

**Development and evaluation of a
theoretical model to predict Medicines
Adherence in people with Mild to
Moderate Intellectual Disability and
Diabetes: a mixed methods study**

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Keywords

Medicines, medications, intellectual disability, type 1 diabetes, type 2 diabetes, depression, side effects, self-efficacy, social support, multivariate analysis, associations, social cognitive theory.

Abstract

Background: Fifty percent of medications are not taken as prescribed. This is a major public health issue yet there is very limited evidence on the factors associated with medicines adherence in people with mild to moderate Intellectually Disabilities and diabetes (IDD). This study evaluated the frequency of, and factors associated with, medicines non-adherence in this group compared to people without ID but with diabetes (non-IDD).

Methods: A systematic review of the literature informed the theoretical model tested. A two-stage, sequential mixed methods study with 111 people with type 1 and 2 diabetes, (IDD = 33, non-IDD = 78) was then carried out. Stage one (quantitative) compared frequency of medication adherence in the group overall, IDD and non-IDD. Univariate and multiple regression analysis evaluated associations between factors (ID, depression, side effects, self-efficacy and perceived level of social support) and medicines non-adherence. Stage two (qualitative) explored findings of stage one with 12 stage one participants' carers using semi-structured interviews.

Results: Data were collected between July 2014 and May 2016. The frequency of medicines adherence was similar in the IDD and non-IDD population (70% vs 62%, $p = 0.41$). The theoretical model did not predict medicines non-adherence. After controlling for support with medicines and complexity of regime (number of medications and use of insulin), depression was an independent predictor in the non-IDD and group overall ($p < 0.001$). In the IDD group, perceived side effects was an important, but non-significant, predictor of non-adherence ($p = 0.06$). Carers' perceptions of adherence and depression were consistent with stage one findings.

Conclusions: Optimising adherence to diabetes medicines is equally challenging in IDD and non-IDD populations. Associations between independent factors and adherence differed between the two groups: in the non-IDD population, depressive symptoms were associated with non-adherence whereas in the IDD population perceived level of side effects appeared most dominant. Due to small sample sizes findings were inconclusive therefore, a sufficiently powered study further investigating the relationship between adherence and side effects in people with ID and diabetes is recommended.

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List of Abbreviations

ADA	American Diabetic Association
ARMS	Adherence to Refill and Medication Scale
BMI	Body Mass Index
CASP	Critical Appraisal Skills Programme
CRPD	Convention for Rights with People with Disability
CSO	Chief Scientists Office
DFBC	Diabetes Family Behaviour Checklist
DHQ	Diet Habits Questionnaire
DKT	Diabetes Knowledge Test
DPP-4i	DPP-4 inhibitor and antidiabetic drug used in Type 2 diabetes
DSM	Diabetes Symptom Measurement
EASD	European Association for the study of Diabetes
EMC	Electronic Monitoring Caps
EPHPP	The Effective Public Health Practice Project tool
FREAG	Faculty Research Ethics and Governance
GDS-LD	Glasgow Depression Scale - Learning Disabilities
GRAMMS6	Quality appraisal tools for mixed methods research
HbA1c	Serum test measuring average glycaemic control over 120 days
ICD-10	International Classification of Disease 10th Revision
ICD-11	International Classification of Disease 11th Revision
ID	People with an Intellectual Disability
IDD	People with an Intellectual Disability and diabetes
IQ	Intelligence Quotient
IRAS	Integrated Research Approval System
ISD	Information Services Division
MARS	Medication Adherence Report Scale
MEMS	Medicines Electronic Monitor System
MMAS8	Morisky Medicines Adherence Scale
mMOS-SS	modified Medical Outcomes Scale - Social Support
MMSE	Mini Mental Score Examination
MOS	Medical Outcomes Study - Social Support Scale
MPR	Medicines Possession Ratio
NHS	National Health Service
NICE	National Institute for Clinical Excellence
NIHR	National Institute for Healthcare Research

NMC	Nursing and Midwifery Council
non-IDD	People without an Intellectual Disability but with Diabetes
NVIVO	Software package used for qualitative data analysis
PASE	Physical Activity Scale for the Elderly
PCS	Perceived Competence Scale
PHQ	Patient Health Questionnaire
PICO	Population, Intervention, Comparison, Outcome
PILS	Participant Information Leaflets
PPI	Patient and Public Involvement
PSM	Perceived Sensitivity to Medicines
RAPPORT	Research with Patient and Public Involvement: A Realist evaluation
RCT	Randomised Control Trial
SDSCA	Summary of Diabetes Self Care
SE	Self-Efficacy
SGLT-2	Oral antidiabetic medicine used in type 2 diabetes
SIGN	Scottish Intercollegiate Guideline Network
SPSS	Software package for statistical analysis of data
TPB	Theory of Planned Behaviour
UK	United Kingdom
UKU-SES-ID	UKU Side Effects Scale for people with Intellectual Disability
WHO	World Health Organisation

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1 Chapter 1: Background and Introduction

1.1 Background

Medicines non-adherence has a significant impact on quality of life, mortality and morbidity. In 2003, the World Health Organisation (WHO) stated that improving medicines adherence may have a greater impact on chronic disease management than any other scientific advance (Sabate, 2003). Vulnerable populations may be at greatest risk of non-adherence, yet the frequency of and factors associated are not known in many populations. One such population is people with Intellectual Disabilities and diabetes (IDD).

This PhD project has an overall aim of developing, testing and evaluating a theoretical model to predict factors associated with medicines non-adherence in people with ID and diabetes. The study is in two parts:

1. Part one is a systematic review of the literature to develop an evidence based theoretical model designed to predict medicines non-adherence in the diabetic population.
2. Part two is in two stages:
 - a. Stage one will test the model developed in part 1 in a cohort of people with ID and diabetes (IDD population) and compare findings with a cohort of people without ID but with diabetes (non-IDD population).
 - b. Stage two will triangulate and corroborate results from stage one by conducting semi-structured interviews with carers of stage one participants. This will further explore and triangulate stage one findings.

This is the first study to develop and test a model of medicines non-adherence people with ID and diabetes. It will also be the first to prospectively compare findings with a

comparison group, namely people without ID but with diabetes. Given the impact that medicines non-adherence has on short and long term mortality and morbidity (Ryan et al, 2014) this study may generate debate in academic and practice communities and influence policy, practice and the direction of future adherence research in people with ID.

This introductory chapter will outline, provide definitions, current evidence and the context of the research. The final section will present my motivation for carrying out this research, the aims of this study, and outline the structure of this PhD thesis.

1.2 Medicines adherence: definitions

“Medicines adherence” is the extent to which patients’ actions match the prescribing recommendations from healthcare professionals (National Institute of Clinical Excellence (NICE), 2009). Previously, terminology used was “medicines concordance” or “compliance”, however “concordance” was a term not clearly understood and “compliance” was associated too closely with blame (Sabaté, 2003). Furthermore, neither “concordance” nor “compliance” reflected the partnership agreement between the service user and the healthcare professional. Therefore “medicines adherence” is the current terminology used to describe how effectively a service user takes their medications, and how aligned it is to recommendations from healthcare professionals.

Prescribing recommendations from healthcare professionals maximise therapeutic effect, alleviate clinical symptoms, minimise adverse drug events and ensure safe and timeous medicines consumption. Optimum medicines adherence is when medicines are taken correctly 80-95% of the time (Osterberg & Blaschke, 2005).

The frequency of adherence in the international and United Kingdom (UK) literature is substantially lower than this. A report published by WHO, which consolidated international

evidence on the rational use of medicines including medication adherence, estimated it at 50% in developed countries and lower in developing and transitional countries (Holloway & Van Dijk, 2011). This estimate has been corroborated in the UK by NICE who reported 30-50% of medications are not taken as prescribed (NICE, 2009).

Since publication of these documents, modest progress towards improving adherence in long term conditions has been made. A meta-analysis of over 376,000 patients from 20 research papers on people with cardiovascular disease reported adherence of 57% over a mean 24 month period (Naderi, Bestwick, & Wald, 2012). Similar rates have been reported in relation to other long term conditions including, hepatitis C, diabetes and asthma (Bårnes & Ulrik, 2015; Davies et al, 2013; Lieveld, van Vlerken, Siersema, & van Erpecum, 2013).

1.3 Factors affecting adherence

Medicines adherence is a complex behaviour which, outside of the hospital environment, is regulated by service users and/or carers. There are a number of factors which are reported to influence medication adherence (or non-adherence) which include practical, cognitive and socioeconomic factors (WHO, 2003). Practical factors influencing adherence include dexterity to open packs or bottles; cognitive factors include remembering or being able to follow instructions related to taking medicines; socioeconomic factors are cited as ability to pay for treatment regimes.

Psychological factors imply that a person's actions will be influenced by how they think, feel and behave (Bandura, 1986). In the context of medicines adherence, this suggests that beliefs and attitude about illness and proposed treatment will influence how well a patient will adhere to their medication regime.

The complexity of how, why and whether a patient adheres to a treatment regime explains slow improvements in adherence over the last 50 years (DiMatteo, 2004).

Furthermore, external factors such as an increasingly aging population managing more complex regimes (Zogg, Woods, Saucedo, Wiebe, & Simoni, 2012), polypharmacy resulting in more adverse drug events (Capoccia, Odegard, & Letassy, 2016) and more healthcare professionals with legislative authority to prescribe (Department of Health, 2013; Scottish Government, 2016) has increased the number of people taking medicines, the number of medicines being taken by one person and, the number of professionals prescribing medicines.

This complexity highlights the need for adherence interventions to be underpinned by robust evidence which: (1) identifies which factors are most importantly associated with medicines adherence and, (2) designs interventions that will minimise the effect of those factors on adherence. As medicines non-adherence has economic, health and social consequences the need for evidence is a priority.

1.4 Consequences of non-adherence

The aim of healthcare worldwide is to deliver high quality, cost-effective and safe healthcare. In Scotland, where this study took place, the government's vision for the National Health Service (NHS) is to become a leader in healthcare quality. Part of this vision is a 'realistic medicine' strategy which advocates interventions to reduce unnecessary cost, reduce unnecessary variation in practice and improve health inequalities (NHS Scotland, 2016). Medicines non-adherence is costly and reduces drug efficacy resulting in increased mortality and morbidity in those who are non-adherent (Nieuwlaat et al, 2014).

NHS Information Services Department (ISD) reported that the net cost of prescribing, that is, the gross cost minus patient charges, in Scotland in 2013/14 was £1,146 million (ISD, 2014). Applying this cost to adherence statistics from NICE, namely 30-50% medications are not taken as prescribed (NICE, 2009), the financial consequences of non-adherence may be as high as £573 million per year in unused or unwanted medication.

From the service users' perspective, suboptimal adherence may result in overdose, progression of disease, unnecessary hospital admission, antimicrobial resistance, treatment failure and death (Holloway and Van Dijk, 2011; Ryan et al, 2011; Wasserfallen, 2001).

Seven to ten percent of hospital admissions are related to adverse drug events (Aljadhey et al, 2013; Chan Nicklason and Vial, 2001), a proportion of which are related to medication adherence. Raschetti et al (1999) reported 4.3% (n = 243) of presentations to an Emergency department in Italy (n = 5497) were attributed to adverse drug events and, of those, 55% were a direct result of medicines non-adherence. More recently a Swiss study reported adverse drug events were related to non-adherence in 30% of presentations and clinical deterioration, hospital admission and significant cost implications was a consequence of this (Wasserfallen et al, 2001).

To reduce the financial and economic impact of adherence, researchers in the field of adherence literature have called for high quality research in groups most susceptible to medicines non-adherence (Nieuwlaat et al, 2014; Ryan et al, 2014; Viswanathan et al, 2012).

1.5 Groups at greatest risk of non-adherence

Groups who are particularly susceptible to non-adherence are those with long term medical conditions and minority populations. WHO identified that the groups most susceptible to medicines non-adherence are people with diabetes, asthma, depression, epilepsy and hypertension (Sabaté, 2003).

A meta-analysis carried out by Dimatteo (2004) of 569 studies between 1948 and 1998 concluded that diabetes medicines adherence was amongst the lowest at 66%. Subsequent research has revealed service users with diabetes are at greater risk of hospital admission due to non-adherence to prescribed regimes (Malhotra, Karan, Pandhi, & Jain, 2001; Wasserfallen et al, 2001). Moreover, a systematic review of 21 studies, six of which were conducted in the

UK, cited diabetes medicines non-adherence as the most common cause of hospital admission related to adverse drug events (Al Hamid, Ghaleb, Aljadhey, & Aslanpour, 2014).

The international adherence literature estimates diabetes medication adherence to be around 36-93% (Mann, Ponieman, Leventhal, & Halm, 2009; Sabaté, 2003). This wide variation in adherence frequency is likely due to variation in sample populations, study design and adherence measurements; therefore the exact figure remains unclear. Nonetheless this evidence indicates a shortfall in target adherence rates in people with diabetes (Osterberg & Blaschke, 2005, Bailey and Kodack, 2011).

1.6 Diabetes mellitus: cause, prevalence and treatment

Diabetes mellitus is a common long term condition in the UK and worldwide, and is a result of the pancreas not producing enough or any insulin, a hormone responsible for the regulation of blood sugar. It is characterised by elevated levels of blood glucose which, if poorly controlled, will result in cardiovascular and microvascular complications.

There are three major types of diabetes: type 1, type 2 and gestational diabetes. Type 1 diabetes is characterised by a deficiency in insulin production, occurs in childhood or as a young adult, with genetic and autoimmune factors being responsible. Type 2 results from the body's ineffective use of insulin (insulin resistance). Type 2 diabetes is most common and accounts for 90% of the diabetic population (Diabetes UK, 2017). Onset is most common during adulthood and attributed to lifestyle factors, particularly high energy diets and sedentary lifestyle. Gestational diabetes occurs during pregnancy.

Over the last 20 years there has been a dramatic rise in the incidence of type 2 diabetes. The global report on diabetes published by WHO (2016) states type 2 diabetes worldwide has risen from 4.7% in 1980 to 8.4% in 2014. In 2012 alone it was responsible for 1.5 million deaths worldwide and is predicted to be the seventh leading cause of death worldwide by 2030.

Its complications are stroke, heart disease, renal failure and blindness (WHO, 2016). In the UK, prevalence amongst the adult population is around 5% and is expected to rise to 9% by 2025 (Diabetes UK, 2012). This is due to longer life expectancy, high energy diets, low activity levels and increasing obesity. These statistics are concerning and, to prevent the continued rise in diabetes, regular physical exercise, adopting healthy eating habits and maintaining normal body weight is essential.

Once a person has received a diagnosis of diabetes, goals shift from prevention to disease management. The goals of treatment are to maintain effective glycaemic control thereby reducing risk of short and long term complications, such as hypoglycaemia or hyperglycaemia cardiovascular disease, renal impairment, visual impairment and amputation (Kuo et al, 2003).

Internationally, the gold standard measure of glycaemic control is serum Haemoglobin A1c (HbA1c). This provides an average estimate of glycaemic control in a 120-day period.

Good glycaemic control is dependent on adherence to prescribed diabetes self-care behaviours such as medication regimes, clinic appointments, foot care and changes in diet and exercise regimes optimising cardiovascular health and maintaining adequate weight control. NICE has issued guidance for type 1 and type 2 diabetes (NICE, 2015a, b), which recommends HbA1c to be maintained between 48 mmol/mol (6.5%) and 58 mmol/mol (7.5%).

In people with diabetes, studies have demonstrated significant correlations between glycaemic control and medicines non-adherence, that is to say as medication adherence decreases glycaemic control worsens (Lee et al, 2013; Wong et al, 2015). Furthermore, in low income service users in the US, it is a more significant predictor of poor control than any other area of diabetes self-care (Osborn, Mayberry, & Kim, 2016). Thus, diabetes medication adherence to plays a key role in good glycaemic control and long term health of people with diabetes.

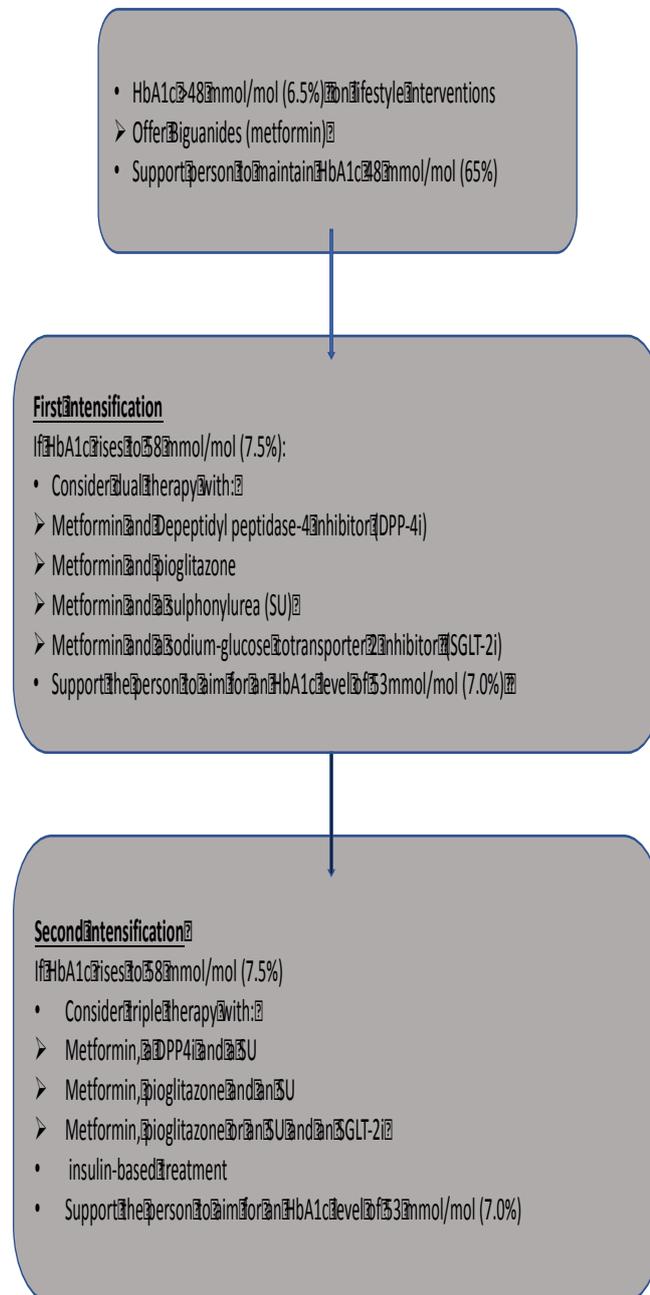
1.6.1 Pharmacological management: Type 1 and type 2 diabetes

In type 1 diabetes pharmacological management involves a combination of short, medium or long acting insulin via continuous or intermittent injection. Dose is dependent on frequent blood glucose monitoring and adjusting insulin dose to attain normoglycaemia. Side effects are related to localised pain, oedema or erythema at injection sites, or systemic side effects for example hypo or hyperglycaemia. Non-adherence to insulin is life threatening. Overdose can result in hypoglycaemia, and coma; underdose or omission causes ketoacidosis. Consequently, adherence in this population is particularly important.

Treatment of type 2 diabetes is dependent on residual islet cell function, and depending on choice of medication, will either stimulate insulin secretion in the pancreas or reverse insulin resistance by acting on muscle, fat and the liver to increase glucose utilization. Side effects range from gastric upset and diarrhoea, hypoglycaemia and changes in weight (BNF, 2017). People with Type 2 diabetes, whose glycaemic control cannot be maintained with diet and exercise alone will be commenced on one or two oral glucose lowering agents. If glycaemic control remains suboptimal insulin therapy will be considered (Figure 1.1) (NICE 2015b).

Selection of and intensity of treatment will be dependent on age, clinician and patient preferences, expected adherence to treatment, tolerability of side effects, body mass index and the presence of existing comorbidities, for example cardiovascular disease. Hence HbA1c targets defined by NICE are individualised according to these factors (NICE, 2015b).

Figure 1.1: NICE guidance: Pharmacological management of Type 2 diabetes (NICE 2015b)



1.7 Adherence in minority diabetic populations

Although much has been clarified about adherence rates and consequences of non-adherence in people with diabetes, understanding of medicines adherence is far from complete. Specific concerns about adherence in minority groups is highlighted in NICE (2009) guidance which recommends medicines adherence research in minority and vulnerable groups should not only establish the frequency of adherence but factors influencing, and barriers to, medicines adherence.

This concern may be attributed to evidence which suggests that glycaemic control and medication adherence is suboptimal. In a retrospective study in the US (n = 43,455) adherence to anti-diabetic, antihypertensive and lipid lowering therapy in Asian and Pacific Islanders was compared to the Caucasian population. It reported that Asian and Pacific Islanders had significantly lower medication adherence than the white population (Juarez, Tan, Davis, & Mau, 2014). A second US study suggested that medicines non-adherence may be a contributing factor to these poorer health outcomes. This study, prospectively observed minority Hispanic patients (n = 908) over a seven-year period and compared diabetic complications in those with good and suboptimal adherence. It found those with poor medication were more likely have renal impairment and higher mortality than those with good adherence (Kuo et al, 2003). This finding suggests diabetic medicines non-adherence a significant patient safety and public health issue in minority groups.

In the UK, a minority vulnerable group that has a high prevalence of diabetes and shorter life expectancy are people with ID, yet the frequency of medicines adherence and the factors associated with medicines non-adherence are unknown. The role of carers in supporting medicines adherence are also unknown.

1.8 Intellectual Disability: definition, prevalence and risk of diabetes

WHO defines ID as a significantly reduced ability to understand new or complex information or learn and apply new skills (WHO, 2013). The International Classification of Diseases (ICD-10) has categorised ID in 5 broad categories according to intelligence quotient (IQ); namely borderline, mild, moderate, severe and profound (WHO, 1996). More recently, ID is characterised as

‘..a group of developmental conditions characterized by significant impairment of cognitive functions, which are associated with limitations of learning, adaptive behaviour and skills.’ (Bertelli, Munir, Harris & Salvador-Carulla, 2016)

Therefore, ID covers a broad spectrum of developmental conditions which ranges from those living independently with no carer support to those requiring intensive support from highly skilled carers. It also incorporates those with limited practical and social skills. Currently there are an estimated 1.5 million people in the UK with an intellectual disability (Mencap, 2013) and, in Scotland, 26,000 adult have been assessed as having ID (Scottish Government, 2013). Due to the broad nature of the definition and differences in classification of ID in health and welfare systems compared to public health databases the exact number of people with ID remains uncertain.

What is known is that people with ID are living longer (Coppus, 2013), and, consequently, diagnosis and treatment of long term conditions and more complex treatment regimens are common (Haveman et al, 2011). Type 1 and type 2 diabetes are common long term conditions in people with ID. De Winter (2012a) suggests that diabetes prevalence in the ID population may be comparable to the non-ID population, however, there are claims that this may be due to underreporting or underdiagnosis (Tyler, Schramm, Karafa, Tang, & Jain, 2010) or poorer life expectancy (Haveman et al, 2011) and actual prevalence of people with ID and diabetes is higher.

Research carried out in the UK with people with ID, diabetes prevalence is reported in the range of 4%-19% (Diabetes UK, 2009; Haveman et al, 2011; Reichard & Stolzle, 2011; Tyler et al, 2010), which is higher than people without ID. A recently published systematic review of 29 studies worldwide noted prevalence rates in the people with ID between 0.4% and 25% (MacRae et al, 2015). Current local prevalence of diabetes and intellectual disability is estimated at 7%.

Genetic factors, chromosomal abnormalities (Schmidt et al, 2012; Taggart, Coates, & Truesdale-Kennedy, 2013), low levels of activity (Oppewal, Hilgenkamp, van Wijck, & Evenhuis, 2013), high energy diets and abdominal obesity (Rimmer, Yamaki, Lowry, Wang, & Vogel, 2010) put people with ID at high risk of diabetes. Despite these risk factors there is an absence of data on how people with ID manage their diabetes, yet there are a number of reasons why adherence may be suboptimal in this minority population.

Longer life expectancy combined with cognitive impairment, poor health literacy and known health inequalities suggest this group may be at high risk of non-adherence (Allerton, Welch, & Emerson, 2011; Becker, Thames, Woo, Castellon, & Hinkin, 2011; Emerson & Baines, 2011; Ettenhofer et al, 2009; Hawkins et al, 2012; Martinez-Aran et al, 2009). Moreover, glycaemic control is suboptimal in people with ID. A UK study conducted by Taggart et al (2013) with 186 ID service users found that over 50% had suboptimal glycaemic control. This was attributed to poor diet, inactivity, abdominal obesity or lack of social support however the influence of medicines adherence on glycaemic control in this population was not considered. Given the association between glycaemic control and medicines adherence in people without ID (Lee et al, 2013; Wong et al, 2015), it is prudent to establish whether a similar association exists in people with ID.

1.9 Why this study is necessary

Developing and testing an evidence based predictive model of medicines non-adherence in people with ID is important for two reasons. Firstly, if medicine adherence is suboptimal it may provide an alternative explanation for suboptimal glycaemic control. Subsequent research could focus on optimising adherence through targetted interventions thus improving glycaemic control and the long term health of people with ID and diabetes. Secondly, developing and testing a predictive model of medicines non-adherence may identify characteristics of those at greatest risk of medicines non-adherence and allow interventions to be proitised to those most vulnerable.

By corroborating results obtained in stage one with carers' views acknowledges their contribution to the evidence base. An international expert forum on adherence purported that interdisciplinary solutions and patient involvement are crucial for the development of interventions (Holloway & Van Dijk, 2011). Carers are part of the interprofessional group responsible for supporting medicines management in people with ID and diabetes, and therefore, it is crucial that carers contribute to this research by offering their perspective of diabetic medicines adherence and associated factors.

1.10 Motivation for conducting this research

I qualified as a nurse in 1992, and worked in critical care and coronary care in Scotland and the United States of America. During this time I gained experience in caring for incapacitated and vulnerable populations and, in 1997, undertook an MPhil in Law and Ethics in Medicine at the University of Glasgow. This allowed me to explore the legal and ethical context of caring for vulnerable groups. On completion, I took a senior practitioner post in acute medicine and, in 2006, combined this with an academic post leading a non-medical prescribing programme. During this time I qualified as a non-medical prescriber and gained clinical experience as an advanced practitioner in acute medicine where I treated a wide range

of vulnerable groups, including people with ID. My decision to move into academic work full-time in 2013 coincided with commencing part-time PhD studies and my desire to explore an aspect of prescribing in vulnerable groups was further developed.

As a non-medical prescriber, and programme leader of advanced practice and non-medical prescribing, I read widely in pharmacology, the psychology of adherence and challenges associated with prescribing in vulnerable populations. Following discussion with senior academics in my department, it became apparent that there was limited literature on medicines adherence in vulnerable groups, and, at the time of commencing my PhD, none focussing specifically on people with ID.

The shift from institutional to community care, increased life expectancy, multiple comorbidities and polypharmacy (Cooper et al, 2015; O'Dwyer, Peklar, McCallion, McCarron, & Henman, 2016) led me to believe that this group may be particularly susceptible to medicines non-adherence and became the focus of this research study. This coupled with the desire to carry out an impactful, medicines focussed, original research project led me to the topic area that is the focus of this thesis.

Developing an evidence base on the frequency of and factors associated with adherence in people with ID will inform the future direction of research, practice and policy in this area. A freedom of information request stated that in 2016, 35,000 nurses and midwives were registered as prescribers (Nursing and Midwifery Council, NMC, 2016). This highlighted that skills in prescribing and medicines management are pivotal to the role of NMC registrants. Medicines adherence is integral to prescribing and medicines management and, if optimised, will minimise harm and improve quality of life of those receiving treatment, which is of particular importance for those with complex health and social care needs.

1.11 Research question and aims of this study

This PhD study will seek to fill the current knowledge gaps with regard to medicines adherence in people with ID and diabetes (IDD). The paucity of evidence on medicines adherence in minority populations and poorer health outcomes, particularly in diabetes, has made this the focus of this PhD thesis. The overall aims of this study are:

1. to carry out a systematic review of the literature to establish factors most frequently associated with adherence in people with diabetes,
2. to propose an evidence based theoretical model of medication adherence based on key findings from the systematic review,
3. to test the proposed theoretical model in a cohort of IDD and compare findings to a cohort of non-IDD.
4. Based on findings accept or reject the proposed theoretical model and, if rejected, propose predictors of medicines non-adherence in IDD and non-IDD thus informing future policy, clinical practice and research in this area.

Thus, this PhD thesis will address the following research questions:

1. What is the frequency of dependent factors (glycaemic control and medication adherence) and independent factors (depression, side effects, self-efficacy and level of social support) in the IDD compared to the non-IDD population?
2. Whilst controlling for regime complexity and support with medicines, does the proposed theoretical model predict medication adherence in the group overall, IDD and non-IDD population?
3. Is the frequency of, and factors associated with, adherence consistent with the views of carers supporting diabetes medicines management?

1.12 Methodological approach

The aims and research questions of this study were addressed by using a mixed methods design. Development of a theoretical model necessitated a systematic review of the literature. This revealed two findings, first, an absence of literature in medication adherence in people with IDD and second, in the general diabetic population, a theoretical model of factors associated with medicines non-adherence aligned to Banduras social cognitive theory. This purports that the interaction between cognitive capacity, biological, affective, social and behavioural abilities will determine how a person thinks, feels and acts.

The next phase was prospective, quantitative and observational in design. In stage one; face to face interviews were conducted with IDD and non-IDD participants. Validated questionnaires were used to collect data in both groups. A multiple regression analysis generated some unique and novel findings, which were further explored and triangulated with carers in stage two, the qualitative stage of the study.

Stage two was important because data collection instruments had never been used in people with IDD and carers' accounts provided a perspective on stage one result. This was important because of reported assumptions that people with ID lack capacity to participate in research, provide unreliable results and, for these reasons, excluded from participation (McDonald & Patka, 2012, McDonald et al, 2009). This stage sought to rebut this and, instead, actively include this population, thus emphasising to the research community their ability and contribution to the research process.

1.13 Thesis outline

This thesis has eight chapters, the background, context and aims have been outlined in this chapter. Chapter two will present the systematic review, which comprehensively investigated and established the current evidence on medication adherence in people with diabetes. Bandura's model of social cognitive theory was aligned to the findings from the

systematic review and this formed the theoretical framework within which this study was designed. Findings from the systematic review revealed that: cognitive impairment, perceived side effects, depressive symptoms, level of social support and confidence predicted diabetic medicines non-adherence in people with diabetes, but there was no available evidence on the frequency of, and factors associated with medication adherence in the IDD population. Based on these findings it was proposed the PhD study investigated Banduras social cognitive theory model and its role in predicting medicines non-adherence in the IDD and non-IDD population.

Chapter three provides an overview of methodological approach. A sequential, two stage, mixed methods approach was used in this study. In this chapter justification for the priority, timing and sequencing of each stage is presented. This is followed by a detailed account of the procedure followed in the quantitative and qualitative stages on sampling, recruitment, data collection and analysis. This chapter concludes with ethical considerations during data collection and write up.

Chapter four and five presents stage one quantitative results obtained from IDD and non-IDD participants. A total of 111 participants were recruited (IDD n = 33, non-IDD n = 78) Results relating to the reliability of instruments used and descriptive data relating to demographic and health characteristics of the study population are presented. In addition, medication adherence, glycaemic control, demographic and health characteristics in the IDD and non-IDD groups are compared.

Chapter five presents the results of an evaluation of the performance of the model to predict medicines non-adherence in the group overall and in the IDD and non-IDD groups. To test the capability of the proposed model univariate and multiple regression analyses were performed and, whilst controlling for confounders (support with medicines and regime complexity) statistical associations between medication adherence and independent factors (depression, side effects, self-efficacy and perceived level of social support) were investigated.

Chapter six presents results from stage two the qualitative phase. Informed by preliminary results from stage one, a topic guide was developed and semi-structured interviews were conducted with carers of stage one participants. A thematic analysis of results was informed by Braun and Clarke's (2006) theoretical framework. Following alignment of stage one and stage two results, findings from each stage were compared, corroborated and, where possible, verified.

Chapter seven fully integrates and discusses key findings from stage one and two, considering them in the context of the wider literature. In the context of the aims of the study, the first part of this discussion evaluates the overall fit of Banduras model of social cognitive theory in predicting medication adherence in the group overall, the IDD or non-IDD groups and proposes a revised predictive model of medication adherence. The second part compares findings from this study to previous adherence research and provides possible explanations for the differences and similarities between the IDD and non-IDD population in terms of demographic, health characteristics, glycaemic control and medicines adherence. This chapter concludes with a commentary of strengths and weaknesses of the study and how these limitations may be addressed in future research.

Chapter eight provides recommendations for policy, practice and research based on the findings from this study. Social cognitive theory does not predict medication adherence and therefore this is not recommended as model of predicting adherence, rather, biological factors, depression and side effects are the most important predictors of adherence. Key recommendations are that, if reasonable adjustments are made, people with ID are reliable and willing research participants. Greater pharmacovigilance and monitoring for side effects of medication in people with IDD may improve adherence, however further research to corroborate findings from this study is recommended.

This PhD study has contributed to the evidence base by investigating the frequency of, and factors associated with, medicines adherence in people with IDD. The findings may inform the development of interventions to reduce long term mortality and morbidity in people with ID and diabetes.

2 Chapter 2: Systematic review of the literature

2.1 Introduction and aim of literature review

This chapter will present the findings of a systematic review. This chapter will:

1. Critically appraise the current research evidence on factors associated with medicines adherence in the diabetic population,
2. report on the quality of current evidence and,
3. propose an evidence based theoretical framework designed to predict medicines non-adherence in people with and without ID and diabetes.

A systematic review is a methodology that will rigorously search, appraise and synthesise current research evidence in order to address a specific research question (Aveyard, 2010). It collates a body of evidence in one area of practice and provides a judgement of the quality of the current evidence available. Narrative synthesis involves collating the results from each of the systematically selected papers appraising the quality of, and identifying key characteristics from, those studies.

This chapter is in four sections, the first of which will describe the methods used to search, appraise and synthesise the evidence. Secondly a quality appraisal and characteristics of the studies selected for review will be presented. Thirdly a discussion of the results will be set out and finally a theoretical framework for this PhD study will be proposed.

2.2 Methods

A systematic review follows a rigorous and replicable research methodology. Bettany (2016) proposes six steps to a systematic review :

1. defining the question and identifying aims,
2. devising search inclusion criteria,
3. identifying search strategy inclusive of data bases,
4. selecting appropriate articles and data extraction,
5. synthesising evidence using quality appraisal and key characteristics of the study, and
6. making recommendations.

Once the question and aims of the systematic review were defined, the next step was to develop clear inclusion and exclusion criteria for the search. Use of inclusion and exclusion criteria identifies the reasons for an article being rejected or included in the review. In this review following identification of the inclusion and exclusion criteria, a comprehensive and systematic search of literature using predefined key words took place. Titles, abstracts and full-text articles were reviewed and articles were selected on the basis that they met the predefined inclusion criteria.

Once the articles had been selected data were extracted and analysed. Data analysis has two main parts. The first is appraisal of the quality and the second is extraction of key themes from the selected papers. Quality appraisal is carried out using a validated or recommended instrument for either quantitative or qualitative research or in the case of mixed methods, both. Using narrative synthesis, key characteristics of studies are grouped together in either table or chart format allowing comparisons to be drawn between them. This thematic approach not only identifies similarities and differences in study design and results, but also gaps in the literature. Grouping and synthesising research in this way provides a collective analysis of

research which is stronger than just reporting on one published study. As a result, it can provide strong evidence for developing research studies and clinical practice.

2.2.1 Defining the question and identifying aims

Development of an answerable and focussed research question is essential. Developing a research question was challenging but, is a key element of study; hence, it was designed to be unambiguous, answerable and relevant to the area of research.

A common approach to developing a research question, adopted by the Cochrane Collaboration and recommended in the literature is the Population Intervention Comparison or Context and Outcome (PICO) (Bettany, 2016). Using this framework, the research question for the systematic review was developed and refined (Table 2.1).

Table 2.1: PICO framework used to develop research questions for systematic review

Population	Adult ID and non-ID diabetic population
Intervention	Diabetic medication (Oral hypoglycaemic or insulin)
Comparisons or context	Factors associated with adherence
Outcome	Adherence to prescribed diabetic medication.

This research question for the systematic review was:

What factors are associated with diabetic medication adherence in the adult IDD and non-IDD diabetic population?

Further detail was added to the question to clarify the question and sought to address:

1. factors associated with diabetes medicines adherence in the non-IDD population,
2. factors associated with diabetes medicines adherence in the adult IDD population, and,
3. gaps in the literature associated with diabetes medicines adherence in the IDD population that prevent comparisons from being drawn about the frequency of, and factors associated with, medicines adherence in the IDD and the non-IDD population.

2.2.2 Inclusion criteria

An inclusion criterion helps to identify what literature needs to be included to answer the research question and what does not. Criteria for this review are detailed below (Table 2.2). It articulates what the researcher is looking for in the research, focusses the literature search and, for the reader, identifies the scope and relevance of the review.

Table 2.2: Inclusion criteria for systematic review

Type of study	Primary quantitative research, quantitative or mixed methods
Study design	Observational
Language	English
Timeframe	January 2003-April 2014
Population	IDD and non-IDD adults aged 18 or over who were type 1 or type 2 diabetics,
Intervention	Receiving oral hypoglycaemic medication or insulin therapy,
Context	factors associated with adherence, and
Outcome	studies which used a validated measure of medicines adherence and a statistical estimate of the association between factors (for example, depression, self-efficacy etc.) and medication adherence

Primary, peer reviewed research is the best available evidence and was the first inclusion criteria. Observational studies were selected because the overall study objective was to establish the frequency of, and factors associated with, adherence rather than testing whether an intervention improved medication adherence.

To maintain the currency of the research reported and, taking into account the comprehensive systematic review on treatment adherence (DiMatteo, 2004), the search was limited to articles published from January 2003 to the date when ethical approval for the study was sought in April 2014. This provided the most up to date evidence which informed the design of theoretical model. Finally, to ensure that highest quality research was selected only those which used a validated instrument to measure medication adherence and demonstrated a statistical association between factors were included.

2.2.3 Identifying search strategy inclusive of databases

The literature search was carried out in June 2014 by the author. A comprehensive online search was carried out using four online English language databases: Medline, CINAHL, psych INFO and Psychological and Behavioural Sciences databases. A search strategy for each of the databases was employed using combinations of the keywords outlined in Table 2.3. Truncation was used to allow for variations in the word to be included in the search: for example, using “*medic**” instead of “*medication*”, allowed for the search to include “*medicines*”, “*medicine*” and “*medications*”, thus generating a broader search of the literature. Reference lists from retrieved articles relevant to the research aims were reviewed and advice was taken from the university librarian, clinical and academic experts in ID, diabetes and medicines adherence to ensure inclusion of unpublished, grey or government literature.

Table 2.3: Search terms entered Medline, CINAHL, Psych INFO and Psychological and Behavioural science databases

Domain	Keywords
Intellectually disabled	Learning disab* or mental retard* or intellectual disab*, developmental disab*
Adults	Adult* not adoles* or child*.
Factors associated	influence or factors influencing or motivation or barriers or beliefs or fears
Adherence	medicines adherence or concordance or compliance or noncomplian* or non-complian* or nonadheren* or non-adherence or patient complian* or complian* or comply or complies or complying or adher*
Diabetes	Diabetes Mellitus OR Diabetes Mellitus, Type 1 OR Diabetes Mellitus, Type 2
Medications	Medic* or drugs or oral hypoglycaemics or insulin

2.2.4 Selection of articles, data extraction and management

Selection of appropriate articles involved removing duplicates, followed by a review of titles and abstracts, excluding those which were irrelevant. The full text of remaining articles were imported into a reference management system and read in full to verify they met inclusion criteria.

Data from articles that fully met inclusion criteria were extracted and organised to identify: the quality of existing evidence, key characteristics of the studies, and factors associated with adherence.

A second reviewer, a member of the supervision team, independently reviewed and rated the quality of papers using the same EPHPP tool (see below) to verify findings and factors associated with adherence. The independent reviewer then cross checked and referenced jointly with the PhD candidate. Any disparities were discussed and resolved throughout the review and critiquing process. To ensure the process was transparent, a Prisma chart detailing reasons for rejecting or including articles was created (Figure 2.1).

2.2.5 Synthesis of evidence: quality appraisal of quantitative studies

Appraisal of quantitative studies was assessed using a quality assessment tool for published by the Effective Public Health Practice Project (EPHPP) (Effective Public Health Practice Project, 2004). Recent research compared this assessment tool to the Cochrane Collaboration Risk of Bias Tool and found that each had different constructs and analysed the evidence in differing ways (Armijo-Olivo, Stiles, Hagen, Biondo, & Cummings, 2012), but one was not superior to the other. EPHPP was chosen for its relative simplicity, its widespread use and its applicability to public health topics. Medicines adherence, health inequalities and diabetes are key public health topics, so was considered an appropriate quality assessment tool for this review.

The tool appraises studies in eight component ratings namely:

1. selection bias,
2. study design,
3. control of confounding factors,
4. blinding of outcome assessors and participants,
5. data collection methods,
6. withdrawal and dropout rates,
7. intervention integrity, and
8. analyses

Each of the eight criteria was rated as strong, moderate, weak or not applicable according to the assigned component ratings. A full outline of the methodology underpinning this quality appraisal of the quantitative studies in accordance with the 8 component ratings is set out in Sections 2.2.5.1 to 2.2.5.8.

2.2.5.1 *Selection bias*

The EPHPP appraisal instrument requires judgement on whether selection bias was strong, moderate or weak. The extent of selection bias will determine the external validity of a study and generalisability of the results. External validity of a study should be determined by an evaluation of participant demographics, subject pool, sampling population and sampling strategy (Cunningham, 2013). Participant demographics informs a judgement of whether the study population is representative. If gender, age range or other demographic data are higher or lower than the general population the results of the study may not be generalizable.

The subject pool and sampling population may also determine the external validity of a study, for example, studies that select from one sample population or one database may result in skewed demographics. Those which are sampled from several sources, for example,

outpatient departments, general practitioners and specialist databases provide a sample population more representative of the general population under investigation.

Probability, as opposed to non-probability sampling has greater external validity (Newell & Burnard, 2011). The former applies random or stratification techniques and is likely to be the most representative, unbiased sample of the population as different units in the selection have equal likelihood of being selected (Cunningham, 2013). For practical reasons, it is often not chosen. For example, in difficult to reach populations, homeless, medically underserved or minority groups there are a limited pool of potential participants and it is a case of recruiting as many as possible. In studies involving these groups, non-probability, convenience or snowball sampling may be the only practical, cost effective method of recruitment. This was taken into consideration when appraising the studies in this review and, if a minority or hard to reach population were the target population, alternatives to random or stratification were considered. Selection bias criteria also includes an estimate of what percentage of selected individuals agreed to participate. An evaluation of this was carried out for each of the studies included in the review and, if more than 60% of those selected agreed to participate the study met this criterion.

To reflect the rating developed by the EPHPP and recommendations made by Cunningham (2013) a strong rating was assigned to studies which satisfied three or more of the four criteria for selection bias namely, (1) the study reflected the demographic of the general diabetic population, (2) the study sampled from a variety of sources, (3) the study used probability sampling and (4) the study had an agreement rate of greater than 60%. A moderate rating was given to those which satisfied two of the above criteria and a weak rating to those which met one or fewer.

2.2.5.2 *Appraisal of study design*

According to the hierarchy of evidence (Vogt, 2011), and EPHPP, a cross-sectional design is the lowest level of evidence whereas a Randomised Controlled Trial (RCT) is the highest. RCTs are the gold standard in evidence-based medicine for eliminating bias, maintaining objectivity and proving whether the study intervention is effective or not. A systematic review has challenged this and purported that a well-designed observational studies can generate as robust and externally valid data as RCTs (Benson & Hartz, 2000) however this is not a widely held view. In cross-sectional observational studies measurements are observed at a single point in time, and, unlike interventional studies, causality cannot be proven, only associations between dependent and independent factors reported. To maintain consistency with EPHPP, cross-sectional studies were assigned a weak rating, RCTs strong and other methodologies moderate.

2.2.5.3 *Control of confounding factors*

Confounding factors are extraneous variables (for example, age, gender, number of medications, complexity of regime) which are accounted for during statistical analysis of data to detect an association, or correlation, between the dependent and independent variables. If, in a study, there is failure to account for prognostic confounding factors, validity may be affected. Extraneous variables may mediate the relationship between the intervention and outcome, and if not accounted for, may result in misinterpretation of associations between dependent and independent variables. Selection of confounding variables are based on existing evidence from the literature, pilot studies, or data from the study population.

There are 3 main ways to control for confounders: matching, stratification and modelling (Vogt, 2011). In matching 2 groups with similar characteristics can be compared to determine whether outcome measures are similar in the study and comparison group. . In stratification, study participants are divided into subgroups, for example, classifying age into decades or

classifying number of medications into more or less than four. The effect of this confounder is controlled for during data analysis. In a modelling approach, information on the dependent factor (e.g. adherence) and confounding factors are incorporated in a regression equation.

For this review, important prognostic confounders were those defined in the EPHPP tool (2004). Studies were assigned a weak rating if no prognostic confounders were controlled for, moderate if two or more prognostic factors were controlled for and strong if all were controlled for.

2.2.5.4 Blinding of outcome assessors and participants.

Blinding is a method of eliminating bias in RCTs and refers to concealment of group allocation for one or more individuals in a research study. Typically, RCTs have a study and control arm. Participants randomised to the control arm usual care and placebo and study arm may receive usual care plus study intervention. Blinding randomisation to study and control arms protects against bias influencing results. In this systematic review, as all studies selected were observational this criterion was not applicable and, therefore, excluded.

2.2.5.5 Data collection methods

A well-designed study will apply appropriate data collection strategies and, in quantitative research, use validated instruments to detect the effect of an intervention or, in observational studies, associations between dependent and independent factors. In this review, an evaluation of methods of data collection and instruments used to collect data allowed for studies to be assigned a weak, moderate or strong rating. This section will describe how conclusions were made about the quality of data collection methods used in selected diabetic medication adherence research.

Quantitative observational studies administer questionnaires face to face, via the internet, by post or by telephone. Remote data collection elicits a large amount of data and encourages standardised responses which are generalizable. Questionnaires may be complex or lengthy

and, if administered remotely, clarification of questions may not be possible. This may produce less reliable results and exclude those with low levels of literacy, cognitive impairment or low self-efficacy from participating, or, if they do participate, give unreliable results (Newell & Burnard, 2011).

With smaller sample sizes, face to face interviews permit the researcher to clarify any points during the interview. This method is favoured in research with vulnerable groups, those with lower health literacy, or language barriers who would otherwise be unable or unwilling to participate (Newell & Burnard, 2011). In qualitative studies, this approach permits deep exploration of the study subject matter and is the most common approach to data collection. Conversely, face to face interviews are time consuming and require impartiality and consistency by those collecting data. Bias when asking questions may influence participant responses, thus affecting validity of results. Therefore, judgement on the appropriateness of data collection methods was based on achieving representative participation from the target population and obtaining impartial, non-biased responses.

Using validated data collection instruments provides a structured and consistent approach. They have been tested for their psychometric properties, verified for internal and external validity and produce results that are easy to summarise, compare and generalise. Altering statements or selecting extracts from validated data collections instruments affects validity and generalisability of the reported results.

In the context of medicines adherence, validated instruments have their challenges. DiMatteo (2004) argues self-report medicines adherence (dependent) instruments should be corroborated with objective adherence markers, for example, blood tests, urine samples or clinical observations. Conversely, others argue this is unnecessary because of the good internal and external validity of self-report instruments (Morisky, Ang, Krousel-Wood, & Ward, 2008; Morisky, Green, & Levine, 1986).

Poor recall, or a desire to provide an acceptable response, may result in self-report instruments underestimating non-adherence. A recent systematic review suggested prescription refills may be more objective as the participant is not being directly observed, or questioned, on their adherence behaviour (Nieuwlaat et al, 2014). However, a limitation of this measurement is that it provides evidence that a repeat prescription has been collected rather than actual medicines consumption. Furthermore, self-report adherence instruments have similar validity to other measures of adherence (Gonzalez et al, 2013). This lack of consensus on the most reliable instrument to evaluate adherence resulted in a decision that, quality rating was based on whether dependent and independent factors used validated measurement instruments to collect the data rather than the specific approach.

Thus, this criterion was appraised in three ways (1) appropriateness of data collection strategies (2) use of validated instruments for independent measures and (3) use of validated instruments for dependent measures. A strong rating was assigned if all three criteria were met, moderate if two out of three criteria met or weak if one or none criterion was met.

2.2.5.6 Withdrawal and dropout rate

The EPHPP tool considers withdrawal and dropout rates as an important factor. Withdrawal and dropout are when research participants do not complete the study protocol. This may be due to personal circumstances, adverse events or health reasons, but the consent process informs the participant of their right to withdraw without giving reasons and without their ongoing treatment or future participation being affected. Research governance requires investigators to report withdrawal and dropout rates, as well as reasons for withdrawal. This is an essential component of assessing the quality of the study.

A high withdrawal and drop-out rate is significant in studies carrying out specific measures at multiple time points and there is a risk of incomplete data sets, absence of follow-up and participants excluded from analysis. This may affect the number of participants and the

credibility of study findings. Cross-sectional study design generally involves a single measurement at a single point in time, however some carry out test retest reliability thus collecting data at two or more time points. Therefore, in accordance with the EPHPP criteria, a not applicable rating to this criterion was used for studies of cross sectional design with a single time-point measurement. In those with a longitudinal study design a strong rating was assigned to studies which (1) recorded the number of, and reasons for, dropouts and, (2) if 60-100% completed the study. A moderate rating was assigned if less than 60% completed the study and a weak rating if there was no record of percentage completing the study.

2.2.5.7 *Intervention integrity*

Blinding of assessors and participants is not a feature of cross sectional research therefore, this criterion was not applicable.

2.2.5.8 *Data Analyses*

An appraisal of the use of statistical methods use was carried out. The assignment of a good, moderate or weak rating was based on whether statistical methods were outlined and the relevance of the test to study outcomes. If all criteria were met, a strong rating were assigned and, if only partially met, a moderate or weak rating.

2.2.6 Quality appraisal of qualitative stages in mixed methods studies

Researchers argue that criteria-based critical appraisal of qualitative literature stifles creativity and removes the subjective element that is central to this type of research (Dixon-Woods, Shaw, Agarwal, & Ja, 2004). Whilst it is acknowledged that this has some justification, to validating and benchmarking results against other evidence, the results must still be credible and trustworthy. Hannes (2011) argues critical appraisal of qualitative research should focus on the methodological soundness rather than their contribution to science, stating that those with methodological flaws may generate new insights into a phenomenon but the reliability of the results may be questionable. Consequently, qualitative and quantitative research methodologies require a consistent and objective approach to data collection and analysis thus withstanding logical and systematic scrutiny.

2.2.6.1 Appraisal of qualitative stages in mixed methods studies

Qualitative stages in this review were evaluated according to criteria detailed in Table 2.4. Core criteria described by Hannes (2011) was supplemented with the Critical Appraisal Skills Programme (CASP) (2017) for qualitative research. Hannes criteria was selected over others because of its alignment with quantitative research, but was not detailed enough for the researcher to provide an adequate appraisal of the research. For example, although it is implicit that an analysis of the process of ethical approval should take place in any appraisal of research, this is not explicit when evaluating studies using this criterion. Therefore, questions from CASP were mapped to core criteria (Table 2.4) and conclusions as to whether the qualitative phases of selected studies were high or low quality.

Table 2.4: Quality appraisal criteria applied to qualitative papers

Criteria (Hannes, 2011)	CASP questions
Credibility (whether the findings hold true) e.g. member checks, independent analysis	Have ethical issues been considered? Was data analysis rigorous? Is there a clear statement of findings?
Transferability of details of study participants, demographics	Clear statement of aims? Recruitment strategy appropriate? How valuable is the research?
Dependability of methods chosen, dependability, reflexivity, debriefing	Is qualitative methodology appropriate? Was research design appropriate to aims? Data collected in a way that addressed research issue?
Conformability of background information on researcher, effect of researcher at each stage of the process	Relationship between researcher and participant adequately considered?

2.2.7 Global rating of studies

A global rating of strong, moderate or weak was assigned to each paper according to the ratings assigned to each criterion. In accordance with the EPHPP tool papers were rated as weak if there were two or more weak ratings, moderate if one weak rating or strong if no weak ratings were assigned. The same criteria for global rating was applied the quantitative phase of mixed methods studies included in this review.

2.3 Data synthesis

Methods for data synthesis range from meta-analysis, numerical synthesis or narrative synthesis. A narrative approach was agreed by the researcher and supervisors as sufficiently rigorous and did not require the highly specialist skills of a team of researchers carrying out a meta-analysis. Furthermore, meta-analysis can only take place if similar approaches to data analysis in the primary research papers takes place and the heterogeneity of the papers included in this review meant it was unsuitable.

Narrative synthesis does not answer questions of effectiveness, instead was to establish associations between medicines non-adherence and independent factors. There is no gold standard guidance on the structure and format for narrative synthesis, however a four part format recommended by the Cochrane Public Health Group (Jackson, 2012) provided guidance for the review namely:

1. an evaluation of the quality takes place and a preliminary synthesis of the studies,
2. a description of the key characteristics and themes of the studies,
3. exploration of the relationships and findings from different studies with the intention of identifying a theoretical framework, and
4. explanation of the absence of data between studies to identify gaps in research knowledge.

This approach to narrative synthesis was adopted, and the next section will present findings from the systematic review of the literature. First search results will be set out, followed by a quality appraisal of the paper and, lastly a narrative synthesis of study characteristics designed to address the aims (section 2.2.1).

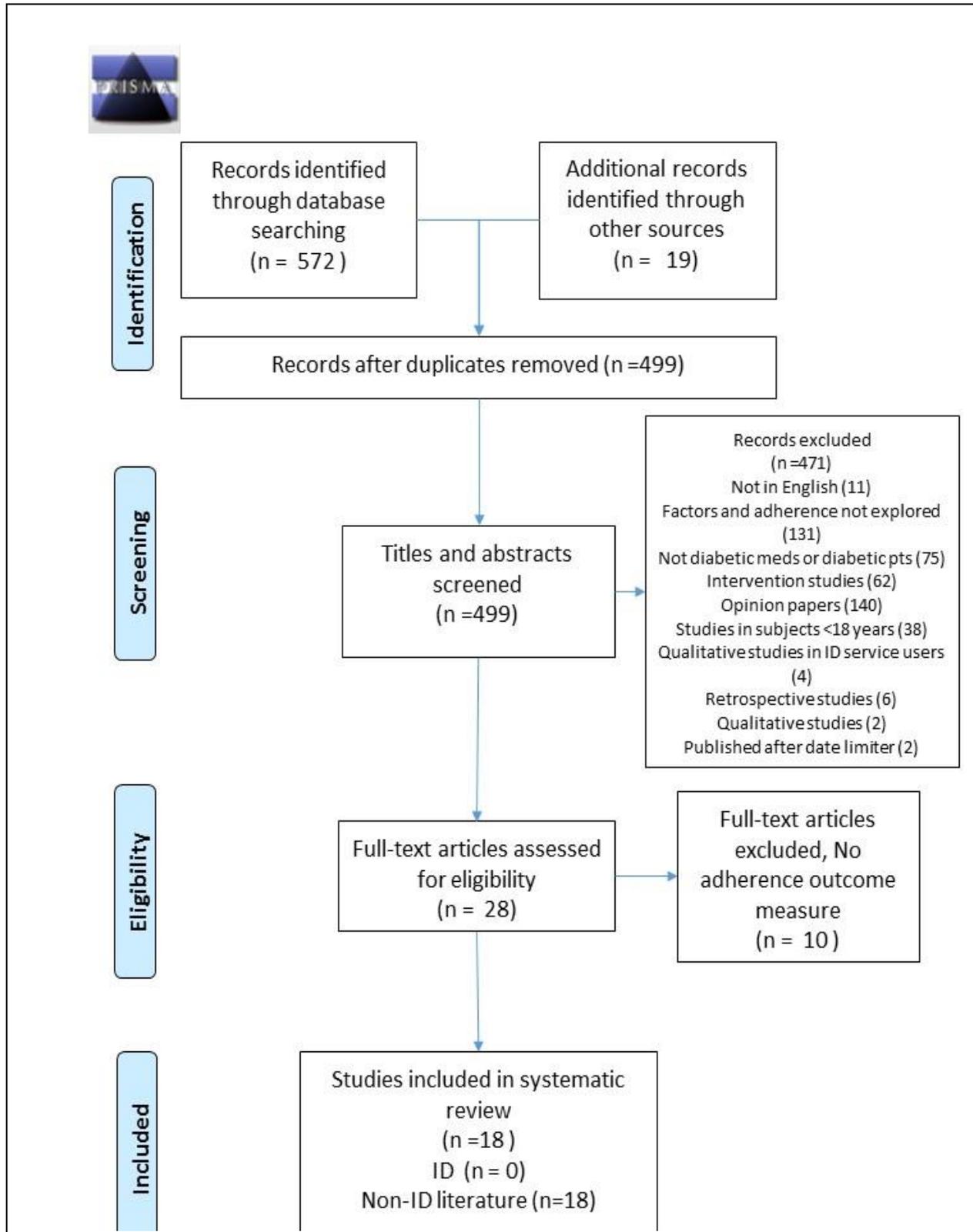
2.4 Findings

2.4.1 Search results

A total of 591 articles were retrieved. After removal of duplicates, 499 article titles and abstracts were screened and 471 were rejected because of not meeting the inclusion criteria (figure 2.1). The reasons for articles not meeting the inclusion criteria are outlined in Figure 2.1. Four studies were identified and explored treatment and diabetes management in the ID population (Cardol, Rijken, & Valk, 2012a, 2012b; Dysch, Chung & Fox, 2012; Hale, Trip, Whitehead, & Conder, 2011) but did not meet the inclusion criteria as they were qualitative studies. This resulted in 28 articles being selected for secondary evaluation.

Following review of the full text articles, 10 articles were rejected because there was no statistical estimate of the association between factors and adherence. This resulted in 18 articles meeting inclusion criteria. (Figure 2.1). Of those, two were mixed methods (Farmer, Kinmonth, & Sutton, 2006; Mayberry & Osborn, 2012) and 16 quantitative (Bailey, Barner, Weems, Leckbee, Solis, Montemayor & Pope, 2012; Broadbent, Donkin, & Stroh, 2011; Chao, Nau, Aikens, & Taylor, 2005; de Vries, Keers, Visser, De Zeeuw, Haaijer-Ruskamp, Voorham & Denig 2014; Gonzalez, Safren, Delahanty, Cagliero, Wexler, Meigs, & Grant, 2008; Grant, Devita, Singer, & Meigs, 2003; Kilbourne, Reynolds, Good, Sereika, Justice, & Fine 2005; Mann, Ponieman, Leventhal, & Halm, 2009; Nau, Aikens, & Pacholski, 2007; Nelson, McFarland, & Reiber, 2007; Odegard & Gray, 2008; Osborn & Egede, 2012; Pollack, Purayidathil, Bolge, & Williams, 2010; Schoenthaler, Schwartz, Wood, & Stewart, 2012; Sweileh, Zyoud, Abu Nab'a, Deleq, Enaia, Nassar. & Al-Jabi, 2014).

Figure 2.1: Search Results



2.5 Quality appraisal

Tables 2.5 and 2.6 outline the methodological quality of the reviewed papers. Seven studies were assigned an overall rating of moderate (Chao et al, 2005; Gonzalez et al, 2008; Kilbourne et al, 2005; Nelson et al, 2007; Osborn et al, 2012; Schoenthaler et al, 2012) and 11 assigned a weak rating (Bailey et al, 2012; Broadbent et al, 2011; de Vries et al, 2014; Farmer et al, 2006; Grant et al, 2003; Mayberry et al, 2012; Nau et al, 2007; Nelson et al, 2007; Odegard et al, 2008; Pollack et al, 2010; Sweileh et al, 2014).

The main limitations of the mixed methods and quantitative studies were their cross-sectional nature, the lack of control for confounders and the limited use of validated data collection instruments. Strengths were in data collection methods and analyses. An overview of the quality of the studies included in the review follows and the quantitative and mixed methods studies will be discussed in the context of the EPHPP tool and qualitative aspects of mixed methods studies will be addressed using criteria outlined previously in section 2.2.6. This approach is intended to provide a thorough quality appraisal of the studies included in this review.

Table 2.5: Quality appraisal of studies which reported medicines adherence in adults with diabetes using EPHPP quality assessment tool (n=18)

Study	Selection bias	Design	Confounders	Data collection methods	Dropout	Analysis	Overall rating
(Chao et al, 2005)	moderate	weak	moderate	moderate	N/A	strong	moderate
(Schoenthaler et al, 2012)	moderate	weak	moderate	strong	N/A	strong	moderate
(Osborn et al 2012)	moderate	weak	moderate	strong	N/A	strong	moderate
(Bailey et al, 2012)	weak	weak	weak	moderate	N/A	weak	weak
(Broadbent et al, 2011)	weak	weak	weak	weak	N/A	weak	weak
(Pollack et al, 2010)	moderate	weak	weak	strong	N/A	strong	weak
(Mann et al, 2009)	weak	weak	weak	moderate	N/A	strong	weak
(Gonzalez et al, 2008)	strong	weak	moderate	moderate	moderate	strong	moderate
(Kilbourne et al, 2005)	moderate	weak	moderate	strong	N/A	strong	moderate
(Odegard et al, 2008)	weak	weak	weak	moderate	N/A	strong	weak
Rosen et al, (2003)	weak	weak	moderate	strong	N/A	strong	weak
(Grant et al, 2003)	moderate	weak	weak	moderate	N/A	strong	weak
(Nau et al, 2007)	moderate	weak	moderate	weak	N/A	strong	weak
(Nelson et al, 2007)	moderate	weak	moderate	strong	N/A	strong	moderate
(de Vries et al, 2014)	moderate	weak	weak	strong	N/A	strong	weak
(Sweileh et al, 2014)	moderate	weak	weak	strong	N/A	strong	weak
(Mayberry et al, 2012)	moderate	weak	weak	strong	N/A	strong	weak
(Farmer et al, 2006)	strong	weak	weak	strong	N/A	strong	weak

Table 2.6: Quality appraisal of qualitative phases of mixed methods studies which reported medicines adherence in adults with diabetes (n = 2).

Study	Credibility	Transferability	Dependability	Conformability	Overall rating
(Mayberry & Osborn, 2012)	strong	moderate	moderate	moderate	strong
(Farmer et al, 2006)	strong	moderate	moderate	moderate	strong

2.5.1.1 *Selection bias*

All studies recruited according to inclusion and exclusion criteria and whether the sample was likely or somewhat likely to be representative of the target population.

All papers outlined demographic details of the study population. The mean age of participants were 50-67 years. All but two studies had similar male to female ratio of participants (Nelson et al, 2007).

Four studies sampled participants from more than one source (Farmer et al, 2006; Gonzalez et al, 2008; Nelson et al, 2007; Schoenthaler et al, 2012). Fourteen studies sampled from one source (Bailey et al, 2012; Broadbent et al, 2011; Chao et al, 2005; de Vries et al, 2014; Grant et al, 2003; Kilbourne et al, 2005; Mann et al, 2009; Mayberry & Osborn, 2012; Nau et al, 2007; Odegard et al, 2008; Osborn et al, 2012; Pollack et al, 2010; Sweileh et al, 2014), four papers used probability sampling (Chao et al, 2005; Farmer et al, 2006; Grant et al, 2003; Nau et al, 2007) and 14 used non-probability sampling (Bailey et al, 2012; Broadbent et al, 2011; de Vries et al, 2014; Gonzalez et al, 2008; Kilbourne et al, 2005; Mann et al, 2009; Mayberry et al, 2012; Nelson et al, 2007; Odegard et al, 2008; Osborn et al, 2012; Pollack et al, 2010; Rosen et al, 2003; Schoenthaler et al, 2012; Sweileh et al, 2014) .

Twelve studies detailed the percentage of the population that agreed to participate and, of those, six studies noted a response rate greater than 60% (Farmer et al, 2006; Gonzalez et al, 2008; Kilbourne et al, 2005; Nelson et al, 2007; Osborn et al, 2012; Pollack et al, 2010). Six studies noted a response rate of less than 60% (Broadbent et al, 2011; Chao et al, 2005; de Vries et al, 2014; Grant et al, 2003; Nau et al, 2007; Schoenthaler et al, 2012). The remaining six studies did not provide detail on the recruitment rate (Bailey et al, 2012; Mann et al, 2009; Mayberry et al, 2012; Odegard et al, 2008; Rosen et al, 2003; Sweileh et al, 2014).

Based on the criteria outlined in Section 2.2.5.1, two studies were assigned a strong rating (Farmer et al, 2006; Gonzalez et al, 2008), ten moderate (Chao et al, 2005; de Vries et al, 2014; Grant et al, 2003; Kilbourne et al, 2005; Nau et al, 2007; Nelson et al, 2007; Osborn & Egede, 2012; Pollack et al, 2010; Schoenthaler et al, 2012; Sweileh et al, 2014) and six weak ratings (Bailey et al 2012; Broadbent et al, 2011; Mann et al, 2009; Mayberry et al, 2012; Odegard et al, 2008; Rosen et al 2003).

2.5.1.2 *Study design*

All studies were cross-sectional in design (Table 2.5 and 2.6). The cross-sectional design of studies resulted in all quantitative studies, including those which had a quantitative stage (Farmer et al, 2006; Mayberry et al, 2012) being assigned a weak rating.

With regard to the qualitative aspects of mixed methods studies, Farmer et al (2006), sought associations between medication adherence and health beliefs by connecting the results of the qualitative stage with the quantitative stage. This is described as sequential exploratory design (Andrew, Halcomb, & Dawson, 2013). This method allows for survey instruments to be designed with a specific population in mind, perhaps making it more relevant to the study population. This may be a particularly relevant method when a minority or hard to reach population is the study group, when there are no validated instruments available for data collection, or if it is a recognised method for collecting data on that particular factor. In this study, the factor to be explored was health beliefs and research paradigm was the theory of planned behaviour (TPB). This approach recommends that a new questionnaire is developed for each study group via a pilot study (Ajzen, 1985). Although this may affect the external validity of a study it is a recognised methodology which promotes flexibility in questionnaire design (Darker & French, 2009). Two studies have found that participants find TPB questionnaires difficult to interpret which they suggest resulted in unreliable results (Darker et

al, 2009; French, Cooke, McLean, Williams, & Sutton, 2007), however this was not highlighted as a limitation in the reviewed article (Farmer et al, 2006).

The second mixed methods study (Mayberry & Osborn, 2012) used a method described as concurrent nested mixed methodology (Andrew et al, 2013). Focus groups were combined with medicines adherence scores to determine whether themes associated with diabetes service users' perceptions of family members were also associated with adherence and glycaemic score. Validated instruments were used to measure adherence, family knowledge, family supportive behaviour and glycaemic control. Both studies were assigned a moderate rating (dependability) for the qualitative stage of the study.

2.5.1.3 *Controlling for confounders*

A total of eight studies controlled for some, but not all, confounders (Chao et al, 2005; Gonzalez et al, 2008; Kilbourne et al, 2005; Nau et al, 2007; Nelson et al, 2007; Osborn & Egede, 2012; Rosen et al, 2003; Schoenthaler et al, 2012) and were assigned a moderate rating. The ten remaining studies had no evidence of controlling for age, sex, socioeconomic status or health status (Bailey et al, 2012; Broadbent et al, 2011; de Vries et al, 2014; Farmer et al, 2006; Grant et al, 2003; Mann et al, 2009; Mayberry & Osborn, 2012; Odegard & Gray, 2008; Pollack et al, 2010; Sweileh et al, 2014) and were assigned a weak rating. None were assigned a strong rating because no study controlled for all prognostic confounders.

2.5.1.4 *Data collection methods*

Eight studies used self-administered questionnaires (Broadbent et al, 2011; Chao et al, 2005; de Vries et al, 2014; Nau et al, 2007; Nelson et al, 2007; Pollack et al, 2010; Schoenthaler et al, 2012; Sweileh et al, 2014) and those with smaller samples sizes (Grant et al, 2003; Odegard et al, 2008), potentially vulnerable participants (Gonzalez et al, 2008; Kilbourne et al, 2005; Osborn et al, 2012; Rosen et al, 2003), minority populations (Bailey et al, 2012) or

mixed methods design (Farmer et al, 2006; Mayberry et al, 2012) used face to face or telephone surveys. Mixed methods studies used a combination of self-administered and face-to-face questionnaires and semi-structured interviews.

Measurement instruments for independent and dependent factors selected were based on the current adherence literature, theories related to adherence psychology, preliminary qualitative interviews or a combination of the above. Eight studies used validated tools for both independent and dependent factors (de Vries et al, 2014; Kilbourne et al, 2005; Nelson et al, 2007; Osborn et al, 2012; Pollack et al, 2010; Rosen et al, 2003; Schoenthaler et al, 2012; Sweileh et al, 2014). Five studies used adapted, or extracts from, measurement instruments to explore independent or dependent factors (Bailey et al, 2012; Gonzalez et al, 2008; Grant et al, 2003; Mann et al, 2009; Odegard et al, 2008). Two studies altered or used extracts from both validated independent and dependent measurement instruments (Broadbent et al, 2011; Nau et al, 2007).

In mixed methods studies, one study carried out qualitative interviews based on a theoretical model, theory of planned behaviour (TPB) and informed the design of the survey instrument (Farmer et al, 2006). The other merged qualitative data with quantitative results to seek associations between qualitative perceptions of family support, medicines adherence and glycaemic control (Mayberry et al, 2012). Hence, both mixed methods studies adopted a valid and reliable qualitative data collection strategies and use of validated medicines adherence instruments which resulted in both assigned a strong rating.

Ten articles were assigned a strong rating (de Vries et al, 2014; Farmer et al, 2006; Kilbourne et al, 2005; Mayberry & Osborn, 2012; Nelson et al, 2007; Osborn et al, 2012; Pollack et al, 2010; Rosen et al, 2003; Schoenthaler et al, 2012; Sweileh et al, 2014), 6 moderate (Bailey et al, 2012; Chao et al, 2005; Gonzalez et al, 2008; Grant et al, 2003; Mann et al, 2009; Pollack et al, 2010) and 2 a weak rating (Broadbent et al, 2011; Nau et al, 2007)

2.5.1.5 *Withdrawal and dropout rates*

Withdrawal and dropout rates were not applicable in 13 studies (Table 4). Dropout rates in the remaining three were 16% (Farmer et al, 2006), 27% (Mayberry et al, 2012) and 60% (Gonzalez et al, 2008) and were assigned a moderate rating.

2.5.1.6 *Data Analyses*

Two studies did not detail the statistical tests performed to establish associations between dependent and independent variables (Bailey et al, 2012; Broadbent et al, 2011) and were assigned a weak rating. The remaining studies used appropriate statistical tests for their studies and were assigned a strong rating for this criterion. Appropriate analysis was carried out on the qualitative aspects of the mixed methods studies and were assigned a strong rating for credibility of the qualitative finding (Farmer et al, 2006; Mayberry et al, 2012)

2.5.2 **Overall quality evidence of studies included in the review.**

As all studies had at least one weak rating, no studies were assigned an overall strong rating, seven studies were assigned a moderate (Chao et al, 2005; Farmer et al, 2006; Gonzalez et al, 2013; Kilbourne et al, 2005; Nelson et al, 2007; Osborn et al, 2012; Schoenthaler et al, 2012) and eleven a weak rating (Bailey et al, 2012; Broadbent et al, 2011; de Vries et al, 2014; Grant et al, 2003; Mann et al, 2009; Mayberry et al, 2012; Nau et al, 2007; Odegard et al, 2008; Pollack et al, 2010; Rosen et al, 2003; Sweileh et al, 2014).

Having appraised the quality of research evidence, according to Jackson (2012), the next stage of a narrative systematic review is to review the key characteristics of the studies and identify themes associated with the included studies. .

2.6 **Key characteristics of the studies and themes of study findings**

. Table 2.7 provides an overview of the studies and will be followed by an appraisal of key emergent themes.

Table 2.7: Key characteristics of studies included in systematic review

Study and setting	Design	Aim	Population	Data collection (strategy and instruments)	Analysis	Findings	Comments	Global quality rating
(Chao et al, 2005), USA	Cross-sectional Quantitative Health belief model	Associations between depression and adherence	Sample size: 445 Gender: 50.1% female Age: 56.3 (±11.4 years) Mode ethnicity: Caucasian 78% Comorbidities: ≥1 86.7% Diabetes type: All type 2 diabetes Mean time with diabetes: 7.3 years Income: \$50,000-\$75,000 Schooling: Not recorded	Postal questionnaire Dependent Items from Morisky Medicines Adherence Score (MMAS) and Medicine Adherence Rating Scale (MARS) Independent Depression (PHQ-9) Extracts from validated tools for meds sense, disease perception and perceived barriers	Structural equational modelling Programme SAS Reliability Cronbach's alpha Model fit when $\chi^2/df < 3$	Response rate 48%. 51.8% adherent. Perceived side effect barriers and self-efficacy acted as mediators between depressive symptoms and medication adherence.	Extracts from validated tools.	moderate
(Schoenthaler et al, 2012), USA	Cross-sectional Quantitative	Associations between psychosocial, sociodemographic, disease and physician service user relationship on adherence	Sample size: 608 Gender: 52% female Age: 62.1 (SD 9.2) Mode ethnicity: NR Comorbidities: ≥1 24% Time since diagnosis: 5.4 years Diabetes type: type 2 Schooling: Not recorded	Interviews and self admin questionnaires Dependent Oral medicine possession ratio (MPR) for 2 years prior to start of study Independent Diabetes knowledge test (DKT-13) Beliefs about meds (BMQ) Social support (MOS-19)	Multiple linear regression Two sided tests p <0.05 significant	Response rate not reported Adherence rates not reported High levels of social support and those on oral meds associated with higher adherence.	Participants had lower HbA1c than those who declined to participate. Unclear as to how many diabetes meds prescribed. Retrospective analysis of meds adherence MPR only accounts for oral meds and is measure of prescription filled not consumption.	moderate
(Osborn et al 2012), USA	Cross-sectional Quantitative	Associations between the role of social support on depression and medication adherence with social support as mediator	Sample size: 138 Gender: 79.1% female Age: 62.9 (SD 11years) Mode ethnicity: 71.4 African American Comorbidities: NR Diabetes type: type 2 Length of time: Not recorded Income: NR Schooling: 65% high school education or greater	Self-administered Questionnaire Dependent MMAS-4 HbA1c Independent Depression – PHQ-10 Social support - MOS-19	SPSS Bootstrapping	43% Adherent Depressive symptoms have an indirect effect on medication adherence through a lack of social support	No theoretical model	moderate
(Bailey et al, 2012), USA	Cross-sectional Quantitative	Associations between barriers and adherence	Sample size: 58 Gender: 43% female Age: 50 (SD10.3) Mode ethnicity: 85% Hispanic Comorbidities: ≥1 50% Time since diagnosis: NR Diabetes type: unknown Income: 77%, \$20,000 Schooling: 30% college	Self-administered questionnaire Dependent MMAS8 Independent Perceived sensitivity to meds Complementary meds use Non-validated tool for barriers	Reliability tested SAS package P < 0.05	44% adherent Cost most prevalent reason for non-adherence, followed by no refills (repeat prescription)	Small Hispanic population	weak

Study and setting	Design	Aim	Population	Data collection (strategy and instruments)	Analysis	Findings	Comments	Quality rating
(Broadbent et al, 2011), New Zealand	Cross-sectional. Quantitative	Association between medicine beliefs and adherence.	Sample size: 157 patients Gender: type 1 51% female, type 2 42% female Age: type 1 43.2 + 20.57, type 2 58.3_+ 11.27 Mode ethnicity: not reported Comorbidities: not reported Time since diagnosis: not reported Diabetes type: 79% type 2 diabetes Income: not reported Level of schooling: not reported	Self-administered questionnaire Dependent GRIVAS score Independent Belief about medicines scores (BMQ)	Not reported	86% adherent to insulin Lower perceived consequences of diabetes, lower distress and fewer symptoms associated with adherence	Tool adapted from original validated instruments Adherence to oral hypoglycaemic not reported.	weak
(Pollack et al, 2010), USA	Cross-sectional Quantitative	Association between drug side effects and adherence	Sample size: 2074 Gender: 47.4% female Age: 60.1 years_+ 10.8 Mode ethnicity: 13.3% non-white Comorbidities: unknown Diabetes type: type 2 diabetes Length of time with diabetes: 8.9 years Income: not reported Level of schooling: not reported	Self-administered internet based survey Dependent MMAS-4 (MMAS) Independent Diabetes symptom measurement (DSM) Tolerability measurements tool devised for study (not validated)	SPSS software Univariate frequencies Chi Square ANOVA Multivariate regression	Adherence rates not reported Constipation, diarrhoea, hypoglycaemia significantly associated with non-adherence	Only one independent variable validated	weak
(Mann et al, 2009), USA	Cross-sectional Leventhal's self-regulation theory	Association between disease, medication beliefs and adherence in Hispanic population	Sample size: 151 Gender: 68% women, Age: 57 (SD 11) Mode ethnicity: Caucasian 54% Comorbidities: > 1 >80% Diabetes type: All type 2 diabetes Length of time with diabetes: 13 years. Income: 89% \$30,000 Level of schooling: 51% <high school education	Face to face interview Dependent MMAS-4 Independent Brief illness perception questionnaire Beliefs about medicines questionnaire (BMQ) Disease specific self-efficacy Regime complexity Depression (PHQ-9)	STATA statistical software Chi-square tests – predictors of adherence Multivariable logistic regression univariate analysis –stepwise elimination	72% adherent Illness perceptions and medication belief, side effects, complex regimes and self-efficacy predicted non-adherence	Minority group Use of self-reported scale No objective measure No measure of cultural differences	weak
(Gonzalez et al, 2008), USA	Cross-sectional Longitudinal	Association between depressive symptoms and diabetes self-care at 0 and 9 months	Sample size: 208 Gender: 49% women, 51% male Age: 65.5 (±11.6) Mode ethnicity: Caucasian 86% Comorbidities: mean 3.2 Diabetes type: All type 2 diabetes Length of time: 9.4 years ±6.9 Income: not reported Level of schooling: .80% high school	Self-report measure – interviews Dependent Summary of Diabetes Self-Care (SDSCA) Independent Harvard Department of Psychiatry/National Depression Screening Day Scale (HANDS)	SPSS Descriptive statistics (means) Linear regression models.	Adherence not reported. Higher baseline levels of depression predicted poorer medication adherence. 1 point increase in depression score predicted non-adherence.	DSCA is validated. Medicines adherence is part of scale rather than an independent measure of medicines adherence.	moderate

Study and setting	Design	Aim	Population	Data collection (and instruments)	Analysis	Findings	Comments	Global quality rating
(Kilbourne et al, 2005), USA	Cross-sectional/ follow-up. Quantitative	Association between depression and adherence to oral hypoglycaemic medication	Sample size: 203 Gender: 100% male Age: 67 years (± 10) Mode ethnicity: 17% non-white Comorbidities: not reported Diabetes type: All type 2 diabetes Length of time 59% >10 years Income: not reported Level of schooling: not reported	Face to face and mailed survey (9 months) Dependent Electronic monitoring caps (EMC) Pharmacy refill data Independent Depression (PHQ-9)	SAS statistical package Non-parametric tests for significance between depressed and non-depressed groups Multiple logistic regression	65% reported good overall adherence Patients with depression were associated with poorer adherence	Findings limited to those in veterans' healthcare facility. All male population. Behaviour change due to knowledge that medication consumption was being monitored.	moderate
(Odegard et al 2008), USA	Cross-sectional Quantitative	Factors associated with medication adherence in adults with poorly controlled type 2 diabetes	Sample size: 77 Gender: Male 55.8% female 44.2% Age: 52 years + 10.9 Mode ethnicity: NR Comorbidities: unknown Diabetes type: type 2 diabetes Length of time with diabetes: 7 years Income: not reported Level of schooling: 80% high school education	Questionnaire interview. Dependent Part of 4 item Morisky Medication Adherence Score (MMAS) Independent Challenges to medication adherence based on a previously validated tool (not validated)	Statistical package not reported. Bivariate linear regression	Adherence not reported Adherence barriers identified as cost, remembering doses, reading prescription labels	Did not use full validated MMAS Forgetfulness often associated with socially acceptable way of saying does not want to take medication	weak
(Rosen et al, 2003), USA	Cross-sectional Quantitative	Association between cognitive function and adherence to metformin (OAD)	Sample size: 79 Gender: 100% male Age: 65 years (range 41-85) Mode ethnicity: not reported Comorbidities: not reported Diabetes type: All type 2 diabetes Length of time: not reported Income: not reported Level of schooling: Average 13 years	Questionnaire Dependent Medicines Electronic monitoring caps (MEMS) Independent Validated MMSE and neurocognitive tests	Statistical package not reported Multiple logistic regression, Stepwise multiple regression of variables significantly correlated with adherence Statistical significance $p < 0.05$	% of population adherent not reported. Mild association between neuropsychological functioning and adherence to oral anti-diabetic medicine.	Cross-sectional study unclear how administered Sample size small? underpowered study 30-day study – short timeframe Hawthorne effect Male only study not generalizable findings to the wider population.	weak
(Grant et al, 2003), USA	Cross-sectional Quantitative	Association between side effects, medication benefits, polypharmacy and adherence	Sample size: 128 Gender: 61% female Age: 66 years (± 12) Mode ethnicity: 88% white Comorbidities: not reported Diabetes type: All type 2 diabetes Length of time not reported Income: not reported Level of schooling: not reported	Telephone interview Dependent Self-reported questions derived from validated tools Independent No validated tool to assess polypharmacy	SAS statistical package Spearman's correlation coefficient to correlate adherence rates with number of prescribed medication $P < 0.05$ statistically significant	Adherence rates not reported Side effects and negative perceptions about whether medication was beneficial associated with non-adherence Polypharmacy does not affect medication adherence	Information was passed onto primary care physician – may have influenced patient responses. White population results not generalizable to minority groups.	weak

Study and setting	Design	Aim	Population	Data collection (strategy and instruments)	Analysis	Findings	Comments	Global quality rating
(Nau et al, 2007), USA	Cross-sectional Quantitative	Association between gender depression and medication adherence.	Sample size: 391 Gender: 49.9% female. Age: 56 years (SD 11.1) Mode ethnicity: 78.3% white Comorbidities: ≥ 1 86% Diabetes type: All type 2 diabetes Length of time: not reported Income: 21%: \$25,000 Level of schooling: .65.5% college or higher education	Postal questionnaire Independent 4 item scale similar -to Medicine adherence report scale (MARS) Dependent Depression (PHQ-8) Non-validated tool for measure of social support Non-validated tool for measure of self-efficacy	SPSS statistical package 2x2 factorial analysis P < 0.05 statistically significant	Adherence to medication poorer in men with depression compared to women	Assessment of depression was with depression score rather than full psychological assessment. Scale may have been invalidated as was adapted from original tool.	weak
(Nelson et al, 2007), USA	Cross-sectional Quantitative	Association between self-efficacy, readiness to change and provider advice and diabetes self-care (including medication adherence).	Sample size: 717 Gender: 4% female Age: 22% 30-54 44% - 55-64 34 \geq 65 years Mode ethnicity: not reported Comorbidities: ≥ 1 $\geq 90\%$ Diabetes type: All type 2 diabetes Length of time: not reported Income: not reported Level of schooling: not reported	Mailed survey Independent Summary of diabetes self-care activities (SDSCA) Dependent Physical Activity Scale for the Elderly (PASE) Diet Habits questionnaire (DHQ)	STATA statistical package ANOVA or T-tests Multivariate linear regression analysis to detect associations between diabetes self-care behaviours and HbA1c	Higher self-efficacy scores associated with higher adherence	Study was on older men – results may not be applicable to younger men or women No specific medicines adherence scale used.	moderate
(de Vries et al, 2014), Netherlands	Cross-sectional Quantitative	Association between medication beliefs, treatment complexity and non-adherence.	Sample size: 133 Gender: 50% Age: 66 Mode ethnicity: not reported Comorbidities: not reported Diabetes type: type 2 diabetes Length of time: 7 years Income: not reported Level of schooling: 40% middle or high education	Mailed survey Independent MARS Prescription data Dependent Beliefs about medicine scale Medication regime complexity index	Sample size not calculated Between group comparisons Mann-Whitney U P < 0.01 significant) One way analysis of variance P < 0.05 significant	50% selected on basis of non-adherence Treatment complexity associated with non-adherence	Selection bias due to moderate response rate Postal survey excluded those with poor health literacy or cognitive impairment.	weak
(Sweileh et al, 2014), Palestine	Cross-sectional Quantitative	Association between medication beliefs, diabetes knowledge Demographic factors and medication adherence.	Sample size: 405 Gender: 53.3% female Age: 58.3 Mode ethnicity: NR Comorbidities: ≥ 2 Diabetes type: type 2 Length of time: 7 years Income: not reported Level of schooling: 17.5% >high school education.	Self-reported questionnaire Independent MMAS8 Dependent Beliefs about Medicines Questionnaire (BMQ) Michigan Knowledge Scale	Sample size calculated at 385 SPSS package Mean and median Factors associated with adherence- Univariate analysis Significance p < 0.05	57.3% adherent Association between marriage and high diabetic knowledge, adverse events, beliefs about medicines and adherence.	Not number of meds but belief about efficacy and harm of medicine. Not representative of the Arab Palestinian population No data on glycaemic control.	weak

Study and setting	Design	Aim	Population	Data collection (strategy and instruments)	Analysis	Findings	Comments	Global quality rating
(Mayberry et al, 2012), USA	Cross-sectional Mixed methods	Association between family members support and participants' medication adherence.	Sample size: 61 Gender: 69% women, 31% male Age: 57.1 (\pm 8.6) Mode ethnicity: Caucasian 67% white, 28% African American 5% other Comorbidities: not reported Diabetes type: All type 2 diabetes Length of time: not reported Income: 83% \$30,000-\$60,000 Level of schooling: 75% high school degree	Focus groups Questionnaire for demographics Independent Adherence to refills and medication scale (ARMS), Dependent HbA1c Diabetes Family Behaviour Checklist (DFBC)	STATA statistical package Descriptive statistics t-test and Mann Whitney U NVIVO 9 for qualitative data Thematic analysis	Non-supportive behaviour by family members associated with poor medication adherence and higher HbA1c levels	Single site recruitment No validated score to measure level of family support.	weak
(Farmer et al, 2006), UK	Cross-sectional Mixed methods	Association of medication taking beliefs and medicines adherence	Sample size: 121 Gender: 52.1% male Age: 66 years (+8) Mode ethnicity: not reported Comorbidities: not reported Diabetes type: All type 2 diabetes Length of time: 6 years (median) Income: not reported Level of schooling: not reported	Interviews and Questionnaires Independent Medicine adherence report scale (MARS) Dependent Questionnaire based on interview Non-validated medicines for diabetes scale	STATA statistical package Spearman's rank correlation Mann-Whitney U to detect between group differences	Side effects (weight gain) associated with adherence Taking diabetic medication would lead to weight gain is associated with adherence (side effects)	. Validated tools not used for data collection of independent factors No objective measure of diabetes control e.g. HbA1c	weak

2.6.1 Location and study design

Of the studies included in the review 14 were conducted in the USA (Bailey et al, 2012; Chao et al, 2005; Gonzalez et al, 2008; Grant et al, 2003; Kilbourne et al, 2005; Mann et al, 2009; Mayberry & Osborn, 2012; Nau et al, 2007; Nelson et al, 2007; Odegard & Gray, 2008; Osborn & Egede, 2012; Pollack et al, 2010; Rosen et al, 2003; Schoenthaler et al, 2012), one in New Zealand (Broadbent et al, 2011), one in the UK (Farmer et al, 2006), one in the Netherlands (de Vries et al, 2014) and one in Palestine (Sweileh et al, 2014).

Sixteen studies were cross-sectional (Bailey et al, 2012; Broadbent et al, 2011; Chao et al, 2005; de Vries et al, 2014; Gonzalez et al, 2008; Grant et al, 2003; Kilbourne et al, 2005;. Mann et al, 2009; Nau et al, 2007; Nelson et al, 2007; Odegard et al, 2008; Pollack et al, 2010; Rosen et al, 2003; Schoenthaler et al, 2012; Sweileh et al, 2014), and two were mixed methods (Farmer et al, 2006; Mayberry et al, 2012).

Four studies applied a theoretical framework to inform study design (Chao et al, 2005; Farmer et al, 2006; Mann et al, 2009; Nelson et al, 2007); namely; the health beliefs model (Chao et al, 2005); theory of planned behaviour ((Farmer et al, 2006); Leventhal's self-regulation theory (Mann et al, 2009) and readiness to change model (Nelson et al, 2007).

2.6.2 Aims

In four studies the primary aim was to explore the association between independent factors (such as depression, self-efficacy, health beliefs, and social factors) and diabetes treatment adherence (including appointments, diabetes foot care, medicines adherence, diet and exercise) in the general adult diabetic population (Gonzalez et al, 2008; Nelson et al, 2007; Pollack et al, 2010;). Fourteen studies explored the association between independent factors and medicines adherence only (Bailey et al, 2012; Broadbent et al, 2011; Chao et al, 2005; de Vries et al, 2014; Farmer et al, 2006; Grant et al, 2003; Kilbourne et al, 2005; Mann et al, 2009;

Mayberry et al, 2012; Nau et al, 2007; Odegard et al, 2008; Osborn et al, 2012; Rosen et al, 2003; Schoenthaler et al, 2012; Sweileh et al, 2014).

Six investigated associations between medication adherence in two or more independent factors (de Vries et al, 2014; Mann et al, 2009; Mayberry et al, 2012; Nau et al, 2007; Nelson et al, 2007; Osborn et al, 2012; Schoenthaler et al, 2012). The remaining studies explored one factor. Of the reviewed papers and 16 identified factors, which were organised into four main themes namely, patient, psychological, medication-related and socioeconomic factors characteristics (Figure 2.2).

2.6.3 Sample sizes and demographic data

Study sample sizes ranged from 50 to 717. Mean age of participants ranged from 35-67 years. The percentage of female participants recruited was 0-53% with 2 studies recruiting > 90% male participants (Nelson et al, 2007; Rosen et al, 2003). One study recruited type 1 and type 2 diabetics (Broadbent et al, 2011), 16 studies recruited type 2 diabetics only (Chao et al, 2005; de Vries et al, 2014; Farmer et al, 2006; Gonzalez et al, 2008; Grant et al, 2003; Kilbourne et al, 2005; Mann et al, 2009; Mayberry et al, 2012; Nau et al, 2007; Nelson et al, 2007; Odegard et al, 2008; Osborn et al, 2012; Pollack et al, 2010; Rosen et al, 2003; Schoenthaler et al, 2012; Sweileh et al, 2014) and one study did not specify what type of diabetes participants had (Bailey et al, 2012).

Time since diagnosis was recorded in 10 studies (Chao et al, 2005; de Vries et al, 2014; Farmer et al, 2006; Gonzalez et al, 2008; Kilbourne et al, 2005; Mann et al, 2009; Odegard et al, 2008; Pollack et al, 2010; Schoenthaler et al, 2012; Sweileh et al, 2014) and all of those 10 studies recorded a diagnosis of diabetes of 5 or more years in the majority of participants.

Ethnicity was recorded in 10 US studies (Bailey et al, 2012; Chao et al, 2005; Gonzalez et al, 2008; Grant et al, 2003; Kilbourne et al, 2005; Mann et al, 2009; Mayberry et al, 2012; Nau et al, 2007; Osborn et al, 2012; Pollack et al, 2010), but not in others (Broadbent et al,

2011; Farmer et al, 2006; Nelson et al, 2007; Odegard et al, 2008; Rosen et al, 2003; Schoenthaler et al, 2012). Those that recorded ethnicity reported the majority of participants were Caucasian with the exception of three studies that recruited from African-American (Osborn et al, 2012), Hispanic (Bailey et al, 2012) and Arab Palestinian (Sweileh et al, 2014) ethnicity.

Average income, level of education, and comorbidities were not consistently recorded in any studies with only two studies recording all three (Mann et al, 2009; Osborn et al, 2012).

2.6.4 Recruitment methods

Three studies recruited from medical databases (Chao et al, 2005; Nau et al, 2007; Pollack et al, 2010), 13 from community practices or outpatient diabetic clinics (G. Bailey et al, 2012; Broadbent et al, 2011; de Vries et al, 2014; Farmer et al, 2006; Gonzalez et al, 2008; Grant et al, 2003; Kilbourne et al, 2005; Mann et al, 2009; Nelson et al, 2007; Odegard et al, 2008; Osborn et al, 2012; Schoenthaler et al, 2012; Sweileh et al, 2014) and two from a combination of two or more sources (Mayberry et al, 2012; Rosen et al, 2003).

2.6.5 Data collection

Four studies conducted researcher administered interviews (Grant et al, 2003; Mann et al, 2009; Odegard et al, 2008; Osborn & Egede, 2012) , 11 completed self-administered questionnaires (Bailey et al, 2012; Broadbent et al, 2011; Chao et al, 2005; de Vries et al, 2014; Farmer et al, 2006; Kilbourne et al, 2005; Nau et al, 2007; Nelson et al, 2007; Pollack et al, 2010; Rosen et al, 2003; Sweileh et al, 2014), three completed a combination of the two (Gonzalez et al, 2008; Mayberry et al, 2012; Schoenthaler et al, 2012). All but one study (Farmer et al, 2006) used validated or extracts from validated questionnaires.

2.6.5.1 *Dependent variables*

Thirteen studies used validated self-reported medicine adherence scales (Bailey et al, 2012; Broadbent et al, 2011; Chao et al, 2005; de Vries et al, 2014; Farmer et al, 2006; Grant

et al, 2003; Mann et al, 2009; Mayberry et al, 2012; Nau et al, 2007; Odegard et al, 2008; Osborn et al, 2012; Pollack et al, 2010; Sweileh et al, 2014), two studies used self-report adherence diabetes self-care scales (Gonzalez et al, 2008; Nelson et al, 2007). The remaining studies used Medicines Electronic Monitoring System (MEMS) (Rosen et al, 2003), monitoring of prescription refills (Kilbourne et al, 2005), and Medicine Possession Ratios (MPR) (Schoenthaler et al, 2012). Two studies adapted validated medicines adherence instruments to meet the needs of the study population or research aims (Broadbent et al, 2011; Grant et al, 2003).

Four studies corroborated adherence measurements with biochemical markers, HbA1c or blood glucose (Mann et al, 2009; Mayberry et al, 2012; Odegard et al, 2008; Rosen et al, 2003).

2.6.5.2 *Independent variables*

Nine studies used validated measurement instruments (Broadbent et al, 2011; de Vries et al, 2014; Gonzalez et al, 2008; Kilbourne et al, 2005; Nelson et al, 2007; Osborn et al, 2012; Rosen et al, 2003; Schoenthaler et al, 2012; Sweileh et al, 2014). Socio-demographic data included age, gender and number of medications. Measurement instruments for psychological factors related to depression were the patient health questionnaire (PHQ-8,9) (Chao et al, 2005; Kilbourne et al, 2005; Mann et al, 2009; Nau et al, 2007; Osborn et al, 2012; Schoenthaler et al, 2012) and Harvard Department of Psychiatry/National Depression Screening Day Scale (HANDS) (Gonzalez et al, 2008). Cognitive function using 5 brief neuropsychological tests and Mini mental status exam (MMSE) was used in only one study (Rosen et al, 2003).

Self-efficacy was measured by one using the Perceived Competence in Diabetes Scale (Nelson et al, 2007) and three studies measured self-efficacy using a non-validated method (Chao et al, 2005; Mann et al, 2009; Nau et al, 2007). Illness beliefs were measured with the Brief Illness Perception Questionnaire (Broadbent et al, 2011). Measurement instruments for

medication-related factors were the Brief Medication Questionnaire (Odegard et al, 2008) and Beliefs about Medicines Questionnaire (Chao et al, 2005; Mann et al, 2009; Schoenthaler et al, 2012) Social factors were measured using the 19-item Medical Outcome Study (MOS) (Osborn et al, 2012; Schoenthaler et al, 2012) and one study use a non-validated instrument (Mayberry et al, 2012). Two studies developed a non-validated measurement instrument for measuring barriers to adherence (Bailey et al, 2012), the other tolerability (Pollack et al, 2010) and one study used extracts from validated tools (Chao et al, 2005). One study designed a questionnaire based on 33 qualitative interviews (Farmer et al, 2006).

2.6.6 Data Analysis

The primary quantitative research studies applied a variety of statistical methods to analyse and report data. To detect correlations between dependent and independent variables, two studies used Spearman's Rank correlation (Farmer et al, 2006; Grant et al, 2003) To establish independent predictors of adherence, 10 studies used multiple logistical regression analysis techniques (de Vries et al, 2014; Gonzalez et al, 2008; Kilbourne et al, 2005; Mann et al, 2009; Nelson et al, 2007; Odegard et al, 2008; Pollack et al, 2010; Rosen et al, 2003; Schoenthaler et al, 2012; Sweileh et al, 2014), 1 study used structural equation modelling (Chao et al, 2005), 1 study carried out a factor analysis (Nau et al, 2007) and one performed bootstrapping (Osborn et al, 2012) to establish the mediating effect of social support and depression on adherence. Two studies did not describe statistical methods (Bailey et al, 2012; Broadbent et al, 2011). In all studies, statistical significance was defined as p value of <0.05. SAS, STATA 7.0 or SPSS statistical analysis programmes were used to analyse data.

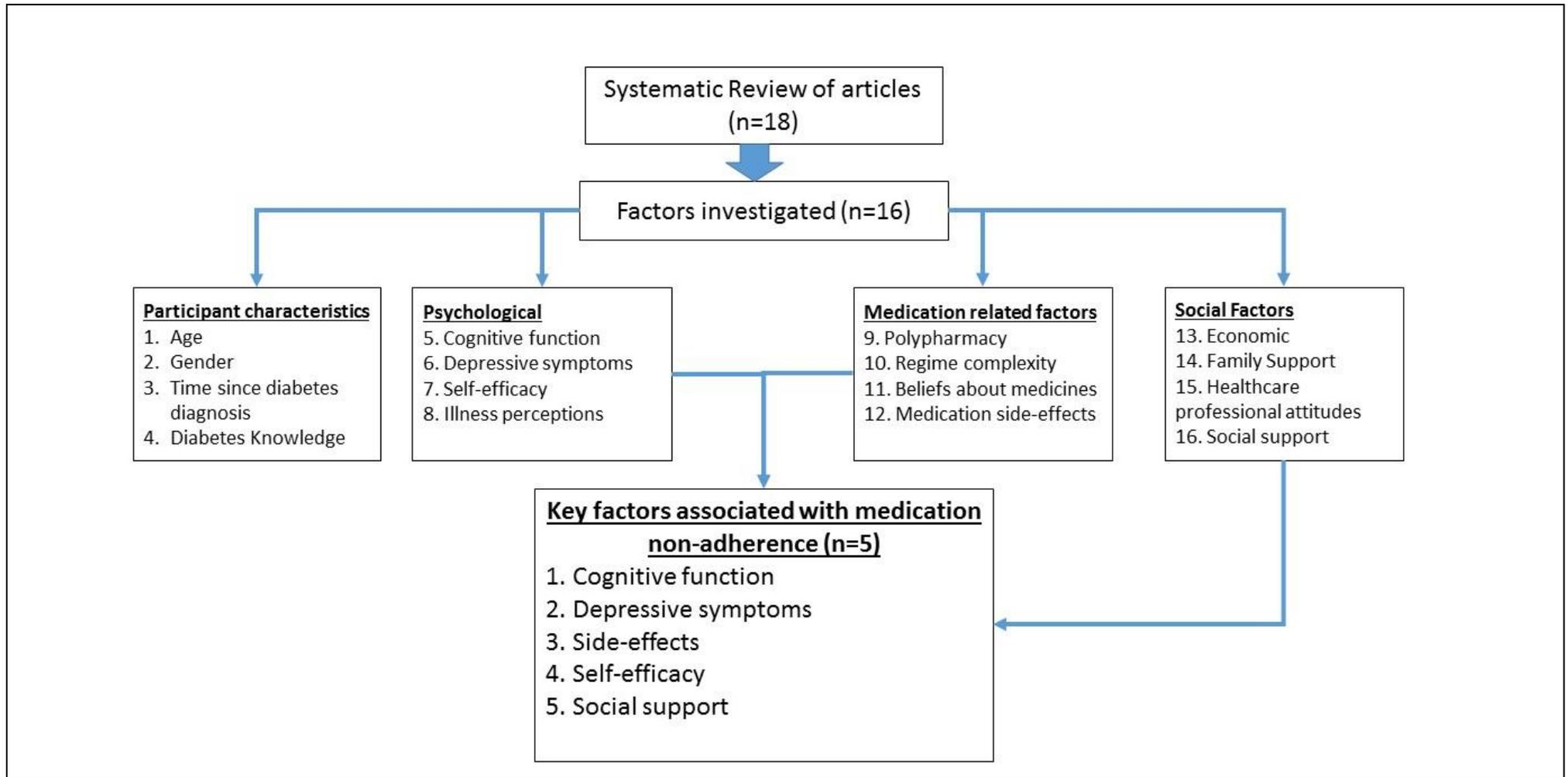
Nine studies controlled for confounders, such as, age sex, time since diagnosis, other comorbidities and education (Chao et al, 2005; Farmer et al, 2006; Kilbourne et al, 2005; Mayberry & Osborn, 2012; Nau et al, 2007; Nelson et al, 2007; Osborn & Egede, 2012; Rosen et al, 2003; Schoenthaler et al, 2012). The qualitative aspects of the mixed methods studies

carried out a thematic analysis of data from interviews and focus groups using NVIVO software (Udo, 2014)

2.7 Frequency of, and factors associated with adherence

Seven studies reported medication adherence rates and, of those, the mean frequency of adherence was 60% ((n =1152) (range 44% - 86%) (Bailey et al, 2012; Broadbent et al, 2011; Chao et al, 2005; Kilbourne et al, 2005; Mann et al, 2009; Osborn et al, 2012). Sixteen factors were investigated for associations with adherence, of those, five were most frequently identified as having statistically significant associations with medication adherence namely depression, self-efficacy, medication side effects and social support and regime complexity (figure 2.2). Participant characteristics (for example demographics or time since diagnosis), illness perceptions and medication beliefs were not associated with adherence.

Figure 2.2: Summary of factors associated with medication adherence in the diabetic population



2.8 Factors and associations with diabetic medicines adherence

2.8.1 Demographic factors

Two studies reported no strong association between age or gender and medicines adherence (Grant et al, 2003; Nau et al, 2007). One study reported no association between time since diagnosis, level of education, diabetes knowledge and medication adherence (Schoenthaler et al, 2012). The remaining did not report associations between medicines adherence and demographic factors.

2.8.2 Psychological factors

One study noted an association between cognitive function and medicines adherence (Rosen et al, 2003). Six studies cited depressive symptoms as a factor associated with medication adherence (Chao et al, 2005; Gonzalez et al, 2008; Kilbourne et al, 2005; Mann et al, 2009; Nau et al, 2007; Osborn et al, 2012) with one of those identifying that being male and having depressive symptoms was associated with non-adherence (Nau et al, 2007). Four studies found an association between low self-efficacy and non-adherence in adult diabetics (Chao et al, 2005; Mann et al, 2009; Nau et al, 2007; Nelson et al, 2007). Chao et al (2005) noted that the association between depression and medication adherence is mediated by self-efficacy and people with diabetes and depressive symptoms may be less motivated and less confident in self-management thus have lower adherence. Two studies explored illness perceptions which were found by one study to have some association with adherence (Broadbent et al, 2011) but appeared to be less important than self-efficacy and depression in another (Mann et al, 2009).

2.8.3 Medicines-related factors

One study reported that polypharmacy (Grant et al, 2003) did not negatively influence adherence in the adult diabetic population. Two studies suggested that regime complexity was associated with non-adherence (Mann et al, 2009; Sweileh et al, 2014). Five studies identified

an association between side effects, and medication adherence (Chao et al, 2005; Farmer et al, 2006; Grant et al, 2003; Mann et al, 2009; Pollack et al, 2010).

2.8.4 Socioeconomic factors

Two studies reported cost as a factor (Bailey et al, 2012; Odegard et al, 2008). Two studies identified that healthcare provider advice and perceived satisfaction with physicians' ability to educate the patient was associated with better adherence (Nelson et al, 2007; Schoenthaler et al, 2012). Three studies reported that social and family support was associated with medicines adherence (Mayberry et al, 2012; Osborn et al, 2012; Schoenthaler et al, 2012). High levels of shared decision-making and social support had a positive impact on medication adherence (Schoenthaler et al, 2012) and poor social support increased depressive symptoms and decreased diabetic medication adherence (Osborn et al, 2012). Non-supportive family behaviour was associated with lower medication adherence (Mayberry et al, 2012).

2.9 Discussion

This review sought to establish the factors associated with diabetic medicines adherence in the IDD and non-IDD populations. The limitations to this review are that it has not been an exhaustive systematic review of all peer-reviewed, 'grey' and unpublished diabetic medicines adherence literature nor has it comprehensively reviewed the medicines adherence literature outside diabetes. Nevertheless, this review has identified the gaps in the research evidence related to people with diabetes and in particular people with ID and diabetes.

Most importantly, this systematic review has revealed the absence of quantitative research on the frequency of, and factors associated with, medication adherence in people with IDD. Secondly, research conducted in the non-IDD diabetic population on medication adherence is of weak quality with only a small proportion conducted in the UK. Finally, there are statistically significant factors associated with adherence in the diabetic population are aligned to Banduras Social Cognitive Theory which require further exploration. This section

will discuss in detail the findings from this review and conclude with proposing a theoretical framework within which this PhD study will be framed.

2.9.1 The absence of evidence: intellectual disability and medicines adherence

The absence of any empirical evidence on the frequency of, and factors associated with, adherence in the IDD population is a key finding from this review. Given the high prevalence of diabetes, poor glycaemic control, shorter life expectancy and high rates of polypharmacy, this is a much-needed area of research, which if investigated, and findings acted upon, will have a positive impact on both mortality and morbidity in this population.

However, people with ID are a hard to reach, potentially vulnerable population making recruitment to studies challenging. In addition, assessing capacity to consent to participate and data collection can be more challenging and time consuming which makes this group a more labour-intensive study population than the general population (Carey & Griffiths, 2017).

Nonetheless, when there is evidence of health inequalities (Haveman et al, 2011) that may be reversed with interventions supported by good quality empirical evidence, research with this population is essential. This is a key recommendation of the UN Convention of Rights of People with Disability (CRPD) (UN, 2007) calling for international communities to develop evidence based interventions for this population, and for them to be participants in research. At a national level, NICE recommended that the focus of adherence research should be targeted at minority and hard to reach populations, and with no data on the people with IDD, this group must be prioritised.

As outlined in chapter 1, prevalence of diabetes in people with ID is at least as high as the general population (McRae et al, 2015) and blood glucose control is suboptimal (Taggart et al, 2013). In people with diabetes but without ID, studies have found that medicines non-adherence (Morisky et al, 2008; Wong et al, 2015), is a more significant predictor of glycaemic control than any other area of diabetes self-care (Osborn et al, 2016).

If similar findings were reported in the IDD population, optimising adherence may improve glycaemic control, reduce mortality and morbidity, improve health outcomes and reduce health inequalities. Alternatively, if medicines adherence is optimal in this group but glycaemic control poor, the focus of diabetes research can be diverted to other areas of self-care, for example diet and exercise. Without this evidence, interventions to improve glycaemic control in people with IDD may be misplaced. Therefore, it is essential to establish the frequency of diabetic medicines adherence in this group. Given the challenges with recruiting to studies from this population, the paucity of evidence and to address NICE recommendations (2009), this research will also seek to establish factors associated with adherence in people with IDD.

During the initial search, four qualitative studies conducted with people with IDD were found (Cardol et al, 2012a, 2012b; Dysch et al, 2012; Hale et al, 2011). These were excluded at the screening stage of the review due to not meeting the inclusion criteria. Exclusion of the studies due to the use of qualitative research approaches and no specific exploration on medication adherence. Nevertheless, they provide an insight into the care of people with ID and diabetes. An overview of this literature will follow and where possible compared to findings from this PhD systematic review.

Two qualitative studies suggest that depression has a negative impact on treatment adherence in people with ID and diabetes (Dysch et al, 2012, Hale et al, 2011). The first, a phenomenological study of four patients from the UK (Dysch et al, 2012) reported that one participant felt that mood may affect adherence to medication. The second, conducted in New Zealand with people with IDD and their carers (n=14), indicated that mood may affect self-management of the condition (Hale et al, 2011). Neither of these studies specifically explored medication adherence but, when their findings are considered in the context of (1) the high incidence of depression and anxiety (McGillivray & McCabe, 2007), (2) poor glycaemic

control (Taggart et al, 2013) in the ID population and (3) evidence from this review of an association between depression and non-adherence in people with diabetes, it provides a rationale to explore associations between depression and diabetic medicines adherence in people with ID.

Considering self-efficacy and social support, a grounded theory study conducted in the Netherlands with 17 carers (Cardol et al, 2012a), suggested that some carers adopted coercive strategies in people with IDD to optimise treatment. Although focussing on the outcome of optimising treatment adherence, it was interpreted as impinging on autonomy, and lowering self-efficacy in people with IDD. A more recent qualitative study conducted (Trip, Conder, Hale & Whitehead, 2015) with 17 support workers working in New Zealand reported those with low confidence may rely on carers for social support and, if a person with IDD refuses to adhere to a treatment regime, carers intervene. These studies suggest that carers may mitigate the effect of low confidence by employing persuasive or coercive support.

These four studies have made a valuable contribution to the evidence base, but what is not known is the effect of low confidence and support provided by carers on medicines adherence in this population. Further research is needed to establish whether the association between medicines adherence and self-efficacy is as important in people with IDD as in the non-IDD population or whether other factors, for example, carer support prevail.

The final factor identified in this review was medicines side effects. Evidence from this systematic review has revealed it is a significant and commonly reported factor associated with adherence in the non-IDD population. However, this review found no literature on the impact of side effects on diabetic medicines adherence in people with IDD. The absence of evidence is not known but possible reasons may be: (1) it is a challenging area to research in this population, (2) people with ID and diabetes and their carers have a limited understanding of

medicine side effects or, (3) clinicians' awareness of the risks associated with polypharmacy and introducing complex regimes, resulting in side effects not identified as problematic.

Recent research has highlighted the challenges with exploring symptoms and signs in people with ID (Osugo, Morrison, Allan, Kinnear, & Cooper, 2017). This Scottish cross-sectional study with people with ID (n = 1023) reported unexplained symptoms as 3.8 times higher than the general population, however the relationship between these symptoms and type or number of medicines was not reported. The high incidence of polypharmacy in people with ID (O'Dwyer et al, 2016), combined with evidence of higher adverse drug events associated with polypharmacy in the non-ID population (Al Hamid et al, 2014), suggests that unexplained symptoms in people with ID may, in part, be attributed to medicines side effects, yet, there is no evidence to support or reject this hypothesis in the IDD population. If research demonstrated that unexplained symptoms were attributable to medicines side effects then medicines review and removal of unnecessary medication could reduce side effects, improve adherence and quality of life in people with ID. Conversely if side effects were not attributed to unexplained symptoms, this line of investigation could be excluded from future research.

This limited understanding of side effects in people with ID extends to carers. A survey with a sample of 25 carers supporting people with ID living in the community in Wales (Fretwell & Felce, 2007) found that their knowledge of side effects with antipsychotic medication was limited and identified a need for more education in this area. Although the small sample size prevents any firm conclusions it does suggest that carers may be reticent to explore side effects in this group.

Conceivably, health care professionals caring for people with IDD may be adopting approaches that minimise side effects in this group. A recent UK-based qualitative study with 30 clinicians supporting people with ID and diabetes suggested that they simplified and minimised changes to diabetic medicines to reduce the risk of adverse drug events (Brown et

al, 2017). This may support the view that side effects are not as problematic in people with ID compared to those without, however more extensive research is required to support or reject this finding.

Limited evidence on the presence, impact and understanding of side effects in people with IDD suggests that further research is necessary. By prospectively comparing the frequency of side effects and its association with medication adherence in people with diabetes with and without ID in this PhD study will identify whether: (1) clinicians are effectively managing diabetic medicines in people with IDD; (2) carers are better informed about side effects than previously reported or, (3) more research is required in this area.

2.9.2 Quality of diabetic adherence studies

The overall quality rating of the studies that met the inclusion criteria for this systematic review was weak to moderate. The observational nature of the selected studies was the main reason why studies were assigned no more than a moderate rating; however, studies were weak across the range of EPHPP quality criteria. The next section will discuss the criteria that resulted in studies receiving a weak rating, namely, study design, data collection methods and controlling for confounders.

The primary aim of the search was to establish factors associated with medicines adherence in the IDD and non-IDD population rather than establishing the interventions that may improve medicines adherence. Hence the weak rating for study design may be a feature of the inclusion criteria of the search rather than a true reflection of the methodological quality of the studies included. The articles which met the inclusion criteria were not necessarily poorly designed observational studies; rather they were robust studies of their type but, when compared to the standard hierarchy of evidence where randomised controlled trials are considered the best available evidence and social science or observational studies the lowest available, there was no alternative but to categorise all studies in the review as weak.

This weak rating may be also be as a result of selecting an appraisal tool designed to critique randomised controlled trials, as there is some evidence that well designed observational studies can generate as robust externally valid results as randomised trials (Benson et al, 2000). By selecting an instrument more closely aligned to observational studies, for example, CASP, may have produced different results. However as previously discussed in Section 2.2.5 the EPHPP tool was used because of its relative simplicity, widespread use and its applicability to public health topics.

However, it was not only study design that led to many studies receiving weak rating, as this tool requires 2 or more criteria to be weak before this rating is assigned, studies were weak in other criteria, for example, data collection methods and controlling for confounders (Table 2.5).

With regard to data collection methods, a low rating was assigned due to alteration of validated instruments. The absence of controlling for confounders made it difficult to draw conclusive comparisons between the studies as extraneous factors which were not controlled for during regression analysis, thus confounders may have influenced adherence in the study population. However, correlations between socio-demographic status and medicines adherence have been modest (Dimatteo, 2004; Gherman et al, 2011) which may have influenced those studies in this review that did not control for them.

NICE (2009) has identified the need for better quality adherence research, particularly in minority groups. This PhD study will address the gap by conducting high quality medicines adherence research that will explore the frequency of and factors associated with medicine adherence from a sample of IDD and non-IDD service users using validated data collection instruments and controlling for potential confounders, regime complexity and support with medicines.

Establishing the most important factors associated with non-adherence will inform which interventions may be effective in optimising medication adherence in both the IDD and non-IDD population in the future. Therefore, a methodologically strong observational study from which recommendations for an interventional study in the IDD population can be made may set the direction of future research in this area.

2.9.3 Paucity of UK research

This systematic review has demonstrated the dearth of UK-based adherence studies. Despite concerns about medication adherence in the UK by NICE, 17 of the studies in this review took place outside the UK, primarily in the USA. This may be reflective of the availability of funded research in the UK compared to the USA. Moreover the location where the study took place may not be of concern because of the international consensus on the importance of medicines adherence (Sabaté, 2003) and the likely generalisability of adherence results reported from elsewhere in the developed world.

Socio-demographic and cultural factors do not have an effect on medicines adherence (Osterberg & Blaschke, 2005), so it is likely that results from non-UK studies are transferable to the UK. Conversely healthcare commissioning in the US is very different to that of the UK. In the UK healthcare is government funded, not for profit, free at the point of entry to care and predominantly community based. The USA has a predominantly hospital-based, insurance-driven system which requires service users to make a financial contribution to healthcare at the point of delivery. In two studies, from USA, the cost of prescription refills was identified as a factor associated with non-adherence and the recent changes in prescription charging in Scotland and exemptions from prescription charges for people with diabetes in the UK may mean that the results of these studies are not be relevant to people with diabetes residing in the UK.

Furthermore, the paucity of medicines adherence research conducted in the UK, suggests that there may be scope for further exploration of medicines adherence. This study will address this gap in the UK literature by conducting a study based in Scotland, UK.

2.9.4 Adherence and factors associated with adherence in the non-IDD population

Studies included in this review did not consistently report overall adherence rates for their study population, with only seven studies doing so. As a result, it was not clear whether the participants selected in the remaining 11 studies were representative of both the adherent and non-adherent diabetic population. Reporting the proportion of those adherent in all studies would have provided an estimate of whether the study population was representative of both groups.

This review identified 16 factors (figure 2.1) associated with medicines adherence in the adult diabetic population of which four (depressive symptoms, self-efficacy, side effects and social support) having statistically significant associations. This section will present some of the wider literature supporting the recommendation that, for the proposed study design, these four factors should be examined in one study to establish which of those is most important.

2.9.5 Depressive symptoms

Depressive symptoms can result in low self-confidence, decreased energy, and feelings of hopelessness which have a negative effect on self-care activities (Katon, 2010). The articles included in this review suggest that symptoms of depression affect medicines adherence and the six articles which explored the association between the two detected a negative effect (Chao et al, 2005; J. S. Gonzalez et al, 2008; Kilbourne et al, 2005; Mann et al, 2009; Nau et al, 2007; Osborn & Egede, 2012). This is consistent with a meta-analysis that reported a significant association between medicines adherence and depression (Gonzalez et al, 2008). Furthermore, poorer health outcomes are evident in those with depression and diabetes. A US study of over

2000 diabetics reported those with depression were less likely to adopt a healthy diet or regular exercise regime (Katon et al, 2010) which, alongside medicines adherence, are key components of effective self-management. One US study of 4,184 adult diabetic patients reported that those with depression had poorer glycaemic control which was associated with a greater risk of diabetes complications and increased mortality (Lin et al, 2009). Hence detecting depressive symptoms is key in optimising adherence.

2.9.6 Self-efficacy

Self-efficacy is defined as belief in one's own ability to perform a certain task (Bandura, 1986). Translating this to diabetes and medicines adherence, it suggests that if an individual believes that they can take their medication as recommended by the prescriber then they are more likely to be adherent to that medication. It is therefore related to confidence and capability. This review suggests that in the general diabetic population there is an association between self-efficacy and adherence when measured against other factors, for example, depression and illness perceptions. A recent meta-analysis of 48 studies has supported the finding that self-efficacy has an association with medicines adherence (Gherman et al, 2011). Moreover, this review suggests that, when measured against depression, low self-efficacy may be a more significant indicator of poor adherence than depressive symptoms. Mann (2009) reported a stronger association between self-efficacy and adherence when compared to depression and adherence. This is an important finding, particularly when considering interventions to improve adherence in a patient. For example, if a patient has low self-efficacy but no symptoms of depression an intervention to improve self-efficacy may improve adherence. Conversely, if a patient has symptoms of depression and low motivation an intervention to improve mood may be necessary to improve adherence (Chao et al, 2005).

2.9.7 Beliefs about medicines and side effects

Self-regulation theory suggests that one's beliefs will influence how information is interpreted and experienced and how behaviour is guided (Cameron & Leventhal, 2003). Applying this theory to medication beliefs, if a patient believes that medicines are beneficial they are likely to adhere to treatment and, if a patient believes that a drug has unpleasant side effects and it makes them feel worse rather than better, they may be more inclined to stop treatment. In the context of diabetes medications, nausea, anorexia and diarrhoea are common unpleasant side effects of metformin, which may influence the patient's motivation to continue taking the medication. Five studies included in this review found evidence to support this logic, and side effects were the medicine-related factor most frequently associated with non-adherence in the adult diabetic population (Chao et al, 2005; Farmer et al, 2006; Grant et al, 2003; Mann et al, 2009; Pollack et al, 2010). This suggests that medication beliefs are important but that experiencing side effects may be a more specific factor associated with adherence. Pollack (2010) also reported that medicine side effects had a significant impact on health-related quality of life. A low quality of life may negatively affect self-efficacy and mood and these factors combined with side effects may have a cumulative negative effect on adherence.

2.9.8 Social Support

Finally results from this review suggest that social support has an impact on medicines adherence. The five studies that investigated social, healthcare or family support found an association between perceived positive support and adherence (Mayberry & Osborn, 2012; Nelson et al, 2007; Osborn & Egede, 2012; Schoenthaler et al, 2012). This finding has been corroborated by Gherman (2011) who reported a positive relationship with the physician had a positive effect on medicines adherence. Creating a health and social network which is perceived by the patient to be supportive is an important factor associated with adherence (Schoenthaler et al, 2012). In the IDD literature it has been suggested that they gained

confidence from the social support they received; however, no links between this and medication adherence were made (Hale et al, 2011).

A recent literature review recommended that intervention studies should be designed to test the impact of different types of social support on medication adherence (Miller & DiMatteo, 2013). However, Mayberry et al (2012) suggests it may not be the type but the perceived benefit of support which is important. This US study (n=61) cited that some support, although well intentioned may impinge upon a person's self-confidence and result in relationship conflict and rebellion. In the context of medicines adherence, this will positively impact on the aim of support (medicines optimisation) but how this is achieved may not be person centred. Person centred interventions appear to have a positive impact on people with ID. A qualitative study conducted in New Zealand with people with IDD (n = 14) and their support workers (n = 17) (Whitehead et al 2016), reported person centred interventions that promoted shared decision-making enhanced autonomy in this population, however the effect on medicines adherence was not explored. Exploring perceived level of social support with people with diabetes, carers' perception of their role in medicines adherence and relating this to objective medicines adherence measures will further explore whether it is type rather than perceived benefit of support which influences medicines adherence. Furthermore, comparing perceived level of social support in the IDD group to the non-IDD group may identify whether needs are similar.

2.9.9 Justification for investigating identified factors

This systematic review has reported important associations between factors associated with adherence. The purpose of this study is to take those factors and investigate them in IDD participants and prospectively compare them to a cohort of non-IDD participants. Each of these factors has the potential to impact on the others and, as far as the author is aware these factors have not been included in the same study before. For example, Osborn et al

(2012) explored the relationship between depressive symptoms, medication adherence and social support and suggested that social support may contribute to improved adherence however, the role of self-efficacy and medicines side effects were not explored.

If these factors were explored in one study, one hypothesis is that low self-efficacy and depressive symptoms may be offset by the level of social support provided. To explain more fully, if the patient perceives their support network to be satisfactory, their depressive symptoms may lessen, they may have greater confidence in their ability to manage their medicines and be more open in their beliefs about the effect that treatment is having on their life. It may also increase awareness about side effects and strategies to avoid them.

This study design also acknowledges that medicines adherence is a complex behaviour and the extent to which a patient will adhere to medication regimes are associated with social, behavioural and cognitive considerations. To explore these factors concurrently in both the IDD and non-IDD population may also identify which is most dominant in each group and provide evidence for future research in this area.

2.10 Proposal of a theoretical framework to inform this PhD study design.

A research proposal should be based on findings from previous research that (1) identifies the research problem and (2) provides a rationale for investigating the problem. This systematic review has identified that there is no evidence on medication adherence and associated factors in the IDD population, it is unclear which is the most important factor associated with medication adherence in people with diabetes and improve health outcomes in this population a good quality empirical research study is essential.

A theoretical framework provides a structured perspective through which to explore and understand the research topic. It is beneficial because it provides a basis for a hypothesis and choice of research methods. In the context of this study, to understand adherence behaviour in

the IDD population and how this relates to the general diabetic population it is important that concepts are defined and measured using a theoretical framework to explain the relationship between them. In this section, a discussion of existing theoretical frameworks included in the review and those presented in the wider adherence literature will take place. It will be concluded that a framework derived from the findings of this systematic review and based on social cognitive theory is the best fit for this study.

2.10.1 Theoretical frameworks applied to studies included in reviewed studies

2.10.1.1 *Health beliefs model*

Chao (2005) applied the health beliefs model which purports that the probability of engaging in a health behaviour is based on several personal beliefs; the perceived threat, the perceived benefits versus the perceived barriers, the perceived confidence (self-efficacy) and cues to action. This model supports the idea that adherence may be better understood if we try to understand the underpinning beliefs and motivations of those taking part. This is a person-centred approach, takes account of the underpinning principles associated with self-management interventions, for example, cognitive behavioural therapy or motivational interviewing. It is also consistent with NICE recommendations related to medicines optimisation. However, the results from this review did not suggest that a personal belief of perceived threat is a factor associated with adherence nor is there any suggestion in the IDD qualitative literature that adherence was impaired due to a fear of becoming unwell. Consequently, this model has been rejected.

2.10.1.2 *Self-regulation theory*

Mann (2009) used Leventhal's self-regulation theory which states that behaviour is regulated by one's beliefs. If a person believes that a certain behaviour (medicines adherence) will have a positive outcome on the goal (for example, improved health) then he or she will likely to adhere. Conversely if a person believes that certain behaviour (medicines adherence)

may have a negative outcome (such as, increased side effects or poor perception of health) then he or she is less likely to adhere (Cameron et al., 2003). Although Mann (2009) did explore the association of depression and self-efficacy on this self-regulation theory, the role of external influences, for example, social, family or health professional support, was not explored. This theory appears to address the individual's internal psychological motivations to adhere to treatment, however does not address the association between the psychological and social factors. Osborn suggests that social support is an important mediator for medicines adherence in type 2 diabetes, particularly in the presence of depression (Osborn & Leonard Egede, 2012). Furthermore, this review has suggested social support is a factor associated with adherence and, therefore, self-regulation theory was not a suitable theoretical model to underpin this research project.

2.10.1.3 *Readiness to change.*

Nelson (2007) applied the readiness to change model which identifies six stages of change that an individual will go through prior to instigating and sustaining behaviour change. The model was first developed by Prochaska et al. (cited in Leonard, 2013) and the six stages consist of pre-contemplation, contemplation, preparation, action, maintenance and relapse. This model was unsuitable for the proposed study for several reasons. Firstly, Nelson combined this model with self-efficacy and appropriate advice from medical providers to detect whether a stage of the readiness to change model and self-efficacy was associated with adherence to diabetes self-care. Therefore, this model was tested as a predictor of medicines adherence rather than a research paradigm underpinning the research study. The readiness to change model is not a validated measurement instrument and therefore associations of readiness to change to medication adherence should be interpreted with caution (Brug, Conner, Harré, Kremers, & McKellar, 2005; Norcross, Krebs, & Prochaska, 2011). The use of this model as a predictor rather than a research paradigm may also suggest that it is not appropriate to use in adherence

studies. Additionally, it explores one aspect of behaviour change instead of considering other aspects, for example, social circumstances and psychological health.

2.10.1.4 *Theory of planned behaviour*

A model more closely aligned with the proposed study was the theory of planned behaviour applied by Farmer (2006). This theory outlines three sets of behaviour that influence intentions and behavioural beliefs (taking medication will make me feel better), normative beliefs (my support worker will approve of me taking medication) and control beliefs (changes to my daily routine will make it more difficult to take my medication) (Ajzen, 1985). This theory requires a two stage, mixed method design (one qualitative and one quantitative). The first stage is face to face interviews to identify the key themes and to provide a structured topic guide for stage two questionnaires. There are, however, concerns relating to application of this theoretical model in this study.

Firstly, conducting semi-structured interviews prior to quantitative interviews may influence the behaviour of those participating in both stages of the study. If there is a large sampling pool to select from this may not be significant, however, with a smaller sampling pool, for example, people with IDD, it will be difficult to avoid using the same group of participants in stage one and two. This PhD study will be conducted in a health board with limited eligible IDD participants who will be eligible to participate.

Secondly, carrying out a semi-structured, qualitative interview prior to collecting quantitative data on the frequency of medicines adherence may result in participants or their carers becoming more aware of adherence behaviour and inadvertently changing behaviour before stage two data is collected. If adherence improves because of reflection on interviews from stage one overall, although positive, it may skew the results and overestimate the frequency of adherence in this group. For this reason, this model has been rejected.

2.10.2 Proposed theoretical framework

The theoretical models presented in this systematic review are not suitable for this research. However, a framework to provide a rationale for research design is beneficial. In this study, the theoretical framework is derived from a systematic review of the literature and the results are closely aligned to social cognitive theory.

Bandura's (1986), social cognitive theory states that actions are influenced by 4 main mechanisms namely, internal personal factors, affective and biological events, behavioural patterns and environmental factors. This theory acknowledges that human behaviour cannot be explained in terms of social structures or psychological factors alone, instead, it is the interaction between the two. Therefore, this theory states that behaviour of an individual will be related to their level of cognition, biological and affective factors which will be mediated by their socioeconomic conditions, family support, or social support which in turn will influence their aspirations and self-efficacy.

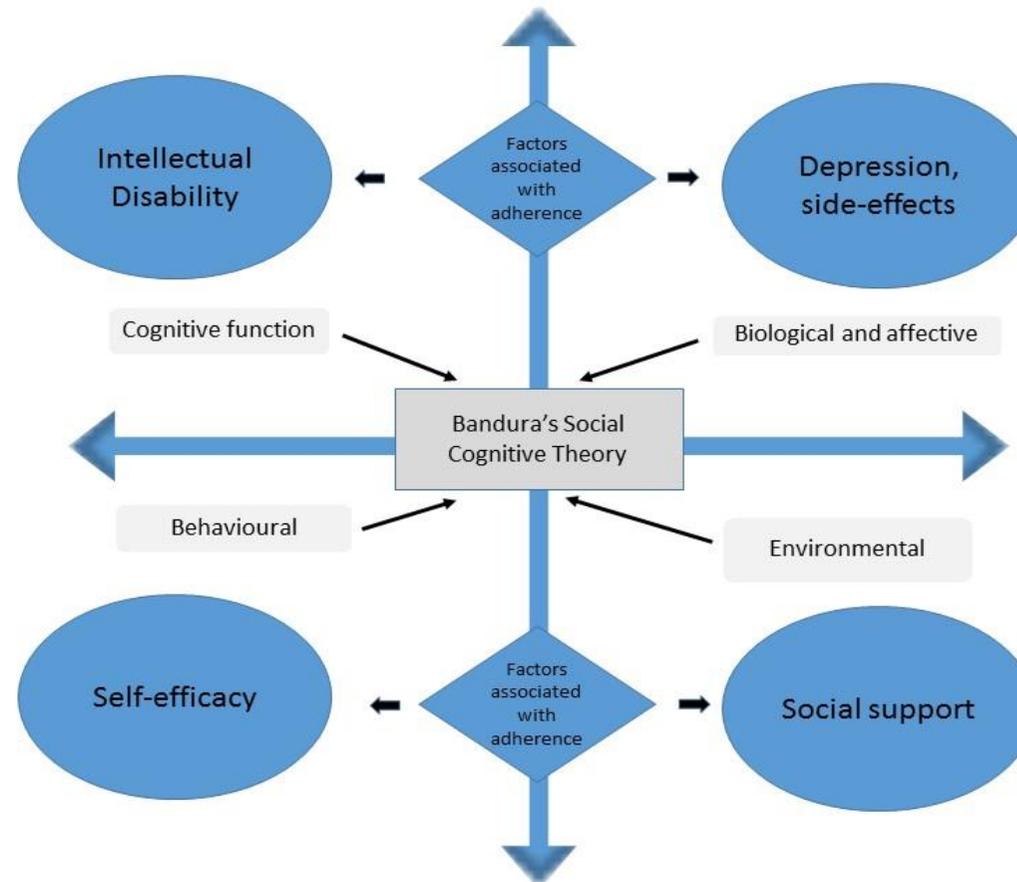
This systematic review revealed that (1) depressive symptoms, (2) side effects (affective and biological events), (3) self-efficacy (behavioural patterns) and (4) level of social or family support (environmental factors) are associated with medicines adherence in the non-IDD population.

Furthermore, Bandura states that personal factors such as cognition are a feature of this theory. This systematic review suggested that cognitive impairment affects adherence to medication (Rosen et al, 2003). People with ID may experience a range of cognitive impairment from borderline, very mild to profound. The target population in this study are those with mild to moderate ID whose cognitive and social functioning may range from the ability to live independently requiring minimal support to those requiring a higher level of carer support to optimise adherence. As there is no evidence on the impact that mild to moderate ID

has on adherence this study will explore whether mild to moderate ID, or other factors, are associated with adherence in this population.

In summary, based on the evidence derived from this systematic review, Bandura's Social Cognitive Theory is aligned most strongly. The proposed theoretical model (Figure 2.3) has been derived from results from studies conducted with the non-IDD population. This theoretical framework has not been tested previously in non-IDD medicines adherence research and the first to prospectively explore medicines adherence research in people with IDD.

Figure 2.3: Theoretical model derived from systematic review which informed study design



2.10.3 Summary of discussion

The initial aims of this systematic review were to (1) appraise the current research evidence on factors associated with medicines adherence in the diabetic population, (2) report on the quality of existing evidence and (3) propose an evidence based theoretical framework to predict medication adherence in people with and without ID and diabetes. The findings from this systematic review suggest there are three main shortcomings in the available evidence. Firstly, there is no published literature on medicines adherence in the IDD population. Secondly it is not known whether factors associated with adherence are the same in the IDD population and non-IDD population. Nor is it clear which of the factors identified from this review is most dominant in the non-IDD population.

This study is believed to be the first to establish the frequency of and factors associated with adherence in the IDD population. Research of this nature will identify whether the needs of the IDD population in terms of medication adherence are greater, different, less or the same as those in the non-IDD population. It will be the first to investigate associations between intellectual disability, depression, self-efficacy, side effects and social support, considering the effect regime complexity and support with medicines may have on these factors.

Carrying out a prospective study comparing demographics, adherence and associated factors in the IDD and non-IDD population will integrate people with ID into the research community. For example, prospectively comparing the IDD and non-IDD population and associations between depression and medicines adherence will detect whether depression is an independent predictor of non-adherence regardless of the presence of an intellectual disability, or, whether the presence of depressive symptoms combined with an intellectual disability puts the person with diabetes at greater risk of medicines non-adherence. Alternatively, if similar findings are identified in both populations, targeted interventions to support all service users

with depressive symptoms and diabetes may improve glycaemic control, quality of life and reduce mortality and morbidity, thus reducing health inequalities.

Therefore, this study will provide a unique contribution to gaps in adherence research. A theoretically informed evidence base will positively impact on medicines adherence and the lives of people with ID and diabetes. This may improve diabetic health, reduce the burden of disease and improve the quality of care provided to them by carers. In the wider context, this research may also inform the direction of future adherence research in other vulnerable groups, for example, people with dementia, mental health problems and those with more severe intellectual disabilities.

The methodology and methods by which these will be achieved will be outlined in the next chapter. This will clearly set out the philosophical underpinning of the research study design and the study protocol.

3 Chapter 3: Methods

3.1 Introduction

This chapter describes the approaches adopted to answer research questions and aims. The first section presents a critical appraisal of research paradigms, followed by a justification of the chosen research approach, the research design and methods. Each stage of the study will be detailed and include sampling strategy, recruitment procedures and timeline, data collection methods and analysis. Ethical consideration will be presented in the final section.

3.1.1 Research questions

The overarching research questions were derived from the results of the systematic review reported in chapter two and are:

1. What is the frequency of dependent (glycaemic control and medicines adherence) and independent factors (depression, side effects, self-efficacy and level of social support) in the IDD population compared to the non-IDD population?
2. Whilst controlling for regime complexity and support with medicines, does the proposed theoretical model predict medication adherence in the group overall, the IDD and non-IDD diabetic population?
3. Is the frequency of and factors associated with adherence consistent with the views of carers supporting diabetes medicines management?

3.2 Overview of study design

The PhD student was the researcher and was responsible for all aspects of the project including design, ethical approval, selection and recruitment, data collection and analysis. The project had a supervisory team of three consisting of two experts in learning disabilities and one in social sciences research. One supervisor was an expert in quantitative and the other two qualitative methodology.

To meet the research questions a cross-sectional, two stage sequential mixed methods study was designed, quantitative followed by qualitative. The first stage, quantitative, provided (1) descriptive statistics in the IDD and non-IDD groups, (2) verification of the reliability of instruments used, (3) correlations between medication adherence instruments and biomedical markers, (4) statistical estimates of the frequency of and factors associated with adherence in the IDD and non-IDD population and (5) testing the theoretical model and its ability to predict medication adherence in the IDD and non-IDD population.

Stage two was qualitative and provided an in-depth exploration of the interaction between carers and factors associated with adherence. This second stage was designed to triangulate the quantitative results and explain the interaction between support for medicines management on one hand and psychological, biomedical and social factors associated with adherence in the other, in the study population.

3.3 Methodology

3.3.1 Research paradigms

Research paradigms are defined as theoretical perspectives or, in simple terms, models or examples (Corbetta, 2003). They involve setting down a set of beliefs and demonstrating how they have influenced the research design. Corbetta (2003) outlines three factors which shape a research paradigm, firstly, ontology, meaning the way that reality is constructed, what is reality or how something works; secondly, epistemology, meaning how we know something and what our relationship is to that knowledge, and, finally, methodology or how we go about finding out about knowledge.

To achieve this, consideration of the three main research paradigms is necessary namely, positivist, constructivist, and pragmatic paradigms. Following consideration of all three, it will be concluded that the method that will most effectively answer the research questions is a pragmatic paradigm using mixed methods quantitative and qualitative research design. A justification for this will be presented followed by the methods that the research study will follow during each stage of the study.

3.3.2 Positivist paradigms

This involves collecting data that is objective, generalizable and quantifiable. This is achieved through collecting sufficient quantities of numerical data to allow for statistical analysis to test predetermined hypotheses (Creswell, 2014). Where it is hypothesised that the cause is related to the effect, confounders can be eliminated through carefully selected eligibility criteria and appropriate, systematic, statistical analysis. This aims to eliminate bias and increase objectivity. In this paradigm, there is a structured standardized approach to methods resulting in easily replicable studies and findings from a variety of studies to be compared.

This paradigm is deductive and, provided the sample population is sufficiently large and representative of the general population, findings are generalizable and can be impact on policy and practice through proof or rejection of a hypothesis. However, proving or disproving a hypothesis will only be valid if sufficient rigour is applied to research design. Lack of rigour will invalidate research findings and render the research poor quality. It is therefore important to consider what constitutes rigour in positivist paradigms or quantitative research.

3.3.2.1 *Rigour and positivist paradigms*

Designing a study with sufficient rigour involves adopting a methodology that eliminates bias, maximises objectivity and generalisability (Armijo-Olivo et al, 2012). The four key markers associated with rigour in a positivist paradigm are validity, reliability, replicability and generalisability (Cunningham, 2013) and are key features of quality appraisal tools, such as, the EPHPP tool applied in the systematic review presented in chapter 2 (Effective Public Health Practice Project, 2004).

Validity is related to the extent to which a concept is accurately measured in a study (Creswell, 2014; Jason, 2008). Specifically, it will be concerned with how the researcher sampled the study population, selected and applied data collection instruments, applied statistical tests to test hypotheses and, whether congruency in sampling, analysis and presentation of findings is trustworthy, reliable and therefore, generalizable.

Selection bias may occur if the sample population is drawn from one site, clinical area or demographic. Probability sampling techniques are the most common ways to produce unbiased results and techniques such as random sampling, systematic sampling, stratified sampling or cluster sampling are ideal. Random sampling involves taking the whole population and sampling by chance meaning that each member of the population has equal chance of being selected (or not). Systematic sampling is when every Xth person in the sample is invited to participate, stratified sampling is when a group from the sample is selected to participate and

cluster sampling is when a cluster (e.g. household or ward area) is randomly selected to participate in a study.

With regard to data collection instruments, using a validated instrument during data collection and controlling for external influences or bias (confounders) when analysing data will increase the validity of the research (Pounder, 1993). Validity may also be assessed by measuring the correlation between two measurement instruments measuring the same or similar outcomes. If those results are similar the results have greater validity.

Reliability of results is related to the internal consistency of the measurement instrument using a statistical test, for example, Cronbach's alpha. How the instrument responds during repeated measures with the same respondent or against an instrument measuring a similar outcome will also test reliability.

Replicability is concerned with whether repeated application of the same methods will produce the same results if carried out by another researcher. Transparency in recruitment, data collection and analysis is important to allow for replicable results.

Finally, generalisability is the applicability of the results to the larger population or similar situations. Results that are generalizable are more meaningful because there is greater likelihood of applicability to a large cross section of society, and may have greater impact on policy than those that are not.

3.3.2.2 *Limitations of positivist paradigms*

There are limitations associated with this approach; it is inflexible and does not explain contextual factors that may interpret or explain erroneous results or outliers more fully. Validated instruments do increase objectivity but collecting data on sufficiently large numbers is expensive and time-consuming and, if not analysed using appropriate statistical tests, may yield invalid results.

Some would argue this paradigm oversimplifies a complex world with many interactions influencing the outcome of any given situation (O'Cathain & Thomas, 2006). This is a particularly relevant point when conducting health services research. Quantitative studies may prove or disprove a hypothesis but they will not inform how or why intervention was successful or not, nor the reasons for associations in one group but not another.

To fully understand the findings of a study, interviewing those delivering or receiving care using a more constructivist approach may provide in-depth exploration and more comprehensively inform future policy or research. In the context of this study it has limitations in that it does not address the exploratory aspects of research question three.

3.3.3 Constructivist paradigms

Constructivist paradigms will generate a rich description of viewpoints, beliefs and meaning (Corbetta, 2003; Hannes, 2011; Murphy & Dingwall, 1998). Within a constructivist paradigm there are two main approaches, (inductive and deductive) with a third (abductive) emerging.

To explain further, a deductive approach is concept-driven and tests existing theories and models; inductive approaches look at similarities in the data and generate themes from these (Creswell, 2014). Inductive tells a story and purely describes the phenomenon as it emerges from the data whereas deductive explains a phenomenon in the context of the world and existing concepts and theories thus translating easily back to the practice setting.

There are limitations to both (Graneheim, 2017); Inductive is at risk of describing situations rather than analysing and exploring in more depth, and deductive may not identify new or emergent themes which did not fit the explanatory or theoretical model. A third approach, an abductive approach promotes movement backwards and forward between inductive and deductive. The latter approach suggests a more flexible and in-depth approach to qualitative research (Udo, 2014).

Common to all approaches is the acknowledgement of the importance of the role of the researcher and context of the study in shaping those views and producing the final report. Epistemologically, the researcher's relationship to the research process will shape the research design and interpretation of results (Findlay & Gough, 2003). This subjectivity is a key difference between constructivist and positivist paradigms and the ability to explain concepts and theories through the analytical lens of the researcher is unique to this approach (Kumsa, Chambon, Yan, & Maiter, 2015).

Within constructivist paradigms there are three main methodologies namely phenomenology, ethnography and grounded theory. Following a brief overview and critique of these, a fourth paradigm, the generic approach, will be argued as a methodology suitable for this study.

3.3.3.1 *Common approaches to qualitative research*

A phenomenological approach is a conscious experience from the first person or subjective point of view. It offers a reflective and deep exploration of a real world experience (Creswell, 2014). This qualitative methodology provides an in-depth exploration of self, perception of the world and others, linguistic activity, social interaction and culture. In summary, it is the exploration of lived experiences and how they are perceived, or explained, by the research participant.

Ethnography provides a broader approach within which qualitative research is structured and is built upon the social science specialism, anthropology (Murphy & Dingwall, 1998). This is the study of cultures and behaviours within society, and ethnography is the study of culture groups in their natural setting over a long period of time. It is therefore a descriptive account of social life and culture within research setting. This approach should not be interpreted beyond the case it describes; instead it is a form of story-telling which provides a snapshot of the participants lives, culture, thoughts and feelings (Karen & Reilly, 2009). It is a method of

deep research involving large amounts of time observing, recording and interpreting the culture and behaviours of the group.

Finally, grounded theory methodology is iterative and involves generating theories from the data collected. It is complex and starts with general broad questions from which themes emerge and form tentative links with theory (Draper, 2001). The data obtained and themes emerging from the data inform subsequent interviews. Data collection ends when the researcher concludes that there are no new themes emerging from the data and thus ‘saturation’ has been reached.

3.3.3.2 *Generic qualitative approaches*

Generic qualitative approaches are research that is not guided by an explicit set of philosophical assumptions in the form of the known qualitative methodologies, rather the approach is guided by the research question posed (Caelli, Ray, & Mill, 2003). Thorne (2004) suggests that this methodology has genuinely practical application and bridges the theory practice gap (Auta, Strickland-Hodge & Maz, 2017). Therefore, a generic approach encourages new ways of looking at recurring problems, has the potential to develop research innovation and promote excellence in constructivist paradigms by being more flexible and practical, however there is some scepticism towards this research approach.

This scepticism appears to be as a result of (1) lack of philosophical underpinning to support methodology, (2) lack of literature to support the research approach and (3) opacity in relation to methods adopted (Caelli, et al, 2003). In the next section these criticisms are acknowledged but rebutted, arguing that the emphasis should be on the robustness of the methods rather than the philosophy underpinning the methodology. Instead, articulation of a transparent and ethical research process, contextual to the research question and demonstrates robustness, credibility and validity during research design, data collection and analysis takes precedence over the pursuit of a specific research methodology will be argued.

3.3.3.2.1 *Limitations of generic constructivist paradigms*

Generic qualitative approaches have been criticised as being ‘...not good science’ and, without a philosophical underpinning for research, are a mismatch of different methodologies (Kahlke, 2014). However, grounding oneself in a research methodology that makes linear theoretical assumptions about the research approach may not be a logically sound approach either. To propose any methodology is fundamentally correct may be a difficult philosophical stance to adopt. For example, phenomenology assumes that one in-depth subjective viewpoint will describe a phenomenon most accurately, and, acknowledging it does provide an in-depth description and interpretation of that situation, it does not allow for the consideration of cultural and societal perspectives that ethnography may do. Neither of these approaches appear to put any emphasis on ‘data saturation’, where data collection is halted when there are no new concepts emerging, which is a fundamental feature of grounded theory methodology.

Adopting a more generic methodology requires consideration of all research methodologies, contextualisation to the proposed research study and, deliberation as to which of these is best suited to addressing the research question. This process may not be as rigorous if a strong philosophical stance is adopted where certain rules and assumptions are made and without consideration of alternatives. In addition, some commentators suggest that the myriad of philosophical approaches associated with qualitative research adds to the confusion and scepticism associated with constructivist paradigms (Smith, Bekker, & Cheater, 2011; Thorne, 2011; J. Williams, 2013). They purport that less emphasis on philosophical standpoint and more on alignment to research questions and aims may result in greater understanding of constructivist paradigms.

A lack of literature to support this research approach also attracts criticism. Caelli (2003) argues that a robust research framework is built upon its use by a well-established research community whose experience is reported in the literature. Without this, it is argued, quality of

the research may be compromised, resulting in lack of rigour and invalidating results. However, a body of literature supporting this approach can be found (Auta et al, 2017; Caelli et al, 2003; Cooper & Endacott, 2007; Kahlke, 2014; Kennedy, 2016; Smith et al, 2011; Williams, 2013), suggesting that support is growing for this approach.

3.3.3.2 Rigour and constructivist paradigms

Like any craft or skill, there are certain rules and guidance that are best practice and will help others to develop that skill. Best practice in qualitative research is structured and transparent whilst preserve flexibility and creativity.

Therefore, a well-designed research framework consisting of broad assumptions about the nature of knowledge, theoretical framework, methodology and methods and techniques or procedures used to analyse and gather data will improve external validity of qualitative research (Cresswell et al, 2007). These rules are not dissimilar to quantitative research and a number of commentators have proposed frameworks (Caelli et al, 2003; Kennedy, 2016; Tracy, 2010), however the gold standard for measurement of rigour is that proposed by Lincoln and Gubba (Brown, Elliott, Leatherdale, & Robertson-Wilson, 2015). They propose five main criteria: credibility, confidence in the findings, transferability, such as, applicability of findings to other situations, dependability, and confirmability (Draper, 2001). These concepts have similarities to quantitative research in that they suggest that credibility is aligned to validity, transferability to objectivity, dependability and confirmability. Although there may be similarities, the differences lie in how these criteria are met when using a constructivist research approach. These differences will be outlined in the section below.

3.3.3.3 *Credibility*

Credibility is a key marker in both qualitative and quantitative research and, although reached through different means, it has the same goal, that is, to make the results believable and give readers sufficient trustworthy evidence to act on the findings of the research. Credibility in constructivist research is characterised by its richness, relevance and methods used to collect and analyse data and is achieved through detailing methods of sampling and data collection, triangulation of results or third party verification of findings during data analysis (Bourgeault, 2010).

Unlike positivist paradigms, there is no absolute number or statistical calculation that determines sufficient sample sizes producing significant results. Therefore, the amount of data, number of participants and length of interviews are dependent on the aim of the research. However, if the length of interview is insufficient to allow for the generation of rich exploratory and explanatory data, credibility of results may be called into question. Moreover, credibility of findings is determined by the sample population, the uniqueness of the data, the types of questions asked and the level of verification of the data once collected. Whether a population is conveniently sampled, according to pre-set criteria, or selected by a named informant and how this is justified and aligned to the research question is an important factor when assessing the quality of a constructivist paradigm (Draper, 2001). For example, if the researcher is exploring the perceptions of parents, sampling only mothers may skew the result and introduce bias as the male parent group have been excluded.

When analysing qualitative data choosing, organising and analysing data in qualitative research is led by inductive analysis (Straus and Corbin, 2008), patterns and emergent themes come from the data rather than being derived from an external source, for example, literature or research aims. However, data presented in this way may produce irrelevant results unrelated to the research question and may affect the transferability of findings. A more structured

approach consists of three main questions that should be posed when analysing qualitative research: (1) ‘what is the data telling me’, (2) ‘what is it I want to know’, (3) ‘what is the relationship between what the data is telling me and what I want to know’ (Caelli et al, 2003). These three questions provide a focussed approach to data analysis that answers the research question and identifies new themes emerging from the data. Once data has been analysed by the researchers, confirming those results through third party verification is important.

3.3.3.4 *Dependability and confirmability*

Verification of the data by an independent party, for example, a second researcher or research participants, will improve the dependability and confirmability of the results. Tracy (2010) describes multiple approaches to meeting these two quality criteria including thick description, multivocality and impartiality. This verification of data typically occurs in all research approaches and confirms the methods adopted in data analysis were accurate and were free from bias. The most frequently used method to confirm findings and create dependable results is triangulation. This is a method of collecting data from a number of different sources, or using different methods to collect the same information (Moran-Ellis et al, 2006). For example, ethnographic studies may be combined with semi-structured interviews to confirm or dispel emergent themes from the initial stage of the study, or interviews with parents and carer on the same subject may be a feature of qualitative research. Equally, qualitative methodology may be employed to triangulate quantitative findings.

3.3.3.5 *Transferability*

Acknowledging the researcher’s relationship with the process (reflexivity) is an intrinsic aspect of transferability. Reflexivity, rather than being viewed as bias, is regarded as a strength within contemporary qualitative research as it allows the unique understandings of the researcher to be transparent within the study findings (Findlay & Gough, 2003). Berger (2015) argues that researchers focus on self and its role in the creation of knowledge, and

how the researcher's bias, values and attitudes may shape the interpretation of the data. To ignore the subjective position of the researcher is to reject the key protagonist in the research process.

Furthermore, allowing researchers to position themselves in this way and acknowledge the challenges, support and unexpected results of the study will generate discussion within the readership. If readers can identify similarities between the researcher and their own experiences, contextualisation and testing of results in their own cultures may happen more readily (Berger, 2015). This transparency within a sufficiently robust study will produce verifiable results that will not only have relevance to the academic community, but demonstrate new knowledge and future areas of clinical research. Moreover, answering the questions posed will have relevance to clinical practice by directing resources to support those most in need and ultimately have an impact on health outcomes.

However some are concerned that applied research is tainted and risks introducing bias and interfering with the research process (Corbin & Strauss, 2008; Karen & Reilly, 2009). This view suggests that research is for research sake, an end rather than a means to an end. This viewpoint preserves the craft and art of methodology grounded research and has specific relevance to the academic community. However, a balance between strict alignment to theoretical qualitative approaches and building robust evidence to inform practice is vital for healthcare research.

In summary, positivist and constructivist approaches are at opposing ends of the methodological spectrum particularly in relation to objectivity and interpretation of truth; however, the principles of rigour, relevance and transferability apply to both. The difference is in how rigour is presented and evaluated and whether the methodology adopted answers the research questions. Taking an ideological stance and claiming one approach is superior to another, does not acknowledge the strengths of problem focussed research.

3.3.4 Pragmatic paradigms

Pragmatic paradigms involve designing a research study that is best suited to the research questions and driven by anticipated consequences (Teddlie & Tashakkori, 2009). This is in contrast to adhering to a strict research philosophy or paradigm, for example, a positivist or constructivist approach (Andrew et al, 2013). Protagonists of positivist or constructivist paradigms tend to focus on the differences between the two approaches and their incompatibilities as opposed to supporters of pragmatic paradigms who seek out similarities between approaches and how a combination of approaches can answer the research question (Smith et al, 2011). Pragmatic paradigms shift the emphasis from the philosophical standpoint to problem solving, and are interested in the social construct within which the problem exists. Pragmatic paradigms tend to favour mixed methods approaches to answer the research questions. This is method adopted for this PhD study.

Ozawa (2014) identified from the literature around 19 definitions of mixed methods research and is a method of research that mixes quantitative and qualitative data in a single or series of research studies to answer the research questions (Cresswell et al, 2007). Core characteristics are; firstly, both qualitative and quantitative data is collected and analysed using sufficient rigour and sample sizes to generate meaningful results; secondly, data is integrated during collection, analysis or discussion and the study is framed in a philosophical or theoretical model of research.

This research approach one of the fastest growing areas and now accounts for around 30% of health services research (O'Cathain, Murphy, & Nicholl, 2007a) . This growth may be due to recognition in the research community that there are strengths and weaknesses in all research methodologies, and one size does not fit all. However, the credibility of this research approach is dependent on rigour and how integration of the stages take place.

3.3.5 Rigour and mixed methods research

O’Cathain et al (2006) purports rigour in mixed methods studies involves a clear justification and applying relevant rules and standards of rigour to each stage . The GRAMMs6 criteria for assessing rigour in mixed methods research is emerging as a popular appraisal tool (Brown et al, 2015; Cameron, Dwyer, Richardson, Ahmed, & Sukumaran, 2013).

Specifically, the six criteria include:

1. a clear justification for this research approach,
2. how methodological rigour was applied to each stage of the study including theoretical underpinning, purpose, sequencing and stage of integration,
3. methods for each stage including sampling, collection and recruitment and how rigour was applied to each stage of the research approach.
4. how each stage was integrated including where integration occurred, how it occurred and who participated in it,
5. identifying limitations of integrating methods and
6. insights gained from integrating methods.

In the next section, a justification of this research approach will be provided, the approach to methodological rigour, will be described and limitations of mixed methods will be addressed.

3.4 Justification for a mixed methods approach

The researcher’s philosophical position is that conducting health services research with service users requires designing a study to explain complex interactions. Epistemologically, the world-view and the background of the researcher will influence the interpretation of research findings and subsequent development of meaningful and actionable recommendations. This is also consistent with the theoretical framework underpinning this

study that a person's actions (medicine adherence in this study) are explained by complex interactions between social, cognitive, environmental and biological factors.

Adopting either a constructivist or positivist research approach is not aligned to the researcher's philosophical position, nor would doing so fully address the research questions set out in Section 3.1.1. Qualitative methodology would not address research questions 1 and quantitative methods would not answer research question 2. It is acknowledged that a qualitative approach in medicines adherence in the IDD population is a valid study design and would generate new knowledge, but it would not address the overall aim, that is, to establish the frequency of, and factors associated with, medicines adherence. Without numerical data to quantify the frequency of adherence and to explore statistical associations between medicines adherence and independent factors, the research questions cannot be answered. Hence, this study requires a mixed methods approach using both qualitative and quantitative methodology.

Therefore, a two-stage cross-sectional, explanatory mixed methods design was adopted to answer the research questions.

Without this new knowledge, interventions to improve adherence in people with IDD have no evidence to support them, and may misdirect healthcare and research resources. Table 3.1 illustrates the questions and philosophical approach to each stage. The overall design was intended to draw on the strengths of each approach whilst addressing weaknesses of the other.

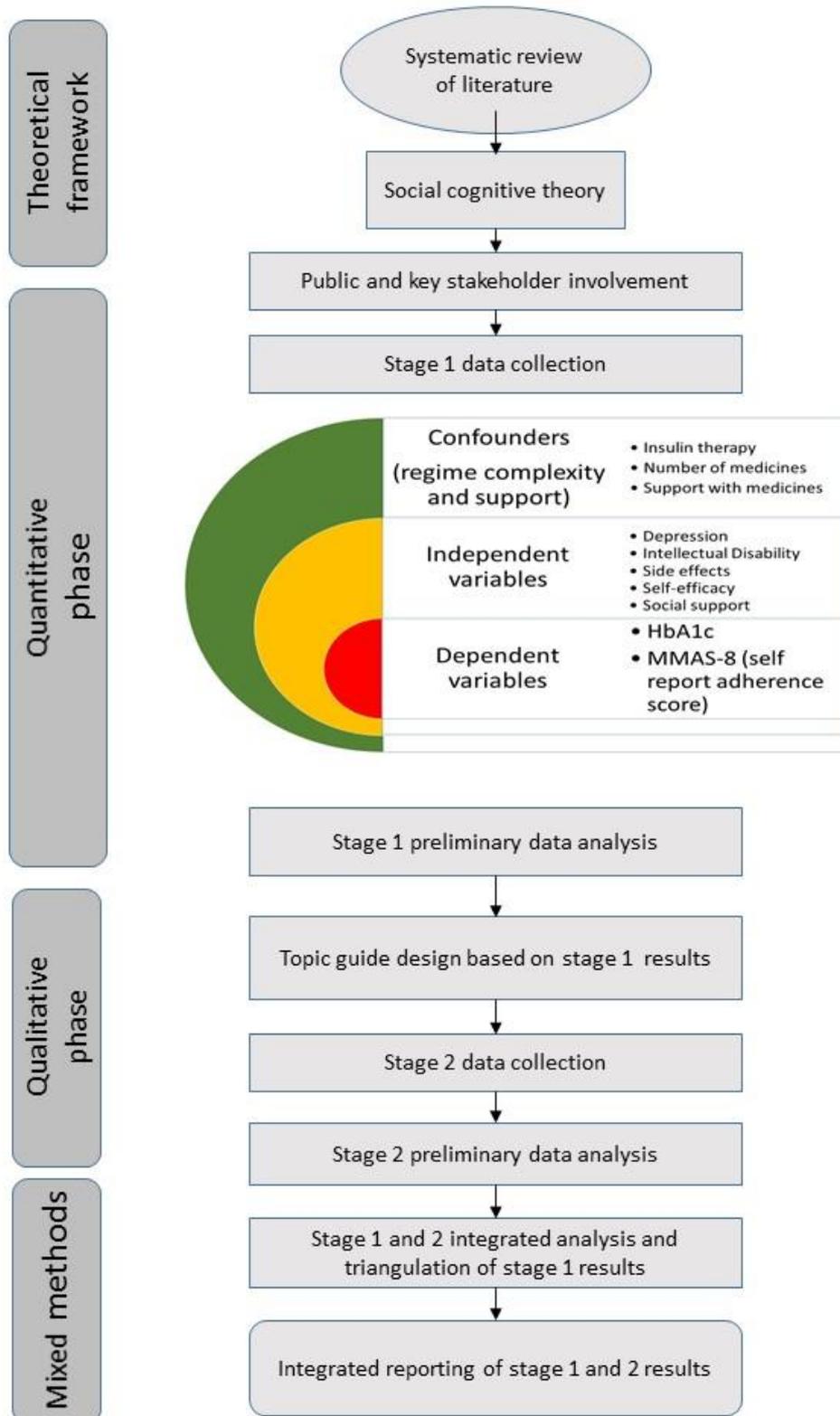
Table 3.1: Research questions aligned to philosophical underpinning

	Research question	Ontology	Epistemology	Methodology	Paradigm
1.	What is the frequency of medicines adherence (glycaemic control and medication adherence) and associated factors (depression, side effects, self-efficacy and level of social support) in the IDD population compared to the non-IDD population?	Objective	Experimental testing hypotheses	Quantitative	Positivist
2.	Whilst controlling for regime complexity and support with medicines, does the proposed theoretical model predict medication adherence in the group overall, the IDD and non-IDD population?	Objective	Experimental testing hypotheses	Quantitative	Positivist
3.	Are the frequencies of, and factors associated with, adherence consistent with the views of carers supporting diabetes medicines management?	Interpretative / Explanatory	Explaining/ verifying theory	Quantitative	Constructivist

3.4.1 Study design

Figure 3.1 provides a diagrammatic illustration of study design. For research questions 1 and 2, a quantitative comparison between the IDD and non-IDD diabetic populations was undertaken because it was unclear whether similar factors were associated with medicines adherence in the groups. The research was prospective and designed to be sufficiently comprehensive to make an objective and generalizable estimate of the frequency of medicines adherence in the study population. Research question three was explanatory and interpretative and therefore, qualitative. Predominantly, it was seeking a more in-depth explanation and triangulation of findings from research questions 1 and 2. However, identifying emergent new theories was important, therefore an abductive approach (Graneheim et al, 2017) was adopted.

Figure 3.1: study design



3.5 Methodological rigour

Methodological rigour is associated with priority, sequencing and stages of integration. Taking each one of these in turn, and for ease of explanation, each of these concepts will be contextualised to this study.

3.5.1 Priority of methods

Priority of methods means emphasis, or weighting, placed on each stage of the study. Each stage may have either equal weighting or greater emphasis may be placed on either the qualitative or quantitative (Teddlie & Tashakkori, 2009). The primary aim of this study was to establish associations between dependent and independent factors in the IDD and non-IDD population, therefore greater priority and weighting was placed on the quantitative stage.

3.5.2 Sequencing

In explanatory mixed methods the collection and analysis of quantitative data is followed by collection and analysis of qualitative data (Cresswell et al, 2007). The benefits of this approach are that it has two distinct stages that are straightforward to implement, and, for a lone researcher, allows one stage of data to be collected at a time. In this study, preliminary analysis of stage one data before qualitative interviews with carers supported triangulation of stage one results.

Stage two was particularly important for the IDD population. Despite a high proportion of people with ID affected by diabetes and other medical conditions (Amanda & Hayley, 2011; Haveman et al, 2011; Torjesen, 2013) they are rarely recruited to, and, often excluded from, research (Witham, Beddow, & Haigh, 2015). During research design, discussions with experts in the field of ID and scoping of the ID research literature, highlighted barriers to recruitment that risked the ID sample being insufficiently powered to produce credible and reliable associations between adherence and associated factors.

Barriers to recruitment are practical, ethical and restricted by using gatekeepers for access to potential participants (Jepson, 2015; Witham et al, 2015). A systematic review reported recruitment to studies was far greater when ID participants were recruited directly rather than through a carer or significant other (Cleaver, Ouellette-Kuntz, & Sakar, 2010). This suggests carers exercise caution when nominating people with ID for research. Their intention is to protect the interests of this vulnerable group perhaps fearing participation will unnecessarily burden a person with ID (Jepson, 2015; McDonald, Keys, & Henry, 2008; Morrisey, 2012). This may be because of limited understanding of the value of research, or a fear of exploitation of vulnerable groups based on unethical practice in previous research (Kars et al, 2016).

To mitigate barriers, triangulating the first stage with a second qualitative stage was agreed by the research team to be methodologically viable, and aligned to previous studies in people with ID (Cuthill, Espie, & Cooper, 2003; Tvetter, Bakken, Røssberg, Bech-Pedersen, & Bramness, 2016). This approach provided a carer perspective of stage one results, and, if results from stage one and two were consistent and coherent, evidenced carer and stage one participant perspectives were aligned. Conversely, incongruous views of adherence and associated factors between stage one and two would require further exploration.

Although using face-to-face interviews, rather than online or postal questionnaires, facilitated accuracy of stage one data collection, it did not fully explain anomalies emerging from the quantitative data. If, for example, there was a mismatch between HbA1c and medicines adherence scores in the one population, but not in the other, exploration of other aspects of diabetes care with carers would be required to provide more in-depth explanation. Therefore, the second stage provided an opportunity for further investigation and explanation of potential anomalies.

Finally, there is very limited evidence on factors associated with adherence in the IDD population. To identify new and emergent themes, it was important to explore with carers whether there were any additional factors that influenced diabetes medicines adherence in the IDD population. Acknowledging effective glycaemic control involves a healthy lifestyle and adherence to medicines, an exploration of which were perceived by carers to be most challenging was important. A qualitative approach was therefore essential to validity and reliability of results, to explain any inconsistencies in the data and to identify any additional factors associated with diabetic treatment adherence.

3.5.3 Stages of integration

Integrating data in mixed methods research is achieved by comparing and contrasting results after analysis of each stage, or, analysing the data collected from each stage simultaneously (Teddlie and Tashakkori, 2009). Analysing the two data sets separately using recognised methods of data analysis preserves the integrity of each and permits flexibility when reporting and publishing results. In this study, the results from each stage are reported separately in chapters 4, 5, and 6. Integration occurred during design of topic guide, analysis and reporting of results. Thematic analysis of data in stage two was based around the topic guide and preliminary results from stage one. In chapter 6, stage two results are considered in the context of preliminary stage one results. Full integration and triangulation of results did not occur until the discussion chapter of this thesis where both sets of results were compared, contrasted and analysed.

3.5.4 Limitations of research approach

In a systematic review (Brown et al, 2015) of 23 mixed methods studies in education research, it was reported that none of the studies fully met the above criteria. This was largely because rigour in each research approach was not fully explained in the selected review papers. O’Cathain’s (2007b) review of 75 health services research papers published over a 10 year

period revealed similar findings, but also suggested that integration of qualitative and quantitative results was rarely discussed in proposals or papers. This suggests that in mixed methods research qualitative and quantitative stages are presented independently resulting in a consecutive rather than integrated reporting of results (Brown et al, 2015). O’Cathain (2007a). This lack of integration during the results stage of a research study may affect the credibility of this research approach.

Pragmatic paradigms and, specifically, mixed methods approaches can test the skills, resources and philosophical standpoint of the researcher and often will require a large multi skilled research team to effectively implement. Although this does not lend itself to PhD research the skills of the supervisory team and previous knowledge and skills of this PhD student facilitated mixed methods research in this study. In this study, the supervisory team had expertise in qualitative and quantitative research and the PhD student had carried out both qualitative and quantitative research previously, therefore this experience supported a mixed methods approach. Although the process is resource intensive and results in an extensive report, agreement within the team was there was no alternative paradigm to comprehensively answer the research questions.

In summary, this section of the thesis has provided a justification for the study design, and has justified the mixed methods approach, sequencing and weighting of stages taking into consideration context of this research project. In accordance with GRAMMS6 criteria, the next section of this chapter will outline the methods for each stage of the study.

3.6 Methods

A breakdown of each stage of the study outlining the hypotheses or, in the qualitative stage, aims to be explored will be presented. Following an outline of service user and key stakeholder feedback, a detailed description of procedure and timeline, sampling, recruitment, data collection, and data analysis for stages one and two will be presented. As ethical considerations in stages one and two are similar these will be discussed in the final section of the chapter.

3.7 Key stakeholder engagement on instruments and study design

Involving key stakeholders in adaptation of instruments and study procedure had four aims:

1. To verify comprehension of information contained in participant information leaflets (PILS), consent forms and data collection instruments (Appendices 3-8) with key stakeholders including people with IDD
2. To revise data collection methods and instruments as necessary
3. To test comprehension and duration of an IDD service user interview
4. To identify a group of named informants who would seek out eligible IDD and non-IDD participants.

3.7.1 Procedure and timeline

A purposive sample of NHS Lothian specialist ID and diabetic nurses, allied health professionals, carers and medical consultants with an interest in diabetes and ID together with two people with mild to moderate ID were invited to comment on the data collection instruments. For ease, the researcher requested to attend any existing meetings and with key stakeholders namely, learning disability nurses, general practitioners and diabetes specialists.

The research procedure, PILs, consent and data collection instruments were reviewed and commented on for comprehension, accessibility and time taken to complete. Major changes to the instruments would invalidate the results of the study, therefore minor amendments to the

layout rather than content was sought. These changes were intended to identify the use of explanatory symbols and minor linguistic changes to clarify those statements that people with ID may have found confusing. In so doing, the intention was to maximise the ability for those with mild to moderate ID to fully comprehend all items within the scale.

This stage also provided data on the average time for each interview. Data collection was carried out by the researcher in participants' homes or any other suitable place of their choosing. All participants were given the opportunity to have a support person with them during the consent and data collection stage. The interviews were timed and a mean time calculated.

Identification of named informants occurred at this stage. Named informants were general practitioners, clinical managers, specialist nurses and general practice managers. A database of named informants was held on a password protected computer. Once identified, they were informed of the study via email and at management and specialist practitioner forums. This gave named informants the opportunity to meet with the researcher, and seek any clarification on the study's purpose and participant inclusion criteria. It also confirmed their agreement to be contacted to identify participants. As this aspect of the study was exploratory there was no statistical evaluation, instead the outcome of each aim is presented below. This took place between June and July 2014.

3.7.2 Verification of Participant Information Leaflets (PILS), consent forms and data collection instruments with key stakeholders

Ten key stakeholders commented on consent forms, recruitment and data collection methods. The PhD supervisory team (n = 3), one ID nurse specialist, a research assistant, one diabetes specialist research nurse, an ID nurse manager and a professor of endocrinology and diabetes commented on the comprehension of PILS, consent and data collection instruments, recruitment and method for collecting HbA1c results. A speech and language therapist offered

advice on readability specifically on the questionnaires. Three recommendations were made for the participant information sheets and questionnaires by specialists in ID practice and research.

The first was to modify sentence construction to short sentences in an easy read format and to use Board maker® to provide a pictorial representation of the text. Easy read is recommended for use by the British Institute for people with Learning Disabilities (BILD) to improve comprehension of text materials for people with intellectual disabilities. Board maker® is an assistive device which uses facial expressions and symbols to explain the text within a document. It has previously been used in studies with patients with ID and was used to validate the GDS-LD, a scale used in this study to assess depressive symptoms (Cuthill et al, 2003).

Secondly, researchers in the field of ID recommended development of a very brief participant information sheet that could be distributed to generate interest in the study with the full participant information sheet distributed after this. This was intended to provide a staged introduction about the study to the IDD population.

Thirdly, the diabetes research nurse and professor in endocrinology recommended, for ease of data collection of HbA1c results, that they could be drawn from a central database by a NHS employed diabetes specialist research nurse.

3.7.3 Comprehension and duration of an IDD service user interview

Following linguistic modification and insertion of explanatory symbols the instruments were tested on 2 people with ID and diabetes in a face to face interview. Time to complete the questionnaires was also recorded.

One interview was conducted in the presence of a carer and one with the IDD participant only. Neither participant wished to complete the questionnaire alone and instead sought the

support of the researcher to insert their response to the questionnaires and explain more complex questions. Although the presence of a carer was beneficial to provide further explanation to the IDD participant as additional explanations were required for the perceived sensitivity to medicines and self-efficacy scales, both participants could answer the questions with ease.

Participant 1 took 40 minutes to give informed consent and complete the questionnaire and participant 2, one hour. Mean time was calculated at 50 minutes. This gave the researcher an estimated time to allocate for interviews. To ensure an unhurried approach to the data collection participants were allocated 1 hour for all stage one interviews.

3.7.4 Identification of named informants

Named informants disseminated information about the study throughout their networks. Named informants included 7 key stakeholders, 2 general practitioners, 1 specialist diabetes research nurse, 1 diabetes specialist nurse, 2 ID nurses and one informant from a private social support service. These were drawn from all regions within the local NHS board, Community Health Partnerships and City Council.

3.7.5 Outcome of key stakeholder involvement

Recommendations from key stakeholders were reflected upon by the research team and amendments were made to PILs, consent forms and data collection instruments (Appendix 3-8). Time allocated to interviews, HbA1c data collection and contact with named informants were added to the research protocol and enhanced study design.

3.8 Stage 1: quantitative

Stage one answered research questions 1 and 2:

1. What is the frequency of medicines adherence (glycaemic control and medication adherence) and associated factors (depression, side effects, self-efficacy and level of social support) in the IDD population compared to the non-IDD diabetic population?
2. Whilst controlling for regime complexity and support with medicines, does the proposed theoretical model predict medication adherence in the group overall, the IDD and non-IDD diabetic population?

3.8.1 Sampling strategy

Sampling was based on achieving a representative sample of the study population whilst also achieving sufficient sample sizes for statistical power. Following NHS and university ethical approval (Appendix 2), a convenience sample of adult mild to moderate IDD and non-IDD participants over the age of 16 years was drawn from central diabetic databases, community and acute care ID liaison teams, social support organisations, out-patient departments and general practices in NHS Lothian.

3.8.2 Sample size

To generate sufficient statistical power for a multiple regression analysis a sample of $n = 109$ was required. The number of participants was derived from a power analysis using G*Power 3.1.5 (Faul, Erdfelder, Lang, & Buchner, 2007) with $\alpha = 0.05$ and power $(1 - \beta) = 0.80$, and assuming a medium effect size ($f^2 = 0.15$). This was to detect the significance of each of the independent factors (ID, depression, self-efficacy, side effects and social support) associated with medicines adherence.

3.8.3 Inclusion/exclusion criteria

The inclusion and exclusion criteria are outlined in Table 3.2. Given the paucity of research in IDD services users and no available research on comparisons between IDD and non-IDD participants this research was conducted with those who could independently consent. Stage one inclusion criteria sought to strike a balance between recruiting participants who could independently consent and be explicit enough to avoid recruiting those who did not have capacity to consent to participate. Involving the IDD population in this study carried the risk of recruiting those unable to consent, hence, after review of the inclusion/exclusion criteria, the direct care team nominated potential participants. The Age of Legal Capacity (Scotland) (1991) states that 16 years of age is when someone reaches adulthood, therefore this was the age cut-off in this study.

As medicines adherence was the primary aim of this study, only those on pharmacological treatment were considered eligible to participate, and, to reduce the risk of deterioration in physical health during the study only those who were medically fit were recruited. Although this may have excluded those with the most challenging adherence behaviour it was less of a risk to recruit those who were medically fit to take part.

Table 3.2: Stage one inclusion/exclusion criteria.

IDD Participants		Non-IDD participants	
Inclusion criteria	Exclusion criteria	Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> ➤ capacity to consent independently to the study ➤ identified by the direct care team as having a mild to moderate ID ➤ diagnosis of type 1 or type 2 diabetes ➤ prescribed oral glucose lowering agents and/or insulin therapy ➤ medically fit ➤ over 16 years of age ➤ able to communicate in English 	<ul style="list-style-type: none"> ➤ unable to consent independently ➤ did not have type 1 or type 2 diabetes ➤ diabetes was controlled with diet alone ➤ unable to communicate in English ➤ medically unfit to participate in the study 	<ul style="list-style-type: none"> ➤ capacity to consent independently to the study ➤ diagnosis of type 1 or type 2 diabetes ➤ prescribed oral glucose lowering agents and/or insulin therapy ➤ medically fit ➤ over 16 years of age ➤ communicate in English 	<ul style="list-style-type: none"> ➤ unable to consent independently ➤ did not have type 1 or type 2 diabetes ➤ their diabetes was controlled with diet alone ➤ unable to communicate in English ➤ medically unfit to participate in the study

3.8.4 Recruitment strategy and timeline

Distribution of healthcare professional information sheets to GP surgeries, and community ID groups, voluntary organisations, carer groups, community, acute care, ID and diabetic teams by the researcher informed them about the study (Appendix 3). The named informant was invited to identify potential participants.

The named informant provided potential participants with an initial information sheet (Appendix 4) and a point of contact to express interest. If interest was expressed in participating in the study, the named informant contacted the researcher who contacted the potential participant to further inform them of the study. At this stage, a full patient information leaflet was sent (Appendix 5).

Potential participants were given a minimum of 48 hours to consider whether they wished to be part of the study. This was considered sufficient time to consider the project and discuss participation with significant others. They were also informed of their rights namely; (1) to withdraw from the study at any time, (2) to refuse consent or make a complaint, (3) to discuss any aspect of the study with the researcher or an independent advisor, (4) that their usual management and care will not be affected during the study and (5) to have a nominated person present during the interview. The latter point was to enable clarification during the interview to be made in language the participant was accustomed to. The carer could rephrase questions in a format that the participant understood and provide illustrative examples that were contextual to the participant.

If the potential participant did not agree to take part, to avoid recontacting them, the participant was assigned a non-participant, non-identifiable code which was stored in a secure, password protected database. If the participant did agree to be included in the study, the researcher arranged a mutually convenient time to administer the questionnaire via a face-to-face interview.

Interview location was in the participant's home, at a research office location, or any other suitable place of their choosing. Usual diabetic treatment was continued during the study and all were given the opportunity to have a support person with them during consent and data collection. An opportunity to ask questions prior to consent was offered to all participants. Only individuals who provided written consent or, in cases of illiteracy or disability, verbal consent witnessed by the participant's carer were included in the study.

Prior to commencing the interview, written consent was obtained (appendix 7) to

1. Administer the questionnaires in form of an interview,
2. Obtain permission from the service user to contact a relevant NHS primary care provider or research specialist nurse to record the most recent outpatient clinic HbA1c levels from his or her medical records.
3. To identify and contact a carer/significant other who may be willing to participate in the qualitative stage of the study.

Participants were offered a break during the interview if they experienced fatigue or distress as a result of the questions being asked.

On completion of the interview HbA1c data was requested from the service users' medical records by the researcher. A copy of the signed consent form from the service user stating that they agree to have this information disclosed to the researcher was presented to the primary care provider or research specialist nurse in person or via letter, fax or email. The HbA1c level collected at an outpatient clinic and within 6 months of the interview was recorded by the researcher. This took place between November 2014 and January 2016.

3.8.5 Data collection

Demographic, dependent and independent variables were measured using a variety of validated instruments, of which one, the Glasgow Depression Score-LD had been tested and validated in

the IDD and non-IDD population (Appendix 8). The remainder had not been tested in this population however during the key stakeholder exercise all instruments were tested for linguistic comprehension and ability to complete. None were problematic for the IDD population to complete; therefore, all instruments were suitable.

3.8.5.1 *Demographic data*

Included in baseline data collection was the participant's age, gender, level of ID (where applicable), educational level, level of living and social support, time since diabetes diagnosis, type of diabetes, and drug history. This was obtained from the patient and corroborated with one other source, for example, the carer, primary care provider or healthcare professional. To ensure accuracy of medication records, participants were instructed to bring their medication, or repeat prescription to the interviews for recording with patient information. These data allow for between group comparisons (group overall, IDD and non-IDD groups).

Data relating to a service user received support with medications, number of medications prescribed and whether the service user was on insulin were recorded. This was defined as regime complexity and was selected due to it being a simpler method of assessing the effect of regime complexity than the 65-item Medication Complexity Regime Index (de Vries et al, 2014). During multiple regression analysis, these data were controlled for as it was known that they may be potential confounders.

3.8.5.2 *Dependent variables*

Two dependent variables were used: a validated self-report adherence measurement instrument and serum HbA1c.

3.8.5.2.1 *Self-report adherence measure (MMAS8)*

Morisky medicine adherence score (MMAS8) (Morisky et al, 2008) instrument is a revised version of the 4-item Morisky medicines adherence scores (MMAS) (Morisky et al, 1986) and has been used in previous diabetes medicines adherence studies (Mann et al, 2009;

Pollack et al, 2010). The MMAS8 was initially validated for use in an outpatient setting in 1367 patients (Morisky et al, 2008). The instrument was found to be reliable ($\alpha = 0.83$) and had a significant correlation with blood pressure control and the previous four item score MMAS ($p < 0.05$). Since its introduction, the MMAS8 has been validated for use in diabetic patients (Al-Qazaz et al, 2010; Lee et al, 2013) and been used in diabetes adherence studies (Bailey et al, 2012). MMAS8 is an 8 item self-reporting medicines adherence instrument asks the participant to state yes or no to a series of questions and receives one point for each correct answer (Appendix 8). Scores of 8 indicate good medicines adherence, 6 or 7 medium adherence and less than 6 poor adherence.

3.8.5.2.2 Measurement of glycaemic control

HbA1c is an international and gold standard measure of glycaemic control and provides an average measurement of blood glucose control over 120 days. The higher the HbA1c the poorer the glycaemic control and the greater risk of complications. In this study, HbA1c was presented as a dichotomous and continuous variable. Good glycaemic control is a target HbA1c of 6.5 - 7.5% (48-58 mmol/mol) for diabetic patients (SIGN, 2010). As a dichotomous variable poor diabetic control was defined as HbA1c $> 7.5\%$ or > 58 mmol/mol.

3.8.5.3 Independent (predictor) variables.

Five independent variables were measured namely, ID, depression, side effects, self-efficacy and perceived level of social support. An outline and rationale for selection of each of the data collection instruments follows.

3.8.5.3.1 ID

Diagnosis of any medical condition is based on aetiology and meeting evidence-based criteria that provides a diagnosis. The international classification of diseases (ICD-10) has categorised ID in five broad categories according to Intellectual Quotient (IQ) and classifications, namely, borderline, mild, moderate, severe and profound (WHO, 1996).

However, this may only focus on only one aspect of intellectual function and may not provide a holistic assessment of ID. Previous studies reported that classification of ID severity was rarely formally documented (Cardol et al, 2012b; Dysch, et al, 2012; Hale et al, 2011; Taggart et al, 2013) and, during study design, key stakeholders concurred. Furthermore, in the health board where the study took place there was no central database providing information on classification of people with ID. For these reasons, identification of borderline, mild, moderate, severe or profound ID was requested from named informants, or carers who had observed potential participants in the practical, academic and social context.

3.8.5.3.2 Depression

The Glasgow Depression Scale for People with ID (GDS-LD) is a 20-item scale which has been psychometrically test for use in patients with mild to moderate ID and correlates highly with depression scores used in the non-ID population (Cuthill et al, 2003). The participant rates their symptoms across a 3-point Likert scale from 'never/no' to 'always/a lot'. Five questions were reverse scored (Questions 3, 4, 5, 9 and 20)

Cuthill et al (2003) reported GDS-LD to be internally reliable ($\alpha = 0.9$) and, using a cut-off score of 13, was 96% sensitive and 90% specific when screening for depression. This study screened IDD and non-IDD depressive symptoms as well as depression, therefore the cut-off score was not as important as exploring whether medicines non-adherence was associated with higher GDS-LD scores.

3.8.5.3.3 Self-efficacy

The Perceived Competence in Diabetes Scale, (PCS), is a validated 4-item scale that assesses the respondent's confidence in their ability to manage their diabetes care (Williams, et al, 1998). For each of the four components, the scale ranges from 1 (not at all true) to 7 (very true) and the score is calculated 0-100. A higher score indicates greater self-efficacy.

This scale was used in one study included in the literature review (Nelson et al, 2007); and, with no other validated measure available, it was selected for this study.

3.8.5.3.4 Medicines side effects.

The Perceived Sensitivity to Medicines Scale (PSM) (Horne et al, 2013) is a validated five-item questionnaire is scored on a five-point Likert-type scale. Individual item scores are summed to provide a total PSM score ranging from 5 to 25. Higher PSM scores are suggested to have an association with medicines non-adherence. It is a shortened revised version of the validated Beliefs about Medicines Questionnaire (BMQ) (Horne & Weinman, 1999). The BMQ is an 18-item scale which covers broader concepts relating to medicines such as overuse and harm, necessity and concerns, rather than medicines side effects. Selected items from it have been used in diabetes medicines adherence studies (Kurlander, Kerr, Krein, Heisler, & Piette, 2009; Mann et al, 2009). In the systematic review (Chapter 2) medicines side effects, rather than medicines beliefs, was a factor associated with adherence (Chao et al, 2005; Farmer et al, 2006, Grant et al 2003; Mann et al, 2009; Pollack et al 2010).

Therefore, a scale focussing on medicines side effects was sought. The Perceived Sensitivity to Medicines (PSM) scale was selected because (1) it is simple to administer, (2) focuses on medicines side effects and (3) is a concise 5-item scale. This scale was validated in a sample of 1,166 participants from five groups with a range of health needs. The PSM scale had good correlation with the BMQ across all study groups ($r=0.3-.36$, $p < 0.001$) (Horne et al, 2013). Individual item scores were summed to provide a total PSM score ranging from 5 to 25 (the higher the score the greater the perceived level of side effects).

3.8.5.3.5 Social support

The modified Medical Outcomes Study Social Support Survey (mMOSS-SS) is a validated 8-item social support survey (Moser, Stuck, Silliman, Ganz, & Clough-Gorr, 2012). It is a shortened questionnaire derived from the 19-item Medical Outcomes Study Survey

(MOSS) used by Schoenthaler et al (2012) to explore social factors associated with diabetes medicines adherence.

The mMOSS-SS was validated in a sample of > 3,000 women across three study populations. Results showed good internal reliability ($\alpha = 0.88, - 0.93$) and was comparable to MOSS in terms of external reliability and validity. Participants rate each of the items across a five-point Likert scale, and the score is totalled and calculated 0 - 100. A higher score indicates a greater perceived level of social support. The mMOSS-SS score was less burdensome than the 19-item MOSS score and was considered more user-friendly for all research participants including, most importantly, people with ID.

3.8.6 Data Analysis

Data analysis was carried out using SPSS version 20.0. SPSS is software that provides an entire analytical package including data storage, analysis and reporting (Brace, Kemp, & Snelgar, 2013). Selection of the appropriate test, interpretation and presentation of results is dependent on the knowledge and skills of the researcher but does provide a mechanism for storage and accurate analysis of numerical data.

All data were entered systematically and screened for missing data. Laerd Online Statistics (2017) and Brace et al (2013) were used to guide selection of appropriate statistical tests. An analysis plan was agreed and verified by the research team and department statistician. The plan consisted of overall and between group comparisons (IDD and non-IDD participants) of demographic, dependent and independent variables; correlation between HbA1c and MMAS8; reliability of measures and a 3-step univariate and multiple regression analysis. A total of 11 hypotheses were tested. Statistical significance was defined as a probability level of $p = <0.05$, that is the probability that the difference occurred by chance is less than 5%. This is a recognised and satisfactory criteria for statistical significance (Brace et al, 2013).

3.8.7 Baseline demographic and health statistics and testing internal validity

Prior to addressing the research questions, comparisons between the IDD and non-IDD groups were carried out. Descriptive statistics summarise data and provide an overview of the data collected. Associations between the dependent factor (medication adherence) and biomedical markers were established and internal reliability of dependent and independent measurement instruments was assessed. This was to investigate whether the IDD and non-IDD population were similar across factors, for example, gender, living situation, level of education and work situation.

Health characteristics were measured in the context of diabetes health and comparisons were made between the number and type of medication, insulin therapy and HbA1c in the IDD and non-IDD population. Once these comparisons were investigated, demographic and health characteristics that were statistically significantly different in the two groups were tested for associations between these factors and medication adherence. This was to verify that differences between the two groups were not associated with adherence and that the group overall could be analysed. The three hypotheses tested were:

- I. There would be no statistical difference in the demographics of the IDD and non-IDD population.
- II. The instruments used to measure independent factors would demonstrate good internal reliability.
- III. There would be a negative association between MMAS score and HbA1c score in the group overall, the IDD, and non-IDD population – specifically the lower the MMAS8 the higher the HbA1c in the sample population.

3.8.7.1 *Measurement of statistical difference in demographics of IDD and non-IDD groups*

To test whether frequency counts were distributed similarly in terms of demographic factors, parametric and non-parametric tests were performed. SPSS established descriptive statistics of the group overall frequencies demographic characteristics and health characteristics from the questionnaires (appendix 8) were reported.

Chi-squared test was used for categorical variables and for parametric data, independent T test were performed (Laerd, 2017). Where nominal variables were used mean and standard deviation were reported to ensure that central tendency and dispersion were also reported. For nominal variables with outliers on box plot inspection median values were reported, and Mann Whitney U tests were performed to detect statistical significance between the two groups. In all cases if results were not statistically significant hypothesis I would be upheld.

3.8.7.2 *Internal reliability of independent factors*

To evaluate the measures and test the reliability of the measures, a reliability analysis using Cronbach's Alpha was conducted in the IDD and non-IDD groups

It is widely agreed that internal consistency of a measure should be tested prior to any other statistical analysis to ensure internal reliability of the measurement instruments used. Cronbach's alpha measures the random error rate of a particular scoring instrument and, the closer the result is to 1, the lower the random error rate and the greater the reliability (Brace et al, 2013). Rather than relying on published scores of previous studies, Cronbach's Alpha should be tested each time the measurement instrument is administered as the score will alter according to those participating in the study. This test was of importance in this study because apart from the GDS-LD none of the data collection instruments used in this study had been used in the IDD population. The result of the test is expressed as a number between 0 and 1

with $\alpha = 0.7 - 0.9$ demonstrating a good level of internal consistency (Brace et al, 2013; Laerd, 2017). If internal consistency of instruments was good hypothesis II would be upheld.

3.8.7.3 *Associations between MMAS8 score and HbA1c scores in (1) group overall, (2) the IDD and (3) non-IDD groups.*

To test correlations between MMAS8 and HbA1c score, Spearman's Rank Order correlation was performed. This calculates a co-efficient (r_s) that measures the strength and direction between two continuous variables (Laerd, 2017). The coefficient value (r_s) strength of correlation in the context of statistical significance of the correlation coefficient (p value) were reported.

A linear regression was then carried out to determine the effect of medication adherence on glycaemic control in each group. In this study it provided an estimate of the HbA1c according to MMAS8 and whether an elevated HbA1c could predict a poor adherence score. Once assumptions of tests were met for both tests the results were reported (Brace et al, 2013; Laerd, 2017). The value, effect size and confidence intervals were reported as r , r^2 and % respectively. According to Brace (2013) r values of 0 - 0.2 are considered weak, 0.3 - 0.6 moderate, 0.7 - 1 strong. Studies that have measured the association between HbA1c and MMAS8 and demonstrated that there was a strong negative association between the two (Hill-Briggs et al, 2005; Schectman, Nadkarni, & Voss, 2002; Wong et al, 2015): as adherence scores fall, HbA1c increased. A similar correlation between HbA1c and MMAS8 was predicted in the group overall, in the IDD and non-IDD population.

If a negative correlation between medication adherence score and HbA1c was reported in the group overall, the IDD and non-IDD groups, hypothesis III would be upheld.

3.8.8 Research Question 1

What is the frequency of dependent factors (glycaemic control and medication adherence) and independent factors (depression, side effects, self-efficacy and level of social support) in the IDD compared to the non-IDD population? To address this research question four hypotheses were tested:

- IV. There would be no difference in HbA1c in the IDD compared to the non-IDD groups.
- V. There would be no difference in MMAS8 in the IDD compared to the non-IDD groups.
- VI. Reported reasons for non-adherence in MMAS8 in the IDD and non-IDD groups would not be equal.
- VII. The frequency of independent factors in the IDD and Non-IDD groups would not be equal.

3.8.8.1 *Frequency of dependent variables (HbA1c and medicines adherence (MMAS8)) in overall, IDD and non-IDD groups and between group comparison*

Frequency of dependent variables in the group overall were expressed as percentage and numerical data. To detect statistically significant differences between the IDD and non-IDD groups with continuous variables HbA1c and MMAS8, parametric and non-parametric tests were performed with the two tailed T-test and Mann Whitney U respectively. HbA1c and MMAS8 were calculated as mean values (standard deviations) and, if outliers were detected, non-parametric tests were performed using median scores.

Chi-squared tests were applied to dichotomous variables, namely, optimal and suboptimal medicines adherence and optimal and suboptimal glycaemic control. A

dichotomous, HbA1c value > 58mmol (7.5%) was defined as suboptimal glycaemic control (SIGN, 2010) and MMAS8 less than 6 was defined as suboptimal medication adherence.

If the frequency of dependent factors was not equal and there was a statistically significant difference between the two groups hypothesis IV would be upheld.

3.8.8.2 *Frequency of reported reasons for non-adherence in MMAS8 in the overall, IDD and non-IDD groups and between group comparison*

To report reasons for non-adherence in the IDD and non-IDD population frequency of items within the MMAS8 that were reported as incorrect were measured. Differences in responses were reported by comparing percentages of responses and presented in table format. Chi squared tests were performed to determine whether differences between two groups were significant.

3.8.8.3 *Frequency of independent variables and comparisons of independent variables in the group overall, the IDD and non-IDD groups.*

Mean and median depression (GDS-LD), side effects (PSM), confidence (PCS) and social support (mMOS-SS) scores were calculated in the (1) group overall, (2) the IDD and (3) non-IDD group. Frequency of independent variables in the group overall were expressed as a percentage and in numerical terms. To compare IDD and non-IDD groups, frequency and median or mean scores of independent factors were reported. To detect statistically significant differences between the two groups, parametric and, if evidence of outliers, non-parametric tests were performed. Outliers were detected using visual inspection of box plots. If outliers were detected, non-parametric tests were performed using Mann-Whitney U; otherwise, a parametric independent T-test was performed.

If frequency of dependent factors was not equal, and there was a statistically significant difference between the IDD and non-IDD groups hypothesis VI would be upheld.

3.8.9 Research Question 2:

Whilst controlling for regime complexity and support with medicines, does the proposed theoretical model predict medication adherence in the group overall, the IDD and non-IDD population?

3.8.9.1 *Research hypotheses*

To address this research question four hypotheses were tested:

- VIII. After controlling for confounders, the overall model of medicines adherence would significantly predict medicines non-adherence in the group overall, the IDD and non-IDD population
- IX. After controlling for confounders, support with medicines and regime complexity, ID would predict medicines non-adherence in the group overall
- X. After controlling for confounders, support with medicines, and regime complexity, depression would predict adherence in the non-IDD group
- XI. After controlling for confounders, support with medicines, and regime complexity depression perceived level of social support would predict adherence in the IDD group.

The purpose of these analyses was to establish which independent factors predicted medicines non-adherence. Correlation between the most important factors, mean scores and medicines non-adherence were also investigated. This modelling tested: (1) whether Bandura's social cognitive theoretical model was predictive of adherence, (2) which independent factors were associated with adherence and (3) whether cut-off scores of statistically significant independent factors could predict medicines non-adherence in the group overall in the IDD and non-IDD population.

3.8.9.2 *After controlling for confounders, the overall model of medicines adherence will significantly predict medicines non-adherence*

To investigate whether the overall model predicted medicines non-adherence, a multiple regression analysis was carried out. Multiple regression is used to predict a score of an independent variable based on multiple dependent variables (Brace et al, 2013; Laerd, 2017). Carrying out this type of test acknowledges that human behaviour is influenced by many interrelated variables. In multiple regression there is a correction for the correlations among the predictor variables (Laerd, 2017).

The procedure was a three-step procedure (1) the purposeful selection of independent variables entered in the regression model; (2) regression analysis; (3) repeating the regression analysis whilst controlling for potential confounders.

The first step, purposeful selection, began with a univariate analysis of each independent variable. A significant result from univariate analysis was defined as a p-value < 0.15 in the group overall. This p value was selected across all groups as a p-value < 0.05 may fail to identify variables known to be important. This was important in this study as all factors were selected due to their significant association with adherence in previous studies.

The second step, a multiple regression, by analysing selected variables simultaneously using the enter function on SPSS to detect the predictive value of the overall model and, which variables were significant or important predictors of adherence. These steps were repeated for the group overall, the IDD group and the non-IDD group.

The final step was to investigate whether confounding independent factors had any effect on medication adherence using hierarchical multiple regression. Confounding and independent variables were entered sequentially into the model. Confounding variables and independent variables were then inputted simultaneously using the enter function. The effect of these potential confounder variables was removed by using hierarchical multiple regression (Laerd,

2017). The measure of most importance is the r^2 and r^2 changes in p values after controlling for confounders.

Confounding variables controlled for were: (1) support with medications, and (2) regime complexity (number of medicines and use of insulin). These factors were selected based on results from the systematic review reporting associations between adherence and support and complexity of regime.

Univariate, sequential and hierarchical multiple regression results were expressed in the standard form as the r^2 which is the proportion of variance in the dependent variable which is explained by the independent variables. Cohen's classification of effect size was used signifying a $r^2=0-0.2$ small effect size, $r^2=0.2-0.5$ medium effect size and $r^2=0.5-0.8$ large effect size (Brace et al, 2013; Cohen, 1988). Statistical significance and F ratio (F) of the overall model and between dependent and independent variables were also reported. Statistical significance provides an estimate of how the overall model predicted medication adherence, and which independent factor was the most important predictor of medication adherence and F ratio is the variance due to the manipulation of the factor(s) divided by the variance due to error. If the overall model was statistically significant hypothesis VII would be upheld.

3.8.9.3 Determining which independent factor was statistically significantly associated with adherence in the group overall, IDD and non-IDD groups.

To investigate which independent factors were predictors of adherence the model table was inspected to determine which factors were associated with adherence in the group overall, the IDD and non-IDD group before and after controlling for confounders. If ID was the most important predictor of adherence hypothesis VIII would be upheld. If depression score was significantly associated with medicines non-adherence in the IDD and non-IDD groups then hypotheses IX and X would be upheld.

3.8.9.4 *Determining correlations between mean score of independent factors significantly associated with medicines non-adherence in the group overall, IDD group and non-IDD group.*

To determine predictors of adherence according to mean score, results from the model were examined. A linear regression was performed using the syntax function on SPSS on those which were most importantly associated with adherence either before or after controlling for confounders, in the group overall, the IDD group or the non-IDD group. This was to provide a comprehensive estimate of adherence according to significant factors across all groups. A similar procedure was followed as detailed in 3.6.4.3. This was to predict which mean score within the independent factor was associated with medicines non-adherence in each of the groups and propose scores from significant independent factors that may predict medicines non-adherence. The score was reported as a mean value across each of the MMAS8 scores from 4, 5 meaning poor adherence, 6, 7 meaning medium adherence and 8 meaning excellent adherence.

3.9 Stage two: Qualitative

Stage two followed stage one and provided an in-depth exploration of those results. This intended to find out more about the stage one results in addition to verifying the accounts of medicines adherence from stage one participants. Following the same format as stage one methods, stage two will outline sampling, recruitment, data collection and analysis strategies. The final section will outline how stage one and two data were integrated and triangulated.

Stage two of the study was designed to address research question 3:

1. Is the frequency of, and factors associated with adherence, consistent with the views of carers supporting diabetes medicines management?

The aims of this stage were to:

1. Triangulate stage one self-reported scores with carers' perceptions of dependent and independent factors.
2. Explore how carers support stage one participants in medicines adherence
3. Explore the views of carers regarding the relationship between medicines adherence and independent factors (depression side effects self-efficacy and social support)
4. Explore other factors associated with diabetes care, for example diet and exercise

An outline of the methods used to address the research question and associated aims are presented in the next section.

3.9.1 Sampling strategy

Sampling was based on achieving a purposive sample of the study population and obtains sufficient data to have confidence in that there were no new emergent themes. As the express intention of this stage was to verify and triangulate the data collected in stage one a representative sample was not the priority. Stage two was conducted using semi-structured interviews with a sample of carers from IDD and non-IDD participants.

Predetermined inclusion and exclusion criteria (Table 3.3) were devised to ensure that carers had sufficient knowledge of service users' behaviour in relation to medicines adherence, that the service user had consented to the researcher speaking to the carer, that the carer met the age of legal capacity, and that the service user was able to communicate in English without the aid of a translator.

Table 3.3: Stage two inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> ➤ supported the stage one participant for a minimum of 6 months, ➤ had been nominated by the IDD or non-IDD stage one participant to participate in the study ➤ were over 16 years of age, ➤ able to communicate in English ➤ had capacity to consent to the study 	<ul style="list-style-type: none"> ➤ supported the stage one participant for less than 6 months, ➤ had not been nominated by the stage 1 participant to participate in the study. ➤ were less than 16 years of age, and ➤ unable to communicate in English ➤ Did not have capacity to consent to the study.

3.9.2 Sample size

Sampling was based on preliminary results from stage one. Provided stage one participants agreed for carers to participate and met inclusion criteria, they were sent an invitation letter to take part in stage two of the study. To provide a diverse range of views of carers target numbers of participants were between 10 and 15, which equated to around 10-15% of the stage one study population. This was sufficient to provide an in-depth exploration of medication adherence of a cross-section of stage one population and provide a sufficient data to verify stage one results, to explore any inconsistent findings in stage one and identify any additional factors associated with adherence in the study population.

3.9.2.1 *Recruitment strategy and timeline*

Data were collected over a pre-specified period to ensure the currency of the data collected in relation to stage one results. On completion of the stage one interview with the participant the researcher requested permission to invite the carer to take part in stage two. If the stage one participant agreed that the carer could be contacted, a stage two participant information sheet (Appendix 9) was given to the stage one participant, and the researcher requested that the information was passed onto the participant's carer. A database of carers agreeing to participate was created and all were followed up within 12 months of completing stage one data collection with a letter inviting the carers to participate in this stage of the study. This included the information sheet about the study (appendix 9).

Once participants expressed an interest in the study, they were informed by the researcher about the aims of the study and were given at least 48 hours to consider whether they wished to participate. If the participant agreed, the researcher discussed the study in more depth and a time and place to obtain consent to conduct the interview was arranged.

Participation was voluntary, confidential and anonymous and participants were free to withdraw at any time during the study without giving a reason. Contact details of an

independent research advisor not related to the study were also given, so that they could discuss any aspect of the study with an academic not connected to the study. Stage two data collection took place between January and May 2016.

3.9.2.2 *Data collection*

A topic guide for interview was devised following a preliminary analysis of stage one data (appendix 12). This was based on the theoretical framework from the systematic review and encompassed the questions related to medication adherence and the factors associated with adherence which were investigated with stage one participants. The topic guide was intended to provide the carer with the opportunity to recount their experience of managing medicines, thereby exploring the same factors with the carers as the stage one participants. To allow for free discussion of the topic of managing diabetes treatment, a final question was added which explored the most challenging part of diabetes care overall.

Interviews were digitally recorded and transcribed verbatim. When there was a lack of clarity in either audio or written transcripts explanation was sought from the participant to confirm meaning.

3.9.3 *Data analysis*

3.9.3.1 *Software package*

NVIVO software was used to collate data and organise themes. NVIVO is a software package designed to assist in the management and analysis of qualitative data (Udo, 2014). Use of software packages has increased in popularity with over 400 qualitative papers outlining its use in qualitative data analysis (Flick, 2013). Its benefits are twofold: it clearly outlines to external reviewers how data has been coded and organised into themes and it allows for verification of themes by a second reviewer thereby enhancing the credibility of findings. For large multicentre qualitative studies, it allows for merging of data thus strengthening the impact

of qualitative research (Pope, Ziebland, & Mays, 2000). It results in a more flexible, systematic and transparent approach to analysis of qualitative data than manual coding.

However, unlike SPSS it does not make any analytic decisions: this is the responsibility of the research team. NVIVO and all other qualitative software packages do not teach researchers how to analyse data nor do they provide a standardized method of data analysis. Furthermore, it is a generic data analysis tool designed for any qualitative research approach rather than focussing on specific qualitative approach, for example, ethnography, grounded theory or phenomenology. Therefore, rigour in data analysis and presentation of findings is demonstrated by clearly articulating the method by which conclusions were drawn and through verification of themes identified and, although the view that a second analyst should be involved has been contested (Pope et al, 2000), it is considered good practice to have a second person verify themes (UK, 2017).

In this study data analysis was carried out using the thematic analysis method involving the supervision team to sense-check data, discuss themes and verify against findings. The next section of this thesis will outline the step by step method by which qualitative data was analysed.

3.9.3.2 *Exploration of data according to factors associated with adherence and additional factors associated with diabetes management*

All data were analysed thematically and in the context of the stage two research question and associated aims. Thematic analysis involves the systematic analysis of qualitative data to explore and understand in depth the research question posed. It is a method of identifying and analysing patterns in qualitative data whilst maintaining structure focussing on the research questions. Braun and Clarke (2006) argue that thematic analysis is not a methodology rather it is a method of analysing data within qualitative research. They describe six phases of thematic analysis:

1. Familiarisation with the data: This is an integral part of all qualitative analysis. Data is read and re-read the data and audio-recordings are listened to. Initial analytic observations are noted;
2. Coding: Data items are categorised and collated in relevant data extracts. This allows for deep analysis and understanding of the data. In this study stage one and two data sets and service user and carer data sets were matched and analysed together to create an in-depth explanation of the research questions and verification of stage one results. Results of stage one participants were presented in table format and analysed in the context of stage one findings;
3. Searching for themes: A theme is a coherent and meaningful pattern in the data relevant to the research question. This ‘searching’ is an active process and culminates in collating all the coded data relevant to each theme. Themes were arranged according to stage one dependent and independent factors with an additional theme addressing other factors related to adherence;
4. Reviewing the themes: This involves checking that the themes ‘work’ in relation to both the coded extracts and the full data set. At this stage, a story about the

data is emerging and themes split, combined or deleted. It synthesises the evidence and helps to select relevant information and discard less relevant. At this stage, themes are checked against each other and back to the original data set until themes emerging from data are internally coherent, consistent and distinctive. In the context of this study, themes were reviewed by an expert in the field of qualitative research. This verification allowed for themes to be confirmed and for additional emergent themes to be identified that may have been missed by the primary researcher;

5. Defining and naming themes: The themes are defined and quotes selected according to relevance to identified theme. A detailed analysis of each theme is outlined. It synthesises the evidence and helps to select relevant information and discard less relevant. Data was defined in the context of the topic guide and the research question.
6. Writing up: Writing-up involves weaving together the analytic narrative and data extracts to tell the reader a coherent and persuasive account of the qualitative data. To improve cohesiveness in this study, the findings will be considered in the context of stage one data, the researcher's relationship to the study and the existing research literature on the subject. This transparency, particularly in relation to the researcher's position in the research process is intended to help those reading the research to apply findings to other settings and contexts.

3.10 Integration of quantitative and qualitative data

Integration of qualitative and quantitative data occurred in two parts. The first part, in stage two, occurred during analysis and the second during discussion of findings. The sequential design of the study allowed for a preliminary analysis of stage one data prior to

finalising the topic guide and collection of stage two data. Once stage two topic guides was finalised and data collected, participant data from stage one was matched with the carer of the stage two participants using SPSS.

Themes from within one data set were contrasted with the other. This concurrent integration contextualised the qualitative data, verified data collected in stage one was authentic and explored any incongruous results. This met the first two aims of this exploratory phase of the study.

Exploring with carers additional factors associated with adherence described in more depth the concept of medicines adherence and carer involvement in the study population which met the third aim of stage two. There was no integration of qualitative and quantitative data at this point because this was inductive and established new and emergent themes associated with glycaemic control.

The second part of integration occurred during the discussion chapter and stage two results were at this point fully integrated with stage one results. This was intended to create a synergy between the two sets of data and to know more about medicines adherence particularly in the IDD population. Integration at this stage is described by Moran-Ellis (2006) as theoretical integration; it takes findings from each stage of the study and brings them together in an explanatory framework.

3.11 Ethical considerations

Prior to commencing the study, ethical approval was sought from the Integrated Research Approval System (IRAS) and Edinburgh Napier University Faculty Research Ethics Approval Group (FREAG) (Appendix 2).

3.11.1 Risks and burdens to research participants

Given that this was a cross-sectional study, the risk of adverse events was low. In both stages, any problems arising for taking part in the study were addressed through their routine care. The contact details of the PhD student, research supervisor and independent advisor were available should participants or their carers have had any queries outside of attending their sessions. If participants wished to withdraw from the study, they continued to receive their routine treatment by a clinician from their direct care team.

3.11.2 Inclusion/exclusion criteria

In both stages, the inclusion/exclusion criteria were based on factors associated with the research questions and to ensure that eligible participants were not unfairly excluded from the study.

In stage one, exploring medicines adherence across the range of people with IDD i.e., from borderline to severe, would have produced a fully inclusive and comprehensive study allowing comparisons to be drawn between a broad range of people with ID and people without ID. However, this study had to be conducted in accordance with legislation and specifically the Adults with Incapacity (Scotland) Act 2000 (Scottish Government, 2000) which states that participants without capacity to consent can only be recruited if similar research cannot be done by involving adults who can consent. As this was the first study to explore medicines adherence in the IDD population, research involving only those who had capacity to independently consent to participation were included.

In stage two, between 10 and 15 nominated paid or voluntary carers were interviewed. These participants were selected on the basis that stage one participants had nominated them and they were willing to participate in the study. No carer was unfairly excluded from the study and all nominated carers/significant others were invited to participate in interviews.

3.11.3 The consent process

In both stages, participants who did not have the intellectual capacity to consent were excluded from participating in the study. Consent was obtained using a standard consent preform (Appendix 7). In both stages participants were informed of the study purpose and design in the initial information sheet and, again, prior to giving consent.

Written or verbal informed consent was obtained from stage one and two participants. In stage one, if verbal consent was obtained, the record of consent was documented and the carer who witnessed the consent process was requested to verify assent by the participant by signing the consent form. The purpose of the signature, by the witness, was not to provide consent to participate in the study, rather it was evidence that a witness was present during the consent process and they agreed that the participant was fully informed of the risks and benefits of, and alternatives to, participating in the study. In both stages at the start of all interviews, participants were informed of their right to withdraw from the study at any point.

In stage one and two when seeking informed consent to take part in the study, it was made clear that responses to questionnaires and interviews would be kept confidential. If any participant's response indicated that either the participant or another person was at risk of harm, then, in the interests of participant or public safety, a member of the participant's direct care team, or, in the case of carers, line manager, was informed immediately so that appropriate action could be taken. This was made explicitly clear to all participants when seeking informed consent to take part. The participant was also informed of the disclosure to the direct care team or line manager. This is in accordance with the Nursing and Midwifery Council's (NMC) code of conduct (2015) Standard 16.

3.11.4 Assessing capacity to participate

In stage one, there was a risk that mild to moderate IDD participants may not fully understand in broad terms the aims and outcomes of the research, the risks and benefits of

participating and what would happen if they refused consent to participate. Therefore, capacity to consent and participate in research was assessed prior to commencing data collection and was ongoing during data collection. This was assessed by firstly building a rapport with the participant, ensuring that they understood in broad terms the nature of the study that they could retain that information and use that information to come to a decision about whether they would like to take part. In stage one, as an additional safeguard prior to commencing the study, the researcher liaised with clinical staff to ensure that participants were medically and psychologically fit to participate in data collection.

3.11.4.1 *Maximising capacity to consent*

In stage one, during data collection, participants had the opportunity to have a nominated representative present. The researcher communicated slowly and clearly, and chose a quiet location with minimal interruptions. When administering the questionnaires, concepts and questions were introduced one point at a time and teach-back techniques were used to verify and check understanding. This acknowledged a recent systematic review of six articles which suggested that, although research evidence was poor, additional time and teach back were strategies that may have some effect on improving understanding of the proposed procedure in participants with low levels of health literacy (Tamariz, Palacio, Robert, & Marcus, 2013).

Stage one IDD participants were also given more time to answer questions and more time was allocated for their interviews. It was also acknowledged that IDD participants' capacity to participate may increase or decrease at different times of the day, and it was therefore important to liaise with the carer to ensure that the interview took place at a time where capacity was maximised. These two strategies were to ensure that the participant felt at ease and not under pressure to provide answers without considering all possible options. This approach was consistent with an observational study carried out by Jepson et al (2015) and consistent with UK and Scottish Codes of Practice (Scottish Government, 2000).

In stage one, the presence of the main carer may have influenced the responses that the participant gave, therefore, prior to commencing data collection, it was stressed to the carers that the only the participant's views and perceptions were important at this stage and that the carer would have the opportunity to share their perspective in the next stage of the study.

If at any time during stage one or two, the researcher was concerned that the participant did not have capacity to consent, then he or she would be no longer eligible to participate in the study, he or she would be withdrawn, data would be destroyed and the participant would continue with usual care.

3.11.5 Data collection

All stage one data collection instruments had been validated and used in routine practice and research without any documented adverse events. The questionnaires chosen in the study were selected based on their routine use in clinical practice and in other research studies, their psychometric properties which have shown them to be valid and reliable measures and their relative simplicity and ease of use.

In stages one and two informed consent was gained prior to taking part in the study which detailed the types of questions they would be asked. Any participant who was unhappy about completing such questionnaires was unlikely to consent to take part in the study.

In stage one request for HbA1c results were made to general practitioners and diabetes specialist nurses. These results were matched to the data recorded from stage one and stored with the participants' data set on a password protected computer.

3.11.5.1 *Minimising harm during data collection*

The Helsinki Declaration outlines the principle of minimizing (or eliminating) harm as:

'[protection of] the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects' (Leavitt, 2006)

In stage one, the questionnaires asked participants to identify and rate emotions and feelings they may have recently experienced. Such questions form the basis of a good standard of routine care and practice within diabetic services; however, it was acknowledged that this may cause distress for some participants.

If this did lead to distress, the researcher, if necessary, suspended data collection, addressed the issue and, offered a debrief on the aspect of the questionnaire causing distress. Where necessary the participant was encouraged to discuss the area of concern with a member of their direct care team. Following debrief, the participant was given the opportunity to continue, take a break or withdraw from the study.

3.11.5.2 Physical or psychological illness during data collection

In stages one and two, if, during any part of the study, there was any concern that the patient was manifesting signs of physical or psychological illness then participation was suspended and his or her nominated healthcare professional was informed. If, the participant's physical or psychological condition was deemed to be a medical emergency, appropriate and reasonable interventions (including contact of emergency services) would be taken to preserve life or prevent serious deterioration in physical or psychological health.

In stage one, if there was evidence that medicines adherence was so severely compromised that it put the patient at risk of physical or psychological harm, participation was suspended and the participants direct care team was contacted to discuss how to prevent further deterioration in physical or psychological health. In all cases the situation was documented and the participant was either invited to participate at a later stage or withdrawn from the study.

3.11.6 Maintaining confidentiality

During stages one and two interviews were carried out in an environment which protected the participant's right to privacy yet maximised their ability to understand, retain and process the questions set out in the interview schedule. Where necessary, and to support the participant

during the interview, a nominated representative was also present. Where this occurred, the representative also ensured that the participants' right to privacy and freedom of speech was protected at all times.

If, during the interview, the participant became upset or disclosed information which exposed them or others to physical or psychological harm, the interview was discontinued, and consent obtained to contact the direct care team. If the researcher had evidence to suggest that it was in the greater public interest to discuss information disclosed with relevant professional agencies rather than maintain participant confidentiality, this was carried out without the consent of the participant.

3.11.7 Data access and storage

Once data had been collected all hard copies of completed questionnaires used in the study were anonymised using a coding system and any personal identifiable information removed. These were stored in a locked cabinet, in a secure office at Edinburgh Napier University. Participant consent forms, contained names, contact details and the identifiable code of the participant so that relevant questionnaire scores could be matched to the same participant and that carer participants can be matched to IDD service user participants. If the participant decided to withdraw from the study the patient information was stored in such a way that it was easily identifiable and, one identified was destroyed in accordance with data protection legislation. Personal details were stored 3-6 months after the study has ended.

Following data collection, data were coded and uploaded onto a secure password protected database for analysis. Any publication of direct quotes was anonymised and any identifiable information coded and stored in a secure password protected Edinburgh Napier University server. Patient outcome data from the study was stored on Edinburgh Napier University computers for data analysis. Verification of results was carried out by research supervisors. Research data generated from the study will be stored for five years.

3.11.8 Risk management of the researcher

The researcher is a registered adult nurse and is required to be fully compliant with the NMC Code of Conduct (2015). The researcher was a Ph.D. student, in possession of an NHS Lothian ‘research passport’ and was fully compliant with relevant health board policies and procedures.

The researcher was adherent to NHS Lothian’s lone worker policy which provided protection for the researcher when carrying out field research in isolation. Prior to commencing data collection, the researcher had a mobile phone and undertook Violence and Aggression e-learning, and face to face lone worker training.

During the data collection stage, the date, time and location of the interview were recorded in the researcher’s electronic diary. In the event of adverse circumstances the researcher’s administrator, line manager and research supervisors had access to this. If the investigator visited participants in their own home, pre/post appointment contact was made with a nominated member of Edinburgh Napier staff. If the interviews took place in a research office, this was carried out during office hours and there was access to a telephone and emergency equipment if required.

3.12 Summary

This chapter has outlined the methodology, methods and ethical considerations that were applicable to the proposed project. A pragmatic paradigm underpinned the philosophical approach and the mixed methods research design sought to answer the research questions posed.

Using methods that were conducive to maximising recruitment, participation and rigour intended to produce meaningful results that would inform policy and practice.

In the next three chapters, results will be presented. Stage one results will be presented in chapters 4 and 5 and stage two results in chapter 6. Chapter 4 will present the results from the patient and public involvement exercise, demographic and health characteristics and correlations between dependent variables. Chapter 5 will explore frequencies of, and factors associated with, adherence followed by correlations of significant factors and adherence scores. The final results chapter will report qualitative results.

4 Chapter 4: Stage 1 Results – Descriptive statistics

4.1 Introduction

This chapter will present descriptive statistics drawing demographic and health characteristic comparisons between the IDD and non-IDD groups and conclude with data on the reliability of instruments and associations between glycaemic control and medication adherence in the IDD and non-IDD groups.

The questions will be addressed in the order in which they were presented in chapter 3. The hypotheses tested will also be presented in this section. Where appropriate, illustrative tables will be presented and referred to in the text.

4.2 Descriptive Results: Sample

4.2.1 Sampling

Recruitment took place between September 2014 and December 2015. To achieve as representative a sample as possible healthcare professional information and initial participant information was distributed to all general practices within NHS Lothian Community Health Partnerships (CHP) (n = 124) and advertised in a general practice regional newsletter, diabetic outpatient clinics (n = 2), diabetic clinical research facility (n = 1) and specialist community ID services (n = 3). Information was also distributed via Edinburgh city council to social support organisations that care for people with intellectual disabilities.

4.2.2 Sample Size

Table 4.1 outlines recruitment statistics of 164 patients who met the inclusion criteria and were approached to participate in the study. The sample of 50 (30%) eligible IDD participants was obtained from the following sources: 17 (34%) IDD participants were identified through a diabetes database by a specialist diabetes research nurse, 16 (32%) from a GP practice, six

(12%) from a previous ID research study, two (4%) from consultant endocrinologists, seven (4%) from specialist community ID services and two (4%) from social support organisations. All IDD participants were attendees at a regional diabetic outpatient clinic. The sample of 114 (70%) eligible non-IDD participants was recruited from a regional diabetic outpatient clinic.

Of those 164 eligible, 111 (68%) were recruited to the study. The distribution IDD/non-IDD participants were 30 and 78 (30%, 70%) respectively. Non-participation is outlined in Table 4.1 The reasons for those unable to contact or for non-attendance were unknown and after a second attempt to contact the participant was withdrawn from the study.

In both groups 31 (19%) did not have time to be interviewed and 2 (4%) declined because there was no reward incentive for participating. Five (3%) in the group did not meet the inclusion criteria. Two (4%) in the IDD population did not meet the inclusion criteria due to lacking capacity to independently consent to the study. Three (2%) in the non-IDD population 2% did not meet the inclusion criteria because in 2 cases (4%) there was diet controlled and in one case (1%) commencing medication only the six months prior to data collection.

Table 4.1: Participant recruitment following identification by named informants by IDD and non-IDD groups and reasons for non-participation

Variable	Group overall (n= 111)	IDD (n = 33)	Non-IDD (n =78)
Participants approached (%)	164	50 (30)	114 (70)
Declined to participate (%)	31 (19)	11 (22)	20 (18)
Did not meet inclusion criteria (%)	5 (3)	2 (4)	3 (2)
Unable to contact after agreeing to participate. (%)	10 (6)	4 (10)	10 (8)
Did not attend interview (%)	3 (2)	0 (0)	3 (2)
Participants recruited (%)	111 (68) ^a	33 (66)	78 (68)

4.2.3 Baseline demographic and health statistics and testing internal reliability

Prior to data analysis, descriptive statistics and testing of reliability of instruments were conducted. This included baseline demographics and corroboration of medication adherence scores with glycaemic control. As outlined in the methods chapter this was to test the homogeneity of the group overall. The following hypotheses were tested:

- I. There would be no statistical difference in the demographics of the IDD and general population.
- II. The instruments used to measure independent factors would demonstrate good internal reliability.
- III. There would be a negative association between adherence score (MMAS8) and glycaemic control (HbA1c) score in the group overall, the IDD and non-IDD population– specifically the lower the MMAS8 the higher the HbA1c in the sample population.

The following section will present the demographic characteristics of the group overall followed by statistical comparisons between demographics of the IDD and non-IDD population. This will test hypothesis I. This will be followed by an outline of reliability of instruments and correlations of HbA1c and MMAS8. This will test hypotheses II and III.

4.2.3.1 *Demographic characteristics of the group overall, IDD and non-IDD groups*

Table 4.2 presents the characteristics of the group overall. Median age of all participants was 62 years and 55 (49%) were female. In the group overall, 82 (74%) did not complete secondary school education, 35 (31%) of participants lived alone and 17 (15%) were in paid employment.

Ninety participants (81%) had been diagnosed with type 1 or type 2 diabetes for more than 6 years and 83 (75%) had type 2 diabetes. Ninety (81%) were prescribed more than 4 medications and 24 (27%) had support with taking medications from a paid or unpaid carer. Thirty-five (42%) of type 2 diabetics in the group overall were prescribed insulin.

Table 4.2: Demographic characteristics of the study population

Socio demographics	Group overall n = 111	IDD n = 33	Non-IDD n = 78	p value
Median age	62	51	64	0.05* ^{MWU}
IDD (%)	33 (30)	-	-	
Female (%)	55 (50)	15 (45)	40 (51)	0.575 ^{chi}
<Secondary School education (%)	82 (74)	30 (90)	52 (66)	<0.05* ^{chi}
Employed (%)	17 (15)	15 (45)	2 (3)	<0.05* ^{chi}
Lives alone (%)	35 (31)	17 (51)	18 (23)	< 0.05* ^{chi}
Type 2 diabetes (%)	83 (75)	27 (82)	56 (72)	0.266 ^{chi}
Type 1 diabetes (%)	28 (25)	6 (18)	22 (28)	0.266 ^{chi}
Prescribed insulin (%)	63 (57)	9 (27)	54 (69)	0.05* ^{chi}
Type 2 diabetics prescribed insulin (%)	35 (42)	3 (11)	32 (57)	0.05* ^{chi}
Support with medications (%)	27 (24)	23 (70)	4 (5)	0.05* ^{chi}
>4 medicines prescribed (%)	93 (84)	28 (84)	65 (83)	0.84 ^{chi}
Diabetes >6 years (%)	90 (81)	24 (72)	66 (85)	0.14 ^{chi}

*statistically significant difference in the IDD and non-IDD population

^{chi} Chi squared test for significance (ordinal variable).

^{MWU} non-parametric Mann Whitney U test as outliers detected continuous data

4.2.3.2 *Demographics of IDD compared to non-IDD group*

The male: female ratio was similar in both groups. The IDD population had a lower median age (51 vs 64 years), a lower level of high school education (66% vs 90%), higher employment status (45% vs 3%) and were more than twice as likely to live alone (51% vs 23%).

In the IDD compared to the non-IDD population those diagnosed with diabetes for more than six years (72% vs 85%) and proportions of type 1 and type 2 diabetes (82% vs 72%) were similar. A higher proportion of IDD participants received support with medicines management from a paid or family carer (70% vs 5%).

Similar proportions in the IDD compared to the non-IDD population had 4 or more medicines prescribed (84% vs 83%), however an overall lower proportion of IDD participants were prescribed insulin (24% vs 66%) and a lower proportion of type 2 diabetics in the IDD group were prescribed insulin (11% vs 57%).

4.2.3.3 *Statistical comparisons of demographics between the IDD and non-IDD population.*

A chi-squared test was carried out for categorical variables to compare IDD and non-IDD groups. Statistical significance was defined as a value of $p < 0.05$. The only continuous variable was age and on visual inspection of a box plot (fig 1) outliers ($n = 2$) were noted. After confirming that this was not a measurement or data entry error a Mann-Whitney U test was performed to test for homogeneity between the IDD and non-IDD groups.

The male: female ratio was similar in both groups. The IDD group had lower median age ($p < 0.05$) and lower level of secondary school education ($p < 0.05$). A higher proportion of the IDD group were employed ($p = 0.05$) and lived alone ($p < 0.05$).

Further comparisons between the two groups showed no statistical difference in proportions of type 1 and type 2 diabetes ($p = 0.27$), length of time with diabetes ($p = 0.14$) or number of medicines prescribed ($p = 0.84$).

A higher proportion of IDD participants received support with medicines management ($p < 0.05$). However, a lower proportion of IDD participants were prescribed insulin ($p < 0.05$) and a lower proportion of IDD type 2 diabetics were prescribed insulin ($p < 0.05$).

It was therefore concluded that there were statistically significant differences in sociodemographic characteristics, support with medicines and the proportion of participants with IDD, type 2 diabetes and prescribed insulin. Hypothesis I stating no difference in demographic and health characteristics was rejected.

4.2.4 Internal reliability of measurement instruments

Internal reliability of measures was tested using Cronbach's Alpha with a value of 0.7-0.9 demonstrating a good level of internal consistency across all instruments in both groups

Table 4.3 outlines results in the group overall, IDD and non-IDD groups. MMAS8, GDS-LD Perceived sensitivity to medicines (PSM), self-efficacy (PCS) and perceived level of social support (mMOSS-8) all displayed good internal consistency. It was therefore concluded that all dependent and independent measurement instruments demonstrated good internal reliability in the IDD and non-IDD groups and hypothesis II was accepted.

Table 4.3: Internal reliability of dependent (medication adherence) and independent (depression, medication side effects, self-efficacy and social support) measurement instruments.

Scale	Group overall	IDD Cronbach's α	Non-IDD Cronbach's α
Medication adherence (MMAS8) (8-item scale)	0.7	0.7	0.7
Depression (GDS-LD) (20-item scale)	0.8	0.8	0.8
Medication side effects (PSM) (5-item scale)	0.9	0.8	0.9
Self-Efficacy (PCS) (4-item scale)	0.9	0.9	0.9
Social support (mMOS-SS) (8-item scale)	0.9	0.9	0.9

4.2.5 Association between medication adherence scores (MMAS8) and glycaemic control (HbA1c)

Correlation between MMAS8 and HbA1c was tested using Spearman's correlation coefficient. To establish predictions of HbA1c according to MMAS8 scores a linear regression was performed. Tables 4.4 and 4.5 present results in tabular format. Prior to reporting results assumptions of test were met which were that the relationship was non-monotonic in the group overall, IDD and non-IDD groups as assessed by visual inspection of scatterplots.

Table 4.4: Linear regression to determine whether HbA1c predicted MMAS8 score as a continuous variable in the group overall IDD and non-IDD population.

Result	Group overall (n = 111)	IDD (n = 33)	Non-IDD (n = 78)
r ₂	2%	1%	3%
Adjusted r ₂	1%	0%	2%
p value	0.1	0.5	0.8

Table 4.5: Linear regression to determine whether HbA1c could predict MMAS8 score as a dichotomous variable (poor adherence MMAS < 6, good adherence MMAS > 6) in the group overall, non-IDD and IDD groups.

	Group overall (n = 111) HbA1c	IDD group (n = 33) HbA1c	Non-IDD group (n = 78) HbA1c
Poor adherence (MMAS8 < 6)	<i>67mmol/mol (8.3%) (CI 62-72)</i>	<i>71 mmol/mol (8.7%) (CI 56-84)</i>	<i>66 mmol/mol (8.2%) (CI 61-71)</i>
Medium or good adherence (MMAS8 ≥ 6)	<i>63mmol/mol (7.9%) (CI 59-66)</i>	<i>65 mmol/mol (8.1%) (CI 55-74)</i>	<i>61 mmol/mol (7.7%) (CI 58-66)</i>

4.2.5.1 *Correlation between HbA1c and MMAS8 as continuous variables.*

With HbA1c and MMAS8 as continuous variables there was a significant negative correlation between HbA1c and MMAS8 score in the overall group (Spearman's r_s (111) = 0.199, $p = 0.04$), and in the non-IDD group (Spearman's r_s (78) = 0.224, $p = 0.05$). In the IDD group correlation was non-significant (Spearman's r_s (33) = 0.136, $p = 0.44$).

4.2.5.2 *Predictions of adherence according to mean HbA1c scores*

A linear regression to determine whether HbA1c values predicted MMAS8 adherence score as a continuous variable in the group overall, the IDD and non-IDD groups was carried out. Prior to linear regression assumptions were tested. There was independence of variables as assessed by a Durbin Watson statistic in the group overall (2.32), IDD (2.33) and non-IDD (2.30). Linearity was established by visual inspection of a scatterplot (Appendix 12). The residuals were normally distributed as assessed by a normal probability plot and histogram (Appendix 12).

The results are presented in Table 4.4. In the group overall, linear regression established that HbA1c as a continuous variable accounted for 0-3% of the variation of MMAS8 score, no effect according to Cohen (1988). HbA1c did not significantly predict MMAS8 score, as a continuous variable in the group overall (Adjusted $r_2 = 2\%$, $p = 0.1$); IDD group (Adjusted $r_2 = 0$, $p = 0.5$) or non-IDD group (Adjusted $r_2 = 3\%$, $p = 0.08$).

This non-significance may have been due to small sample size, therefore data were explored using MMAS8 as a dichotomous variable, defined as poor adherence (MMAS <6), or good adherence (MMAS8 \geq 6) in the group overall, IDD and non-IDD groups.

In the group overall, poor adherence (MMAS <6) was predictive of a 4 mmol/mol (4-5%) increase in HbA1c from a baseline of 63 mmol/mol. In the IDD population, poor adherence was predicted with a 6 mmol/mol (6%) increase in HbA1c from a baseline of 65 mmol/mol and, in the non-IDD population, poor adherence was predicted with a 5mmol/mol (5%) increase

in HbA1c from a baseline of 61 mmol/mol. Of interest, mean HbA1c was suboptimal across all groups even when scores of 6 (medium or good adherence) or more were reported.

These results suggest a negative correlation between HbA1c and medication adherence scores in the group overall and non-IDD groups and IDD groups. This correlation was significant in the group overall, non-IDD population but not in the IDD population.

With MMAS8 as a continuous variable, HbA1c did not significantly predict medication adherence in the group overall, the IDD or the non-IDD population. However, suboptimal adherence (MMAS8 <6) was associated with an increase in HbA1c in the group overall, the IDD and non-IDD population. Hypothesis III stating that there was a negative correlation between HbA1c and adherence score was upheld.

4.2.6 Summary

Table 4.6 summarises results from the hypotheses tested in this chapter. Analysis of demographic and reliability data showed significant differences in the IDD and non-IDD population in age, level of education, and living alone. There were significant differences in people with ID and type 2 diabetes who were prescribed insulin with a lower proportion of those participants receiving insulin therapy yet a higher proportion receiving support with medicines by carers.

All measurement instruments displayed good internal reliability in the IDD and non-IDD groups. There was a (non-significant) inverse relationship between HbA1c and medicines adherence scores in the IDD group

Correlations between MMAS8 and HbA1c were similarly negative across the group overall, IDD and non-IDD population. Although results failed to reach statistical significance in the IDD group results reveal that, as HbA1c increases, adherence to medication decreases.

Table 4.6 Results from hypothesis testing

	Hypothesis	Outcome
I	There would be no statistical difference in the demographics of the IDD diabetic and non-IDD population.	Rejected
II	The instruments used to measure independent factors would demonstrate good internal reliability.	Upheld
III	There would be a negative association between adherence score (MMAS8) and glycaemic control (HbA1c) score in the group overall, the IDD and non-IDD population– specifically the lower the MMAS8 the higher the HbA1c in the sample population.	Upheld

5 Chapter 5: Frequencies and associations between dependent and independent factors and testing of theoretical model

5.1 Introduction

This chapter will present findings from analysis of dependent and independent factors in the group overall, the IDD and non-IDD groups. The following research questions will be addressed:

1. What is the frequency of dependent factors (MMAS8 and HbA1c) and independent factors (depression, side effects, self-efficacy and level of social support) in the IDD population compared to the Non-IDD population?
2. Whilst controlling for regime complexity and support with medicines, does the proposed theoretical model predict medication adherence in the group overall, the ID and non-ID diabetic population?

Descriptive data for dependent and independent factors will be presented for the group overall and comparisons between the IDD and non-IDD groups. This will be followed by statistical comparisons between the IDD and non-IDD group.

Next, research question 2 will be addressed. Results from univariate and multiple regression analyses and the factors which are important predictors of adherence in the group overall, the non-IDD and IDD groups will be presented. This will determine how well the proposed model predicts medicines non-adherence. Lastly, threshold scores of independent factors which predict medicines adherence will be determined.

To address research question 1 the following hypotheses were tested:

- IV. There would be no difference in HbA1c in the IDD compared to the non-IDD groups.
- V. There would be no difference in MMAS8 in the IDD compared to the non-IDD groups.
- VI. Reported reasons for non-adherence in MMAS8 in the IDD and non-IDD groups would not be equal.
- VII. The frequency of independent factors in the IDD and Non-IDD groups would not be equal.

5.1.1 HbA1c and MMAS8 medicines adherence scores in overall, IDD and non-IDD groups

Table 5.1 provides an outline of findings in the group overall, IDD and non-IDD population. In the group overall, median HbA1c was 61 mmol/mol and 67 (61%) of participants had poor glycaemic control (HbA1c >58 mmol/mol, >7.5%) 67%. In the group overall 63% self-reported good adherence (MMAS \geq 6) to diabetic medicines. Mean adherence score recorded by MMAS8 score was 6.37 (SD 1.71).

A lower proportion of IDD compared to non-IDD participants had poor glycaemic control (54% vs 62%). Median HbA1c was lower in the IDD group (60 mmol/mol, (7.6%) vs 61mmol/mol, (7.7%)).

Comparisons of medication adherence between the IDD and non-IDD groups revealed similar mean adherence scores but a higher proportion of the IDD population reporting MMAS8 \geq 6 signifying good adherence (70% vs 62%).

Table 5.1: Comparison of dependent variables (medicines adherence and HbA1c) in the group overall, IDD group and non-IDD group.

Variable	Group overall (n = 111)	IDD group (n= 33)	Non-IDD Group (n = 78)	p value
HbA1c >58 mmol/mol (7.5%) suboptimal glycaemic control (%)	67 (61)	18 (54)	49 (62)	0.42 ^{chi}
HbA1c mmol/mol median	61	60	61	0.82 ^{MWU}
Medicines adherence MMAS8 ≥6 (Good adherence) (%)	70 (63)	23 (70)	48 (62)	0.41 ^{chi}
Mean medicines adherence score (SD)	6.4 (1.7)	6.5(1.6)	6.3 (1.7)	0.65 ^{ITT}

^{chi} Chi squared test for significance (ordinal variable).

^{MWU} non-parametric Mann Whitney U test as outliers detected in continuous data

^{ITT} Independent T-test as parametric continuous data.

5.2 Research question 1

5.2.1 Statistical comparison of dependent factors (HbA1c and MMAS8) in IDD and non-IDD groups.

Appendix 12 shows results from tests of assumptions. Visual inspection of box plots revealed outliers in both the IDD and non-IDD groups in HbA1c measurements, and no outliers in MMAS8 measurements. Distribution of HbA1c and MMAS8 scores were similar as assessed by visual inspection of scatterplots. Therefore, assumptions for making comparisons between the two groups were met.

To detect whether there were statistically significant differences between HbA1c and MMAS8 in the IDD compared to the non-IDD groups, Mann Whitney-U test and independent t-test were applied to HbA1c and MMAS8 respectively. A chi-squared test was performed to compare the frequency of poor glycaemic control and poor adherence in the two groups. Results are presented in Table 5.1.

Median HbA1c, as assessed by Mann-Whitney U test was not statistically significantly different between the IDD and non-IDD groups, ($U = 1,325, z = 0.25, p = 0.82$). The frequency of suboptimal glycaemic control (HbA1c) in the IDD and non-IDD groups using a chi-squared test revealed no statistically significant difference between the two groups ($p = 0.42$).

Adherence scores (MMAS8) in the IDD and non-IDD groups revealed a similar picture. Mean MMAS8, as assessed by independent t-test was not statistically significant ($p = 0.65$). Optimum adherence scores ≥ 6 in the IDD and non-IDD groups using a chi-squared was not statistically significant ($p = 0.41$).

There was no statistically significant difference in glycaemic control (HbA1c) and adherence score (MMAS8) in the IDD and non-IDD group. Hypotheses IV and V, that there would be no difference in HbA1c and MMAS8, were upheld.

5.2.1.1 *Comparison of MMAS8 scores in the overall, IDD and non-IDD groups*

Table 5.2 provides a detailed analysis of responses to the component items of the MMAS8 in the group overall, IDD and non-IDD groups. Comparisons between IDD and non-IDD groups were made using the Chi square test.

Items within the scale were marked ‘correct’ or ‘incorrect’ assigning a score of 1 when the ‘correct’ response was provided by the participant (Morisky, 1998). The correct or incorrect score does not refer to a mistake or error by the participant but reflects the wording used in the validated instrument (Appendix 8). To maintain consistency and allow for between study comparisons, the same terminology is used to report results in this study.

The most common reason for non-adherence within the MMAS8 in both the IDD and non-IDD population was forgetting to take medication (36% vs 50% $p = 0.19$) with similar proportions in each group reporting days when they did not take their medication.

A higher proportion of IDD participants reported non-adherence because diabetes medications made them feel worse (18% vs 8% $p = 0.17$). A lower proportion of IDD participants reported forgetting diabetic medication when travelling or leaving home (3% vs 22% $p = 0.02$). Therefore, the reasons for non-adherence in the IDD population compared to the non-IDD population were not equal and hypothesis VI was partially upheld.

Table 5.2: Frequency n (%) of responses in the group overall, IDD and non-IDD groups, Chi square comparisons between IDD and non-IDD group.

Morisky MMAS8 adherence scale (correct answer ^T)		Overall n = 111 (%)	IDD n = 33 (%)	Non- IDD n = 78 (%)	Chi Square p value
1.	Do you sometimes forget to take your diabetes medication? (N)	51 (54)	12(36)	39 (50)	0.19
2.	Over the past 2 weeks, were there any days when you did not take your diabetes medication? (N)	27 (24)	7(21)	20(25)	0.62
3	Have you ever cut back or stopped taking your diabetes medication without telling your doctor because you felt worse when you took it? (N)	12 (10)	6 (18)	6 (8)	0.17**
4	When you travel, or leave home, do you sometimes forget to bring along your diabetes medications? (N)	18 (16)	1 (3)	17 (22)	0.02*
5	Did you take your diabetes medication yesterday? (Y)	3 (3)	33 (0)	3 (4)	0.55
6	When you feel like your diabetes is under control, do you sometimes stop taking your medications? (N)	3 (3)	2(6)	1 (1)	0.21**
7	Do you ever feel hassled about sticking to your diabetes treatment plan (N)	26 (23)	11(33)	15 (19)	0.11
8	How often do you have difficulty remembering to take all your diabetic medications (never, sometimes, always)	43 (39)	12 (36)	31 (40)	0.73

^T Possible responses: yes/no; correct response = 1 point; incorrect response = 0 points. Possible responses: never (1 point); almost never, sometimes, quite often, always (0 points). Possible scale range = 0-8. Poor adherence MMAS<6, Medium= 6, 7, Good =8.

*statistically significant p < 0.05

**expected count less than 5 so exact test was selected for Pearson's chi squared.

5.2.2 Comparison of independent variables (depression, side effects, self-efficacy and social support in the IDD and non-IDD groups.

In this study depression using GDS-LD was defined as a score of >13, however as outlined in chapter 2 depressive or anxiety symptoms were also of importance in this study, so actual scores were also recorded and reported as a median value. The remaining factors (side effects, self-efficacy and social support) had no defined cut-offs therefore median scores are reported. Table 5.3 provides a summary of findings. Median scores were reported due to outliers detected on boxplot inspection (Appendix 13)

Median depression scores, using GDS-LD (range 0-40), were below the defined cut-off threshold score of 13, signifying depressive symptoms were low in the group overall, in the IDD and non-IDD groups. The frequency of depression was higher (GDS-LD >13) in the IDD compared to the non-IDD groups (36% vs 17.9%) and higher median depression scores were detected in the IDD group, (mean 10.9 vs 8.3, median 11 vs 8).

Higher median scores of perceived side effects using the PSM scale (range 5-25), were reported in the IDD compared to non-IDD groups (14 vs 10).

Lower median self-efficacy scores using PCS scale (range 0-100) were detected in the IDD group compared to non-IDD group (75 vs 93), signifying that the IDD population had lower levels of self-confidence compared to the non-IDD population.

Comparison of perceived levels of social support using the mMMOS-SS (range 0-100) between the two groups revealed lower median scores in the IDD group (78 vs 88).

In summary, the results indicate that the IDD population had a higher frequency of depression, greater perceived side effects from their diabetes medication, lower confidence and lower perceived levels of social support compared to the non-IDD group.

5.2.2.1 *Statistical analysis of independent variables in IDD and non-IDD groups.*

Appendix 13 illustrates testing of assumptions. On visual inspection of box plots, outliers across all variables were noted. Distribution of depression, side effects and self-efficacy variables across the IDD and non-IDD groups were not similar as assessed by visual inspection. It was concluded that the data was not normally distributed and non-parametric, Mann-Whitney-U tests was performed to test comparisons of independent variables between the two groups. Table 5.3 provides an outline of results.

There was a statistically significant difference in depression score ($U=977$, $z = 154.6$, $p < 0.05$), sensitivity to medicines ($U=741$, $z=-3.5$, $p < 0.05$) and self-efficacy scores ($U=1884$, $z=3.91$, $p < 0.05$) in the IDD and non-IDD groups. There was no statistically significant difference in median mMOS-SS scores ($U= 1563$, $z=1.79$, $p = 0.73$).

The hypothesis that independent factors in the IDD and non-IDD groups would not be equal was upheld.

Table 5.3: Comparisons of independent variables (depression, side effects, self-efficacy and perceived level of social support) in the group overall, IDD group and non-IDD groups.

Variable	Group overall (n = 111)	IDD group (n = 33)	Non- IDD group (n = 78)	Mann Whitney U-test p value
Median depression score GDS-LD	8	11	8	<0.05*
Depression score >13, n = (%)	26 (23)	12 (36)	14 (18)	
Median perceived sensitivity to medicines (PSM) or side effects score	11	14	10	<0.05*
Median self-efficacy score PCS	93	75	93	<0.05*
Median perceived level of social support mMOS-SS	85	78	88	0.73

*statistically significant difference between the IDD and the non-IDD groups.

5.3 Research Question 2:

Whilst controlling for regime complexity and support with medicines, does the proposed theoretical model predict medication adherence in the group overall, the IDD and non-IDD population?

This research question was met by testing the following hypotheses.

- VIII. After controlling for confounders, the overall model of medicines adherence would significantly predict medicines non-adherence in the group overall, the IDD and non-IDD groups.
- IX. After controlling for confounders, support with medicines and regime complexity, IDD would predict medicines non-adherence in the group overall.
- X. After controlling for confounders, support with medicines, and regime complexity depression would predict adherence in the non-IDD group.
- XI. After controlling for confounders, support with medicines, and regime complexity perceived level of social support would predict adherence in the IDD group.

5.3.1 Association between medicines adherence and independent factors (depression, self-efficacy, ID, social support and medicine side effects)

Prior to univariate or multiple regression, a number of assumptions were tested and reported as follows. There was linearity as assessed by partial regression plots and a plot of studentized residuals against the predicted values. There was independence of residuals, as assessed by a Durbin-Watson statistic of 2.2. There was homoscedasticity, as assessed by visual inspection of a plot of studentized residuals versus unstandardized predicted values. There was no evidence of multicollinearity, as assessed by tolerance values greater than 0.1. There were no studentized deleted residuals greater than ± 3 standard deviations, no leverage values greater

than 0.2, and values for Cook's distance above 1. Therefore, assumption of normality was met, as assessed by Q-Q Plot.

Univariate analysis was performed and results outlined in Table 5.4. Any independent factor with $p < 0.15$ were considered for inclusion into the regression model was then selected for step two. A multiple regression with MMAS8 as a continuous outcome was performed in SPSS by entering independent factors into the model simultaneously using the enter function for the group overall, the non-IDD and IDD groups. The third step was to control for any extraneous confounding variables using hierarchical multiple regression by sequentially entering confounding variables followed by independent factors into the model. A linear regression was then performed on the most important factors emerging from the model in the group overall, the IDD and non-IDD groups to estimate predictions of independent factors and medicines adherence.

5.3.1.1 *Step 1: Univariate analysis.*

Table 5.4 presents results of univariate analysis. Linear regression established that IDD did not statistically significantly predict medicines adherence in the group overall ($F(1,109) = 0.213$, $p = 0.6$). Furthermore, perceived level of social support (mMOS-SS) did not statistically significantly predict in the group overall ($F(1,109) = 0.992$, $p = 0.32$), the IDD ($F(1,31) = 0.900$, $p = 0.35$) and non-IDD groups ($F(1,76) = 0.439$, $p = 0.51$).

Depression score (GDS-LD) statistically significantly predicted medicines adherence in the group overall, $F(1,109) = 24.3$, $p < 0.001$ and accounted for 17% of the variation in adherence score, a small effect size. An even greater effect was evident in the non-IDD population where depression statistically significantly predicted adherence, $F(1,76) = 35.3$, $p < 0.000$ and accounted for 30% of the variation in the adherence score, a medium effect size. There was no statistically significant prediction of adherence according to depression

score $F(1, 31) = .92$, $p = 0.18$ which accounted for 2% of the variation in adherence score, a small effect size.

Side effects (PSM) statistically significantly predicted medicine adherence in the group overall $F(1, 109) = 4.2$, $p = 0.04$ and accounted for 3% of the variation in adherence score, a small effect size. Side effects approached statistical significance in the IDD group $F(1, 31) = 3.6$, $p = 0.06$ and accounted for 8% of the variance in adherence score, a small effect size. Side effects did not significantly predict adherence in the non-IDD population $F(1, 76) = 2.407$, $p = 0.12$.

Self-efficacy did not predict medications adherence in the group overall $F(1, 109) = 1.266$, $p = 0.26$, or in the IDD group $F(1, 31) = 0.299$, $p = 0.59$. In the non-IDD group self-efficacy statistically significantly predicted medicines adherence $F(1, 76) = 5.123$, $p = 0.02$ and accounted for 5% of the variance in the adherence score.

In summary, depression, side effects and self-efficacy satisfied selection for multiple regression analysis.

Table 5.4: Univariate analysis of MMAS8 and independent factors (ID, depression, side effects, self-efficacy and social support)

	Group overall			IDD			Non-IDD		
	r ² (adjusted r ²)	F	p	r ² (adjusted r ²)	F	p	r ² (adjusted r ²)	F	p
ID (ID)	0% (0%)	(1,109) =0.213	0.6	-	-	-	-	-	-
Depression GDS-LD ^c	18% (17%)	(1,109) =24.3	<0.000*	5% (2%)	(1,31) =9.2	0.18	31% (30%)	1,76=35.3	<0.000*
Side effects (PSM) ^c	3% (3%)	(1,109) =4.2	0.04*	10% (8%)	(1,31) =3.6	0.06*	3% (2%)	1,76=2.407	0.125*
Self-efficacy (PCS) ^c	1% (0)	(1,109) =1.266	0.26	1% (0%)	(1,31) =0.299	0.59	6% (5%)	1,76=5.123	0.02*
Social support (mMOS-SS)	0% (0%)	(1,109) =0.992	0.32	2% (0%)	(1,31) =0.90	0.35	0% (0%)	1,76=0.439	0.51

*significant factors p < 0.15; ^c factors meeting selection for multiple regression analysis

5.3.1.2 *Step 2: Multiple regression analysis*

Results of step 2 of the multiple regression are outlined in Tables 5.5 and 5.6. In the group, overall r^2 for the model was 19%, with an adjusted r^2 of 17%, a small effect size. Multiple regression analysis showed the model statistically significantly predicted medicines adherence ($F(3,107) = 8.42, p < 0.001$). However, depression was the only independent predictor of medicines adherence in the group overall ($p = <0.001$). Factors that were not statistically significant predictors of adherence were side effects ($p = 0.35$) and self-efficacy ($p = 0.36$).

In the IDD group, overall r^2 for the model was 19% with an adjusted r^2 of 11%, a small effect size. The model did not predict adherence in the IDD population ($F(3, 29) = 2.30, p = 0.09$). No factor was an independent predictor of adherence, however results suggested that medicines side effects approached statistical significance ($p = 0.06$). Factors that were not significant predictors of adherence were depression ($p = 0.09$) and self-efficacy ($p = 0.36$).

In the non-IDD group, overall r^2 for the model was 32% with an adjusted r^2 of 30%, a medium effect size. The model predicted adherence in the non-IDD population ($F(3, 74) = 11.9, p < 0.001$). However, depression was the only independent predictor of adherence in the non-IDD population ($p < 0.001$). Factors that were not significant predictors of adherence were side effects ($p = 0.54$) and self-efficacy ($p = 0.48$).

Table 5.5: Standardised and unstandardized regression coefficients for the variables entered into the model (depression, side effects and self-efficacy: Group overall, IDD and non-IDD groups).

	Group overall (n=111)				IDD (n=33)				Non-IDD (n=78)			
	B	SE _B	β	p	B	SE _B	β	p	B	SE _B	β	p
Depression (GDS-LD)	-0.132	0.30	-0.423	P < 0.001	-0.075	0.04	-0.294	P = 0.09	-0.202	0.39	-0.565	P < 0.001
Side effects (PSM)	-.032	-0.35	-0.084	P = 0.35	-.057	-0.32	-0.328	P = 0.06	-.028	-0.045	-0.064	P = 0.35
Self-efficacy (PCS)	-.004	0.007	-0.620	P = 0.53	-.010	0.011	-0.159	P = 0.36	-.007	0.09	0.072	P = 0.53

Table 5.6 Overall model fit for variables entered into the model (depression, side effects and self-efficacy): Group overall, IDD and non-IDD groups.

	Group overall (n = 111)	IDD (n = 33)	Non-IDD (n = 78)
r ₂ (adjusted r ₂)	18 (17)	19 (10)	32 (30)
F	(3,107) =8.41	(3,29) =2.30	(3,74) = 11.86
p value	<0.001	0.09	<0.001

5.3.1.3 Step 3: *Multivariate analysis controlling for confounders*

Testing of the proposed theoretical model and ability to predict medicines adherence in the group overall, IDD and non-IDD groups after controlling for confounders (regime complexity and support with medication) was carried out. Tables 5.7 and 5.8 detail the changes in significance (p value) after controlling for support and regime complexity (number of medicines and whether on insulin therapy) in the group overall, non-IDD and IDD groups.

In the group overall, after controlling for confounders, r_2 for the model was 22%, with an adjusted r_2 of 17%, a small effect size. The model of side effects, self-efficacy and depression predicted medicines adherence ($F(6, 104) = 4.75, p < 0.001$) but depression was the only independent predictor of medicines adherence ($p < 0.001$). After controlling for confounders, side effects ($p = 0.25$) and self-efficacy ($p = 0.9$) were not statistically significant predictors of adherence.

In the IDD group, after controlling for confounders r_2 for the model was 10%, with an adjusted r_2 of 0%, no effect. The overall model did not statistically significantly predict medicines adherence ($F(6, 26) = 1.52, p = 0.2$). However, side effects approached statistical significance ($p = 0.06$) and was the most important factor in predicting medicines adherence. Depression ($p = 0.15$) and self-efficacy ($p = 0.16$) were not statistically significant predictors of adherence.

In the non-IDD group, after controlling for confounders r_2 for the model was 34%, with an adjusted r_2 of 29%, a medium effect size. The overall model predicted medicines adherence ($F(6, 71) = 6.131, p < 0.001$). After controlling for confounders depression was the only independent predictor of medicines adherence ($p < 0.001$). After controlling for confounders factors that were not predictors of adherence were side effects ($p = 0.5$) and self-efficacy ($p = 0.4$). Therefore, across all groups, controlling for potential confounders, namely support and regime complexity (number of medicines and insulin therapy) had minimal effect on the model.

Table 5.7: Multiple regression: Unadjusted and adjusted values to predicted factor associated with adherence with MMAS8 as continuous variable after controlling for potential confounders (support with medicines and regime complexity): Group overall, IDD and non-IDD

	Overall Group n = 111			IDD n = 33			Non-IDD n = 78		
	Unadjusted model B (95% CI)	p value	Adjusted model p value ^d	Unadjusted model B (95% CI)	p value	Adjusted model p value ^d	Unadjusted model B (95% CI)	p value	Adjusted model p value ^d
Depression (GDS-LD)	-0.134(-0.190, - 0.073)	<0.001*	<0.001*	-0.75(-0.165, - 0.015)	0.10	0.15	-.202(-279-0.124)	<0.001*	<0.001*
Side effects (PSM)	-0.032 (-0.100, 0.37)	0.36	0.25	-0.112(-0.228,0.005)	0.06	0.06**	0.28(-0.062, 0.118)	0.55	0.50
Self-efficacy (PCS)	-0.004(-0.018, 0.014)	0.53	0.89	-0.010(-0.033,0.013)	0.96	0.16	0.007(-0.012, 0.025)	0.48	0.40

^d Controlled for support with medication, no of medicines and if on insulin (regime complexity).

*statistically significant

**most important but not statistically significant.

Table 5.8: Overall fit for variables entered the model after controlling for support with medicines and regime complexity, group overall, IDD and non-IDD groups.

	Group overall (n = 111)	IDD (n = 33)	Non-IDD (n = 78)
r ₂ (adjusted r ₂)	22% (17%)	10% (0%)	34% (29%)
F	(6,104) = 4.75	(6,26) = 1.52	(6,71) = 6.131
p value	<0.001	0.2	<0.001

5.3.1.4 *Summary of predictors of adherence*

In the group overall, univariate analysis showed that IDD was not a significant predictor of adherence. Therefore, hypothesis IX was rejected.

The overall model did not predict medicines adherence in the group overall, the non-IDD or IDD population, therefore hypothesis VIII was rejected.

In the group overall and non-IDD population, multiple regression analysis revealed depressive symptoms was the only statistically significant predictor of adherence therefore hypothesis X was upheld. In the IDD population perceived level of social support did not predict adherence and therefore hypothesis XI was rejected. In fact, in the IDD population no factor significantly predicted adherence however, side effects was the most important factor associated with adherence and was approaching statistical significance in the IDD population.

5.3.2 Predicting non-adherence according mean GDS-LD and PSM score adherence in the group overall, IDD and non-IDD groups.

To establish whether GDS-LD and PSM scores predicted non-adherence in the group overall, in the IDD and non-IDD groups a linear regression of those factors was performed. These results are outlined in Table 5.9.

As depression increased medicines adherence scores decreased, suggesting increased symptoms of depression predicts medicines non-adherence across all the groups. Regarding side effects the prediction was not clear in the group overall or the non-IDD group, but in the IDD groups perceived level of side effects increased as medicines adherence score decreased.

In the group overall, and in the non- IDD group, mean depression score of 11 predicted medicines non-adherence, with a 1 point increase in depression score resulting in a 1 point decrease in adherence score. There was no linear association between side effects and medicines adherence in the group overall. This suggests that a GDS-LD depression score of >10 predicts non-adherence to diabetic medicines in a mixed cohort of IDD and non-IDD diabetic service users and in a cohort of non-IDD service users.

In the IDD group, a mean depression score of 12 predicted medicines non-adherence, with a 1 point increase in mean depression score indicating a 1 point decrease in adherence. A linear association between side effects and medicines non-adherence was noted, with a 1 point increase in side effects score indicating a 1 point decrease in adherence score. A GDS-LD score of 12 predicted medicines non-adherence in the IDD population. A PSM score of 16 or more appeared to predict suboptimal adherence in the IDD population.

Table 5.9: MMAS8 score and predicted Depression (GDS-LD) and Side effects (PSM) scores in the group overall.

Adherence^t (MMAS8)	Depression (GDS-LD)			Side effects (PSM)		
	Group overall	IDD	Non-IDD	Group overall	IDD	Non-IDD
4	12 (10.7-13.9)	13 (9.2-17.4)	11 (10.4-13.4)	13 (11.6-14.5)	17 (13.5-19.5)	12 (10.3-13.3)
5 ^x	11 (9.7-12.1)	12 (9.1-15.4)	10 (9.2-11.5)	12 (11.4-13.6)	16 (13.3-17.8)	11 (10.2-12.5)
6	10 (8.9-10.5)	11 (9.1-13.8)	8 (7.8-9.7)	12.0 (11.2-12.9)	15 (12.9-16.3)	11 (10.1-11.9)
7	8 (7.2-9.1)	10 (8.1-12.8)	7 (6.2-8.2)	12 (10.6-12.4)	14 (11.9-15.3)	10 (9.6-11.6)
8	7 (5.5-8.1)	9 (6.4-12.6)	5 (4.3-6.9)	11 (9.9-12.2)	13 (10.4-14.9)	10 (9.9-11.5)

Data presented as mean (95% CI)

^tPossible scale range = 0-8. Poor adherence MMAS<6, Medium= 6, 7, Good =8.

^x score of 5 or less - poor adherence

5.3.2.1 *Summary of frequency of and factors associated with adherence*

Results from the hypotheses tested in this chapter are outlined in Table 5.10. Hypotheses IV, V, VI, VII and X were upheld and VIII, IX and XI rejected. The IDD population had a higher median HbA1c, yet the frequencies of suboptimal glycaemic control and medicines adherence were similar in the IDD and non-IDD groups.

Reasons for non-adherence did not statistically significantly differ between the two groups with forgetting to take medications reported most frequently. A clinically important finding was a higher percentage of IDD participants reported not taking medicines because it made them feel worse when they did, and a higher percentage of the non-IDD population reported forgetting to medicines when travelling or going out.

Higher depressive symptoms, side effects and lower confidence were reported in the IDD than non-IDD participants. There was no difference in perceived levels of social support.

Univariate and multivariate analysis revealed the model did not significantly predict medicines non-adherence in the group overall the IDD and non-IDD populations. ID was not a significant factor associated with adherence and, in the group overall and non-IDD population depression was the only statistically significant factor. This will be further expanded upon in the discussion chapter.

In the IDD population, univariate analysis revealed that perceived level of social support was not a predictor of adherence thus rejecting the hypothesis that this was the most important factor associated with adherence, instead side effects was the most important predictor of adherence but failed to reach statistical significance in this group.

Linear regression revealed that a depression score of 10 or greater predicted poor medicines adherence in the group overall and in the non-IDD group. Comparing this to the IDD group depression scores of 12 predicted medicines non-adherence.

Linear regression revealed that a PSM score of 16 may predict poor adherence in the IDD but not in non-IDD population. Self-efficacy and perceived level of social support were not statistically significant in the group overall, IDD or non-IDD groups, therefore it was concluded that these factors were not associated with adherence.

Table 5.10: Results of hypotheses testing IV – XI

	Hypothesis	Outcome
IV	There would be no difference in HbA1c in the IDD compared to the non-IDD groups	Upheld
V	There would be no difference in MMAS8 in the IDD compared to the non-IDD groups.	Upheld
VI	Reported reasons for non-adherence in MMAS8 in the IDD and non-IDD groups would not be equal.	Upheld
VII	The frequency of independent factors in the IDD and Non-IDD groups would not be equal.	Upheld
VIII	After controlling for confounders, the proposed model of medicines adherence would significantly predict medicines non-adherence in the group overall, IDD and non-IDD groups.	Rejected
IX	After controlling for confounders, support with medicines and regime complexity, ID would predict medicines non-adherence in the group overall.	Rejected
X	After controlling for confounders, support with medicines, and regime complexity, depression would predict adherence in the non-IDD group.	Upheld
XI	After controlling for confounders, support with medicines, and regime complexity perceived level of social support would predict adherence in the IDD group.	Rejected

6 Chapter 6: Qualitative Results

6.1 Stage two – Qualitative stage

The objectives of this stage were to triangulate and further explain the results from stage one and to identify emergent new themes. As outlined in chapter 3, this is termed an “abductive” approach and is a combination of deductive and inductive approaches (Graneheim et al, 2017). Stage two sought to address research question 3: Is the frequency of, and factors associated with, adherence consistent with the views of carers supporting diabetes medicines management?

The aims of this stage were to:

1. Triangulate stage one self-reported scores with carers’ perceptions of dependent and independent factors
2. Explore how carers support stage one participants with medicines adherence
3. Explore the views of carers regarding the relationship between medicines adherence and independent factors (depression, side effects, self-efficacy and social support)
4. Explore other factors associated with diabetes care, for example, diet and exercise with carers.

An abductive thematic analysis based on stage one results was carried out. The primary intention was to corroborate data collected during phase one to provide a more in-depth explanation and analysis of medicines adherence behaviour in the sample population.

As it was important to identify new emergent themes associated with adherence to diabetes care an inductive approach was also part of this stage. This was particularly important in the IDD population, due to the paucity of evidence on medicines adherence in

the IDD literature. The systematic review which provided the theoretical framework for this study was based on non-IDD literature, therefore it was conceivable that additional themes associated with adherence in the IDD population could emerge.

Finally, it acknowledged that medicines were only a part of diabetic management. Although the overall aim of the study was to investigate medicines adherence, diet and exercise are of equal importance. By exploring other aspects of diabetes care it contextualised medicines adherence within overall diabetes care, establish how carers supported service users, and explored whether one aspect of care was prioritised over another.

This chapter is in three parts. First, stage two participant demographics will be presented; followed by triangulation of stage one and two findings (research aim 1). Secondly, themes emergent from analysis of data will be presented in the context of research aims 2, 3 and 4. Finally, a discussion of findings in the context of the wider literature will be presented. Throughout, and where possible, comparisons between the IDD and non-IDD population and stage one and two findings will be made.

6.2 Data collection and reporting

Following a preliminary analysis of stage one data, a topic guide was devised to meet the aims (Appendix 12). The main topics were how carers supported medicines adherence and the influence that depression, side effects, confidence and social support had on their approach to support. Additional and emergent themes were explored by asking the carers about other aspects of diabetes care that the stage one participant found challenging.

Qualitative interviews took place between January and May 2016 and interviews took place in each stage one participant's home. Stage one participants were not present during the interviews. Following consent the topic guide interviews with carers were administered in face

to face semi-structured interviews. Interviews were 15 and 35 minutes in duration and audio-recorded. On completion, they were transcribed *verbatim* and identifiable information removed to protect participant confidentiality.

To further protect participant confidentiality and to ensure that carers' views reflected their own perspective on the service users' medicines adherence and associated factors, stage one results relating to the person that they cared for were not discussed. Instead, overall stage one results were discussed with carers during the interview. To further protect confidentiality pseudonyms were used during the reporting of stage two.

The secondary data reported in this stage (Table 6.3) were collected during stage one of the study and related to medicines adherence, diabetic control and factors associated (depression, side effects, self-efficacy and social support). These data were matched to their stage two carers' transcripts to meet aims 1, and 3.

Analysis was in accordance with procedure outlined in chapter 3. An unpaid carer was defined as a relative, friend or neighbour who supported the IDD or non-IDD participant and a paid carer was someone employed by a health and social care agency. Any ambiguous data was checked with the interviewee and results were verified by one of the research supervisors: an expert in qualitative research.

6.3 Results

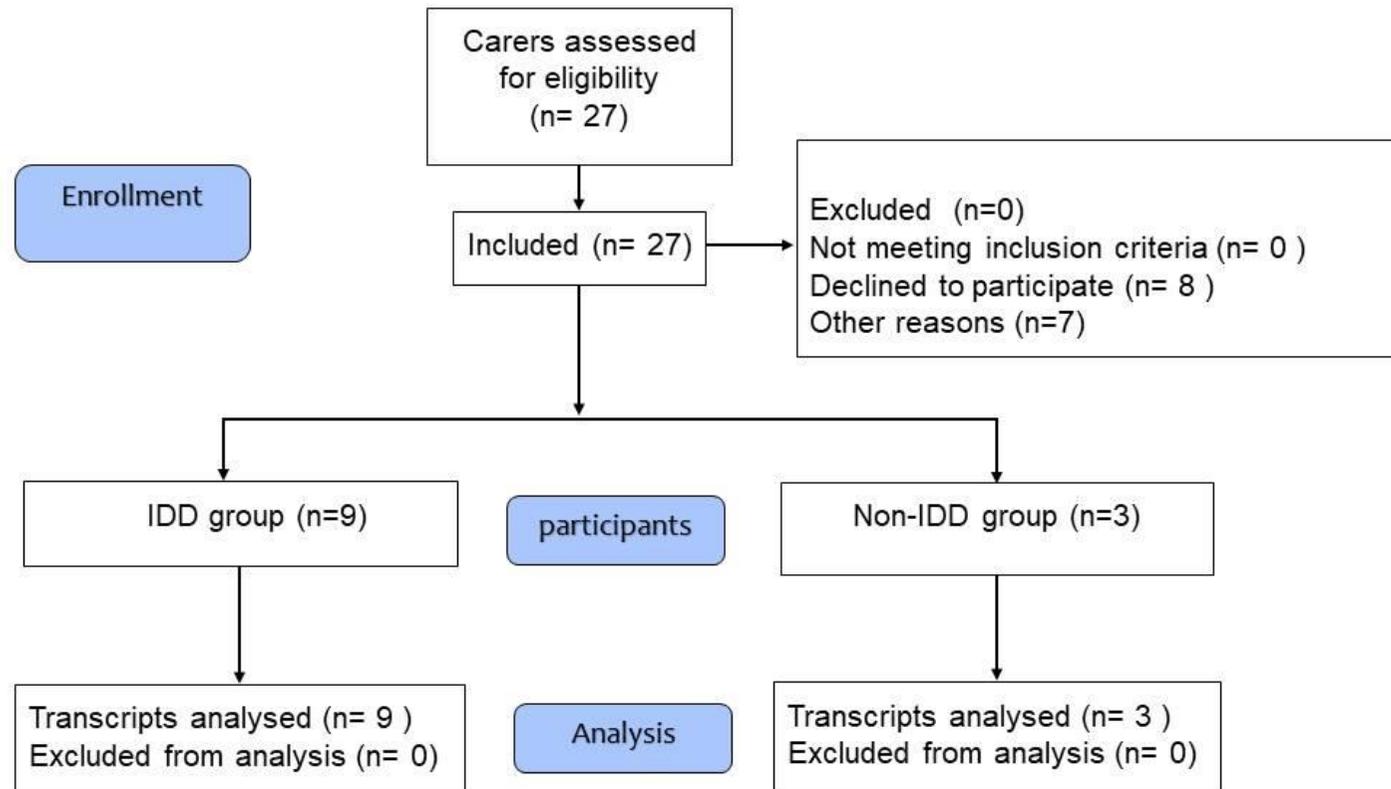
6.3.1 Demographics

Figure 6.1 outlines recruitment. In the group overall, (n = 111), 27 received help from a paid or unpaid carer with their medications, and all met inclusion criteria (IDD group n = 23, non-IDD group n = 4). Sixteen were unpaid carers and 11 were paid. All carers were invited to take part and 12 were recruited: 9 carers from IDD population, 3 carers from non-IDD population.

In the IDD carer population, of the 23 approached, 8 declined to participate, 3 could not be contacted to arrange interview and 2 did not attend for interview. One participant had died between stage one and two, and, after contacting the carer, it was agreed that it would be too distressing to interview her and therefore participation was withdrawn. This resulted in 9 carers for people with IDD participating.

In the non-IDD carer group, 4 carers were approached, one did not attend for interview resulting in three of the IDD carer population participating.

Figure 6.1: Stage two recruitment



6.3.2 Descriptive statistics and matching of stage one and stage two participants

Descriptive statistics are outlined in Table 6.1. In the group overall, 12 carers were recruited, of which 4 were paid and 8 unpaid carers. Matching stage two data with stage one data revealed that in the group overall, 4 carers supported participants with suboptimal adherence and 7 carers supported participants with suboptimal glycaemic control (HbA1c > 58 (> 7.5%)).

Comparing type of carer in IDD and non-IDD groups: in the IDD carer group, 4 received paid carer support and 5 unpaid carer support. In the non-IDD group all support was provided by an unpaid carer.

Three carers supported IDD participants with suboptimal adherence compared to one in the non-IDD group. With regard to glycaemic control, in the IDD group 5 carers supported participants with suboptimal glycaemic control compared to two in the non-IDD group

In the group overall, carers supported 7 participants with depressive symptoms (GDS-LD >10), of whom the majority (n = 6) were IDD participants. Side effects scores (PSM >15) were elevated in 3 of stage one participants all of whom were people with IDD. Carers supported 3 with low self-efficacy of which 2 were IDD participants, and no stage one participants whose carers participated in stage two in either group had low perceived levels of social support.

Table 6.1: Descriptive statistics including adherence and glycaemic control

	Total (n = 12)	IDD (N = 9)	Non-IDD (n = 3)
Paid carer	4	4	0
Unpaid carer	8	5	3
MMAS <6 (poor adherence)	4	3	1
HbA1c >58 mmol/mol (poor glycaemic control)	7	5	2
Depression score >10	7	6	1
Side effects >15	3	3	0
Self-efficacy <35	3	2	1
Social support <50	0	0	0

6.4 Findings: triangulation

The first aim of this stage was to triangulate carers' accounts with stage one results and corroborate stage one and two findings in relation to independent factors affecting medicines adherence, namely; depression, side effects, self-efficacy and social support. Table 6.2 illustrates alignment of stage two results with stage one.

Table 6.2: Triangulation of stage one and stage two results

^p Pseudonym used

	IDD									Non-IDD		
Stage one Participant ^p	Mark	Hamish	Carl	Karen	Simon	Claire	Brian	John	Jess	Fiona	Jane	Ian
Carer ^p	Barbara	Keith	Louise	Robert	Jennifer	Jim	Mary	Alex	Susan	Chris	Kevin	Sarah
Dependent factors												
Medicines Adherence (MMAS8)	8	5	6	5	8	8	6	5	8	4	8	8
* Triangulation with stage two results	√	√	√	√	√	√	√		√	√	√	√
HbA1c mmol/mol*	102	100	42	45	60	46	75	59	46	56	73	76
Independent factors												
Depression score (GDS-LD) *	5	26	11	17	6	12	17	5	21	7	10	3
Triangulation with stage two results	√	√	√	√	√	√	√	√	√	√	√	√
Side effects (PSM)*	9	11	14	25	13	9	9	22	19	6	9	10
Triangulation with stage 2 results	√			√	√	√			√		√	
Self-efficacy (PCS)*	78	54	96	68	28	78	36	93	32	100	28	100
Triangulation with stage 2 results	√	√	√		√		√	√			√	√
Social support (mMOS-SS)*	85	55	100	75	98	100	68	90	95	60	100	100
Triangulation with stage 2 results	√	√	√	√				√	√			

*data obtained from stage 1 results

6.4.1.1 *Triangulation of stage one and two: dependent factors (adherence)*

Eleven carers' reports of adherence were matched with stage one participant reports. Many in the IDD and non-IDD population reported that those with high adherence scores took medications *'fine'* and that they were *'used to it'*. Others with poor adherence reported that participants were often non-adherent due to become frequently distracted or forgetting; for example, Keith, a paid carer, reported Hamish, an IDD participant, was:

'... very easily distracted....so if something comes up he's very good at going away and not taking his insulin stuff with him' (MMAS8 score 5).

6.4.1.2 *Triangulation of stage one and two results: independent factors (depression, self-efficacy, side effects and social support).*

Corroboration of stage one and two results revealed alignment of reports of depressive symptoms (Table 6.2). Due to the relationship between depression and adherence further evidence of this is explored and analysed in Section 6.4.3.

Alignment of stage one and two results on side effects was less clear. Half of carers were not aware of perceived side effects even when high scores were reported by stage one participants. In those that had discussed side effects, in a minority of cases it was apparent that carers and stage one accounts were aligned as low side effects scores were also reported by stage one participants; for example, Mary, a family carer, stated that Brian (an IDD participant):

'...has never mentioned side effects to me' (PSM score 9, MMAS8 score 6).

A carer of a non-IDD participant, Kevin believed that side effects were an inevitable consequence of drug treatment, but that Jane was not affected by side effects.

'Well basically she realises that every tablet has some sort of side effect and she takes them.' (PSM Score 9, MMAS8 score 8).

In IDD and non-IDD carer populations, eight were aware of stage one participants' levels of confidence and were aligned to self-efficacy scores reported in stage one. Jim, an unpaid

carer for Claire, a person with IDD, stated he believed her to be ‘60%’ confident in managing her treatment and she had reported a medium to high self-efficacy score (PCS) of 78. Similarly, in the non-IDD population, Jane reported a low self-efficacy score and Kevin, her family carer corroborated this by stating her confidence was low due to a visual impairment.

Finally, carers’ accounts of social support triangulated with stage one results in some of the IDD but none of the non-IDD group. Keith a paid carer, described how Hamish, an IDD participant, had quite an erratic social circle which was also reflected in Hamish’s low social support score (mMOS-SS).

‘when he has a fall out with his family or with his friends as well, then it brings on the arrogance in the opposite way in being that ‘I don’t need anybody, I can do things myself’ which then turns into being a bit depressed’ (MMAS8 score 5, mMOS-SS = 55)

These results suggest that stage two results triangulated with adherence and depression scores and moderately with self-efficacy and social support self-report scores in stage one. With side effects, alignment between stage one and two results was less clear due to half of carers not exploring side effects with the stage one participant. It was concluded that stage one results were aligned to stage two accounts in medicines adherence and depression, confidence and social support, however side effects scores were only partially aligned.

The alignment between medicines adherence, associated factors and support provided by carers will now be explored further with an analysis of qualitative findings under themes and subthemes emerging from the qualitative data.

6.5 Emergent themes

Using NVIVO software, data were organised and coded under three main categories:

1. Mode of help
2. Exploration of medicines adherence in the context of independent factors

-
- a. depression
 - b. medicines side effects
 - c. confidence
 - d. social support
3. Other factors associated with diabetic control

Three themes emerged from data analysis namely:

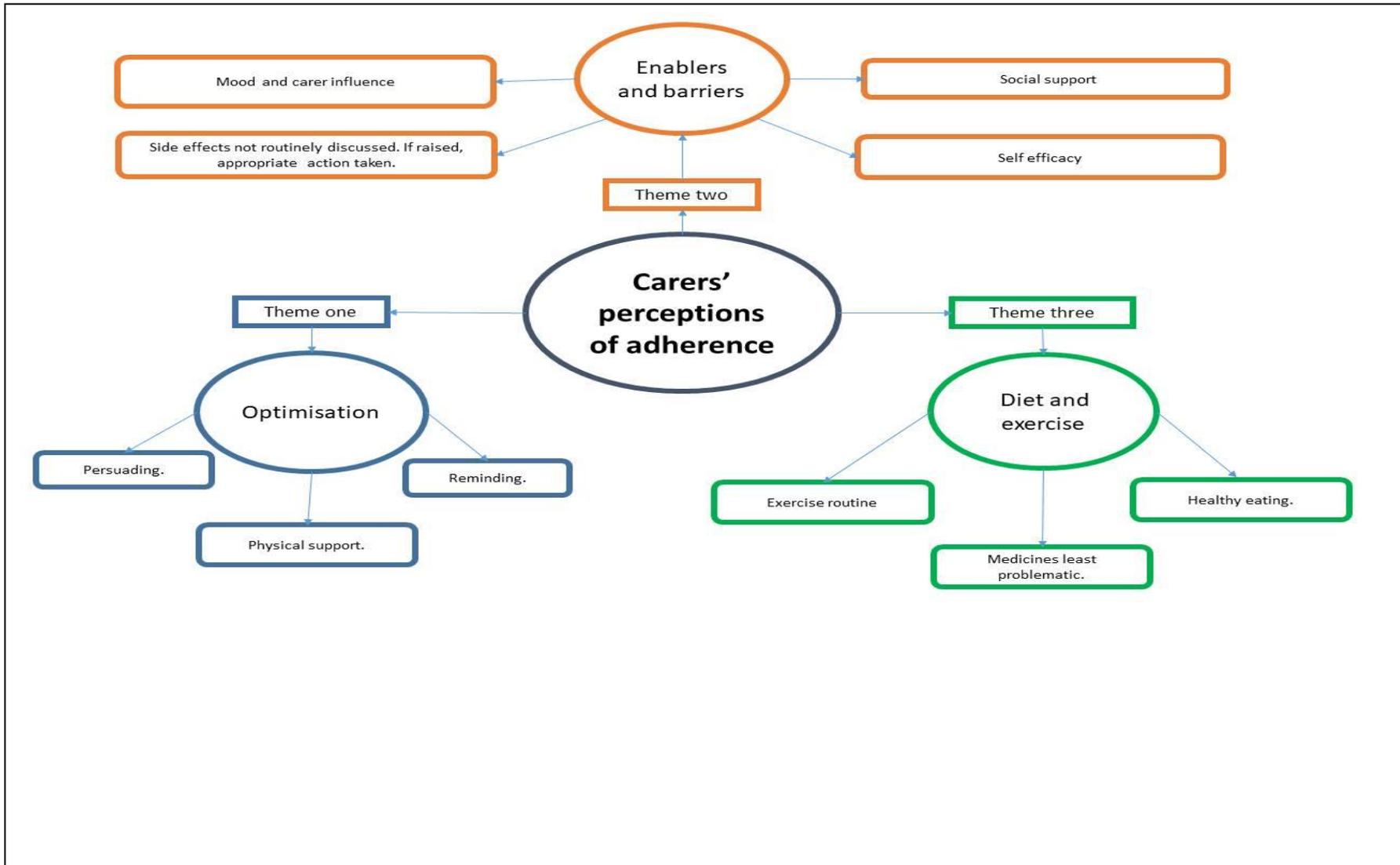
1. Optimisation.
2. Enablers and barriers.
3. Diet and exercise.

Table 6.3 presents a description of themes and descriptors. Within these themes subthemes were identified (Figure 6.2).

Table 6.3: Themes and theme descriptors

	Theme	Theme descriptor
1.	Optimisation	Optimisation strategies were defined as any type of psychological or physical assistance which the carer interpreted as support for the IDD or non-IDD participant to take prescribed diabetic medicines. Prescribed diabetic medicines was defined as a pharmacological treatment regime recommended by a prescriber or other healthcare professionals (for example diabetes specialist nurses, district nurse or pharmacist) designed to optimise glycaemic control.
2.	Enablers and barriers	How IDD and non-IDD carers interpreted the influence of depression side effects, self-efficacy and social support had on compliance of the stage one participant to prescribed diabetic medicines.
3.	Diet and exercise	Carers' interpretation of stage one participants' adherence to diet and exercise recommendations and how this compared to adherence to diabetic medicines.

Figure 6.2 Emergent themes and subthemes



6.5.1 Theme 1: Optimisation

Table 6.4 illustrates carer's responses with regard to optimisation of medicines. The qualitative data suggested that all carers optimised medicines management using one or more strategies and frequently provided opportunities for participants to self-manage medicines whilst balancing this with support strategies. Within this theme, reminding, persuading and physical support emerged as subthemes.

Table 6.4: Theme 1: Optimisation: Carers' responses

	IDD										Non-IDD		
Stage one participant ^P	Mark	Hamish	Carl	Karen	Simon	Claire	Brian	John	Jess		Fiona	Jane	Ian
Carer	Barbara 301	Keith 302	Louise 312	Robert 304	Jennifer 305	Jim 306	Mary 311	Alex 308	Susan 309		Chris 310	Kevin 307	Sarah 303
Reminding			√					√			√		√
Persuading				√		√	√		√				
Physical support	√	√			√		√					√	

6.5.1.1 *Reminding*

Qualitative data suggested that those in the ‘habit’ of taking medicines and reporting good adherence often needed verbal or visual prompts, suggesting that reminders are necessary even for people who have lived with diabetes for several years. This approach was common in carers of IDD and non-IDD participants. For example, Sarah, the family carer of Ian (non-IDD participant), used non-verbal prompts to support adherence by putting medicines on his breakfast plate. This was despite Ian being diabetic for 14 years, in the habit of taking medications and Sarah’s confidence that he would be able to manage his medicines independently. Likewise, Jim a family carer of Claire, (an IDD participant) felt that she would forget or lack motivation to take medicines:

‘I think that if it wasn’t for somebody like myself, that was maybe just reminding her and helping her with the medication then she would probably have stopped taking a wee while ago.’ (MMAS8 score 8, HbA1c 46).

This mode of help was used by carers regardless of whether they were paid or unpaid and assisted in maintaining optimum adherence in both the IDD and non-IDD group.

6.5.1.2 *Persuading*

A second subtheme emergent from the qualitative data was persuading. This approach to optimisation was a mode of support provided by carers of the IDD but not the non-IDD population. For participants who reported suboptimal adherence scores, carers in the IDD group acknowledged stage one participants’ reluctance to take their medications, however carers perceived they had a role in persuading them to take their medication..

One reason carers used to persuade stage one participants to take medicines was the positive effect on health. Susan, a paid carer of IDD participant, Jess, stated:

‘...we always manage to get her to take them; she knows that if she doesn’t take her medication she becomes unwell.’ (MMAS8 score 8, HbA1c 46)

Louise adopted a similar strategy with Carl, an IDD participant:

'Sometimes he can become stubborn, so he has to be coaxed and you do have to observe that he does take them, but he does have an understanding that he has to take them for his health.' (MMAS8 score 6, HbA1c 42)

There was some evidence that unpaid carers of IDD participants were more direct in their support and used strategies such as 'nagging' and consequentialist threats to persuade people to take medication. Although this persuasive approach may be considered negative behavioural support, it did appear to be effective in supporting medicines adherence in the IDD population as evidenced by good or moderate glycaemic control. Robert, family carer of Karen, an IDD participant, said:

'I say, well there are two ways to look at it, you either take it and you live or you don't take it and you die...when you tell them as blunt as that they usually say alright and they take them' (MMAS8 score 5, HbA1c 43)

Mary, family carer took a similarly direct approach to persuading Brian (IDD participant) to take medication:

'..he thinks they're a pest at times to take, but trying to get through to him, with his learning disability it's hard for him to understand that they're [medications] good for him, they're not bad.' (MMAS8 score 6, HbA1c 75).

These data suggest persuasion was used to encourage IDD participants to take medicines by both paid and unpaid carers, albeit that unpaid carers were more coercive and direct in their approach. This resulted in maintaining good glycaemic control despite poor to medium self-reported adherence. This suggests carers of IDD participants who highlight positive aspects of adherence and consequences of non-adherence in either a persuasive or more direct manner encouraged services users to self-manage and mitigates medicines non-adherence. Considering this in the context of stage one results this may explain John, Carl and Karen's poor or medium self-reported adherence score but good glycaemic control.

6.5.1.3 *Physical support*

The third optimisation strategy emergent from the qualitative data was physical support. This was found predominantly in the IDD population.

The only carer who provided physical support of a non-IDD participant was Kevin, family carer of Jane, who said her visual impairment prevented self-management of diabetes medication.

'...her sight is pretty bad so I've got to lay out her tablets and give her insulin and that's it.' (MMAS8 score 8, HbA1c 73)

The remainder of physical support was provided by carers of IDD participants. Service users were noted by carers to adhere to medicines but only with their or other healthcare professionals' support. The data also suggested support needs shifted between the IDD participant, the carer and healthcare provider. These approaches were described in a way that attempted to maximise autonomy, optimise medicine adherence and promote good glycaemic control. For example, Susan's (a paid carer) account of supporting Jess, included attempts to give her full autonomy when managing her medicines. However, support shifted back to carers when she overdosed on her medication. This illustrated Susan's motivation to optimise Jess' autonomy whilst preserving safety:

'When she had her medication in a cabinet in her bedroom she opened it and she took an overdose of her medication, so that's why we hold onto it.... we hand her the blister pack and she always knows which day, which time it is.'

Ongoing attempts by Susan to shift support back to the IDD participant were also evident:

'We've been starting to get her to count how many she has each time as well, so she knows in the afternoon there's three tablets, so she knows that, she knows which ones, so she's getting to know what she's taking and what time she's taking them at.' (MMAS8 score 8, HbA1c 46)

This approach to promoting autonomy was supported by Keith's (paid carer) account of promoting medicines adherence with Hamish, an IDD participant. In this case, Hamish had

poor medicines adherence, an uncontrolled HbA1c and poor compliance with diet and exercise. Realising the tension between controlling Hamish's diabetes whilst also respecting his autonomy, Keith had taken the time to educate himself and Hamish on his diabetes thereby promoting self-management:

'When he's happy, we try and support him in a way that he's forward thinking and he's happy and by talking to him through doing the therapy we've got a better understanding now as well, so we're just talking more and addressing the issues, so if you address the issues he's more likely to understand and to take his insulin.' (MMAS8 score 5, HbA1c 100).

When this did not improve adherence and glycaemic control, Keith and the team of carers intensified support and shifted care to a specialist diabetic nurse and developed a person-centred plan for diabetes management:

We have two protocols based on eating or non-eating, so if he's having his breakfast we'll follow the eating protocol, if he's not we follow the non-eating protocol. We record it in his book, Hamish takes his own insulin but we record that he's taken his insulin. (MMAS8 score 5, HbA1c 100)

A third case illustrating a person-centred approach to medicines adherence was Mark, an IDD participant, and his paid carer, Barbara. When Mark's type 2 diabetes required insulin therapy, care shifted from self-management to the carer and healthcare professional. In this case, due to a needle phobia, autonomy was surrendered by the IDD participant and insulin treatment managed by the carer and district nurse, thus optimising medicines adherence. Barbara reported Mark had needed a lot of persuasion and ongoing support to accept insulin treatment:

'...it took us about a year...there is always a staff member in with him when the nurses come in to give him his injections because he requested it, so yeah that's what we did.' (MMAS8 score 8, HbA1c 102).

For others, this 'shifting' between physical support and promoting autonomy was less clear. Jennifer's accounts of support revealed no evidence, and perhaps, due to optimum

adherence and good glycaemic control, a reluctance to promote self-management. With Simon, an IDD participant, she did ‘the lot’ as although he had ‘no problem’ with taking medicines she was unsure of his ability to manage his own medications.

‘He would take the readings on his machine, he can do that but I wouldn't say he would be capable of knowing exactly the amount of insulin he should have and I wouldn't want him to have that responsibility either.’ (MMAS8 score 8, HbA1c 60).

Jennifer did not provide a reason for limiting Simon’s opportunity to self-manage, therefore it was unclear whether she had tried and been unsuccessful, she had assumed he was unable to self-manage, or that she was concerned that self-management may result in poorer self-management.

These carers’ accounts suggest that the need to maintain optimum adherence by providing physical support is more evident in the IDD population than the non-IDD population. Reminding was common to both the IDD and non-IDD populations, with persuasion and physical support more a feature of those supporting people with IDD.

The qualitative data suggests that when providing physical support to optimise adherence carers reported a tension between balancing care needs and promoting independence. This tension has been previously described in the IDD population by Cardol (2012a) as impinging on autonomy to minimise harm. Although this may be interpreted as paternalistic, in the majority of cases, accounts described in this stage were akin to findings by Whitehead (2016), and were targeted at protecting from harm, optimising choice and increasing independence.

Some carers in this study were proactive at encouraging independence and testing ability to self-manage, whereas others were more reticent to do so. An interesting observation was that paid carers in this study appeared to encourage self-management more than unpaid carers. The reasons for this were not explored in this study but may be attributed to a higher level of

professional support and education provided to paid carers. Although participant numbers were small in this study, further exploration in this area could support or reject this theory.

In summary, carers of both IDD and non-IDD participants are aware of the medicines adherence behaviour of service users and the support they provided appeared to have a positive effect at optimising adherence. This suggests the mode of support provided by the carer population is dynamic and proportionate to the physical or psychological needs of the person with diabetes, which, in many cases, will promote self-management and autonomy.

6.5.2 Theme 2: Enablers and barriers.

This theme addressed the third research aim which was to explore the views of carers of medicines adherence in the context of the factors explored in stage one: depression, side effects, self-efficacy and social support. These factors were specifically explored in the qualitative interviews because they were identified in the literature as barriers to adherence and investigated in stage one. Thus the subthemes were predetermined by the literature and stage one.

Four subthemes emerged from within the data which were organised in the overarching theme: barriers and enablers (table 6.5). The first two subthemes were related to mood and how carers influenced it. Subthemes three and four were related to side effect which were not routinely discussed, but if evident appropriate action taken. Self-efficacy was explored with carers and emerged as a subtheme which suggested there was no clear relationship between level of confidence and adherence. Lastly, the perception that social stability was an important factor associated with adherence was evident in the IDD, but not the non-IDD, carer population.

Table 6.5: Theme 2: Enablers and barriers

	IDD										Non-IDD		
Stage one Participant ^P	Mark	Hamish	Carl	Karen	Simon	Claire	Brian	John	Jess		Fiona	Jane	Ian
Carer	Barbara 301	Keith 302	Louise 312	Robert 304	Jennifer 305	Jim 306	Mary 311	Alex 308	Susan 309		Chris 310	Kevin 307	Sarah 303
Depression													
Mood		√	√	√		√	√		√				
Carer influence		√	√	√		√	√		√				
Side effects													
Not routinely discussed		√	√				√	√	√		√		√
appropriate actions	√			√	√								
Self-efficacy								√			√		
Social support	√	√	√	√	√	√	√	√	√				

6.5.2.1 *Depression: Mood and adherence*

As part of the semi-structured interviews carers were invited to consider the impact that mood had on adherence to medication. Previous research has demonstrated a negative association between depressive symptoms and positive behaviour in the IDD population (McGillivray et al, 2007), however a link between depressive symptoms and medicines non-adherence has not been reported.

Carers of those in the non-IDD population did not express any clear insight into the effect low mood had on motivation. This may be a reflection on the carer sample population as stage one participants they were caring for did not have high GDS-LD scores. Their perception was that mood did not influence how they adhered to medications. A typical response was given by Sarah, family carer of Ian, a non-IDD participant

'He's got older and maybe a wee bit quicker tempered but I don't see much difference at all from taking and not taking.' (GDS-LD 3, MMAS8 score 8)

In contrast, there was a clear perception of the link between mood and medicines adherence in the majority of carers of IDD participants and, all that had elevated depression scores (GDS-LD > 10) reported a negative relationship between depressive symptoms and medicines adherence. Jim, an unpaid carer of Claire (an IDD participant) said:

'...if she's depressed, I think she'd just say, 'well I'm not taking it, there's no point'. I quite firmly believe that.' (GDS-LD score 12, MMAS8 score 8)

This perception of mood affecting adherence was also evident in Mary, and unpaid carer of Brian:

'...when he's a bit low with it he says, 'why should I bother taking this, why should I, this is not helping me.' (GDS-LD score 17, MMAS8 score 6).

This was evident in those with lower depression scores and with carers offering paid support. Louise, Carl's carer stated:

'...if he's in a kind of stropmy mood the he might prolong taking his medicines to make you coax him...he usually finds this quite funny and he will eventually take them (GDS-LD score 11, MMAS8 score 6)

Keith, Hamish's carer raised an interesting link between glycaemic control and depressive symptoms, which may have explained his poor adherence but also extended to other aspects of diabetes care. He associated physiological changes in blood glucose levels with mood, a phenomenon reported in both type 1 and type 2 diabetes (Strandberg et al, 2015; Whitworth et al, 2016).

'...when he's comfort eating, his readings are shooting up through the roof so that has a physical effect on him...his ketone levels are high which is making him feel even more unwell.... and depressed and it's a really hard cycle to get out of.' (GDSLD score 26, MMAS8 score 5).

Conversely, carers of IDD participants with minimal or no depressive symptoms did not view mood to have a relationship with medicines adherence. Jennifer, a family carer of Simon, illustrated this point:

'He just doesn't have a mood, he just goes with the flow....he gets himself ready and I give him the injection and he's quite happy with that. He never has anything to say about it' (GDS-LD score 6, MMAS8 score 8)

6.5.2.2 Depression: Carers influence

Carers of IDD participants not only displayed an awareness of the effect of low mood on medicines non-adherence but also attempted to reduce the impact of the risk by offering more intense support during times of low mood. This mode of help was commensurate with the level of help required and followed a similar pattern outlined in Section 6.4.2.

For example, Susan (paid carer of Jess) reported that low mood manifested itself in a reluctance to take medications which could be overcome with persuasion:

'...if her mood is low... if something has happened she's reluctant to take her medication. But then, she always will come around and she will take it (GDS-LD score 21, MMAS8 score 8)

Robert, a family carer of Karen, displayed a similar level of support but a more coercive approach:

'If it was coming up to the anniversary of a death of a family member, she would maybe get a bit more, 'why me' and I'd just tell her, look I am in the same boat but I've got to do it if I want to keep living so I suggest that you think about it...it's better to keep taking the tablets.' (GDS-LD score 17, MMAS8 score 5)

Mary, Brian's family carer, offered more physical support by preparing insulin injections and ensuring that he was prepared should Brian become hypoglycaemic.

'We just make sure that he's got his needle loaded up and he's got his blue strips, if he needs anything, if he has a hypo we're there for him to give him his juice or his Haribos to take to get his blood sugar back up.' (GDS-LD score 17, MMAS8 score 6)

Unfortunately, due to non-IDD participants not having depression, comparisons could not be drawn between the IDD and non-IDD population. However, emergent from the qualitative data is the view that that carers of people with IDD perceive medicines adherence to be influenced by mood. .

This suggests carers in the IDD population are aware of the risk of depressive symptoms on adherence and subsequently offered those with depressive symptoms additional physical or psychological support to sustain or improve medicines adherence. This may explain results from stage one in people with IDD whereby no significant association between depression and medicines adherence was detected. Results from this stage infer carers anticipate low mood and intervene to avoid non-adherence. It also suggests that support provided to IDD participants who have depressive symptoms is effective and, if a similar awareness of

depression was evident in the non-IDD population, and were supported by carers, adherence in the non-IDD population may also improve.

6.5.2.3 *Side effects: not routinely discussed*

Carers did not routinely discuss side effects with stage one participants. For example, Alex, a family carer of John, an IDD participant, was not aware of any side effects.

'It wasn't doing any good until they introduced that other tablet, that Metformin, and they increased the dosage as well, and he's been on the Metformin for a year/18 months maybe.... I think he realises they are doing him good...cause if he doesn't take them his blood sugar is sky high' (PSM score 22, MMAS8 score 5).

Susan's, a paid carer, account of Jess's perception of side effects, who perceived side effects were not an issue:

'I don't think she thinks that there's any issue with any side effects. I think the effects of them doing her good far outweigh what she could maybe think were side effects.' (PSM score 19, MMAS8 score 8).

This absence of discussion between carer and participant made it unclear as to whether side effects affected adherence scores however data suggested when side effects were highlighted carers took appropriate action.

6.5.2.4 *Side effects – taking action*

In a minority of cases, carers in the IDD population sought to reduce the risk of non-adherence as a result of side effects by taking appropriate action and shifting care back to the healthcare professional for a review of medications. The most common side effect reported by carers was diarrhoea and medicines were altered if referred to a prescriber.

'.... he was having diarrhoea...and we took that information back to the doctor and obviously, they changed his medication.' (Barbara carer of Mark, IDD participant PSM score 9, MMAS8 score 8).

'.... there used to be one tablet was awful bad for giving you diarrhoea but I think that one has been changed.' (Robert carer of Karen IDD participant PSM score 25, MMAS8 score 5).

In summary, carers' perceptions of side effects side effects on medicines adherence remains unclear because they did not routinely discuss side effects with those they were caring for. However, carers that did discuss side effects also supported the participant to take appropriate action and discuss symptoms with healthcare professionals. This intervention by carers may mitigate poor adherence to medications in the IDD population. However, due to half of the participants being unaware of side effects, firm conclusions cannot be drawn from the data.

6.5.2.5 *Self-efficacy*

Qualitative data suggested carers did not perceive a coherent relationship between self-efficacy and adherence. For example, Louise felt Carl was not confident enough to manage his own diabetes, stating:

'...I'm confident that he would understand he needs to take them but I think he wouldn't totally understand if he didn't take them the effect it would have on him' (PCS score 99, MMAS8 score 6)

Similarly, Mark, an IDD participant had a good confidence score but Barbara believed he *'could not manage his medicines on his own'* (PCS score 78, MMAS8 score 8)

Another example of incoherence of the relationship between confidence and adherence scores was found in the accounts provided by Chris (carer of a non-IDD participant) and Alex (an IDD participant).

In the case of Fiona (a non-IDD participant), Chris her carer reported that she forgot to take her medicine but remembered at critical points, e.g. prior to meal times, and found strategies to adjust her medicines to their lifestyle.

'she is always very busy, so food will go down on the table and only then does she think to go and find her testing kit. (PCS score 99, MMAS8 score 4)

Alex, a carer of John, suggested that he habitually took his medication, and was confident in how he managed his diabetes.

'I think he is totally confident. It's just something that he has to do and he's got into the routine, and he does it and that's it, it's part of life' (Alex carer of John, IDD participant, PCS score 93, MMAS8 score 5)

This incongruity may be explained by Fiona and John having developed confidence in managing their diabetes which is not fully adherent to the health professionals' recommendations, but maintains glycaemic control and appears to suit to their lifestyle.

Overall these results suggest that there is lack of clear relationship between self-efficacy and medicines adherence. This may suggest self-efficacy and medicines adherence is a more complex interaction than other factors associated with adherence explored in this study.

6.5.2.6 Social support

This subtheme explored with carers the influence social support had on medicines adherence. Thematic analysis suggested there was some evidence of a relationship between support and adherence in carers of IDD participants but less so in non-IDD participants.

All carers in the IDD population appeared to value social stability and linked this to medicines adherence. A typical example of this was described by Barbara, a paid carer, who thought that Mark put a great deal of importance on this when receiving support with his medication:

'He needs his social support...he knows someone comes in at such and such a time and if they don't, he starts to panic...' (mMOS-SS 85, MMAS8 score 8).

This was also similar to paid carer Louise's interpretation of Carl's perception of support:

'He's got good staff support to help him understand, to explain to him, good explanations and I think that's just what Carl needs.' (mMOS-SS 100, MMAS8 score 6)

The impact of an erratic social situation also appeared to influence medicines adherence. Without routine support and friendship paid carer Keith noted that this had a rebound effect on Hamish's diabetes management which affected mood, diet and attitude to those who supported him:

'when he has a fall out with his family or with his friends as well it brings on the arrogance... that [he can do things himself] which then turns into being a bit depressed, upset which can then go into the eating.' (mMOS-SS score 55, MMAS8 score 5).

Keith also described the effect of an unstable social environment on medicines adherence:

'When it's a good day he's good and he'll take his novo rapid on time the right amount, when he kind of gets that arrogance swing to it because of his friends are being kind of arrogant and a bit cocky, then he's kind of like 'I'll take it when I want to take it' (mMOS-SS score 55, MMAS8 score 5).

Less importance was placed on the relationship between social support and adherence by non-IDD carers. For example, Sarah, a family carer, reported that if Ian was on his own *'he would still take his medicines, I honestly believe it'* and this was also similar to the views of Chris, a family carer of Fiona:

'very well socially supported but I don't see that necessarily influencing her level of adherence or not' (mMOS-SS score 60, MMAS8 score 4).

In summary, carers of IDD participants perceived there to be a relationship between social support and adherence. However, this differed for carers in the non-IDD population. An explanation for this may be that IDD carers were predominantly paid carers and played a far

more active role in supporting adherence through persuasion and physical help. This may have a dual effect of promoting adherence and providing social contact. In contrast, non-IDD carers were spouses and therefore social contact extended beyond adherence.

6.5.3 Theme 3: Diet and exercise.

This theme explored additional aspects of diabetes care with carers. This theme adopted a more inductive approach and explored with carers broader concepts relating to diabetes management. Three subthemes emerged from this theme (table 6.6) namely, medicines were least problematic, exercise routine and healthy eating. Exploration of additional factors associated with diabetes treatment revealed that diet and, to a lesser extent, exercise was perceived to be more problematic than medicines adherence in both the IDD and non-IDD groups.

Table 6.6 Theme 3: Diet and exercise

	IDD									Non-IDD		
Stage one Participant ^P	Mark	Hamish	Carl	Karen	Simon	Claire	Brian	John	Jess	Fiona	Jane	Ian
Carer	Barbara 301	Keith 302	Louise 312	Robert 304	Jennifer 305	Jim 306	Mary 311	Alex 308	Susan 309	Chris 310	Kevin 307	Sarah 303
Medicines least problematic	√		√					√	√	√		
exercise routine	√	√	√	√					√			
healthy eating		√	√		√	√	√				√	√

6.5.3.1 *Medicines adherence least problematic*

When carers were asked to comment on which they found most challenging from diet, exercise and medications, medicines adherence was viewed as least problematic. This was attributed to the support provided by the carer to promote medicines adherence and that taking medicines was ‘easy’ whereas diet and exercise required more self-motivation to maintain.

Susan illustrated this point:

‘So, I’d say the medicines is probably the least challenging to be honest because the support’s there and we support her to take it, whereas the exercise and the diet is something which more has to come from Jess more than us’ (HbA1c 46, MMAS8 score 8).

6.5.3.2 *Exercise routine*

Exercise was perceived as problematic; most carers of both IDD and non-IDD participants suggested that there was a lack of interest in participating in any form of moderate activity. Typical responses came from Barbara who said:

‘[Mark]... will walk maybe just down to the bus stop so he can get a bus, he doesn’t do any other exercise’.

Chris agreed that moderate exercise was not something he and Fiona regularly took stating:

‘... exercise is the thing that both of us need to keep reminding ourselves to have’.

Carers of IDD participants who had greatest success with exercise were those that treated it as a social occasion or incorporated it into daily life. Alex described how John incorporated exercise into his daily life, stating:

‘... exercise is not a problem because it’s built into his working life.’

Mary, a family carer of Brian, said:

‘He’ll go swimming with the girlfriend and that’s exercise for him’. He walks; he’s got a good walk when he gets off the bus to work so that’s exercise.’ HbA1c 73, MMAS8 score 6)

Louise went for a walk with Carl encouraging at least some exercise. Others described walking to the bus, shops or when at work as sufficient exercise. Although these activities support physical activity, carers' perceptions of sufficient exercise fall short of current government recommendations. This was a similar finding to Hale (2011) who found some enthusiasm by IDD participants and their carers to take part in exercise but that intensity of exercise and the feeling that it was a socially isolating activity did not encourage participation.

6.5.3.3 *Healthy eating*

All carers noted that they had an active role in encouraging a healthy diet. In half of the accounts diet was the most challenging factor. In particular, carers of IDD participants suggested that diet was the most challenging because there was tension between promoting independence and protecting from harm. Barbara, Marks carer, said:

'...he has been known to go down to the local chip shop and get himself a fish supper.'
(HbA1c 102, MMAS8 score 8)

Mary described a similar challenge when caring for Brian:

The diet is the hard bit, telling him what he's got to watch what he's eating and if he has something sweet he has to remember that he's got to up his insulin' (Mary, HbA1c 75, MMAS8 score 6)

This theme was also seen within the non-IDD population:

'.... I know in the morning he has porridge...but he won't take a cup of tea unless there's a biscuit there' (Sarah, HbA1c 73, MMAS8 score 8)

Similar findings have been reported in the literature, (Gill & Fazil, 2013) supporting the finding that diet quality is suboptimal in the IDD population (Ptomey, Goetz, Lee, Donnelly, & Sullivan, 2013) and an ongoing challenge for those supporting people with diabetes (Cardol et al, 2012a; Rouse & Finlay, 2016; Trip, 2015).

6.6 Discussion

Findings from this stage have shown carers have a good insight into the requirement and nature of support needs. Adherence support ranged from empowering participants to self-manage medications by using simple reminders, to preserving health and wellbeing by providing full treatment monitoring with specialist nurse input.

This person-centred approach to diabetes care is similar to previously published observations (Rouse & Finlay, 2016; Whitehead, 2016). Both Rouse and Whitehead provide descriptions of carers of people with IDD as having a dual responsibility of promoting autonomy by encouraging self-management and managing risk through monitoring adherence behaviour.

A unique finding of this research compared to previous studies is that carers' medicine adherence support commensurate to the needs of people with IDD. Stage one participants who reported good adherence needed only reminders to take medicines whereas those with medium adherence or on more complex medicines regimes who reported poor adherence received more intensive support from carers. This alignment suggests that the level of care and support provided is not driven by the desire to assume control over the service user but by a personal or professional duty to optimise treatment and health outcomes. *Prima facie* the caregivers' legal duty of care is to balance respecting autonomy whilst protecting from harm, the preservation of physical and psychological health (Scottish Government, 2000) and findings from this study suggest that these principles are reflected in carers actions

This is the first study to explore perceptions of medicines adherence and associated factors in a group of carers of people with IDD. Verification of results from stage one demonstrated that people with IDD recruited in this study were reliable reporters of adherence. Therefore, the instruments used show promise for future research in people with IDD. The credibility of the perceived side effects to medicines score was less reliable. This may reflect carers' not

discussing medicine side effects with participants rather than incongruous responses from stage one. Furthermore, it has highlighted some key points in relation to the how carers support medicines adherence, the impact of factors on adherence and the direction of future research in medicines adherence in the IDD population. These are significant findings given the high prevalence of diabetes (MacRae et al, 2015), polypharmacy (O'Dwyer et al, 2016) and poor health indicators (Reichard & Stolzle, 2011; Shireman, Reichard, Nazir, Backes, & Greiner, 2010; Tyler et al, 2010) in this population.

With regard to factors associated with adherence, previous research has reported that depression is as prevalent in the IDD population as the general population and has demonstrated depression has an effect on cognitive function (Esbensen & Benson, 2005). The association between depression and medicines adherence is well documented in the non-IDD literature (Gonzalez et al, 2008; Gonzalez et al, 2008). However, to date, as far as the author is aware no data has been published on the association between depressive symptoms, adherence to diabetic medicines and what support is provided by carers to IDD service user who are experiencing psychological distress.

Results from this study suggest that carers of people with IDD were aware of the effect that mood had on medicines adherence and the impact depression had on all aspects of diabetic treatment. The final point is particularly important as the consequences on overall health of non-adherence to diabetic treatment and depressive symptoms is poorer diet (Silverman et al, 2015), shorter life expectancy, increased hospitalisation (Prisciandaro et al, 2011) and poorer glycaemic control (Wagner, Tennen, & Osborn, 2010). Carers of IDD participants did attempt to mitigate the effect of depression on diabetes care which was modified according to mood and anxiety. Comparisons of care between the IDD and non-IDD population were unable to be drawn, because no non-IDD participants in stage two reported depressive symptoms in stage one.

Many carers were unaware of the side effects experienced by people with IDD. As a result, alignment between carers' perception of side effects and service-users reporting of side effects is less clear than the other topic areas explored. In current IDD literature side effects of psychotropic medications are documented, yet carers' knowledge of side effects in psychotropic medicines appears to be limited (Fretwell et al, 2007). However, in the areas of side effects and diabetic medicines it is unknown or whether people with IDD take their medicines regardless of side effects due to the carers.

Comparing this to the non-IDD literature the association between side effects and diabetic medicines adherence is well documented (Capoccia et al, 2016; Mann et al, 2009; Ryan et al, 2014). Results from this research suggest that medicines adherence in people with IDD is similar to the non-IDD; therefore it is logical to postulate that side effects have the same association with adherence in the IDD population. However, to prove this hypothesis, further research is necessary.

With regard to self-efficacy, there was no consistent pattern between levels of confidence adherence and support provided. In some cases, low confidence resulted in greater support from carers; in others, higher confidence did not change the support provided and, in some, when people with diabetes showed increased levels of confidence carers responded with less support. Furthermore, findings suggested that as confidence increased and support decreased, adherence to medications reduced. Although previous studies have demonstrated an association between self-efficacy and adherence (Mann et al, 2009; Williams & Bond, 2002), the results from this stage suggest that the interaction between the two is complex, does not follow any pattern and requires further exploration.

Social support and its effect on medicines adherence were perceived to have greater importance by carers for the IDD rather than the non-IDD population. This may be explained by IDD participants having higher levels of depression and lower levels of confidence both of

which may require more active support from their carers without which there may be less likelihood of successful self-management. Although the effect of social support in the general population is not a specific finding in this study it has been reported in previous published research (Kim et al, 2015).

The approaches and challenges associated with support are similar in the IDD and non-IDD diabetic population. However, carers of people with and without IDD found other aspects of diabetes care, such as diet and exercise more problematic than medicines adherence. In this study, the data suggests that this may be because medicines adherence is more easily controlled by the carer whereas diet and exercise relies on intrinsic motivation.

Negative behaviour of stage one participants reported by carers with regard to diet and exercise were a theme throughout the data. This has been reported previously in both the IDD (Ptomey et al, 2013) (Cardol et al, 2012b; Trip et al, 2015) and general population (Hankó et al, 2007; Morse, Ciechanowski, Katon, & Hirsch, 2006) but this study suggests that little progress in reducing this negative behaviour has been made. Strategies which appeared to promote positive behaviour were to integrate physical activity into daily life and promote healthy eating were evident in this study. Therefore, to optimise diabetic health any future interventions to improve medicines adherence should consider how diet and exercise can also be improved.

6.6.1 Limitations of stage two

There are limitations in this stage of the study. The sample was a small subset of participants recruited from stage one of the study. Of those that received support with medicines adherence fewer than half agreed to take part. Although some of the sample population were carers supporting those with suboptimal adherence, all were self-selected. The reasons for those declining to participate are unknown.

The number recruited from the non-IDD population were small, only four people in this group received support for medicines management from carers. This prevented comparisons between the IDD and non-IDD groups.

6.6.2 Conclusions

In conclusion, this stage of the study has addressed the research question of whether the frequency of, and factors associated with medicines adherence are consistent with the views of carers. Key findings are as follows:

1. IDD participants self-reporting of adherence, depression, confidence and social support are aligned to carers perceptions
2. Carers strategies to optimise adherence are proportionate to the needs of service users
3. Further exploration of the impact of side effects on adherence in the IDD population is needed
4. The relationship between depressive symptoms and non-adherence is evident in this group of carers of people with IDD

To achieve the greatest gain in adherence, diabetic wellbeing and quality of life the main recommendation from this stage is to target medicines adherence interventions on IDD participants with depressive symptoms who have suboptimal adherence and limited support with medications, as the findings from this study suggest that carers effectively mitigate the risk of non-adherence in those with depression. A second recommendation is to further explore the effect of side effects on medicines adherence in the IDD population. These two recommendations will be discussed further in chapter 7 in the context of full integration and triangulation of stage one and two findings.

7 Chapter 7: Discussion

7.1 Introduction

The overall aim of this study was to develop, test and evaluate a theoretical model to predict those at greatest risk of medicines non-adherence in people with IDD. Following a systematic review of the literature, a two stage, sequential mixed methods study applying Banduras Social Cognitive theory (1986) was carried out. This research design was unique because:

1. It developed and tested a theoretical model designed to predict medicines non-adherence in people with IDD and prospectively compared findings to the non-IDD population.
2. It prospectively tested factors associated with medicines non-adherence in a cohort of diabetic service users, drawing comparisons between the IDD and non-IDD population.
3. It established the frequency of, and tested predictors of non-adherence in the IDD population.

This PhD study, revealed similarities, and differences in the frequency of, and factors associated with medicines adherence in the IDD and non-IDD population. Key findings were as follows:

1. The theoretical model proposed did not predict medicines non-adherence in this sample of IDD and non-IDD participants.
2. Biological factors, namely side effects and depression, were the most important predictors of medicines non-adherence in this study cohort.
3. The IDD population had higher levels of depression, more medicines side effects and lower confidence than the non-IDD population.

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4. Depression was an independent predictor of medicines non-adherence in a mixed group of IDD and non-IDD diabetics.
 5. Side effects was the most important factor associated with non-adherence in the IDD population.
 6. Health and treatment characteristics of the IDD compared to the non-IDD population were not equal; particularly age and proportion of IDD type 2 diabetics on insulin therapy.
 7. Medicines adherence and glycaemic control were similar in the IDD compared to the non-IDD population.

This PhD has made a contribution to understanding the phenomenon of medicines non-adherence in people with diabetes with and without ID. The results are of importance to people with IDD because this subgroup has higher mortality and morbidity from diabetes than the general diabetic population (Balogh, Lake, Lin, Wilton, & Lunsky, 2015). Therefore, this research study has generated some preliminary findings and contributed to understanding of what factors may predict medicines non-adherence in this population and, how management of this condition may be improved.

Dissemination of these findings to carers and healthcare professionals has the potential to impact positively on the lives of people with diabetes with and without ID. For example, the study provides evidence for routine screening for the presence of symptoms of depression and, particularly in the IDD population, side effects. If these factors are identified with implementation of targeted, person-centred interventions, there is potential to improve medicines adherence in both groups. Consequently, the long term debilitating effect of prolonged suboptimal glycaemic control may be reduced, resulting in improved quality of life and life expectancy of people with diabetes.

This chapter will systematically discuss these findings. Throughout this discussion results from both stages of the study will be integrated and appraised. Conclusions will be drawn based on logical analysis of this study's findings and in the context of existing policy, clinical guidance and research evidence.

Based on these conclusions, in Chapter 8, the final chapter of this thesis, a proposal for the focus and direction of medicines adherence research, policy and clinical practice in the IDD and non-IDD populations will be made. Recommendations will be based on promoting participation of people with ID in research, further testing of MMAS8 and testing interventions to improve medicines adherence in the IDD, and the non-IDD population.

This chapter is in four sections. Prior to discussing key findings an appraisal of the reliability and validity of results are reported. This will be considered in the context of the sample size; instruments used and stage one and two results. This is presented prior to discussing findings because, except for GDS-LD, the instruments had not been tested in people with IDD. Thirdly, key differences and similarities of demographic and health characteristics, including glycaemic control and medicines adherence will be presented. The chapter will conclude with an appraisal of strengths and limitations and a reflection on my learning during this PhD.

7.2 Reliability of instruments

The results from this study revealed a number of findings in terms of reliability of instruments and future application to research and clinical practice. First and most importantly, was the medicines adherence measurement instrument, MMAS8, shows promise as a simple and reliable method for screening for medicines adherence in the IDD population. Independent measurement instruments (GDS-LD, PSM, PCS and mMOS-SS) also demonstrated good internal consistency and there was some correlation with stage two data. As all instruments

have previously been validated for use in the non-ID population (Cuthill et al, 2003; Horne et al, 2013; Morisky et al, 2008; Morisky et al, 1986), the focus of this discussion will be on the reliability and credibility of results obtained from the IDD population.

7.2.1 Reliability of dependent factors (MMAS8)

As previous studies had established the reliability and validity of MMAS8 (Lee et al, 2013; Morisky et al, 2008) in the non-IDD population it was not necessary to test for construct validity. However, in the IDD population validation of the instruments with a factor analysis was desirable as it would further demonstrate the reliability of results and ratify it as a medicines adherence screening instrument in the people with ID.

A sample of 42 was necessary to statistically test the construct validity of MMAS8. Despite a final attempt to contact all named informants to identify additional participants, the sample remained at 33. This shortfall in recruitment in the IDD group called into question the reliability of MMAS8 as an approach for monitoring adherence in the research or clinical environment in people with ID.

Studies in people with ID commonly have small numbers of participants. A systematic review of randomised controlled trials conducted in people with ID (n = 53) reported a median sample size of 48 participants (Mullhall, Taggart, Coates, McAloon & Hassiotis, 2018) in the cognitive disability population, including people with ID. Identification and recruitment was cited as a common reason for this. These challenges are not only common in interventional studies, but also in studies testing instrument validity (Cuthill et al, 2003, Tveter et al, 2016). To overcome these, alternative methods to evaluate instrument validity have been reported in the ID literature. Validation of the GDS-LD depression score was carried out by comparing results of ID participants with and without depression (n = 38) against a validated depression scoring tool and corroborating findings with carers (Cuthill et al, 2003). The study concluded that GDS-LD was a valid and reliable tool and recommended for use in people with ID.

Similarly, Tveter et al (2016) tested the reliability and feasibility of a side effects score, UKUSERS-ID, in a sample of people with ID (n = 22) using reliability tests and face validity using focus groups. This study concluded that it was a feasible screening tool for people with ID. This suggests that experts in the field of ID research are adopting alternative and pragmatic approaches to testing validity and reliability of instruments. Given the recruitment challenges in studies involving people with ID, mixed methods approaches similar to Tveter and Cuthill and those used in this PhD study may offer a way forward for future research in this population.

Despite sample size falling short of testing instrument validity, reliability of MMAS8 was tested using: (1) scale reliability (2) inter-test reliability using correlation between MMAS8 and HbA1c, and (3) observer reliability triangulating stage one and two results.

A measure of scale reliability (Cronbach's alpha scores) showed good internal consistency of the instrument in the IDD population which was identical to results in the non-IDD group ($\alpha = 0.7$ vs 0.7). Inter-test reliability was assessed by correlating HbA1c and MMAS8 scores in the IDD population, comparing results with the non-IDD population and with results from published studies. The results revealed that, in the IDD population, as HbA1c increased, medicines adherence decreased. Similar correlation and prediction were evident in the non-IDD population suggesting inter-rater reliability of MMAS8.

A 6 point mmol/mol (0.6%) increase in HbA1c from a mean score of 65 mmol (8.1%) (CI, 55-74 mmol/mol) predicted a change from optimal to suboptimal adherence (MMAS8 < 6). The non-IDD group displayed similar findings in that, a 5 mmol/mol (0.5%) point increase in HbA1c from a mean score of 61mmol/mol (CI, 58 - 66) predicted a change from optimal to suboptimal adherence. This is aligned to previous studies reporting an increase in HbA1c is associated with a lower MMAS8 score (Lee et al, 2013; Wong et al, 2015).

Finally, good inter-observer reliability of MMAS8 in the IDD population was also evident when stage one and stage two results were integrated. Many carers' accounts of service users' medicines adherence were consistent with the self-report scores by the participants in stage one. This independent corroboration of results by carers adds further strength to the reliability of MMAS8 in the IDD population.

These findings in the IDD population have not been reported before. What is particularly novel is the negative association between MMAS8 and HbA1c in the IDD population. This is a clinically important finding and suggests that, if a person with IDD presents with a suboptimal HbA1c, the use of MMAS8 may alert a clinician that suboptimal medicines adherence may be contributing factor. Furthermore, breaking down the items within the MMAS8 scale and evaluating responses within the scale may identify reasons for non-adherence, for example, forgetting, travelling away from home, complexity of regime or side effects.

The correlation between HbA1c and MMAS8 provides preliminary evidence that optimising medicines adherence may have a role to play in improving glycaemic control in the IDD population. This finding is consistent with the general diabetic literature (Simpson, Lin, & Eurich, 2016) and suggests that optimising medicines adherence may achieve HbA1c levels closer to NICE targets (2015b). If findings from this study are replicated in a larger sample population, MMAS8 could be widely implemented as a cost-effective way of reducing the burden of microvascular complications associated with poor glycaemic control in this population.

Other recent studies have advocated the use of self-report instruments to assess medicines adherence because compared to other methods (e.g. medicine electronic monitoring (MEMS) and prescription refills) self-report methods were as accurate in detecting non-adherence (Gonzalez et al, 2013; Lee et al, 2013). This is in contrast to a recent Cochrane review that recommended prescription refill as the preferred and most objective measure of adherence

(Nieuwlaat et al, 2014). However, as discussed in Chapter 3, prescription refills indicate only that the prescription has been collected from the pharmacy and not whether the medicines have been taken. Furthermore, the relative simplicity and low cost of MMAS8 makes it a viable instrument for use in future medicines adherence research in people with IDD.

Although correlation between HbA1c and MMAS8 was non-significant in the IDD compared to the non-IDD population, the internal consistency, inter-test, inter-rater and observer reliability of results suggest that this non-significance is due to an underpowered study rather than no association between the two measures. This adds weight to further testing of MMAS8 in adherence research with the IDD population.

Nonetheless, results should be interpreted with caution and it is recommended that MMAS8 be further tested with a larger sample to generate sufficient power to fully test the construct validity of this instrument. If findings are reproduced in a larger study, and a significant correlation between HbA1c and MMAS8 is shown this will support its use as a screening tool for non-adherence in people with IDD.

7.2.2 Reliability of independent factors (depression, side effects, confidence and social support)

Similar to MMAS8, measurement instruments for independent factors had previously been validated in the non-IDD population but there were insufficient numbers in the IDD population to test construct validity of the instruments selected to measure independent factors.

Depression score (GDS-LD), medicines side effects score (PSM), self-efficacy (SE) and social support (m-MOS-SS) all showed good internal consistency with Cronbach's α of 0.8 - 0.9 in the IDD population. Similar findings were reported in the non-IDD population (Cronbach's $\alpha = 0.8 - 0.9$). Corroboration of results from IDD participants presented in stage one was carried out in stage two by conducting semi-structured interviews. Themes emerging

from the qualitative data suggested that carer's perceptions were aligned to some, but not all, stage 1 results.

7.2.2.1 *Depression score (GDS-LD)*

Reliability of GDS-LD in the IDD population had previously been reported and the instrument showed good internal consistency in this study. In relation to depression, six stage one participants with symptoms of depression participated in stage two (GDS-LD >10) and in all cases carers verified that symptoms of depression, but not necessarily a diagnosis of depression, were present in the person that they cared for. This suggests that results of GDS-LD in the IDD population were reliable. The validity of GDS-LD has previously been shown by Cuthill et al. (2003) and, therefore, this is not a new finding. It did, however, add credibility to results in this study.

7.2.2.2 *Side effects (PSM)*

The internal consistency of PSM in the IDD population was good (0.8). However, the qualitative data suggested that at least half of participating carers did not routinely screen or discuss side effects with the service user. Therefore, although the side effect instrument (PSM) shows promise and may provide an indication of whether people with IDD perceive they are experiencing side effects from their diabetic medication, further research is required to conclusively establish reliability and validity of the PSM score in the IDD population.

To date, there are no reports on the frequency of side effects in people with IDD, or that carers routinely screen for side effects (perceived or otherwise) in people with ID and diabetes. A possible explanation is the non-specific nature of side effects. Often, it is not clear whether the perceived side effect is a worsening symptom of an existing clinical condition, a new symptom or medicines side effects. This may be even less clear in the ID population, due to the high frequency of unexplained complex symptoms (Osugo et al, 2017). Due to the complexity and non-specificity of symptoms and side effects carers may avoid this discussion.

Avoiding or not actively seeking out discussions about side effects is recognised in the wider ID literature (Fretwell et al, 2007). The findings from this PhD study suggest that that a standardized side effects screening tool may establish whether a person with IDD believes they are experiencing side effects. Further testing of the instrument in this population may encourage carers and health care professionals to be proactive about exploring side effects, and highlight more readily those who perceive they are experiencing side effects severe enough to have a negative impact on adherence.

7.2.2.3 *Self-efficacy (PCS) and perceived level of social support (mMOSS-SS)*

The last two independent variables, self-efficacy and social support, internal consistency was good (Cronbach's $\alpha = 0.9$) and, in stage two reports, the majority of carers' accounts of self-efficacy were aligned to participant self-reports. Carers' accounts of social support were aligned to most of IDD participant perceptions of social support. This may be because those who participated in stage two support people with IDD effectively and, as a result, feel confident in managing their medicines. Therefore, the sample of carers who agreed to participate in this study were self-selecting, knew their participant well, had a good relationship with the person they were caring for and actively optimised adherence. As a result, stage two sampling may have been bias towards a proactive group of carers.

This potential for biased sampling is not isolated to this study and is an issue to consider for all research projects using human participants. Those willing to take part may be those who are most confident and pro-active in the target population. Furthermore, the perceptions of social support and confidence by carers have been reported previously in the ID literature. Three qualitative studies of 17 carer participants in each demonstrated social contact and emotional support provided by paid and unpaid carers may improve confidence and adherence to diabetic treatment (Cardol et al, 2012a; Trip et al, 2015; Whitehead, 2016).

In summary, the internal consistency of independent variables as measured by Cronbach's alpha was good. Observer reliability in stage two reports from carers were aligned to self-reports of depression in stage one, however results are less conclusive with regard to side effects, self-efficacy and social support.

Therefore, although good internal consistency and qualitative findings add to the reliability of results reported in this study, further testing using larger sample sizes to fully internally and externally validate the instruments used in this study would ratify use in future adherence research in people with IDD.

7.2.3 Evaluation of the theoretical model and its ability to predict medicines non-adherence

The testing of the theoretical model addressed research question 2:

Whilst controlling for regime complexity and support with medicines, does the proposed theoretical model predict medication adherence in the group overall, the IDD and non-IDD diabetic population?

Key results discussed in this section are (1) the theoretical model did not predict medicines adherence, (2) ID was not a significant predictor of medicines adherence; and (3) after controlling for confounding variables, support with medicines and regime complexity, depression was the most important and only statistically significant predictor of medicines adherence in the non-IDD population and group overall and, (4) in the IDD population, side effects was the most important predictor of adherence.

These findings will be discussed in the context of stage two findings, demographics of the study population and in the context of the wider literature. Based on conclusion drawn from this discussion recommendations for future research will be made.

7.2.4 Capability of theoretical model in predicting medicines non-adherence

Bandura's social cognitive theory and factors derived from the diabetic medicines adherence literature did not predict medicines adherence in the group overall. This could not be attributed to an underpowered study because 109 participants was sufficient power to generate a medium effect size (Faul et al, 2007). In chapter two, consideration was given to four other theoretical models used previously in adherence research: health beliefs model, self-regulation theory, readiness to change and theory of planned behaviour. These models were not aligned to results from the systematic review (Chapter 2), and social cognitive theory was selected on the basis that it was closely aligned to findings from the review.

As far as the author is aware this model has not been tested in diabetic medicines adherence study and results suggest that biological and affective factors are those which predict medicines non-adherence. In the following sections an analysis of each of the factors tested will be presented thus providing an explanation why social cognitive theory has not been proven.

7.2.5 Cognitive factors: ID

Banduras theory suggests that cognitive function will predict how people think, feel and behave. In this study one hypothesis was, because people with ID may have reduced cognitive function, they would have lower frequency of adherence and therefore ID would predict medicines non-adherence.

Results revealed ID accounted for 30% (n = 33) of the total (n = 111) study population. Univariate analysis revealed no statistically significant association between ID and medicines adherence ($p = 0.6$). This is an important and never previously reported finding, particularly given that poor cognitive function is associated with non-adherence (Feil et al, 2009; Tomlin & Sinclair, 2016) and social, intellectual and cognitive dysfunction is a feature of people with ID (Cooray et al, 2015).

Cognitive impairment in people with ID ranges from mild to profound however in this study recruitment included people with mild to moderate intellectual disability only. The weak association with medicines adherence identified in the study may be attributable to recruitment of those at the higher functioning end of ID. Cognitive function was not formally assessed and therefore, definitive conclusions cannot be made, however more than 50% of IDD participants were employed and living independently. This denotes a level of social and cognitive function that may be similar the non-IDD population.

The absence of association between medicines adherence and people with IDD may also be attributed to the support provided by carers. Stage two results revealed carers of people with IDD employed strategies such as reminding, persuading, coercing, and physical support to optimise adherence. This vigilance by carers and, when needed, shifting care back to diabetes specialist services, may have been a confounder on the effect that ID has on non-adherence.

Nonetheless finding that ID is not associated with medicines adherence is positive. It suggests that reasonable adjustments can and are being made by carers and healthcare professionals to tailor diabetes care to the needs of the individual, thereby optimising adherence. For example, a simple twice daily medicines regime may be sufficiently complex for this group.

However, although carers may be maintaining medicines adherence at the same level as the non-IDD population, which is commendable, it is important to note that in the overall study cohort the frequency of those with optimal adherence was only 70%. This reflects only a small improvement in adherence rates reported by Dimatteo et al (2004), but is lower than adherence targets of 80-95%.

To meet this target and improve the overall health of people with diabetes a 10-15% increase in those adherent to diabetes treatment is necessary. This may be achieved through

effective service user and carer led interventions, improving the overall health and wellbeing of the IDD and non-IDD population. Therefore, further research supporting people with ID and carers to optimise healthcare resources by employing person centred, evidence based medicines adherence interventions using qualitative and quantitative outcome measures is recommended (NICE, 2009; UN, 2007).

7.2.6 Biological and affective factors: depressive symptoms

Social cognitive theory purports actions will be based on the individual's resilience and motivation; therefore, mood may influence how a person thinks, feels and behaves. Applying this theory medicines adherence research depression or depressive symptoms may affect how adherent individual is to their prescribed medication regime.

In this study, univariate and multiple regression analysis revealed depressive symptoms was a statistically significant, and the most important, predictor of medicines non-adherence in the group overall and non-IDD population ($p < 0.001$), yet depressive symptoms were not a predictor of adherence in the IDD population.

The association between depressive symptoms and medicines adherence in the non-IDD population is commonly reported. Primary research studies conducted in the general diabetic population (Chao et al, 2005; Kilbourne et al, 2005; Lerman et al, 2009; Silverman et al, 2015) and narrative, systematic reviews and meta-analyses have consistently proven the association between depressive symptoms, depression and medicines adherence (Capoccia et al, 2016; Gonzalez et al, 2008; Tiktin, Celik, & Berard, 2016). This study has further corroborated these findings and reinforces the importance of more intensive monitoring for non-adherence in people with depression or depressive symptoms.

Yet, the finding that there was no statistical association between depression and adherence in the IDD group has not been reported previously. This finding is even more notable as the IDD group were twice as likely to report depressive symptoms (36% vs 17.9%) when

compared to the non-IDD group, and reported significantly higher total depression scores when compared to the non-IDD group (GDS-LD 11 vs 8, $p < 0.05$).

In the context of existing research, a higher prevalence of depression in the ID population is not remarkable. A recent cross-sectional study from all GP practices in Scotland ($n = 1445$) has reported a higher prevalence of depression in the IDD population compared to the non-IDD population (15.8% vs 10.6% $p < 0.001$) (Cooper et al, 2015). Thus, it suggests that the sample of IDD participants obtained may be representative of the population.

However, what is remarkable is that the higher prevalence of depression in this study population did not yield significant associations between depression and medicine adherence in the IDD population.

The absence of statistically significant associations may be for two reasons, (1) sample size and (2) effective carer interventions. It may simply be that the numbers recruited in the IDD population were too small to detect a significant effect between depression and medicines adherence. There were 33 participants recruited from the IDD population, and 36% to demonstrate a moderate effect a power calculation required a sample of 111 (Faul et al, 2007) therefore the lack of association may have been a sampling or type 1 error.

An alternative explanation may be evident in stage two qualitative findings. This revealed how carers of people with IDD played an effective mediating role in mitigating non-adherence, particularly when the IDD participant was displaying symptoms of low mood. In their accounts, carers of IDD participants were cognisant of the impact that depression had on adherence and modified assistance. Carers of the IDD population perceived a particularly positive effect on those with high levels of anxiety or depression and where necessary escalated support to healthcare services to optimise adherence.

This may in part help to understand and explain the absence of association between depression and adherence in this group, that is, if carers are optimising medicines adherence in people with IDD and depression, using strategies such as reminding, persuading and physical support they may reduce the effect that depression has on adherence in this population.

The qualitative findings have provided a unique insight into explaining why depression, or depressive symptoms, were not associated with adherence in people with IDD; that is, effective support provided by carers reduced non-adherence. Although the link between mood and adherence has been inferred previously in the ID literature (Cardol et al, 2012a; Hale et al, 2011; Trip et al, 2015), this this is the first study to link qualitative findings to quantitative adherence data in people with IDD.

Qualitative findings also suggested that depressive symptoms in the IDD population impacts on other aspects of diabetes care. For example, findings suggested those with depressive symptoms and IDD had low motivation to exercise and maintain a healthy diet. This is consistent with recent evidence in the non-IDD population suggesting that when depression is combined with cognitive impairment this will not only affect medicines adherence, but also adherence to diet and exercise (Li et al, 2017), however this is the first to explore this association between depression and medicines adherence in people with IDD.

Findings from this aspect of are novel and but should be interpreted with caution. It appears that carers reduce the risk of non-adherence in people with ID, diabetes and depression by offering effective support and encouragement, however, due to the small numbers recruited from the IDD population in this study, this requires further investigation. If the methodology applied in this study was replicated in a larger multi-centre study, recruitment numbers could be sufficient to make a more confident statistical estimate of the relationship between medicines adherence and depression in people with IDD, thus proving or disproving the hypothesis that depression is not a factor associated with adherence in people with IDD. In

addition, further in-depth qualitative research into the role that carers play in mitigating non-adherence in people with IDD and depressive symptoms is required which may provide evidence for effective interventions to improve adherence.

7.2.7 Biological factors: side effects

The theoretical model proposed that actions are determined by biological factors which in this study were beliefs about medication side effects. The hypothesis was within social cognitive theory perceived side effects predicted medicines non-adherence.

Univariate analysis of the results investigating the relationship between side effects and medicines adherence revealed that side effects in the IDD population, was trending towards statistical significance ($p = 0.06$, r_2 8%) and was the most important factor. Conversely in the non-IDD population, there was no statistical significance between side effects and medicines adherence ($p = 0.125$, r_2 2%).

This difference in association between side effects scores and medicines adherence in the IDD compared to the non-IDD population may be attributed to higher side effects scores in the IDD population. Descriptive statistics from this study showed a significant difference in median side effects scores (PSM) in the IDD compared to the non-IDD population (14 vs 10, $p < 0.05$). This evidence was corroborated following analysis of frequency of reported items within MMAS8, which revealed that side effects was the second most commonly reported reason for non-adherence with 18% ($n = 6$). In contrast in the non-IDD group it was ranked as the fourth most important reason after travelling and ‘feeling hassled’ about taking their diabetic regime.

In the research literature, it is known that there is a higher prevalence of comorbidities in people with ID (Haveman et al, 2011). Consequently, there may be a higher risk of polypharmacy and subsequent risk of drug interactions, adverse drug events and increased medication side effects. A UK study of 753 ID participants reported polypharmacy (5 or more

drugs) in more than 50% of cases (O'Dwyer et al, 2016). However, an increasingly aging general diabetic population, living longer into advanced old age, and with more long-term conditions, has as great a risk of polypharmacy and side effects as in the non-IDD population (Caughey, Barratt, Shakib, Kemp-Casey, & Roughead, 2017; Noale et al, 2016).

In this study, comparisons between the IDD and non-IDD groups revealed no difference in frequency of those prescribed 5 or more medications. This suggests that polypharmacy is equally prevalent, therefore it may be the type, rather than number of, medications which account for side effects being a more important factor in the people with ID.

Evidence from this study to support this view is a significantly lower proportion of people with ID and type 2 diabetes compared to the non-IDD population was prescribed insulin (11% vs 57%, $p < 0.05$). As this difference was not attributed to age, length of time with diabetes or inferior glycaemic control, it may suggest a more proactive approach to glycaemic control in the non-IDD population. There are clinically important reasons for this difference in practice, for example, avoiding hypoglycaemia or an overly complex treatment regime, however the results of this study suggests there are possible unintended consequence of this in the IDD population namely (1) a higher intensity of side effects, and (2) side effects being the most important factor associated with adherence.

This supports the theory that it is type, rather than number of medicines, which is important. NICE guidance sets out guidance for optimising glycaemic control (NICE, 2015b). As outlined in chapter 1 (Fig 1.1), first line diabetes treatment recommendations are biguanides (metformin), second line treatment are gliptins (DPP-4 inhibitors), sulphonyl urea and glifozins (SGLT-2 inhibitors) combined with biguanide, and third line treatment is these plus the addition of insulin. In this study, the finding that a higher proportion of the non-IDD population were on insulin, yet diabetic control and time since diagnosis were similar, suggests that they

are accelerated more rapidly through the treatment algorithm and prescribed insulin earlier than people with ID and type 2 diabetes.

Previous research suggests there are differences in side effects according to the treatment prescribed and side effects may be less with second and third line treatment. For example, metformin is first line treatment for type 2 diabetes and one of the most commonly drugs prescribed in diabetes. It is reported to be a safe drug with few drug-drug interactions (May & Schindler, 2016), however, there are more side effects associated with this medicine compared to insulin with gastric side effects from metformin particularly problematic (Stein, Lamos, & Davis, 2013) (Bianchi, Daniele, Dardano, Miccoli, & Del Prato, 2017). For example, in a retrospective study in the USA (n = 2074) greater side effects were associated with oral treatment and there was a significant association between side effects and medicines adherence (Pollack et al, 2010) and, gastric side effects were poorly tolerated.

With regard to second line treatment a recent study by Flood (2017) conducted in the United States on 168 type 1 and type 2 diabetics found the newer generation of medications, DPP-4 inhibitors and SGLT-inhibitors, were preferable due to fewer side effects. Finally, third line treatment is insulin, the greatest adverse event of which is hypoglycaemia few reports of gastric side effect. Furthermore, recent studies suggest the risk of hypoglycaemia is no greater than oral diabetic medications (Vos et al, 2016; Wright, Burden, Paisey, Cull, & Holman, 2002). Therefore, those earlier in the diabetic medicines treatment algorithm may experience more side effects resulting in a more significant impact on medicine adherence.

In this study, fewer people with IDD were prescribed insulin yet more had side effects. This may not affect glycaemic control but may account for the differences in frequency of reported side effects, higher overall side effects scores and more important associations between medicines side effects and adherence in people with IDD. Associations between side effects and adherence is consistent with findings from existing research in the non-IDD

population (Chao et al, 2005; Farmer et al, 2006; Grant et al, 2003; Mann et al, 2009; Pollack et al, 2010) but, as far as the author is aware, in the IDD population this finding is new and may have implications for future diabetic medicines management and prescribing practice in this group. This will be revisited in section 7.4.2

The association between higher side effects and non-adherence in people with IDD may be viewed as proactive approach to self-management and the person with IDD ‘taking action’ however it is, by definition, non-adherence (NICE, 2009) and may result in poorer health outcomes. A reason for the person with IDD ‘taking action’ without referral back to the prescriber is evident in the qualitative stage of this study. The data suggested that carers of people with IDD did not appear to routinely explore side effects with stage one participants and a mismatch between service user and carer perceptions of side effects emerged.

However when side effects were noted by carers the qualitative data did suggest that appropriate action was taken. For some, it was considered accepted as a consequence of treatment by service users and carers and, even when offered an alternative to existing treatment, one non-IDD participant chose to continue. For others, when prescribers were alerted to the presence of side effects, treatment was reviewed, action taken and, where indicated, modified.

These findings may explain the variation in association between medicines adherence and side effects in the IDD compared to the non-IDD population in this study but the importance of these findings is limited by sample size. Nonetheless it suggests the need to provide additional support to carers and prescribers on the impact of side effects on adherence in people with IDD. An appreciation of the consequences of side effects on adherence may encourage carers to be proactive with regard to exploring side effects more fully, taking appropriate action and referring to a prescriber for medicines review, treatment and dose adjustments thus reducing side effects and optimising adherence.

As outlined in chapter 6, carers provide effective support with medicines and, with support, findings from this study suggests people with IDD are as adherent to medicines as the non-IDD population. Adherence in the IDD population may improve further if carers are proactively addressing side effects. Educating carers on pharmacovigilance and healthcare professionals on the impact of side effects may help to review treatment options and individualise care. Clinician-led interventions and regular medicines review similar to those outlined by NHS Scotland's (2015) guidance may reduce side effects. By addressing this, diabetic management may be more effective, medicines adherence may improve, resulting in a significant impact on diabetic health and quality of life in this population. The effectiveness of an intervention of this type could be evaluated more rigorously in an interventional study, which would include exploring the effect that medicines review and screening for side effects has on medicines adherence in the IDD population.

The impact that side effects have on adherence in people with IDD has never been reported, therefore this is a novel and unique finding from this study. This requires further investigation, both in the research and clinical practice environment. Most importantly, to further validate the findings from this study, a sufficiently powered study is necessary to (1) definitively quantify the impact of side effects on medicines adherence in the IDD population, and (2) to establish whether a specific diabetic medicine is associated with non-adherence.

7.2.8 Behavioural factors: Self-efficacy

Social cognitive theory purports that belief in oneself to change behaviour will promote a change in behaviour. In the context of medicine adherence, if an individual has the confidence that their actions will improve health they will adhere to medicines.

In this study, univariate analysis suggested that self-efficacy was a predictor of adherence in the non-IDD group ($p = 0.02$) but not in the IDD population ($p = 0.59$). However, multiple regression analysis revealed self-efficacy was not a significant predictor of adherence

in either group ($p = 0.36$, $p = 0.51$), nor was it the most important predictor of adherence in either the IDD or non-IDD population, before or after controlling for confounding variables.

Median self-efficacy scores were lower in the IDD population. In stage two the qualitative data indicated that there was a lack of confidence by carers in the abilities of the IDD participants to manage medicines independently. This is not surprising as confidence is known to impede self-management of diabetes (Cardol et al, 2012b; Hale et al, 2011). This could result in people with ID developing learned reliance, which has previously been reported in the literature (Gill et al, 2013; Rasaratnam, Crouch, & Regan, 2004), suggesting that IDD participants are similar to those recruited to previous studies.

However, the absence of significant association between self-efficacy and medicines adherence is contrary to previous studies carried out in the general diabetic population (Nakahara et al, 2006; Williams & Bond, 2002). A meta-analysis conducted by Gherman et al. (2011) demonstrated a significant association between self-efficacy and diabetes self-care adherence, which included medicines adherence. Mann et al. (2009) carried out a study in the US with type 2 diabetics ($n = 151$) and reported that self-efficacy was a significant factor associated with medicines adherence. Neither of these studies measured self-efficacy alongside depression, side effects and social support. Therefore, this is the first study that has considered all the above factors concurrently and results suggests that depression and side effects are more important predictors of medicines adherence than self-efficacy in the IDD and non-IDD population.

A possible explanation for this may be in the stage two findings. Carers' accounts of stage one participants suggested that those reporting low confidence were receiving support from a carer to take their medication. Conversely, some participants with high confidence who reported poor adherence with prescribed medicines regime may have skewed the results. With regard to the latter, carers' perceptions were stage one participants developed flexibility in how

they managed their medicines, which may not have been in strict accordance with the prescribers' recommendations. Although defined by the service user as non-adherent, their adequate glycaemic control despite low adherence scores suggests they could effectively manage their diabetes treatment in accordance with their lifestyle without having a detrimental effect. This 'expert patient' behaviour was only reported in a minority of cases yet may provide an insight into the effectiveness of a more individualised approach to care.

Hence, findings from this study suggest self-efficacy is not a strong predictor of adherence in either the IDD or non-IDD population. When considered in the context of the other factors explored in this study, this is a new finding in both the IDD and non-IDD population as previous studies have reported an association between the two (Mann et al, 2009; Williams et al, 2002). It also suggests that carers support those with low confidence and those with high levels of confidence manage their diabetes in a way that suits their lifestyle rather than being fully adherent to prescribed treatment. Therefore, this suggests that development and testing of strategies to improve adherence in both the IDD and non-IDD population should not be focused on improving self-efficacy but on reducing the effect of more significant factors, namely; depression and side effects.

7.2.9 Environmental factors: social support

Banduras cognitive theory hypothesises that the influence of environmental factors and norms will have an impact on the extent to which someone is adherent to a recommended programme of care or regime. Results from the systematic review suggested that social support was a factor associated with medicines adherence in diabetes therefore; social support was hypothesised to be a factor associated with adherence. Univariate analysis revealed it was a poor predictor of medicines adherence in the IDD population ($p = 0.35$) and the non-IDD population ($p = 0.51$).

The non-significance in both groups is unremarkable because median social support (mMOS-SS) scores were similar in the IDD and non-IDD groups (78% vs 88%, $p = 0.73$). This suggests that the emotional and social support provided to IDD participants was similar to that of non-IDD participants. This, again, is a new finding as perceived levels of social support have never been compared in the IDD and non-IDD population. It is particularly notable because, in this study a higher percentage of people with IDD lived alone (51% vs 23%) and had a higher frequency of depressive symptoms (36% vs 18%) when compared to the non-IDD population.

This may have led to an expectation that IDD participants would have higher perceptions of social and emotional isolation as this is often a feature of depressive symptoms, however this was not the case and, in fact, people with and without ID had similar perceptions of social support. The similarity in mMOS-SS scores may be for two reasons. First, carers of IDD participants may be receiving effective support from carers, their workplace and social groups; and secondly, the non-IDD participants who overall were older and beyond retirement age may experience loneliness and social isolation similar to the IDD population. This merits further research, particularly considering previous findings suggesting a negative association between social and emotional support and medicines adherence.

The mediating effect of social support on adherence is well documented (Costa, Pereira, & Pedras, 2012; Mayberry & Osborn, 2012) and there is evidence that the mediating effect on depression will have a positive impact on medicines adherence (Kim et al, 2015; Osborn & Egede, 2012). The difference in results between this and previous studies may be attributable to the type of instrument used to collect data. For example, Kim (2015) conducted a study of type 1 and 2 diabetics residing in Korea ($n = 314$) using an instrument that measured only emotional support. The mMOSS-SS tool measures perceived level of social support, including perceived level of support with meals, housework and transportation, as well as emotional support. Therefore, this instrument provides a more holistic evaluation of perceptions of

support encompassing both practical and emotional support rather than emotional support alone.

Another finding from Kim et al. (2015) was the positive effect that social support had on depressive symptoms and adherence. This finding is consistent with the stage two findings from the IDD population whereby qualitative data suggested carers were effective at managing medicines adherence and depressive symptoms. Furthermore, carers of the IDD population did appear to support the suggestion that social support was associated with medicines adherence but, is just not as important a factor as depression or side effects.

The positive role that effective social support plays in medicines adherence in people with IDD was emergent from the qualitative data, but was not a significant predictor in stage one. There are two possible reasons for this, first, the study was not sufficiently powered to detect a significant association, and secondly, carers are mitigating the possible effect of poor social support on medicines adherence by providing effective support. Therefore, these findings and previous evidence, suggest a larger scale study with sufficient power focussing on perceived level of social support is required.

7.2.10 Predictors of adherence according to mean scores of depression and side effects in the IDD and non-IDD population.

The final analysis established if there was a threshold where depression and side effects scores could reliably predict medicines non-adherence important in the IDD and non-IDD groups. To draw comparisons between the two groups, depression, side effects and adherence in both the IDD and non-IDD populations were analysed.

Using MMAS8 score of 5 as a marker of non-adherence, higher depression scores as measured by the GDS-LD were associated with non-adherence in both the IDD and non-IDD population and with cut-off GDS-LD scores of 10 and 12 respectively. The specificity and sensitivity of the GDS-LD as a depression screening tool is greatest at 13 (Cuthill et al, 2003).

However, this study has shown that this may fail to identify IDD and non-IDD service users who are non-adherent. This study suggests that adherence is mediated not only by depression but also by depressive symptoms. Therefore, the higher cut-off defined by Cuthill et al. (2003) may not be sufficiently sensitive to detect non-adherence. This is supported by stage two carer reports in the IDD population who suggested that GDS-LD scores less than 13 may impact on medicines adherence. Therefore, it is recommended that if GDS-LD is to be used to identify non-IDD or IDD patients at risk of non-adherence a cut-off of 10 or 12 respectively would be optimal.

With regard to side effects, PSM threshold scores indicating high or low side effects have not been defined, nor has the instrument been used as a predictor of adherence. Results from this study suggested that, a cut off MMAS8 score of 5 denoted higher side effects scores in the IDD but not the non-IDD population. A cut-off PSM score of 16 appears to predict adherence in the IDD population, however there was no clear cut off in the in non-IDD population (table 5.9) as the same score predicted both medium and poor adherence. This corroborates the finding that the trend towards significance is in the IDD but not in the non-IDD population. This finding is clinically significant because it demonstrates the potential of the PSM scale to establish a threshold whereby side effects are sufficiently intolerable that they affect adherence in the IDD population. Given the frequency of non-specific symptoms reported by Osugo (2017) this may assist in identifying those at risk of both side effects and non-adherence.

These instruments had never been tested in this way previously and the purpose of doing so was to generate some preliminary data on a clinically relevant threshold for depression and side effects that predicted non-adherence. Given the linear association between adherence and depressive symptoms and side effects in the IDD population, the argument that the study was insufficiently powered is strengthened. It also provides weight to the argument that a larger scale study is needed to corroborate or reject the findings from this research. However, the

finding that cut-off scores for depression (GDS-LD = 12) and side effects (PSM = 16) may predict medicines adherence in the IDD population has important clinical significance which has not previously been reported. For example, if similar associations are shown in future research it may identify people who are at greatest risk of non-adherence and allow resources aimed at optimising adherence to be targeted more effectively.

In summary, the proposed model of medicine adherence applying Banduras social cognitive theory did not predict medicines adherence in group overall, the IDD or non-IDD populations. Instead, this study suggests that a new model to predict medicines adherence is emerging namely: affective and biological factors are those which are important predictors of adherence in the diabetic population. Furthermore, this study has reinforced previous findings that presence of depressive symptoms predicts non-adherence in a mixed group of people with diabetes with and without ID.

Most importantly, a unique finding from this study is the finding that perceived side effects are an important predictor of non-adherence in people with IDD, and the higher the PSM score the less likely the person with ID and diabetes will adhere to prescribed diabetic medicines. Although the sample of people with IDD were small this study and further study is necessary, this has provided some preliminary insights into the reasons why this group are non-adherent to medicines and perceptions of carers. The findings suggest that further work with a larger sample size is necessary to further test predictive value of side effects and medicines non-adherence in people with IDD.

7.3 Key findings: comparisons of demographic and health characteristics

This section will discuss the keys results from demographic data and Research Question 1 namely: What is the frequency of dependent factors (glycaemic control and medicines

adherence) and independent factors (depression, side effects, self-efficacy and level of social support) in the IDD compared to the Non-IDD population?

Results from the baseline health and treatment characteristics revealed two key findings: first, the difference in age between the IDD and non-IDD groups, and second, the lower proportion of insulin prescribing in people with ID and type 2 diabetes. As key findings of independent factors were discussed in Section 6.8 this section will focus on dependent factors, glycaemic control and medicines adherence. Comparisons have not prospectively been reported between glycaemic control previously and rates of adherence in the IDD and non-IDD population a novel finding from this study was that there was no difference in glycaemic control or frequency of adherence in the two groups.

7.3.1 Age differences

In this study, the IDD group compared to the non-IDD group were significantly younger (51 vs 64 years), yet there was no statistical difference in those diagnosed with diabetes for more than six years. As type 1 diabetes is predominantly diagnosed in childhood or adolescence, and the prevalence of type 2 diabetics in both groups were similar (82% vs 72%, $p = 0.27$) this result is attributed to evidence that suggests people with ID are diagnosed with type 2 diabetes at a younger age.

Earlier onset of type 2 diabetes in the ID population has been attributed to poorer diet (Hale et al, 2011; Haveman et al, 2011; Taggart et al, 2013), and more sedentary lifestyles (Cardol et al, 2012a; Haveman et al, 2011) resulting in higher rates of obesity (Melville et al, 2008) from a younger age (Rimmer et al, 2010). In addition, due to genotypes in ID there is a higher prevalence of type 2 diabetes (Bojesen, Høst, & Gravholt, 2010; Laurier et al, 2015; Nordstrøm, Paus, Retterstøl, & Kolset, 2016). This finding that people with ID are diagnosed with type 2 diabetes earlier than those without is consistent with a population-based study conducted in North America of over 28,000 people (Balogh et al, 2015). There was a

statistically significant higher prevalence of diabetes in the ID population at ages: 50-59, 30-49 and 30-39. Early onset diabetes is a concern as those diagnosed with diabetes at a younger age have an increased risk of microvascular and macrovascular complications, including retinopathy, nephropathy and neuropathy (Stratton et al, 2000). These complications impact on life expectancy, quality of life and cost of ongoing healthcare provision.

Tight parameters for glycaemic control will significantly reduce renal and retinal complications (Zoungas et al, 2017). NICE recommend insulin is commenced on people with type 2 diabetes following sustained elevation of HbA1c > 58 mmol/mol (7.5%) whilst on optimised oral therapy (NICE, 2015b).

In this study, median glycaemic control was suboptimal in both the IDD and non-IDD population (median 60 mmol/mol, 8.1% vs 61 mmol/mol, 8.2%). Glycaemic control and medicines adherence are linked (Osborn et al, 2016; Wong et al, 2015), therefore optimising medicines adherence with a view to improving diabetic control in a group of younger people with ID and diabetes is important. The case to improve adherence in this population is further strengthened by Balogh et al (2015) who reported people with ID and diabetes were 2.6 times more likely to be hospitalised. Reasons for hospital admission in this study were not clear, however, a systematic review of 45 papers revealed that poor adherence to medicines is a leading cause of hospital admission in the general diabetic population (Al Hamid et al, 2014). Given the similarity in frequency of adherence in people with IDD compared to those without IDD in this study is it likely these results are transferable to the IDD population.

This study revealed only 70% of people with IDD are adherent to medicines is concerning and this population may benefit from strategies to optimise medicines adherence in the IDD population thus improving glycaemic control, reduce hospital admission and diabetic complications. This is particularly important given people with IDD are diagnosed with

diabetes earlier. Therefore, it is recommended that this area of research is prioritised in this population; this will be discussed and expanded upon in chapter 8.

7.3.2 Frequency of insulin prescribing in the IDD population

In the IDD and non-IDD group, as previously highlighted in chapter 4 (Table 4.2), the number of medications prescribed were similar. The percentages of four or more medications prescribed in each group were 84% vs 83% respectively ($p = 0.84$). This suggests that both the IDD and non-IDD groups have similar rates of prescribing for prevention of complications from diabetes, for example, managing blood pressure, lipids and cardiovascular risk.

However, what is a novel and important finding is the statistically significantly lower proportion of people with ID and type 2 diabetes prescribed insulin compared to the non-IDD population (11% vs 57%, $p < 0.05$). In contrast, there was no statistical difference in diabetic control in the IDD and non-IDD groups, (60 mmol/mol, 8.1% vs 61 mmol/mol 8.2%) ($p = 0.8$, $u = 1,325$). A single measurement of HbA1c obtained in this study is not a marker of a sustained elevation but may indicate a difference in how people with ID and diabetes medicines are managed when compared to the non-IDD population.

NICE guidelines for early treatment with insulin and tight glycaemic control have particular benefit in the young, those with fewer comorbidities and normal Body Mass Index (BMI) (Wallia & Molitch, 2014). Relaxation of target HbA1c is permitted on a case-by-case basis, and if the person is older or frail, has multiple comorbidities or is at risk of hypoglycaemia then starting insulin therapy may be delayed (NG28, NICE 2015a, 2015b).

The benefit in starting insulin early in younger type 2 diabetic (Wallia et al, 2014) is that it can achieve tighter glycaemic control thereby reducing the risk of microvascular complications (for example, retinopathy, nephropathy and neuropathy) (Zoungas et al, 2017) and progression to macro vascular complications (for example, stroke or acute coronary

syndrome) (Stratton et al, 2000) or cognitive impairment (Barnett, Brice, Hanif, James, & Langerman, 2013; Geijselaers, Sep, Stehouwer, & Biessels, 2015).

Despite benefits of insulin treatment efficacy of insulin treatment in type 2 diabetes has been debated. A recent systematic review (n = 20) including over 18,000 patients suggested that insulin therapy compared to oral hypoglycaemic agents had no effect on cardiovascular outcomes (Erpeldinger et al, 2016). Conversely, a Cochrane systematic review of 37 articles and over 3000 patients revealed an overall improvement in glycaemic control when insulin was combined with oral therapy (Vos et al, 2016) which suggests combination therapy with insulin has better overall outcomes. Despite this conflicting evidence on the efficacy of insulin therapy in type 2 diabetes, tight glycaemic control of HbA1c 6.5 - 7.5%, with insulin therapy where necessary, is a current recommendation (NICE, 2015b).

The findings that the IDD population are younger and have suboptimal glycaemic control suggest that the frequency of insulin therapy would be similar in the IDD population compared to the non-IDD population. Indeed, based on NICE recommendations to provide tighter diabetic control in the young and commencing insulin earlier in cases of poor glycaemic control, it would be logical to expect a higher frequency of insulin prescribing in people with ID. However, this study suggests evidence to the contrary, i.e. insulin prescribing is lower despite sustained hyperglycaemia in the IDD population. This suggests a failure to intensify or initiate treatment when clinically indicated (clinical inertia).

Reasons cited for clinical inertia are concerns around harmful effects of treatment, concerns around the ability to manage a treatment regime or clinicians suspecting non-adherence. (Khunti, Davies, & Khunti, 2015). Although the reasons for hesitancy in prescribing insulin in the IDD group were not discussed with clinicians, the next section will explore possible reasons for the disparity in prescribing between the IDD and non-IDD groups.

Harmful effects of insulin are weight gain, risk of hypoglycaemia due to dosing errors and impact on quality of life. (Tamir, Wainstein, Raz, Shemer, & Heymann, 2012; Vos et al, 2016; Wallia et al, 2014). A Cochrane systematic review of 37 trials (n = 3227) compared groups of patients, firstly, on insulin monotherapy and, secondly, combined insulin with oral hypoglycaemic. The results revealed weight gain of up to 2.1 kg in both groups, except those prescribed metformin and insulin (Vos et al, 2016). Weight gain results in suboptimal glycaemic control, cancer, and increased risk of cardiovascular disease, such as stroke or heart disease (Stuart et al, 2011). Therefore, initiating insulin and increasing weight further may do more harm than good. Although BMI was not recorded in this study the literature has reported a high prevalence of obesity in people with ID (de Winter, Bastiaanse, Hilgenkamp, Evenhuis, & Echteld, 2012b; Rimmer et al, 2010), which may explain the differences in treatment. Conversely, prevalence of obesity type 2 diabetes are increasing in the general population (Stuart et al, 2011) with WHO citing obesity approaching an epidemic. This may suggest that the gap between obesity in the IDD and the non-IDD population may be narrowing. Although weight gain is a possible explanation for differences in treatment approaches, the absence of BMI data in this study means that firm conclusions cannot be drawn.

Clinician concerns around hypoglycaemia may be another reason for choosing not to prescribe insulin in the IDD population. As previously highlighted by a recent systematic review (Erpeldinger et al, 2016), insulin is associated with increased risk of hypoglycaemia. There is also a reported association between hypoglycaemia, cognitive impairment and subsequent dementia (Sheen & Sheu, 2016). Other reviews have found no difference in hypoglycaemic events in people with diabetes on insulin; for example, a review by Asche (2012) of 76 publications reported no difference in hypoglycaemic events in those prescribed insulin versus oral hypoglycaemics. Nonetheless, hypoglycaemia is a serious, potentially fatal and avoidable complication of diabetes and with conflicting evidence supporting the long and

short-term benefit of insulin, clinicians may err on the side of caution with the IDD population and choose not to prescribe this treatment.

Instead, clinicians weighing up the benefit of tight glycaemic control versus the risk of hypoglycaemia with insulin therapy may judge risk of weight gain and hypoglycaemia outweighs benefit of tight glycaemic control in the IDD population. The views of clinicians were not obtained in this study, but this explanation is consistent with findings from a qualitative study of 29 healthcare providers to people with IDD by Brown et al. (2017). Clinicians cited concerns about hypoglycaemia as a limiter to tighter glycaemic management in people with ID. Therefore, the decision not to commence insulin may be based on pragmatic clinical judgement. Furthermore, as there was no significant difference in glycaemic control in the IDD group compared to the non-IDD group in this study, the risk of hypoglycaemia and weight gain may outweigh the benefit in introducing insulin therapy.

Brown et al. (2017) also cited lack of effective support for insulin management as a barrier to commencing insulin in people with IDD. Insulin therapy is a more complex treatment than oral hypoglycaemics as monitoring of blood glucose, more frequent insulin dosing and carbohydrate intake monitoring are essential aspects of self-management. Given most IDD participants had support with medicines management this may support the argument for treatment intensification with insulin. Carers could not only support tight glycaemic control through insulin administration but also be educated on serious side effects and how to avoid or manage them.

However, greater reliance on carers to support insulin therapy has resource and quality of life implications. For example, in this study, the qualitative results revealed greater physical support for carers by IDD participants on insulin therapy than those receiving oral treatment suggesting that carer support was more intense and frequent in the former. Intensifying treatment from twice daily oral therapy to a minimum of three times daily insulin therapy

significantly increases care needs for people with IDD. Many carers were paid (55% n = 5) in the IDD population, thus, treatment intensification may put additional financial strain on an already under-resourced health and social care sector.

Regarding the effect of insulin on quality of life, although generalisations about attitudes to insulin therapy cannot be made in this study, Tamir et al. (2012) suggested that people with type 2 diabetes on insulin therapy had a lower quality of life when compared to those on oral treatment. This was mainly due to pain experienced when taking blood tests and could be overcome with education, support and good management; however, it may explain clinicians' caution in prescribing insulin in this group. In the IDD population, commencing insulin may have a greater negative impact on quality of life as it may result in more intensive support, loss of independence and confidence. The qualitative results did not suggest that those on insulin had a poorer quality of life, but the effect of insulin on quality of life would merit a robust evaluation, if more people with IDD are to be commenced on insulin treatment

Finally, clinical inertia has been linked to the likelihood of adherence to a prescribed regime, that is, if a clinician believes non-adherence is a risk they may not escalate or intensify treatment. For example, in a US study by Grant et al (2007) of 2063 patients who, over a 2-year period, showed a relationship between non-adherence and escalation of treatment with those reporting low adherence being less likely to have treatment escalated. Although reasons for selecting different types of diabetes treatment was not explored in this study this may be a topic for future research.

This is the first study to report on the frequency of adherence in the IDD population and, prior to commencing the study, one hypothesis was that adherence in the IDD compared to the non-IDD population would not be equal. This was based on assumptions that people with IDD did not have the cognitive or functional ability to adhere to a prescribed treatment regime. However, the findings suggest this was not the case; instead, results suggest that adherence was

similar in the IDD compared to the non-IDD groups. This similarity may be due to effective prescribing choices by clinicians, and support provided by carers, resulting in the simplest once or twice daily treatment regimens selected for IDD participants. However, the prescribing of simpler medicines regimes in the IDD group may be based on the false assumption that they do not adhere to treatment.

If the latter is correct, choosing not to prescribe insulin may be to the detriment of the IDD population as it may reduce the opportunity for optimum glycaemic control and increase their risk of long-term diabetic complications (Stratton et al, 2000; Zoungas et al, 2017). Given higher rates of hospitalization, shorter life expectancy and poorer overall health in the ID population (Balogh et al, 2015; de Winter et al, 2012a; Emerson, Hatton, Baines, & Robertson, 2016), this hesitancy in prescribing may already be having a negative effect on the health of people with ID and diabetes.

Undoubtedly, the decision to commence insulin is a complex decision and, prior to this study, the best available evidence from the ID literature was that treatment decisions were based around preventing hypoglycaemia and the ability to adhere to more complex treatment plans (Brown et al, 2017). Therefore, this study provides new evidence suggesting that IDD participants, with assistance, can achieve similar rates of adherence to the non-IDD population and more complex treatment can be managed with effective support. The support required does require additional carer resource and has cost implications; however, this needs to be balanced against the consequences of poor glycaemic control, increased hospitalization and poorer overall health which are more prevalent in the IDD compared to the non-IDD population (Balogh et al, 2015, Cooper et al, 2015, Zoungas et al, 2017).

The reporting of descriptive data in this study has revealed differences in prescribing practice between the IDD and non-IDD population. Exploration of the wider research evidence suggests this may be driven by pragmatic clinical judgement in that the decision to commence

insulin requires consideration of not only clinical risk in terms of side effects, but also an assessment of economic benefit, effect on quality of life and likelihood of adhering to treatment (Brown et al, 2017).

These results are from a small population in one health board in Scotland and, as such, should be interpreted with caution. However, the findings are important and do warrant further investigation in a larger cohort of IDD research participants. In the meantime, dissemination of findings may promote reflection on the prescribing choices made by clinicians with and for people with ID and type 2 diabetes. This would ensure prescribing plans were optimised to achieve good glycaemic control and the greatest benefit to short and long term health.

7.4 Key findings: frequency of dependent factors in IDD compared to the Non-IDD population

There are two key findings that have never been reported previously in the literature and warrant discussion namely (1) that there were no statistical differences in glycaemic control and (2) there was no difference in adherence rates with the IDD and non-IDD population were compared.

7.4.1 Glycaemic control

NICE guidance state optimum upper limits of HbA1c are; 48 mmol/mol (6.5%) for type 1 and 58 mmol/mol (7.5%) for type 2 diabetes (NICE, 2015a, 2015b). These targets are particularly important for people who are younger and have type 2 diabetes. This is in accordance with the United Kingdom Prospective Diabetes Study (Stratton et al, 2000) and a recently published meta-analysis concluding that tight glycaemic control prevents renal and retinal microvascular disease in type 2 diabetes (Konig et al, 2013; Zoungas et al, 2017).

In this sample, median HbA1c was suboptimal in both the IDD and non-IDD groups (median 60 mmol/mol, 8.1% vs 61 mmol/mol, 8.2%). Similar proportion of participants in the IDD (54%) and non-IDD groups (62%, $p=0.42$) had suboptimal glycaemic control. Glycaemic control is marginally better in the IDD compared to the non-IDD population, but in both groups glycaemic control exceeds recommended limits by NICE.

Recently, there has been debate among diabetes experts on the efficacy of tight glycaemic control in type 1 diabetes, and, for type 2 diabetes these tight parameters are relaxed for the elderly, and for those with comorbidities, obesity and shorter life expectancy (Rodríguez-Gutiérrez & Montori, 2016). A position statement of the American Diabetic Association (ADA) and European Association for the Study of Diabetes (EASD) (Inzucchi et al, 2012) advocates a more person-centred approach for those groups where a higher HbA1c may be tolerated to protect against risks associated with tight control which include weight gain and

hypoglycaemia. In response to this position statement, a review paper proposed a target HbA1c of 7.6 - 8.5% for the older population (> 65 years of age), those with more comorbidities and longer length of time with diabetes (Mathur, Zammitt, & Frier, 2015). Although this proposed change has not been reflected in NICE guidance they do advocate a person centred approach to attaining HbA1c goals in type 1 and 2 diabetes (NICE, 2015a, 2015b).

These position statements by the ADA and EASD may explain suboptimal glycaemic control in this study. Demographic data from this study showed that although the median age was < 64 years, many participants in the group had diabetes for six or more years and therefore, the need for tight glycaemic control may not be as important as in those diagnosed for less time. Furthermore, people with ID have are more likely to have more comorbidities (Cooper et al, 2015) which may result in a relaxation of HbA1c targets. However, an argument to support tighter glycaemic control in people with IDD is that they cohort were significantly younger, thus more susceptible to long term complications from diabetes. As a result, more intense glycaemic control using insulin therapy may have been expected.

Exploration of clinician prescribing decisions was not part of this study, however, findings from this study revealing poor glycaemic control in a younger IDD population with diabetes, who have lower rates of insulin prescribing, warrants further exploration with clinicians. This would aim to establish the reasons for their prescribing decisions and rationale for suboptimal glycaemic control in this younger vulnerable group.

7.4.2 Medicines adherence

Overall, there was no difference in frequency of adherence in the IDD and non-IDD groups ($p = 0.41$). In the IDD group 70% of participants reported medium or good adherence ($\text{MMAS8} \geq 6$) and in the non-IDD group 62% reported $\text{MMAS8} \geq 6$.

Comparing these results to the general diabetic literature suggests that adherence is slightly lower. For example, a systematic review conducted over a 50-year period suggested

adherence rates at around 74% (DiMatteo, 2004). Prospective studies have revealed similar adherence rates to this. In a study in the US of 151 diabetics attending outpatient clinics 72% of the study population were adherent to treatment (Mann et al, 2009). The results from this study suggest that there has been little change in adherence over the last 15 years.

Comparing results from this study to the ID literature is more challenging as a literature search yielded one published study relevant to the IDD population. This US study was a retrospective analysis of 1500 Medicaid people with developmental disabilities. Results revealed that adherence as measured by medicines possession ratio (MPR) was ‘optimised’, however the percentage of those adherent versus non-adherent was not stated (Patel et al, 2016). Therefore, the present study is the first to report the frequency of adherence in this population. Furthermore, this study reported a non-significant ($p = 0.41$) but higher proportion of IDD participants were adherent to medicines compared to the non-IDD group (70% vs 62%).

The initial hypothesis during study design was that the frequency of medicines adherence would not be equal and that, due to cognitive impairment, and difficulties in managing complex medicines regimes the IDD population would have poorer adherence than the non-IDD population. This hypothesis was based on evidence from several studies that identified cognitive impairment as a factor associated with adherence (Ettenhofer et al, 2009; Martinez-Aran et al, 2009; Tomlin & Sinclair, 2016; Turner, Hochschild, Burnett, Zulfiqar, & Dyer, 2012) and supported by the theoretical framework that informed this study (Bandura, 1986).

An assumption by the researcher was that all IDD participants had cognitive impairment and those without ID did not as they part of the ‘general population’. However, there is emerging evidence that this is not the case and that people with diabetes are at higher risk than the general population of cognitive impairment. The long-term effect of prolonged insulin treatment, frequency of hypoglycaemic events and overall poor health in the non-IDD

population may be factors associated with impaired cognitive function in people with diabetes (Chau et al, 2011; Li et al, 2017; Sheen & Sheu, 2016).

Cognitive impairment not impeding capacity to consent to participate was a requirement of both groups. To maximise inclusion of people with IDD in the study, recruitment and data collection instruments and methods had pictorial and linguistic amendments. These amendments and face to face method of data collection, maximised inclusion for the IDD population, but may have widened recruitment to those in the non-IDD group with mild cognitive impairment or poor literacy who otherwise may have declined to participate if data collection methods were different, for example, a postal or online survey. Therefore, the lower frequency of adherence in the non-IDD population may be attributed to a wider cross-section of the diabetic population participating than previous studies.

A second hypothesis was that level of support would mitigate poor medicines adherence in people with IDD. Previous research has highlighted the role that social and family support plays in motivating non-IDD service users to adhere to prescribed treatment (Feil et al, 2009; Kim et al, 2015; Mayberry & Osborn, 2012; Patel et al, 2016). However, there is no published data on the role of the carer in optimising medicines adherence in people with IDD. In this study, carers reported a variety of methods ranging from verbal reminders, coercion and professional support intended to prompt optimum medicines adherence. Overall these strategies appeared to be commensurate with the help that participants required to optimise medicines adherence, without which adherence rates may have been significantly lower. Yet, perceived level of social support was not associated with non-adherence, this suggests that other factors are more important, i.e. depression and side effects.

In summary, the lower frequency of medicines adherence in the non-IDD group may be due to the data collection approach widening inclusion to those who may not usually participate in research but are at risk of non-adherence. Secondly, in the IDD population a higher

frequency of adherence in the IDD population may be due to effective support provided by carers. Nonetheless, in both groups improvements in medicines adherence are necessary. An effective approach for future adherence research is to involve carers and maximise inclusion of vulnerable groups in development and design of strategies. This may be time consuming but may offer a more egalitarian and inclusive approach to research and which may improve health outcomes in people with diabetes and specifically in minority and vulnerable groups.

7.5 Summary of discussion

The overall aim of the study was to develop and test a theoretical model designed to improve medicines adherence in the IDD population and compare this to the non-IDD population. Both stage one and two have achieved this. It was hypothesised that Bandura's social cognitive theory was an effective model for predicting those at greatest risk of non-adherence. Although the study was underpowered, testing this model in a cohort of IDD and non-IDD people suggests that biological factors (side effects) in the IDD and affective factors (depression) in the non-IDD population may be the most important predictors of medicines non-adherence.

Examination of descriptive statistics revealed that people with IDD were diagnosed with diabetes at a younger age yet, were not as frequently treated with insulin as people without IDD. There are several hypotheses proposed as to the reasons for this and further empirical evidence is required to draw any conclusions from this finding.

Another important finding was that comparisons between the IDD and non-IDD population revealed that the frequency of medicines adherence was no different. However, the results suggest that improvements in adherence are needed in both groups and this in turn will improve glycaemic control.

Findings from this study have not been reported before and have implications for research, policy and practice. Before recommendations are made, strengths and limitations of this study will be presented. This will be followed by a personal reflection on the research process. This section is intended to inform development of further research in this area and to provide an insight into my perspective on the PhD process and research findings.

7.6 Strengths of the study

7.6.1 Research methodology

A major strength was the mixed methods approach. The quantitative stage reported statistically significant differences and estimated predictors of non-adherence. Perhaps the greatest strength of stage two (qualitative) was to allow for further explanation of stage one results, particularly in relation to verification of the self-reported adherence score, further exploration of depression and side effects and associations with adherence in the IDD population. This added impact to the study results, and gave greater certainty to the overall results. An additional advantage of this approach was that the methodology mitigated the potential risk of recruitment challenges and small numbers to permit statistically valid results.

It is always preferable to recruit suitable numbers to fully validate findings. However in the ID population recruitment to studies is a commonly cited issue (Clever et al, 2010; Goldsmith & Skirton, 2015) and, in recognition of this, a number of other studies have adopted a similar mixed methods approach (Cuthill et al, 2003; Tveter et al, 2016). By anticipating the potential for shortfalls in recruitment, and through systematically analysing and triangulating the data obtained in both stages of the study, the reliability and credibility of findings were enhanced. This methodologically, if disseminated to other researchers in the field, could offer a way forward for future research in vulnerable difficult to reach populations.

7.6.2 Recruitment

An additional strength which maximised recruitment to the study was the adaptable approach adopted in where interviews took place, support provided by carers during the interviews and pictorial and linguistic modification of instruments to maximise comprehension.

Prior to commencement of the study, key stakeholder involvement refined the study design and provided named informants with the opportunity to contribute to the development

of the research, improve understanding of the project and optimised access to eligible IDD participants.

Interviewing in a place of participants' choosing encouraged those reluctant or unable to travel to participate in the study to do so and provided a person-centred approach to data collection. When the participant was willing to travel to an office space, the interviews took place in a quiet location near the outpatient department where they were recruited. The participant was made to feel at ease because this location was familiar to them. When the participant was unable to travel, due to cost, or mobility issues, collecting data in their home helped to widen inclusion to those who may not normally participate in research.

Carers of those in the IDD and non-IDD population were invited to stay if the research participant had consented to this. The presence of carers was valuable because it provided support if any items within the questionnaire caused confusion and allowed the carer to provide explanations in terms familiar to the participant. The carers had no input into respondents' answers, however, when required, they provided explanations in terms that the participant could understand, thereby maximising meaningful participation.

Use of Board maker, easy read and giving participants additional time and speaking clearly, in simple language also maximised participation. This approach was applied to participant information leaflets and may have contributed to a high overall recruitment rate (68%, n = 111) and low percentage of participants not attending for interview. In fact, all participants in the IDD group and 98% (n = 78) in the non-IDD group attended after agreeing to take part.

7.6.3 Consent

There were two major strengths associated with consent: firstly, close collaboration with named informants verified capacity to consent, and secondly, and verification of capacity to consent before and during the data collection process.

The Age of Legal Capacity (Scotland) Act (1991) is built on the premise that capacity to consent to treatment and research is presumed unless proven otherwise (Scottish Government, 2000). This suggests that capacity may only be assessed if there is doubt that the person has capacity to consent. However, verification of capacity to consent in this study was essential and, in accordance with research codes of practice and to maintain the reliability of the research, verification of understanding of the research, what would happen to the data and how and where data would be reported was undertaken prior to consent (Palmer & Forrester-Jones, 2016; Tamir et al, 2012).

During the formal consent process and interview, techniques, for example, teach-back, ensuring adequate time for responses and giving regular breaks during the interviews were all used to verify and maximise capacity to consent. This also acknowledged that capacity is not an “all or nothing” principle and that capacity fluctuates and needs to be re-evaluated during the research process. Throughout the interview, it was important to verify capacity and comprehension in a more unstructured way. This approach was presented in a case study (Boahen, 2015) and facilitated a rapport to develop between the researcher and participant, promoted a shared understanding of research purpose and assessed intellectual capability of the participant at various points during the interview process.

Ongoing capacity was verified by contextualising questions and asking participants to describe activities that made them happy or sad, asking participants to describe pictures depicted within the scales and, if in the person’s home, asking the participant about pictures and personal effects. These provided ongoing assessment as well as establishing a rapport and making the participant feel at ease. All those consenting at the beginning could participate and complete the questionnaires and interviews (n = 111).

7.6.4 Data collection

Face to face interviews maximised eligible inclusion. In both stage, it confirmed accurate eligibility to participate; verified capacity to consent to the study; clarified items within the questionnaires in both the IDD and non-IDD groups, which otherwise may have been left blank or misinterpreted.

Face to face interviews were also valued by both IDD and non-IDD participants. Anecdotally some non-IDD participants reported that it was helpful to have a researcher's support in completion of the questionnaires and presence at the time of completing the questionnaires as it provided discussion about any points of confusion. Moreover, use of pictures and symbols and easy read terminology widened access for those who had poor literacy and otherwise been unable to complete the questionnaires on their own. The approach to data collection also allowed the researcher to develop a rapport with participants and identify carers who were willing to participant in stage two.

Furthermore, this approach minimised the risk of missing data and full data sets for all 111 participants were obtained. This demonstrates the effectiveness of a person-centred approach to recruitment, that data collection was acceptable to those participating, minimised non-attendance and provided full data sets.

7.6.5 Data analysis

Use of standardised data analysis procedures, particularly to establish predictors of adherence, allowed for inclusion of this study in future systematic review. Univariate and multiple regression analysis may be more readily understood by clinicians seeking out research that will inform delivery of care. Alternative methods of data analysis to test associations between dependent and independent factors, for example, structural equational modelling could also have been used. However, the most common approach to statistical analysis reported in chapter 2 was univariate and multiple regression analysis (n = 10) for simplicity and

consistency with previous studies it was selected. Stage two data analysis using NVIVO software permitted verification of themes with the research team and transparency in how themes were extracted.

7.6.6 Results

As outlined throughout this discussion chapter, as far as the researcher is aware, this study is the first to investigate medicines adherence and associations with depression, side effects, self-efficacy and perceived social support in people with ID. It has revealed statistically and clinically significant findings: for example, similarities in adherence scores and glycaemic control in the IDD and non-IDD population and dominant factors associated with adherence in the IDD and non-IDD population.

A major strength of this research is that it is the first to report the frequency of diabetic medicines adherence in the IDD population. Prior to commencement of this study, there were no reported studies on medicines adherence in the IDD population of any type. Since completion, a retrospective study has been published (Patel et al, 2016). However as far as this author is aware, this PhD study is the only prospective study to examine medicines adherence in the IDD population.

This study has established which of the five key factors within the theoretical model are most strongly associated with adherence. Previous diabetic medicines adherence studies have explored the association between one or more factors (depression (Chao et al, 2005; Mann et al, 2009; Osborn & Egede, 2012) and/or side effects (Pollack et al, 2010) and/or self-efficacy (D. M. Mann et al, 2009; Nelson et al, 2007) and social support (Mayberry & Osborn, 2012; Schoenthaler et al, 2012)) and their association with adherence in the general population, but not all factors have been investigated in one study. Therefore, the findings from this study are unique for both the IDD and non-IDD population.

Factors associated with adherence differed between the IDD and non-IDD group. Consistent with previous research, this study has demonstrated that depression is the most dominant factor associated with adherence in the non-IDD population. Triangulating quantitative with qualitative results suggested that carers of IDD participants mitigate the effect of depressive symptoms which may explain the absence of significant associations in this group.

In people with IDD, perceived level of side effects appeared the most important factor. Descriptive statistics revealed that people with ID and type 2 diabetes appear to be maintained on the least complex regime, and may experience more side effects than the non-IDD population. The qualitative data suggest that exploration of side effects in people with IDD by carers is infrequent and if more robustly addressed may improve adherence in this population. These differences have not been reported before and could have important implications for how diabetes care is provided to people with IDD. Further exploration of the impact of side effects on medicines adherence may inform development of evidence based interventions to improve long-term morbidity and mortality.

7.7 Limitations of this PhD study

7.7.1 Absence of Patient and Public Involvement exercise.

Patient and public involvement (PPI) is required by most funding bodies and recommended by government as good research practice (National Institute for Healthcare Research, (NIHR), 2017). This is underpinned by the philosophy that research is carried out ‘with’ and ‘about’ members of the public rather than ‘to’ or ‘for’ them. It is intended to put the public at the heart of health and social care research, improving awareness, participation and relevance of research (Brett et al, 2012). There is limited evidence to support its use; however a realistic evaluation of over 129 cases studies (the RAPPORr study) reported that PPI improved study design, methodology and dissemination of results. The RAPPORr study recommended more research is needed to further evaluate PPI and establish methodologies that support a robust and consistent approach (Wilson et al., 2015). In response the National Institute of Healthcare Research (NIHR) in collaboration with the Chief Scientists Office (CSO) in Scotland and Health and Research in Wales are developing national standards and PPI is currently recommended as an integral part of the research cycle as it strengthens the relevance, quality and ethics of the research study (NIHR, 2017).

Despite benefits of PPI, this study did not formally conduct one, instead, it scoped out views of key stakeholders caring for people with IDD. This scoping exercise provided preliminary views on the useability of the instruments used in the study and tested the feasibility of the methodology proposed in the target study population. Feedback from stakeholders was overwhelmingly supportive of the subject area to be studied, the proposed study design and approaches to data collection. In addition, named informants were identified to assist in recruitment and no ethical issues were identified. Therefore it provided the researcher with similar information that a PPI exercise would provide. Given the positive feedback from stakeholders on the study it was viewed by the researcher and the supervisory

team stakeholder engagement was a sufficiently robust approach to inform study design, generate awareness and promote recruitment.

In retrospect public involvement may have provided an alternative and unique perspective to recruitment, for example access to non-IDD or IDD user groups unknown to health care professionals. It may have identified alternative approaches to study design or a lay perspective on medicines adherence. This may have enhanced recruitment and the overall quality of the study. Whilst this is acknowledged as a limitation of this PhD study, obtaining views from key stakeholder and experts in diabetes and intellectual disabilities was a valuable exercise to enhancing recruitment and improved data collection strategies. Nonetheless, any future studies in this area by the researcher will carry out a comprehensive patient and public involvement exercise prior to study implementation.

7.7.2 Study design

A major limitation was the cross-sectional design, meaning a causal link between dependent factors and medicines adherence cannot be made. However, this is the first research study to establish whether ID is associated with medicines adherence and contributes to the UN Convention of Rights with People with Disabilities (CRPD) to establish an evidence base for treatment of people with ID (UN, 2007). Observational studies are the first stage in establishing associations between dependent and independent factors and inform research and clinical practice on the type of interventions that may improve patient outcomes. Publication of these results will inform practice and design of future interventional studies measuring the effect of depressive symptoms or side effects on medicines adherence.

7.7.3 Sampling

A second limitation of the study was the sampling strategy. Ideally random sampling would have been the sampling method of choice; however, adopting this approach may have resulted in a smaller pool of potential ID participants. Therefore, the sampling strategy aimed

to recruit all people with ID and diabetes who met the study inclusion criteria. The absence of a comprehensive local database detailing all people with ID and diabetes meant that named informants identified potential participants. This sampling method resulted in a lack of clarity whether the sample obtained was comprehensive and representative of the total population of people with ID and diabetes.

The subject pool was also a limitation as most non-IDD participants were recruited from one diabetic outpatient department. IDD participants were sampled from a variety of sources including GP practices, ID services, outpatient studies and research databases but all attended 6 monthly appointments with their GP, at another regional outpatient clinic or a learning disabilities clinic. As referral from primary care to diabetic clinics occurs for all type 1 diabetics and for problematic or potentially problematic type 2 diabetics, the sample in this study was representative of a population at risk of poor diabetic control but not necessarily representative of the general diabetic population. These limitations may skew the applicability of results in favour of those with problematic glycaemic control, thereby reducing the generalisability of findings. Therefore, the results establish the most important factors associated with adherence in this population, but may not be representative of the general IDD or non-IDD population.

7.7.4 Recruitment

Failure to meet target recruitment numbers was a limitation. Initially, the target was to sample 111 participants from the IDD population. During this pre-data collection stage, the stakeholders suggested target numbers that were overly ambitious particularly because (1) recruitment was restricted to one health board, (2) no comprehensive regional database identifying people with ID and diabetes exists and (3) those unable to give valid consent were excluded from participation.

Nonetheless, to avoid compromise and to attempt to present conclusive and statistically reliable findings, it was important to meet the recruitment target. In the first six months of

recruitment, the researcher identified named informants, contacted hospital outpatient departments, specialist ID services and general practitioners; advertised the study in the local general practice newsletter; and attended ID nurse specialist forums on numerous occasions. Despite this, only two IDD participants were recruited. Furthermore, only three out of 124 GP practices contacted the researcher to nominate additional potential participants. The reasons for slow recruitment were initially unclear. However, it may just have been the case that the target figure of 111 was over ambitious. This has been verified by a prevalence study published after commencement of this study which gathered data from over one million patient records extracted from 314 GP records in Scotland in 2009 and reported the prevalence of diabetes and learning disability at 6% (Cooper et al, 2015). This equates to around 531 people in Scotland with diabetes and a learning disability, therefore in retrospect a target figure of 111 from one health board was overly ambitious.

After nine months, after discussion with PhD supervisors it was agreed to modify the study to compare the frequency of, and factors associated with medicines adherence, in the IDD and non-IDD population and this modification was approved by the regional ethics committee. This shifted the study from one that focussed solely on people with ID to investigating whether ID was a factor associated with adherence.

To the best of the researcher's knowledge, a study of this type has not been conducted before and, in fact this amendment strengthened the study. It is the first time that prospective comparisons have been made between the IDD and non-IDD population in areas of glycaemic control, medicines adherence and associated factors. Testing Bandura's theoretical framework derived in the IDD and non-IDD population has extended findings to those with a specialist interest in diabetes care in general, not just those caring specifically for people with ID. Therefore, results may generate greater impact than if the study had solely recruited from the IDD population.

In stage two, ineligibility of carers in the non-IDD group limited recruitment. During stage one interviews, most participants reported self-management of their diabetic treatment, whereas the majority of people with IDD received support with medicines. As a result, comparison of carers' perceptions of medicines adherence and related factors between the two groups was limited. This was not a specific aim of this stage but would have facilitated greater integration of findings in stage one and two and allowed inferences to be drawn about how medicines adherence is supported in the IDD and non-IDD population.

Inclusion criteria in non-IDD population could have been extended to family members who observed medicines consumption and, if approved, would have permitted greater comparisons and an analysis of carers who observed how stage one participants managed medicines in addition to those supporting medicines management. However, extending inclusion in this way would have altered the focus of stage two from triangulating stage one results to comparing carers and family members approach to maximising adherence in the IDD and non-IDD population. This was beyond the scope of this thesis, but may be an area of future research. A study focussing on this may allow a more in-depth exploration of identify strengths and weaknesses of support offered by carers and family members living with people who have diabetes with or without ID.

7.7.5 Data collection methods

There were limitations with face-to-face interviews. A minimum of one hour plus travelling time was allocated to each interview therefore, data collection was therefore, more protracted than with online or postal questionnaires. It also may have inadvertently excluded those with busy work or personal lives. This may in part explain why many non-IDD participants who participated were not in paid employment and older. However, overall, the approach was generally considered to maximise inclusion and, with conversions from recruitment to participation in both groups at 65%, a moderately good response rate was

achieved. This shows that people with ID are as willing to participate in research as those without, and builds a case for them to be included in future research.

In retrospect, collecting data on Body Mass Index (BMI) and reporting full drug history may have provided more conclusive findings. It became apparent that this was particularly important in relation to achieving a greater understanding in the differences in drug treatment and reasons for side effects being the most important factor associated with adherence in people with ID. For example, if BMI was similar in both groups then it may have been concluded that the differences in insulin prescribing were not attributed to this. Furthermore, if a full drug history had been taken during the interview, a more definitive conclusion on whether the differences in treatment in the IDD compared to the non-IDD population had an impact on the frequency and intensity of side effects in the IDD group. Consequently, data on BMI and drug history may have advanced understanding on diabetic management in the IDD population even further. Therefore, future research in this area should include the data omitting in this study, thus building on existing research in this area. Despite this omission this study has made an important contribution to diabetic medicines adherence, and the findings have contributed to developing an evidence-based supporting further research that may include interventions to improve adherence in both the IDD and non-IDD population.

7.7.6 Results

The final and most important limitation was that the recruitment numbers in the IDD population prevented definitive conclusions to be made about the validity and future use of dependent and independent instruments. Moreover, small recruitment numbers that were not sufficiently powered to demonstrate the effect of independent variables may have resulted in type 1 errors in stage one. For example, it may be that insufficient power failed to detect the effect of depression on medicines adherence and resulted in side effects being the most important factor associated with adherence in the IDD population. Recruiting greater numbers

to the IDD population may have produced different results. Although corroborating results in stage two verified the credibility and reliability of stage one findings and went some way to explain the incongruous results, caution needs to be used in interpretation of the above findings from this study. These findings therefore should be tested further in a larger scale study to generate statistically reliable results rejecting or upholding hypotheses tested in this study.

7.8 Personal reflection on PhD project

In chapter 1, I detailed my motivation for conducting this research project which was to carry out impactful, medicines focussed, and original research in a vulnerable group. I have achieved medicines focussed and original research and have gained a great deal of knowledge in a variety of research methodologies; narrative systematic review, quantitative and qualitative research. It has highlighted the complexity of the research process, the challenge of gaining expertise in all three and how a team of researchers may be better placed to conduct mixed methods research.

As an academic, I appreciate the need for evidence based practice, particularly in medicines management and non-medical prescribing. Throughout my PhD, I have reflected on the relevance of my research to non-medical prescribing and pre-registration students and, during presentations and teaching, obtained their views on their role in optimising adherence. During my teaching it was apparent that many students were not aware of the health and financial impact of medicines adherence. Raising awareness through my teaching may assist health care professionals to implement strategies to optimise adherence, reduce health inequalities, improve quality of life of those they care for, and deliver a more cost-effective service.

Many of the strengths outlined in this PhD thesis are examples of good research practice, and a reflection of my clinical skills, research and teaching experience. It has also demonstrated the effect that a compassionate and person-centred approach has on recruitment, participation and obtaining complete data sets in both populations. Time spent with research participants was rewarding, revealing and often left me with a sense that I had taken the time to listen and, with some, make a difference to the care they received. This was particularly evident when visiting participants in their homes. For most, they were well cared for by carers and family members, whilst a minority lived alone, felt socially isolated and lacked support for basic health

and social care needs. As a nurse, I could identify those in need of greater support, actively listen to their concerns and where necessary, and with participants' consent, highlight my concerns to the direct care team. In response to this, the direct care team explored their needs in greater depth. Utilising my skills as a registered nurse whilst carrying out research reassured me that I could pursue an academic career whilst using my nursing skills to protect the health and social care needs of research participants.

This PhD has highlighted the value of conducting research with people with ID and investigating medicines adherence in this population, but also the challenges. My biggest disappointment was recruitment which has impeded the impact of this research. Slow identification of potential participants resulted in a smaller sample and inconclusive findings. In future this could be addressed by modifications to methodology including: (1) extending the research to additional health service areas, (2) including carers and incapacitated IDD participants and (3) bypassing the named informants.

Extending recruitment and adopting a multi-centre study design could have generated sufficient power to provide conclusive results in the IDD population. Recruiting from two additional health boards may have provided adequate numbers. However, recruiting from other centres would have required additional financial resource and travel time, which as a lone part-time researcher was beyond the timeframe and budget of this study.

Extending inclusion criteria to IDD participants who lacked capacity to consent to participate in the study was an option. The United Nations advocates inclusion in research and necessity for all treatment provided to all types of IDD participants, including those without capacity, to be supported by an evidence base (UN, 2007). Without inclusion, an evidence base will not be built, and without evidence demonstrating the effect of interventions across the range of people with IDD, health inequalities may not be addressed.

Extending recruitment would have resulted in a more comprehensive study and provided a valuable insight into medicines adherence across the range of people with IDD. It would have also been consistent with my interest in exploring the challenge of medicines management in people across the range of ID. However, one of the overriding conditions attached to involving adults with incapacity in research is that similar research cannot be conducted by involving adults who can consent (Scottish Government, 2000). As there was no evidence on medicines adherence in any people with IDD and, as a novice researcher, I limited recruitment to IDD participants who had capacity to consent.

A third option would have been to bypass named informants and contact participants directly. This approach may have increased recruitment and I was sufficiently skilled and sensitive to screen and respond to the needs of the person with IDD, an essential requirement for direct recruitment (McDonald et al, 2016). However, taking into consideration that I had not worked in this area of practice, my view was that approaching participants through a named informant was less coercive and better aligned to research codes of practice. In addition, I was not employed by the health service, thus making it impossible to access databases or named informants who may identify those with intellectual disabilities and diabetes.

The commitment invested in my PhD to submit on time, whilst working full time has been considerable. With most work completed in my own time, I have sacrificed professional and personal commitments to improve my academic credibility and advance the nursing profession. By committing to developing a grant proposal in this area to further investigate and ratify findings from this research I hope that, with a team of researchers, I can work towards a goal of leading high quality person-centred research in this area whilst maintaining a work-life balance.

In conclusion, despite its limitations, I believe this study has made a limited but valuable contribution to informing best practice in managing diabetes medicines adherence in the IDD

and non-IDD population. I have presented my findings at two conferences, and, at both, they have generated discussion amongst delegates. Post-viva and graduation, my intention is to publish the findings in high quality, peer reviewed journals. The skills I have gained will extend beyond adherence research and be transferable, not only to future research, but to supporting undergraduate and postgraduate study, thereby advancing nursing practice and influencing healthcare policy in the future.

8 Chapter 8: Conclusions and recommendations

8.1 Introduction

This chapter will consolidate all findings from this PhD study and consider their significance in terms of implications for research, policy and practice. As outlined in chapter seven, the study was limited by the numbers recruited in the IDD group. However, this study is the first to have developed and tested a theoretical model of medication adherence in the IDD population. Although results suggest that Banduras social cognitive theory is not a good model fit for predicting adherence as outlined in the discussion chapter affective and biological factors do predict those who are likely to be non-adherent in the diabetic population. The study is therefore of international relevance and interest to those researching and caring for people in this area.

In this chapter, potential implications of the findings on the direction of future research will be presented, followed by policy and, finally, practice.

8.1.1 Implications for future research

An important recommendation is that the focus on research will be on further validating the findings from this study in a larger cohort of IDD participants. In the non-IDD population or a mixed group of IDD and non-IDD participants it is recommended that the focus be on screening for, and developing interventions to reduce the effect of depression on medicines adherence.

8.1.1.1 *Implications for future adherence research: the IDD population.*

Further work on validating findings from this study is a priority. Firstly, further validation of instruments used in this study is required to provide a definitive recommendation on their continued use in clinical practice and future research. Secondly, a sufficiently powered larger

scale study to further test the hypothesis that side effects predict non-adherence, and the significance of a side effects score of 16, is necessary.

Finally, with the wide range of medications available to treat type 2 diabetes, it may be beneficial to carry out a fully controlled interventional study evaluating the effect of adjustments in diabetes treatment on reported side effects, medicines adherence and quality of life. In advance of further research in this area, an education focus is recommended to increase awareness in carers of the effect of side effects on adherence and how prescribers can avoid polypharmacy and effectively screen for side effects.

8.1.1.2 *Implications for future adherence research: the non-IDD population and group overall*

With regard to research, testing an intervention that may improve both symptoms of depression and motivation to adhere to a prescribed treatment regime may set the direction of future adherence research. Given the challenges related to research in the ID population and the homogeneity of the sample population with respect to demographics and health characteristics, designing a study which maximises recruitment from IDD and non-IDD groups with symptoms of depression who are not currently in receipt of support may have an overall benefit. Although interventional studies have been carried out in the non-ID population who have diabetes and depression, none reported inclusion of people with IDD.

One intervention that shows promise in the ID and general population is behavioural activation therapy. This is a person-centred intervention which addresses the needs of the whole person through a series of therapeutic encounters (Jahoda et al, 2015). This intervention is well suited to diabetes care as it is a multi-faceted approach to improving outcomes. Diabetes treatment requires both medicines and lifestyle interventions this may have a positive effect mood and motivation, social integration and medicines adherence. A recent feasibility study protocol has been published which will determine the effect of this intervention on depression

score (Jahoda et al, 2015). With regard to the non-IDD population a study testing behavioural activation therapy and its effect on depression showed a positive effect on outcomes (Choi & Twamley, 2013; Idusohan-Moizer, Sawicka, Dendle, & Albany, 2015; Unwin, Tsimopoulou, Kroese, & Azmi, 2016). Therefore, this may be a starting point for piloting an interventional study in a mixed group of IDD and non-IDD service users, measuring the effect of behavioural activation therapy on depression and medicines adherence.

To detect medicines non-adherence, a possible target for future research is to suggest a GDS-LD screening cut-off at 11 in a mixed group of IDD and non-IDD service users. This cut-off may not only be effective in detecting depressive symptoms and poor adherence but may provide a quantitative marker measuring the effect of an intervention on adherence and mood in future research.

A second area of research is related to the frequency of insulin prescribing in people with ID and type 2 diabetes. To corroborate and fully understand the finding that insulin is less frequently prescribed in people with IDD, a larger scale mixed methods study is recommended to (1) establish the type of medications prescribed in this population, (2) the effect that these medicines may have on perceived level of side effects and (3) clinicians' rationale for their prescribing choices. This may provide a greater insight into the process of decision making in this population, and in the context of findings of the possible relationship between perceived side effects and adherence in people with IDD, may improve adherence.

8.1.2 Implications for policy

This PhD study proposes two possible policy changes in relation to resources for funding support for medicines management and participation in research.

Stage two interviews with carers and corroboration of results with stage one demonstrated that carers play a key role in optimising adherence and preventing further diabetic complications arising from poor adherence. This example of good practice by carers of people

with IDD, particularly in relation to managing adherence during periods of low mood, is an aspect of care to which the non-IDD population may have limited access to.

Government policy may be able to provide greater support by providing additional resource for carer support with medicines, particularly for those with depressive symptoms. Additional funding in this group would allow carers to continue with their support of people with ID and diabetes and allow the non-IDD population with depressive symptoms to have additional access to care and support services. This may provide greater support for the non-IDD population which may have an impact on adherence and long term health.

This study has demonstrated the homogeneity of the IDD and the non-IDD population and similarity in trends in frequency of adherence and HbA1c. This suggests it is reasonable to compare not only findings between the two groups but also to allow for trends in the group overall to be reported. Simple and reasonable adjustments to consent and data collection instruments have maximised inclusion of people with ID in this research. This further strengthens the argument that people with ID can participate in mainstream research and, provided reasonable adjustment is made to recruitment, consent and participation, they are effective contributors. Inclusion in mainstream research is also a requirement of social justice: for participants to be afforded equal weight in society, it is necessary to investigate their needs through research and how this relates to the wider population.

If policy change to enhance recruitment from vulnerable groups was adopted widely by the research community it could provide more generalizable results and a more inclusive research culture. It is important to raise the profile of this group within the research community as it may contribute to addressing health inequalities and provide an evidence base for targeting particularly challenging areas of health and social care in this population.

Continued exclusion from research may prevent minority populations and their carers benefitting from potentially effective treatment, interventions or scientific advances. Furthermore, ill-judged inclusion or exclusion may constitute unethical research conduct, and be counter to the Declaration of Helsinki (1996) and the UN Convention on Rights of People with Disability (2007). Instead, instilling ethical mindfulness in the research and clinical community (that is engendering respect for choice, balancing risk and benefit for participating in the research and adhering to principles of social justice) must be central to the inclusion of this minority population in research studies.

Therefore, research policy should encourage researchers to make reasonable adjustments to study design to maximise vulnerable and minority group inclusion. People with ID should not be actively excluded from research as this study has shown that similar proportions of IDD and non-IDD participants were recruited after initial contact (Table 4.1). Recruitment from these groups may be challenging, and underpowered studies may affect the significance of findings, but including ID participants as a subgroup of a larger study and triangulating results with in-depth qualitative interviews may ratify otherwise inconclusive findings and progress research in vulnerable groups. Therefore, it is recommended that researchers consider the inclusion of vulnerable groups, such as people with ID, in design of future research protocols.

8.1.3 Implications for practice

The findings have several important implications for diabetes practice regarding future use of instruments used in this study, proactively screening for depression and side effects and suggesting changes to treatment that may optimise both adherence and glycaemic control.

8.1.3.1 *Use of MMAS8 in clinical practice*

The use of MMAS8 as an instrument to evaluate medicine adherence has been proven to be useful in the general diabetic population (Wong et al, 2015), however this is the first study to test it with people with ID and diabetes.

The results have demonstrated that MMAS8 may be a useful and reliable self-reported medicines adherence measure in the IDD population. Its internal reliability, correlation with HbA1c and triangulation of stage one results in stage two suggest that with further testing it may be a reliable and simple instrument to use in the IDD population. Despite the limitation that construct validity could not be tested, the MMAS8 shows promise for use in screening for non-adherence in the IDD population. If these preliminary findings are replicated in a sufficiently powered study it would support MMAS8 as a simple and reliable tool identifying those with suboptimal medicines adherence (MMAS8 <6).

If, after further testing, this tool was adopted widely in practice by carers and healthcare professionals, strategies to improve adherence and glycaemic control could be developed. This could also have an impact on prescribing practice. For example, instead of adding to the medicines burden by prescribing additional treatment or, progressing prematurely to insulin therapy, strategies to improve medicines adherence could be implemented. This alternative approach would reduce the burden of polypharmacy, side effects, and unnecessary prescribing, maintain independence, improve quality of life, and reduce the financial impact of over prescribing or progression of diabetic complications.

The prospective comparison between the IDD and non-IDD population with regard to adherence and associated factors is a unique aspect of this study. Results revealed that adherence is similar in the IDD and non-IDD groups and stage two results suggested that carers have a key role in supporting medicines adherence. This has important implications for clinical practice and an awareness that adherence is similar in both groups may reassure clinicians when considering treatment escalation. Conversely, clinicians may be more cautious at escalating treatment if they are aware that adherence is poor and instead take steps to optimise existing treatment before prescribing additional treatment.

8.1.3.2 *Use of GDS-LD in clinical practice.*

The associations between depression and medicines adherence in the group overall and non-IDD population and side effects and adherence in the IDD population suggests that routine screening for depressive symptoms and side effects may identify those at risk of non-adherence. Additional support may improve adherence and glycaemic control and reduce complications related to poor medicines adherence and elevated HbA1c. Moreover, with limited healthcare resources available targeting adherence interventions at service users with both diabetes and depression and no carer support may have the greatest effect on improving this aspect of diabetes care. An alternative to carer interventions may be to fund the implementation a text messaging service to remind those who frequently forget to take their medication. Given findings suggest forgetting is the most commonly reported reason for non-adherence this may have successful outcomes in this population and, in particular, those with depression and diabetes.

8.1.3.3 *Use of PSM side effectsside effects score in clinical practice.*

Results from this study in the IDD population were inconclusive but there was preliminary evidence to suggest that clinicians and carers should explore side effects in this population in more depth.

Formally screening for side effects could alert clinicians to review medications. The Perceived Sensitivity to Medicines scale demonstrated good internal reliability in the IDD population and was simple to administer. If further research replicates results from this study PSM could provide a standardised tool for screening for side effects. Where side effects affect adherence in IDD patients, clinicians could consider the ability of the IDD participant to self-manage, or manage with support, more complex second or third line treatment. This could minimise side effects, maximise quality of life and optimise medicines adherence.

Side effects could also be reduced by encouraging clinicians to carry out regular polypharmacy reviews in the IDD population to reduce unnecessary medications and the risk of adverse or drug interactions. A current recommendation from NHS Scotland (2015) is a medicines review must take place prior to starting new treatment and unnecessary medications should be stopped. The introduction of a polypharmacy ‘app’ for both practitioners and service users may encourage more comprehensive medicines review, highlight existing side effects, reduce drug-drug interactions and reduce the cost of prescribing. An intervention of this type could improve both adherence and perceived side effects in the IDD population.

8.2 Overview

This final chapter has summarised recommendations from this PhD thesis. Recommendations for research, policy and clinical practice are as follow:

1. To fully validate all instruments used in in this study in a sufficiently powered study. This could be carried out whilst evaluating the effect of adjustments of diabetes medications on reported side effects and adherence in this group.
2. To explore how to embed the inclusion of vulnerable groups into research practice. Promoting equality and diversity in research recruitment will widen the applicability of results and give minority groups a voice in research.
3. To develop and test an intervention in a mixed group of people with IDD and non-IDD designed to improve depressive symptoms using medicines adherence as a primary outcome measure. A study of this type may meet policy, practice and research recommendations emerging from this study and may have the most beneficial effect on short and long term effect of adherence and poor glycaemic control.

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4. To fully explore the differences in prescribing practice between people with ID and type 2 diabetes and those without which establishes the reasons for, and consequences of, lower rates of prescribing insulin in people with ID and type 2 diabetes.
 5. Explore in more depth the role of the carer in supporting adherence to diabetic medicines. This study has suggested they have a positive effect on adherence in the IDD population and if similar strategies were adopted in the non-IDD population an equally positive effect on adherence may be shown.
 6. In clinical practice routine use of screening tools for adherence, depression and side effects may highlight to clinicians those at greatest risk of non-adherence.
 7. Education for carers on the effect of side effects on medicines adherence may result in more effective screening for side effects by carers and more effective medicines review in the IDD population. These interventions may highlight the need to start, stop or change treatment and facilitate safe escalation through diabetes treatment algorithms. As a result, it may have an impact on adherence and improve the overall health of the IDD population.

Appendix 1: Search terms and strategy

[Print Search History](#) | [Retrieve Searches](#) | [Retrieve Alerts](#) | [Save Searches / Alerts](#)

<input type="checkbox"/> Select / deselect all		<input type="button" value="Search with AND"/>	<input type="button" value="Search with OR"/>	<input type="button" value="Delete Searches"/>	<input type="button" value="Refresh Search Results"/>		
Search ID#	Search Terms	Search Options	Actions				
<input type="checkbox"/> S22	S17 and S16	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S21	S10 and S13	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S20	S17 and S10	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S19	S18 and S10	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S18	S17 and S7	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S17	S3 and S6	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S16	S14 OR S15	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S15	care*	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S14	(MM "Caregivers") OR (MM "Caregiver Support") OR (MM "Caregiver Burden")	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S13	S11 OR S12	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S12	cognitiv* impair* or mental incapacity or head injury or incapacitated or incapable	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S11	(MM "Delirium, Dementia, Amnestic, Cognitive Disorders+")	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S10	S8 OR S9	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S9	medicines adherence or concordance or compliance or noncompliant* or non-compliant* or nonadherent* or non-adherence or patient compliant* or complian* or comply or complies or complying or adher*	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S8	(MM "Medication Compliance") OR (MM "Patient Compliance+")	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S7	(MH "Insulin") OR (MM "Hypoglycemic Agents+")	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S6	S4 OR S5	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S5	diabet*	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S4	(MM "Diabetes Mellitus") OR (MM "Diabetes Mellitus, Type 1") OR (MM "Diabetes Mellitus, Type 2")	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S3	S1 OR S2	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S2	Learning disab* or mental retard* or intellectual disab*	Search modes - Boolean/Phrase					Rerun View Details Edit
<input type="checkbox"/> S1	(MM "Mental Retardation+")	Search modes - Boolean/Phrase					Rerun View Details Edit

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Appendix 2: Ethical Approval

NRES Committees - North of Scotland

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17 April 2015

Mrs Ruth Paterson
Lecturer, Edinburgh Napier University
Edinburgh Napier University
Room 4.b.38,
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EDINBURGH
EH11 4BN

Dear Mrs Paterson

Study title: The frequency of, and factors associated with, medicines adherence in the mild to moderate intellectually disabled diabetic population (MAIDD) – A mixed methods study
REC reference: 14/NS/0060
Amendment number: AM01 – (Study Team Ref No)
AM02 (REC Ref only)
Amendment date: 30 March 2015
Amendment Summary: The major amendment was that a control group of non Intellectually Disabled (ID) general diabetic patients and a sample of their carers were recruited in addition to the study group of ID service users. This allowed for comparisons to be drawn between the two groups. The knowledge acquired from this research informed future adherence research in vulnerable groups and identify whether behaviour related to medicines adherence is similar, or different in each group. Given that there were a finite number of healthcare resources available the results led to recommendations on what service users were at greatest risk of no adherence and propose strategies or interventions that would maximise medicines adherence in this group.
IRAS project ID: 150517

The above amendment was reviewed at the meeting of the Sub-Committee held in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

NRES Committees - North of Scotland

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10 April 2014

Mrs Ruth Paterson
Lecturer
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Room 4.b.38,
Sighthill Campus
EDINBURGH
EH11 4BN

Dear Mrs Paterson

Study title: **The frequency of, and factors associated with, medicines adherence in the mild to moderate intellectually disabled diabetic population (MAIDD) – A mixed methods study**
REC reference: **14/NS/0060**
IRAS project ID: **150517**

Thank you for your letter of 3 April 2014, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the Lead Reviewer.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Co-ordinator Mrs Carol Irvine, carolirvine@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

University Hospitals Division

Queen's Medical Research Institute
47 Little France Crescent, Edinburgh, EH16 4TJ

FM/NM/approval

19 June 2014

Mrs Ruth Paterson
Edinburgh Napier University
Room 4.b.38
Sighthill campus
Edinburgh
EH11 4BN



Research & Development
Room E1.12
Tel: 0131 242 3330

Email:
R&DOffice@nhslothian.scot.nhs.uk

Director: Professor David E Newby

Dear Mrs Paterson

Lothian R&D Project No: 2014/0225

Title of Research: The frequency of, and factors associated with, medicines adherence in the mild to moderate intellectually disabled diabetic population (MAIDD) - A mixed methods study.

REC No: 14/NS/0060

Patient Information Sheet:
Stage 1, 2, 3 version 2 dated 3 April 2014

Consent Form:
Stage 1, 2, 3 version 2 dated 3 April 2014

Protocol:
Version 2 dated 3 April 2014

I am pleased to inform you that this study has been approved for NHS Lothian and you may proceed with your research, subject to the conditions below. This letter provides Site Specific approval for **NHS Lothian**.

Please note that the NHS Lothian R&D Office must be informed if there are any changes to the study such as amendments to the protocol, recruitment, funding, personnel or resource input required of NHS Lothian. This includes any changes made subsequent to management approval and prior to favourable opinion from the REC.

Substantial amendments to the protocol will require approval from the ethics committee which approved your study and the MHRA where applicable.

Please inform this office when recruitment has closed and when the study has been completed.

I wish you every success with your study.

Yours sincerely

Dr Douglas Young
Principal R&D Manager

CC Professor Mark Strachan, Consultant in Diabetes and Endocrinology Associate Medical Director, WGH

Appendix 3: Healthcare professional information sheet

Study information sheet

My name is Ruth Paterson and I am a PhD student and registered nurse at Edinburgh Napier University. I am conducting a study exploring:

The frequency of, and factors associated with medicines adherence in the mild to moderate intellectually disabled diabetic population (MAIDD) – A mixed methods study

I would like to interview mild or moderate intellectually disabled (IDD) diabetic patients and general diabetic patients, over the age of 16 and a selection of their carers. Participants will have a diagnosis type 1 or type 2 diabetes and be prescribed either insulin or oral anti diabetic drugs, and be able to consent independently to the study. This study has full NHS, Edinburgh City Council and University ethical approval.

The aims of this study are:

1. To explore the prevalence of medicines adherence in the mild to moderate IDD diabetic population.
2. To explore the association between depression, self-efficacy, perceived sensitivity to medicines and social support and medicines adherence in mild to moderate IDD diabetic service users and compare this to the general diabetic population
3. To explore the perceptions of carers/significant others and whether these perceptions are associated with medicines adherence in diabetic service users.

To carry out the proposed research I need some help from experts caring for people with diabetes

I am looking for some help in identifying suitable service users:

- Who have mild or moderate IDD and type 1 or type 2 diabetes, are on diabetic medicines, can consent independently and would be willing to participation in the study.
- Who have type 1 or type 2 diabetes, are prescribed diabetic medicines and can consent independently.

I am aiming to conduct a short interview using validated questionnaires with this group of patients. They can have a support person with them during the interview, they can take breaks as needed, and I will discuss the project with any potential participants you identify..

If you have any service users who may be willing to participate in this study please could you contact me on 0131-455-5663 or email r.paterson@napier.ac.uk. I will then contact them direct and provide further information to them and their carers about the study.

Appendix 4: Initial Participant information sheet –IDD Service User

Do you have a learning disability as well as Diabetes?

If you answered ‘yes’, we need your help.



Hello, my name is Ruth, I am a qualified nurse and a student and I trying to find things out about diabetes and medicines. This is called research.

I want to find out if you take your medicines and



I want to know how you take your medicines and if feeling:
Sad or



Confused or



What you believe about medicines or



You have good help.



Helps you to take your medicines.



To take part you must have diabetes as well as a learning disability.

If you would like to take part
or somewhere that suits you.



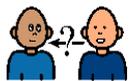
I will come and visit you at your home



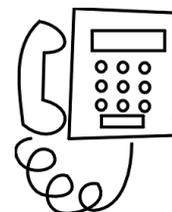
I will explain the research and make sure you still want to take part. I will help you understand



the questions I ask



A friend or parent or partner or carer can be with you.



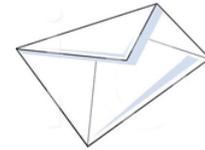
If you would like an information pack you can phone
Ruth on 0131 455 5663 or



If you have a computer you can email Ruth at
r.paterson@napier.ac.uk

Or you can send me a letter:

Ruth Paterson
Mailroom 4.B.36,
School of Nursing, Midwifery & Social Care,
Edinburgh Napier University,
Sighthill Campus,
Sighthill Court,
EH11 4BN.



Thank you for helping me.

**Appendix 5: Full participant information sheet IDD service user
Medicines adherence in the intellectually disabled diabetic population (MAIDD) and general
diabetic population –Frequency of and factors influencing medicines adherence.**



Hello, my name is Ruth, I am a qualified nurse and a student and I trying to find things out about diabetes and medicines. This is called research.

I am going to give you some information. I want to ask  you to be part of my research. You can choose whether or not you want to take part. Your care team know that you have been asked to take part.

You can talk  to your family about the research to you family or friends or anyone else. You do not have to decide straight away.



There may be some questions or words you don't know. You can contact me on 0131-455-5663 or email r.paterson@napier.ac.uk. I will explain  any questions you have.

Who has reviewed the study?

My research teachers and The NRES Committees – North of Scotland (2) has reviewed the study.

Why are you doing this research?

I want to find out how diabetic people take their medicine. This might help us to help you to take medicines better and be healthy.



What do I have to do?



I would like to ask if you forget  to take your diabetic

medicines.  I also want to know if:

- feeling sad  or
- angry ,
- feeling confused  and what you
- believe  about medicines  you are take means that you don't take your medicines. .

I want to ask  your doctor  for the result of a special diabetes blood test (HbA1c) .

I want to find out if you think you have good support  from people  who help you.

I would also like to talk  to one of your family or friends  or carers .

Do I have to do this?

You do not have to be part of this research. It is up to you. If you decide not to do the research, it is OK

nothing changes . Even if you say yes now you can change your mind later and it is still OK.

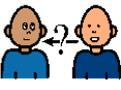
If I say yes what happens to me?

If you want to take part, this is what will happen.



1. I will come and visit you . A friend or parent or partner  or carer  can be with you.

2. I will explain the research and make sure you still want to take part. I will help  you understand  the questions

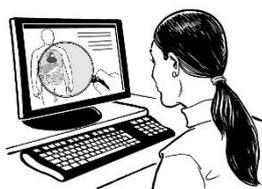
I ask .



3. I will ask  if I can contact your doctor  to ask for your most recent blood level (HbA1c) .

4. I will ask you if I can talk  to the person  who helps

 you with your medicines .



5. I will put your answers on a computer  and use them to report on what I have learned from this research. .

Will it take a long time?



No it will not take long - only about 1 hour. We can take a break

 or stop  at anytime.

Is our interview private?



When you talk to me it is a private . I will not tell anyone about our discussion. But if you tell me something that worries  me, because it may affect your health I will talk to you about speaking to your doctor, nurse or support worker . This is to keep you safe . If you tell me something I am worried  will harm you or others, I have to tell your doctor . If this happens I



I will store the information about you on a computer



with a password I only know. Your name will not be on the form. I will give your information a number which will keep the information private .

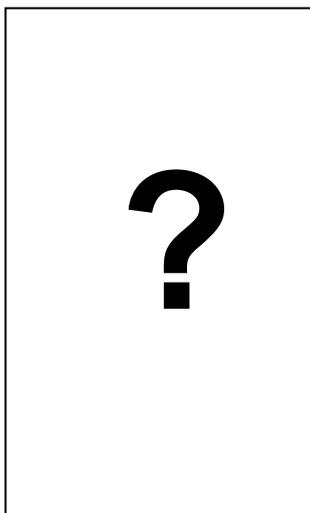


If you have to travel  to where we meet we will give you money  to pay for it.



When I am finished the research, I will tell you what we have learned . I will also give you a letter about the research. After this we will tell more people - other researchers - about what we have learnt. We will do this by going to meetings and sharing reports with people.

Who can I talk to or ask questions to?



You can ask me questions now or later.  There are also lots of other people you can talk to. You can ask the person who gave you this information. You can speak to someone whose contact details are below.

Researcher

Ruth Paterson, r.paterson@napier.ac.uk tel 0131-455-5663

Supervisor,

Professor Michael Brown, m.brown@napier.ac.uk tel -0131-455-5311

Independent advisor

Mr Andy Gibbs – a.gibbs@napier.ac.uk, tel 0131- 455-5301

Thank you for reading this.

Appendix 6: Stage one PIL Non-IDD service user

The frequency of, and factors associated with medicines adherence in the intellectually disabled and general diabetic population. – A mixed methods study **Stage two – Participant Information – general diabetic population**



Hello, my name is Ruth, I am a qualified nurse and a student and I am trying to find out about diabetes and medicines. I am going to give you some information. I want to ask you to be part of my research. You can choose whether or not you want to take part. Your care team know that you have been asked to take part. You can talk about the research to your family, friends or anyone else. You do not have to decide straight away.

Who has reviewed the study?

My research supervisors and The NRES Committees – North of Scotland (2) has reviewed the study. My university ethics committee has also reviewed and approved the study.

Why are you doing this research?

I want to find out how and why diabetic people take their medicine. This might help us help those who find taking medicines difficult.

What is the research about?

I am asking a group of intellectually disabled (IDD) patients about how and why they take their medicines and I would also like to find out how the general diabetic population take their medicines. I want to ask the same questions to IDD diabetics as you and compare the results. This will help us to understand whether the needs of each group are different or the same. There are 3 main parts to the study:

1. I would like to ask you some questions from tried and tested questionnaires about how well you take your medicines and whether symptoms of depression, lack of confidence, medicines side effects or the level of social support you receive affects whether you take your medicines.
2. I would like to ask your doctor for the result of a special diabetes blood test (HbA1c).
3. I would like to find out if you think you have good support from people who help you. If possible I would also like to talk to one of your family or friends or carers, but this is not necessary to participate in the first two parts of the study.

Do I have to do this?

You do not have to be part of this research. It is up to you. If you decide not to do the research, nothing changes and you will continue with your normal diabetic treatment. Even if you say yes now you can change your mind later and it is still OK.

What do I have to do?

If you say yes;

- I will arrange a good time and place to come and ask you the questions. A friend, parent, partner or carer can be with you aswell.
- Once I finish the interview I will ask if I can contact your doctor to ask for your most recent blood level (HbA1c)
- I will ask you if I can talk to the person who helps you with your medicines.
- I will put your answers on a computer and use them to report on what I have learned from this research.

How long will it take?

The questions will take no more than 30 minutes to answer. Anything that you tell me will be confidential. But if you tell me something that worries me, because it may affect your health I will talk to you about speaking to your doctor, nurse or support worker. This is to keep you safe. If you tell me something I am worried will harm you or others, I have to tell your doctor. If this happens I will tell you I am going to talk to them.

What will happen to the results?

When I am finished interviewing everyone, I will tell you what we have learned. I will also give you a letter about the research. After this we will tell other researchers through meetings and publishing my research. This will help us to understand medicines management in diabetic patients better.

Who can I talk to or ask questions to?

You can ask me questions now or later. There are also lots of other people you can talk to. You can speak to someone whose contact details are below.

Researcher

Ruth Paterson, r.paterson@napier.ac.uk tel 0131-455-5663

Supervisor,

Professor Michael Brown, m.brown@napier.ac.uk tel -0131-455-5311

Independent advisor

Dr Barbara Neades – b.neades@napier.ac.uk tel 0131- 455-5315

Thank you for reading this.

Appendix 7: Stage one consent form

Medicines adherence in the intellectually disabled diabetic population (MAIDD) –Frequency of and factors influencing medicines adherence

Name of Researcher: Ruth Paterson

Participant number

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Please initial box

- 1 I confirm that I have read and understand the information sheet dated 3/4/14 (Version 2.) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

- 2 I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

- 3 I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from NHS Lothian, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

- 4 I agree to my GP being informed of my participation in the study.

- 5 I agree to take part in the above study.

Name of Participant	Date	Signature
Name of Person taking consent (if different from researcher)	Date	Signature
Researcher	Date	Signature

Appendix 8: Stage one questionnaires

Participant number

--	--	--

Dear Participant

My name is Ruth,

Thank you for agreeing to take part in **the MAIDD study**. We would like to find out about your experience of taking your diabetes tablets or injections. This booklet has questions about how well you take your medication and if your mood, confidence, and thoughts about your medication or support affect your choice to take your medication. I will be with you help you to complete the questionnaire and you can also have a friend, relative or carer with you when you are completing the questionnaire.

I also would like to ask if we contact your doctor for information about your other medications and illnesses, how long you have had diabetes, diabetic blood tests. The information that we are requesting in the back of this booklet. All information gathered during this project will be stored in a locked office and on a password protected computer which me and my supervisors will only have access to.

We know that it is difficult to sometimes answer questions but please try to answer the questions as best you can, and remember!

THERE ARE NO RIGHT OR WRONG ANSWERS

The researcher will be there to help you answer the question but not give you the answers, it is very important that you are able to tell us what your experience is.

You are able to stop the interview at anytime, take a break or request to stop the study, you do not have to give a reason for this. This is your choice and will not affect any help you need with taking tablets or any other part of your care and treatment.

Please tick the box ✓ to the one answer that best describes your feelings. Do not select more than one answer unless you are asked to do so.

Thank you for taking the time to complete this questionnaire!

Part one: About You.

We won't be asking for your name in this booklet of questions, but we would like to start by asking you some questions about yourself.

1. Date of birth:.....

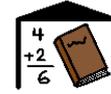
2. Gender

Male Female (Please tick one box)

3. Who is your doctor.....

.....
Address.....

.....
can we contact them Yes/No.



4. What is the highest level of education you have completed?

- No schooling completed
- Primary school
- Secondary school no qualification
- Secondary school with qualifications
- Some college credit, no degree
- Trade/technical/vocational training
- University education

5. Level of Learning Disability:

Borderline [] Mild [] Moderate [] Unknown []



6. Where do you live?

Own home [] Family Home [] Supported Living Scheme []
Residential Home [] Nursing Home [] Homeless []
Hospital [] Other: _____



7. Who do you live with?

Self [] With Partner [] With parents/relatives [] Other people with learning disabilities [] Other: _____

8. What medication are you on? (verify with GP letter, rpt prescription or actual



medications)

Medicine	Dose	Frequency	Comments

9. How long have you had diabetes?

< 1 yr [] 1– 2 yrs [] 2-5 yrs [] 6 yrs plus [] Don't know []

Support when taking medication.

10. Who helps you to take your diabetic medication?

Self [] With Partner or parents/relatives [] Paid carer [] unpaid carer [] Other:

11. How long have they helped your for?

Less than 6 months [] more than 6 months []



Taking my medications = MMAS8 Questionnaire We would like to find out how well you are able to take your diabetic medicines. With Ruth's help please answer the following questions with a yes or no.

	Morisky question (correct answer)	Response
1.	 Do you sometimes forget to take your diabetes medication? (N)	
2.	Over the past 2 weeks, were there any days when you did not take your diabetes Medication  ? (N)	
3	Have you ever cut back or stopped  taking your diabetes medication without telling your doctor because you felt worse  when you took it? (N) <i>Have you taken less of your medication. Did you tell your doctor or carer? (N)</i>	
4	When you travel or leave home,  do you sometimes forget  to bring along your diabetes medications  ? (N)	
5	Did you take your diabetes medication  yesterday  ? (Y)	
6	When you feel like your diabetes is under control  , do you sometimes stop  taking your medications? (N) <i>When you feel well do you stop taking your diabetic medicine, (N)</i> <i>If your blood sugar is good do you stop taking your medication? (N)</i>	
7	Do you ever feel hassled  about sticking to your diabetes treatment plan (N)	

8	<p>How often do you have difficulty remembering to take all of your diabetic medications (never, sometimes, always) </p> <p><i>Do you have difficulty remembering to take your diabetes medicine? (No)</i></p>	
---	---	--

a Possible responses: yes/no; correct response = 1 point; incorrect response = 0 points.
 possible responses: never (1 point); almost never, sometimes, quite often, always (0 points). Possible scale range = 0-8.
 Non adherence = score ≥ 6

About how I am feeling and my mood:



Please answer all the questions.

With the researchers please rate your feelings, and **put a sticker in the box that best describes your mood. It may be helpful to think about how you have felt in the last week.** If you do not know which answer to give to a question, **please choose the ONE** that best suits your mood. This can often be your first answer.

Glasgow Depression Score (GDS – LD)

<p>1. Have you felt sad? </p> <p><i>Have you felt upset? Have you felt miserable?</i></p> <p><i>Have you felt depressed?</i></p>	<p>Never/no</p> <p>0</p>	<p>Sometimes</p> <p>1</p>	<p>Always/a</p> <p>lot</p> <p>2</p>
<p>2. Have you felt as if you are in a bad mood? </p> <p><i>Have you felt bad-tempered?</i></p> <p><i>Have you felt as if you want to shout at people?</i></p>	<p>Never/no</p> <p>0</p>	<p>Sometimes</p> <p>1</p>	<p>Always/a</p> <p>lot</p> <p>2</p>

<p>3. Have you enjoyed the things you have done?</p>  <p><i>Have you had fun?</i> <i>Have you enjoyed yourself?</i></p>	<p>Never/no 0</p>	<p>Sometimes 1</p>	<p>Always/a lot 2</p>
<p>4. Have you enjoyed talking to people and being with other people?</p>  <p><i>Have you liked having people around you?</i> <i>Have you enjoyed other people's company?</i></p>	<p>Never/no 0</p>	<p>Sometimes 1</p>	<p>Always/a lot 2</p>
<p>5. Have you made sure you have washed yourself, worn clean clothes, brushed your teeth and combed your hair?</p> <p><i>Have you taken care of the way you look?</i> <i>Have you looked after your appearance?</i></p> 	<p>Never/no 0</p>	<p>Sometimes 1</p>	<p>Always/a lot 2</p>
<p>6. Have you cried?</p> 	<p>Never/no 0</p>	<p>Sometimes 1</p>	<p>Always/a lot 2</p>
<p>7. Have you felt tired during the day?</p>  <p><i>Have you gone to sleep during the day?</i> <i>Have you found it hard to stay awake during the day?</i></p>	<p>Never/no 0</p>	<p>Sometimes 1</p>	<p>Always/a lot 2</p>
<p>8. Have you felt you are a horrible person?</p> <p><i>Have you felt others don't like you?</i></p> 	<p>Never/no 0</p>	<p>Sometimes 1</p>	<p>Always/a lot 2</p>
<p>9. Have you been able to pay attention to things (such as watching TV)?</p> <p><i>Have you been able to concentrate on things (like television programmes)?</i> <i>What is your favourite [television programme]? Are you able to</i></p>	<p>Never/no 0</p>	<p>Sometimes 1</p>	<p>Always/a lot 2</p>

<p><i>watch it from start to finish?</i></p> 			
<p>10. Have you found it hard to make decisions?  <i>Have you found it hard to decide what to wear, or what you would like to eat, or do?</i> <i>Have you found it hard to choose between two things? [Give concrete example if required.]</i></p>	<p>Never/no 0</p>	<p>Sometimes 1</p>	<p>Always/a lot 2</p>
<p>11. Have you found it hard to sit still?  <i>Have you fidgeted when you are sitting down?</i> <i>Have you been moving about a lot, like you can't help it?</i></p>	<p>Never/no 0</p>	<p>Sometimes 1</p>	<p>Always/a lot 2</p>
<p>12. Have you been eating too little?  <i>Have you been eating too much?</i> <i>Do people say you should eat more/less?</i> <i>[Positive response for eating too much OR too little is scored]</i></p>	<p>Never/no 0</p>	<p>Sometimes 1</p>	<p>Always/a lot 2</p>
<p>13. Have you found it hard to get a good night's sleep? <i>[Ask questions to clarify information. If a positive response is given to one of the following, score positively.]</i> <i>Have you found it hard to fall asleep at night?</i> <i>Have you woken up in the middle of the night and found it hard to get back to sleep?</i> <i>Have you woken up too early in the morning? [Clarify time.]</i></p>  <p>When do you go to bed?</p>	<p>Never/no 0</p>	<p>Sometimes 1</p>	<p>Always/a lot 2</p>

When do you get up?			
14. Have you felt that life is not worth living? <i>Have you wished you could die?</i> <i>Have you felt you do not want to go on living?</i> 	Never/no 0	Sometimes 1	Always/a lot 2
15. Have you felt as if everything is your fault? <i>Have you felt as if people blame you for things?</i> <i>Have you felt that things happen because of you?</i> 	Never/no 0	Sometimes 1	Always/a lot 2
16. Have you felt that other people are looking at you, talking about you, or laughing at you? <i>Have you worried about what other people think of you?</i>	Never/no 0	Sometimes 1	Always/a lot 2
17. Have you become very upset if someone says you have done something wrong or you have made a mistake? <i>Do you feel sad if someone tells you . . . /gives you a row? Do you feel like crying if someone tells you . . . /gives you a row?</i> 	Never/no 0	Sometimes 1	Always/a lot 2
18. Have you felt worried?  <i>Have you felt nervous?</i> <i>Have you felt tense/wound up/on edge?</i> <i>Have you been stressed?</i>	Never/no 0	Sometimes 1	Always/a lot 2
19. Have you thought that bad things keep happening to you?  <i>Have you felt that nothing nice ever happens to you anymore?</i>	Never/no 0	Sometimes 1	Always/a lot 2
20. Have you felt happy when something good happened? [If nothing good has happened in the past week]	Never/no 0	Sometimes 1	Always/a lot 2

*If someone gave you a nice present,
would that make you happy?*



You and your medicines



We would like to talk about you and your diabetic medicines and how you think your body reacts to medicines. Please put a sticker in the box that best describe your thoughts..

The key is as follows.

	1	2	3	4	5
	Strongly disagree 	Disagree 	Neither agree nor disagree 	Agree 	Strongly agree. 
My body is very sensitive to medicines;					
My body overreacts to medicines;					
I usually have stronger reactions to medicines than most people;					
I have had a bad reaction to medicines in the past;					
Even very small amounts of medicines can upset my body.					

How well do you manage your diabetes?

These 4 questions are to see how confident you are in managing your diabetes medicines; we appreciate that some of you may have a carer or family member who may help you with your diabetes medicines. It may be helpful to think of a time when your carer or family member was not able to help you – how confident did you feel?

1. I feel confident in my ability to manage my diabetes

						
<u>Not true</u>	<u>sometimes true</u>	<u>always true</u>				
<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>

2. I am capable of handling my diabetes now.

						
<u>Not true</u>	<u>sometimes true</u>	<u>always true</u>				
<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>

3. I am able to do my own routine diabetic care now.

						
<u>Not true</u>	<u>sometimes true</u>	<u>always true</u>				
<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>

4. I feel able to meet the challenge of controlling my diabetes.

						
<u>Not true</u>	<u>sometimes true</u>	<u>always true</u>				
<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>

People who help you.



We would like to find out how much support you have in your day to day life.

	1	2	3	4	5
<u>If you needed it, how often is someone around</u>	 None of the time	 A little of the time	 Some of the time	 A lot of the time	 All of the time
To help you if you were confined to bed? 					
To take you to the doctors? 					
To help you prepare your meals if you couldn't do it yourself? 					
To help you with daily chores if you were sick? 					
To have a good time with? 					
To turn to for help with a problem? 					
Who understands your problems? 					
To love and make you feel wanted? 					

To help us find out the views of the person who helps you to take your diabetic medication we would like to also talk to them. Could you please give them this information letter, so that they can help us with this part of the research.

Letter given to participant. Y/N

Thank you for completing this questionnaire.

Appendix 9: Stage two Participant information sheet

Stage two - MAIDD Participant information sheet



Hello, my name is Ruth, I am a qualified nurse and a student at Edinburgh Napier University and I am doing some research about diabetes and medicines. I have spoken to the person with diabetes that you help and they agreed to give you this information sheet.

What is the study?

We would like to find out about how well the Intellectually Disabled (IDD) service users take their diabetic medication. We would like to compare this to how the general diabetic population take their medication. Therefore I would like carers of service users with diabetes who are over the age of 16 years to participate in the study. You have been invited to participate because someone you help take their diabetic medicines has taken part in this study and I have asked them to give you this information.

Aim of the study?

The study will help me find out how well IDD service users take their medicines (adherence) and whether their needs are different to the general diabetic population. I would like to interview carers about their experience of how well diabetics take medication and if mood, confidence, and thoughts about medication affect whether or not they take medication. I would also like to ask how much help they get and whether you think it is enough. We would also like to explore how you support patients when taking their medicines. By finding this out we will have a better idea about the needs of this group when looking at ways to support medicines management.

Who has reviewed the study?

My research teachers and The NRES Committees – North of Scotland (2) and the university ethics committee have reviewed the study.

What does the study involve?

As part of this study I will be asking you some questions. The questions are based on the interviews I have carried out with diabetic patients. I will give you time before the interview to read the questions and write down your thoughts.

The interview will take place at a time and place that suits you. The interview will be digitally recorded and anonymised. We will refund you any travel expenses and offer you refreshments during the interview.

What happens next?

If you would like to take part in the study please just contact me, the researcher, either by phone or email. I will ask if you have any questions and check that you still would like to be part of the study. If you are still happy to take part I will arrange a time and day which suits you. My contact

details are – Ruth Paterson – telephone 0131-455-5663 (there is an answering machine) or email r.paterson@napier.ac.uk.

Do I have to take part?

You do not have to take part and if you do, you can stop the interview at anytime, take a break or request to not be part of the study anymore, you do not have to give a reason for this. This is your choice and will not affect any part of your life as a carer.

What will happen to the information I give?

All information will be stored in a safe locked cupboard or on a computer with a password which the research team will only have access to. We will not put your name on any of your answers this is to make sure that we dont know who gave us the information and the information is only used for the research. We will match your interview to the IDD service user who nominated you so that we can look at the results altogether. The information will be used for a PhD study and may be published in a healthcare journal. If we do publish from this study noone will know who said what during the study.

Do you have any other questions?

If you have any questions about the study you can speak to someone in the research team or someone who is not part of study team but knows about research. The contact details are below.

Researcher

Ruth Paterson, r.paterson@napier.ac.uk tel 0131-455-5663.

Supervisor,

Professor Michael Brown, m.brown@napier.ac.uk tel -0131-455-5311

Independent advisor

Dr Barbara Neades – b.neades@napier.ac.uk, tel 0131- 455-5315

Thank you for reading this.

Appendix 10: letter to stage two participants

Ruth Paterson
Lecturer/Researcher
Room 4. b.36
Edinburgh Napier University
Sighthill Campus
Edinburgh
EH11 4BN
Tel 0131-455-5663
Email r.paterson@napier.ac.uk

Dear Mr

RE:

I am a PhD student and a registered nurse at Edinburgh Napier University and I interviewed for my research as part of stage one. At that time they agreed that I could also speak to someone who helps to remind them or to help take their medication and I am contacting you to see if you would be willing to take part. They nominated you as someone who helps them to take their medicines.

I am writing to provide you with an information sheet and if possible, I would like to arrange a time to meet with you and conduct a short 30 minute interview about the help you give to I also enclose a participant information sheet.

If you are willing to take part I will contact you in the next few weeks to arrange a time to come and see you. Please contact me on the number above or via email if you would not like to take part otherwise I will be in touch before the end of February to arrange to come and see you.

If you have any questions about this study or would like further information please do not hesitate to contact us at the details below. Alternatively you can contact an independent advisor not connected with the study. The name of the independent advisor is Dr Barbara Neades, Senior Lecturer, Edinburgh Napier University. Contact details are b.neades@napier.ac.uk.

We would like to take this opportunity to thank you for your assistance.

Appendix 11: Stage two consent form

Centre Number: Study Number:
Participant Identification Number for this trial:

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Stage two participant IDD

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Title of Project: MAIDD

Name of Researcher: Ruth Paterson

Please initial box

- | | | |
|---|--|--------------------------|
| 1 | I confirm that I have read and understand the information sheet dated 3/4/14 (Version 2.) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. | <input type="checkbox"/> |
| 2 | I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. | <input type="checkbox"/> |
| 4 | I agree to being audio recorded | <input type="checkbox"/> |
| 5 | I agree to take part in the above study. | <input type="checkbox"/> |

Name of Participant

Date Signature

Name of Person taking consent
(if different from researcher)

Date

Signature

Researcher

Date Signature

Appendix 12: Stage two topic guide

Explanatory note – This is a brief outline of what is proposed to be discussed, the actual schedule will not be decided until stage two analysis but the format is likely to be.

Introduction. Thanks for agreeing to participation – this is the final part of the MAIDD study. This part is exploring the views of the carers.

First going to start with some information to confirm that you are matched with the correct IDD service user.

1. Can you just confirm the person that you are caring for and who nominated you to participate in the study?
2. Can you just tell me what relationship (if any) you are to this person?
3. How do you help them take their diabetic medicines?
4. Question based on MMAS:
5. Part of the patient part of the study was to look at how well the patient felt they took their medication, can you give me a bit of information about how you think „,takes their medicine.
 - A. What do you see as the barriers to xxx taking medicines
 - B what do you see as the things that help xxx to take medicines (break down into insulin and meds if necessary)

6. Mood (depression) questions

One area we explored with the patient was mood and whether or not he or she had low mood or depression.

- a. Can you talk a bit about how you think xxx mood affects how well they take their medicine,
- b. Does this affect how you support him or her taking medications?

7. Confidence (Self efficacy) questions

We also asked him or her whether he or she felt confident in managing their medications.

- a. Can you tell me a bit about how confident he or she feels in managing his or her medication?
- b. Do you feel confident in supporting him or her managing treatment – if yes why? /if no why?

8. Beliefs about medicines.

We asked whether worries about side effects from the medications or whether they felt the medications are doing them any good.

- a. Can you talk a bit about whether you think has any worries about side effects or whether they feel the medicines help them control their diabetes?
- b. Do you have any views about the diabetes medicines that your patient takes (insulin or pills)? Side effects/do they work

9. Social support

Finally we asked service users what they thought about their level of social support.

- a. What is your impression of how this impacts on taking their diabetes medicines?

There are 3 main parts to diabetes self care – one medicines, 2 exercise 3 diet.

In your view what do you think is the most challenging for xxx. Can you explain to me why that is? (Explore where medicines adherence fits into all of this.)

Appendix 13: testing of assumptions (linearity of MMAS8 and HbA1c)

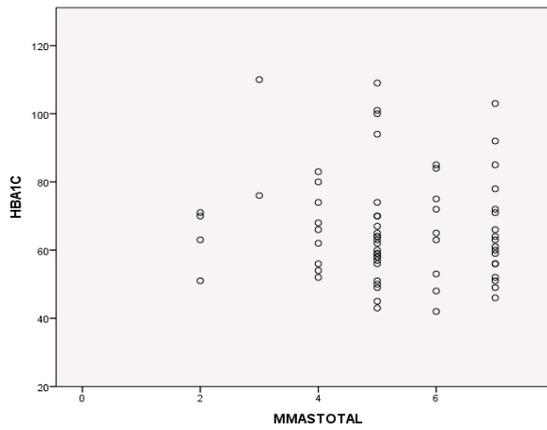


Fig 13.1: Scatterplot of correlation between HbA1c and MMAS8 (whole sample (n = 111))

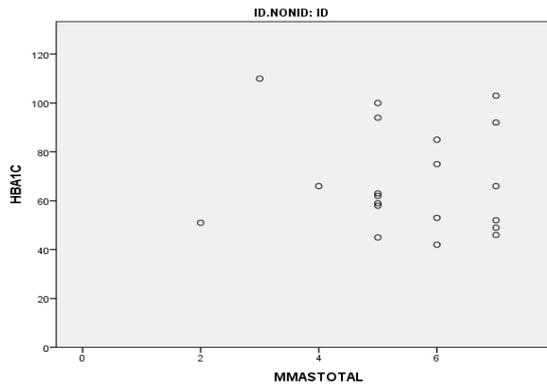


Fig 13.2: Scatterplot of correlation between HbA1c and MMAS8 (IDD sample (N = 33))

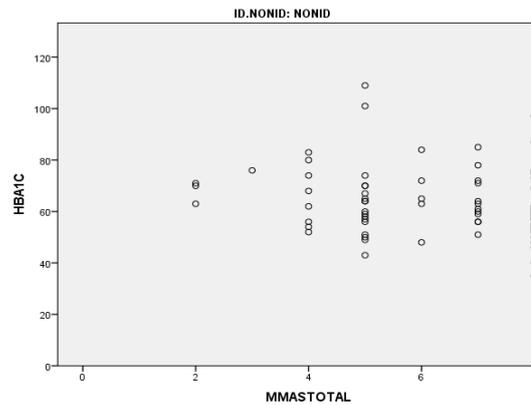


Fig13.3: Scatterplot of correlation between HbA1c and MMAS8 (Non-IDD sample (N = 78))

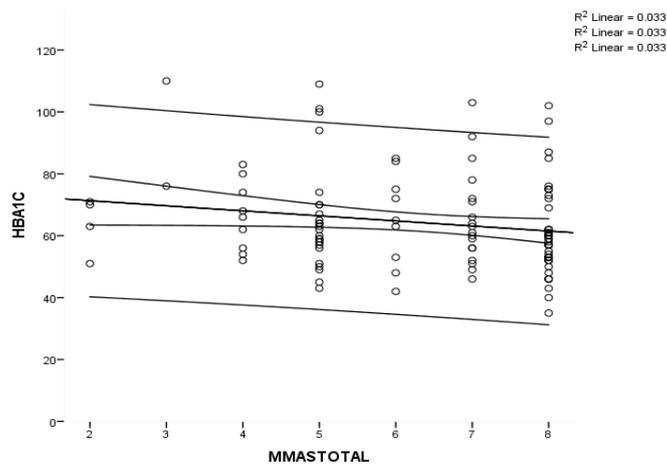


Fig 13.4: Scatterplot and linearity of MMAS8 and HbA1c

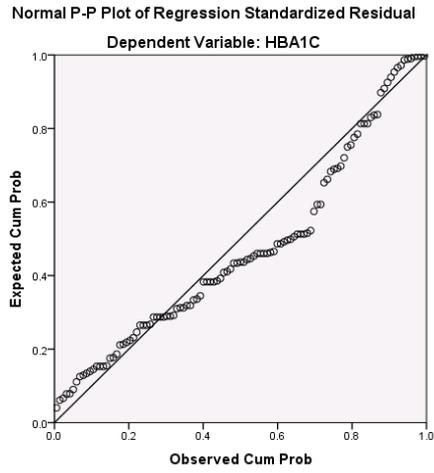


Fig 13.5: Normal P-Plot of regression dependent variable HbA1c

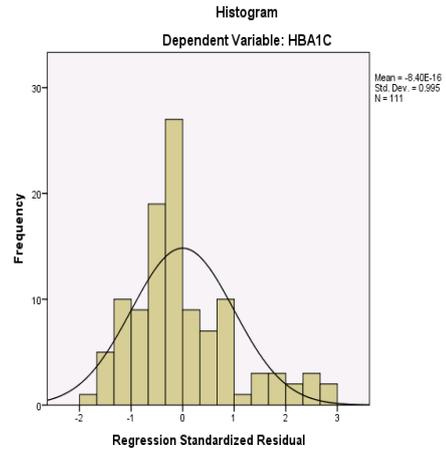


Fig 13.6: distribution of HbA1c on histogram

Appendix 14: Boxplots: dependent and independent factors

Dependent factors: glycaemic control and medicines adherence (HbA1c and MMAS8)

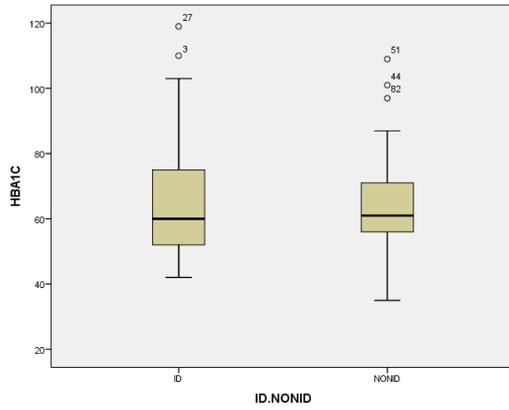


Fig 14.1: HbA1c in IDD and non-IDD groups

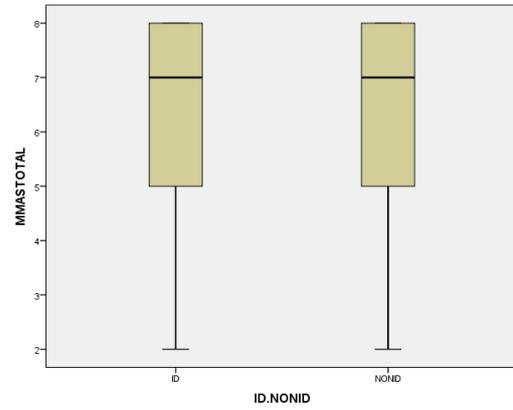


Fig 14.2: MMAS8 in IDD and non-IDD groups

Independent factors: Self-efficacy, social support, side effects and depression

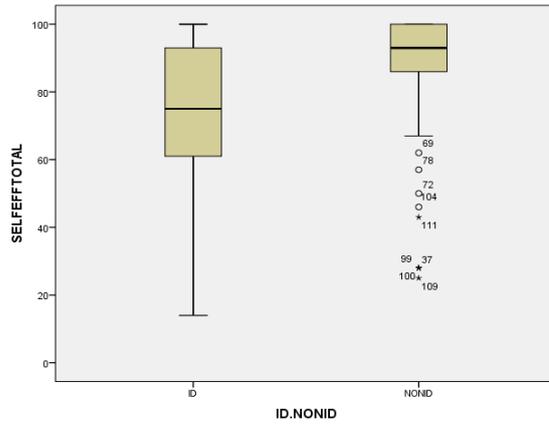


Fig 14.3: self-efficacy score in IDD and non-IDD groups

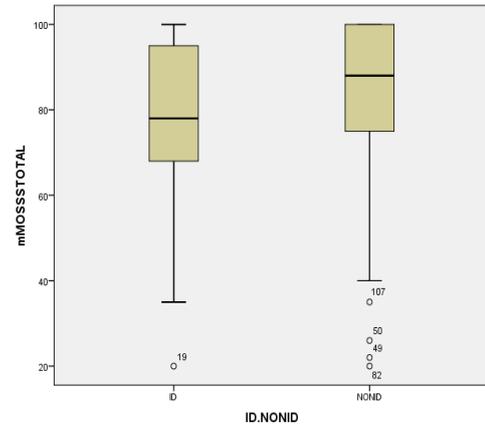


Fig 14.4: social support score in IDD and non-IDD groups

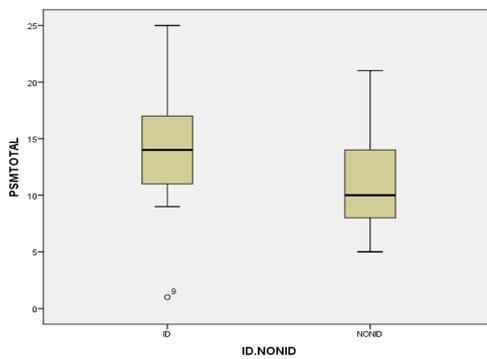


Fig 14.5: side effects score in IDD and non-IDD groups

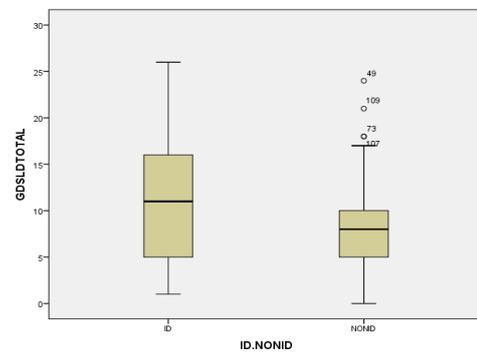


Fig 14.6: depression score in IDD and non-IDD groups

Appendix 15: References

- Adults with Incapacity Act, Part 5 Medical Treatment and Research (2000)
- Age of Legal Capacity (Scotland) Act. (1991). from http://www.legislation.gov.uk/ukpga/1991/50/pdfs/ukpga_19910050_en.pdf
- Ajzen, I. (1985). *From intentions to actions: A theory of planned behaviour in Action control: From cognition to behaviour* (K. J & B. J Eds.). New York: Springer Verlag.
- Al-Qazaz, H., Hassali, M. A., Shafie, A. A., Sulaiman, S. A., Sundram, S., & Morisky, D. E. (2010). The eight-item Morisky Medication Adherence Scale MMAS: Translation and validation of the Malaysian version. *Diabetes Research & Clinical Practice*, 90(2), 216-221. doi: 10.1016/j.diabres.2010.08.012
- Al Hamid, A., Ghaleb, M., Aljadhey, H., & Aslanpour, Z. (2014). A systematic review of hospitalization resulting from medicine-related problems in adult patients. *British Journal Of Clinical Pharmacology*, 78(2), 202-217. doi: 10.1111/bcp.12293
- Aljadhey, H., Mahmoud, M. A., Mayet, A., Alshaikh, M., Ahmed, Y., Murray, M. D., & Bates, D. W. (2013). Incidence of adverse drug events in an academic hospital: a prospective cohort study. *International Journal For Quality In Health Care: Journal Of The International Society For Quality In Health Care / Isqua*, 25(6), 648-655. doi: 10.1093/intqhc/mzt075
- Allerton, L. A., Welch, V., & Emerson, E. (2011). Health inequalities experienced by children and young people with intellectual disabilities: A review of literature from the United Kingdom. *Journal of Intellectual Disabilities*, 15(4), 269-278. doi: 10.1177/1744629511430772
- Amanda, R., & Hayley, S. (2011). Diabetes Among Adults With Cognitive Limitations Compared to Individuals With No Cognitive Disabilities. *Intellectual and Developmental Disabilities*, 49(3), 141-154.
- Andrew, S., Halcomb, E., & Dawson, B. (2013). *Mixed methods research for nursing and the health sciences*. United Kingdom: Dawson Books.
- Armijo-Olivo, S., Stiles, C. R., Hagen, N. A., Biondo, P. D., & Cummings, G. G. (2012). Assessment of study quality for systematic reviews: a comparison of the Cochrane Collaboration Risk of Bias Tool and the Effective Public Health Practice Project Quality Assessment Tool: methodological research. *Journal of Evaluation in Clinical Practice*, 18, 12-18. doi: 10.1111/j.1365-2753.2010.01516.x
- Asche, C. V., Bode, B., Busk, A. K., & Nair, S. R. (2012). The economic and clinical benefits of adequate insulin initiation and intensification in people with type 2 diabetes mellitus. *Diabetes, Obesity & Metabolism*, 14(1), 47-57. doi: 10.1111/j.1463-1326.2011.01487.x
- Auta, A., Strickland-Hodge, B., & Maz, J. (2017). There is still a case for a generic qualitative approach in some pharmacy practice research (Vol. 13, pp. 266-268).
- Aveyard, H. (2010). *Doing a literature review in health and social care : a practical guide* (3rd ed.). S.l.]: VLeBooks.
- Bailey, C., & Kodack, M. (2011). Patient adherence to medication requirements for therapy of type 2 diabetes. *International Journal of Clinical Practice*, 65(3), 314-322. doi: 10.1111/j.1742-1241.2010.02544.x
- Bailey, G., Barner, J., Weems, J., Leckbee, G., Solis, R., Montemayor, R., & Pope, N. (2012). Assessing Barriers to Medication Adherence in Underserved Patients With Diabetes in Texas. *Diabetes Educator*, 38(2), 271-279. doi: 10.1177/0145721711436134

- Balogh, R. S., Lake, J. K., Lin, E., Wilton, A., & Lunsy, Y. (2015). Disparities in diabetes prevalence and preventable hospitalizations in people with intellectual and developmental disability: a population-based study. *Diabetic Medicine: A Journal Of The British Diabetic Association*, 32(2), 235-242. doi: 10.1111/dme.12573
- Bandura, A. (1986). *Social foundations of thought and action: a social cognitive theory*. London: Prentice Hall.
- Bårnes, C. B., & Ulrik, C. S. (2015). Asthma and adherence to inhaled corticosteroids: current status and future perspectives. *Respiratory Care*, 60(3), 455-468. doi: 10.4187/respcare.03200
- Barnett, A. H., Brice, R., Hanif, W., James, J., & Langerman, H. (2013). Increasing awareness of hypoglycaemia in patients with Type 2 diabetes treated with oral agents. *Current Medical Research & Opinion*, 29(11), 1503-1513. doi: 10.1185/03007995.2013.834250
- Becker, B. W., Thames, A. D., Woo, E., Castellon, S. A., & Hinkin, C. H. (2011). Longitudinal change in cognitive function and medication adherence in HIV-infected adults. *AIDS and Behavior*, 15(8), 1888-1894. doi: 10.1007/s10461-011-9924-z
- Benson, K., & Hartz, A. J. (2000). A comparison of observational studies and randomized, controlled trials. *The New England Journal Of Medicine*, 342(25), 1878-1886.
- Berger, R. (2015). Now I see it, now I don't: researcher's position and reflexivity in qualitative research. *Qualitative Research*, 15(2), 219-234. doi: 10.1177/1468794112468475
- Bertelli, M. O., Munir, K., Harris, J., & Salvador-Carulla, L. (2016). 'Intellectual developmental disorders': Reflections on the international consensus document for redefining 'mental retardation-intellectual disability' in ICD-11. *Advances in Mental Health and Intellectual Disabilities*, 10(1), 36-58. doi: 10.1108/AMHID-10-2015-0050
- Bettany-Saltikov, J. (2016). *How to do a systematic literature review in nursing : a step-by-step guide* (Second edition / Josette Bettany-Saltikov and Robert McSherry. ed.). London: Open University Press/McGraw Hill Education.
- Bianchi, C., Daniele, G., Dardano, A., Miccoli, R., & Del Prato, S. (2017). Early Combination Therapy with Oral Glucose-Lowering Agents in Type 2 Diabetes. *Drugs*, 77(3), 247-264. doi: 10.1007/s40265-017-0694-4
- Boahen, G. (2015). Researching the Mental Capacity Act 2005: Reflections on governance, field relationships, and ethics with an adult who did not consent. *Ethics and Social Welfare*, 9(4), 375-389. doi: 10.1080/17496535.2015.1072571
- Bojesen, A., Høst, C., & Gravholt, C. H. (2010). Klinefelter's syndrome, type 2 diabetes and the metabolic syndrome: the impact of body composition. *Molecular Human Reproduction*, 16(6), 396-401.
- Bourgeault, I. (2010). *The SAGE Handbook of Qualitative Methods in Health Research*. London: SAGE Publications.
- Brace, N., Kemp, R., & Snelgar, R. (2013). *SPSS for psychologists* (5th Edition ed.). Basingstoke: Routledge.
- Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology *Qualitative Research in Psychology* (pp. 77-101): Taylor and Francis.
- Brett, J., Staniszewska, S., Mockford, C., Herron-Marx, S., Hughes, J., Tysall, C., Suleman R. (2012) Mapping the impact of patient and public involvement on health and social care research: a systematic review, *Health Expectations*, 17, pp 637-650 doi: 10.1111/j.1369-7625.2012.00795.x

-
- Broadbent, E., Donkin, L., & Stroh, J. C. (2011). Illness and treatment perceptions are associated with adherence to medications, diet, and exercise in diabetic patients. *Diabetes Care, 34*(2), 338-340. doi: 10.2337/dc10-1779
- Brown, K. M., Elliott, S. J., Leatherdale, S. T., & Robertson-Wilson, J. (2015). Searching for rigour in the reporting of mixed methods population health research: a methodological review. *Health Education Research, 30*(6), 811-839. doi: 10.1093/her/cyv046
- Brown, M. (2015). Review: Research involving people with a learning disability – methodological challenges and ethical considerations. *Journal of Research in Nursing, 20*(6), 447-448. doi: 10.1177/1744987115592084
- Brown, M., Taggart, L., Karatzias, T., Truesdale, M., Walley, R., Northway, R., Davies, M. (2017). Improving diabetes care for people with intellectual disabilities: a qualitative study exploring the perceptions and experiences of professionals in diabetes and intellectual disability services. *Journal of Intellectual Disability Research, 61*(5), 435-449. doi: 10.1111/jir.12369
- Brug, J., Conner, M., Harré, N., Kremers, S., & McKellar, S. W., S. (2005). The Transtheoretical Model and stages of change: a critique: Observations by five Commentators on the paper by Adams, J. and White, M. (2004) Why don't stage-based activity promotion interventions work? *Health Education Research, 20*(2), 244-258. doi: 10.1093/her/cyh005
- Caelli, K., Ray, L., & Mill, J. (2003). 'Clear as Mud': Toward Greater Clarity in Generic Qualitative Research. *The International Journal of Qualitative Methods, 2*(2).
- Cameron, L., & Leventhal, H. (2003). *The self-regulation of health and illness behaviour*. London: Routledge.
- Cameron, R., Dwyer, T., Richardson, S., Ahmed, E., & Sukumaran, A. (2013). Lessons from the field: Applying the Good Reporting of A Mixed Methods Study (GRAMMS) framework. *Electronic Journal of Business Research Methods, 11*(2), 53-64.
- Capoccia, K., Odegard, P. S., & Letassy, N. (2016). Medication adherence with diabetes medication: A systematic review of the literature. *The Diabetes Educator, 42*(1), 34-71. doi: 10.1177/0145721715619038
- Cardol, M., Rijken, M., & Valk, H. L.-d. (2012a). Attitudes and dilemmas of caregivers supporting people with intellectual disabilities who have diabetes. *Patient Education & Counseling, 87*(3), 383-388.
- Cardol, M., Rijken, M., & Valk, H. L.-d. (2012b). People with mild to moderate intellectual disability talking about their diabetes and how they manage. *Journal of Intellectual Disability Research, 56*(4), 351-360. doi: 10.1111/j.1365-2788.2011.01472.x
- Carey, E., & Griffiths, C. (2017). Recruitment and consent of adults with intellectual disabilities in a classic grounded theory research study: Ethical and methodological considerations. *Disability & Society, 32*(2), 193-212. doi: 10.1080/09687599.2017.1281793
- CASP UK, (2017). Critical Skills Appraisal Programme (CASP). Retrieved from <https://casp-uk.net/>
- Caughey, G. E., Barratt, J. D., Shakib, S., Kemp-Casey, A., & Roughead, E. E. (2017). Medication use and potentially high-risk prescribing in older patients hospitalized for diabetes: a missed opportunity to improve care? *Diabetic Medicine, 34*(3), 432-439. doi: 10.1111/dme.13148
- Chan, M., Nicklason, F., & Vial, J. H. (2001). Adverse drug events as a cause of hospital admission in the elderly. *Internal Medicine Journal, 31*(4), 199-205.
- Chao, J., Nau, D. P., Aikens, J. E., & Taylor, S. D. (2005). The mediating role of health beliefs in the relationship between depressive symptoms and medication adherence in persons with diabetes. *Research in Social & Administrative Pharmacy, 1*(4), 508-525.

- Chau, P. H., Woo, J., Lee, C. H., Cheung, W. L., Chen, J., Chan, W. M., . . . McGhee, S. M. (2011). Older people with diabetes have higher risk of depression, cognitive and functional impairments: implications for diabetes services. *The Journal Of Nutrition, Health & Aging, 15*(9), 751-755.
- Choi, J., & Twamley, E. W. (2013). Cognitive rehabilitation therapies for alzheimer's disease: A review of methods to improve treatment engagement and self-efficacy. *Neuropsychology Review*. doi: 10.1007/s11065-013-9227-4
- Cleaver, S., Ouellette-Kuntz, H., & Sakar, A. (2010). Participation in Intellectual Disability Research: A Review of 20 Years of Studies. *Journal of Intellectual Disability Research, 54*(3), 187-193. doi: 10.1111/j.1365-2788.2010.01256.x
- Cohen, J. (1988). *Statistical Power Analysis for the Behavioral Sciences.*: Routledge.
- Cooper, S., & Endacott, R. (2007). Generic qualitative research: a design for qualitative research in emergency care? *Emerg Med J, 24*(12), 816. doi: 10.1136/emj.2007.050641
- Cooper, S., McLean, G., Guthrie, B., McConnachie, A., Mercer, S., Sullivan, F., & Morrison, J. (2015). Multiple physical and mental health comorbidity in adults with intellectual disabilities: population-based cross-sectional analysis. *BMC Family Practice, 16*(1), 1-11. doi: 10.1186/s12875-015-0329-3
- Cooray, S. E., Bhaumik, S., Roy, A., Devapriam, J., Rai, R., & Alexander, R. (2015). Intellectual disability and the ICD-11: Towards clinical utility? *Advances in Mental Health and Intellectual Disabilities, 9*(1), 3-8. doi: 10.1108/AMHID-10-2014-0036
- Coppus, A. M. W. (2013). People with intellectual disability: what do we know about adulthood and life expectancy? *Developmental Disabilities Research Reviews, 18*(1), 6-16. doi: 10.1002/ddrr.1123
- Corbetta, P. (2003). *Social Research Theory, Methods and Techniques*. London: SAGE Publications.
- Corbin, J. M., & Strauss, A. (2008). *Basics of Qualitative Research (3rd ed.): Techniques and Procedures for Developing Grounded Theory*. Thousand Oaks.
- Costa, V., Pereira, M. G., & Pedras, S. (2012). Partner support, social-cognitive variables and their role in adherence to self-monitoring of blood glucose in type 2 diabetes. *European Diabetes Nursing, 9*(3), 81-86. doi: 10.1002/edn.212
- Cresswell, J. W., & Plano Clark, V. L. (2007). *Mixed Methods Research*. London: Sage publications.
- Creswell, J. W. (2014). *Research design : qualitative, quantitative, and mixed methods approaches* (Fourth edition, international student edition. ed.). Los Angeles, Calif. ; London: SAGE.
- Cunningham, C. J. L. (2013). *Understanding and conducting research in the health sciences* (First Edition. ed.). Hoboken, New Jersey: John Wiley & Sons, Inc.
- Cuthill, F. M., Espie, C. A., & Cooper, S.-A. (2003). Development and psychometric properties of the Glasgow Depression Scale for people with a learning disability: Individual and carer supplement versions. *The British Journal of Psychiatry, 182*(4), 347-353. doi: 10.1192/bjp.182.4.347
- Darker, C. D., & French, D. P. (2009). What sense do people make of a theory of planned behaviour questionnaire? *Journal of Health Psychology, 14*(7), 861-871. doi: 10.1177/1359105309340983
- Davies, M. J., Gagliardino, J. J., Gray, L. J., Khunti, K., Mohan, V., & Hughes, R. (2013). Real-world factors affecting adherence to insulin therapy in patients with Type 1 or Type 2 diabetes mellitus: a systematic review. *Diabetic Medicine: A Journal Of The British Diabetic Association, 30*(5), 512-524. doi: 10.1111/dme.12128

Department of Health (2013) The Medicines Act 1968 and the Human Medicines Regulations (Amendment) Order. London: Department of Health

- de Vries, S. T., Keers, J. C., Visser, R., de Zeeuw, D., Haaijer-Ruskamp, F. M., Voorham, J., & Denig, P. (2014). Medication beliefs, treatment complexity, and non-adherence to different drug classes in patients with type 2 diabetes. *Journal Of Psychosomatic Research, 76*(2), 134-138. doi: 10.1016/j.jpsychores.2013.11.003
- de Winter, C. F., Bastiaanse, L. P., Hilgenkamp, T. I. M., Evenhuis, H. M., & Echteld, M. A. (2012a). Cardiovascular risk factors (diabetes, hypertension, hypercholesterolemia and metabolic syndrome) in older people with intellectual disability: results of the HA-ID study. *Research in Developmental Disabilities, 33*(6), 1722-1731. doi: 10.1016/j.ridd.2012.04.010
- de Winter, C. F., Bastiaanse, L. P., Hilgenkamp, T. I. M., Evenhuis, H. M., & Echteld, M. A. (2012b). Overweight and obesity in older people with intellectual disability. *Research in Developmental Disabilities, 33*(2), 398-405. doi: 10.1016/j.ridd.2011.09.022
- Diabetes UK. (2009). Learning disabilities and diabetes. from http://www.diabetes.org.uk/About_us/News_Landing_Page/Diabetes-UK-launches-DVD-to-help-people-with-learning-disabilities/
- DiMatteo, M. R. (2004). Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Medical Care, 42*(3), 200-209.
- Dixon-Woods, M., Shaw, R., Agarwal, S., & Ja, S. (2004). The problem of appraising qualitative research. *Quality and Safety in Health Care, 13*, 223-225.
- Draper, P. (2001). Handbook of Qualitative Research , 2nd edition edited by Norman K. Denzin and Yvonna S. Lincoln. Sage, Thousand Oaks, 2000, 1144 pages, £69.00, ISBN 0 761 91512 5 (Vol. 33, pp. 847-847). Oxford UK.
- Dysch, C. M., Chung M.C., Fox J., (2012). How Do People with Intellectual Disabilities and Diabetes Experience and Perceive their Illness? *Journal of Applied Research in Intellectual Disabilities, 25*(1), 39-49. doi: 10.1111/j.1468-3148.2011.00641.x
- Effective Public Health Practice Project (EPHPP) (2004). Quality assessment tool for quantitative studies. from <http://www.ehphp.ca/tools.html>
- Emerson, E., & Baines, S. (2011). Health inequalities and people with learning disabilities in the UK. *Tizard Learning Disability Review, 16*(1), 42-48. doi: 10.5042/tldr.2011.0008
- Emerson, E., Hatton, C., Baines, S., & Robertson, J. (2016). The physical health of British adults with intellectual disability: cross sectional study. *International Journal For Equity In Health, 15*, 11-11. doi: 10.1186/s12939-016-0296-x
- Erpeldinger, S., Rehman, M. B., Berkhout, C., Pigache, C., Zerbib, Y., Regnault, F., Boussageon, R. (2016). Efficacy and safety of insulin in type 2 diabetes: meta-analysis of randomised controlled trials. *BMC Endocrine Disorders, 16*, 1-15. doi: 10.1186/s12902-016-0120-z
- Esbensen, A. J., & Benson, B. A. (2005). Cognitive variables and depressed mood in adults with intellectual disability. *Journal of Intellectual Disability Research, 49*(7), 481-489.
- Ettenhofer, M. L., Hinkin, C. H., Castellon, S. A., Durvasula, R., Ullman, J., Lam, M., Foley, J. (2009). Aging, neurocognition, and medication adherence in HIV infection. *American Journal of Geriatric Psychiatry, 17*(4), 281-290. doi: 10.1097/JGP.0b013e31819431bd
- Farmer, A., Kinmonth, A., & Sutton, S. (2006). Measuring beliefs about taking hypoglycaemic medication among people with Type 2 diabetes. *Diabetic Medicine: A Journal Of The British Diabetic Association, 23*(3), 265-270.

- Faul, F., Erdfelder, E., Lang, A. G., & Buchner, A. (2007). G*power 3: A flexible statistical power analysis program for the social, behavioural and biomedical sciences. *Behavior Research Methods*, 39(2), 175-191.
- Feil, D. G., Pearman, A., Victor, T., Harwood, D., Weinreb, J., Kahle, K., & Unützer, J. (2009). The role of cognitive impairment and caregiver support in diabetes management of older outpatients. *International Journal of Psychiatry in Medicine*, 39(2), 199-214.
- Findlay, L., & Gough, B. (2003). *Reflexivity: A Practical Guide for Researchers in Health and Social Science*. London: Blackwell.
- Flick, U. (2013). *The SAGE Handbook of Qualitative Data Analysis*. London: SAGE Publications.
- Flood, E. M., Bell, K. F., de la Cruz, M. C., & Ginchereau-Sowell, F. M. (2017). Patient preferences for diabetes treatment attributes and drug classes. *Current Medical Research And Opinion*, 33(2), 261-268. doi: 10.1080/03007995.2016.1253553
- French, D. P., Cooke, R., McLean, N., Williams, M., & Sutton, S. (2007). What do people think about when they answer theory of planned behaviour questionnaires? A 'think aloud' study. *Journal of health psychology*, 12(4), 672.
- Fretwell, C., & Felce, D. (2007). Staff Knowledge of the Side Effects of Anti-Psychotic Medication. *Journal of Applied Research in Intellectual Disabilities*, 20(6), 580-585. doi: 10.1111/j.1468-3148.2006.00356.x
- Geijselaers, S. L. C., Sep, S. J. S., Stehouwer, C. D. A., & Biessels, G. J. (2015). Glucose regulation, cognition, and brain MRI in type 2 diabetes: a systematic review. *The Lancet. Diabetes & Endocrinology*, 3(1), 75-89. doi: 10.1016/S2213-8587(14)70148-2
- Gherman, A., Schnur, J., Montgomery, G., Sassu, R., Veresiu, I., & David, D. (2011). How are adherent people more likely to think? A meta-analysis of health beliefs and diabetes self-care. *The Diabetes Educator*, 37(3), 392-408.
- Gill, J., & Fazil, Q. (2013). Derogation of "duty of care" in favour of "choice"? *Journal of Adult Protection*, 15(5), 258-270. doi: 10.1108/JAP-12-2012-0028
- Goldsmith, L., & Skirton, H. (2015). Research involving people with a learning disability – methodological challenges and ethical considerations. *Journal of Research in Nursing*, 20(6), 435-446. doi: 10.1177/1744987115591867
- Gonzalez, J., Peyrot, M., McCarl, L. A., Collins, E. M., Serpa, L., Mimiaga, M. J., & Safren, S. A. (2008). Depression and diabetes treatment nonadherence: a meta-analysis. *Diabetes Care*, 31(12), 2398-2403.
- Gonzalez, J. S., Safren, S. A., Delahanty, L. M., Cagliero, E., Wexler, D. J., Meigs, J. B., & Grant, R. W. (2008). Symptoms of depression prospectively predict poorer self-care in patients with Type 2 diabetes. *Diabetic Medicine*, 25(9), 1102-1107.
- Gonzalez, J. S., Schneider, H. E., Wexler, D. J., Psaros, C., Delahanty, L. M., Cagliero, E., & Safren, S. A. (2013). Validity of medication adherence self-reports in adults with type 2 diabetes. *Diabetes Care*, 36(4), 831-837. doi: 10.2337/dc12-0410
- Graneheim, U. H., Lindgren, B.-M., & Lundman, B. (2017). Methodological challenges in qualitative content analysis: A discussion paper. *Nurse Education Today*, 56, 29-34. doi: 10.1016/j.nedt.2017.06.002
- Grant, R., Adams, A. S., Trinacty, C. M., Zhang, F., Kleinman, K., Soumerai, S. B., Ross-Degnan, D. (2007). Relationship between patient medication adherence and subsequent clinical inertia in type 2 diabetes glycemic management. *Diabetes Care*, 30(4), 807-812.

-
- Grant, R. W., Devita, N. G., Singer, D. E., & Meigs, J. B. (2003). Polypharmacy and medication adherence in patients with type 2 diabetes. *Diabetes Care*, 26(5), 1408-1412.
- Hale, L. A., Trip, H. T., Whitehead, L., & Conder, J. (2011). Self-Management Abilities of Diabetes in People With an Intellectual Disability Living in New Zealand. *Journal of Policy & Practice in Intellectual Disabilities*, 8(4), 223-230. doi: 10.1111/j.1741-1130.2011.00314.x
- Hankó, B., Kázmér, M., Kumli, P., Hrágyel, Z., Samu, A., Vincze, Z., & Zelkó, R. (2007). Self-reported medication and lifestyle adherence in Hungarian patients with Type 2 diabetes. *Pharmacy World & Science: PWS*, 29(2), 58-66.
- Hannes, K. (2011). Chapter 4 - Critical appraisal of qualitative research. In J. Noyes, A. Booth, H. K., H. A., H. J., L. S. & L. C. (Eds.), *Supplementary Guidance for Inclusion of Qualitative Research in Cochrane Systematic Reviews of Interventions. Version 1: Cochrane Collaboration Qualitative Methods Group*.
- Haveman, M., Perry, J., Salvador-Carulla, L., Walsh, P. N., Kerr, M., Valk, H. L.-d., Weber, G. (2011). Ageing and health status in adults with intellectual disabilities: Results of the European POMONA II study. *Journal of Intellectual & Developmental Disability*, 36(1), 49-60. doi: 10.3109/13668250.2010.549464
- Hawkins, L. A., Kilian, S., Firek, A., Kashner, T. M., Firek, C. J., & Silvet, H. (2012). Cognitive impairment and medication adherence in outpatients with heart failure. *Heart & Lung: The Journal Of Critical Care*, 41(6), 572-582. doi: 10.1016/j.hrtlng.2012.06.001
- Hill-Briggs, F., Gary, T. L., Bone, L. R., Hill, M. N., Levine, D. M., & Brancati, F. L. (2005). Medication adherence and diabetes control in urban African Americans with type 2 diabetes. *Health Psychology*, 24(4), 349-357.
- Holloway, K., & Van Dijk, L. (2011). The world medicines situation 2011: the rational use of medicines. retrieved from http://www.who.int/medicines/areas/policy/world_medicines_situation/WMS_ch14_wRational.pdf
- Horne, R., Faasse, K., Cooper, V., Diefenbach, M. A., Leventhal, H., Leventhal, E., & Petrie, K. J. (2013). The perceived sensitivity to medicines (PSM) scale: an evaluation of validity and reliability. *British Journal of Health Psychology*, 18(1), 18-30. doi: 10.1111/j.2044-8287.2012.02071.x
- Horne, R., & Weinman, J. (1999). Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *Journal Of Psychosomatic Research*, 47(6), 555-567.
- Idusohan-Moizer, H., Sawicka, A., Dendle, J., & Albany, M. (2015). Mindfulness-based cognitive therapy for adults with intellectual disabilities: An evaluation of the effectiveness of mindfulness in reducing symptoms of depression and anxiety. *Journal of Intellectual Disability Research*, 59(2), 93-104. doi: 10.1111/jir.12082
- Inzucchi, S. E., Bergenstal, R. M., Buse, J. B., Diamant, M., Ferrannini, E., Nauck, M., . . . Matthews, D. R. (2012). Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach: Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Spectrum*, 25(3), 154-171.
- Information Services Department.(ISD) (2014). Prescribing and medicines: prescription cost and analysis. from <https://isdscotland.scot.nhs.uk/Health-Topics/Prescribing-and-Medicines/Publications/2014-06-24/2014-06-24-Prescribing-PrescriptionCostAnalysis-Report.pdf>
- Jackson, N. (2012). Systematic review of health promotion and public health interventions. Retrieved from

https://ph.cochrane.org/sites/ph.cochrane.org/files/uploads/HPPH_systematic_review_handbook.pdf website:

- Jahoda, A., Melville, C. A., Pert, C., Cooper, S. A., Lynn, H., Williams, C., & Davidson, C. (2015). A feasibility study of behavioural activation for depressive symptoms in adults with intellectual disabilities. *Journal of Intellectual Disability Research*, 59(11), 1010-1021. doi: 10.1111/jir.12175
- Jason, O. (2008). *Best Practices in Quantitative Methods*.
- Jepson, M. (2015). Applying the Mental Capacity Act to research with people with learning disabilities. *British Journal of Learning Disabilities*, 43(2), 128-134. doi: 10.1111/bld.12122
- Juarez, D. T., Tan, C., Davis, J. W., & Mau, M. M. (2014). Using quantile regression to assess disparities in medication adherence. *American Journal of Health Behavior*, 38(1), 53-62. doi: 10.5993/AJHB.38.1.6
- Kahlke, R. M. (2014). Generic Qualitative Approaches: Pitfalls and Benefits of Methodological Mixology. *International Journal Of Qualitative Methods*, 13, 37-52.
- Karen, O., & Reilly, M., (2009). *Key Concepts in Ethnography*. London.
- Kars, M. C., van Thiel, G. J. M. W., van der Graaf, R., Moors, M., de Graeff, A., & van Delden, J. J. M. (2016). A systematic review of reasons for gatekeeping in palliative care research. *Palliative Medicine*, 30(6), 533-548. doi: 10.1177/0269216315616759
- Katon, W. (2010). Depression and diabetes: unhealthy bedfellows. *Depression & Anxiety (1091-4269)*, 27(4), 323-326. doi: 10.1002/da.20683
- Katon, W. J., Russo, J. E., Heckbert, S. R., Lin, E. H., Ciechanowski, P., Ludman, E., Von Korff, M. (2010). The relationship between changes in depression symptoms and changes in health risk behaviors in patients with diabetes. *International Journal of Geriatric Psychiatry*, 25(5), 466-475. doi: 10.1002/gps.2363
- Kennedy, D. M. (2016). Is it any clearer? Generic qualitative inquiry and the VSAIEEDC model of data analysis.(Report). *The Qualitative Report*, 21(8), 1369.
- Khunti, S., Davies, M. J., & Khunti, K. (2015). Clinical inertia in the management of type 2 diabetes mellitus: a focused literature review. *British Journal of Diabetes & Vascular Disease*, 15(2), 65-69. doi: 10.15277/bjdv.2015.019
- Kilbourne, A. M., Reynolds, C. F., Good, C. B., Sereika, S. M., Justice, A. C., & Fine, M. J. (2005). How does depression influence diabetes medication adherence in older patients? *The American Journal Of Geriatric Psychiatry: Official Journal Of The American Association For Geriatric Psychiatry*, 13(3), 202-210.
- Kim, C.-J., Schlenk, E. A., Kim, D. J., Kim, M., Erlen, J. A., & Kim, S.-E. (2015). The role of social support on the relationship of depressive symptoms to medication adherence and self-care activities in adults with type 2 diabetes. *Journal of Advanced Nursing*, 71(9), 2164-2175. doi: 10.1111/jan.12682
- Konig, M., Lamos, E. M., Stein, S. A., & Davis, S. N. (2013). An insight into the recent diabetes trials: what is the best approach to prevent macrovascular and microvascular complications? *Current Diabetes Reviews*, 9(5), 371-381.
- Kumsa, M. K., Chambon, A., Yan, M. C., & Maiter, S. (2015). Catching the shimmers of the social: from the limits of reflexivity to methodological creativity. *Qualitative Research*, 15(4), 419-436. doi: 10.1177/1468794114538897
- Kuo, Y., Raji, M. A., Markides, K. S., Ray, L. A., Espino, D. V., & Goodwin, J. S. (2003). Inconsistent use of diabetes medications, diabetes complications, and mortality in older Mexican Americans over a 7-year period: data from the Hispanic Established Population for the Epidemiologic Study of the Elderly. *Diabetes Care*, 26(11), 3054-3060.

-
- Kurlander, J. E., Kerr, E. A., Krein, S., Heisler, M., & Piette, J. D. (2009). Cost-Related Nonadherence to Medications Among Patients With Diabetes and Chronic Pain: Factors beyond finances. *Diabetes Care*, *32*(12), 2143-2148. doi: 10.2337/dc09-1059
- Laerd. (2017). Laerd statistics. retrieved from <https://statistics.laerd.com/>
- Laurier, V., Lapeyrade, A., Copet, P., Demeer, G., Silvie, M., Bieth, E., . . . Jauregi, J. (2015). Medical, psychological and social features in a large cohort of adults with Prader–Willi syndrome: Experience from a dedicated centre in France. *Journal of Intellectual Disability Research*, *59*(5), 411-421. doi: 10.1111/jir.12140
- Leavitt, F. J. (2006). Dissecting bioethics. Is any medical research population not vulnerable? *Cambridge Quarterly of Healthcare Ethics*, *15*(1), 81-88.
- Lee, W.-Y., Ahn, J., Kim, J.-H., Hong, Y.-P., Hong, S. K., Kim, Y. T., Morisky, D. E. (2013). Reliability and validity of a self-reported measure of medication adherence in patients with type 2 diabetes mellitus in Korea. *The Journal Of International Medical Research*, *41*(4), 1098-1110. doi: 10.1177/0300060513484433
- Leonard, H. S. (2013). *The Wiley-Blackwell handbook of the psychology of leadership, change and organizational development*. Hoboken, N.J.: Wiley-Blackwell.
- Lerman, I., Díaz, J. P. M., Ibarguengoitia, M. E. R., Pérez, F. J. G., Villa, A. R., Velasco, M. L., Rodrigo, J. A. R. (2009). Nonadherence to insulin therapy in low-income, type 2 diabetic patients. *Endocrine Practice: Official Journal Of The American College Of Endocrinology And The American Association Of Clinical Endocrinologists*, *15*(1), 41-46.
- Li, C.-L., Chiu, Y.-C., Bai, Y.-B., Lin, J.-D., Stanaway, F., & Chang, H.-Y. (2017). The occurrence of depressive symptoms and cognitive impairment and its relationship with self-care behaviors among community dwelling older adults with diabetes. *Diabetes Research And Clinical Practice*, *129*, 73-78. doi: 10.1016/j.diabres.2017.03.025
- Lieveld, F. I., van Vlerken, L. G., Siersema, P. D., & van Erpecum, K. J. (2013). Patient adherence to antiviral treatment for chronic hepatitis B and C: a systematic review. *Annals Of Hepatology*, *12*(3), 380-391.
- Lin, E. H., Heckbert, S. R., Rutter, C. M., Katon, W. J., Ciechanowski, P., Ludman, E. J., Von Korff, M. (2009). Depression and increased mortality in diabetes: unexpected causes of death. *Annals of Family Medicine*, *7*(5), 414-421. doi: 10.1370/afm.998
- MacRae, S., Brown, M., Karatzias, T., Taggart, L., Truesdale-Kennedy, M., Walley, R., . . . Davies, M. (2015). Diabetes in people with intellectual disabilities: A systematic review of the literature. *Research in Developmental Disabilities*, *47*, 352-374. doi: 10.1016/j.ridd.2015.10.003
- Malhotra, S., Karan, R. S., Pandhi, P., & Jain, S. (2001). Drug related medical emergencies in the elderly: role of adverse drug reactions and non-compliance. *Postgraduate Medical Journal*, *77*(913), 703-707.
- Mann, D. M., Ponieman, D., Leventhal, H., & Halm, E. A. (2009). Predictors of adherence to diabetes medications: the role of disease and medication beliefs. *Journal of Behavioral Medicine*, *32*(3), 278-284. doi: 10.1007/s10865-009-9202-y
- Martinez-Aran, A., Scott, J., Colom, F., Torrent, C., Tabares-Seisdedos, R., Daban, C., Vieta, E. (2009). Treatment nonadherence and neurocognitive impairment in bipolar disorder. *Journal of Clinical Psychiatry*, *70*(7), 1017-1023. doi: 10.4088/JCP.08m04408
- Mathur, S., Zammitt, N. N., & Frier, B. M. (2015). Optimal glycaemic control in elderly people with type 2 diabetes: what does the evidence say? *Drug Safety*, *38*(1), 17-32. doi: 10.1007/s40264-014-0247-7

- May, M., & Schindler, C. (2016). Clinically and pharmacologically relevant interactions of antidiabetic drugs. *Therapeutic Advances in Endocrinology and Metabolism*, 7(2), 69-83. doi: 10.1177/2042018816638050
- Mayberry, L. S., & Osborn, C. Y. (2012). Family support, medication adherence, and glycemic control among adults with type 2 diabetes. *Diabetes Care*, 35(6), 1239-1245. doi: 10.2337/dc11-2103
- McDonald, K., & Patka, M. (2012). 'There is no black or white': Scientific community views on ethics in intellectual and developmental disability research. *Journal of Policy and Practice in Intellectual Disabilities*, 9(3), 206-214. doi: 10.1111/j.1741-1130.2012.00348.x
- McDonald, K. E., Conroy, N. E., Kim, C. I., LoBraico, E. J., Prather, E. M., & Olick, R. S. (2016). Is safety in the eye of the beholder? Safeguards in research with adults with intellectual disability. *Journal of Empirical Research on Human Research Ethics*, 11(5), 424-438. doi: 10.1177/1556264616651182
- McDonald, K. E., Keys, C. B., & Henry, D. B. (2008). Gatekeepers of science: attitudes toward the research participation of adults with intellectual disability. *American Journal Of Mental Retardation: AJMR*, 113(6), 466-478. doi: 10.1352/2008.113:466-478
- McDonald, K. E., Kidney, C. A., Nelms, S. L., Parker, M. R., Kimmel, A., & Keys, C. B. (2009). Including adults with intellectual disabilities in research: Scientists' perceptions of risks and protections. *Journal of Policy and Practice in Intellectual Disabilities*, 6(4), 244-252. doi: 10.1111/j.1741-1130.2009.00225.x
- McGillivray, J. A., & McCabe, M. P. (2007). Early detection of depression and associated risk factors in adults with mild/moderate intellectual disability. *Research in Developmental Disabilities*, 28(1), 59-70. doi: 10.1016/j.ridd.2005.11.001
- Melville, C. A., Cooper, S. A., Morrison, J., Allan, L., Smiley, E., & Williamson, A. (2008). The Prevalence and Determinants of Obesity in Adults with Intellectual Disabilities. *Journal of Applied Research in Intellectual Disabilities*, 21(5), 425-437. doi: 10.1111/j.1468-3148.2007.00412.x
- Mencap. (2013). More about learning disability. Retrieved 2/09/13, 2013
- Miller, T. A., & Dimatteo, M. R. (2013). Importance of family/social support and impact on adherence to diabetic therapy. *Diabetes, Metabolic Syndrome And Obesity: Targets And Therapy*, 6, 421-426.
- Moran-Ellis, J., Alexander, V. D., Cronin, A., Dickinson, M., Fielding, J., Sleney, J., & Thomas, H. (2006). Triangulation and integration: processes, claims and implications. *Qualitative Research*, 6. doi: 10.1177/1468794106058870
- Morisky, D., Ang, A., Krousel-Wood, M., & Ward, H. J. (2008). Predictive validity of a medication adherence measure in an outpatient setting. *Journal Of Clinical Hypertension (Greenwich, Conn.)*, 10(5), 348-354.
- Morisky, D., Green, L., & Levine, D. (1986). Concurrent and predictive validity of a self-reported measure of medication adherence. *Medical Care*, 24(1), 67-74.
- Morrisey, B. (2012). Ethics and Research Among Persons With Disabilities in Long-Term Care. *Qualitative Health Research*, 22(9), 1284-1297. doi: 10.1177/1049732312449389
- Morse, S. A., Ciechanowski, P. S., Katon, W. J., & Hirsch, I. B. (2006). Isn't this just bedtime snacking? The potential adverse effects of night-eating symptoms on treatment adherence and outcomes in patients with diabetes. *Diabetes Care*, 29(8), 1800-1804.
- Moser, A., Stuck, A. E., Silliman, R. A., Ganz, P. A., & Clough-Gorr, K. M. (2012). The eight-item modified Medical Outcomes Study Social Support Survey: psychometric

-
- evaluation showed excellent performance. *Journal Of Clinical Epidemiology*, 65(10), 1107-1116. doi: 10.1016/j.jclinepi.2012.04.007
- Mullhall, P., Taggart, L., Coates, V., McAloon, T. & Hassiotis, A, (2018), A systematic review of the methodological and practical challenges of undertaking randomised controlled trials with cognitive disability populations. *Social Science Medicine*, 29 (200), 114-128
- Murphy, E., & Dingwall, R. (1998). Qualitative methods in health services research. In N. Black, J. Brazier, R. Fitzpatrick & B. Reeves (Eds.), *Health services research methods*. London: BMJ Books.
- Naderi, S., Bestwick, J., & Wald, D. (2012). Adherence to drugs that prevent cardiovascular disease: meta-analysis on 376,162 patients. *American Journal of Medicine*, 125(9), 882-887. doi: 10.1016/j.amjmed.2011.12.013
- Nakahara, R., Yoshiuchi, K., Kumano, H., Hara, Y., Suematsu, H., & Kuboki, T. (2006). Prospective study on influence of psychosocial factors on glycemic control in Japanese patients with type 2 diabetes. *Psychosomatics*, 47(3), 240-246.
- Nau, D. P., Aikens, J. E., & Pacholski, A. M. (2007). Effects of gender and depression on oral medication adherence in persons with type 2 diabetes mellitus. *Gender Medicine*, 4(3), 205-213.
- Nelson, K. M., McFarland, L., & Reiber, G. (2007). Factors influencing disease self-management among veterans with diabetes and poor glycemic control. *Journal Of General Internal Medicine*, 22(4), 442-447.
- Newell, R., & Burnard, P. (2011). *Research for Evidence-Based Practice in Healthcare*: Wiley-Blackwell.
- NHS Scotland (2016) Health and Social Care Delivery Plan, retrieved from: <http://www.gov.scot/Resource/0051/00511950.pdf>
- NHSScotland (2015). Polypharmacy guidance. Retrieved October, 2017, from <http://www.sehd.scot.nhs.uk/publications/DC20150415polypharmacy.pdf>
<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000011.pub4/abstract>
- NICE. (2009). Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence. Retrieved July, 2012, from <http://www.nice.org.uk/CG76>
- NICE. (2013). Medicines and prescribing support from NICE. Retrieved November, 2013, from <http://www.nice.org.uk/mpc/index.jsp>
- NICE. (2015a). Type 1 Diabetes in Adults: diagnosis and management. Retrieved June, 2017, from <https://www.nice.org.uk/guidance/ng17>
- NICE. (2015b). Type 2 Diabetes in Adults: management. Retrieved June, 2017, from <https://www.nice.org.uk/guidance/ng28>
- Nieuwlaat, R., Wilczynski, N., Navarro, T., Hobson, N., Jeffery, R., Keepanasseril, A., . . . Haynes, R. (2014). Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews*, 11.
- NIHR. (2017). Public Involvement Standards Development. Retrieved from <https://sites.google.com/nih.ac.uk/pi-standards/home>
- Noale, M., Veronese, N., Cavallo Perin, P., Pilotto, A., Tiengo, A., Crepaldi, G., & Maggi, S. (2016). Polypharmacy in elderly patients with type 2 diabetes receiving oral antidiabetic treatment. *Acta Diabetologica*, 53(2), 323-330. doi: 10.1007/s00592-015-0790-4
- Norcross, J. C., Krebs, P. M., & Prochaska, J. O. (2011). Stages of change. *Journal of Clinical Psychology*, 67(2), 143. doi: 10.1002/jclp.2758

- Nordstrøm, M., Paus, B., Retterstøl, K., & Kolset, S. O. (2016). The prevalence of metabolic risk factors of atherosclerotic cardiovascular disease in Williams syndrome, Prader–Willi syndrome, and Down syndrome. *Journal of Intellectual & Developmental Disability, 41*(3), 187-196. doi: 10.3109/13668250.2016.1167845
- Nursing and Midwifery Council (NMC) (2015), The **code**: Professional standards of practice and behaviour for nurses and midwives. London: **NMC** retrieved from <https://www.nmc.org.uk/globalassets/sitedocuments/nmc-publications/nmc-code.pdf>
- Nursing and Midwifery Council (NMC) (2016) Freedom of information request, unpublished email.
- O'Cathain, A., Murphy, E., & Nicholl, J. (2007a). Integration and publications as indicators of 'yield' from mixed methods studies. *Journal of Mixed Methods Research, 1*. doi: 10.1177/1558689806299094
- O'Cathain, A., Murphy, E., & Nicholl, J. (2007b). Why, and how, mixed methods research is undertaken in health services research in England: a mixed methods study. *BMC Health Services Research, 7*(1), 1-11. doi: 10.1186/1472-6963-7-85
- O'Cathain, A., & Thomas, K. (2006). Combining qualitative and quantitative methods. In C. Pope & N. Mays (Eds.), *Qualitative Research in Health Care*. Oxford: Blackwell Publishing.
- O'Dwyer, M., Peklar, J., McCallion, P., McCarron, M., & Henman, M. C. (2016). Factors associated with polypharmacy and excessive polypharmacy in older people with intellectual disability differ from the general population: a cross-sectional observational nationwide study. *BMJ Open, 6*(4), e010505-e010505. doi: 10.1136/bmjopen-2015-010505
- Odegard, P. S., & Gray, S. L. (2008). Barriers to medication adherence in poorly controlled diabetes mellitus. *The Diabetes Educator, 34*(4), 692-697. doi: 10.1177/0145721708320558
- Oppewal, A., Hilgenkamp, T. I. M., van Wijck, R., & Evenhuis, H. M. (2013). Cardiorespiratory fitness in individuals with intellectual disabilities-A review. *Research in Developmental Disabilities, 34*(10), 3301-3316. doi: 10.1016/j.ridd.2013.07.005
- Osborn, C. Y., & Egede, L. E. (2012). The relationship between depressive symptoms and medication nonadherence in type 2 diabetes: the role of social support. *General Hospital Psychiatry, 34*(3), 249-253. doi: 10.1016/j.genhosppsych.2012.01.015
- Osborn, C. Y., Mayberry, L. S., & Kim, J. M. (2016). Medication adherence may be more important than other behaviours for optimizing glycaemic control among low-income adults. *Journal of Clinical Pharmacy & Therapeutics, 41*(3), 256-259. doi: 10.1111/jcpt.12360
- Osterberg, L., & Blaschke, T. (2005). Adherence to medication. *The New England Journal Of Medicine, 353*(5), 487-497.
- Osugo, M., Morrison, J., Allan, L., Kinnear, D., & Cooper, S. A. (2017). Prevalence, types and associations of medically unexplained symptoms and signs. A cross-sectional study of 1023 adults with intellectual disabilities. *Journal of Intellectual Disability Research*. doi: 10.1111/jir.12372
- Ozawa, S., & Pongpirul, K. (2014). 10 best resources on ... mixed methods research in health systems. *Health Policy And Planning, 29*(3), 323-327. doi: 10.1093/heapol/czt019
- Palmer, N., & Forrester-Jones, R. (2016). Are people with intellectual and developmental disabilities who lack capacity to consent at risk of being excluded from research?: Ethical implications of the UK Mental Capacity Act 2005. *Journal of Intellectual Disability Research, 60*(7-8), 805-805.

-
- Patel, I., Erickson, S. R., Caldwell, C. H., Woolford, S. J., Bagozzi, R. P., Chang, J., & Balkrishnan, R. (2016). Predictors of medication adherence and persistence in Medicaid enrollees with developmental disabilities and type 2 diabetes. *Research in Social & Administrative Pharmacy, 12*(4), 592-603. doi: 10.1016/j.sapharm.2015.09.008
- Pollack, M. F., Purayidathil, F. W., Bolge, S. C., & Williams, S. A. (2010). Patient-reported tolerability issues with oral antidiabetic agents: Associations with adherence; treatment satisfaction and health-related quality of life. *Diabetes Research & Clinical Practice, 87*(2), 204-210. doi: 10.1016/j.diabres.2009.11.023
- Pope, C., Ziebland, S., & Mays, N. (2000). Qualitative research in health care - Analysing qualitative data (Reprinted from *Qualitative Research in Health Care*). *Br. Med. J., 320*(7227), 114-116.
- Pounder, D. G. (1993). *Rigor in Traditional Quantitative Methods*.
- Prisciandaro, J. J., Gebregziabher, M., Grubaugh, A. L., Gilbert, G. E., Echols, C., & Egede, L. E. (2011). Impact of psychiatric comorbidity on mortality in veterans with type 2 diabetes. *Diabetes Technology & Therapeutics, 13*(1), 73-78. doi: 10.1089/dia.2010.0092
- Ptomey, L., Goetz, J., Lee, J., Donnelly, J., & Sullivan, D. (2013). Diet Quality of Overweight and Obese Adults with Intellectual and Developmental Disabilities as Measured by the Healthy Eating Index-2005. *Journal Of Developmental And Physical Disabilities, 25*(6). doi: 10.1007/s10882-013-9339-z
- Rasaratnam, R., Crouch, K., & Regan, A. (2004). Attitude to medication of parents/primary carers of people with intellectual disability. *Journal Of Intellectual Disability Research., 48*(Pt 8), 754-763.
- Raschetti, R., Morgutti, M., Menniti-Ippolito, F., Belisari, A., Rossignoli, A., Longhini, P., & La Guidara, C. (1999). Suspected adverse drug events requiring emergency department visits or hospital admissions. *European Journal of Clinical Pharmacology, 54*(12), 959-963.
- Reichard, A., & Stolze, H. (2011). Diabetes among adults with cognitive limitations compared to individuals with no cognitive disabilities. *Intellectual & Developmental Disabilities, 49*(3), 141-154. doi: 10.1352/1934-9556-49.2.141
- Rimmer, J. H., Yamaki, K., Lowry, B. M., Wang, E., & Vogel, L. C. (2010). Obesity and obesity-related secondary conditions in adolescents with intellectual/developmental disabilities. *Journal of Intellectual Disability Research, 54*(Part 9), 787-794. doi: 10.1111/j.1365-2788.2010.01305.x
- Rodríguez-Gutiérrez, R., & Montori, V. M. (2016). Glycemic Control for Patients With Type 2 Diabetes Mellitus: Our Evolving Faith in the Face of Evidence. *Circulation: Cardiovascular Quality & Outcomes, 9*(5), 504-512. doi: 10.1161/CIRCOUTCOMES.116.002901
- Rosen, M. (2003). Neuropsychological Correlates of Suboptimal Adherence to Metformin. *Journal of Behavioral Medicine, 26*(4), 349.
- Rouse, L., & Finlay, W. M. L. (2016). Repertoires of responsibility for diabetes management by adults with intellectual disabilities and those who support them. *Sociology of Health & Illness, 38*(8), 1243-1257. doi: 10.1111/1467-9566.12454
- Ryan, R., Santesso, N., Hill, S., Lowe, D., Kaufman, C., & Grimshaw, J. (2011). Consumer-oriented interventions for evidence-based prescribing and medicines use: an overview of systematic reviews. *Cochrane Database Of Systematic Reviews (Online)*(5), CD007768.
- Ryan, R., Santesso, N., Lowe, D., Hill, S., Grimshaw, J., Prictor, M., . . . Taylor, M. (2014). Interventions to improve safe and effective medicines use by consumers: an overview

- of systematic reviews. *The Cochrane Database Of Systematic Reviews*, 4, CD007768. doi: 10.1002/14651858.CD007768.pub3
- Sabaté E, e. (2003). Adherence to long-term therapies:evidence for action. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3068890/>
- Schectman, J. M., Nadkarni, M. M., & Voss, J. D. (2002). The association between diabetes metabolic control and drug adherence in an indigent population. *Diabetes Care*, 25(6), 1015-1021.
- Schmidt, F., Kapellen, T. M., Wiegand, S., Herbst, A., Wolf, J., Fröhlich-Reiterer, E. E., Holl, R. W. (2012). Diabetes mellitus in children and adolescents with genetic syndromes. *Experimental And Clinical Endocrinology & Diabetes: Official Journal, German Society Of Endocrinology [And] German Diabetes Association*, 120(10), 579-585. doi: 10.1055/s-0032-1306330
- Schoenthaler, A. M., Schwartz, B. S., Wood, C., & Stewart, W. F. (2012). Patient and Physician Factors Associated With Adherence to Diabetes Medications. *Diabetes Educator*, 38(3), 397-408. doi: 10.1177/0145721712440333
- Scottish Government. (2013). *The Keys to Life _ Improving the quality of life for people with learning disabilities.*: Retrieved from <http://www.scotland.gov.uk/Publications/2013/06/1123>.
- Scottish Government (2016), Non-medical prescribing retrieved from: <http://www.gov.scot/Topics/Health/NHS-Workforce/Pharmacists/Non-Medical-Prescribing>
- Sheen, Y.-J., & Sheu, W. H. H. (2016). Association between hypoglycemia and dementia in patients with type 2 diabetes. *Diabetes Research & Clinical Practice*, 116, 279-287. doi: 10.1016/j.diabres.2016.04.004
- Shireman, T. I., Reichard, A., Nazir, N., Backes, J. M., & Greiner, K. A. (2010). Quality of diabetes care for adults with developmental disabilities. *Disability And Health Journal*, 3(3), 179-185.
- Silverman, J., Krieger, J., Kiefer, M., Hebert, P., Robinson, J., & Nelson, K. (2015). The relationship between food insecurity and depression, diabetes distress and medication adherence among low-income patients with poorly-controlled diabetes. *Journal Of General Internal Medicine*, 30(10), 1476-1480. doi: 10.1007/s11606-015-3351-1
- Simpson, S. H., Lin, M., & Eurich, D. T. (2016). Medication Adherence Affects Risk of New Diabetes Complications: A Cohort Study. *Annals of Pharmacotherapy*, 50(9), 741-746. doi: 10.1177/1060028016653609
- Smith, J., Bekker, H., & Cheater, F. (2011). Theoretical versus pragmatic design in qualitative research. *Nurse Researcher*, 18(2), 39.
- Stein, S. A., Lamos, E. M., & Davis, S. N. (2013). A review of the efficacy and safety of oral antidiabetic drugs. *Expert Opinion On Drug Safety*, 12(2), 153-175. doi: 10.1517/14740338.2013.752813
- Strandberg, R. B., Graue, M., Wentzel-Larsen, T., Peyrot, M., Thordarson, H. B., & Rokne, B. (2015). Longitudinal relationship between diabetes-specific emotional distress and follow-up HbA1c in adults with Type 1 diabetes mellitus. *Diabetic Medicine: A Journal Of The British Diabetic Association*, 32(10), 1304-1310. doi: 10.1111/dme.12781
- Stratton, I., Adler, A., Neil, H., Matthews, D., Manley, S., Cull, C., Holman, R. (2000). Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *British Medical Journal*, 321(7258), 405-421.

-
- Stuart, A. R., Grzegorz, D., Jiten, V., Kamlesh, K., Marcel, K., & Robert, J. L. (2011). Impact of weight gain on outcomes in type 2 diabetes. *Current Medical Research & Opinion*, 27(7), 1431-1438. doi: 10.1185/03007995.2011.585396
- Sweileh, W. M., Zyoud, S. e. H., Abu Nab'a, R. J., Deleq, M. I., Enaia, M. I., Nassar, S. a. M., & Al-Jabi, S. W. (2014). Influence of patients' disease knowledge and beliefs about medicines on medication adherence: findings from a cross-sectional survey among patients with type 2 diabetes mellitus in Palestine. *BMC Public Health*, 14(1), 94-94. doi: 10.1186/1471-2458-14-94
- Taggart, L., Coates, V., & Truesdale-Kennedy, M. (2013). Management and quality indicators of diabetes mellitus in people with intellectual disabilities. *Journal of Intellectual Disability Research*, 57(12), 1152-1163. doi: 10.1111/j.1365-2788.2012.01633.x
- Tamariz, L., Palacio, A., Robert, M., & Marcus, E. N. (2013). Improving the informed consent process for research subjects with low literacy: A systematic review. *Journal Of General Internal Medicine*, 28(1), 121-126. doi: 10.1007/s11606-012-2133-2
- Tamir, O., Wainstein, J., Raz, I., Shemer, J., & Heymann, A. (2012). Quality of life and patient-perceived difficulties in the treatment of type 2 diabetes. *The Review Of Diabetic Studies: RDS*, 9(1), 46-54. doi: 10.1900/RDS.2012.9.46
- Teddle, C., & Tashakkori, A. (2009). *Mixed Methods Research: intergrating quantitative and qualitative approaches in the social and behavioural sciences*. London Sage publications.
- Thorne, S. (2011). Toward methodological emancipation in applied health research. *Qualitative Health Research*, 21(4), 443. doi: 10.1177/1049732310392595
- Tiktin, M., Celik, S., & Berard, L. (2016). Understanding adherence to medications in type 2 diabetes care and clinical trials to overcome barriers: A narrative review. *Current Medical Research And Opinion*, 32(2), 277-287. doi: 10.1185/03007995.2015.1119677
- Tomlin, A., & Sinclair, A. (2016). The influence of cognition on self-management of type 2 diabetes in older people. *Psychology Research and Behavior Management*, 9.
- Torjesen, I. (2013). People with learning disabilities are dying 16 years earlier than their counterparts, inquiry finds. *BMJ: British Medical Journal*, 346(7900), 1-1.
- Tracy, S. J. (2010). Qualitative Quality: Eight “Big- Tent” Criteria for Excellent Qualitative Research. *Qualitative Inquiry*, 16(10), 837-851. doi: 10.1177/1077800410383121
- Trip, H., Conder J., Hale L., Whitehead L. (2015). The role of key workers in supporting people with intellectual disability in the self-management of their diabetes: a qualitative New Zealand study. *Health and Social Care in the Community*.
- Turner, A., Hochschild, A., Burnett, J., Zulfiqar, A., & Dyer, C. B. (2012). High prevalence of medicines non-adherence in a sample of community-dwelling older adults with adult protective services-validated self-neglect. *Drugs & Aging*, 29(9), 741-749. doi: 10.1007/s40266-012-0007-2
- Turner, L., Shamseer, L., Altman, D. G., Weeks, L., Peters, J., Kober, T., Moher, D. (2012). Consolidated standards of reporting trials (CONSORT) and the completeness of reporting of randomised controlled trials (RCTs) published in medical journals. *Cochrane Methodology Review Group*(11). doi: 10.1002/14651858.MR000030.pub2
- Tveter, A. L., Bakken, T. L., Røssberg, J. I., Bech-Pedersen, E., & Bramness, J. G. (2016). Short communication: reliability and validity of the UKU Side Effect Rating Scale for adults with intellectual disabilities. *Advances in Mental Health & Intellectual Disabilities*, 10(3), 166-171. doi: 10.1108/AMHID-10-2015-0051

- Tyler, C. V., Jr., Schramm, S., Karafa, M., Tang, A. S., & Jain, A. (2010). Electronic health record analysis of the primary care of adults with intellectual and other developmental disabilities. *Journal of Policy and Practice in Intellectual Disabilities*, 7(3), 204-210. doi: 10.1111/j.1741-1130.2010.00266.x
- Udo, K. (2014). *Qualitative Text Analysis: A Guide to Methods, Practice & Using Software*. London.
- UN. (2007). Convention on the Rights of Persons with Disabilities. Retrieved June, 2017, from <https://www.un.org/development/desa/disabilities/convention-on-the-rights-of-persons-with-disabilities.html>
- Unwin, G., Tsimopoulou, I., Kroese, B. S., & Azmi, S. (2016). Effectiveness of cognitive behavioural therapy (CBT) programmes for anxiety or depression in adults with intellectual disabilities: A review of the literature. *Research in Developmental Disabilities*, 51-52, 60-75. doi: 10.1016/j.ridd.2015.12.010
- Viswanathan, M., Golin, C. E., Jones, C. D., Ashok, M., Blalock, S. J., Wines, R. C. M., Lohr, K. N. (2012). Interventions to Improve Adherence to Self-administered Medications for Chronic Diseases in the United States: A Systematic Review. *Annals of Internal Medicine*, 157(11), 785-795. doi: 10.7326/0003-4819-157-11-201212040-00538
- Vogt, W. P. (2011). *SAGE Quantitative Research Methods*.
- Vos, R. C., van Avendonk, M. J., Jansen, H., Goudswaard, A. N., van den Donk, M., Gorter, K., Rutten, G. E. (2016). Insulin monotherapy compared with the addition of oral glucose-lowering agents to insulin for people with type 2 diabetes already on insulin therapy and inadequate glycaemic control. *The Cochrane Database Of Systematic Reviews*, 9, CD006992.
- Wagner, J. A., Tennen, H., & Osborn, C. Y. (2010). Lifetime depression and diabetes self-management in women with Type 2 diabetes: a case-control study. *Diabetic Medicine: A Journal Of The British Diabetic Association*, 27(6), 713-717.
- Wallia, A., & Molitch, M. E. (2014). Insulin therapy for type 2 diabetes mellitus. *Journal of the American Medical Association*, 311(22), 2315-2325. doi: 10.1001/jama.2014.5951
- Wasserfallen, J.-B., Livio, F., Buclin, T., Tillet, L., Yersin, B., & Biollaz, J. (2001). Rate, type, and cost of adverse drug reactions in emergency department admissions. *European Journal of Internal Medicine*, 12(5), 442-447. doi: [http://dx.doi.org/10.1016/S0953-6205\(01\)00159-5](http://dx.doi.org/10.1016/S0953-6205(01)00159-5)
- Whitehead, L. C., Trip, H. Hale, L.A. & Conder, J. (2016). Negotiated autonomy in diabetes self-management: the experiences of adults with intellectual disability and their support workers. *Journal of Intellectual Disability Research*, 60(4), 389-397.
- Whitworth, S. R., Bruce, D. G., Starkstein, S. E., Davis, W. A., Davis, T. M. E., & Bucks, R. S. (2016). Lifetime depression and anxiety increase prevalent psychological symptoms and worsen glycemic control in type 2 diabetes: The Fremantle Diabetes Study Phase II. *Diabetes Research And Clinical Practice*, 122, 190-197. doi: 10.1016/j.diabres.2016.10.023
- WHO. (1996). *ICD-10 guide for mental retardation*. Geneva: World Health Organisation Retrieved from http://www.who.int/mental_health/media/en/69.pdf.
- WHO. (2013). Definition: intellectual disability. Retrieved 25/08, 2013, from <http://www.euro.who.int/en/what-we-do/health-topics/noncommunicable-diseases/mental-health/news/news/2010/15/childrens-right-to-family-life/definition-intellectual-disability>
- WHO. (2016). Global report on diabetes. Retrieved June, 2017, from http://apps.who.int/iris/bitstream/10665/204871/1/9789241565257_eng.pdf?ua=1

-
- Williams, J. (2013). Generic qualitative research: is it a second rate option? *International Journal Of Qualitative Methods*, 12, 834-834.
- Williams, K. E., & Bond, M. J. (2002). The roles of self-efficacy, outcome expectancies and social support in the self-care behaviours of diabetics. *Psychology, Health & Medicine*, 7(2), 127-141. doi: 10.1080/13548500120116076
- Wilson, P., Mathie, E., Keenan, J., McNeilly, E., Goodman, C., Howe, A., . . . Peckham, S. (2015). ReseArch with Patient and Public invOLvement: a RealisT evaluation – the RAPPORT study. doi: 10.3310/hsdr03380
- Witham, G., Beddow, A., & Haigh, C. (2015). Reflections on access: too vulnerable to research? *Journal of Research in Nursing*, 20(1), 28-37. doi: 10.1177/1744987113499338
- World Medical Organisation (WMO). (1996). Declaration of Helsinki. *British Medical Journal*, 313(7070), 1448-1449.
- Wong, M. C. S., Wu, C. H. M., Wang, H. H. X., Li, H. W., Hui, E. M. T., Lam, A. T., Morisky, D. E. (2015). Association between the 8-item Morisky medication adherence scale (MMAS-8) score and glycaemic control among Chinese diabetes patients. *Journal Of Clinical Pharmacology*, 55(3), 279-287. doi: 10.1002/jcph.408
- Wright, A., Burden, A., Paisey, R., Cull, C., & Holman, R. (2002). Sulfonylurea inadequacy: efficacy of addition of insulin over 6 years in patients with type 2 diabetes in the U.K. Prospective Diabetes Study (UKPDS 57). *Diabetes Care.*, 25(2), 330-336.
- Zogg, J., Woods, S., Saucedo, J., Wiebe, J., & Simoni, J. (2012). The role of prospective memory in medication adherence: a review of an emerging literature. *Journal of Behavioral Medicine*, 35(1), 47-62. doi: 10.1007/s10865-011-9341-9
- Zoungas, S., Arima, H., Gerstein, H. C., Holman, R. R., Woodward, M., Reaven, P., Chalmers, J. (2017). Effects of intensive glucose control on microvascular outcomes in patients with type 2 diabetes: a meta-analysis of individual participant data from randomised controlled trials. *The Lancet. Diabetes & Endocrinology*. doi: 10.1016/S2213-8587(17)30104-3