| 35 | 107 | 16 | 17 | 4 | 0 | 0 | 1 | 21 | 81.0 | 64.2 | 97.7 |
| 36 | 208 | 16 | 17 | 4 | 0 | 0 | 1 | 21 | 81.0 | 64.2 | 97.7 |
| 37 | 281 | 17 | 17 | 4 | 0 | 0 | 0 | 21 | 81.0 | 64.2 | 97.7 |
| 38 | 13 | 11 | 21 | 5 | 0 | 0 | 1 | 26 | 80.8 | 65.6 | 95.9 |
| 39 | 143 | 11 | 21 | 4 | 1 | 0 | 1 | 26 | 80.8 | 65.6 | 95.9 |
| 40 | 166 | 12 | 21 | 5 | 0 | 0 | 0 | 26 | 80.8 | 65.6 | 95.9 |
| 41 | 27 | 17 | 16 | 4 | 0 | 0 | 1 | 20 | 80.0 | 62.5 | 97.5 |
| 42 | 42 | 12 | 20 | 4 | 1 | 0 | 1 | 25 | 80.0 | 64.3 | 95.7 |
| 43 | 74 | 17 | 16 | 4 | 0 | 0 | 1 | 20 | 80.0 | 62.5 | 97.5 |
| 44 | 78 | 23 | 12 | 3 | 0 | 0 | 0 | 15 | 80.0 | 59.8 | 100.2 |
| 45 | 83 | 12 | 20 | 4 | 1 | 0 | 1 | 25 | 80.0 | 64.3 | 95.7 |
| 46 | 92 | 12 | 20 | 5 | 0 | 0 | 1 | 25 | 80.0 | 64.3 | 95.7 |
| 47 | 178 | 12 | 20 | 5 | 0 | 0 | 1 | 25 | 80.0 | 64.3 | 95.7 |
| 48 | 184 | 12 | 20 | 5 | 0 | 0 | 1 | 25 | 80.0 | 64.3 | 95.7 |

| Overall adherence in individual patients ranked from patient with highest adherence to lowest- continued | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| # | Patient Key | N/A | Yes | NO | NOJ | IDs | IDq | applicability | Adherence (%) | 95% CI min | 95% CI max |
| 49 | 222 | 22 | 12 | 3 | 0 | 0 | 1 | 15 | 80.0 | 59.8 | 100.2 |
| 50 | 287 | 12 | 20 | 5 | 0 | 0 | 1 | 25 | 80.0 | 64.3 | 95.7 |
| 51 | 299 | 8 | 23 | 6 | 0 | 0 | 1 | 29 | 79.3 | 64.6 | 94.1 |
| 52 | 46 | 13 | 19 | 4 | 0 | 1 | 1 | 24 | 79.2 | 62.9 | 95.4 |
| 53 | 88 | 13 | 19 | 5 | 0 | 0 | 1 | 24 | 79.2 | 62.9 | 95.4 |
| 54 | 176 | 13 | 19 | 5 | 0 | 0 | 1 | 24 | 79.2 | 62.9 | 95.4 |
| 55 | 277 | 13 | 19 | 5 | 0 | 0 | 1 | 24 | 79.2 | 62.9 | 95.4 |
| 56 | 120 | 19 | 15 | 4 | 0 | 0 | 0 | 19 | 78.9 | 60.6 | 97.3 |
| 57 | 122 | 9 | 22 | 6 | 0 | 0 | 1 | 28 | 78.6 | 63.4 | 93.8 |
| 58 | 29 | 14 | 18 | 4 | 0 | 1 | 1 | 23 | 78.3 | 61.4 | 95.1 |
| 59 | 171 | 15 | 18 | 5 | 0 | 0 | 0 | 23 | 78.3 | 61.4 | 95.1 |
| 60 | 22 | 11 | 21 | 6 | 0 | 0 | 0 | 27 | 77.8 | 62.1 | 93.5 |
| 61 | 43 | 19 | 14 | 4 | 0 | 0 | 1 | 18 | 77.8 | 58.6 | 97.0 |
| 62 | 116 | 19 | 14 | 4 | 0 | 0 | 1 | 18 | 77.8 | 58.6 | 97.0 |
| 63 | 198 | 11 | 21 | 5 | 1 | 0 | 0 | 27 | 77.8 | 62.1 | 93.5 |
| 64 | 41 | 6 | 24 | 6 | 0 | 1 | 1 | 31 | 77.4 | 62.7 | 92.1 |
| 65 | 66 | 15 | 17 | 4 | 1 | 0 | 1 | 22 | 77.3 | 59.8 | 94.8 |
| 66 | 82 | 15 | 17 | 4 | 1 | 0 | 1 | 22 | 77.3 | 59.8 | 94.8 |
| 67 | 161 | 16 | 17 | 5 | 0 | 0 | 0 | 22 | 77.3 | 59.8 | 94.8 |
| 68 | 168 | 16 | 17 | 5 | 0 | 0 | 0 | 22 | 77.3 | 59.8 | 94.8 |
| 69 | 213 | 15 | 17 | 5 | 0 | 0 | 1 | 22 | 77.3 | 59.8 | 94.8 |
| 70 | 97 | 12 | 20 | 5 | 0 | 1 | 0 | 26 | 76.9 | 60.7 | 93.1 |
| 71 | 159 | 11 | 20 | 5 | 0 | 1 | 1 | 26 | 76.9 | 60.7 | 93.1 |
| 72 | 182 | 11 | 20 | 6 | 0 | 0 | 1 | 26 | 76.9 | 60.7 | 93.1 |
| 73 | 266 | 25 | 10 | 3 | 0 | 0 | 0 | 13 | 76.9 | 54.0 | 99.8 |
| 74 | 290 | 8 | 23 | 7 | 0 | 0 | 0 | 30 | 76.7 | 61.5 | 91.8 |
| 75 | 146 | 20 | 13 | 4 | 0 | 0 | 1 | 17 | 76.5 | 56.3 | 96.6 |
| 76 | 62 | 17 | 16 | 5 | 0 | 0 | 0 | 21 | 76.2 | 58.0 | 94.4 |
| 77 | 81 | 16 | 16 | 5 | 0 | 0 | 1 | 21 | 76.2 | 58.0 | 94.4 |
| 78 | 214 | 17 | 16 | 5 | 0 | 0 | 0 | 21 | 76.2 | 58.0 | 94.4 |
| 79 | 289 | 16 | 16 | 5 | 0 | 0 | 1 | 21 | 76.2 | 58.0 | 94.4 |
| 80 | 20 | 13 | 19 | 5 | 1 | 0 | 0 | 25 | 76.0 | 59.3 | 92.7 |
| 81 | 47 | 12 | 19 | 6 | 0 | 0 | 1 | 25 | 76.0 | 59.3 | 92.7 |
| 82 | 103 | 13 | 19 | 6 | 0 | 0 | 0 | 25 | 76.0 | 59.3 | 92.7 |
| 83 | 226 | 12 | 19 | 5 | 1 | 0 | 1 | 25 | 76.0 | 59.3 | 92.7 |
| 84 | 262 | 12 | 19 | 6 | 0 | 0 | 1 | 25 | 76.0 | 59.3 | 92.7 |
| 85 | 8 | 8 | 22 | 5 | 0 | 2 | 1 | 29 | 75.9 | 60.3 | 91.4 |
| 86 | 59 | 8 | 22 | 7 | 0 | 0 | 1 | 29 | 75.9 | 60.3 | 91.4 |
| 87 | 172 | 8 | 22 | 6 | 0 | 1 | 1 | 29 | 75.9 | 60.3 | 91.4 |
| 88 | 204 | 6 | 22 | 5 | 1 | 1 | 3 | 29 | 75.9 | 60.3 | 91.4 |
| 89 | 9 | 9 | 21 | 7 | 0 | 0 | 1 | 28 | 75.0 | 59.0 | 91.0 |
| 90 | 16 | 9 | 21 | 6 | 1 | 0 | 1 | 28 | 75.0 | 59.0 | 91.0 |
| 91 | 114 | 13 | 18 | 5 | 1 | 0 | 1 | 24 | 75.0 | 57.7 | 92.3 |
| 92 | 139 | 22 | 12 | 4 | 0 | 0 | 0 | 16 | 75.0 | 53.8 | 96.2 |
| 93 | 141 | 17 | 15 | 5 | 0 | 0 | 1 | 20 | 75.0 | 56.0 | 94.0 |
| 94 | 156 | 13 | 18 | 6 | 0 | 0 | 1 | 24 | 75.0 | 57.7 | 92.3 |
| 95 | 170 | 26 | 9 | 3 | 0 | 0 | 0 | 12 | 75.0 | 50.5 | 99.5 |
| 96 | 210 | 9 | 21 | 6 | 1 | 0 | 1 | 28 | 75.0 | 59.0 | 91.0 |
| 97 | 237 | 13 | 18 | 5 | 1 | 0 | 1 | 24 | 75.0 | 57.7 | 92.3 |

| Overall adherence in individual patients ranked from patient with highest adherence to lowest- continued | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| # | Patient Key | N/A | Yes | NO | NOJ | IDs | IDq | applicability | Adherence (%) | 95% CI min | 95% CI max |
| 98 | 249 | 14 | 18 | 5 | 1 | 0 | 0 | 24 | 75.0 | 57.7 | 92.3 |
| 99 | 38 | 7 | 23 | 7 | 1 | 0 | 0 | 31 | 74.2 | 58.8 | 89.6 |
| 100 | 99 | 6 | 23 | 7 | 0 | 1 | 1 | 31 | 74.2 | 58.8 | 89.6 |
| 101 | 48 | 14 | 17 | 5 | 0 | 1 | 1 | 23 | 73.9 | 56.0 | 91.9 |
| 102 | 135 | 14 | 17 | 6 | 0 | 0 | 1 | 23 | 73.9 | 56.0 | 91.9 |
| 103 | 199 | 14 | 17 | 5 | 1 | 0 | 1 | 23 | 73.9 | 56.0 | 91.9 |
| 104 | 252 | 15 | 17 | 6 | 0 | 0 | 0 | 23 | 73.9 | 56.0 | 91.9 |
| 105 | 5 | 18 | 14 | 5 | 0 | 0 | 1 | 19 | 73.7 | 53.9 | 93.5 |
| 106 | 37 | 18 | 14 | 5 | 0 | 0 | 1 | 19 | 73.7 | 53.9 | 93.5 |
| 107 | 101 | 18 | 14 | 5 | 0 | 0 | 1 | 19 | 73.7 | 53.9 | 93.5 |
| 108 | 125 | 15 | 14 | 5 | 0 | 0 | 4 | 19 | 73.7 | 53.9 | 93.5 |
| 109 | 234 | 18 | 14 | 5 | 0 | 0 | 1 | 19 | 73.7 | 53.9 | 93.5 |
| 110 | 106 | 22 | 11 | 4 | 0 | 0 | 1 | 15 | 73.3 | 51.0 | 95.7 |
| 111 | 203 | 22 | 11 | 4 | 0 | 0 | 1 | 15 | 73.3 | 51.0 | 95.7 |
| 112 | 230 | 8 | 22 | 8 | 0 | 0 | 0 | 30 | 73.3 | 57.5 | 89.2 |
| 113 | 256 | 7 | 22 | 8 | 0 | 0 | 1 | 30 | 73.3 | 57.5 | 89.2 |
| 114 | 64 | 11 | 19 | 7 | 0 | 0 | 1 | 26 | 73.1 | 56.0 | 90.1 |
| 115 | 4 | 15 | 16 | 6 | 0 | 0 | 1 | 22 | 72.7 | 54.1 | 91.3 |
| 116 | 40 | 15 | 16 | 6 | 0 | 0 | 1 | 22 | 72.7 | 54.1 | 91.3 |
| 117 | 84 | 15 | 16 | 5 | 1 | 0 | 1 | 22 | 72.7 | 54.1 | 91.3 |
| 118 | 126 | 15 | 16 | 6 | 0 | 0 | 1 | 22 | 72.7 | 54.1 | 91.3 |
| 119 | 181 | 15 | 16 | 5 | 1 | 0 | 1 | 22 | 72.7 | 54.1 | 91.3 |
| 120 | 236 | 15 | 16 | 6 | 0 | 0 | 1 | 22 | 72.7 | 54.1 | 91.3 |
| 121 | 260 | 13 | 16 | 5 | 0 | 1 | 3 | 22 | 72.7 | 54.1 | 91.3 |
| 122 | 305 | 15 | 16 | 5 | 1 | 0 | 1 | 22 | 72.7 | 54.1 | 91.3 |
| 123 | 175 | 9 | 21 | 6 | 1 | 1 | 0 | 29 | 72.4 | 56.1 | 88.7 |
| 124 | 235 | 8 | 21 | 7 | 1 | 0 | 1 | 29 | 72.4 | 56.1 | 88.7 |
| 125 | 138 | 20 | 13 | 5 | 0 | 0 | 0 | 18 | 72.2 | 51.5 | 92.9 |
| 126 | 273 | 17 | 13 | 4 | 0 | 1 | 3 | 18 | 72.2 | 51.5 | 92.9 |
| 127 | 288 | 19 | 13 | 5 | 0 | 0 | 1 | 18 | 72.2 | 51.5 | 92.9 |
| 128 | 113 | 12 | 18 | 7 | 0 | 0 | 1 | 25 | 72.0 | 54.4 | 89.6 |
| 129 | 223 | 13 | 18 | 7 | 0 | 0 | 0 | 25 | 72.0 | 54.4 | 89.6 |
| 130 | 261 | 10 | 18 | 7 | 0 | 0 | 3 | 25 | 72.0 | 54.4 | 89.6 |
| 131 | 57 | 16 | 15 | 6 | 0 | 0 | 1 | 21 | 71.4 | 52.1 | 90.8 |
| 132 | 118 | 9 | 20 | 6 | 1 | 1 | 1 | 28 | 71.4 | 54.7 | 88.2 |
| 133 | 238 | 24 | 10 | 4 | 0 | 0 | 0 | 14 | 71.4 | 47.8 | 95.1 |
| 134 | 147 | 10 | 17 | 6 | 1 | 0 | 4 | 24 | 70.8 | 52.6 | 89.0 |
| 135 | 163 | 13 | 17 | 6 | 1 | 0 | 1 | 24 | 70.8 | 52.6 | 89.0 |
| 136 | 212 | 13 | 17 | 6 | 1 | 0 | 1 | 24 | 70.8 | 52.6 | 89.0 |
| 137 | 276 | 13 | 17 | 6 | 1 | 0 | 1 | 24 | 70.8 | 52.6 | 89.0 |
| 138 | 284 | 13 | 17 | 6 | 1 | 0 | 1 | 24 | 70.8 | 52.6 | 89.0 |
| 139 | 31 | 20 | 12 | 4 | 1 | 0 | 1 | 17 | 70.6 | 48.9 | 92.2 |
| 140 | 71 | 20 | 12 | 5 | 0 | 0 | 1 | 17 | 70.6 | 48.9 | 92.2 |
| 141 | 153 | 21 | 12 | 5 | 0 | 0 | 0 | 17 | 70.6 | 48.9 | 92.2 |
| 142 | 233 | 21 | 12 | 4 | 1 | 0 | 0 | 17 | 70.6 | 48.9 | 92.2 |
| 143 | 258 | 20 | 12 | 3 | 2 | 0 | 1 | 17 | 70.6 | 48.9 | 92.2 |
| 144 | 217 | 11 | 19 | 7 | 1 | 0 | 0 | 27 | 70.4 | 53.1 | 87.6 |
| 145 | 283 | 10 | 19 | 8 | 0 | 0 | 1 | 27 | 70.4 | 53.1 | 87.6 |
| 146 | 11 | 17 | 14 | 6 | 0 | 0 | 1 | 20 | 70.0 | 49.9 | 90.1 |

| Overall adherence in individual patients ranked from patient with highest adherence to lowest- continued | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| # | Patient Key | N/A | Yes | NO | NOJ | IDs | IDq | applicability | Adherence (%) | 95% CI min | 95% CI max |
| 147 | 18 | 18 | 14 | 5 | 1 | 0 | 0 | 20 | 70.0 | 49.9 | 90.1 |
| 148 | 127 | 18 | 14 | 5 | 1 | 0 | 0 | 20 | 70.0 | 49.9 | 90.1 |
| 149 | 200 | 4 | 21 | 8 | 0 | 1 | 4 | 30 | 70.0 | 53.6 | 86.4 |
| 150 | 293 | 18 | 14 | 6 | 0 | 0 | 0 | 20 | 70.0 | 49.9 | 90.1 |
| 151 | 295 | 18 | 14 | 5 | 1 | 0 | 0 | 20 | 70.0 | 49.9 | 90.1 |
| 152 | 61 | 14 | 16 | 7 | 0 | 0 | 1 | 23 | 69.6 | 50.8 | 88.4 |
| 153 | 108 | 14 | 16 | 5 | 1 | 1 | 1 | 23 | 69.6 | 50.8 | 88.4 |
| 154 | 117 | 15 | 16 | 6 | 1 | 0 | 0 | 23 | 69.6 | 50.8 | 88.4 |
| 155 | 195 | 14 | 16 | 7 | 0 | 0 | 1 | 23 | 69.6 | 50.8 | 88.4 |
| 156 | 242 | 11 | 16 | 7 | 0 | 0 | 4 | 23 | 69.6 | 50.8 | 88.4 |
| 157 | 267 | 15 | 16 | 7 | 0 | 0 | 0 | 23 | 69.6 | 50.8 | 88.4 |
| 158 | 112 | 11 | 18 | 7 | 1 | 0 | 1 | 26 | 69.2 | 51.5 | 87.0 |
| 159 | 152 | 24 | 9 | 4 | 0 | 0 | 1 | 13 | 69.2 | 44.1 | 94.3 |
| 160 | 160 | 12 | 18 | 7 | 1 | 0 | 0 | 26 | 69.2 | 51.5 | 87.0 |
| 161 | 296 | 24 | 9 | 4 | 0 | 0 | 1 | 13 | 69.2 | 44.1 | 94.3 |
| 162 | 102 | 22 | 11 | 5 | 0 | 0 | 0 | 16 | 68.8 | 46.0 | 91.5 |
| 163 | 91 | 19 | 13 | 4 | 2 | 0 | 0 | 19 | 68.4 | 47.5 | 89.3 |
| 164 | 130 | 18 | 13 | 5 | 1 | 0 | 1 | 19 | 68.4 | 47.5 | 89.3 |
| 165 | 270 | 18 | 13 | 6 | 0 | 0 | 1 | 19 | 68.4 | 47.5 | 89.3 |
| 166 | 227 | 12 | 15 | 7 | 0 | 0 | 4 | 22 | 68.2 | 48.7 | 87.6 |
| 167 | 23 | 12 | 17 | 7 | 1 | 0 | 1 | 25 | 68.0 | 49.7 | 86.3 |
| 168 | 52 | 12 | 17 | 8 | 0 | 0 | 1 | 25 | 68.0 | 49.7 | 86.3 |
| 169 | 87 | 13 | 17 | 6 | 1 | 1 | 0 | 25 | 68.0 | 49.7 | 86.3 |
| 170 | 165 | 10 | 17 | 6 | 2 | 0 | 3 | 25 | 68.0 | 49.7 | 86.3 |
| 171 | 272 | 12 | 17 | 8 | 0 | 0 | 1 | 25 | 68.0 | 49.7 | 86.3 |
| 172 | 286 | 10 | 17 | 7 | 0 | 1 | 3 | 25 | 68.0 | 49.7 | 86.3 |
| 173 | 121 | 9 | 19 | 7 | 1 | 1 | 1 | 28 | 67.9 | 50.6 | 85.2 |
| 174 | 6 | 14 | 16 | 6 | 2 | 0 | 0 | 24 | 66.7 | 47.8 | 85.5 |
| 175 | 105 | 13 | 16 | 8 | 0 | 0 | 1 | 24 | 66.7 | 47.8 | 85.5 |
| 176 | 119 | 13 | 16 | 7 | 0 | 1 | 1 | 24 | 66.7 | 47.8 | 85.5 |
| 177 | 124 | 16 | 12 | 6 | 0 | 0 | 4 | 18 | 66.7 | 44.9 | 88.4 |
| 178 | 157 | 19 | 12 | 6 | 0 | 0 | 1 | 18 | 66.7 | 44.9 | 88.4 |
| 179 | 183 | 16 | 14 | 7 | 0 | 0 | 1 | 21 | 66.7 | 46.5 | 86.8 |
| 180 | 188 | 11 | 16 | 6 | 1 | 1 | 3 | 24 | 66.7 | 47.8 | 85.5 |
| 181 | 245 | 25 | 8 | 4 | 0 | 0 | 1 | 12 | 66.7 | 40.0 | 93.3 |
| 182 | 253 | 17 | 12 | 6 | 0 | 0 | 3 | 18 | 66.7 | 44.9 | 88.4 |
| 183 | 254 | 14 | 16 | 8 | 0 | 0 | 0 | 24 | 66.7 | 47.8 | 85.5 |
| 184 | 257 | 17 | 14 | 7 | 0 | 0 | 0 | 21 | 66.7 | 46.5 | 86.8 |
| 185 | 274 | 11 | 14 | 6 | 0 | 1 | 6 | 21 | 66.7 | 46.5 | 86.8 |
| 186 | 292 | 14 | 16 | 7 | 1 | 0 | 0 | 24 | 66.7 | 47.8 | 85.5 |
| 187 | 294 | 13 | 16 | 8 | 0 | 0 | 1 | 24 | 66.7 | 47.8 | 85.5 |
| 188 | 44 | 14 | 15 | 7 | 0 | 1 | 1 | 23 | 65.2 | 45.8 | 84.7 |
| 189 | 115 | 14 | 15 | 8 | 0 | 0 | 1 | 23 | 65.2 | 45.8 | 84.7 |
| 190 | 297 | 15 | 15 | 8 | 0 | 0 | 0 | 23 | 65.2 | 45.8 | 84.7 |
| 191 | 35 | 18 | 13 | 7 | 0 | 0 | 0 | 20 | 65.0 | 44.1 | 85.9 |
| 192 | 98 | 17 | 13 | 7 | 0 | 0 | 1 | 20 | 65.0 | 44.1 | 85.9 |
| 193 | 21 | 21 | 11 | 5 | 1 | 0 | 0 | 17 | 64.7 | 42.0 | 87.4 |
| 194 | 278 | 21 | 11 | 5 | 1 | 0 | 0 | 17 | 64.7 | 42.0 | 87.4 |
| 195 | 15 | 23 | 9 | 5 | 0 | 0 | 1 | 14 | 64.3 | 39.2 | 89.4 |
| 196 | 228 | 13 | 16 | 8 | 1 | 0 | 0 | 25 | 64.0 | 45.2 | 82.8 |

| Overall adherence in individual patients ranked from patient with highest adherence to lowest- continued | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| # | Patient Key | N/A | Yes | NO | NOJ | IDs | IDq | applicability | Adherence (%) | 95% CI min | 95% CI max |
| 197 | 244 | 12 | 16 | 9 | 0 | 0 | 1 | 25 | 64.0 | 45.2 | 82.8 |
| 198 | 275 | 13 | 16 | 9 | 0 | 0 | 0 | 25 | 64.0 | 45.2 | 82.8 |
| 199 | 90 | 15 | 14 | 8 | 0 | 0 | 1 | 22 | 63.6 | 43.5 | 83.7 |
| 200 | 194 | 12 | 14 | 7 | 1 | 0 | 4 | 22 | 63.6 | 43.5 | 83.7 |
| 201 | 215 | 15 | 14 | 8 | 0 | 0 | 1 | 22 | 63.6 | 43.5 | 83.7 |
| 202 | 148 | 19 | 12 | 7 | 0 | 0 | 0 | 19 | 63.2 | 41.5 | 84.8 |
| 203 | 167 | 18 | 12 | 7 | 0 | 0 | 1 | 19 | 63.2 | 41.5 | 84.8 |
| 204 | 209 | 16 | 12 | 5 | 1 | 1 | 3 | 19 | 63.2 | 41.5 | 84.8 |
| 205 | 51 | 10 | 17 | 8 | 2 | 0 | 1 | 27 | 63.0 | 44.7 | 81.2 |
| 206 | 33 | 22 | 10 | 6 | 0 | 0 | 0 | 16 | 62.5 | 38.8 | 86.2 |
| 207 | 45 | 10 | 15 | 7 | 0 | 2 | 4 | 24 | 62.5 | 43.1 | 81.9 |
| 208 | 185 | 21 | 10 | 6 | 0 | 0 | 1 | 16 | 62.5 | 38.8 | 86.2 |
| 209 | 246 | 14 | 15 | 8 | 1 | 0 | 0 | 24 | 62.5 | 43.1 | 81.9 |
| 210 | 259 | 21 | 10 | 5 | 1 | 0 | 1 | 16 | 62.5 | 38.8 | 86.2 |
| 211 | 301 | 10 | 15 | 8 | 0 | 1 | 4 | 24 | 62.5 | 43.1 | 81.9 |
| 212 | 169 | 15 | 13 | 8 | 0 | 0 | 2 | 21 | 61.9 | 41.1 | 82.7 |
| 213 | 239 | 17 | 13 | 8 | 0 | 0 | 0 | 21 | 61.9 | 41.1 | 82.7 |
| 214 | 298 | 17 | 13 | 8 | 0 | 0 | 0 | 21 | 61.9 | 41.1 | 82.7 |
| 215 | 196 | 24 | 8 | 5 | 0 | 0 | 1 | 13 | 61.5 | 35.1 | 88.0 |
| 216 | 30 | 20 | 11 | 7 | 0 | 0 | 0 | 18 | 61.1 | 38.6 | 83.6 |
| 217 | 80 | 14 | 14 | 9 | 0 | 0 | 1 | 23 | 60.9 | 40.9 | 80.8 |
| 218 | 145 | 13 | 14 | 9 | 0 | 0 | 2 | 23 | 60.9 | 40.9 | 80.8 |
| 219 | 221 | 14 | 14 | 9 | 0 | 0 | 1 | 23 | 60.9 | 40.9 | 80.8 |
| 220 | 280 | 7 | 17 | 9 | 1 | 1 | 3 | 28 | 60.7 | 42.6 | 78.8 |
| 221 | 2 | 12 | 15 | 10 | 0 | 0 | 1 | 25 | 60.0 | 40.8 | 79.2 |
| 222 | 14 | 23 | 9 | 6 | 0 | 0 | 0 | 15 | 60.0 | 35.2 | 84.8 |
| 223 | 32 | 22 | 9 | 5 | 1 | 0 | 1 | 15 | 60.0 | 35.2 | 84.8 |
| 224 | 67 | 17 | 12 | 7 | 1 | 0 | 1 | 20 | 60.0 | 38.5 | 81.5 |
| 225 | 109 | 15 | 12 | 6 | 1 | 1 | 3 | 20 | 60.0 | 38.5 | 81.5 |
| 226 | 151 | 17 | 12 | 7 | 1 | 0 | 1 | 20 | 60.0 | 38.5 | 81.5 |
| 227 | 206 | 22 | 9 | 6 | 0 | 0 | 1 | 15 | 60.0 | 35.2 | 84.8 |
| 228 | 63 | 15 | 13 | 7 | 0 | 2 | 1 | 22 | 59.1 | 38.5 | 79.6 |
| 229 | 94 | 15 | 13 | 8 | 1 | 0 | 1 | 22 | 59.1 | 38.5 | 79.6 |
| 230 | 104 | 15 | 13 | 9 | 0 | 0 | 1 | 22 | 59.1 | 38.5 | 79.6 |
| 231 | 129 | 16 | 13 | 9 | 0 | 0 | 0 | 22 | 59.1 | 38.5 | 79.6 |
| 232 | 19 | 21 | 10 | 6 | 1 | 0 | 0 | 17 | 58.8 | 35.4 | 82.2 |
| 233 | 89 | 21 | 10 | 7 | 0 | 0 | 0 | 17 | 58.8 | 35.4 | 82.2 |
| 234 | 134 | 20 | 10 | 6 | 1 | 0 | 1 | 17 | 58.8 | 35.4 | 82.2 |
| 235 | 137 | 20 | 10 | 7 | 0 | 0 | 1 | 17 | 58.8 | 35.4 | 82.2 |
| 236 | 271 | 21 | 10 | 7 | 0 | 0 | 0 | 17 | 58.8 | 35.4 | 82.2 |
| 237 | 131 | 13 | 14 | 9 | 1 | 0 | 1 | 24 | 58.3 | 38.6 | 78.1 |
| 238 | 132 | 12 | 14 | 7 | 1 | 2 | 2 | 24 | 58.3 | 38.6 | 78.1 |
| 239 | 250 | 23 | 7 | 3 | 2 | 0 | 3 | 12 | 58.3 | 30.4 | 86.2 |
| 240 | 36 | 19 | 11 | 4 | 4 | 0 | 0 | 19 | 57.9 | 35.7 | 80.1 |
| 241 | 186 | 18 | 11 | 8 | 0 | 0 | 1 | 19 | 57.9 | 35.7 | 80.1 |
| 242 | 207 | 18 | 11 | 8 | 0 | 0 | 1 | 19 | 57.9 | 35.7 | 80.1 |
| 243 | 218 | 18 | 11 | 8 | 0 | 0 | 1 | 19 | 57.9 | 35.7 | 80.1 |
| 244 | 251 | 18 | 11 | 8 | 0 | 0 | 1 | 19 | 57.9 | 35.7 | 80.1 |
| 245 | 300 | 7 | 15 | 7 | 0 | 4 | 5 | 26 | 57.7 | 38.7 | 76.7 |
| 246 | 49 | 16 | 12 | 7 | 1 | 1 | 1 | 21 | 57.1 | 36.0 | 78.3 |

| Overall adherence in individual patients ranked from patient with highest adherence to lowest- continued | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| # | Patient Key | N/A | Yes | NO | NOJ | IDs | IDq | applicability | Adherence (%) | 95% CI min | 95% CI max |
| 247 | 76 | 16 | 12 | 8 | 1 | 0 | 1 | 21 | 57.1 | 36.0 | 78.3 |
| 248 | 269 | 9 | 16 | 11 | 0 | 1 | 1 | 28 | 57.1 | 38.8 | 75.5 |
| 249 | 291 | 7 | 17 | 13 | 0 | 0 | 1 | 30 | 56.7 | 38.9 | 74.4 |
| 250 | 1 | 14 | 13 | 10 | 0 | 0 | 1 | 23 | 56.5 | 36.3 | 76.8 |
| 251 | 12 | 14 | 13 | 10 | 0 | 0 | 1 | 23 | 56.5 | 36.3 | 76.8 |
| 252 | 69 | 14 | 13 | 10 | 0 | 0 | 1 | 23 | 56.5 | 36.3 | 76.8 |
| 253 | 110 | 11 | 13 | 9 | 1 | 0 | 4 | 23 | 56.5 | 36.3 | 76.8 |
| 254 | 224 | 11 | 13 | 8 | 1 | 1 | 4 | 23 | 56.5 | 36.3 | 76.8 |
| 255 | 68 | 21 | 9 | 7 | 0 | 0 | 1 | 16 | 56.3 | 31.9 | 80.6 |
| 256 | 140 | 18 | 9 | 3 | 2 | 2 | 4 | 16 | 56.3 | 31.9 | 80.6 |
| 257 | 190 | 21 | 9 | 6 | 1 | 0 | 1 | 16 | 56.3 | 31.9 | 80.6 |
| 258 | 232 | 19 | 9 | 6 | 1 | 0 | 3 | 16 | 56.3 | 31.9 | 80.6 |
| 259 | 247 | 22 | 9 | 7 | 0 | 0 | 0 | 16 | 56.3 | 31.9 | 80.6 |
| 260 | 72 | 12 | 14 | 10 | 0 | 1 | 1 | 25 | 56.0 | 36.5 | 75.5 |
| 261 | 189 | 10 | 15 | 10 | 1 | 1 | 1 | 27 | 55.6 | 36.8 | 74.3 |
| 262 | 248 | 19 | 10 | 7 | 1 | 0 | 1 | 18 | 55.6 | 32.6 | 78.5 |
| 263 | 304 | 17 | 11 | 9 | 0 | 0 | 1 | 20 | 55.0 | 33.2 | 76.8 |
| 264 | 10 | 24 | 7 | 5 | 1 | 0 | 1 | 13 | 53.8 | 26.7 | 80.9 |
| 265 | 26 | 11 | 14 | 12 | 0 | 0 | 1 | 26 | 53.8 | 34.7 | 73.0 |
| 266 | 54 | 9 | 15 | 10 | 2 | 1 | 1 | 28 | 53.6 | 35.1 | 72.0 |
| 267 | 96 | 20 | 9 | 8 | 0 | 0 | 1 | 17 | 52.9 | 29.2 | 76.7 |
| 268 | 70 | 18 | 10 | 8 | 1 | 0 | 1 | 19 | 52.6 | 30.2 | 75.1 |
| 269 | 111 | 17 | 10 | 8 | 1 | 0 | 2 | 19 | 52.6 | 30.2 | 75.1 |
| 270 | 179 | 16 | 11 | 8 | 2 | 0 | 1 | 21 | 52.4 | 31.0 | 73.7 |
| 271 | 24 | 14 | 12 | 9 | 2 | 0 | 1 | 23 | 52.2 | 31.8 | 72.6 |
| 272 | 180 | 12 | 12 | 10 | 1 | 0 | 3 | 23 | 52.2 | 31.8 | 72.6 |
| 273 | 155 | 17 | 8 | 5 | 0 | 3 | 5 | 16 | 50.0 | 25.5 | 74.5 |
| 274 | 201 | 22 | 6 | 6 | 0 | 0 | 4 | 12 | 50.0 | 21.7 | 78.3 |
| 275 | 225 | 16 | 11 | 11 | 0 | 0 | 0 | 22 | 50.0 | 29.1 | 70.9 |
| 276 | 53 | 12 | 12 | 13 | 0 | 0 | 1 | 25 | 48.0 | 28.4 | 67.6 |
| 277 | 158 | 15 | 11 | 12 | 0 | 0 | 0 | 23 | 47.8 | 27.4 | 68.2 |
| 278 | 191 | 16 | 10 | 7 | 4 | 0 | 1 | 21 | 47.6 | 26.3 | 69.0 |
| 279 | 154 | 18 | 9 | 10 | 0 | 0 | 1 | 19 | 47.4 | 24.9 | 69.8 |
| 280 | 73 | 22 | 7 | 8 | 0 | 0 | 1 | 15 | 46.7 | 21.4 | 71.9 |
| 281 | 25 | 13 | 11 | 12 | 0 | 1 | 1 | 24 | 45.8 | 25.9 | 65.8 |
| 282 | 197 | 13 | 11 | 11 | 2 | 0 | 1 | 24 | 45.8 | 25.9 | 65.8 |
| 283 | 285 | 9 | 11 | 9 | 1 | 3 | 5 | 24 | 45.8 | 25.9 | 65.8 |
| 284 | 79 | 15 | 10 | 12 | 0 | 0 | 1 | 22 | 45.5 | 24.6 | 66.3 |
| 285 | 231 | 15 | 10 | 11 | 1 | 0 | 1 | 22 | 45.5 | 24.6 | 66.3 |
| 286 | 216 | 15 | 9 | 10 | 1 | 0 | 3 | 20 | 45.0 | 23.2 | 66.8 |
| 287 | 243 | 13 | 9 | 8 | 0 | 3 | 5 | 20 | 45.0 | 23.2 | 66.8 |
| 288 | 142 | 15 | 8 | 7 | 0 | 3 | 5 | 18 | 44.4 | 21.5 | 67.4 |
| 289 | 303 | 19 | 8 | 10 | 0 | 0 | 1 | 18 | 44.4 | 21.5 | 67.4 |
| 290 | 65 | 21 | 7 | 9 | 0 | 0 | 1 | 16 | 43.8 | 19.4 | 68.1 |
| 291 | 128 | 19 | 7 | 8 | 1 | 0 | 3 | 16 | 43.8 | 19.4 | 68.1 |
| 292 | 264 | 21 | 7 | 9 | 0 | 0 | 1 | 16 | 43.8 | 19.4 | 68.1 |
| 293 | 144 | 12 | 9 | 8 | 0 | 4 | 5 | 21 | 42.9 | 21.7 | 64.0 |
| 294 | 219 | 23 | 6 | 8 | 0 | 0 | 1 | 14 | 42.9 | 16.9 | 68.8 |
| 295 | 58 | 25 | 5 | 4 | 3 | 0 | 1 | 12 | 41.7 | 13.8 | 69.6 |
| 296 | 3 | 14 | 9 | 13 | 1 | 0 | 1 | 23 | 39.1 | 19.2 | 59.1 |

| Overall adherence in individual patients ranked from patient with highest adherence to lowest- continued | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **#** | **Patient Key** | **N/A** | **Yes** | **NO** | **NOJ** | **IDs** | **IDq** | **applicability** | **Adherence (%)** | **95% CI min** | **95% CI max** |
| 297 | 255 | 14 | 7 | 9 | 0 | 2 | 6 | 18 | 38.9 | 16.4 | 61.4 |
| 298 | 302 | 16 | 8 | 11 | 0 | 2 | 1 | 21 | 38.1 | 17.3 | 58.9 |
| 299 | 50 | 15 | 7 | 9 | 0 | 3 | 4 | 19 | 36.8 | 15.2 | 58.5 |
| 300 | 220 | 18 | 6 | 10 | 0 | 1 | 3 | 17 | 35.3 | 12.6 | 58.0 |
| 301 | 136 | 17 | 7 | 13 | 0 | 0 | 1 | 20 | 35.0 | 14.1 | 55.9 |
| 302 | 229 | 13 | 7 | 14 | 1 | 0 | 3 | 22 | 31.8 | 12.4 | 51.3 |
| 303 | 150 | 25 | 3 | 10 | 0 | 0 | 0 | 13 | 23.1 | 0.2 | 46.0 |
| 304 | 263 | 21 | 3 | 8 | 0 | 3 | 3 | 14 | 21.4 | 0.0 | 42.9 |
| 305 | 279 | 17 | 4 | 16 | 0 | 0 | 1 | 20 | 20.0 | 2.5 | 37.5 |
| **Total** | | **4587** | **4534** | **1931** | **118** | **74** | **346** | **6657** | **68.1** | **67.0** | **69.2** |

# Appendix 9

# Findings from MAT application in the UK

Level of adherence to individual audit tool criteria in 328 patients from all study practices in the UK (n= 14104 criteria)

| Criterion | | NOJ (%) | NO (%) | YES (%) | N/A (%) | IDQ (%) | IDS (%) | Applicable (%) | % Adherence (95%CI) | % Adjusted Adherence |
|---|---|---|---|---|---|---|---|---|---|---|
| **1** | Invited to structured diabetes education programme. | 3 (0.9) | 243 (74.1) | 82 (25) | 0 | 0 | 0 | 328 (100) | 25.0 (20.3-29.7) | 25.9 |
| **2** | Recorded target $HbA_{1c}$. | 0 | 328 (100) | 0 | 0 | 0 | 0 | 328 (100) | 0.0 | 0.0 |
| **3** | A record of at least two $HbA_{1c}$ measurements in the previous 15 months. | 4 (1.2) | 91 (27.8) | 233 (71) | 0 | 0 | 0 | 328 (100) | 71.0 (66.1-75.9) | 72.3 |
| **4** | An $HbA_{1c}$ recorded at <7 % as their most recent value | 16 (4.9) | 169 (51.5) | 140 (42.7) | 0 | 0 | 3 (0.9) | 328 (100) | 42.7 (37.3-48.0) | 47.6 |
| **5** | On metformin or sulphonylurea. | 0 | 9 (3.6) | 239 (96.4) | 80 (24.4) | 0 | 0 | 248 (75.6) | 96.4 (94.0-98.7) | 96.4 |
| **6** | Patients with a stable $HbA_{1c} \geq 7\%$ are on more than one agent. | 1 (0.9) | 42 (35.9) | 74 (63.2) | 170 (51.8) | 41 (12.5) | 0 | 117 (35.7) | 63.2 (54.5-72.0) | 64.1 |
| **7** | Not on more than two agents added to metformin | 0 | 2 (1.9) | 106 (98.1) | 220 (67.1) | 0 | 0 | 108 (32.9) | 98.1 (59.6-100.7) | 98.1 |
| **8** | Patients on a gliptin, pioglitazone or a glinide are co-prescribed metformin or a sulphonylurea. | 0 | 2 (4) | 49 (96) | 277 (84.5) | 0 | 0 | 51 (15.5) | 96.1 (90.8-101.4) | 96.1 |
| **9** | Patients with a stable $HbA_{1c} \geq 7.5\%$ despite the dual therapy should be on a third oral agent | 0 | 21 (58.3) | 15 (41.7) | 282 (86) | 10 (3) | 0 | 36 (11) | 41.7 (25.6-57.8) | 41.7 |
| **10** | Patient with BMI >25 $kg/m^2$ is on metformin. | 24 (8.7) | 58 (21.1) | 193 (70.2) | 51 (16) | 2 (0.6) | 0 | 275 (83.4) | 70.2 (64.8-75.6) | 78.9 |
| **11** | Patients on metformin therapy have an estimated GFR is >45 ml/min/1.73 $m^2$ | 1 (0.5) | 6 (2.8) | 208 (95.4) | 110 (33.5) | 0 | 3 (1.3) | 218 (66.5) | 95.4 (92.6-98.2) | 95.9 |
| **12** | Patients on metformin with GFR ≤45 ml/min/1.73 $m^2$ have had their RFTs measured within the past 12 months | 0 | 0 | 7 (100) | 318 (96.9) | 3 (0.9) | 0 | 7 (2.2) | 100.0 | 100.0 |

| Criterion | | NOJ (%) | NO (%) | YES (%) | N/A (%) | IDQ (%) | IDS (%) | Applicable (%) | % Adherence (95%CI) | % Adjusted Adherence |
|---|---|---|---|---|---|---|---|---|---|---|
| **13** | On metformin and do not have a current estimated GFR <30 ml/min/1.73 $m^2$ | 0 | 2 (0.9) | 212 (97.7) | 111 (33.8) | 0 | 3 (1.4) | 217 (66.2) | 97.7 (95.7-99.7) | 97.7 |
| **14** | Patient on a second or third line agent is co-prescribed metformin and/or a sulphonylurea. | 0 | 9 (11) | 73 (89) | 246 (75) | 0 | 0 | 82 (25) | 89.0 (82.3-95.8) | 89.0 |
| **15** | Patient on insulin has previously received oral glucose lowering therapy. | 0 | 2 (6.3) | 30 (93.7) | 295 (90) | 1 (0.3) | 0 | 32 (9.7) | 93.8 (85.4-102.1) | 93.8 |
| **16** | Patient with a stable $HbA_{1c}$ ≥7.5% should be on a second/third line agent. | 3 (4.1) | 25 (34.2) | 45 (61.6) | 231 (70.5) | 24 (7.3) | 0 | 73 (22.3) | 61.6 (50.5-72.8) | 65.8 |
| **17** | Patient on exenatide or liraglutide has a BMI>30 $kg/m^2$. | 0 | 0 | 7 (100) | 321 (97.9) | 0 | 0 | 7 (2.1) | 100.0 | 100.0 |
| **17a** | Patient on exenatide or liraglutide for > 6 months has evidence that it has reduced $HbA_{1c}$ by ≥ 0.5% | 0 | 1 (25) | 3 (75) | 324 (98.8) | 0 | 0 | 4 (1.2) | 75.0 (32.6-117.4) | 75.0 |
| **17b** | Patient on exenatide or liraglutide for > 6 months has evidence that it has reduced body weight by ≥3% | 0 | 1 (25) | 3 (75) | 324 (98.8) | 0 | 0 | 4 (1.2) | 75.0 (32.6-117.4) | 75.0 |
| **17c** | Patient on a liraglutide is prescribed a dose of 1.2 mg daily | 0 | 0 | 2 (100) | 326 (99.4) | 0 | 0 | 2 (0.6) | 100.0 | 100.0 |
| **17d** | Patient on a gliptin and receiving it for > 6 months has evidence that it has reduced $HbA_{1c}$ by ≥ 0.5% | 0 | 4 (19) | 11 (52.6) | 307 (93.6) | 0 | 6 (28.6) | 21 (6.4) | 52.4 (31.0-73.7) | 52.4 |
| **18** | Does not have heart failure. | 0 | 0 | 27 (100) | 301 (91.8) | 0 | 0 | 27 (8.2) | 100.0 | 100.0 |
| **19** | Does not have an osteoporosis. | 0 | 0 | 27 (100) | 301 (91.8) | 0 | 0 | 27 (8.2) | 100.0 | 100.0 |

| | Criterion | NOJ (%) | NO (%) | YES (%) | N/A (%) | IDQ (%) | IDS (%) | Applicable (%) | % Adherence (95%CI) | % Adjusted Adherence |
|---|---|---|---|---|---|---|---|---|---|---|
| **20** | Patient on a thiazolidinedione and receiving it for >6 months has evidence that it has reduced $HbA_{1c}$ by ≥ 0.5%. | 0 | 3 (11) | 12 (44.5) | 301 (91.8) | 0 | 12 (44.5) | 27 (8.2) | 44.5 (25.7-63.2) | 44.4 |
| **21** | Patient previously on first line agent(s) and now on insulin, continues to be prescribed the previous oral therapy | 0 | 10 (33.3) | 20 (66.7) | 298 (90.8) | 0 | 0 | 30 (9.2) | 66.7 (49.8-83.5) | 66.7 |
| **22** | Patient with microalbuminuria or proteinuria is prescribed an ACE inhibitor or an ARB. | 0 | 20 (18.2) | 90 (81.8) | 218 (66.5) | 0 | 0 | 110 (33.5) | 81.8 (74.6-89.0) | 81.8 |
| **23** | Had renal function (serum creatinine/ eGFR) or microalbuminuria checked within past 15 months | 2 | 0 | 320 (97.6) | 0 | 0 | 6 (1.8) | 328 (100) | 97.6 (95.9-99.2) | 98.2 |
| **24** | Had retinal examination within the past 15 months. | 23 (7) | 36 (11) | 269 (82) | 0 | 0 | 0 | 328 (100) | 82.0 (77.9-86.2) | 89.0 |
| **25** | Had neuropathy/ foot check in the past 15 months. | 12 (3.7) | 40 (12.2) | 276 (84.1) | 0 | 0 | 0 | 328 (100) | 84.1 (80.2-88.1) | 87.8 |
| **26** | Patient with diabetic neuropathy is prescribed a tricyclic antidepressant, gabapentin, pregabalin or duloxetine. | 0 | 2 (18.2) | 9 (81.8) | 317 (96.6) | 0 | 0 | 11 (3.4) | 81.8 (59.0-104.6) | 81.8 |
| **27** | Had their blood pressure measured within the past 15 months | 1 (0.3) | 0 | 319 (97.3) | 0 | 0 | 8 (2.4) | 328 (100) | 97.3 (95.5-99.0) | 97.6 |
| **28** | Patient with hypertension is prescribed an ACE Inhibitor or angiotensin II-receptor antagonist (ARB). | 0 | 42 (19.4) | 174 (80.6) | 112 (34.1) | 0 | 0 | 216 (65.9) | 80.6 (75.3-85.8) | 80.6 |
| **29** | Patient prescribed antihypertensive drug therapy has achieved BP < 140/80 mmHg. | 0 | 62 (29.1) | 150 (70.4) | 115 (35.1) | 0 | 1 (0.5) | 213 (64.9) | 70.4 (64.3-76.6) | 70.4 |
| **30** | Patient with treated hypertension and with co-existing kidney, eye or cerebrovascular damage has achieved a blood pressure level < 130/80 mmHg. | 0 | 17 (74) | 6 (26) | 305 (93) | 0 | 0 | 23 (7) | 26.1 (8.1-44.0) | 26.1 |

| Criterion | | NOJ (%) | NO (%) | YES (%) | N/A (%) | IDQ (%) | IDS (%) | Applicable (%) | % Adherence (95%CI) | % Adjusted Adherence |
|---|---|---|---|---|---|---|---|---|---|---|
| **31** | Patient prescribed antihypertensive drug therapy is not prescribed a combination of thiazide diuretic and beta-blocker | 0 | 27 (12.8) | 184 (87.2) | 117 (35.7) | 0 | 0 | 211 (64.3) | 87.2 (82.7-91.7) | 87.2 |
| **32** | Patient with hypertension has a treatment plan that excludes corticosteroids, NSAIDs, carbenoxolone, monoamine-oxidase inhibitor, oral contraceptives | 16 (7.5) | 2 (0.9) | 196 (91.6) | 114 (34.8) | 0 | 0 | 214 (65.2) | 91.6 (87.9-95.3) | 99.1 |
| **33** | Patient with diabetes aged >40 is prescribed a statin | 26 (8.4) | 21 (6.8) | 262 (84.8) | 19 (5.8) | 0 | 0 | 309 (94.2) | 84.8 (80.8-88.8) | 93.2 |
| **34** | Patient on the same dose of a statin for >6 weeks has achieved a re-test total cholesterol level of < 5 mmol/l | 0 | 27 (10.2) | 108 (40.6) | 62 (19) | 0 | 131 (49.2) | 266 (81) | 40.6 (34.7-46.5) | 40.6 |
| **35** | Patient prescribed a simvastatin or atorvastatin not co-prescribed macrolide antibiotics or ketoconazole or itraconazole | 0 | 0 | 265 (99.6) | 62 (19) | 0 | 1 (0.4) | 266 (81) | 99.6 (98.9-100.4) | 99.6 |
| **35a** | Patient prescribed >20mg simvastatin not co-prescribed verapamil | 0 | 1 (0.4) | 264 (99.6) | 63 (19.2) | 0 | 0 | 265 (80.8) | 99.6 (98.9-100.4) | 99.6 |
| **36** | Patient with a triglyceride level > 4.5mmol/L (whether on a statin or not) is prescribed a fibrate | 0 | 13 (92.9) | 1 (7.1) | 139 (42.3) | 175 (53.4) | 0 | 14 (4.3) | 7.1 (-6.3-20.6) | 7.1 |
| **37** | Patient with triglyceride level of 2.3-4.5 mmol/L despite statin therapy is prescribed a fibrate | 0 | 28 (100) | 0 | 142 (43.2) | 158 (48.2) | 0 | 28 (8.6) | 0.0 | 0.0 |
| **38** | Patient who continues to smoke has been offered smoking cessation advice (e.g. structured behavioural support and NRT or bupropion | 0 | 6 (9.4) | 58 (90.6) | 264 (80.5) | 0 | 0 | 64 (19.5) | 90.6 (83.5-97.8) | 90.6 |
| **Total** | | **132 (2)** | **1373 (21.3)** | **4769 (74)** | **7242 (51.3)** | **414 (3.0)** | **174 (2.7)** | **6448 (45.7)** | **74.0 (72.9-75.0)** | **76.0** |

## Appendix 10

## Pharmaceutical care plan from Ejim E

# Pharmaceutical Care of Patients with Long Term Conditions: Structured Assessment

**Name**

**Number**
**CHI (DoB)**

**Address**

**On disease self management plan ❑**

**Smoker ❑**
**Past Smoker ❑**

**Pack Years:**
**Under cessation ❑**

**Specialist Advice ❑ Diet ❑Exercise ❑ Smoking**

**Male ❑ Female ❑**

**Body Weight:** kg

**Height:** M

**BMI** Kg/m²

**Blood Pressure** mm Hg

| Dates (Sys/ Dia) | | | | |
|---|---|---|---|---|
| | | | | |

**PEFR** Litres/hr

| Dates / Value | | | | |
|---|---|---|---|---|
| | | | | |

**GFR** ml/min ❑ >50 ❑ 30-50 ❑ <30

**Cholesterol** ~~mmol/L~~

| Dates / Value | | | | DEXA scan | |
|---|---|---|---|---|---|
| | | | | | |

**Known Allergies**

**High risk Medication user**
**❑ Corticosteroids ❑ High dose inhaled steroids**
**❑ Warfarin ❑Digoxin ❑ MTX Others:**

**Social Circumstances**

**❑ Lives alone ❑ Housebound ❑ Professional carer ❑Family carer**

| | Relevant Medical History | Relevant Past Medication | Date |
|---|---|---|---|
| 1 | | | |
| 2 | | | |
| 3 | | | |
| 4 | | | |
| 5 | | | |
| | | | |
| 6 | | | |
| 7 | | | |
| 8 | | | |
| 9 | | | |
| 10 | | | |

**Current Medication**

| | | | |
|---|---|---|---|
| 1 | | 7 | |
| 2 | | 8 | |
| 3 | | 9 | |

**Disease Specific Monitoring Data**

**Past MI Date(s)**
**CVD Risk: %/10yr**

**Lipid profile**

**TC ≥4 mmol/L ❑**
**HDL <1 mmol/L ❑**
**LDL ≥ 2mmol/L ❑**

**Diabetes Profile**
**Diabetes Risk: %/10yr**

**$HbA_{1c}$ mmol/L: date**
**[Target <7mmol/L]**

**Diabetes Complications**
**Neuropathic pain ❑**
**Microalbuminuria ❑**
**Last check dates: Eye : Foot**

**Pulmonary Function**
**COPD Prognosis index:**
**Predicted 3yrs**
**Mortality:**
**Hospitalisations:**
**Exacerbations:**

**MRC DYPSNOEA SCORE /yr**
**1❑ 2 ❑ 3 ❑ 4 ❑ 5❑**

**❑ Mild ❑ Moderate ❑ Severe**
**$FEV_1$ ≥80% 50-79% 30-49%**

| Stage | COPD / Asthma |
|---|---|
| 1❑ | SABA |
| 2❑ | + Anticholinergic / + Inhaled steroid / + LABA |
| 3❑ | |
| 4❑ | + Inhaled steroid / minus LABA + Add on |
| 5❑ | + Add on / + Oral steroid |

**Exacerbations: in past yr**
**[LABA indicated if >1]**

**Vaccination**
**❑ Pneumonia ❑ Influenza**

**Standard Checks**

| | | √ | Care issue |
|---|---|---|---|
| CHD Prevention | **Smoker** offered entry to cessation programme | | ❑ |
| | **10yr CHD risk ≥20% , Age>40** on aspirin 75mg | | ❑ |
| | **As above plus Diabetes & FH** on Statin (MTD) | | ❑ |
| | **0n aspirin** achieved a BP ≤ 150/90mm/Hg | | ❑ |
| | **Aspirin C/I,** on Clopidogrel 75mg | | ❑ |
| | **Stroke or TIA history** on dipyridamole 200mg BD | | ❑ |
| | **TC≥4mmol/L** on Statin unless C/I | | ❑ |
| | **Patients with CHD** Prescribed aspirin & statin | | ❑ |
| | | | ❑ |
| Hypertension | **Hypertensive patient** on treatment | | ❑ |
| | Not prescribed combination of thiazide & b/blocker | | ❑ |
| | **↑BP, ≤55yr, non-black** on ACE inhibitor | | ❑ |
| | **↑BP, >55yr, black** on thiazide diuretics/ Ca Blocker | | ❑ |
| | **Heart failure patient on** ACE inhibitor -target dose | | ❑ |
| | **Diabetes + Angina, Hypertension** on ACE inhibitor | | ❑ |
| | **Diabetes/CVD /Chronic Renal Failure** blood pressure optimised (≤130/≤80) | | ❑ |
| Diabetes | **AII antagonist** indicated ❑/use verified ❑ | | ❑ |
| | **BMI> 26(F)/27(M) kg/m²** on metformin | | ❑ |
| | **+ BP Controlled, CVD≥20%** on aspirin 75mg | | ❑ |
| | **+ CVD, TC<5, HDL<1** started on gemfibrozil | | ❑ |
| Lung Disease | **Suitability of multiple inhaler prescribing ; on >2 inhalers** has response confirmed | | ❑ |
| | **On inhaled steroid ❑** not > twice daily | | ❑ |
| | **Oral steroid/6mths** annual diabetes, BP & FRAX | | ❑ |
| | FRAX assessment (if >800 mcg/day) | | ❑ |
| | **COPD/asthma** candidate for LABA | | ❑ |
| | **Oral steroid/6mths** is also on inhaled high dose | | ❑ |

## Monitoring Notes

**Next 12 month review date:**

| | | | | | | |
|---|---|---|---|---|---|---|
| **4** | | **10** | | **Obesity Profile** | | |
| **5** | | **11** | | **Target Wt:** **kg** | | |
| **6** | | **12** | | **Fracture Risk** **%/10yr** **FRAX:** | | |

| **INDIVIDUALISED CARE ISSUES** | | | | | | |
|---|---|---|---|---|---|---|
| | **Date** | **Patient Education Documentation Additional Checks** | **Therapeutic Plan Changes** (Individualisations/ Dosage change/ Treatment interruption/ Management of co-morbidity) | **Date** | **Patient Education Documentation Additional Checks** | **Therapeutic Plan Changes** (Individualisations/ Dosage change/ Treatment interruption/ Management of co-morbidity) |
| *Specify* | **1** | | | **4** | | |
| *Action* | | | | | | |
| *Output (Initial)* | | | | | | |
| *Specify* | **2** | | | **5** | | |
| *Action* | | | | | | |
| *Output (Initial)* | | | | | | |
| *Specify* | **3** | | | **6** | | |
| *Action* | | | | | | |
| *Output (Initial)* | | | | | | |

## Appendix 11

## keywords used during literature review

| **keywords used during literature review** |
|---|
| Diabetes prevalence in the UK |
| Aetiology of diabetes |
| Type-2 diabetes |
| Pathophysiology of type-2 diabetes |
| Prevalence of type-2 diabetes in the UK |
| Type-2 diabetes risk factors |
| Type-2 diabetes and obesity |
| Microvascular complications of diabetes |
| Diabetic retinopathy |
| Diabetic nephropathy |
| Diabetic neuropathy |
| Macrovascular complications of diabetes |
| Type-2 diabetes and risk of cardiovascular disease |
| Management of type-2 diabetes |
| Non-pharmacological management of type-2 diabetes |
| Anti-hypoglycaemic agents |
| Antidiabetic agents |
| Metformin |
| Sulphonylureas |
| Thiozolidinediones |
| Meglitanides |
| Acarbose |
| insulin |
| Measuring quality of care |
| Quality improvement of care in clinical settings |
| Clinical audit |
| Medication assessment tool |
| Clinical guidelines |