Receptiveness and Resistance: Perceptions of Insulin Use in Type 2 Diabetes

by

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Submitted in fulfilment of the requirements for the degree of Doctor of Philosophy (Psychology)

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I am the author of the thesis entitled Receptiveness and Resistance: Perceptions of Insulin Use in Type 2 Diabetes

submitted for the degree of Doctor of Philosophy

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Manuscripts Included in Thesis

The following manuscripts published or submitted for publication form empirical chapters in the current thesis. Authorship statements for each publication are included in Appendix A. Journal permissions are presented in Appendix B.

Refereed Journal Articles


Submitted for Publication


Associated Conference Presentations


ADEA Annual Scientific Meeting, Adelaide.


Additional Manuscripts

The following report and published manuscripts co-authored by the PhD candidate are associated with the current research but are not presented in this thesis.

Refereed Journal Articles


Speight, J., Browne, J.L., Holmes-Truscott, E., Hendrieckx, C., Pouwer, F. (2012). Diabetes MILES – Australia (Management and Impact for Long-term Empowerment and Success): Methods and sample characteristics of a national survey of the psychological aspects of living with type 1 or type 2 diabetes in

**Submitted for Publication**


**Non-Refereed Report**

Abstract

Type 2 diabetes (T2D) is a progressive chronic condition requiring timely treatment intensification to prevent/delay the development of long-term complications associated with prolonged hyperglycaemia. Despite the proven efficacy of insulin therapy in reducing hyperglycaemia (and international guidelines recommending early initiation), insulin uptake and intensification are commonly delayed in practice. Several barriers exist at the systemic and healthcare professional levels, while people with T2D may also be reluctant to intensify treatment.

The aim of this thesis was to investigate attitudes to insulin therapy among adults with T2D, focusing on the constructs of ‘psychological insulin resistance’ (PIR) and ‘receptiveness’. This program of doctoral research was designed to generate new knowledge in relation to: a) the measurement of these constructs; b) the occurrence of, and factors associated with, PIR and receptiveness to insulin initiation; c) the demographic, clinical and psychological predictors of actual insulin uptake; and d) attitudes toward insulin post-initiation, perceptions of benefits and consequences of insulin, and attitudes to further treatment intensification.

A mixed methods approach was taken, using data from three studies: 1) a national cross-sectional survey of adults with T2D, 2) a two-armed, 12-month, cluster randomised controlled trial (RCT) in a primary care setting, testing a new model of care designed to facilitate timely insulin initiation among adults with T2D for whom insulin is clinical indicated, 3) an exploratory qualitative interview study with adults with insulin-treated T2D. This thesis presents the findings of those studies in six empirical reports.
The Insulin Treatment Appraisal Scale (ITAS) is a widely used measure of insulin appraisals. Data from the national survey (Study 1a; paper 1) confirmed its psychometric properties in an Australian population, separately for insulin-treated and non-insulin-treated sub-samples. The scale was acceptable and psychometrically sound in both groups but the use of the subscale (ITAS Negative and Positive) scores is recommended in preference to the Total scale.

Factors associated with ITAS Negative scores among adults with non-insulin-treated T2D were examined (Study 1b; paper 2). Negative insulin appraisals were associated with the emotional burden of diabetes (diabetes-related distress) and concerns about current diabetes medications (i.e. oral hypoglycaemic agents). This suggests that identifying and addressing these issues may help to improve receptiveness to future treatment intensification.

PIR/receptiveness has commonly been quantified as ‘hypothetical willingness’, or intention, to begin insulin – but the validity of this measure in predicting actual insulin uptake has never been tested. At baseline, 19% of RCT participants were ‘very willing’ to begin insulin therapy, if recommended, and this was associated with higher socioeconomic status, less negative and more positive insulin appraisals (Study 2a; paper 3). Controlling for study arm allocation, greater intention and higher HbA1c independently predicted insulin initiation at 12 months (Study 2b; paper 4). Thus, interventions to promote timely insulin initiation should aim to reduce PIR and improve receptiveness among people with T2D.

Change in negative, but not positive, insulin appraisals at 12 months was associated with insulin uptake among RCT participants, corroborating previous research. However, experience with insulin alone may not mitigate the negative
impact of insulin therapy universally. In the national survey, adults with insulin-treated T2D reporting higher ITAS Negative scores were more likely to report worse general and diabetes-specific emotional wellbeing, and lower diabetes-specific self-efficacy and satisfaction with blood glucose, than those with less negative insulin appraisals (Study 1c; paper 5). In the final qualitative study (Study 3; paper 6), in addition to the perceived benefits of using insulin (e.g. improved blood glucose levels), adults with insulin-treated T2D also identified disadvantages, some of which are not captured within the ITAS. Further, while most participants reported receptiveness to insulin intensification, the perceived inconvenience of additional insulin injections and concerns about more intensive insulin regimens were barriers for some. These findings highlight the impact of PIR and receptiveness beyond insulin uptake and the need to identify and address ongoing, or new, concerns throughout treatment progression.
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>BMQ</td>
<td>Beliefs about Medications Questionnaire</td>
</tr>
<tr>
<td>DDS</td>
<td>Diabetes Distress Scale</td>
</tr>
<tr>
<td>DES-SF</td>
<td>Diabetes Empowerment Scale – Short Form</td>
</tr>
<tr>
<td>GAD-7</td>
<td>Generalised Anxiety Disorder, 7-item version</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Haemoglobin A1c; a measure of average blood glucose over an 8-12 week period</td>
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<tr>
<td>HCP</td>
<td>Healthcare Professional</td>
</tr>
<tr>
<td>IRSAD</td>
<td>Index of Relative Socioeconomic Advantage and Disadvantage</td>
</tr>
<tr>
<td>ITAS</td>
<td>Insulin Treatment Appraisal Scale</td>
</tr>
<tr>
<td>MARS</td>
<td>Medication Adherence Rating Scale</td>
</tr>
<tr>
<td>MILES</td>
<td>Management and Impact for Long-term Empowerment and Success</td>
</tr>
<tr>
<td>PAID</td>
<td>Problem Areas In Diabetes</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>Patient Health Questionnaire, 9-item version</td>
</tr>
<tr>
<td>PIR</td>
<td>Psychological Insulin Resistance</td>
</tr>
<tr>
<td>RACGP</td>
<td>The Royal Australian College of General Practitioners</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised Controlled Trial</td>
</tr>
<tr>
<td>SMBG</td>
<td>Self-Monitoring of Blood Glucose</td>
</tr>
<tr>
<td>SPSS</td>
<td>Statistical Package for Social Sciences</td>
</tr>
<tr>
<td>T2D</td>
<td>Type 2 Diabetes</td>
</tr>
<tr>
<td>GLP-1</td>
<td>Glucagon-Like Peptide-1</td>
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Outline of Thesis

The aim of this research was to examine attitudes toward insulin therapy, or psychological insulin resistance (PIR) and receptiveness, among adults with type 2 diabetes (T2D) in Australia. This program of the research was designed to contribute to our understanding of a) the measurement and b) the occurrence of, and factors associated with, PIR and receptiveness among Australians with non-insulin-treated T2D, c) the demographic, clinical and psychological predictors of actual insulin uptake, d) attitudes toward insulin post-initiation, perceptions of benefits and consequences of insulin, and attitudes to further treatment intensification.

This thesis consists of 10 chapters, including six independent but related empirical papers, (Chapters 4-9), reporting on data collected from three research studies (1) Diabetes MILES – Australia, a national cross-sectional survey, 2) Stepping Up, a cluster randomised controlled trial (RCT), and 3) Insulin Appraisals, a qualitative study). Figure 1 provides a schematic representation of the research aims of this thesis, the study in which relevant data were collected, and the resulting empirical paper(s).
Chapter 1 (Introduction) describes the condition, management, and prevalence of T2D as well as the problem of delayed insulin intensification. In Chapter 2 (Literature Review), the concepts of PIR and receptiveness are defined and barriers to as well as facilitators of insulin initiation, ongoing use, and intensification are examined. Chapter 3 (Methodology) summaries the methods used, and the research
questions asked of the three broad research studies. A detailed description of the methods is provided in Appendix C.

The first empirical study (Chapter 4, Paper 1: Further investigation of the psychometric properties of the insulin treatment appraisal scale among insulin-using and non-insulin-using adults with type 2 diabetes: Results from Diabetes MILES – Australia) uses cross-sectional data (Study 1: Diabetes MILES – Australia) to undertake psychometric validation of an existing measure of insulin therapy appraisals within an Australian sample. Chapters 5 and 6 both examine attitudes towards insulin and associated factors among adults with non-insulin-treated T2D. In Chapter 5 (Paper 2: Explaining psychological insulin resistance in adults with non-insulin-treated type 2 diabetes: The roles of diabetes distress and current medication concerns. Results from Diabetes MILES – Australia), negative attitudes towards insulin therapy are examined among those not yet using insulin at a national level, drawing upon data from Study 1 (Diabetes MILES – Australia). The relationship between negative attitudes towards insulin and general and diabetes-specific wellbeing and beliefs about medications is examined. In Chapter 6 (Paper 3: Willingness to initiate insulin among adults with type 2 diabetes in Australian primary care: Results from the Stepping Up study), attitudes towards insulin and hypothetical insulin uptake are examined among a clinical sample (Study 2: Stepping Up RCT) of adults with T2D for whom insulin has been clinically indicated. In this paper, clinical, demographic and psychological factors associated with hypothetical willingness to begin insulin were identified.

Chapter 7 (Paper 4: Predictors of insulin uptake among adults with type 2 diabetes in the Stepping Up study) presents longitudinal data (baseline and 12-month
follow-up) gathered in the Stepping Up RCT. Paper 4 examines 1) demographic, clinical and psychological predictors of actual insulin uptake, controlling for the Stepping Up intervention, and 2) change in attitudes towards insulin as a function of the intervention and insulin uptake.

In Chapters 8 and 9 (Papers 5 and 6), the research focus moves to the exploration of insulin appraisals among those already using insulin. Chapter 8 (Paper 5: Negative appraisals of insulin therapy are common among adults with type 2 diabetes using insulin: Results from Diabetes MILES – Australia cross-sectional survey), using data from Study 1 (Diabetes MILES – Australia), examines whether negative insulin appraisals are common among adults with T2D already using insulin therapy and identifies demographic, clinical, self-management and psychosocial outcomes that differ for those with more and less negative insulin appraisals. Chapter 9 (Paper 6: The impact of insulin therapy and attitudes towards insulin intensification among adults with type 2 diabetes: A qualitative study) reports on qualitative findings of an interview study (Study 3: Insulin Appraisals) involving adults with T2D who have initiated insulin use within the past four years. This paper aims to identify positive and negative consequences of insulin use, post-initiation, and attitudes to ongoing use and insulin intensification.

Finally, Chapter 10 (General Discussion) presents an integrated synthesis of the thesis. In this chapter, the findings of the empirical papers are summarised and discussed in relation to the literature reviewed in Chapter 2. Strengths and limitations of the empirical studies are discussed, as well as clinical and research implications, and recommendations for future research.
Chapter 1: Introduction

This chapter describes T2D, its prevalence, and management. The problem of delayed insulin initiation and intensification is introduced.

1.1. What is Type 2 Diabetes?

T2D is a chronic condition characterised by the inability of the pancreatic beta cells to produce sufficient or effective insulin (insulin deficiency) or the body to use it effectively (insulin resistance). Insulin is required for the body to convert glucose into energy. T2D is a progressive condition, with complete beta cell failure generally occurring within 10 years of onset for most individuals (U.K. Prospective Diabetes Study Group, 1995). Loss of beta cell function causes an increase of glucose circulating in the blood stream, otherwise known as hyperglycaemia. The body reacts to hyperglycaemia by secreting more insulin, resulting in exhaustion of the beta cells and, eventually, less production of insulin and/or insulin resistance. Prolonged, untreated hyperglycaemia increases the risk of developing micro-vascular complications (e.g. neuropathy, nephropathy, retinopathy) and macro-vascular complications (e.g. peripheral vascular diseases, heart disease) (Adler et al., 2002; Stratton et al., 2000).

Symptoms of hyperglycaemia include lethargy, increased thirst and frequent urination, blurred vision, loss of sensation, poor wound healing and increased fungal or bacterial infections. However, in its early stages T2D may be asymptomatic and go undiagnosed for several years (American Diabetes Association, 2004). The Royal Australian College of General Practitioners’ (RACGP (2014)) clinical guidelines for the management of T2D indicate that clinical testing should be conducted if a person is experiencing the above symptoms, has risk factors for T2D, or exhibits clinical
signs of insulin resistance. T2D may be diagnosed through measurement of fasting or random blood glucose, oral glucose tolerance testing, or glycated haemoglobin (HbA1c), a measure of the average amount of glucose in the bloodstream over an 8-12 week period. Specifically, diagnostic criteria include, on two separate occasions: HbA1c ≥6.5% (48 mmol/mol), fasting blood glucose of ≥7.0 mmol/L or a two-hour post-prandial oral glucose of ≥11.0 mmol/L.

1.2. Causes of Type 2 Diabetes

The exact cause of T2D is unknown but risk factors are well established. Risk factors may be non-modifiable (i.e. genetic predisposition, family history, age) or potentially modifiable (i.e. overweight or obesity, poor nutrition and physical inactivity). As T2D most commonly develops in adults over the age of 40 years, clinical guidelines suggest that all individuals be screened for T2D every three years from this age (The Royal Australian College of General Practitioners and Diabetes Australia, 2014). However, T2D is increasing among people of younger ages, including adolescents (Dunstan et al., 2002; Lammi et al., 2007; Pinhas-Hamiel & Zeitler, 2005; SEARCH for Diabetes in Youth Study Group et al., 2006), largely associated with modifiable risk factors.

Landmark studies have demonstrated that T2D can be prevented in up to 58% of cases through lifestyle modifications (Lindström et al., 2006; Tuomilehto et al., 2001). Indeed, physical activity and dietary modifications are recommended in diabetes care guidelines (The Royal Australian College of General Practitioners and Diabetes Australia, 2014). However, personal efforts at undertaking lifestyle modifications and reducing weight may be hampered by the so-called ‘obesogenic’ environment (e.g. lack of public space, availability of energy dense/low cost foods,
large portion sizes) (Egger & Swinburn, 1997; Swinburn et al., 2011). A singular focus on the modifiable risks alone, ignoring the non-modifiable risks and the role of environment, may lead to unintended consequences (Browne, Zimmet, & Speight, 2011). The perception of T2D as a ‘lifestyle disease’ may create or reinforce stigma around diabetes and obesity (Browne, Ventura, Mosely, & Speight, 2013; Kalra & Baruah, 2015; Schabert, Browne, Mosely, & Speight, 2012). Recent Australian and international research has highlighted that adults with T2D experience diabetes-related stigma, including feeling blamed for bringing the condition on themselves (Browne et al., 2013; Stuckey et al., 2014).

1.3. Prevalence of Type 2 Diabetes Globally and in Australia

T2D is a global emergency with over 400 million adults currently living with the condition and this number is expected to rise to 642 million by 2040 (International Diabetes Federation, 2015). Approximately 1.2 million Australians are registered with the National Diabetes Services Scheme (NDSS), of which 86% have T2D (National Diabetes Services Scheme, 2016a), and it is estimated that for every four adult Australians with diagnosed T2D, another lives with the condition undiagnosed (Australian Bureau of Statistics, 2013).

T2D was the sixth leading cause of death in Australia in 2011, accounting for 10% of all deaths (Australian Institute of Health and Welfare, 2014), and diabetes is expected to be the leading cause of disease burden by 2023 for males and the second leading cause for females (Australian Institute of Health and Welfare, 2010). The

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1 Australians with diabetes are eligible to register with the National Diabetes Services Scheme (NDSS) to access a large range of subsidised diabetes self-management products and services. The NDSS is an initiative of the Australian Government and is administered with the assistance of Diabetes Australia.
indirect cost of diabetes to the Australian community is nearly $15 billion annually and this is expected to double by 2025 (Australian Government Department of Health, 2015)

1.4. Management of Type 2 Diabetes

While there is no known cure for T2D, lifestyle modifications, such as increased physical activity, weight loss and healthy eating, and a range of pharmacological treatments can be effective in managing hyperglycaemia. Guidelines recommend a staged pharmacological management plan with increasing intensification of treatment from lifestyle modifications, to the introduction of oral hypoglycaemic agents (OHAs), glucagon-like-peptide-1 (GLP1) receptor agonists and insulin therapy (Gunton, Cheung, Davis, Zoungas, & Colagiuri, 2014; International Diabetes Federation, 2012; Inzucchi et al., 2015; Nathan et al., 2009).

The efficacy of pharmacological therapies is determined largely by their impact on blood glucose levels, which is clinically assessed in terms of HbA1c. The standard recommended target HbA1c for people with T2D is <7% (<53 mmol/mol) (International Diabetes Federation, 2012), though individualisation of targets is recommended. The American Diabetes Association and the European Association for the Study of Diabetes position statement on the management of hyperglycaemia in T2D highlights the need to consider both non-modifiable clinical characteristics (i.e. disease duration, life expectancy, established comorbidities, medication side effects) as well as potentially modifiable characteristics (i.e. access to resources and support systems, and attitudes, ability and desire to undertake the treatment change) to determine the optimal HbA1c target for each presenting individual with T2D (Inzucchi et al., 2015). Timely intensification of treatment and achieving, and
maintaining, optimal HbA1c is associated with significantly reduced risk of the development or progression of micro-vascular complications (U.K. Prospective Diabetes Study Group, 1998). HbA1c should be assessed every 3-6 months (The Royal Australian College of General Practitioners and Diabetes Australia, 2014).

Blood glucose may be assessed through self-monitoring, which typically involves the use of a lancet device to finger prick, adding a drop of blood onto a blood testing strip, and finally inserting the strip into a blood glucose meter, which displays the blood glucose reading in terms of millimols per litre of blood (mmol/L). Self-monitoring of blood glucose (SMBG) can be used, for example, to identify, and inform treatment of, hyperglycaemia or hypoglycaemia (defined as a low blood glucose reading <3.5 mmol/L (Frier, 2009)), and, to reflect on glucose patterns. The recommended target blood glucose range for a person with diabetes is 6-8 mmol/L pre-prandial (pre-meal) and 6-10 mmol/L two hours postprandial (post-meal) (Colagiuri, Dickinson, Girgis, & Colagiuri, 2009). Use and frequency of SMBG depends on the individual’s circumstances and therapeutic aims. Among adults with non-insulin-treated T2D, SMBG has been found to provide limited clinical benefits in terms of glycaemia improvements (Malanda et al., 2012). Consequently, in July 2016, the Australian Federal Government implemented a new policy to restrict the access to subsidised test strips for people with non-insulin-treated T2D. Access will now be provided only in cases where an authorised healthcare professional (HCP) ‘considers it clinically necessary’ (Australian Government Department of Health, 2016). SMBG remains recommended for people with T2D using insulin therapy. Other ‘clinically necessary’ cases may include during pregnancy or when changes in treatment, lifestyle or health require monitoring of blood glucose patterns (The Royal Australian College of General Practitioners and Diabetes Australia, 2014).
While there is little evidence for the effectiveness of the routine recommendation of ‘unstructured’ SMBG (Malanda et al., 2012), a ‘structured’ approach to SMBG, for example, a three-day period of intensive monitoring and recording at specific times in the week prior to a HCP consultation, has demonstrated clinical benefit (Speight, Browne, & Furler, 2013). Trials of structured SMBG among adults with non-insulin-treated T2D have demonstrated effectiveness in terms of reduced HbA1c, as well as offering benefits for emotional wellbeing (Polonsky et al., 2011) and confidence in diabetes self-care (Fisher et al., 2012). Thus, it has been argued that the government restriction is short-sighted (Speight, Browne, & Furler, 2015), and should instead advocate for a focused, structured approach to SMBG among those not using insulin to inform T2D management.

1.4.1. Insulin therapy

Insulin therapy is the only diabetes management option that can maintain optimal blood glucose levels throughout the progression of beta cell failure. Through the prevention of diabetes-related complications, insulin use can contribute indirectly to maintaining both quantity and quality of life (Pouwer & Hermanns, 2009). International guidelines emphasise the early consideration and initiation of insulin therapy among people with T2D for whom target glycaemic outcomes are not achieved with maximum OHAs (Inzucchi et al., 2015; Nathan et al., 2009).

Insulin must be injected through the skin subcutaneously. Less invasive modes of administration are the focus of much research, including, for example, inhaled, oral and nasal insulins (Shah, Patel, Maahs, & Shah, 2016). However, to date, no alternatives to subcutaneously-injected insulin are approved for use in Australia. Insulin injections may be delivered either using a syringe and vial, a preloaded or
reusable insulin ‘pen’ injector, or an insulin pump. An insulin pump is a small programmable device worn outside the body that delivers insulin through a plastic tube connected to a fine needle inserted under the skin. Insulin syringes and pen needles are freely available from the NDSS for Australians with T2D using insulin therapy. However, insulin pump consumables (tubing and needles) are not currently subsidised by the NDSS for people with insulin-treated T2D.

In addition to the invasive nature of insulin injections, there are two main side effects of insulin therapy: hypoglycaemia and weight gain. Hypoglycaemia, a blood glucose level <3.5 mmol/L (Frier, 2009), is caused by a relative excess of insulin in the body. This may be due to too much insulin injected or ‘on-board’, increased physical activity, or consuming less carbohydrates (glucose) than required. Early symptoms of hypoglycaemia vary but can include shaking, sweating, light-headedness, confusions, and mood change. If the individual is awake and able to swallow, hypoglycaemia can be treated with consumption of a quick-acting glucose (e.g. juice, jellybeans), followed by SMBG and additional long-acting carbohydrate (e.g. toast) if required. If hypoglycaemia is not treated early, and blood glucose continues to drop, the person may experience an episode of severe hypoglycaemia, characterised by the inability to self-treat, and require the assistance of another person for recovery (Strachan & Frier, 2013). The other key side effect of insulin is weight gain: an increase (approximately 2-4 kilograms) is commonly reported after insulin initiation (Holman et al., 2007; Pontiroli, Miele, & Morabito, 2011; U.K. Prospective Diabetes Study Group, 1998). Reasons for weight gain include the reduction in calorie loss due to the body’s improved ability to absorb glucose and an increase in calorie intake to feed insulin doses and/or combat hypoglycaemia (Strachan & Frier, 2013).
There are five categories of insulin available, differing in terms of how quickly they begin working and how long they last, which informs how many times they should be taken per day and at what times of day (e.g. once-daily injections, 30 minutes before a meal) (NPS MedicineWise, 2016). For people with T2D, the RACGP and Diabetes Australia (2014) recommend that the initiation of insulin involve the prescription of either a once-daily injection of basal insulin (long-acting insulin, lasts up to 24 hours) or a once-daily injection of pre-mixed insulin (combination of both intermediate acting insulin, lasting 16-24 hours, and either short or rapid fast-acting insulins) injection taken prior to the largest meal of the day. The insulin dosage may then be adjusted in the short term in response to changes in glucose levels. If HbA1c is not within target after three months or more following initiation of once-daily insulin injections, insulin intensification may be required. Insulin intensification may include an increased dose or additional injections (e.g. a single additional injection or several meal-related injections per day), which may require changes in the type of insulin used (e.g. addition of pre-prandial short-acting insulin or pre-mixed insulin injections).

1.4.2. Healthcare professional(s) and self-care roles

Clinical guidelines for the management of diabetes highlight the need for person-centred (or patient-centred) care (Inzucchi et al., 2012; The Royal Australian College of General Practitioners and Diabetes Australia, 2014). Person-centred care is “respectful of and responsive to individual patient preferences, needs, and values, and ensuring that patient values guide all clinical decisions” (Institute of Medicine Committee on Quality of Health Care in America, 2001). The role of the HCP in the management of T2D is to assess the health of the person with T2D and provide
timely recommendations for treatment (such as insulin initiation) in the context of the person’s needs, priorities and abilities. Ongoing diabetes education (both directly and through referral to specialists and structured diabetes education programs as necessary) is needed to provide the person with diabetes with adequate understanding with which to make informed treatment decisions and undertake optimal daily diabetes self-management (e.g. SMBG, monitor/adjust (multiple) daily injections, manage food intake and physical activity in relation to glucose levels). T2D self-management is a life-long, and daily, responsibility for a person living with the condition, and is often complicated by the need to concurrently manage one or more additional chronic condition (i.e. multimorbidity) (Luijks et al., 2012; Struijs, Baan, Schellevis, Westert, & van den Bos, 2006; Teljeur, Smith, Paul, Kelly, & O’Dowd, 2013). While the role of the HCP is prescription and communication, it is the person with T2D, not the HCP, who must perform the daily management of diabetes and live with the consequences of their decisions (Anderson, 1985).

1.5. The Problem: Delayed Insulin Initiation or Intensification and Insulin Omission

Despite the proven efficacy of insulin in reducing hyperglycaemia and delaying/slowing progression of diabetes-related complications (U.K. Prospective Diabetes Study Group, 1998), there exists a mismatch between the number of people with T2D using insulin and the number who have a Hba1c and diabetes history suggestive of the need to initiate insulin (S. Khunti, Davies, & Khunti, 2015). For example, in the Australian ‘Fremantle Study’, transition to insulin occurred at a median diabetes duration of eight years and a median Hba1c of 9.4% (79mmol/mol) (Davis, Davis, & Bruce, 2006). This is corroborated by more recent data indicating
that only 24% of Australians with T2D (approximately 250,000 people) are using insulin to manage their diabetes (National Diabetes Services Scheme, 2016b), despite reports that mean HbA1c is above target (8%, 64 mmol/mol) (National Association of Diabetes Centres, 2009; Swerissen, Duckett, & Wright, 2016). A recent review of chronic disease management in Australian primary care reported that 40% of adults with T2D did not have blood glucose data recorded, and of those with recorded data only one in four had within target HbA1c (≤7.0%, ≤53 mmol/mol) (Swerissen et al., 2016). Similar results have been found internationally. In Canada, the mean diabetes duration and HbA1c prior to insulin initiation is nine years and 9.5% (80mmol/mol) respectively (Harris, Kapor, Lank, Willan, & Houston, 2010); in the USA (Curtis & Lage, 2014) and the UK (Blak, Smith, Hards, Maguire, & Gimeno, 2012), mean HbA1c at insulin initiation was 8.6% (70mmol/mol) and 9.3% (78mmol/mol) respectively; and a multi-country primary care study reported a mean of 8.9% (74mmol/mol) (K. Khunti, Damci, Meneghini, Pan, & Yale, 2012). In a South London prospective observational cohort study of newly diagnosed adults with T2D (N=1,335), one-third of the 7% who had initiated insulin at follow-up had experienced an insulin initiation delay according to clinical guidelines and the authors ascertained that a further 10% of the overall sample required insulin therapy but had not yet commenced (Keij, Ismail, & Winkley, 2016).

Beyond insulin initiation, delayed intensification and insulin omission (i.e. purposefully or mistakenly skipping an insulin injection, or taking less insulin than required) may cause prolonged hyperglycaemia among people with T2D already using insulin. Among those already using insulin, recent studies have explored time until, and HbA1c at the time of, insulin intensification, suggesting a mismatch between clinical practice and clinical guidelines (Fulcher, Roberts, Sinha, & Proietto,
Rates of insulin omission vary across studies (Davies et al., 2013). For example, a previous US study reported that 20% of adults using insulin therapy skip their injections often or some of the time (Rubin, Peyrot, Kruger, & Travis, 2009), while in a more recent US study, 46% of participants reported ‘non-adherence’ to their insulin regimen over the two weeks prior (Osborn & Gonzalez, 2016).

The delay in insulin initiation and intensification may be, in part, due to a lack of recommendation/prescription by the HCP known as clinical inertia (which is discussed elsewhere: Shaefer, 2006). It may also be due to a phenomenon known as ‘psychological insulin resistance’ (PIR), negative attitudes to insulin therapy experienced by a person with T2D which may lead to reluctance to commence or intensify insulin therapy (Leslie, Satin-Rapaport, Matheson, Stone, & Enfield, 1994). In contrast, positive attitudes, or receptiveness, to insulin therapy may be associated with insulin uptake. The focus of this thesis is on understanding PIR and receptiveness to insulin therapy initiation, use, and intensification among Australian adults with T2D throughout treatment progression.
1.6. References


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Chapter 2: Literature Review: Understanding Attitudes towards Insulin among Adults with Type 2 Diabetes

2.1. The Literature Review in Context

In this chapter, the terms ‘psychological insulin resistance’ (PIR) and insulin ‘receptiveness’ are defined and a synthesis of existing research exploring attitudes to insulin therapy among adults with T2D is presented. In addition, quantitative measures of PIR and receptiveness and associated concepts are explored. Throughout, gaps in the existing literature are identified, serving to provide a rationale for the research undertaken.

The program of research described in this thesis commenced in 2012, and since that time, research examining PIR has developed considerably, with new publications focused on PIR including: systematic reviews (S. Khunti, Davies, & Khunti, 2015; Ng, Lai, Lee, Azmi, & Teo, 2015), qualitative studies (e.g. Hu, Amirehsani, Wallace, & Letvak, 2013; Y. K. Lee, Low, Lee, & Ng, 2015; Patel, Stone, McDonough, et al., 2015) and cross-sectional quantitative studies (Fu, Wong, Chin, & Luk, 2016; Gherman & Alionescu, 2015; Machinani, Bazargan-Hejazi, & Hsia, 2012). Prior to 2012, no interventions to reduce PIR had been developed or evaluated, but recent years have seen the publication of intervention pilots to improve attitudes toward or education about insulin therapy (e.g. Patel, Stone, Hadjiconstantinou, et al., 2015). Until recently, a major limitation of PIR research was the lack of longitudinal research assessing change in insulin appraisals and predictors of insulin uptake. This, too, is changing with the inclusion of measures of insulin appraisals in recent longitudinal multi-centre studies (Keij, Ismail, &
Winkley, 2016; Odawara, Ishii, Tajima, & Iwamoto, 2016) and trials (Hermanns et al., 2015; Liebl et al., 2013). Finally, the inclusion of insulin omission and/or reluctance to intensify insulin therapy in the conceptual understanding of PIR was uncommon at the commencement of this program of research. A recent systematic review has highlighted the need for additional research in this area (Polinski et al., 2012). The study chapters, which were submitted for publication from 2013 to 2016, may draw attention to gaps in the literature that no longer exist, and exclude references to more recent literature. However, important research conducted after 2012 is incorporated within this chapter, with reference to its recency.

2.2. Defining Psychological Insulin Resistance and Receptiveness

Diabetes self-management typically requires a multitude of daily decisions and behaviours, for example: undertaking, and possibly recording and responding to, SMBG; dietary modifications and increased physical activity (for weight management and/or in response to glucose levels); as well as, administration of medications throughout the day. A key determinant of undertaking a health behaviour, for example: insulin use, is an individual’s attitudes or beliefs about the behaviour and its intended outcome (Michie, Johnston, Francis, Hardeman, & Eccles, 2008). Negative perceptions of the physical or psychological impact of insulin use may lead to a reluctance to initiate insulin therapy.

PIR has been conceptualised as negative attitudes toward insulin which may lead to a reluctance to use insulin therapy among people with T2D, typically referring to initiation of insulin rather than ongoing use. Although this concept first appeared in the field 20 years ago (Leslie & Satin-Rapaport, 1995; Leslie, Satin-Rapaport, Matheson, Stone, & Enfield, 1994), research has grown significantly over
the past decade. Systematic reviews provide an overview of the definitions and components of PIR, its impact on diabetes management, as well as a synthesis of the measures and predictors of, and proposed interventions to reduce, PIR (Brod, Kongsø, Lessard, & Christensen, 2009; Gherman et al., 2011; Ng et al., 2015; Wang & Yeh, 2012). Receptiveness has been quantified as a lack of PIR, exhibited through willingness to initiate insulin (Jenkins, Hallowell, Farmer, Holman, & Lawton, 2010; Polonsky, Hajos, Dain, & Snoek, 2011). In this thesis, receptiveness is conceptualised as positive attitudes toward insulin therapy.

In addition to being relevant to the initiation of insulin, PIR and receptiveness are likely to have explanatory value in relation to ongoing use of insulin therapy (e.g. the omission of insulin in those already using insulin) and treatment intensification (e.g. receptiveness to additional injections per day and/or changes in insulin types). However, few researchers include the omission of insulin or avoidance of treatment intensification in their definitions or discussion of these constructs. In the current thesis, PIR and receptiveness are discussed, and explored, in relation to both insulin initiation (incorporating attitudes to, and barriers and facilitators of, insulin initiation) and ongoing use of insulin therapy and insulin intensification.

2.3. Attitudes towards Insulin Therapy: Evidence from Qualitative Studies

Understanding attitudes toward insulin therapy among people with T2D, and how they develop, has been the aim of a vast body of qualitative research. In addition, a number of studies exploring ‘illness perceptions’ or ‘medication beliefs’ more broadly among adults with T2D, have contributed to the study of the PIR and receptiveness. Qualitative examination of attitudes to insulin therapy have been conducted across the globe, including studies examining the attitudes of specific
subgroups (e.g. Chinese Canadians (Ho & James, 2006), the Bangladeshi population living in East London (Khan, Lasker, & Chowdhury, 2008)).

Qualitative studies of PIR have employed focus groups, interviews or a combination of both, including people with non-insulin-treated and/or insulin-treated T2D. Research including those already using insulin typically focuses on perceived barriers to insulin initiation rather than the experience of using insulin post-initiation. Further, few studies have examined attitudes to insulin intensification among those already using insulin therapy.

In some studies, both people with T2D and HCP participants are included. HCPs are asked to reflect on their own beliefs about insulin, systemic barriers and enablers of insulin initiation, as well as their beliefs about the attitudes held by people with T2D (Furler, Spitzer, Young, & Best, 2011; Jenkins et al., 2010; Tan et al., 2011). To date, only one qualitative study of PIR has been undertaken in Australia (Furler et al., 2011). That study included people with T2D (N=14) and HCP (N=12) participants, but reported mainly on HCP attitudes towards insulin initiation within primary care and HCP roles in the initiation and education of insulin therapy (Furler et al., 2011).

The following is a synthesis of the negative and positive attitudes to, or consequences of, insulin therapy identified in previous qualitative research of adults with T2D, discussed in relation to: a) the perceived necessity of insulin initiation; b) perceived or real negative consequences of insulin initiation; c) perceived benefits of insulin initiation; and d) the formation of attitudes towards insulin.
2.3.1. The perceived necessity of insulin initiation

People with T2D not yet using insulin commonly believe or assert insulin to be unnecessary for achieving optimal blood glucose control. They discredit the efficacy of insulin (K. W. Chen, Tseng, Huang, & Chuang, 2012; Tapu-Ta'ala, 2011), assert that they are able to improve their blood glucose levels without insulin (Bogatean & Hâncu, 2004; Guimarães et al., 2010; Hunt, Valenzuela, & Pugh, 1997; Khan et al., 2008; Noakes, 2010; Tan et al., 2011), and indicate a preference for alternative therapies, such as herbs or dried fruit (K. Brown, Avis, & Hubbard, 2007; Ho & James, 2006; Mull, Nguyen, & Mull, 2001). In one study, participants described insulin as “(in) fashion these day”, a personal preference of the HCP rather than a therapeutic necessity (Bogatean & Hâncu, 2004).

Concerns about the necessity of insulin are particularly common in studies including participants of non-Western ethnic heritage. In these studies, barriers to insulin initiation include the perception that insulin is an unnatural or chemical substance that causes an imbalance in the body (K. Brown et al., 2007; Mull et al., 2001). HCPs report patients’ distrust of Western doctors or medications as a barrier to insulin initiation (Haque, Emerson, Dennison, Navsa, & Levitt, 2005; Y. K. Lee, P. Y. Lee, & C. J. Ng, 2012; Patel, Stone, Chauhan, Davies, & Khunti, 2012). Religious beliefs are also cited by some respondents with T2D as a barrier to insulin initiation (Khan et al., 2008; Noakes, 2010); HCPs in Malaysia note that their patients of Muslim religion remain concerned about the origin of insulin (Y. K. Lee et al., 2012). In addition to the perception that insulin is an unnatural product, some

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2Up until the 1980s, insulin was derived from animal sources, including bovine, equine and porcine. Under the Muslim faith, the consumption or use of animal products must comply with strict religious standards in order to be considered lawful.
perceived the actual task of injecting, and being dependent on, a foreign substance into one’s body as unnatural or not ‘normal’ (Morris, Povey, & Street, 2005).

Conversely, two studies have suggested that people with T2D may not be as psychologically resistant as previously documented (Jeavons, Hungin, & Cornford, 2006), with PIR being greatly over-emphasised and, in fact, receptiveness being a more common experience (Jenkins et al., 2010). Indeed, with few exceptions (Khan et al., 2008), prior qualitative research does not focus exclusively on participants who have refused insulin initiation and the qualitative examination of barriers of insulin therapy frequently includes people with T2D who were already using insulin. Thus suggesting that even those reporting negative attitudes or barriers to insulin therapy may be receptive to insulin therapy. In an interview following participation in the Treat To Target in Type 2 Diabetes (4-T) trial, people with T2D reported being upset or disappointed when recommended insulin but quickly accepting insulin initiation in response to observing the reduced effectiveness of oral medications and recognising that their diabetes had progressed (Jenkins et al., 2010). Other studies have also reported that a person’s perception of discomfort caused by diabetes symptoms may influence his/her likelihood of viewing insulin initiation as necessary. For example, those who feel the acute discomfort of hyperglycaemia are more likely to acknowledge a need for insulin or express a desire to progress to the next phase of treatment (Bogatean & Hâncu, 2004). Similarly, diabetes nurse specialists report that patients who felt unwell were more willing to convert to insulin (Phillips, 2007b), and older African Americans with more symptomatic T2D or severe complications report following their medical regimen more aggressively (Chin, Polonsky, Thomas, & Nerney, 2000). Similarly, in a recent interview study of adults with T2D living in the UK the necessity of insulin was determined by participants in two different ways:
some participants relied on their HbA1c results to alert them of the inability of OHAs
to maintain glucose control, while others reported that insulin would be required
when diabetes-related complications had developed (Patel, Stone, McDonough, et al., 2015). However, T2D may be experienced as asymptomatic, with no symptoms
of prolonged hyperglycaemia recognised as out of the ordinary, and those not yet
using insulin may not be encouraged to monitor, or understand, their blood glucose
levels (Speight, Browne, & Furler, 2015). Thus, with no physical signs of the sub-
optimal management of the condition, people with T2D may not perceive treatment
intensification as necessary. Further, negative consequences of insulin therapy may
outweigh possible positive consequences and/or the perceived necessity of the
insulin use (Patel, Stone, McDonough, et al., 2015).

2.3.2. Perceived or real negative consequences of insulin initiation

Research exploring attitudes towards insulin has typically focused on
identifying barriers to insulin initiation among adults with non-insulin-treated T2D or
attitudes held prior to initiation among those already using insulin. Thus, there is a
vast literature revealing the perceived negative aspects of insulin initiation. While
diabetes duration and primary treatment (i.e. insulin injections, OHAs, lifestyle
modifications) are commonly provided, studies including people with insulin-treated
T2D only occasionally describe the average number of years participants have been
using insulin, and rarely specify any eligibility inclusion criteria for this. In some
cases, participants may be asked to reflect on their experience of, and attitudes held
prior to, insulin initiation years after the actual event. For example, in a study that
aimed to identify barriers to insulin initiation among Chinese people with T2D living
in Canada, the sample of five participants had been using insulin for between one
and 11 years (Ho & James, 2006). Thus, it is unclear whether the identified attitudes did, in fact, form prior to or after initiation, whether these attitudes changed over time, or whether they are accurately remembered. Furthermore, despite the frequent inclusion of adults with insulin-treated T2D, only a minority of studies have sought to understand ongoing barriers to, or consequences of, insulin therapy use after initiation (Morris et al., 2005; Phillips, 2007a), or negative attitudes to insulin intensification (Jenkins, Hallowell, Farmer, Holman, & Lawton, 2011).

The following section provides a summary of the negative consequences of insulin therapy, which may be a barrier to insulin uptake, or an experienced consequence post insulin initiation. People with T2D report the most important aspect of a given diabetes treatment is its impact on blood glucose control (Guimarães et al., 2009), but satisfaction with treatment goes beyond its effectiveness, incorporating experience also (e.g. convenience/flexibility and side effects). Potential negative experiences of insulin that are frequently raised as barriers to insulin initiation include: physical consequences; lifestyle consequences; and the implied meaning or symbolism of insulin use and consequences for self-identity.

2.3.2.1. Physical consequences

One of the most common themes to emerge from the literature concerns insulin injection anxieties. People with T2D perceive insulin injections as an invasive and painful treatment (e.g. Guimarães et al., 2010; Ho & James, 2006; Tan et al., 2011) and a preference for non-injectable insulin treatments has been identified (e.g. Guimarães et al., 2010; Hayes, Bowman, Monahan, Marrero, & McHorney, 2006). In addition to a fear of needles, insulin therapy is also perceived to be a more
complex treatment regimen. Worry and disbelief in one’s ability to self-inject or adjust insulin doses, and concerns about the negative consequences of injecting incorrectly, are frequently raised (e.g. Bogatean & Hâncu, 2004; K. W. Chen et al., 2012; Hassali et al., 2013; Morris et al., 2005).

People with T2D, regardless of whether they currently use insulin, commonly report concerns about the side effects of insulin. Most commonly, these side effects include hypoglycaemia, weight gain (e.g. Guimarães et al., 2010; Tan et al., 2011), and bruising from injection sites (Hayes et al., 2006). Hypoglycaemia is a concern among those already using insulin who express avoidance of increasing their insulin dose so as not to increase the likelihood of experiencing hypoglycaemia (Simon, Gude, Holleman, Hoekstra, & Peek, 2014; Tong, Vethakkan, & Ng, 2015). In a comparison of beliefs about insulin held by Brazilians and Canadians, Guimarães et al. (2010) noted that, while both groups expressed insulin anxiety and a preference for non-injectable treatments, Brazilians were more concerned about hypoglycaemia and the cost of insulin, while Canadian participants were most concerned about weight gain as well as the convenience of injections and their timing. The cost of insulin, injection devices and consumables is also reported elsewhere as a barrier to insulin treatment for people with T2D, most commonly in ethnic minority participant groups (Guimarães et al., 2010; Hayes et al., 2006; Hunt et al., 1997; Khan et al., 2008; Noakes, 2010).

2.3.2.2. Lifestyle and social consequences

Insulin therapy is generally perceived to be an intensive and burdensome self-management activity. For some individuals, the burden of self-injecting and adjusting insulin doses is something they do not feel able to manage, thus increasing
their dependence on family members and HCPs to support them in these activities (K. W. Chen et al., 2012; Guimarães et al., 2010; Khan et al., 2008; Tan et al., 2011). However, the inconvenience of insulin and the hassle it places on eating times and restrictions surrounding daily activities are more commonly reported negative consequences (Abu Hassan et al., 2013; Singh, Cinnirella, & Bradley, 2012). Further, after integrating insulin therapy into one’s lifestyle, the addition of more injections per day may again be cause for concern. For example, in the few qualitative studies exploring attitudes towards insulin intensification, participants reported concerns about the need to juggle their daily routine to make time for additional injections and wishing to avoid injecting in public (Jenkins et al. 2011), as well as a preference for fewer injections per day (Simon et al., 2014).

The potential for needing to inject insulin in a public space and the consequential social embarrassment is a concern (Abu Hassan et al., 2013; Shiu, Kwan, & Wong, 2003). Chinese participants report feeling that if they inject in public, others may perceive them as drug addicts or it may draw negative attention to them as the public feel the condition is self-induced (Shiu et al., 2003). Social stigma surrounding diabetes has been an overlooked and potentially underestimated phenomenon, the occurrence and impact of which is only now coming to the fore (Browne, Ventura, Mosely, & Speight, 2013; Kalra & Baruah, 2015; Schabert, Browne, Mosely, & Speight, 2012). Fears about injecting in public have consequences for optimal diabetes self-management with reports of missing or delaying insulin doses due to social embarrassment (Jenkins et al., 2011; Shiu et al., 2003). Further, Bangladeshi people living in London report that the stigma associated with insulin has negative implications for relationships and marriage prospects (Khan et al., 2008).
A commonly reported belief is that needing insulin indicates an increase in the severity of the condition. In an Australian study, participants rated T2D as being ‘mild’ if managed with dietary modifications, more serious if requiring oral hypoglycaemic agents, and more serious again if diabetes-related complications had occurred, but most severe if managed with insulin (Dunning & Martin, 1997). The belief that insulin indicates a more serious stage of diabetes relates also to the erroneous beliefs held by people with T2D that insulin is the cause of serious diabetes complications, such as blindness and amputations, or even death (e.g. K. W. Chen et al., 2012; Hu, Amirehsani, Wallace, & Letvak, 2012); insulin is an end-stage treatment or last resort treatment (e.g. Brod, Alolga, & Meneghini, 2014; Hassali et al., 2013; Hayes et al., 2006; Hu et al., 2012); and insulin is a punishment for ‘failing’ to self-manage their diabetes previously (e.g. Bogatean & Hâncu, 2004; Hayes et al., 2006). For example, some report feeling shocked when insulin therapy is finally prescribed, previously considering it only to be a threat, and anger that they are being unfairly punished for sub-optimal diabetes management (Morris et al., 2005). For some people with T2D, the recommendation of insulin initiation felt like a loss of control of their body (Vermeire, Van Royen, Coenen, Wens, & Denekens, 2003), or led to a sense of powerlessness and a feeling that they are being controlled by their condition and medications (Hayes et al., 2006; Morris et al., 2005).

Perceived benefits of insulin initiation

Understanding negative beliefs about, and barriers to, insulin use has been the primary focus of qualitative research, with benefits or positive aspects of insulin therapy infrequently reported. When positive aspects of insulin are reported, they are
generally concentrated on the positive physiological consequences of insulin and reported mainly by those already using insulin. Prior to insulin initiation, understanding that insulin is an effective treatment, which may lower blood glucose levels and, therefore, reduce the risk of developing diabetes-related complications, acts as a facilitator of insulin acceptance (Abu Hassan et al., 2013). Post-insulin initiation, participants identify that insulin is more effective at lowering blood glucose levels than other medications, in addition to delaying complications and enabling them to live longer (Guimarães et al., 2010; Morris et al., 2005; Vinter-Repalust, Petriček, & Katić, 2004). Further, many participants view using insulin as a positive step in their treatment, which has led to increased understanding of their diabetes and its treatment, improved diabetes, as well as increased personal control over the management of their condition.

A small-scale interview study investigating attitudes towards insulin therapy before and after a HCP-led educational intervention about insulin, concluded that after receiving education, participants were more accepting of insulin therapy and reported that injecting insulin therapy seemed much easier than expected (Hassali et al., 2013). Similarly, a general relief felt after injecting insulin for the first time is commonly reported by both HCPs and people with T2D (Furler et al., 2011; Hayes et al., 2006; Jenkins et al., 2010; Morris et al., 2005; Noakes, 2010; Phillips, 2007a, 2007b; Tapu-Ta'ala, 2011), and insulin pens and devices are reportedly much easier to use than expected (Hu et al., 2012; Jenkins et al., 2010; Phillips, 2007a; Tan et al., 2011; Vinter-Repalust et al., 2004). Similarly, Vijan et al. (2005) reported the perceived burden of injections tends to decrease following insulin use, while Ratzmann (1991) reported that negative perceptions of insulin diminished four months after initiation, except for the perception that insulin means diabetes has
reached a more serious stage. Morris et al. (2005) reported that for those participants whose resistance to insulin had lessened after insulin initiation, a realisation that insulin was actually helping, rather than hindering, was common. This suggests that the initiation of insulin itself may attenuate negative insulin appraisals.

2.3.4. Formation of attitudes towards insulin therapy

Understanding what influences the development of attitudes toward insulin and how they change over time can assist in the development of strategies and interventions to increase receptiveness to insulin therapy among those with T2D, and, in turn, improve the timely initiation of insulin therapy. The in-depth qualitative investigation of attitudes held by those with T2D either before or after insulin initiation provides insights into how these attitudes may have developed and what may have influenced resistance or receptiveness towards insulin. Hunt et al. (1997) proposed that the formation of attitudes towards insulin is grounded within three sources: self-experience, experience of others, and relationships with their HCPs. These are discussed below in reference to more recent literature.

2.3.4.1. Self-experience

As discussed earlier (Section 2.3.1.), perceiving insulin initiation as necessary may be influenced by a person’s experience of symptom discomfort caused by prolonged hyperglycaemia or their understanding of their own diabetes progression. For example, the provision of information and tools required to understand changes in blood glucose patterns and recognise symptoms of hyperglycaemia may allow the person with T2D to recognise the inefficacy of their current treatment and take personal responsibility for the management of their condition (Fisher et al., 2012). Self-experience as a potential enabler of psychological insulin receptiveness is also
evidenced through the relief commonly reported after injecting insulin for the first time (Furler et al., 2011; Hayes et al., 2006; Jenkins et al., 2010; Morris et al., 2005; Noakes, 2010; Phillips, 2007a, 2007b; Tapu-Ta'ala, 2011), whereby this experience may increase self-confidence and autonomy in the management of their diabetes (Fisher et al., 2012) and provide a sense of power over one’s body (Furler et al., 2011; Morris et al., 2005; Vinter-Repalust et al., 2004). Similarly, for some who are already injecting insulin, additional injections per day is of little concern due to already being familiar with the requirements of the treatment, while for others new injection experiences (such as additional injections during the day, perhaps in public) may cause greater concern (Jenkins et al., 2011). In addition to injection administration, self-experience of insulin therapy side effects plays a role in optimal insulin use after initiation. People with T2D report not fully understanding hypoglycaemia until they have actually experienced it (Nair, Levine, Lohfeld, & Gerstein, 2007). Hunt et al. (1997) noted that participants who described experiencing negative side effects of insulin therapy, such as hypoglycaemia, perceived insulin to be more harmful and felt discouraged to continue taking their insulin therapy.

2.3.4.2. Influence of others

Wolffenbuttel et al. (1993) proposed that the most important determinant of intention to initiate insulin is the ‘subjective norm’, defined as the opinion of ‘significant others’ (e.g. usual HCPs, family and friends). Amongst a Mexican American sample, Hunt et al. (1997) reported observations of others’ experience with insulin as well as conversations with those using insulin as an important contributor to the development of beliefs about insulin therapy. Observing family
members use insulin therapy successfully has been reported as a facilitator of insulin initiation among people with T2D (Abu Hassan et al., 2013; Patel, Stone, McDonough, et al., 2015), and family history of insulin use has been associated with less negative attitudes towards insulin (K. P. Lee, 2015). However, people with T2D frequently report discussions or experiences with family members and friends about the negative aspects of insulin use which may heighten concern about insulin therapy initiation (Ho & James, 2006; Hu et al., 2012; e.g.Khan et al., 2008; Patel, Stone, McDonough, et al., 2015). For example, in a study exploring the meaning of insulin use to a group of Hispanic Americans with T2D and their families, family misconceptions about insulin and lack of support was a barrier to optimal diabetes management (Hu et al., 2012). Families and friends may perceive insulin, rather than the possible several years of prolonged hyperglycaemia, as causing deterioration in health (e.g. Bogatean & Hâncu, 2004; Hu et al., 2012; Hu et al., 2013). HCPs also report the negative influence of family and friends on the initiation of insulin, particularly among those with non-Western cultural heritage (Jeavons et al., 2006; Y. K. Lee et al., 2012; Patel et al., 2012). Lee et al. (2015) suggested that the role of the family in the decision to initiate insulin varies according to the family dynamic, from the family playing an active role in helping to gather information and attend clinic to avoiding sharing personal health information. Both HCPs and people with T2D have discussed the inclusion of families in diabetes education (e.g. clarifying family member roles in the individual’s health care) (Hu et al., 2012; Patel et al., 2012) and peer group education (Bogatean & Hâncu, 2004; Noakes, 2010; Patel et al., 2012; Phillips, 2007a, 2007b; Vinter-Repalust et al., 2004) as possible enablers of insulin initiation.
2.3.4.3. Relationship with healthcare professionals

HCPs commonly report patients’ beliefs and cultural or familial barriers as influencing the decision to initiate insulin, but rarely discuss their own influence on their patients. The impact of interactions between HCPs and people with T2D, and how insulin appraisals might be shared through these interactions, is a potential enabler, or barrier, to both the timely recommendation and the initiation of insulin. For example, Karter et al. (2010) have found that people with T2D who do versus do not fill their initial prescription of insulin therapy differ according to their interactions with their HCP. Those who report not filling their prescription were significantly more likely to report that the risks and benefits of insulin therapy were not well explained to them and were significantly less likely to have received insulin training from a doctor, nurse or education class, compared to those who filled their insulin prescription. People with T2D identify early discussion of insulin within care and good rapport with their HCP as potential facilitators of insulin receptiveness (Abu Hassan et al., 2013; Bogatean & Hâncu, 2004; Jenkins et al., 2010; Noakes, 2010; Patel, Stone, McDonough, et al., 2015; Phillips, 2007a; Tan et al., 2011; Vinter-Repalust et al., 2004), and HCPs highlight the importance of early education and discussion about diabetes and its treatment (J. B. Brown et al., 2002). However, HCPs attempts to engage people with T2D in their diabetes self-management often include inaccurate and harmful language use which may, in effect, delay insulin initiation (Speight, Conn, Dunning, & Skinner, 2012). For example, HCPs may use the need for insulin as a veiled threat to improve self-management long prior to the need to initiate insulin, which reinforces among people with T2D the idea of insulin as a ‘last resort’ option and as a punishment for suboptimal medical outcomes (Morris et al., 2005; Phillips, 2007a; Tan et al., 2011). Struggling to reach treatment
goals can be frustrating and promote feelings of failure and self-blame (Beverly et al., 2012; Krall et al., 2014), and contribute to the negative and emotional reactions to insulin recommendation commonly reported (Jeavons et al., 2006; Morris et al., 2005; Phillips, 2007b).

Studies exploring HCPs’ attitudes suggest that they have preconceived ideas about patients’ willingness to initiate insulin or their likelihood of taking insulin as recommended (Haque et al., 2005; Y. K. Lee et al., 2012; Patel et al., 2012; Tan et al., 2011). They report their expectation of patients’ emotional reactions to insulin as a barrier to insulin recommendation (Furler et al., 2011; Jeavons et al., 2006; Jenkins et al., 2010; Y. K. Lee et al., 2012; Phillips, 2007b; Tan et al., 2011). The assumption that patients will be distressed by the idea of insulin may influence HCP-patient communications and, perhaps, discourage HCPs from introducing insulin therapy in earlier consultations (K. W. Chen et al., 2012; Noakes, 2010; Tan et al., 2011), or encourage HCPs’ preference to discuss the benefits of insulin therapy and downplay or ignore possible risks or barriers to insulin (Y. K. Lee, Lee, & Ng, 2013).

HCPs report a number of barriers, beyond those expressed by the person with T2D, which contribute to the delayed recommendation of insulin therapy, or clinical inertia. These barriers may delay or prevent early education about and discussion of insulin within care, thus not adequately assisting people with T2D to formulate an understanding of, or positive attitudes, about treatment intensification. First, HCPs may hold beliefs about insulin that are incorrect or inconsistent with optimal care. For example, some HCPs report avoiding insulin initiation in people who are obese, ‘non-adherent’, have diabetes-related co-morbidities, or due to the increased risk of hypoglycaemia (Haque et al., 2005; Hayes, Fitzgerald, & Jacober, 2008;
Ratanawongsa et al., 2012). HCPs who have lower belief in the efficacy of insulin, and non-specialist HCPs report a higher preference to delay insulin initiation until absolutely necessary (Peyrot et al., 2005). Second, HCPs have varying levels of experience and knowledge of initiating insulin in people with T2D and they report feeling that they require further education in insulin initiation, including clear practice guidelines, hands-on experience and supervision (Greaves et al., 2003). Hence, a number of HCPs report anxiety and lack confidence in their knowledge and abilities to initiate insulin and may be overwhelmed by the specifics of initiating insulin (Furler et al., 2011; Tan et al., 2011). Lacking diabetes-specific education and confidence may reduce motivation to discuss or initiate insulin and a preference to refer patients to specialists (Haque et al., 2005; P. Y. Lee, Y. K. Lee, & C. J. Ng, 2012; Y. K. Lee et al., 2012; Tan et al., 2011).

Finally, the logistical limitations of health consultations are frequently raised by HCPs as a barrier to insulin initiation. These include language barriers (Haque et al., 2005; Jeavons et al., 2006; P. Y. Lee et al., 2012; Y. K. Lee et al., 2012; Patel et al., 2012); restricted consultation times (e.g. Furler et al., 2011; Greaves et al., 2003; P. Y. Lee et al., 2012; Patel et al., 2012); and a lack of continuity of care (e.g. Greaves et al., 2003; Haque et al., 2005; P. Y. Lee et al., 2012; Tan et al., 2011). The perceived lack of time and ease of communication has led some HCPs to report that the ability to educate patients about insulin devices, algorithms and injecting is too difficult and may be avoided, and some report deferring initiation until the next appointment or for another HCP to handle (Y. K. Lee et al., 2012; Tan et al., 2011). Given HCPs also report consultation times and the complexity of insulin therapy being barriers to insulin recommendation, it is not surprising then that people with
T2D who may be naïve to insulin therapy commonly perceive insulin therapy as complex and difficult.

### 2.3.5. Summary of qualitative research identifying attitudes to insulin

A vast body of exploratory qualitative research has been conducted with the aim of identifying attitudes towards insulin among people with T2D to better understand how these attitudes form and why people with T2D may choose to delay insulin initiation. An extensive list of attitudes towards, and potential barriers and facilitators of, insulin initiation is synthesised above. To date, one qualitative study of PIR has been undertaken in Australia, which focused largely on HCP perceptions of insulin initiation (Furler et al., 2011). While we may expect to find similar results among Australian adults with T2D, as found elsewhere, further research is required to corroborate this assumption.

While many qualitative studies include adults with insulin-treated T2D, most focus on understanding attitudes towards insulin prior to, or at the time of, initiation. With a few exceptions, little research has examined the experience of actual insulin use, including ongoing barriers to optimal insulin use (Morris et al., 2005; Phillips, 2007a), or attitudes toward the intensification of insulin therapy (Jenkins et al., 2011; Simon et al., 2014). To advance the field of knowledge, additional research including people already using insulin needs to explore possible ongoing, or unforeseen, positive or negative consequences of insulin use and how these consequences might impact on participants’ diabetes self-management (i.e. insulin omission) and attitudes toward insulin intensification. Further qualitative research is needed to explore ongoing facilitators and barriers of optimal insulin use and drivers of willingness to intensify insulin in the real world.
2.4. **Quantifying Psychological Insulin Resistance and Receptiveness and Associated Factors**

In accordance with the traditional focus of PIR research (identifying barriers to insulin initiation), insulin refusal rates among people with T2D may provide a useful quantification of the rate of PIR. Similarly, the reverse may also be true, in that rates of insulin initiation at the time of recommendation may be helpful in quantifying receptiveness to insulin therapy. Many studies have explored delay of insulin initiation from a clinical perspective, e.g. time to and proportion of insulin uptake among those with T2D who clinically require insulin (for example: Keij et al., 2016; K. Khunti, Damei, Meneghini, Pan, & Yale, 2012). However, it is unclear what proportion of the delayed insulin initiation is due clinical inertia (i.e. lack of prescription/recommendation of insulin by the HCP), and what proportion is due to insulin refusal or delay by the person with diabetes who has PIR. Limited data are available on the proportion of people with T2D recommended insulin who refuse, delay or immediately initiate insulin.

The landmark UK Prospective Diabetes Study (UKPDS), a 20-year multicentre trial of glycaemic therapies among newly diagnosed adults with T2D, provided early insight into the proportion of people with T2D who refuse insulin therapy. Eligible newly diagnosed participants referred between 1977 and 1987 \((N=2,520)\) were allocated to receive diet alone, or diet plus one of four pharmacological treatments (including insulin therapy) (U.K. Prospective Diabetes Study Group, 1995). Of those allocated to receive insulin \((N=676)\), 27% refused this form of therapy (U.K. Prospective Diabetes Study Group, 1995). In comparison, less than half as many participants refused prescribed OHA medications. In a single clinic study exploring
PIR among a UK Bangladeshi population, 58% of those recommended insulin therapy \((N=212)\) immediately commenced insulin (Khan et al., 2008). A further 22% initiated insulin within three months. However, one in five participants remained unwilling to commence insulin regardless of receiving two counselling sessions (Khan et al., 2008). In a recently published multi-centre longitudinal study undertaken in Japan, 57% of adults with T2D who were recommended insulin therapy \((N=130)\) had commenced insulin within four months (Odawara et al., 2016). This proportion significantly differed according to the qualification of the participant’s primary HCP, whereby those receiving care from a Japan Diabetes Society accredited specialist were less likely to refuse insulin (30%) than those receiving care from general practitioners (68%). However, data collection took place over a decade prior to publication.

The above studies suggest that insulin refusal rates, a behavioural consequence of PIR, may range from 20% to 43% of those recommended insulin, depending on the support received, the study setting (i.e. clinical trial, real-word cohort study) and population. Further research is required to better understand real-world, cross-country insulin refusal rates. PIR and receptiveness have been more commonly measured quantitatively in two main ways: through the assessment of 1) hypothetical intention to commence insulin therapy, and 2) attitudes towards insulin, or insulin appraisals. These methods of measuring PIR and receptiveness are described below.

### 2.4.1. Hypothetical insulin refusal and acceptance

The proportion of people with T2D who may be receptive to insulin or reluctant when prescribed is commonly inferred through the proportion of people who report being hypothetically willing/unwilling to initiate insulin. This is generally
assessed using a single item, e.g. “If your doctor recommended that you start insulin, how willing would you be to take it?” (Polonsky et al., 2011). This wording, or similar, has been used internationally (Gherman & Alionescu, 2015; Larkin et al., 2008; K. P. Lee, 2015; Nur Azmiah, Zulkarnain, & Tahir, 2011; Polonsky, Fisher, Dowe, & Edelman, 2003; Polonsky, Fisher, Guzman, Villa-Caballero, & Edelman, 2005; Polonsky et al., 2011; Wong et al., 2011; Woudenberg, Lucas, Latour, & Scholte op Reimer, 2012). Rates of ‘unwillingness’ vary considerably across samples. For example, in a recent multi-national study, the reported proportion of people with T2D ‘not at all willing’ to initiate insulin differed between countries, from 6% (Spain) to 37% (Italy), with an average of 17% (Polonsky et al., 2011). In contrast, the average proportion of participants who reported being receptive, i.e. moderately or very willing, to insulin initiation across countries was 48%, with a further 35% ambivalent. In Singaporean and Malaysian samples of adults with T2D, rates of ‘unwillingness’ have been reported as high as 71% (Wong et al., 2011) and 51% (Nur Azmiah et al., 2011), respectively. The proportion of Australians with T2D (un)willing to begin insulin is unknown.

To date, research exploring willingness to commence insulin has most often been conducted using convenience or clinical samples of people at various stages of diabetes progressions, not only among those for whom insulin has been clinically indicated (e.g. prolonged hyperglycaemia on maximum OHA dosage). Thus, studies quantifying ‘willingness’ to begin insulin may include a substantial proportion of people who report being ‘unwilling’, not only because they display PIR, but because they are aware that insulin would be an inappropriate or unnecessary treatment progression at this stage of their diabetes. Further, these single items do not capture any information about why a person is willing or unwilling to initiate insulin. Thus,
the item is often accompanied by other single items or scales that explore the positive and/or negative attitudes toward insulin which contribute to PIR/receptiveness.

2.4.2. Insulin appraisals among adults with non-insulin-treated T2D

Questionnaires may be used to measure positive or negative insulin appraisals (attitudes), which may contribute to PIR or receptiveness. Study-specific items have been used to quantify prevalence of negative attitudes towards insulin within certain populations (e.g. Ahmed et al., 2010; Wong et al., 2011), predictors of such attitudes (e.g. Peyrot et al., 2005), how such attitudes differ by hypothetical willingness to begin insulin (Polonsky et al., 2011), and actual insulin uptake (Odawara et al., 2016). However, such items are commonly unvalidated, with little description provided of the item wording or development, and scale brevity is often prioritised over comprehensiveness, validity, or reliability. As such, it is unclear whether these items have comprehensively assessed the range of attitudes towards insulin among a specific group and whether these items, and the study findings, are generalisable across T2D population groups, and indeed whether they would be sensitive to change in attitudes.

In 2007, the development and validation of three PIR scales were published: the ‘Barriers to Insulin Treatment’ (BIT) questionnaire developed in Germany for people with non-insulin-treated T2D (Petarak et al., 2007); the ‘Insulin Treatment Appraisal Scale’ (ITAS), developed in the USA, measuring PIR in people with T2D, both insulin-treated and non-insulin-treated (Snoek, Skovlund, & Pouwer, 2007); and the ‘Study the Hurdles of Insulin Prescription’ (SHIP) questionnaire for use with people with type 1 diabetes or T2D (Martinez et al., 2007). All three measures include both positive and negative aspects of insulin initiation. SHIP is not specific
to T2D, is not easily accessible and has not been widely used, thus it is not discussed further. The BIT questionnaire, which was designed for people with T2D not yet using insulin, and the ITAS, designed for both non-insulin-users and insulin-users, are both discussed in detail in the following section. More recently, the 13-item Chinese Attitudes to Starting Insulin Questionnaire (Ch-ASIQ) has been published (Fu et al., 2013). Ch-ASIQ was developed specifically for Chinese primary care patients with non-insulin-treated T2D, with a focus on the concerns of older adults. This scale has been used only once since its validation (Fu et al., 2016). In addition to these questionnaires, developed specifically to assess PIR in people with T2D, a number of others are relevant, but not specific, to PIR. For example: a measure of fear of self-injecting or self-testing (Snoek, Mollema, Heine, Bouter, & Van Der Ploeg, 1997), insulin-specific treatment satisfaction (e.g. Anderson et al., 2004), and concerns about hypoglycaemia (Polonsky, Fisher, Hessler, & Edelman, 2015). However, these measures either focus too specifically on a single issue that might affect willingness to use insulin, or they assess satisfaction with insulin without identifying factors influencing satisfaction. Furthermore, these scales may not be developed specifically for people with T2D and therefore they may not fully capture the concerns specific to this population.

2.4.2.1. Barriers to Insulin Treatment questionnaire

The development of the BIT questionnaire involved the compilation of a pool of 35-items by an expert panel of diabetes HCPs based on clinical experience, interviews with people with T2D and literature review (Petrak et al., 2007). This pool of items was then tested in a survey of 488 German adults with non-insulin-treated T2D, followed by item reduction analysis. The resulting final items were then
validated in a different sample of 449 adults with non-insulin-treated T2D who were categorised as receiving ‘insufficient’ diabetes pharmacological treatment, defined as an Hba1c ≥7.5% (58mmol/mol). The BIT questionnaire was developed and validated for people with T2D who were not currently using insulin therapy. However, the scale has been used, although not validated, among participants already using insulin therapy (Bahrmann et al., 2014; Hermanns et al., 2015). Following statistical validation, the German questionnaire was translated into English, which involved a vigorous validation process, including: forward and backward translations, item review by HCPs, and cognitive debriefing with English-speaking adults with T2D.

The BIT questionnaire includes 14 items comprising five subscales: fear of injection and self-testing; expected positive insulin-related outcomes; expected hardship from insulin treatment; stigmatisation by insulin injections; and fear of hypoglycaemia (Petrak et al., 2007). Each item is presented as a statement about insulin therapy with response options on a ten point scale from ‘completely disagree’ (0) to ‘completely agree’ (10). Authors suggest total and subscale scores can be calculated by taking a mean of item scores. The total scale and subscales show satisfactory internal reliability (Cronbach’s α=0.62-0.85) (Petrak et al., 2007).

Items included in the BIT questionnaire refer more commonly to the physical aspects of insulin use or technical concerns, such as side effects and pain, compared to the meaning of insulin, e.g. feelings of failure/self-blame or increased diabetes severity. In the validation sample, the most highly endorsed subscales related to expectations about positive insulin-related outcomes and fear of hypoglycaemia (Petrak et al., 2007), which has been replicated in more recent studies using the BIT questionnaire (Bahrmann et al., 2014; Nam, Chesla, Stotts, Kroon, & Janson, 2010;
Petrak, Herpertz, Stridde, & Pfützner, 2013). The two-item fear of hypoglycaemia subscale is preceded by a statement indicating that insulin can lead to low blood glucose. Such ‘scene-setting’ does not feature elsewhere in the questionnaire and likely increases endorsement of these items among those with T2D who may be otherwise unaware of the increased possibility of experiencing hypoglycaemia as a side effect of insulin therapy.

### 2.4.2.2. Insulin Treatment Appraisal Scale

The ITAS is a commonly used measure of PIR, and Chinese and Romanian versions have been validated (Chang, Huang, Li, Liao, & Chen, 2010; Gherman & Alionescu, 2015). The ITAS was developed with the aim of capturing current insulin appraisals among those with T2D, regardless of insulin use (Snoek et al., 2007). Item generation was informed by literature review, discussion with HCPs and clinical experience with people with insulin-treated and non-insulin-treated T2D. Authors proposed a 20-item scale, including 16 statements referring to the negative aspects of insulin use and four referring to the positive aspects of insulin. Items include positive aspects of insulin use as well as potential physical, social and symbolic consequences of insulin use. Response options range, on a 5-point Likert scale, from ‘strongly disagree’ (1) to ‘strongly agree’ (5). The ITAS was conceptualised as a two-dimensional scale (positive and negative) with a single underlying construct: insulin therapy appraisals. Consistent with this, exploratory factor analyses reveal a two-factor structure. Subscales are calculated by taking a sum of relevant items and the total score is calculated by summing all 20 items after reverse scoring the positively worded items. Higher scores indicate more negative insulin appraisals for the total ITAS score (Cronbach’s $\alpha=0.89$) and negative subscale score (Cronbach’s $\alpha=0.90$),
while for the positive subscale score, higher scores indicate less negative insulin appraisals (Cronbach’s α=0.64) (Snoek et al., 2007). Consistent with findings from the BIT questionnaire, in the majority of studies employing the ITAS, the positively-worded statements are highly endorsed (agreed or strongly agreed with) by those not yet using insulin therapy (C. C. Chen et al., 2011; Larkin et al., 2008; Snoek et al., 2007; Woudenberg et al., 2012). However, the item referring to the increased risk of hypoglycaemia is not endorsed as commonly as would be expected given the results of the BIT questionnaire.

Unlike the BIT questionnaire, the ITAS (Snoek et al., 2007) was developed for use with people with T2D regardless of insulin use, which enables assessment of insulin appraisals between treatment groups, and before and after insulin initiation. However, factor analysis and internal reliability assessments were conducted on the sample as a whole, across treatment groups. Thus, statistical validity should be re-assessed separately for each treatment group to ensure the 20 items, and total and subscale scores, perform consistently between groups.

2.4.3. **The role of hypothetical willingness and insulin appraisals in the prediction of actual insulin uptake**

The discriminatory power of the BIT questionnaire and the ITAS has been assessed in relation to a hypothetical choice made by adults with non-insulin-treated T2D about whether to begin insulin therapy. Using the BIT questionnaire in a cross-sectional study, the attitudes of participants who hypothetically chose to initiate insulin were significantly less negative and endorsement of expectations about positive insulin-related outcomes was significantly greater compared to those who choose not to initiate injectable insulin therapy (Petrak et al., 2013; Petrak et al.,
2007), although the positive insulin-related outcomes subscale was the most highly endorsed regardless of hypothetical choice. This suggests that even those participants who hold strong negative appraisals of insulin therapy may be commonly aware of the positive aspects of insulin therapy, perhaps due to HCPs’ tendency to prefer comprehensive education about the benefits of insulin therapy over the risks or barriers (Y. K. Lee et al., 2013). In addition, Woudenberg et al. (2012) and Larkin et al. (2008) both reported in cross-sectional studies that participants who were ‘willing’ to initiate insulin if recommended display lower, less negative, total ITAS scores than those who are ‘unwilling’. However, assessment of willingness is hypothetical and items have never been validated to determine their discriminant validity, i.e. their ability to identify actual refusals versus those showing initial or hypothetical reluctance but initiating insulin.

In the first longitudinal study employing the ITAS, 73 adults with non-insulin-treated T2D, who required treatment intensification, completed the ITAS at baseline and at three months follow-up (Hermanns, Mahr, Kulzer, Skovlund, & Haak, 2010). In this time, 44 participants switched to insulin therapy and 29 remained on OHAs. Those who transferred from oral treatment to insulin displayed slightly lower ITAS scores (less negative insulin appraisals) at baseline than those remaining on OHAs, suggesting that they were more receptive to the prospect of initiating insulin (Hermanns et al., 2010). Further, a cohort study comparing attitudes about insulin (measured using study-specific non-validated items) among a purposively selected sample of people with T2D who did and did not fill their prescription for insulin initiation found that those who did not fill their initial prescription displayed significantly more negative attitudes towards insulin (Karter et al., 2010).
At the time of undertaking the current program of research, no further evidence in support of the relationship between insulin appraisals and insulin uptake was available. More recently, Odawara et al. (2016) reported that in a longitudinal study of Japanese adults with T2D for whom insulin was recommended (N=130), those who initiated insulin (57%) reported significantly less negative, and more positive, insulin appraisals, at baseline, compared with those who remained on OHAs. Insulin appraisals were measured using a study-specific questionnaire. Elsewhere, the BIT questionnaire has been shown to be predictive of time to insulin initiation, whereby more negative appraisals among adults with newly diagnosed T2D were associated with a longer time to insulin initiation after accounting for diabetes-related emotional distress (Keij et al., 2016). However, these studies have not investigated this association in the context of other known correlates (see Section 2.4.5) of PIR and insulin uptake. Prospective research is needed, using validated measures of attitudes towards insulin, as well as accounting for the effect of other known or potential correlates of PIR, to corroborate the finding that attitudes towards insulin are predictive of willingness to begin insulin and, indeed, actual insulin uptake.

2.4.4. Psychological insulin resistance and receptiveness in people with T2D using insulin

Most research into PIR has focused on gauging willingness to, or attitudes towards, insulin initiation among those who have not yet commenced insulin. Once insulin has been initiated the concept of PIR might be considered of less relevant. Consistent with this, adults with insulin-treated T2D report less negative Total ITAS scores compared to those using OHAs (Bahrmann et al., 2014; C. C. Chen et al., 2011; Hermanns et al., 2010; Snoek et al., 2007). This may be due to one, or both, of
the two following reasons: 1) those who commence insulin display less negative attitudes towards insulin prior to insulin initiation (as discussed above); and 2) insulin experience may attenuate negative insulin appraisals. Indeed, when assessing hypothetical treatment preferences, adults with T2D using insulin place significantly less importance on treatment administration type (oral versus injection) (Casciano, Malangone, Ramachandran, & Gagliardino, 2011) and significantly greater importance on glucose control, in comparison to the frequency of administration per day (Hauber, Johnson, Sauriol, & Lescrauwaet, 2005), than those not using insulin. Further, people with T2D who transfer from oral treatment to insulin therapy display significantly less negative insulin appraisals, as measured using the ITAS (Hermanns et al., 2010; Liebl et al., 2013) or study-specific items (Odawara et al., 2016), significantly greater self-efficacy in insulin therapy (Hayes et al., 2013), and improved general treatment satisfaction (Wilson, Moore, & Lunt, 2004), after initiating insulin, suggesting that the use of insulin modifies attitudes.

However, certain negative ITAS items are commonly endorsed by people with insulin-treated T2D. For example, the top areas of concern in the ITAS validation study, including a sample of people with insulin-treated T2D in the US, were side effects, inflexibility and pain of insulin use (Snoek et al., 2007). Chen et al. (2011) reported that Chinese people using insulin were more concerned about the meaning of insulin, endorsing items regarding diabetes severity and previous treatment failure. Both groups commonly agreed that using insulin was associated with friends and family becoming more concerned about them. Furthermore, the mean and standard deviations of observed ITAS scores in insulin-treated versus non-insulin-treated participants suggests that at least a minority of people with T2D using insulin display negative evaluations of insulin therapy equivalent to those not using insulin.
Among those already using insulin, research has focused on medication-taking behaviours (i.e. omission: purposively skipping an injection) and associated factors, rather than PIR explicitly (e.g. Karter et al., 2010; Peyrot, Barnett, Meneghini, & Schumm-Draeger, 2012b; Peyrot, Rubin, Kruger, & Travis, 2010). Rates of insulin omission vary widely across studies. A recent systematic review of 17 studies examining insulin-taking behaviours among those with type 1 diabetes or T2D concluded that self-reported insulin ‘adherence’ ranged from 43% to 86% (Davies et al., 2013). In the Global Attitudes of Patients and Physicians study, 35% of participants across eight countries reported omitting their insulin on at least one day within the last month (Peyrot, Barnett, Meneghini, & Schumm-Draeger, 2012a), while in the more recent US study, 46% of participants reported ‘non-adherence’ to their insulin regimen over the prior two weeks (Osborn & Gonzalez, 2016).

Negative experiences or attitudes towards insulin therapy among those already using insulin may lead to insulin omission or delay of insulin injections. Quantitative research has examined reasons for, and implications of, insulin omission in T2D. For example, insulin omission among adults with type 1 diabetes and T2D may be related to stress or emotional problems, embarrassment of injecting in public, dissatisfaction with insulin treatment, the challenge of taking insulin every day at regular times as well as pain and side-effects caused by injections (Davies et al., 2013; Farsaei, Radfar, Heydari, Abbasi, & Qorbani; Peyrot et al., 2012b; Peyrot, Rubin, Kruger, et al., 2010). Similarly, a recent study found that self-reported insulin omission was associated with negative impact of diabetes treatment on quality of life among Japanese participants with T2D (Mashitani et al., 2015). These data suggest that negative attitudes to, or experience of, insulin therapy may be commonplace for some people with T2D using insulin and may act as a barrier to optimal diabetes
management. Research is required to further explore change in insulin appraisals post insulin initiation, possible ongoing barriers to optimal insulin use, and factors associated with negative attitudes towards insulin therapy among those using insulin.

In addition to insulin omission, negative attitudes to insulin therapy may also contribute to a person’s resistance or receptiveness to further treatment change, such as intensification. Survey data suggest that a third of adults with T2D using insulin are troubled by (Zambanini et al. 1999) or not motivated to consider (Martinez et al. 2007) the possibility of additional daily insulin injections. However, research exploring PIR among adults with insulin-treated T2D rarely incorporates measures of receptiveness to intensify insulin therapy. In a recent study of PIR among adults attending primary care in Hong Kong, participants were asked an alternative to the hypothetical willingness item: “Will you agree to *titrate* insulin treatment, if advised…?” (K. P. Lee, 2015). Among those with insulin-treated T2D, 9% indicated that insulin titration would be “unacceptable”. Further, research is needed to identify rates of receptiveness/refusal to intensification of insulin therapy and understand attitudes, including barriers or concerns that may be distinct from those observed in relation to insulin initiation.

2.4.5. **Factors associated with psychological insulin resistance and receptiveness**

A growing body of research aims to identify healthcare system and clinical characteristics that add to the prediction of insulin uptake in large cohort studies of adults with T2D (Danne et al., 2015; K. Khunti et al., 2016; K. Khunti, Wolden, Thorsted, Andersen, & Davies, 2013; Shah, Hux, Laupacis, Zinman, & van Walraven, 2005). However, psychosocial factors are rarely measured in these
studies. Cross-sectional and some prospective research has examined demographic, clinical and/or psychosocial factors associated with attitudes towards insulin, willingness to begin insulin therapy and insulin omission. For example, the international Diabetes Attitudes Wishes and Needs (DAWN) study provided an initial insight into potential predictors of PIR in people with T2D from 13 countries (including Australia) using unvalidated single items about perceived efficacy of insulin, self-blame for needing insulin, and adherence to treatment (Peyrot et al., 2005). Participants with a stronger belief in the efficacy of insulin were younger, had more diabetes-related complications, poorer relationships with HCPs, reported suboptimal diabetes outcomes, more diabetes-related distress and more frequent self-monitoring of blood glucose. The DAWN study was the first to assess demographic, clinical, behavioural and psychosocial correlates of attitudes towards insulin, and is the only quantitative study of PIR in Australia to date. However, further research is needed to corroborate these findings and, ideally, would use validated measures of attitudes towards insulin (i.e. BIT, ITAS) and/or independent variables (e.g. diabetes-related distress) rather than unvalidated single items. The section below describes the demographic, clinical, behavioural, and emotional characteristics associated with PIR or receptiveness among adults with non-insulin-treated and, where available, insulin-treated T2D.

2.4.5.1. Demographic and clinical characteristics

There are inconsistent findings regarding the association of PIR with age, gender, ethnicity and education. However, where an association has been found, those who report being unwilling to begin insulin or those with more negative insulin appraisals are consistently more likely to be women (e.g. Fu et al., 2016; Nam et al.,
2010; Nur Azmiah et al., 2011; Polonsky et al., 2003; Polonsky, Fisher, Guzman, et al., 2005), older (Peyrot et al., 2005), of ‘non-white’ ethnic orientation (e.g. Makine et al., 2009; Nam et al., 2010; Polonsky, Fisher, Guzman, et al., 2005), and less educated (e.g. C. C. Chen et al., 2011; Wong et al., 2011). Among a sample of low-income Latin and African-American adults with T2D, years living in the US was associated with PIR (Macbinani et al., 2012). Those participants reporting living longer in the US were significantly more willing (hypothetically) to begin insulin and reported less endorsement across all negative insulin attitudes measured. In a recent study of insulin omission in Japan, Mashitani et al. (2015) reported that older adults with T2D were more likely to omit insulin than their younger counterparts. In contrast, a recent systematic review reported that women and those with higher education levels are more likely to report insulin omission, but that age was inconsistently associated with insulin omission (Davies et al., 2013).

With regard to clinical characteristics, studies exploring predictors of insulin prescription and uptake within clinical samples report that those who initiate insulin have a higher HbA1c, longer diabetes duration, more diabetes-related complications and more prescribed OHAs (Danne et al., 2015; K. Khunti et al., 2013). This association with longer diabetes duration and worse glycaemic control may be in part due to the prescription of insulin being delayed by HCPs until absolutely necessary (Peyrot et al., 2005). Further to the delay of prescription, research suggests that people with T2D may be less receptive to insulin initiation, despite clinical need, if experiencing better diabetes outcomes and shorter disease progression. For example, Odawara et al. (2016) reported that those who initiated insulin had a longer diabetes duration (13 years and 11 years) and higher HbA1c (9.9% (84 mmol/mol) and 9.3% (78 mmol/mol), respectively), in addition to less negative insulin appraisals,
compared to those who remained on OHAs. Similarly, in a recent large-scale cross-sectional study of PIR among adults with T2D in China, participants who reported refusing insulin had shorter diabetes duration, fewer complications and a lower HbA1c than those who accepted it (Xiong et al., 2014). Fu et al. (2016) reported a significant negative association between HbA1c and negative attitudes towards insulin among non-insulin treated Chinese with T2D, and in the DAWN study participants with stronger belief in the efficacy of insulin therapy reported more diabetes-related complications and worse perceived diabetes outcomes (i.e. glucose control) (Peyrot et al., 2005). Further, among those already using insulin, it has been reported that those with better glycaemic control (HbA1c), longer diabetes duration, and cardiovascular co-morbidities were less likely to omit insulin than their counterparts (Mashitani et al., 2015). Thus, people with T2D appear to be less likely to refuse, or omit, insulin when they perceive diabetes outcomes to be worse, perhaps due to a lack of awareness of worsening health and the necessity of insulin therapy. However, this delay of insulin, and associated prolonged hyperglycaemia, may increase the risk of diabetes-related complication development. The relationship between receptiveness and perceived diabetes outcomes has similarly been reported in qualitative research (Section 2.3.1.).

2.4.5.2. Diabetes self-management and behavioural characteristics

Current diabetes self-management needs and behaviours may be associated with receptiveness to treatment change. Consistent with the relationship between HbA1c and insulin receptiveness (or resistance) discussed above, a greater awareness of diabetes severity through SMBG and use of multiple daily OHAs may encourage increased receptiveness to insulin therapy. In the DAWN study, participants who
monitored their blood glucose more often reported stronger belief in the efficacy of insulin (Peyrot et al., 2005). In a cross-sectional study of Chinese adults with T2D, an increased number of prescribed OHAs was associated with endorsement of positive insulin self-efficacy beliefs, such as insulin-related knowledge, social support, insulin as a method to improve glucose, confidence in insulin administration, and management of diet in reference to insulin therapy (Fu et al., 2016).

Little further research has explored the relationship between self-management behaviours (i.e. taking medications and/or blood glucose monitoring as recommended) and attitudes toward insulin among adults with T2D not yet using insulin. However, studies have identified perceived suboptimal medication-taking behaviours, or ‘non-adherence’, as a reason for insulin prescription delay among HCPs. For example, Ratanawongsa et al. (2012) reported that 39% of HCPs would delay insulin initiation all or most of the time on the basis of their beliefs about a patient’s likelihood of adherence and 64% of HCPs perceive patient resistance as a reason not to recommend insulin. Similarly, people with T2D categorised as displaying suboptimal medication-taking behaviours were less likely to have medications intensified than those who displayed optimal medication-taking behaviours (Grant et al., 2007) and over 90% of physicians stated that lack of ‘patient compliance’ was a barrier to insulin initiation (Nakar, Yitzhaki, Rosenberg, & Vinker, 2007). In contrast, in the DAWN study, HCPs who perceived their patients to be more ‘adherent’ to treatment recommendations and appointment times were more likely to delay insulin therapy (Peyrot et al., 2005). Further research should be conducted to identify any relationship between self-care behaviours, such
as SMBG and medication taking behaviours, and willingness to begin insulin therapy among those with non-insulin-treated T2D.

With regard to those already using insulin therapy only one study has reported on the relationship between duration of insulin therapy use and negative insulin appraisals using a validated measure (C. C. Chen et al., 2011). Among Chinese adults with T2D using insulin therapy, duration of insulin therapy (<1 year compared to >1 year) was not associated with insulin appraisals (C. C. Chen et al., 2011). This suggests that, after insulin initiation, attitudes towards insulin, although more positive among those using insulin, do not necessarily change (become less negative) with greater insulin experience. Additional studies are needed to corroborate this finding. Further, Chen et al. (2011) also reported that mode of injections (syringe/pen injector) was not related to insulin appraisals. However, in research exploring predictors of insulin omission, switching from a vial/syringe to an insulin pen, or initiating insulin therapy using a pen injector device, was associated with less insulin omission (Davies et al., 2013). The relationship between insulin appraisals and prescribed number of injections per day is not known, to date, but studies report a positive association between injections per day and likelihood of insulin omission (Mashitani et al., 2015; Peyrot, Rubin, Polonsky, & Jennie, 2010). It may be that those using more injections per day perceived insulin to be more intrusive and hold more negative insulin appraisals. Future research should investigate the relationship between insulin use characteristics, such as duration, injections per day, and insulin omission, with negative insulin appraisals among those using insulin therapy.
2.4.5.3. Beliefs about medications

Beliefs about insulin may relate to a person’s broader beliefs about health and medications, or their beliefs about current diabetes medications (i.e. OHAs). Horne et al. (1999) proposed that people hold beliefs about medicines in general (e.g. medicines are overprescribed), as well as beliefs about current medications specific to their diagnosed condition (e.g. insulin therapy is unnecessary for the management of T2D). The Beliefs about Medicines Questionnaire (BMQ) General was developed to assess cognitive representations of perceived ‘overuse’ and ‘harm’ of medications in general, while the BMQ Specific was developed to assess perceived ‘concerns’ about and ‘necessity’ of medications prescribed for personal use (such as OHAs) (Horne et al., 1999). Beliefs about medications, measured using the BMQ Specific and General, have been found to be associated with medication-taking behaviours across a range of chronic conditions, including T2D (Aikens & Piette, 2009; Horne & Weinman, 1999, 2002; Horne et al., 1999). In a cross-sectional study of 803 adults with T2D using various anti-hyperglycaemic medications, including insulin therapy (40%), underuse of treatment was associated with greater concern about current diabetes treatment (Aikens & Piette, 2009).

Beliefs about current medications are likely related to beliefs about, and willingness to commence, medications not currently in use (e.g. insulin use). In the only T2D-specific study to explore the association between PIR and beliefs about current medications (Polonsky et al., 2011), participants with non-insulin-treated T2D who were hypothetically unwilling to commence insulin reported more negative beliefs about current oral medications than those who were receptive to insulin initiation (Polonsky et al., 2011). Thus, identifying and addressing negative beliefs
about current diabetes medications (OHAs) among those not yet insulin-treated may improve receptiveness to further diabetes medications, such as insulin therapy. However, the study conducted by Polonsky et al. (2011) is limited by the use of single items to measure beliefs about current oral medications and the fact that items did not specify whether the medications were for the management of diabetes (condition-specific beliefs) or other purposes (e.g. general medication beliefs). No further research has explored the role of beliefs about general or diabetes-specific medications on attitudes towards insulin therapy. Further research using validated measures, such as the BMQ (Horne et al., 1999), is required to better understand the association between current medication beliefs and PIR or beliefs about future insulin therapy.

2.4.5.4. Emotional wellbeing

The relationship between PIR and emotional wellbeing, such as depression, anxiety, and diabetes-related distress has been a recent focus, perhaps in response to the availability of validated tools to assess PIR. Prevalence of depression and anxiety are reported to be higher amongst people with T2D compared to the general population (Ali, Stone, Peters, Davies, & Khunti, 2006; Grigsby, Anderson, Freedland, Clouse, & Lustman, 2002; Roy & Lloyd, 2012). Depressive symptoms have been found to be associated with impaired self-care behaviours (Gonzalez, Delahanty, Safren, Meigs, & Grant, 2008; Gonzalez et al., 2007), including insulin omission among adults with T2D (Mashitani et al., 2015). It has been suggested that, as depression is associated with reduced energy, perceived self-efficacy and motivation, depressive symptoms may also be associated with increased PIR and reduced likelihood to initiate insulin therapy (Gherman & Alionescu, 2015; Makine
et al., 2009; Nefs, Pop, Denollet, & Pouwer, 2013). Using the WHO-5 questionnaire to assess general emotional wellbeing (Bech, 2004), Snoek and colleagues (2007) found that those with a score above the cut-off indicative of depressive symptomatology displayed significantly higher ITAS scores than those with unimpaired wellbeing. Using various validated measures of depressive symptoms, others also report small-to-moderate significant associations between ITAS scores and depressive symptoms (Gherman & Alionescu, 2015; Larkin et al., 2008; Makine et al., 2009; Woudenberg et al., 2012).

In regards to actual insulin uptake, a recent longitudinal study found that those with T2D experiencing greater severity of depressive symptoms required significantly more time and visits with HCPs training to self-inject, self-adjust and manage other aspects of insulin delivery (Dzida, Karnieli, Svendsen, Sølje, & Hermanns, 2015). However, no significant relationship between depressive symptoms and time to insulin initiation has been found (Iversen et al., 2015; Nefs et al., 2013). A recent cohort study of over 800 adults with T2D in Norway concluded that elevated depression was not associated with time until insulin initiation, but generalised anxiety was a predictor of delayed insulin initiation (Iversen et al., 2015). To date, the relationship between anxiety and attitudes towards insulin has not been explored among those not yet using insulin therapy. Further research is needed to examine the relationship between anxiety symptoms and insulin appraisals.

Diabetes-related distress is the emotional burden associated with living with diabetes (Polonsky et al., 1995). It is commonly measured using either Problem Areas In Diabetes (PAID) questionnaire (Polonsky et al., 1995) or the Diabetes Distress Scale (DDS) (Polonsky, Fisher, Earles, et al., 2005). Diabetes-related
distress is commonly reported among people with T2D. For example, in our cross-sectional survey of Australian adults with diabetes, high or severe diabetes-related distress, measured using the DDS and PAID (Polonsky et al., 1995) respectively, was reported by 12% and 19% of those with T2D (Fenwick et al., 2016). Diabetes-related distress has been found to be moderately-to-strongly associated with depression and researchers in the area have noted that questionnaire measures of depressive symptoms may actually be capturing high levels of diabetes-related distress, rather than symptoms of major depression disorder (Fisher et al., 2007; Gonzalez, Fisher, & Polonsky, 2011). Snoek et al. (2015) proposed a need for better defined depression profiles, and, subsequently, measures, among people with diabetes accounting for the symptomatology of diabetes and diabetes-related distress, which may overlap with the measurement of depressive symptoms. Thus, the association between insulin appraisals and depression measures (noted above) may actually be accounted for, in part, by the contribution of diabetes-related distress. Indeed, Makine et al. (2009) reported that the significant association between depressive symptoms and ITAS scores was reduced after accounting for PAID scores in a cross-sectional study of adults with non-insulin-treated T2D. Elsewhere, a moderate positive relationship has been found between ITAS scores and PAID scores, where more negative attitudes are associated with increased diabetes-related distress (Snoek et al., 2007). Polonsky et al. (2011) reported that adults with T2D from eight countries who were ambivalent about or unwilling to initiate insulin were significantly more likely to endorse single diabetes-related distress items.

Interestingly, the DAWN study found that increased belief in the efficacy of insulin was associated with increased diabetes-related distress (Peyrot et al., 2005), and participants who initiated insulin in a longitudinal study displayed slightly lower
ITAS scores but greater diabetes-related distress (higher PAID scores) at baseline than those who remained insulin naïve (Hermanns et al., 2010). In a large-scale UK prospective cohort study, Keij et al. (2016) reported that diabetes-related distress significantly added to the prediction of time until insulin uptake among newly diagnosed adults with T2D, whereby more distress was associated with a shorter time until insulin initiation. However, after accounting for insulin appraisals, measured using the BIT questionnaire, this independent contribution was no longer significant. These findings seem contradictory to the above positive relationship between PIR and diabetes-related distress, but it is possible that people with T2D who are willing to initiate insulin, and therefore have lower (less negative) ITAS scores, display greater diabetes-related distress due to concerns surrounding their current ineffective diabetes treatment. Indeed, diabetes-related distress may encompass feelings of distress relating to various aspects of living with the condition, including, but not limited to, self-management needs and behaviours (e.g. medication taking) (Polonsky et al., 1995; Polonsky, Fisher, Earles, et al., 2005). Understanding which, if any, aspects of diabetes-related distress (e.g. regimen-related) are more highly associated with PIR, and actual insulin uptake, may be useful in the development of interventions or strategies to reduce PIR.

Few studies have reported on the association between emotional wellbeing and PIR specifically among adults with T2D already using insulin. However, some studies offer a little insight into possible consequences, or correlates, of specific aspects of continued PIR among people with insulin-treated T2D. For example, Mollema et al. (2001) explored psychosocial outcomes in those with type 1 diabetes and insulin-treated T2D comparing those who displayed a fear of insulin injections and those who did not. Increased fear of self-injecting was associated with greater
diabetes-related distress and reduced general emotional wellbeing. In another study, those with greater injection-related anxiety reported greater concern about the possibility of additional injections (Zambanini et al. 1999). Of course, injections are just one of the potentially negative aspects of insulin use and, as such, further research is needed to investigate the emotional impact of ongoing PIR more comprehensively among those with T2D already using insulin.

### 2.4.6. Summary of research quantifying psychological insulin resistance, receptiveness and associated factors

While international and national real-world data is available on the delay of insulin initiation from a clinical perspective (e.g. time to and proportion of insulin use among those with T2D who clinically require insulin), little research has examined the proportion of delayed insulin initiation due to insulin refusal or delay specifically by the person with diabetes (i.e. due to PIR). The landmark UKPDS trial suggests an insulin refusal rate of 27% (U.K. Prospective Diabetes Study Group, 1995), but smaller studies have reported refusal rates from 20% (Khan et al., 2008) to 43% (Odawara et al., 2016). More commonly, PIR and receptiveness have been assessed using self-report questionnaire tools that aim to quantify the proportion of people with T2D who are hypothetically (un)willing to initiate insulin therapy or the possible reasons for this (i.e. negative insulin appraisals).

Willingness to begin insulin therapy among adults with T2D has not been examined within Australia. Elsewhere, depending on the population, study and measure used, the proportion of people with T2D ‘unwilling’ to commence insulin varies substantially from 6% (Polonsky et al., 2011) to 71% (Wong et al., 2011), and may not be reflective of a) willingness to initiate insulin among those for whom
insulin has been clinically indicated (e.g. prolonged hyperglycaemia on maximum OHAs) or b) actual insulin initiation or refusal. To examine whether this is predictive of actual insulin uptake, and gauge a valid representation of the size of the problem of PIR, additional prospective research is required involving people with T2D for whom insulin is clinically indicated.

The ITAS is a widely used validated measure of insulin appraisals, which has the benefit of being suitable for completion by people with non-insulin-treated and insulin-treated T2D. However, the validation of the ITAS was conducted on a sample of adults with T2D with mixed treatment types (including insulin-treated and non-insulin-treated individuals). Additional validation work should be conducted separately by treatment type to ensure the scale performs psychometrically well across, and is acceptable to, both insulin-treated and non-insulin treated populations. To date, no studies have used validated measures of PIR within Australia. Further, scale acceptability, reliability and validity should be assessed within Australia before proceeding with use and analyses of this questionnaire locally.

Cross-sectional, and some prospective, research has examined demographic, clinical, self-management or psychosocial factors associated with attitudes towards insulin, willingness to begin insulin therapy, and insulin uptake. Among adults with non-insulin-treated T2D, identified demographic factors associated with PIR have included age, gender, ethnicity and education, whereby those who report being unwilling to begin insulin or those with more negative insulin appraisals are typically more likely to be women, older, of ‘non-white’ ethnic orientation, and less educated. With regard to clinical characteristics, higher HbA1c, longer diabetes duration and more diabetes-related complications are associated with insulin uptake, in
prospective research, and negative insulin appraisals, in cross-sectional studies. Positive insulin appraisals have been associated with more frequent SMBG and a greater number of prescribed OHAs among non-insulin-treated adults with T2D. However, comprehensive assessment of all of the above demographic, clinical and self-care characteristics in addition to psychosocial measures, preferably using validated tools, is uncommon.

One study has highlighted the role of beliefs about current medications as predictive of receptiveness to future insulin uptake (Polonsky et al., 2011). However, this study employed unvalidated measures and did not distinguish between general medication beliefs and diabetes-specific medication beliefs. Additional research is needed to corroborate this finding, using validated measures of both general medication beliefs and specific current diabetes medication beliefs (i.e. OHAs), as well as accounting for other known correlates of PIR.

Finally, the relationship between PIR and emotional wellbeing, specifically depressive symptoms and diabetes-related distress, has been a recent focus. After accounting for diabetes-related distress, the relationship between depressive symptoms and insulin appraisals is reduced. Furthermore, longitudinal research has shown no significant relationship between depressive symptoms and time to insulin initiation (Iversen et al., 2015; Nefs et al., 2013). In contrast the association between PIR and anxiety symptoms has received little attention, but a recent large (N=800) cohort study suggests generalised anxiety, but not depression, predicts delayed insulin initiation (Iversen et al., 2015). Further research is needed to examine the relationship between anxiety symptoms and insulin appraisals.
A moderate positive association is commonly reported between diabetes-related distress and insulin appraisals, whereby more negative appraisals are associated with greater distress. However, in a longitudinal study, those who initiated insulin therapy displayed slightly lower ITAS scores but greater diabetes-related distress at baseline than those who remained insulin naïve (Hermanns et al., 2010) and a large prospective cohort study reported that diabetes-related distress was associated with a shorter time to insulin initiation (Keij et al., 2016). Additional research is needed to understand the direction and strength of the relationship between diabetes-related distress, PIR and insulin uptake and, further, to examine which, if any, aspects of diabetes-related distress are more highly associated with PIR.

To date, research exploring PIR and associated factors has concentrated on gauging willingness to, or attitudes towards, insulin initiation among those who have not yet commenced insulin. However, some negative insulin appraisals are endorsed by people with insulin-treated T2D and, although rates vary considerably, insulin omission is a relatively common experience. Negative attitudes to, or experience of, insulin therapy may be commonplace for some people with T2D using insulin and may act as a barrier to optimal diabetes management. Research is required to further explore change in insulin appraisals post insulin initiation, possible ongoing barriers to optimal insulin use, and factors associated with negative attitudes towards insulin therapy among those using insulin.

2.5. Conclusions and Direction of Research

T2D is a progressive condition, which is likely to require eventual use of insulin in order to maintain optimal blood glucose and prevent/delay onset of
diabetes-related complications. Around 250,000 Australian adults with T2D currently use insulin (National Diabetes Services Scheme, 2016), but government reports indicate that many more have sub-optimal glycated haemoglobin indicative of complication risk, suggesting that treatment intensification may be needed (Swerissen, Duckett, & Wright, 2016). The delay of insulin initiation may, in part, be due to beliefs held by the person with diabetes, whereby negative perceptions of insulin use may lead to a reluctance to initiate insulin therapy. This is conceptualised as PIR, while the reverse, positive attitudes toward insulin therapy, is known as receptiveness. Beyond insulin initiation, PIR and receptiveness may also have explanatory value in predicting a reluctance to inject as often as recommended or to intensify treatment further.

Qualitative studies have provided a rich description of attitudes towards insulin, and how they may develop, among people with T2D. However, less is known about attitudes post insulin initiation and going forward (e.g. intensification). Further, few qualitative studies have been conducted in the Australian healthcare context, and only one included people with T2D. Thus, little is known about whether these issues are relevant in Australian health context or the extent to which they differ from previous international findings.

Typically, quantitative assessment of PIR has involved the measurement of either: 1) positive and/or negative insulin appraisals or 2) hypothetical ‘willingness’ to initiate insulin. Validated scales of insulin appraisals are freely available, including the ITAS (Snoek et al., 2007) and the BIT questionnaire (Petrak et al., 2007). The widely used ITAS is advantageous in that it can be used among adults with T2D regardless of insulin treatment, allowing for prospective research.
examining change in insulin appraisals. However, the ITAS has not been validated separately by treatment type and, therefore, it is not known whether the scale is acceptable and performs psychometrically well across treatment groups. Hypothetical (un)willingness to initiate insulin therapy has been assessed using a single item and is used as an indicator of likely insulin refusal. However, whether this single item reflects actual refusal rates is yet to be verified. Furthermore, the measurement of willingness to begin insulin in samples that include those who may be years from clinically requiring insulin therapy may limit the validity of this data.

Existing research has highlighted factors associated with PIR among adults with T2D, including demographic and clinical characteristics, self-care behaviours, and general or diabetes-specific emotional wellbeing. However, this research has relied heavily on cross-sectional study design and has rarely comprehensively assessed the role of these factors using valid measures. A reduction in negative insulin appraisals has been demonstrated after insulin initiation and, thus, insulin uptake has been assumed to be synonymous with minimal PIR. However, research shows that certain negative appraisals are apparent among those already using insulin. Furthermore, insulin omission is common among adults with T2D. In-depth, prospective research is required to investigate how PIR changes over time in people with T2D (from non-insulin use to insulin initiation and intensification) and the potential implications of continued PIR in people with T2D using insulin. The aim of this research was to examine attitudes towards insulin among adults with T2D in Australia as well as correlates of, and the capacity for change in, appraisals of insulin. This program of doctoral research was designed to contribute to our understanding of: a) the measurement of insulin appraisals among Australians with T2D, b) the occurrence of, and factors associated with, PIR and intention to begin
insulin therapy among adults with non-insulin-treated T2D within national population level and clinical settings, c) the demographic, clinical and psychological predictors of actual insulin uptake, and d) attitudes toward insulin post-initiation, perceptions of benefits and consequences of insulin, and attitudes to further treatment intensification.
2.6. References


Depressive symptoms prior to and following insulin initiation in patients with type 2 diabetes mellitus: Prevalence, risk factors and effect on physician resource utilisation. *Primary Care Diabetes, 9*(5), 346-353.


people with type 2 diabetes in primary care. *PLoS One, 8*(11), e78865. doi: 10.1371/journal.pone.0078865


Vermeire, E., Van Royen, P., Coenen, S., Wens, J., & Denekens, J. (2003). The adherence of type 2 diabetes patients to their therapeutic regimens: A


Chapter 3: Summary of Methods

The research undertaken for this thesis uses mixed methods and includes analyses of data from three studies, resulting in six empirical papers (Chapter 4 to 9). Brief descriptions of the three studies are provided below along with the research questions that are addressed in Chapters 4 to 9. Research methods specific to each question are detailed in the relevant chapter. A detailed description of the methods of the three studies, as they relate to this thesis, is presented in Appendix C.

3.1. Study 1: Diabetes MILES – Australia Study

Diabetes MILES – Australia was a national cross-sectional survey of adults with type 1 diabetes or T2D. Detailed description of the study rationale, design, methods, and sample characteristics for the study have been published, co-authored by this PhD candidate (Speight, Browne, Holmes-Truscott, Hendrieckx, & Pouwer, 2012). This thesis includes analyses of two sub-samples: adults with insulin-treated and non-insulin treated T2D who completed the ITAS and other questionnaires of relevance. Statistical analyses were driven by three research questions (below) and the findings are presented in three empirical papers (Chapters 4, 5 and 8).

Research Questions:

Study 1a. Is the ITAS an acceptable and psychometrically sound measure of insulin appraisals for use with Australian adults with insulin-treated and non-insulin-treated T2D?

Study 1b. Among those with non-insulin-treated T2D, to what extent do general and diabetes-specific emotional wellbeing and beliefs about medicines contribute to current negative insulin therapy appraisals?
Study 1c. Do adults with insulin-treated T2D display negative insulin appraisals? Do clinical, self-care and psychosocial outcomes differ for those with more and less negative insulin appraisals?

3.2. Study 2: Stepping Up Study

Study 2 was a two-armed, 12-month cluster randomised controlled trial testing the effectiveness of the ‘Stepping Up’ model of care, compared to usual care, to facilitate timely and evidence-based initiation and up-titration of insulin in primary care for eligible adults with non-insulin-treated T2D. The Stepping Up protocol has been published elsewhere, co-authored by this PhD candidate (Furler et al., 2014). Demographic, clinical, self-management and psychosocial data, including insulin appraisals and willingness to begin insulin therapy, was collected at baseline at 12 months among participants with T2D. Statistical analyses of the Stepping Up baseline (Chapter 6) and 12-month follow-up (Chapter 7) datasets were driven by two research questions.

Research questions:

Study 2a. What proportion of Stepping Up participants are hypothetically willing to initiate insulin therapy? What demographic, clinical, self-management and psychosocial factors, including insulin appraisals, are associated with hypothetical willingness to begin insulin?

Study 2b. Controlling for randomisation, to what extent do demographic and clinical factors, emotional wellbeing, attitudes towards insulin and hypothetical willingness to begin insulin at baseline predict actual insulin use among Stepping Up participants at 12 months? Do attitudes toward insulin change, from baseline to 12-
month follow up, as a function insulin initiation and/or model of care (study arm allocation)?

3.3. Study 3: Qualitative Study of Insulin Appraisals

In study 3, exploratory interviews were conducted to elicit an in-depth narrative of the experience of diabetes and treatment progression among adults with T2D currently using insulin therapy. A subset of the collected data are reported in Chapter 9, with thematic analysis driven by the research question below.

Research questions:

Study 3. What is the impact of insulin use, including negative and positive consequences, for adults with T2D already using insulin? What attitudes do participants express about future insulin intensification (e.g. additional insulin injections)?
3.4. References


Chapter 4: Further Investigation of the Psychometric Properties of the Insulin Treatment Appraisal Scale among Insulin-Using and Non-Insulin-Using Adults with Type 2 Diabetes: Results from Diabetes MILES – Australia

Study 1a: Paper 1

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Frans Pouwer Department of Medical and Clinical Psychology, Centre of Research on Psychology in Somatic diseases (CoRPS), Tilburg University, The Netherlands

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*Corresponding author

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3This manuscript was published in Health and Quality of Life Outcomes 12(1): 87. doi:10.1186/1477-7525-12-87. The formatting, structure and referencing style is in accordance with the journal’s requirements. A statement of author contributions is provided in Appendix A.
Abstract

Background

Negative attitudes towards insulin are commonly reported by people with type 2 diabetes mellitus (T2DM) and can act as a barrier to timely insulin initiation. The Insulin Treatment Appraisal Scale (ITAS) is a widely used 20-item measure of attitudes towards insulin. While designed for completion by both insulin using and non-insulin using adults with T2DM, its psychometric properties have not been investigated separately for these groups. Furthermore, the total score is routinely reported in preference to the published two-factor structure (negative/positive appraisals). Further psychometric validation of the ITAS is required to examine its properties.

Methods

The ITAS was completed by a subgroup of 748 Diabetes MILES – Australia study participants with T2DM, who were either insulin using (n = 249; 45% women; mean age = 58 ± 9 years; mean diabetes duration = 13, SD = 8 years) or non-insulin using (n = 499; 47% women; mean age 57 ± 9 years; mean diabetes duration 7 ± 6 years). We replicated the psychometric analyses reported in the ITAS development paper. In addition, we explored factor structure and investigated internal consistency separately for the insulin using and non-insulin using samples.

Results

Factor analyses supported a two-factor structure with good internal consistency (negative subscale α = .90; positive subscale α = .69). Scale performance differed slightly in the insulin using and non-insulin using samples, with some items loading
inconsistently between groups. A one-factor solution was not supported in either sample, with the positive items and some negative items failing to load adequately. Consistent with prior research, negative appraisals were significantly more common among non-insulin using participants compared to those using insulin ($d = 1.04$), while the positive subscale score did not discriminate between groups.

**Conclusions**

The data supported a two factor structure and the positive subscale did not discriminate between insulin using and non-insulin using participants. As such, we recommend use of the negative subscale score in preference to the ITAS total score, and suggest close attention is paid to the relevance of the positive items in the given population.

**Keywords**

Psychological insulin resistance, Type 2 diabetes, Questionnaire, Psychometric validation
Background

Type 2 diabetes mellitus (T2DM) is a progressive condition and most people with this condition will eventually require exogenous insulin to maintain haemoglobin A1c within recommended targets [1,2]. However, a quarter of adults with T2DM report being unwilling to begin insulin therapy [3], commonly reporting concerns about the necessity of insulin, as well as the physical, social and symbolic adverse consequences of insulin use [4]. These negative attitudes, known as ‘psychological insulin resistance’ (PIR), may lead to delays in insulin initiation or sub-optimal use once insulin is prescribed [3,5-8]. PIR is a complex construct that does not simply equate to “fear of the needle”, as people can base their reluctance to use insulin on many different aspects of the therapy. The construct has been operationalised through assessment of attitudes toward insulin (insulin appraisal) [3,9-13].

Two scales have been developed and validated specifically to measure attitudes towards insulin held by people with T2DM. The 14-item ‘Barriers to Insulin Treatment’ (BIT) self-report questionnaire measures attitudes towards insulin amongst people with non-insulin-treated T2DM [13]. BIT items commonly refer to the physical aspects of insulin use or technical concerns (e.g. side effects, pain) rather than the symbolic meaning of insulin initiation (e.g. feelings of failure/self-blame or increased diabetes severity). The Insulin Treatment Appraisal Scale (ITAS) is a 20-item questionnaire, including 16 statements referring to barriers to insulin use and four referring to its benefits (12). Unlike the BIT, the more commonly used ITAS was developed and validated for use by people with T2DM regardless of current treatment type, with the advantage of enabling assessment both before and
after insulin initiation [12]. For non-insulin using respondents, the ITAS assesses expectations about future insulin use, while for those already using insulin, the measure is used to evaluate actual experience with insulin use.

The clinical relevance of the ITAS has been demonstrated. In cross-sectional studies, a difference has been observed between insulin using and non-insulin participants in total ITAS scores of approximately one standard deviation [12,14]. Longitudinal research indicates that the ITAS is sensitive to treatment change from oral medication to insulin injections [15]. Furthermore, higher ITAS scores (indicating more negative appraisal of insulin) are associated with being hypothetically less ‘willing’ to begin insulin if recommended [10]. Previous research has identified associations between ITAS scores and general and diabetes-specific emotional wellbeing among people with T2DM [12,16].

Initial investigation of the structure of the ITAS revealed it to have a two-factor solution, identifying a positive subscale (benefits) and a negative subscale (barriers) [12]. Despite reporting low item commonalities in a one-factor structure, scale developers proposed the use of an ITAS total score (summation of all 20 items), to indicate a person’s overall insulin appraisal. Since the original US study [12], no further work has been published regarding the validation of the two-factor or one-factor structure, and the ITAS total score has been used most commonly [9,10,16]. Despite reports that the ITAS is psychometrically sound for both insulin using and non-insulin using participants [12], psychometric analyses have not been reported separately for these groups. Given that these groups may have either quantitatively or qualitatively different attitudes towards insulin, based on expectations or actual
experience, an investigation is needed of how the scale performs psychometrically in each of these groups separately.

Further psychometric analyses are required to assess the appropriateness of the scale in the two separate samples for which it was intended, as well as to further evaluate the validity of the ITAS total score. Thus, our aim was to further examine the psychometric properties of the ITAS separately among insulin using and non-insulin using adults with T2DM in Australia.

Methods

This analysis utilises a subset of data from Diabetes MILES – Australia, a large-scale, national, cross-sectional survey of Australian adults (aged 18 to 70 years) diagnosed with either type 1 diabetes or T2DM. The survey was conducted in July – August 2011. A detailed description of the methods, response rates and questionnaires has been published elsewhere [17]. Diabetes MILES – Australia received ethics approval from the Deakin University Human Research Ethics committee (reference number: 2011–046).

Participants

Diabetes MILES – Australia surveys were sent out to a random sample of 15,000 National Diabetes Services Scheme (NDSS) registrants. The NDSS register includes >1.1 million registrants living with diabetes in Australia, of whom 87% have T2DM (http://www.ndss.com.au/en/Research/Data-Snapshots/). Survey booklets were matched to the recorded diabetes diagnosis and treatment (confirmed at registration by a health professional): T1DM, T2DM Insulin using or T2DM non-insulin.
The survey was also made available online nationally, with respondents required to self-report their type of diabetes in order to receive the appropriate survey version. The database was cleaned to validate survey versions against self-report diabetes diagnosis, age at diagnosis, and treatment type to ensure the highest level of accuracy possible given the self-report nature of the survey.

Overall, there were 3,338 eligible respondents, of whom 1,962 reported living with T2DM. Of these, 49% (n = 953) were women, the mean ± SD age was 59 ± 9 years and 37% (n = 724) were using insulin. The current analysis focuses on a subsample of participants with T2DM who were invited to complete the ITAS [12] and reported their diabetes treatment type as either insulin using, requiring oral antihyperglycaemic tablets or following lifestyle recommendations. Participants reporting use of glucagon-like peptide-1 (GLP-1) agonist treatment were excluded from the current study. Like insulin, GLP-1 agonist is administered via injection, but differs from insulin use in a number of ways including, its efficacy; potential side effects (e.g. weight loss versus possible weight gain when using insulin) [18]; and the associated stigma of the treatment [19-22]. Therefore participants using GLP-1 injections are not easily classified within either treatment group (insulin using and non-insulin using) relevant to this study.

Measures

The Diabetes MILES – Australia surveys included a set of core measures (completed by all respondents) and various additional measures (included in one or more of the six survey versions). Full details of the measures are published elsewhere [17]. Variables of interest to this study include: demographics (age, gender, relationship status, whether employed in paid work, education level, and body mass
index), diabetes health status (self-reported diabetes type, primary treatment and years living with diabetes), and the ITAS [12].

The ITAS asks respondents to indicate their level of agreement (‘strongly disagree’ = 1 to ‘strongly agree’ = 5) with 20 statements. Scores for 16 negatively-worded items are summed to provide a ‘negative appraisal’ score (16–80); scores for four positively-worded items are summed to provide a ‘positive appraisal’ score (4–20); all twenty items are summed (with positively-worded items reversed) to form a ‘total’ score (20–100). Higher ‘total’ and ‘negative appraisal’ scores indicate more negative attitudes, while higher ‘positive appraisal’ scores indicate more positive attitudes towards insulin. Permission to use the ITAS was granted by the copyright holders.

**Statistical analysis**

Statistical analysis was undertaken using SPSS version 21 (Chicago, USA). Frequencies, means and standard deviation were obtained for ITAS and relevant demographics for insulin using and non-insulin using participants. Acceptability of the scale was assessed by examining completion rates and identifying ceiling effects for negative ITAS items and floor effects for positive ITAS items (i.e. >20% scoring minimum/maximum response) [23]. To replicate the methods described in the ITAS development paper [12], we conducted exploratory factor analysis (EFA) with oblimin rotation on the 20-item scale for the whole sample, as we expected the factors to be correlated. When inspecting the Eigenvalues, we used the Kaiser-criterion (Eigenvalue >1) and reviewed the scree plot to determine the maximum number of factors. In accordance with the original development paper, item loadings were considered optimal if they were >0.40 on one factor and <0.30 on any other.
factor [12]; a less conservative criterion of loading >0.30 (without concern for
double loadings) was also adopted [24]. To replicate the hypothesised optimal scale
structure, and to assess the suitability of the total score, forced two-factor and one-
factor solutions were conducted respectively. Internal consistency was estimated
using Cronbach’s alpha and Guttman’s λ2 [25], where ≥0.70 and <0.90 was
considered reasonable. Item-total correlations were also calculated, with a score of
<0.20 taken to indicate a poor relationship with the total scale score. These
psychometric analyses were conducted for the insulin-using and non-insulin using
samples separately and a forced one-factor solution was also investigated.

Known-groups validity was explored by comparing mean ITAS total, negative
and positive scores between treatment groups. Student t-tests or chi-squares were
conducted to assess between-groups differences in ITAS scores. The association
between demographics and total ITAS scores between groups was explored using
Student t-tests and bivariate correlations. Statistical tests are two-sided with
differences accepted at a significant level of \( p < 0.05 \). Effect sizes are reported using
Cohen’s \( d \).

**Results**

Overall, 887 participants with T2DM completed the Diabetes MILES –
Australia survey versions in which the ITAS was included. Of these, 24 participants
were excluded due to unreported treatment type or reported use of GLP-1 agonist
injections. A further 115 (12.9%) participants were excluded due to non-completion
of at least one ITAS item (see ‘Acceptability’ for further details). Of the 748 eligible
respondents, one third were using insulin to manage their diabetes. Participant
characteristics are shown in Table 1. Within the current sample, 193 participants
(26%) completed the online version of the survey, and 555 (74.2%) completed the hardcopy survey.

Table 1

*Self-reported demographics and clinical characteristics of insulin using and non-insulin using participants*

<table>
<thead>
<tr>
<th></th>
<th>Non-insulin users</th>
<th>Insulin users</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>499 (67%)</td>
<td>249 (33%)</td>
</tr>
<tr>
<td>Female sex</td>
<td>233 (47%)</td>
<td>112 (45%)</td>
</tr>
<tr>
<td>Age - years</td>
<td>57 ± 9 (22 – 70)</td>
<td>58 ± 9 (21 – 70)</td>
</tr>
<tr>
<td>Employment - in paid work</td>
<td>279 (56%)</td>
<td>104 (42%)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>32 (7%)</td>
<td>36 (16%)</td>
</tr>
<tr>
<td>Medium</td>
<td>314 (66%)</td>
<td>157 (67%)</td>
</tr>
<tr>
<td>High</td>
<td>132 (28%)</td>
<td>40 (17%)</td>
</tr>
<tr>
<td>Having a partner</td>
<td>369 (75%)</td>
<td>178 (73%)</td>
</tr>
<tr>
<td>Diabetes duration - years</td>
<td>7 ± 6 (&lt;1 – 35)</td>
<td>13 ± 8 (&lt;1 – 42)</td>
</tr>
<tr>
<td><strong>Primary Treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifestyle modifications</td>
<td>130 (26%)</td>
<td>-</td>
</tr>
<tr>
<td>Blood glucose lowering tablets</td>
<td>369 (74%)</td>
<td>-</td>
</tr>
<tr>
<td>Insulin injections</td>
<td>-</td>
<td>247 (99%)</td>
</tr>
<tr>
<td>Insulin pump</td>
<td>-</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>BMI</td>
<td>31 ± 7 (13 – 78)</td>
<td>34 ± 9 (15 – 92)</td>
</tr>
</tbody>
</table>

NB. Valid percentage reported as n values vary due to missing data on individual variables.
Data are mean ± standard deviation or N (%).
Acceptability

Non-insulin using participants were slightly more likely to have missing data; 83 (14%) non-insulin participants compared to 32 (11%) insulin-using participants missed at least one item. Of the non-insulin using participants with missing data, almost half (n = 39) skipped all 20 items. Thirty-three missed just one item and the remaining 11 missed between 2 and 19 items. The majority of insulin using participants with missing data skipped only 1 item (n = 26), and a further six skipped between 2 and 15 items: none skipped the entire scale. Excluding those who missed the whole scale, each of the 20 ITAS items was completed by ≥98.2% of non-insulin using participants and, similarly, by ≥98.2% of insulin using participants.

Among the four positively-worded ITAS items, no floor effects were apparent amongst either insulin or non-insulin using participants (i.e. ≤20% of participants strongly disagreed with the benefits of insulin). Ceiling effects were apparent for four of the 16 negatively worded items among non-insulin using participants (>20% and <32% strongly agreed with items 1, 2, 5 and 6) but none were apparent among insulin using participants.

Scale structure: whole sample

EFA analyses conducted on the whole sample revealed a maximum of four factors with an Eigenvalue >1, explaining 57.1% of the total variance. The Eigenvalue for (and variance explained by) each factor respectively was 6.7 (33.4%), 2.3 (11.7%), 1.3 (6.4%), and 1.1 (5.7%). Factors three and four were most easily interpretable: the four ‘benefits’ all loaded onto one factor suggesting a ‘positive appraisal’ subscale, and the two side-effect items (‘increases risk of hypoglycaemia’ ‘weight gain’) loaded onto another factor. Eleven negative appraisal items loaded
onto the first factor with the remaining three loading onto the second factor, with no clear interpretation for either.

Given the minimal additional variance explained by a 3- or 4-factor solution, and the aim to replicate the scale structure previously reported [12], a three-factor solution was not investigated. The two-factor solution explained 45% of the total variance with the first factor including all negatively-worded items except ‘weight gain’ and the second factor including the four positively-worded items. Only item 18 (‘family and friends concerns’) loaded >0.3 on more than one factor. The correlation between factors was low ($r = 0.06$), suggesting a Varimax rotation would be more suitable, but the results of this rotation did not differ from the loading pattern obtained using the oblique rotation. A forced one-factor solution explained 33.4% of the variance, with all four positive items and the ‘weight gain’ item failing to load sufficiently. Overall, reliability was satisfactory for the 20-item scale ($\alpha = 0.87; \lambda^2 = 0.89$), the 16-item negative subscale ($\alpha = 0.90; \lambda^2 = 0.91$), and for the positive subscale ($\alpha = 0.69; \lambda^2 = 0.69$). Table 2 displays both the forced one-factor and two-factor solutions, with item loadings for the whole sample (described here) and by treatment type (described below).
Table 2

Forced 1-factor and 2-factor EFA of the ITAS: whole sample and by treatment type

<table>
<thead>
<tr>
<th>Item</th>
<th>Whole sample</th>
<th>Non-insulin users</th>
<th>Insulin users</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total scale</td>
<td>Two factor</td>
<td>Total scale</td>
</tr>
<tr>
<td></td>
<td>Negative subscale</td>
<td>Positive subscale</td>
<td>Negative subscale</td>
</tr>
<tr>
<td>1 Taking insulin means I have failed to manage my diabetes with diet and tablets</td>
<td>0.55</td>
<td>0.54</td>
<td>0.54</td>
</tr>
<tr>
<td>2 Taking insulin means my diabetes has become much worse</td>
<td>0.60</td>
<td>0.59</td>
<td>0.59</td>
</tr>
<tr>
<td>3 Taking insulin helps to prevent complications of diabetes</td>
<td>0.69</td>
<td></td>
<td>0.69</td>
</tr>
<tr>
<td>4 Taking insulin means other people see me as a sicker person</td>
<td>0.65</td>
<td>0.64</td>
<td>0.64</td>
</tr>
<tr>
<td>5 Taking insulin makes life less flexible</td>
<td>0.72</td>
<td>0.71</td>
<td>0.70</td>
</tr>
<tr>
<td>6 I'm afraid of injecting myself with a needle</td>
<td>0.65</td>
<td>0.66</td>
<td>0.58</td>
</tr>
<tr>
<td>7 Taking insulin increases the risk of low blood glucose levels (hypoglycaemia)</td>
<td>0.44</td>
<td>0.43</td>
<td>0.37</td>
</tr>
<tr>
<td>8 Taking insulin helps to improve my health</td>
<td>0.76</td>
<td></td>
<td>0.76</td>
</tr>
<tr>
<td>9 Insulin causes weight gain</td>
<td>0.43</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>10 Managing insulin injections takes a lot of time and energy</td>
<td>0.74</td>
<td>0.74</td>
<td>0.69</td>
</tr>
<tr>
<td>11 Taking insulin means I have to give up activities I enjoy</td>
<td>0.72</td>
<td>0.73</td>
<td>0.70</td>
</tr>
<tr>
<td>Item</td>
<td>Whole sample</td>
<td>Non-insulin users</td>
<td>Insulin users</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>--------------</td>
<td>-------------------</td>
<td>---------------</td>
</tr>
<tr>
<td></td>
<td>Total scale</td>
<td>Two factor</td>
<td>Total scale</td>
</tr>
<tr>
<td></td>
<td>Negative subscale</td>
<td>Positive subscale</td>
<td>Negative subscale</td>
</tr>
<tr>
<td>12 Taking insulin means my health will deteriorate</td>
<td>0.70</td>
<td>0.72</td>
<td>0.66</td>
</tr>
<tr>
<td>13 Taking insulin is embarrassing</td>
<td>0.71</td>
<td>0.73</td>
<td>0.69</td>
</tr>
<tr>
<td>14 Injecting insulin is painful</td>
<td>0.71</td>
<td>0.72</td>
<td>0.69</td>
</tr>
<tr>
<td>15 It is difficult to inject the right amount of insulin correctly at the right time every day</td>
<td>0.68</td>
<td>0.69</td>
<td>0.67</td>
</tr>
<tr>
<td>16 Taking insulin makes it more difficult to fulfil my responsibilities (at work, at home)</td>
<td>0.79</td>
<td>0.80</td>
<td>0.75</td>
</tr>
<tr>
<td>17^Taking insulin helps to maintain good control of my blood glucose</td>
<td></td>
<td>0.74</td>
<td>0.73</td>
</tr>
<tr>
<td>18 Being on insulin causes family and friends to be more concerned about me</td>
<td>0.59</td>
<td>0.56</td>
<td>-0.32</td>
</tr>
<tr>
<td>19^Taking insulin helps to improve my energy levels</td>
<td></td>
<td>0.55</td>
<td>0.50</td>
</tr>
<tr>
<td>20 Taking insulin makes me more dependent on my doctor</td>
<td>0.62</td>
<td>0.61</td>
<td>0.64</td>
</tr>
<tr>
<td>Cronbach’s alpha</td>
<td>0.87</td>
<td>0.90</td>
<td>0.85</td>
</tr>
<tr>
<td>Total variance explained</td>
<td>33.4%</td>
<td>45%</td>
<td>32%</td>
</tr>
</tbody>
</table>

NB. EFA conducted using oblimin rotation. Loadings < ±0.30 have been suppressed from the table for clarity of interpretation. ^positive ITAS items.
Scale structure: by treatment type

In the non-insulin using sample, inspection of the Eigenvalues after EFA revealed a maximum of four factors, explaining 57.2% of the total variance. The Eigenvalues for (and variance explained by) each factor respectively was 6.4 (32.0%), 2.6 (12.9%), 1.4 (6.8%), and 1.1 (5.4%). Only factor four was interpretable, with all four ‘benefits’ loading >0.4, suggesting a ‘positive appraisal’ subscale. Item 7 (‘increased risk of hypoglycaemia’) did not load >0.4 on any factor and six other items loaded ≥ 0.3 onto more than one factor.

An EFA conducted for the insulin using participants revealed a maximum of five factors, explaining 57% of the total variance. The Eigenvalues for (and variance explained by) each factor respectively was 5.4 (27.0%), 2.2 (10.9%), 1.5 (7.7%), 1.2 (6.1%), and 1.0 (5.2%). Once more, one factor included satisfactory loadings for all four positive items while the other factors were unclear. Ten items loaded ≥ 0.3 on two or more factors and two items did not load at all (‘weight gain’ and ‘concern from family and friends’).

The two-factor solution within the non-insulin using group explained 44.9% total variance, with the first factor including 15 of the 16 negative items, and the second factor including all four positive items. Item 7 (‘increases risk of hypoglycaemia’) did not load on either factor, or four of the negative items double-loaded (≥ 0.3) on both factors. Amongst the insulin using group, a two-factor solution explained 38% variance. Factor one included all 16 negative items and factor two included the four positive items.

A forced one-factor solution explained 32% and 27% of the total variance in the non-insulin using and insulin using samples respectively. The positive items did
not load in either group. In the non-insulin using sample, all negative items except for item 7 (‘increases risk of hypoglycaemia’), loaded onto the factor and in the insulin using sample only item 9 (‘weight gain’) did not load.

In the non-insulin using sample, Cronbach’s alpha was 0.85 for the 20-item scale, 0.89 for the 16-item negative subscale, and 0.69 for the positive subscale. Guttman’s λ2 was 0.87, 0.90, and 0.71 respectively. Internal consistency was similar for insulin using participants: for the total scale α = 0.84 and λ2 = 0.85, for the negative subscale α = 0.85 and λ2 = 0.87, and for the positive subscale α = 0.68 and λ2 = 0.69.

Within the total scale, all positive items displayed low item-total correlations; <0.1 for non-insulin participants and <0.32 for insulin using participants. All item-total correlations for negatively worded items were >0.2 for both non-insulin and insulin using participants. When exploring the negative and positive subscales separately, all item-total correlations were above the >0.2 cut off for non-insulin using participants (negative subscale range = 0.31-0.69, positive subscale range = 0.36-0.58) or for insulin using participants (negative subscale range = 0.35-0.63, positive subscale range = 0.38-0.58).

**Known-groups validity**

Table 3 displays, by treatment type, the mean and standard deviation for each of the ITAS items, total score, positive subscale and negative subscale, the t-test significance results and effect sizes showing between group differences, as well as the percentage who agreed or strongly agreed with each item. Non-insulin using participants reported significantly higher (more negative) scores compared to the insulin using participants on all negatively-worded items, except for ‘insulin causes
weight gain’, for which insulin using participants reported higher (more negative) scores. Moderate effect sizes were found between groups for 9 of the 16 negative items ($d$ range = 0.54-0.76), and large effect sizes for 4 items ($d$ range = 0.86-1.08). Item 6 (‘I’m afraid of injecting myself with a needle’) discriminated most highly between groups.
Table 3

*Differences in ITAS scores (items, subscales, and total score) by insulin use*

<table>
<thead>
<tr>
<th>Item</th>
<th>Non-insulin users</th>
<th>Insulin users</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M ± SD</td>
<td>A/SA%</td>
<td>M ± SD</td>
</tr>
<tr>
<td>1</td>
<td>Taking insulin means I have failed to manage my diabetes with diet and tablets</td>
<td>3.5 ± 1.3</td>
<td>58.3%</td>
</tr>
<tr>
<td>2</td>
<td>Taking insulin means my diabetes has become much worse</td>
<td>4.0 ± 1.0</td>
<td>80.2%</td>
</tr>
<tr>
<td>3^</td>
<td>Taking insulin helps to prevent complications of diabetes</td>
<td>3.9 ± 1.0</td>
<td>76.4%</td>
</tr>
<tr>
<td>4</td>
<td>Taking insulin means other people see me as a sicker person</td>
<td>3.3 ± 1.1</td>
<td>46.3%</td>
</tr>
<tr>
<td>5</td>
<td>Taking insulin makes life less flexible</td>
<td>3.6 ± 1.1</td>
<td>58.7%</td>
</tr>
<tr>
<td>6</td>
<td>I'm afraid of injecting myself with a needle</td>
<td>3.3 ± 1.4</td>
<td>47.9%</td>
</tr>
<tr>
<td>7</td>
<td>Taking insulin increases the risk of low blood glucose levels (hypoglycaemia)</td>
<td>3.4 ± 1.0</td>
<td>46.5%</td>
</tr>
<tr>
<td>8^</td>
<td>Taking insulin helps to improve my health</td>
<td>3.8 ± .08</td>
<td>67.7%</td>
</tr>
<tr>
<td>9</td>
<td>Insulin causes weight gain</td>
<td>3.1 ± .08</td>
<td>18.2%</td>
</tr>
<tr>
<td>10</td>
<td>Managing insulin injections takes a lot of time and energy</td>
<td>3.3 ± 1.0</td>
<td>40.9%</td>
</tr>
<tr>
<td>11</td>
<td>Taking insulin means I have to give up activities I enjoy</td>
<td>2.7 ± 1.0</td>
<td>16.8%</td>
</tr>
<tr>
<td>12</td>
<td>Taking insulin means my health will deteriorate</td>
<td>2.8 ± 1.0</td>
<td>18.6%</td>
</tr>
<tr>
<td>13</td>
<td>Taking insulin is embarrassing</td>
<td>2.7 ± 1.1</td>
<td>21.6%</td>
</tr>
<tr>
<td>14</td>
<td>Injecting insulin is painful</td>
<td>3.1 ± 1.0</td>
<td>32.1%</td>
</tr>
<tr>
<td>Item</td>
<td>Non-insulin users</td>
<td>Insulin users</td>
<td>d</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>-------------------</td>
<td>---------------</td>
<td>------</td>
</tr>
<tr>
<td></td>
<td>M ± SD</td>
<td>A/SA%</td>
<td>M ± SD</td>
</tr>
<tr>
<td>15  It is difficult to inject the right amount of insulin correctly</td>
<td>3.0 ± 0.9</td>
<td>23.2%</td>
<td>2.1 ± 1.0***</td>
</tr>
<tr>
<td>every day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16  Taking insulin makes it more difficult to fulfil my responsibilities (at work, at home)</td>
<td>2.8 ± 0.9</td>
<td>17.8%</td>
<td>2.0 ± 0.9***</td>
</tr>
<tr>
<td>17^ Taking insulin helps to maintain good control of my blood glucose</td>
<td>3.9 ± 0.8</td>
<td>74.7%</td>
<td>3.9 ± 0.9</td>
</tr>
<tr>
<td>18  Being on insulin causes family and friends to be more concerned about me</td>
<td>3.6 ± 0.9</td>
<td>57.7%</td>
<td>3.0 ± 1.0***</td>
</tr>
<tr>
<td>19^ Taking insulin helps to improve my energy levels</td>
<td>3.3 ± 0.7</td>
<td>30.9%</td>
<td>3.1 ± 0.9**</td>
</tr>
<tr>
<td>20  Taking insulin makes me more dependent on my doctor</td>
<td>3.4 ± 0.9</td>
<td>47.3%</td>
<td>2.9 ± 1.1***</td>
</tr>
<tr>
<td>Total Score</td>
<td>60.7 ± 10.1</td>
<td>50.2 ± 10.3***</td>
<td></td>
</tr>
<tr>
<td>Positive Subscale</td>
<td>14.9 ± 2.4</td>
<td>14.8 ± 2.6</td>
<td></td>
</tr>
<tr>
<td>Negative Subscale</td>
<td>51.6 ± 10.2</td>
<td>41.2 ± 9.6***</td>
<td></td>
</tr>
</tbody>
</table>

M: mean; SD: standard deviation; A/SA: Agree/Strongly Agree; ^ positive ITAS items, **p < .01, *** p < .001.
Scoring: 1 = Strongly Disagree, 5 = Strongly Agree
There were significant differences between treatment groups for the negative subscale \( t(746) = 13.44, p < 0.001, d = 1.04 \) and total ITAS score \( t(746) = 13.05, p < 0.001, d = 1.03 \). The percentage of participants who agreed with the benefits of insulin was high, regardless of treatment type, and the mean positive subscale score was not significantly different between groups \( t(746) = 0.55, p = 0.582, d = 0.04 \).

Associations between ITAS scores and demographics were comparable between groups. Total ITAS scores were weakly positively correlated with age for both insulin users \( r = -0.29, p < 0.001 \) and non-insulin users \( r = -0.18, p < 0.05 \). No significant relationship was apparent between ITAS scores and diabetes duration for either group (both \( p > 0.607 \)). Between group ITAS scores did not differ by gender (both \( p > 0.558 \) for both) or whether participants reported being in a relationship (both \( p > 0.118 \) for both). Both insulin users \( t(247) = -2.17, p = 0.03 \) and non-insulin users \( t(494) = -3.65, p < 0.001 \) who participated in paid work reported significantly higher ITAS scores (more negative) than those not in paid work.

**Discussion**

In replication of the ITAS development paper [15], EFA and reliability tests were conducted on the whole sample and similar results were observed. However, contrary to the original recommendation to use a single ‘Total ITAS’ score, we believe the two-factor structure appears to be a better representation of the 20-item scale, with only ‘weight gain’ not loading on either scale.

In exploring the two-factor solution for the insulin using and non-insulin using samples separately, we found variation in some item loadings. For non-insulin using participants, item 7 (‘increases risk of hypoglycaemia’) did not load onto either subscale. This might be due to a lack of knowledge among non-insulin using
participants regarding the potential risk of hypoglycaemia caused by insulin use, though almost half of this sample agreed or strongly agreed that this was a risk. In contrast to the whole sample, item 9 (‘weight gain’) loaded onto the negative subscale for non-insulin users and a number of other variables (items 2, 4, 5, 18) had multiple loadings, while all loading strongest on the negative subscale. Only item 18 loaded > 0.4 on both the positive and negative subscale. This might be explained by non-insulin using participants feeling that insulin causing “family and friends to be more concerned about me” would in fact be a benefit of insulin use. Indeed, the item wording is not sufficiently negative for the direction to be clear. For insulin using participants, items 1 (‘insulin means my previous self-care has failed’), 2 (‘insulin means my diabetes is worse’) and 9 (‘weight gain’) were just shy of loading onto the negative subscale (if a stringent criterion of >0.4 was applied) but loaded well when a less conservative criterion (>0.3) was adopted. However these items were the three most highly endorsed among insulin using participants, which suggests they should not be removed from the scale. The forced two-factor solution was the best representation of the 20-item questionnaire for both samples.

Reliability of negative and positive subscales was similar between groups, with the high negative subscale alpha suggesting the possibility for scale reduction. A small number of items performed inconsistently between treatment groups. They maybe candidates for removal or it may be that different items are important for different treatment groups. These items (1, 2, 7, and 9), which also had lower item-total correlations and did not load consistently, were often more highly endorsed by participants than those which performed better statistically, suggesting they have strong face validity. It may be that these items are not performing statistically as well because they are conceptually quite independent of other negative aspects of insulin
use, while the items that load well and display high item-total correlations frequently refer to similar barriers to insulin (e.g. the burden of insulin injections in terms of its effect on lifestyle and responsibilities, as well the technical/physical aspects of having to inject).

Given the high internal consistency reliability of the 20-item total scale, the ITAS total score has been recommended for use to quantify overall insulin appraisal [12]. However, in both the ITAS development paper and our current study, Cronbach’s alpha for the 20-item scale is lower than for the 16-item negative scale, and the positive items display very low item-total correlations. Unsurprisingly, a forced one-factor EFA reveals that the four positive items do not load on the factor for either treatment group. Given these results, we propose that the positive and negative subscales should not be combined to create a total score.

Consistent with international findings adults with non-insulin-treated T2DM report significantly more negative attitudes towards insulin use than those using insulin, with total ITAS scores differing by approximately one standard deviation [12,14,15]. Non-insulin using participants reported higher (more negative) scores on 15 of the 16 items, with ‘weight gain’ the only item for which insulin using participants reported more negative appraisals. This is also consistent with previous research [12,14]. With the exception of ‘weight gain’, the ranking of negative appraisals was similar between the two treatment groups; suggesting similar prioritisation of concerns about insulin between groups and differing only by intensity of endorsement. Ceiling effects were present for four ITAS items among non-insulin using participants, but not for the insulin using participants. However, as these ceiling effects are moderate (<33%), are in line with the expected scoring
direction of non-insulin using participants, and not displayed among insulin using participants, we suggest that they may not be cause for concern necessarily.

While the ‘negative appraisal’ subscale showed strong discriminatory power, the positive subscale did not differ between treatment groups. Similar to previous studies, we found that participants not using insulin commonly endorsed positive statements about insulin [9,10,12,14,15]. This suggests that concerns about insulin initiation, or psychological insulin resistance, may exist independently of the belief that insulin may be beneficial. This may have implications for clinical care. For example, when counselling patients about their diabetes management options, it may be more beneficial to acknowledge, normalise and then minimise their perceived barriers to insulin use rather than emphasising only the actual benefits of insulin use. However, we recommend that the positive items are retained in the scale for further research purposes such as exploring the subscales association with other variables (e.g. self-care behaviours, optimal insulin taking behaviours). For example, previous research has reported optimal medication taking behaviours to be associated with belief in the benefit of the medication [26].

**Strengths and limitations**

The strengths of this study include it being the first study to quantitatively explore PIR in an Australian sample using a validated measure. In addition, it is the only study to further evaluate the psychometric performance of the ITAS since its development. The large sample size and the inclusion of both insulin using and non-insulin using participants to enable separate psychometric analyses are also advantages.
The limitations of Diabetes MILES – Australia are discussed in detail elsewhere [17]. Limitations of specific relevance to the current study are the self-report nature of the diabetes diagnosis for 26% of the sample and the proportion of missing data. The ITAS was developed and validated for use among people with T2DM. Given the self-report nature of Diabetes MILES – Australia, it is impossible to tell whether all participants were accurately classified as having type 2 diabetes. However, it is expected that the following safeguards reduced the likelihood of participants being misclassified. The majority (74%) of respondents had received a pre-determined survey booklet type (specific to their diabetes type and treatment) based on their diabetes diagnosis as reported within the NDSS [17]. These participants had the opportunity to complete the ITAS only if they were registered with the NDSS as having a diagnosis of T2DM; their data were removed from the current analysis if they subsequently reported a diagnosis of type 1 diabetes within the survey booklet. Online participants (26%) received the ITAS for completion only if they self-reported living with T2DM. Thus, any participant who received a type 1 booklet or self-reported online that they had type 1 diabetes would not have had the opportunity to complete the ITAS. Prior literature concludes that self-reported diabetes diagnosis, not type specific, is reasonably accurate when compared to medical data [27,28]. However, to the author’s knowledge, no research has explored the validation of self-reported diabetes type comparing those with type 1 and those with T2DM.

A further limitation of the current analysis was the missing data, which differed by treatment group, suggesting that the scale may be more acceptable or relevant to participants with T2DM using insulin than non-insulin using participants. It is probable that those non-insulin using participants who skipped the scale entirely
perceived it to be irrelevant for them, despite instructions asking non-insulin users “to answer each item based on their current knowledge and thoughts about what insulin therapy would be like”. Hence, we advise future ITAS users to consider including instructions that better emphasise that the questionnaire is to be completed by all participants, not just those already using insulin. After excluding participants who skipped the entire questionnaire, almost three quarters of those with missing data skipped just one item and no particular item displayed substantial non-completion. This indicates acceptability of items among the majority of participants.

Finally, the wording of some ITAS items assumes current or prior use of lifestyle modifications or blood glucose lowering tablets. However, it is possible that proportions of participants with insulin-treated T2DM have not actively managed their diabetes prior to beginning insulin, and therefore, may find some ITAS questions inappropriate. For example: “Taking insulin means I have failed to manage my diabetes with diet and tablets”. As the Diabetes MILES survey did not ask participants to report previous diabetes treatments, we are unable to clarify what proportion, if any, were prescribed insulin immediately after diagnosis of T2DM. This is a potential limitation of the questionnaire and we recommend that future users consider including assessment of prior diabetes management.

Conclusions

In the present study, the 20-item ITAS total score explained less variance and displays lower internal consistency reliability than the 16-item ‘negative appraisal’ score. We recommend that calculation of the 20-item ITAS total score be avoided in preference for the 16-item ‘negative appraisal’ score, with close attention paid to the relevance and usefulness of the ‘positive appraisal’ subscale in the given population.
Our findings support use of the ITAS in both treatment groups. As perceptions of insulin use appear to vary based on expectation versus actual experience, it is unsurprising that certain items performed inconsistently between groups. The ITAS is a relatively brief and easy to complete questionnaire which may be useful clinically to promote discussion with people with T2DM about their concerns regarding insulin use, or to evaluate interventions to reduce PIR.

**Abbreviations**

BIT, Barriers to Insulin Treatment questionnaire; EFA, Exploratory factor analysis; GLP-1, Glucagon-like peptide-1; ITAS, Insulin Treatment Appraisal Scale; NDSS, National Diabetes Services Scheme; PIR, Psychological insulin resistance; T2DM, Type 2 diabetes mellitus

**Competing interests**

JS has received research funding and consultancy fees from Sanofi Diabetes, in addition to support to attend academic meetings from Sanofi Diabetes and Novo Nordisk. FP has acted as an advisory board member and speaker for Novo Nordisk, and as a speaker for Sanofi-Aventis. He has received a grant from Novo Nordisk to support research and he has received funding for travel and accommodation to attend DAWN2 (Diabetes Attitudes Wishes and Needs) International Publication Planning Committee meetings. FP was also a co-author on the ITAS development and validation paper [15].

**Author contributions**

JS conceived The Diabetes MILES Study, and together with FP developed The Diabetes MILES Study International Collaborative. JS is principal investigator of
Diabetes MILES – Australia. EHT was project manager of Diabetes MILES – Australia throughout 2011. EHT conducted all data cleaning and analyses of the measures reported here and prepared the first draft of the manuscript. JS and FP provided advice throughout the analysis and interpretation of results. All authors commented on the initial draft, prepared revisions, and approved the final manuscript.

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References


Chapter 5: Explaining Psychological Insulin Resistance in Adults with Non-Insulin-Treated Type 2 Diabetes: The Roles of Diabetes Distress and Current Medication Concerns. Results from Diabetes MILES—Australia

Study 1b: Paper 2

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Highlights

- Cross-sectional study exploring factors associated with negative insulin therapy appraisals.
- Insulin appraisals moderately associated with diabetes-specific emotional burden.
- Insulin appraisals moderately associated with concerns about diabetes medications.
- Weaker associations observed with general medication beliefs and wellbeing.
- Interventions should look to improve diabetes-specific distress and medicine beliefs.
Abstract

Aims

To investigate the contribution of general and diabetes-specific emotional wellbeing and beliefs about medicines in the prediction of insulin therapy appraisals in adults with non-insulin-treated type 2 diabetes.

Methods

The sample included Diabetes MILES – Australia cross-sectional survey participants whose primary diabetes treatment was oral hypoglycaemic agents (N=313; 49% women; mean±SD age: 57±9 years; diabetes duration: 7±6 years). They completed validated measures of beliefs about the ‘harm’ and ‘overuse’ of medications in general (BMQ General); ‘concerns’ about and ‘necessity’ of current diabetes medications (BMQ Specific); negative insulin therapy appraisals (ITAS); depression (PHQ-9); anxiety (GAD-7), and diabetes distress (DDS-17). Factors associated with ITAS Negative scores were examined using hierarchical multiple regressions.

Results

Twenty-two percent of the variance in ITAS Negative scores (52±10), was explained by: number of complications (β=-0.15, p=0.005), DDS-17 subscale ‘emotional burden’ (β=0.23, p<.001), and ‘concerns’ about current diabetes treatment (β=0.29, p<0.001). General beliefs about medications and general emotional wellbeing did not contribute significantly to the model.
Conclusions

Psychological insulin resistance may reflect broader distress about diabetes and concerns about its treatment but not general beliefs about medicines, depression or anxiety. Reducing diabetes distress and current treatment concerns may improve attitudes towards insulin as a potential therapeutic option.

Keywords

Type 2 diabetes, Psychological insulin resistance, Beliefs about medications, Diabetes distress
Introduction

Despite its proven efficacy among people with progressed type 2 diabetes mellitus (T2DM) [1,2], insulin therapy seems less popular than oral medication. Approximately one quarter of adults with non-insulin-treated T2DM refuse, or report being unwilling to begin, insulin [2, 3, 4]. In the UKPDS, for example, 27% of the participants who were prescribed insulin therapy initially refused this form of therapy, compared to 7-13% in the tablet-treated group [5]. In Australia, around 23% of adults with T2DM are currently using insulin to manage their diabetes [6], despite reports that the mean HbA\textsubscript{1c} of adults with T2DM overall is 8.0% (64 mmol/mol) [7]. Similar results have been found internationally [8-12]. Notwithstanding individual factors and individualised glycaemic targets that cannot be extricated in aggregated national datasets, these data suggest a failure to intensify treatment, e.g. timely insulin initiation, which may be due to the reluctance of the health professional (i.e. clinical inertia [10]) and/or the person with T2DM.

People with T2DM may delay insulin initiation for many reasons, ranging from concerns about the perceived complexity of insulin therapy, to the belief that one has failed if insulin needs to be prescribed. The cluster of negative appraisals of insulin therapy is known as “psychological insulin resistance” [3, 13]. Understanding the factors associated with negative attitudes toward insulin therapy can inform strategies to improve attitudes towards, and uptake of, insulin among people with T2DM.

Previous research has revealed an association between negative appraisals of insulin therapy and impaired emotional wellbeing, including depressive symptoms and diabetes distress [14-17]. In particular, diabetes distress has been shown to
account for a greater proportion of the variance in insulin therapy appraisals than depressive symptoms [15]. While other studies have also observed a moderate, positive relationship between insulin therapy appraisals and diabetes distress [13, 17], it is unclear whether overall diabetes distress or specific components (e.g. regimen-related, physician-related, interpersonal distress) underlie negative insulin therapy appraisals.

In a small longitudinal study, no change in anxiety scores from baseline to follow-up was observed for participants initiating insulin, nor was there any difference in baseline scores between those who initiated insulin and those who did not [14]. Other research has noted a relationship between increased injection-related anxiety (a component of psychological insulin resistance) and increased general anxiety and diabetes distress [18, 19]. However, the association between anxiety and negative insulin therapy appraisals has not been investigated explicitly.

In an international study, participants with non-insulin treated T2DM who reported being hypothetically unwilling to begin insulin displayed increased diabetes distress and more negative beliefs about current oral medications than those who reported willingness to begin insulin if recommended [13]. However, in that particular study, the (unvalidated) single items used to measure beliefs about current oral medications did not specify whether the medications were for the management of diabetes or other purposes. Horne et al [20] suggest that people hold beliefs about medicines in general, as well as beliefs about medications specific to their condition (e.g. T2DM). Further, beliefs about medicines in general are likely to influence an individual’s initial orientation towards medicines (e.g. willingness to begin medication), but condition-specific beliefs about medications are more likely to
influence medication-taking behaviour (e.g. uptake and continuation of therapy as recommended) [21]. Thus, exploration of whether insulin therapy appraisals are associated with broader concerns about medicines in general and/or negative attitudes towards current diabetes-specific medications is required.

Our aim was to investigate the contribution of impaired emotional wellbeing and beliefs about medications (both in general and diabetes-related) to negative appraisals of insulin therapy among adults with non-insulin-treated T2DM.

Participants, Materials and Methods

This study used data from Diabetes MILES – Australia 2011, a national cross-sectional survey of adults with diabetes, focused on psychological and behavioural issues. A detailed description of the methods and questionnaires has been published elsewhere [22]. The study received ethics approval from the Deakin University Human Research Ethics committee (reference number: 2011-046).

Participants

Surveys were posted to a random sample of 15,000 National Diabetes Services Scheme registrants, and an online version was made available and advertised nationally. Overall, 3,338 eligible respondents took part (response rate=18% [22]), of whom 1,941 (58%) self-reported having T2DM (49% (n=953) women; aged 58.5±8.7 years; 45% (n=876) using oral hypoglycaemic agents (OHAs)). The survey consisted of core questions completed by all respondents and, to reduce respondent burden, participants were allocated randomly to an ‘A’ or ‘B’ version. The current analysis was conducted using the 50% subsample of those with T2DM using OHAs who complete the ‘A’ version, which included the Insulin Treatment Appraisal Scale (ITAS).
**Measures**

Demographic characteristics and self-reported clinical data included: age, gender, Socio-Economic Indexes for Areas (SEIFA) decile values for reported residential postcodes [23], body mass index (BMI), diabetes duration, and number of complications.

Several psychological measures were included.

**Negative insulin therapy appraisals**

Appraisals of insulin were assessed using the 20-item ITAS [17]. The measure includes 16 negative and four positive statements about insulin use, against which respondents indicate their level of agreement (strongly disagree=1, strongly agree=5). Scores are summed to provide an ITAS Negative score (range: 16-80) and ITAS Positive score (range: 5-20). The psychometric performance of the ITAS within the current sample has been reported elsewhere [24]. In the current study, the ITAS Negative subscale score is used to represent participants’ negative insulin therapy appraisals.

**Depression and anxiety**

The presence and severity of depressive and anxiety symptoms were assessed using the 9-item Patient Health Questionnaire (PHQ-9) [25] and 7-item General Anxiety Disorder (GAD-7) questionnaire [26]. For each measure, respondents rate the frequency with which they have experienced symptoms over the past two weeks on a 4-point scale (not at all=0, nearly every day=3). Item scores are summed to form a total score (PHQ-9: 0-27; GAD-7: 0-21), where a cut-off score of ≥10 indicates
moderate-to-severe symptoms. Internal consistency in the current sample was satisfactory (PHQ-9: $\alpha=0.89$; GAD-7: $\alpha=0.93$).

**Diabetes-specific emotional distress**

Assessed using the 17-item Diabetes Distress Scale (DDS-17) [27]. Respondents indicate the degree to which each item has been a problem for them over the past month on a 6-point scale (not a problem=1, very serious problem=6). A composite score is derived by summing scores and dividing by 17 items, with a score of $\geq 2$ indicative of moderate-to-high distress, and $\geq 3$ indicative of high distress [28]. The DDS-17 also includes four subscales: emotional burden (5-items), physician-related distress (4-items), regimen-related distress (5-items), and diabetes-related interpersonal distress (3-items). Internal consistency in the current sample was satisfactory for the DDS-17 total score ($\alpha=0.93$) and the four subscales ($\alpha= 0.89-0.93$).

**Beliefs about medications**

The Beliefs about Medications Questionnaire (BMQ) General (8-items) includes subscales addressing perceived ‘harm’ (5 items) and ‘overuse’ (3 items) of prescription medications in general [20]. The BMQ Specific (11-items) includes two subscales representing the perceived ‘necessity’ (5 items) of condition specific medications in maintaining health and ‘concerns’ (6 items) associated with having to take those medications in the long term, referring throughout to “your diabetes medicines”. Items are rated on a 5-point Likert scale (strongly disagree=1, strongly agree=5). Subscale scores are calculated by summing item scores and dividing by the number of items, with higher scores indicating stronger beliefs in the subscale.
concepts. A necessity-concerns differential score is obtained by subtracting the ‘concerns’ score from the ‘necessity’ score, enabling assessment of whether concerns outweigh belief in the necessity of taking the medications [29]. In this sample, the BMQ Specific and General subscales displayed good internal consistency (α=0.79-0.80).

**Statistical analysis**

Statistical analysis was undertaken using SPSS version 21 (Chicago, USA). Missing were replaced according to developer’s recommendations for the DDS-17 (if ≤2 missing items), ITAS, PHQ9 and GAD7 (all if ≤1 missing items). Individuals with missing demographic data required for the statistical analysis (age, diabetes duration, gender, and SEIFA decile) or the BMQ subscales were excluded from the analysis. Pearson’s correlation coefficients, Student’s t-tests, and Chi-square tests were calculated to explore the relationships between the ITAS Negative score and demographics, emotional wellbeing, and beliefs about medications. Where significant relationships existed, those variables were entered stepwise into a hierarchical multiple regression to determine associations with ITAS Negative score (dependent variable): (a) demographics, (b) depression (PHQ9) and anxiety (GAD7), (c) DDS-17 subscale and total scores, (d) BMQ General subscales (‘overuse’ and ‘harm’), and (e) BMQ Specific subscales (‘necessity’ and ‘concern’). Multicollinearity problems were identified using the variance inflation factor (VIF) and tolerance, where values <4 and >0.20 respectively suggest no multicollinearity. Results are reported as mean±SD or %(n). All statistical tests were two-sided and differences were accepted as significant at \( p<0.05 \).
Results

A total of 385 Diabetes MILES – Australia survey participants with self-reported T2DM, reporting OHAs as their sole diabetes treatment, completed the relevant survey version. Of these, 62 were excluded due to missing data. The final sample ($N=313$) was $57\pm9$ years old, with a diabetes duration of $7\pm6$ years, and $49\%$ ($n=152$) were women. Participants had a BMI of $32.2\pm7.0$, which is classified as class 1 Obese. The mean SEIFA Decile was $6.4\pm2.7$, where 1 is the lowest rating area for economic advantage and 10 is the highest rating area. The majority of the sample ($n=195$, 62%) reported no diabetes-related complications. Table 1 details participants’ mean±SD psychosocial outcomes and correlations between measures.
Table 1

*Means, standard deviations and correlations between psychosocial measures*

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>ITAS Positive</th>
<th>BMQ General</th>
<th>BMQ Specific</th>
<th>PHQ-9</th>
<th>GAD -7</th>
<th>DDS-17</th>
<th>Total score</th>
<th>Emotional Burden</th>
<th>Physician distress</th>
<th>Regimen distress</th>
<th>Interpersonal distress</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITAS Negative</td>
<td>52.3±9.5</td>
<td>.20**</td>
<td>.11*</td>
<td>.08</td>
<td>.01</td>
<td>.36**</td>
<td>.25**</td>
<td>.21**</td>
<td>.38**</td>
<td>.41**</td>
<td>.19**</td>
<td>.33**</td>
</tr>
<tr>
<td>ITAS Positive</td>
<td>14.8±2.2</td>
<td>-.15**</td>
<td>-.30**</td>
<td>.19**</td>
<td>-.17**</td>
<td>-.02</td>
<td>-.06</td>
<td>-.05</td>
<td>-.05</td>
<td>-.05</td>
<td>-.03</td>
<td>-.03</td>
</tr>
<tr>
<td>BMQ General</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Overuse</td>
<td>2.8±0.9</td>
<td>.64**</td>
<td>-.13*</td>
<td>.40**</td>
<td>.11</td>
<td>.11*</td>
<td>.20**</td>
<td>.19**</td>
<td>.15**</td>
<td>.10</td>
<td>.20**</td>
<td></td>
</tr>
<tr>
<td>Harm</td>
<td>2.2±0.7</td>
<td>-.12*</td>
<td>.53**</td>
<td>.12*</td>
<td>.11*</td>
<td>.14*</td>
<td>.17**</td>
<td>.12*</td>
<td>.06</td>
<td>.11*</td>
<td></td>
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<tr>
<td>BMQ Specific</td>
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<tr>
<td>Necessity</td>
<td>3.7±0.7</td>
<td>.07</td>
<td>.08</td>
<td>.06</td>
<td>.07</td>
<td>.14*</td>
<td>-.07</td>
<td>.05</td>
<td>.05</td>
<td>.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concerns</td>
<td>2.5±0.7</td>
<td>.27**</td>
<td>.24**</td>
<td>.39**</td>
<td>.47**</td>
<td>.16**</td>
<td>.29**</td>
<td>.29**</td>
<td></td>
<td></td>
<td></td>
<td>.27**</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>6.0±5.6</td>
<td>.76**</td>
<td>.48**</td>
<td>.47**</td>
<td>.19**</td>
<td>.48**</td>
<td>.29**</td>
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</tr>
<tr>
<td>GAD-7</td>
<td>4.4±4.8</td>
<td>.38**</td>
<td>.41**</td>
<td>.17**</td>
<td>.34**</td>
<td>.19**</td>
<td></td>
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<tr>
<td>BMQ General</td>
<td>BMQ Specific</td>
<td>PHQ-9</td>
<td>GAD -7</td>
<td>DDS-17</td>
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</tr>
<tr>
<td>Overuse</td>
<td>Harm</td>
<td>Necessity</td>
<td>Concerns</td>
<td>Total score</td>
<td>Emotional Burden</td>
<td>Physician distress</td>
<td>Regimen distress</td>
<td>Interpersonal distress</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean ± SD</td>
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<tr>
<td>DDS-17</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Total Score</td>
<td>1.8±0.8</td>
<td></td>
<td></td>
<td></td>
<td>.88**</td>
<td>.64**</td>
<td>.87*</td>
<td>.76**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional  Burden</td>
<td>1.9±1.0</td>
<td></td>
<td></td>
<td></td>
<td>.41**</td>
<td>.66**</td>
<td>.61**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physician  distress</td>
<td>1.3 ±0.8</td>
<td></td>
<td></td>
<td></td>
<td>.37**</td>
<td></td>
<td></td>
<td>.41**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regimen  distress</td>
<td>2.1±1.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.52**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interpersonal  distress</td>
<td>1.6±1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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</tr>
</tbody>
</table>

Note: * p < .05, ** p < .01
**Negative insulin therapy appraisals**

Negative insulin appraisals were commonly endorsed by participants; mean ITAS Negative subscale score was 52.3±9.5 (range: 26-80). The top three negative beliefs about insulin endorsed (agreed or strongly agreed with) by participants were “taking insulin means my diabetes has become much worse” (82%, \(n=256\)), “taking insulin makes life less flexible” (63%, \(n=197\)), and “taking insulin means I have failed to manage my diabetes with diet and tablets” (62%, \(n=194\)). Despite the endorsement of negative aspects of insulin use, the majority of participants also endorsed insulin as assisting to “prevent complications of diabetes” (76%, \(n=238\)), “maintain good control of blood glucose” (72%, \(n=226\)), and “improve my health” (67%, \(n=208\)). Higher ITAS Negative scores were significantly associated with younger age (\(r=-0.20, p<0.001\)), and fewer diabetes complications (\(r=-0.14, p<0.014\)). No associations were apparent with duration of diabetes (\(r=-0.04, p=0.468\)), BMI (\(r=0.03, p=0.648\)) or SEIFA decile (\(r=-0.02, p=0.71\)), nor did ITAS Negative scores vary according to gender (\(t=(311)0.151, p=.88\)).

**Emotional wellbeing**

Moderate-to-severe depressive or anxiety symptoms were reported by 24% (\(n=74\)) and 16% (\(n=50\)) of participants, respectively. Higher ITAS Negative scores were associated with increased depressive symptoms (\(r=0.25, p<0.001\)) and increased anxiety symptoms (\(r=0.21, p<0.001\)).

A total of 29% (\(n=90\)) of participants reported moderate-to-high diabetes distress. ITAS Negative scores were moderately and positively related to diabetes distress. All DDS-17 subscales were positively related to ITAS Negative scores, with
the strongest relationships being with ‘emotional burden’ \((r=0.41, p<0.001)\) and ‘regimen distress’ \((r=0.33, p<0.001)\).

**Beliefs about medications**

Average BMQ General subscale scores indicated disagreement with, or uncertainty about, the ‘overuse’ and ‘harm’ of medicines in general. A weak positive correlation was observed between ITAS Negative scores and ‘overuse’ \((r=0.11, p=0.044)\) but not ‘harm’ \((r=0.08, p=0.15)\) (Table 1).

On average, participants indicated that their currently prescribed OHAs were a ‘necessity’ and that they did not have ‘concerns’ about this medication. For 91\% (285) of participants, perceived ‘necessity’ of current diabetes medicines outweighed ‘concerns’ about them. ‘Concerns’ \((r=0.35, p<0.001)\) but not ‘necessity’ \((r=0.01, p>0.05)\) was significantly positively related with ITAS Negative scores.

**Model**

Table 2 displays the results of a hierarchal multiple regression analyses undertaken to assess the contribution of each of the five steps: 1) age and number of complications; 2) depressive and anxiety symptoms; 3) subscales of diabetes-related distress; 4) beliefs about medications in general; 5) beliefs about current diabetes medications, on the dependent variable (ITAS Negative score). Multicollinearity problems were not present according to VIF and Tolerance values. Depressive symptoms, but not anxiety, made a significant contribution to the prediction of ITAS score in step 2. Of the DDS-17 subscales introduced in step 3, only ‘emotional burden’ made a significant contribution and this rendered the contribution of depressive symptoms non-significant. Each step significantly improved the model except for step 4, in which BMQ General ‘overuse’ and ‘harm’ did not contribute to
the model. While BMQ Specific belief in ‘necessity’ did not contribute, ‘concerns’ made a significant independent contribution, increasing the variance accounted for between model 4 and model 5, and reducing the independent contribution of diabetes distress. The final model (step 5 in Table 2), included significant independent contributions from number of complications, DDS-17 ‘emotional burden’, and BMQ Specific ‘concerns’, and accounted for 22% of the variance in negative ITAS scores.
Table 2

Hierarchal multiple regression analyses predicting ITAS Negative score

<table>
<thead>
<tr>
<th>Variables</th>
<th>Step 1 Socio-demographics</th>
<th>Step 2 General emotional wellbeing</th>
<th>Step 3 Diabetes distress</th>
<th>Step 4 General beliefs about medications</th>
<th>Step 5 Specific beliefs about medications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>t</td>
<td>p</td>
<td>β</td>
<td>t</td>
</tr>
<tr>
<td>Age (years)</td>
<td>-0.16</td>
<td>-2.86</td>
<td>.005</td>
<td>-0.11</td>
<td>-1.95</td>
</tr>
<tr>
<td>Number of complications</td>
<td>-0.11</td>
<td>-1.86</td>
<td>.064</td>
<td>-0.12</td>
<td>-2.23</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>0.22</td>
<td>2.68</td>
<td>.008</td>
<td>0.09</td>
<td>1.05</td>
</tr>
<tr>
<td>GAD-7</td>
<td>0.02</td>
<td>-0.28</td>
<td>.784</td>
<td>-0.02</td>
<td>-0.27</td>
</tr>
<tr>
<td>DDS-17 Emotional Burden</td>
<td>0.32</td>
<td>4.04</td>
<td>&lt;.001</td>
<td>0.32</td>
<td>3.99</td>
</tr>
<tr>
<td>DDS-17 Physician-related distress</td>
<td>0.02</td>
<td>0.27</td>
<td>.788</td>
<td>0.02</td>
<td>0.27</td>
</tr>
<tr>
<td>DDS-17 Regimen-related distress</td>
<td>0.06</td>
<td>0.80</td>
<td>.425</td>
<td>0.06</td>
<td>0.79</td>
</tr>
<tr>
<td>DDS-17 Interpersonal distress</td>
<td>0.01</td>
<td>0.10</td>
<td>.92</td>
<td>0.04</td>
<td>0.97</td>
</tr>
<tr>
<td>Step 1 Socio-demographics</td>
<td>Step 2 General emotional wellbeing</td>
<td>Step 3 Diabetes distress</td>
<td>Step 4 General beliefs about medications</td>
<td>Step 5 Specific beliefs about medications</td>
<td></td>
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<tr>
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<td>----------------------------------------</td>
<td>----------------------------------------</td>
<td></td>
</tr>
<tr>
<td>BMQ General: Overuse</td>
<td></td>
<td></td>
<td>0.04</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>BMQ General: Harm</td>
<td></td>
<td></td>
<td>-0.02</td>
<td>-0.15</td>
<td></td>
</tr>
<tr>
<td>BMQ Specific: Necessity</td>
<td></td>
<td></td>
<td>-0.04</td>
<td>-0.67</td>
<td></td>
</tr>
<tr>
<td>BMQ Specific: Concerns</td>
<td></td>
<td></td>
<td>0.29</td>
<td>4.18</td>
<td></td>
</tr>
<tr>
<td>Adj.R²</td>
<td>.04</td>
<td>.09</td>
<td>.18</td>
<td>.19</td>
<td></td>
</tr>
<tr>
<td>F-change (df1,df2)</td>
<td>6.9 (2,299)</td>
<td>9.1 (2,297)</td>
<td>9.8 (4, 293)</td>
<td>0.1 (2, 291)</td>
<td></td>
</tr>
<tr>
<td>p-value (F-chg.)</td>
<td>.001</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>.87</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
</tbody>
</table>
Discussion

Our findings indicate that the majority of adults with T2DM using OHAs endorse negative beliefs about insulin therapy. Further, negative beliefs about insulin therapy are positively associated with number of diabetes-related complications, diabetes-related ‘emotional burden’ and ‘concerns’ about current diabetes treatment (i.e. OHAs). These results suggest that a focus on reducing distress about diabetes and alleviating concerns about its current treatment may act to improve attitudes towards insulin as a potential therapy.

The mean ITAS Negative score, and highly endorsed barriers to insulin treatment, found in the current sample were similar to those reported elsewhere [14-17, 30, 31]. In our sample, approximately one quarter reported a moderate-to-severe level of depressive symptoms or diabetes distress, and one in six reported moderate-to-severe anxiety symptoms. While a weak association between negative insulin appraisals and anxiety was observed, anxiety did not add to the prediction of ITAS Negative scores. Consistent with previous research [15, 32], the contribution of depression scores in the prediction of insulin appraisals was reduced after including diabetes distress. Elsewhere, contradictory results have been reported regarding the prediction of self-care behaviours and HbA1c outcomes by depression and distress [33, 34]. It is likely that the correlation between depression and negative insulin therapy appraisals found here and elsewhere is, at least in part, strengthened by the measurement and symptom overlap between depression and diabetes distress [35]. Prospective research is needed to investigate the causal relationships between diabetes distress, negative insulin therapy appraisals, and insulin uptake.
BMQ Specific ‘concerns’ about OHAs, but not belief in treatment ‘necessity’, was positively associated with negative insulin appraisals and added to the prediction of ITAS scores. Neither of the BMQ General subscales (‘harm’ or ‘overuse’) added to the prediction of ITAS Negative scores when entered (model 4). Horne et al [29] propose that while general beliefs about medicines may be a strong influence in initial orientation towards medicine use, specific beliefs about current medicines are more likely to influence ongoing medication-taking behaviours. The stronger association between negative insulin therapy appraisals and BMQ Specific ‘concerns’ than between insulin appraisals and general beliefs in medicines suggests that people regard the future use of insulin as an extension of current diabetes treatment, rather than as a new medication (despite the difference in administration method, oral versus injection). Furthermore, to maximise treatment use, our findings indicate that current ‘concerns’ about OHAs need to be explored and resolved before any addition of insulin to the treatment regimen.

Given the significant contribution of BMQ Specific ‘concerns’ about current diabetes treatment to the prediction of ITAS Negative scores, it is surprising that the DDS-17 subscale ‘regimen distress’ made no significant independent contribution. Furthermore, we observed only a weak-to-moderate relationship between ‘concerns’ about current treatment and ‘regimen distress’ (Table 1). However, the focus of the regimen-distress subscale is on the perception of the daily management of diabetes (e.g. “not feeling confident in my day-to-day ability to manage diabetes”) and it does not address concerns about, or refer explicitly to, diabetes medications.

Despite endorsing negative aspects of insulin, the majority of participants were aware of the benefits of insulin use (e.g. improved health). Similarly, the ‘necessity’
of current diabetes medications to maintain and improve health was endorsed by the vast majority of participants. This finding suggests that to improve attitudes towards future intensification of treatment, it is likely to be insufficient to focus solely on endorsing the benefits. Interventions are needed to identify, acknowledge and reframe negative attitudes toward current medications rather than focusing singularly on treatment benefits, of which many participants already report being aware.

Diabetes-related ‘emotional burden’ and ‘concerns’ about current diabetes medications were more strongly associated with negative insulin appraisals than general emotional wellbeing (depression / anxiety) and beliefs about medicines in general. This suggests that while participants may have a general mistrust of medicines and or be experiencing impaired general emotional wellbeing (i.e. symptoms of depression or anxiety), this may not necessarily influence or be influenced by negative appraisals of insulin therapy specifically.

Discussion of the general limitations of the Diabetes MILES – Australia study can be found elsewhere [22]. In particular, causality cannot be determined due to the cross-sectional nature of the data. Prospective research is required to understand exactly how the variables interact over time and influence treatment intensification. Further, studies have shown that more negative insulin appraisals (as assessed by ITAS scores) are positively associated with hypothetical unwillingness to initiate insulin if recommended [16, 31], but no prospective research has explicitly studied the influence of negative insulin therapy appraisals on actual insulin initiation. Thus, it is unclear whether or not the factors associated with negative insulin therapy appraisals identified here are in fact determinants of insulin uptake.
One consideration regarding the generalisability of the current study is that the sample includes participants with various diabetes durations, medication dosages, biomedical outcomes, and HbA1c is unknown. Therefore, we should not take the view that all would benefit from treatment intensification in the near future. The Diabetes MILES Study was not designed to include objective biomedical data (e.g. HbA1c). Understanding medication beliefs, emotional well-being and, in particular, insulin therapy appraisals in the context of current HbA1c levels would be of interest in future studies. Further, our results showed that those with more negative attitudes towards insulin also displayed more concerns about current diabetes medications, suggesting that they regard insulin as an extension of current diabetes treatment. Whether insulin is required, or not, these results suggest that participants would benefit from early discussion about the range of diabetes medications, and ways to improve their experience of these medications, with their health professional. Indeed, the recent ADA/EASD position statement on the management of hyperglycaemia in T2DM [36] now includes a ‘patient-centred approach’ and notes that patient attitudes to therapy are ‘potentially modifiable’.

In conclusion, this is the first study, to our knowledge, to investigate (using validated measures) the associations between beliefs about current medicines and attitudes towards future insulin use. Diabetes-related distress and ‘concerns’ about currently prescribed diabetes medicines were more strongly associated with negative insulin therapy appraisals than general emotional wellbeing and beliefs about medicines in general. The findings of this study suggest that negative beliefs about future insulin use may reflect current diabetes distress and treatment concerns. Early intervention and education to improve current experiences of, and attitudes towards diabetes self-management, may improve receptiveness to future medication
intensification. Prospective research is needed to improve our understanding of the causal relationships between diabetes distress, and ‘concerns’ about current medications, and how these may influence negative insulin therapy appraisals and actual insulin uptake, as well as how to reduce barriers to medication intensification.

Conflicts of interest

EHT and TCS have no conflicts to declare. FP has acted as an advisory board member and speaker for Novo Nordisk, and as a speaker for Sanofi-Aventis. He has received a grant from Novo Nordisk to support research and he has received funding for travel and accommodation to attend DAWN2 (Diabetes Attitudes Wishes and Needs) International Publication Planning Committee meetings. The Australian Centre for Behavioural Research in Diabetes has received sponsorship for JS to host or attend educational meetings from Lilly, MSD, Novo Nordisk, Roche Diagnostics Australia and Sanofi Diabetes; and has received consultancy income from Roche Diagnostics Australia and Sanofi Diabetes. JS is a member of the Roche Diagnostics Australia Accu-Chek Advisory Board.

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Chapter 6: Willingness to Initiate Insulin among Adults with
Type 2 Diabetes in Australian Primary Care: Results from
the Stepping Up Study

Study 2a: Paper 3

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Highlights

- Study explores ‘willingness’ to begin insulin among adults with T2DM in primary care.

- Among those for whom insulin is clinically indicated, only 1 in 5 are ‘very willing’ to begin insulin.

- Clinical factors and emotional wellbeing are not independently associated with ‘willingness’.

- Socioeconomic status and insulin appraisals are independently associated with ‘willingness’.

- Early acknowledgement and discussion of attitudinal barriers may improve insulin receptiveness.
Abstract

Aims

To determine ‘hypothetical willingness’ to initiate insulin, and identify associated factors, among adults with type 2 diabetes (T2DM) in primary care for whom insulin is clinically indicated.

Methods

Eligible participants were adults with T2DM with an HbA1c ≥7.5% (58 mmol/mol) and prescribed maximum oral hypoglycaemic agents. A total of 261 participants were recruited from 74 Victorian general practices: mean age 62 ± 10 years; 39% (n = 103) women; diabetes duration 10 ± 6 years; HbA1c 9.0 ± 1.3% (75 ± 14 mmol/mol). Data collected by the Stepping Up Study: demographic and clinical characteristics, ‘willingness’ to initiate insulin, insulin appraisals, depressive symptoms, and diabetes-related distress. A multinomial regression investigated predictors of ‘willingness’.

Results

Nineteen percent (n = 50) were ‘very willing’ to initiate insulin, if recommended. The final regression model ($R^2 = .44$, $\chi^2(12) = 145.91, p < .001$) demonstrated higher socioeconomic status and less negative attitudes to insulin were associated with increased willingness to initiate insulin.

Conclusions

Among adults with T2DM for whom insulin is clinically indicated, only one in five are ‘very willing’ to begin insulin therapy. Independent of demographics, clinical factors and emotional wellbeing, insulin appraisals were associated with ‘willingness’. This study highlights the importance of addressing attitudinal barriers
to insulin therapy among adults with T2DM in primary care to improve insulin receptiveness.

**Keywords**

Type 2 diabetes, Primary care, Insulin therapy
1. Introduction

Due to the depletion of beta cell function over time [1], type 2 diabetes mellitus (T2DM) requires timely intensification of treatment throughout disease progression [2]. Insulin therapy is the most effective glucose lowering treatment option available [3] and [4] but is often delayed [5]. This may be due to a reluctance by health professionals, known as clinical inertia [6], or reluctance among people with T2DM, known as ‘psychological insulin resistance’ [7], [8] and [9].

In the UK Prospective Diabetes Study, 27% of the participants for whom insulin was prescribed initially refused this form of therapy, while just 7–13% refused intensification of tablet treatment [10]. In a qualitative study in a UK Bangladeshi population, one in five participants refused insulin, even after attending counselling about treatment intensification [11]. There has since been little research on the refusal of insulin among people with T2DM, and refusal rates are largely unknown.

Several studies have explored the behavioural concept of ‘hypothetical willingness’ to begin insulin therapy if recommended, where being hypothetically unwilling is regarded as a proxy of insulin refusal [12], [13], [14], [15], [16], [17], [18] and [19]. Approximately 17% of adults with non-insulin-treated T2DM report being hypothetically unwilling to begin insulin, although rates vary across countries [18] and cultural groups [13]. Exploring, and intervening at the level of, insulin appraisals (or attitudes) may be critical in understanding and improving receptiveness toward insulin therapy uptake. Attitudes have been investigated widely using both quantitative [20] and qualitative methods [21].
Despite attitudes being strong predictors of intention [22], little research has investigated the relationship between attitudes towards insulin and hypothetical willingness appropriately. In two previous studies using a validated measure of insulin appraisals, the regression model included attitudes towards insulin as the dependent variable, with hypothetical willingness and other psychosocial variables as predictors [14] and [19]. This is in contrast to the more logical and theoretically-grounded expectation that attitudes (insulin appraisals) would be predictive of intention (willingness) and behaviour (insulin uptake) [22]. Thus, a more suitable approach is to explore the role of attitudes, and associated factors, in the prediction of hypothetical willingness. In other studies, unvalidated or single item assessments of insulin appraisals have been used [13], [16] and [18]. Further research using validated measures to corroborate these findings.

In research exploring attitudes or willingness to initiate insulin, few studies have explored the role of other psychosocial variables (e.g. emotional wellbeing) and/or behavioural factors (e.g. current medication-taking behaviours), in addition to clinical factors (e.g. glycaemic levels). Diabetes-related distress has been shown to be an important underlying predictor of insulin appraisals [23] and [24]. However, willingness to initiate insulin was not explored in these studies and objective clinical data were limited. Where the relationship between emotional wellbeing and willingness to initiate insulin has been explored, depressive symptomatology, rather than diabetes-related distress, has been measured [14] and [19], or unvalidated measures have been used [16]. In summary, a comprehensive analysis is needed of the clinical and psychosocial factors (using validated measures) associated with willingness to begin insulin to guide clinical practice.
Our aims were to: (1) to determine hypothetical willingness to initiate insulin therapy among adults with T2DM for whom insulin is clinically indicated, who receive their diabetes healthcare in general practice, and (2) to identify demographic, clinical and psychosocial factors, including attitudes toward insulin therapy, associated with hypothetical willingness to begin insulin.

2. Participants, materials and methods

Baseline data were collected from adults with T2DM participating in the Stepping Up Study, a cluster randomised trial conducted in 74 general practices across the state of Victoria, Australia. A detailed description of the trial protocol has been published elsewhere [25]. A cross sectional analysis of baseline data collected between October 2012 and June 2014 was undertaken.

Ethical approval was received from the University of Melbourne Health Sciences Human Research Ethics Sub-committee (ID 123740) and Deakin University Human Research Ethics Committee (2012-108). The trial is registered with the Australian New Zealand Clinical Trial Registry (ACTRN12612001028897).

2.1. Participants

Eligible practices were recruited through Medicare Locals (local networks of general practices) and the University of Melbourne Department of General Practice database of teaching and research active practices. Of the 74 participating practices, 77.0% (n = 57) were privately owned; the median (IQR) number of registered patients with a recorded diagnosis of T2DM was 233 (131, 349), and 37.8% (n = 28) were located outside the metropolitan area. Eligible patients were adults with non-insulin-using T2DM, an HbA1c ≥7.5% (58 mmol/mol) in the past 6 months and for whom maximal oral therapy (≥2 oral hypoglycaemic agents (OHAs) at maximum
tolerated doses) had been prescribed or for whom the GP considered insulin initiation appropriate. Patients were ineligible if they were >80 years of age, unable to give consent, had unstable cardiovascular disease, and/or an existing debilitating medical condition.

Potentially eligible patients \((N = 521)\) were identified by the practice and sent a letter stating that study participants may benefit from assessment and more intensive diabetes management (which may include insulin therapy) and inviting the person to attend the practice to learn more about the study. 422 participants responded to this invitation. Upon consent, participants completed the baseline questionnaire and undertook an HbA1c test. Those with HbA1c <7.5\% (58 mmol/mol), were excluded. Following screening, the eligible participating Stepping Up sample included 51\% \((n = 266)\) of the potential population.

2.2. Measures

Full details of the Stepping Up outcome measures are described elsewhere [25]. Measures relevant to the current analysis are detailed below.

*Hypothetical willingness to initiate insulin* was assessed using a single item that asks individuals to indicate how willing they would be to take insulin if recommended by their doctor (‘very’, ‘moderately’, ‘not very’, ‘not at all’) [16]. In prior studies, responses have been recoded as a binary or trichotomised using various cut points [16] and [18]. Given previous scoring inconsistencies, we used all four categories.

*Attitudes towards insulin*: Two measures of attitudes toward insulin were included to enable greater comparability of insulin appraisals of the current sample to participants across national [23] and international data [14], [18], [19] and [26].
(i) The Insulin Treatment Appraisal Scale (ITAS) is a validated 20-item scale that explores participant beliefs and expectations about future insulin use [26]. Respondents indicate their level of agreement with 20 statements on a five-point scale (1 = ‘strongly disagree’ to 5 = ‘strongly agree’). The ITAS was conceptualised as two-dimensional, including a negative insulin therapy appraisal score (the sum score of 16 items, where higher scores indicate more negative appraisals) and a positive insulin therapy appraisal score (the sum of four positive appraisals, where higher scores indicate more positive appraisals). In addition, the scale developers suggested the use of a total ITAS score (sum of all 20 items) [26]. However, in more recent analysis, the total score has not been recommended [27]. As such, the current analysis employs the positive and negative ITAS subscales only.

(ii) A single question tool developed by Polonsky et al. [18], hereafter referred to as the ‘single attitudinal item’, asks participants to identify two out of six statements that best match how they feel about the possibility of starting insulin [18]. Half of these statements are positively worded (e.g. ‘helps you feel better’); and half are negatively worded (e.g. ‘connected to disease worsening’). The number of positive and negative endorsements for each participant is summed to provide a 3-point scale, where 0 = positive attitudes, 1 = mixed attitudes, 2 = negative attitudes. If only one response is selected then scoring is based on whether the response is positive or negative (0 or 2).

Depressive symptoms were assessed using the 9-item Patient Health Questionnaire (PHQ-9) [28]. Respondents rate symptom frequency over the past two weeks on a four-point scale (0 = ‘not at all’ to 3 = ‘nearly every day’). Item scores are summed to form a total score from 0 to 27, where higher scores indicate greater depressive symptoms and scores of ≥10 indicate moderate-to-severe symptoms [28].
Diabetes-related distress was measured using the 20-item Problem Areas In Diabetes (PAID) scale [29]. Respondents rate the extent to which each item is a problem for them on a 5-point scale (0 = ‘not a problem’ to 4 = ‘serious problem’). Item scores are summed and standardised to form a total score from 0 to 100, where scores ≥40 indicate severe diabetes distress [30].

Medication-taking behaviour was assessed using the 6-item Medication Adherence Rating Scale (MARS) [31]. For each item, a parameter relating to suboptimal medication-taking behaviour, participants indicate the frequency with which they behaved accordingly on a 5-point scale (1 = ‘always’ to 5 = ’never’). The scale was adapted, with the developer’s permission, to refer to diabetes-specific medications. A total score (from 6 to 30) is calculated by summing each item score, where higher scores indicate more optimal medication-taking behaviours.

In addition, the following data were retrieved from participants’ medical records: demographics (including: age; gender; country of birth; English as primary language; residential postcode, which was used to determine the Socio-Economic Indexes For Areas Index of Relative Socio-economic Advantage and Disadvantage (SEIFA IRSAD) [32] and clinical data (body mass index (BMI: weight (kg)/Height (m)2); diabetes duration; number of co-morbid conditions [33]; current medications prescribed). Frequency of self-monitoring of blood glucose was self-reported, and baseline HbA1c data were extracted from the study database.

2.3. Statistical analysis

Statistical analysis was undertaken using SPSS version 22 (Chicago, USA). Missing data were rare across psychosocial scales. As imputation procedures for the scales vary across studies (for example: [19] and [24]), a conservative ≤10% rule was
used to replace missing data with the series mean for the PAID and ITAS (i.e. if ≤2 missing items), and PHQ-9 (i.e. if ≤1 missing item). Five participants were excluded due to non-completion of any survey questions or missing data on the dependent variable (‘hypothetical willingness’). One-way ANOVAs and Chi-square tests were calculated to explore the relationships between hypothetical willingness and demographic, clinical, and psychosocial data. Pearson's correlation coefficients were calculated to explore the relationships between independent variables. To explore the prediction of hypothetical willingness, a multinomial logistic regression was conducted, entering in the model all independent variables that differed significantly by hypothetical willingness. A multinomial regression was conducted, as the assumption of proportional odds was not met.

Results are reported as mean ± standard deviation, n(%) or median (interquartile range: IQR). All statistical tests were two-sided and differences were accepted as significant at \( p < .05 \).

3. Results

Of the 266 baseline Stepping Up Study participants, data on psychosocial questionnaires and hypothetical willingness item were available for 261 participants. Table 1 details the demographic, clinical and psychosocial characteristics of the overall sample, and by hypothetical willingness to initiate insulin. On average, participants were 62 years old, diagnosed with T2DM 10 years; 39.5\% (\( n = 103 \)) were women.
Table 1

Demographic, clinical and psychosocial characteristics by willingness to initiate insulin therapy

<table>
<thead>
<tr>
<th></th>
<th>Total sample</th>
<th>Not at all willing</th>
<th>Not very willing</th>
<th>Moderately willing</th>
<th>Very willing</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=261</td>
<td>n=59 (22.6%)</td>
<td>n=76 (29.1%)</td>
<td>n=76 (29.1%)</td>
<td>n=50 (19.2%)</td>
<td></td>
</tr>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender: Women</td>
<td>103 (39.5%)</td>
<td>23 (39%)</td>
<td>34 (44.7%)</td>
<td>31 (40.8%)</td>
<td>15 (30.0%)</td>
<td>Ns</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62±10</td>
<td>62±10</td>
<td>61±10</td>
<td>62±11</td>
<td>63±9</td>
<td>Ns</td>
</tr>
<tr>
<td>In relationship</td>
<td>182 (69.7%)</td>
<td>40 (22.0%)</td>
<td>55 (72.4%)</td>
<td>51 (28.0%)</td>
<td>36 (19.8%)</td>
<td>Ns</td>
</tr>
<tr>
<td>Australia born</td>
<td>161 (61.7%)</td>
<td>29 (49.2%)</td>
<td>49 (64.5%)</td>
<td>49 (64.5%)</td>
<td>34 (68.0%)</td>
<td>Ns</td>
</tr>
<tr>
<td>English as primary language</td>
<td>245 (93.9%)</td>
<td>52 (88.1%)</td>
<td>73 (96.1%)</td>
<td>73 (96.1%)</td>
<td>47 (94%)</td>
<td>Ns</td>
</tr>
<tr>
<td>SEIFA decile</td>
<td>5.8±2.6</td>
<td>4.9±2.9</td>
<td>5.6±2.6</td>
<td>6.5±2.5</td>
<td>5.8±1.9</td>
<td>.003</td>
</tr>
<tr>
<td><strong>Clinical Characteristics &amp; Diabetes Management</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td>9.8±6.4</td>
<td>10.5±7.1</td>
<td>9.4±5.13</td>
<td>10.7±7.6</td>
<td>8.2±5.2</td>
<td>Ns</td>
</tr>
<tr>
<td>Body Mass Index (kg/m^2)</td>
<td>32.7±6.5</td>
<td>33.6±6.5</td>
<td>32.6±6.0</td>
<td>32.6±7.3</td>
<td>31.7±5.9</td>
<td>Ns</td>
</tr>
<tr>
<td>No co-morbid conditions</td>
<td>2.6±1.9</td>
<td>2.4±1.8</td>
<td>2.5±1.9</td>
<td>2.6±2.0</td>
<td>3.1±2.2</td>
<td>Ns</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>9.0±1.3</td>
<td>9.2±1.3</td>
<td>8.8±1.2</td>
<td>8.9±1.3</td>
<td>8.9±1.3</td>
<td>Ns</td>
</tr>
<tr>
<td>(mmol/mol)</td>
<td>75±14</td>
<td>78±15</td>
<td>73±13</td>
<td>74±14</td>
<td>74±14</td>
<td></td>
</tr>
<tr>
<td>SMBG: at least once daily</td>
<td>133 (51.0%)</td>
<td>25 (42.4%)</td>
<td>28 (50.0%)</td>
<td>42 (55.3%)</td>
<td>28 (56.0%)</td>
<td>Ns</td>
</tr>
<tr>
<td>Diabetes medications: number prescribed for diabetes</td>
<td>7.5±3.8</td>
<td>7.1±3.3</td>
<td>7.6±3.9</td>
<td>7.8±4.0</td>
<td>7.7±3.7</td>
<td>Ns</td>
</tr>
<tr>
<td></td>
<td>Total sample N=261</td>
<td>Not at all willing n=59 (22.6%)</td>
<td>Not very willing n=76 (29.1%)</td>
<td>Moderately willing n=76 (29.1%)</td>
<td>Very willing n=50 (19.2%)</td>
<td>Sig</td>
</tr>
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<td>----------------------</td>
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<td>---------------------------</td>
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</tr>
<tr>
<td>MARS total (6-30)</td>
<td>27.3±3.7</td>
<td>27.1±3.8</td>
<td>27.1±3.6</td>
<td>27.1±3.7</td>
<td>27.9±3.5</td>
<td>Ns</td>
</tr>
<tr>
<td><strong>Psychosocial</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHQ-9 total (0-27)</td>
<td>4.5±4.9</td>
<td>5.2±4.8</td>
<td>5.3±5.7&lt;sup&gt;d&lt;/sup&gt;</td>
<td>4.3±4.7</td>
<td>2.8±3.3&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.016</td>
</tr>
<tr>
<td>moderate-to-severe (PHQ-9 total ≥10)</td>
<td>39 (15.0%)</td>
<td>10 (17.2%)</td>
<td>15 (19.7%)</td>
<td>10 (13.2%)</td>
<td>4 (8.0%)</td>
<td></td>
</tr>
<tr>
<td>PAID total (0-100)</td>
<td>19.7±18.2</td>
<td>24.0±21.2&lt;sup&gt;d&lt;/sup&gt;</td>
<td>20.0±17.0</td>
<td>20.0±18.7</td>
<td>13.4±13.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>.021</td>
</tr>
<tr>
<td>severe distress (PAID total: ≥40)</td>
<td>39 (15.0%)</td>
<td>15 (25.4%)</td>
<td>11 (14.5%)</td>
<td>10 (13.2%)</td>
<td>3 (6.0%)</td>
<td></td>
</tr>
<tr>
<td>Single attitudinal item (0-2)</td>
<td>0.9±0.8</td>
<td>1.5±0.7&lt;sup&gt;ed&lt;/sup&gt;</td>
<td>1.3±0.8&lt;sup&gt;ed&lt;/sup&gt;</td>
<td>0.6±0.7&lt;sup&gt;abd&lt;/sup&gt;</td>
<td>0.2±0.5&lt;sup&gt;abc&lt;/sup&gt;</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ITAS Positive (5-20)</td>
<td>14.3±2.0</td>
<td>13.3±1.9&lt;sup&gt;ed&lt;/sup&gt;</td>
<td>14.1±1.9&lt;sup&gt;c&lt;/sup&gt;</td>
<td>15.0±1.8&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>14.9±2.1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ITAS Negative (16-80)</td>
<td>46.9±8.5</td>
<td>50.7±9.1&lt;sup&gt;ed&lt;/sup&gt;</td>
<td>49.1±7.8&lt;sup&gt;d&lt;/sup&gt;</td>
<td>46.1±7.3&lt;sup&gt;ad&lt;/sup&gt;</td>
<td>40.2±6.5&lt;sup&gt;abc&lt;/sup&gt;</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Data are Mean±SD or n(%). Valid percentages reported due to missing varied N’s for each questionnaire. Single attitudinal item: higher scores indicate greater endorsement of negative insulin appraisals; ITAS = Insulin Treatment Appraisal Scale [26], higher scores indicate greater endorsement of negative insulin appraisals (ITAS Negative) or positive insulin appraisals (ITAS Positive); MARS = Medication Adherence Rating Scale [31], higher scores indicate more optimal medication-taking behaviours; PAID = Problem Areas In Diabetes [29], higher scores indicate greater diabetes-related distress; PHQ-9 = Patient Health Questionnaire [28], higher scores indicate more depressive symptoms; SEIFA = SocioEconomic Index For Areas [32], higher scores indicate greater relative socioeconomic advantage and lower disadvantage; SMBG = self-monitoring of blood glucose. Significantly different from

<sup>a</sup>“not at all willing”,  <sup>b</sup>“not very willing”,  <sup>c</sup>“moderately willing”,  <sup>d</sup>“very willing”.  

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Some level of hypothetical willingness to initiate insulin was observed in nearly half of the sample, with 19.2% reporting being ‘very willing’ and 29.1% responding as ‘moderately willing’ to begin insulin therapy if recommended by their doctor. A further 29.1% were ‘not very willing’, with the remaining 22.6% being ‘not at all willing’.

3.1. Participant demographic characteristics

Demographic characteristics did not differ significantly by willingness to initiate insulin, with the exception of SEIFA IRSAD deciles (Brown–Forsythe $F(3, 234.6) = 4.6, p = .003$), where those reporting being ‘not at all willing’ resided in more socio-economically disadvantaged areas than those who were ‘moderately willing’ ($Mean \text{ diff} = -1.61, p = .002$).

3.2. Clinical and diabetes management variables

Clinical characteristics did not differ significantly by hypothetical willingness to initiate insulin therapy. Half ($n = 133$) of the participants reported checking their blood glucose at least daily. Clinical records show a mean current HbA1c of $9.0 \pm 1.3\% (75 \pm 14 \text{ mmol/mol})$ (median $= 8.6\% (70 \text{ mmol/mol})$, IQR $= 8.0, 9.7\% (64, 83 \text{ mmol/mol})$). Ninety per cent of participants had at least one diagnosed co-morbid condition, and a median of two (IQR $= 1–4$) diagnosed co-morbid conditions. The median number of medications prescribed per person on record was seven (IQR $= 5, 10$). A minority ($n = 14, 5.4\%$) were currently using a non-insulin injectable treatment (e.g. exenatide) to manage their diabetes. MARS scores reveal that, on average, participants report taking their diabetes medications as recommended, and this did not differ by hypothetical willingness.
3.3. Emotional wellbeing

Moderate-to-severe depressive symptoms were reported by 15.0% \((n = 39)\) and severe diabetes-related distress was also reported by 14.9% \((n = 39)\). Seven per cent \((n = 19)\) reported both moderate-to-severe depressive symptoms and severe diabetes-related distress. Depressive symptoms and diabetes-related distress both differed by hypothetical willingness to use insulin (PHQ-9: Brown–Forsythe \(F(3, 242.5) = 3.5, p = .016\); PAID: Brown–Forsythe \(F(3, 229.4) = 3.3, p = .021\)). Post-hoc comparisons reveal that participants who report being ‘very willing’ to begin insulin reported significantly less diabetes-related distress than those who reported being ‘not at all willing’ \((Mean \text{ diff} = 10.65, p = .013)\), and significantly less depressive symptoms than those who reported being ‘not very willing’ to begin insulin \((Mean \text{ diff} = 2.54, p = .025)\).

The PAID total score displayed a weak-to-moderate positive correlation with the single attitudinal item score \((r = .251, p < .001)\) and the ITAS negative score \((r = .403, p < .001)\). Similarly, the PHQ-9 showed a weak positive relationship with the single attitudinal item \((r = .268, p < .001)\) and ITAS negative \((r = .281, p < .001)\). There was no significant relationship between the ITAS positive scale and the PAID total or PHQ-9 total scores.

3.4. Attitudes towards Insulin

ITAS negative \((Brown–Forsythe F(3, 229.12) = 19.61, p < .001)\) and ITAS positive scores \((Brown-Forsythe F(3, 225.04) = 9.8, p < .001)\) differed significantly by hypothetical willingness. Post-hoc comparisons revealed that those who were ‘very willing’ to begin insulin reported significantly less negative insulin appraisals than all other groups \((Mean \text{ diff range} = -5.9 \text{ to } -10.5, \text{ all } p < .001)\) and significantly
higher positive ITAS positive scores than those who were ‘not at all willing’ (*Mean diff* = 1.5, *p* < .001). Table 2 shows mean and standard deviations for ITAS items as well as the percentage of participants who endorsed (‘strongly agreed’ or ‘agreed’ with) each item. The most commonly endorsed ITAS negative items were ‘taking insulin means my diabetes has become much worse’ (item 2; *n* = 174; 66.9%) and ‘taking insulin means I have failed to manage my diabetes…’ (item 1; *n* = 133, 51.2%). For all 20 ITAS items, mean scores differed significantly by hypothetical willingness (*p* < .05 to *p* < .001), whereby greater willingness was associated with less negative attitudes, with four exceptions: items 2 (‘insulin means my diabetes has become much worse’), 7 (‘insulin increases the risk of low blood glucose’), 9 (‘insulin causes weight gain’), and 20 (‘insulin makes me more dependent on my doctor’).
Table 2

**Insulin appraisals: mean and standard deviation ITAS item scores and percentage endorsing (agree/strongly agree)**

<table>
<thead>
<tr>
<th>Items</th>
<th>Mean ± SD</th>
<th>Agree or Strongly agree %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  Taking insulin means I have failed to manage my diabetes with diet and tablets</td>
<td>3.3 ± 1.2</td>
<td>51.2%</td>
</tr>
<tr>
<td>2  Taking insulin means my diabetes has become much worse</td>
<td>3.7 ± 0.9</td>
<td>66.9%</td>
</tr>
<tr>
<td>3^ Taking insulin helps to prevent complications of diabetes</td>
<td>3.7 ± 0.8</td>
<td>66.2%</td>
</tr>
<tr>
<td>4  Taking insulin means other people see me as a sicker person</td>
<td>2.9 ± 1.2</td>
<td>33.8%</td>
</tr>
<tr>
<td>5  Taking insulin makes life less flexible</td>
<td>3.0 ± 1.1</td>
<td>32.3%</td>
</tr>
<tr>
<td>6^ I'm afraid of injecting myself with a needle</td>
<td>2.8 ± 1.3</td>
<td>34.2%</td>
</tr>
<tr>
<td>7  Taking insulin increases the risk of low blood glucose levels (hypoglycaemia)</td>
<td>3.3 ± 0.8</td>
<td>36.3%</td>
</tr>
<tr>
<td>8^ Taking insulin helps to improve my health</td>
<td>3.7 ± 0.6</td>
<td>65.3%</td>
</tr>
<tr>
<td>9  Insulin causes weight gain</td>
<td>3.1 ± 0.6</td>
<td>15.4%</td>
</tr>
<tr>
<td>10 Managing insulin injections takes a lot of time and energy</td>
<td>2.9 ± 0.9</td>
<td>22.9%</td>
</tr>
<tr>
<td>11 Taking insulin means I have to give up activities I enjoy</td>
<td>2.4 ± 0.8</td>
<td>7.7%</td>
</tr>
<tr>
<td>12 Taking insulin means my health will deteriorate</td>
<td>2.4 ± 0.8</td>
<td>7.3%</td>
</tr>
<tr>
<td>13 Taking insulin is embarrassing</td>
<td>2.5 ± 0.9</td>
<td>15.8%</td>
</tr>
<tr>
<td>14 Injecting insulin is painful</td>
<td>2.8 ± 0.9</td>
<td>18.2%</td>
</tr>
<tr>
<td>15 It is difficult to inject the right amount of insulin correctly at the right time every day</td>
<td>2.9 ± 0.9</td>
<td>22.4%</td>
</tr>
<tr>
<td>16 Taking insulin makes it more difficult to fulfill my responsibilities (at work, at home)</td>
<td>2.6 ± 0.9</td>
<td>17.8%</td>
</tr>
<tr>
<td>17^ Taking insulin helps to maintain good control of my blood glucose</td>
<td>3.7 ± 0.7</td>
<td>67.2%</td>
</tr>
<tr>
<td>18 Being on insulin causes family and friends to be more concerned about me</td>
<td>3.3 ± 1.0</td>
<td>49.8%</td>
</tr>
<tr>
<td>19^ Taking insulin helps to improve my energy levels</td>
<td>3.3 ± 0.6</td>
<td>31.3%</td>
</tr>
<tr>
<td>20 Taking insulin makes me more dependent on my doctor</td>
<td>3.2 ± 0.9</td>
<td>39.4%</td>
</tr>
</tbody>
</table>

SD: standard deviation; ^ positive ITAS items. Scoring: 1 (strongly disagree) to 5 (strongly disagree).
The distribution of the single attitudinal item total scores indicated an approximately equal sample split between those with positive \( (n = 98, 38.3\%) \), mixed \( (n = 79, 30.9\%) \), or negative \( (n = 79, 30.9\%) \) attitudes toward insulin. Scores differed significantly by hypothetical willingness to initiate insulin (Brown–Forsythe \( F(3, 239.99) = 43.4, p < .001 \)), where mean scores were significantly less negative for those reporting being ‘very willing’ compared to all other groups \( (Mean \text{ diff range} = −.4 \text{ to } −1.3, \text{ all } p < .05) \). The most commonly endorsed single attitudinal item response option was ‘feeling that the disease is getting worse’ if I need to begin insulin \( (n = 107; 41.2\%) \), closely followed by insulin means the ‘opportunity to have better control of my diabetes’ \( (n = 103; 39.6\%) \).

The ITAS negative and single attitudinal item scores were moderately correlated \( (r = .521, p < .001) \). The ITAS positive and single attitudinal item scores displayed a weak, but significant negative relationship \( (r = −.198, p = .001) \). There was no significant relationship between the ITAS positive scale and the ITAS negative.

3.5. Modelling ‘willingness’

The following variables (which had differed significantly by ‘willingness’) were included in a multinomial logistic regression: SEIFA, PHQ-9, PAID, and ITAS negative, ITAS positive and single attitudinal item scores. Total PHQ-9 and PAID scores did not contribute to the model. The final model included SEIFA, ITAS negative, ITAS positive and single attitudinal item scores. Significant main effects were observed for SEIFA \( (p = .002) \), ITAS positive and negative \( (p < .001 \text{ and } p = .001, \text{ respectively}) \), and single attitudinal item scores \( (p < .001) \). Table 3 displays the results of the final significant model \( (\chi^2(12) 145.91, p < .001) \), which correctly predicted 52.5% of hypothetical willingness responses. While socio-economic status
significantly added to the model overall, no significant independent contribution was observed. Increases in ITAS negative and single attitudinal item scores, and a decrease in ITAS positive scores, were significantly associated with being ‘not at all willing’ compared to ‘very willing’ to begin insulin, and ‘not very willing’ compared to ‘very willing’. However, ITAS positive scores did not add to the prediction of ‘moderately willing’ versus ‘very willing’ responses.

Table 3

Multinomial logistic regression analyses predicting hypothetical willingness to begin insulin

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Odds Ratio</th>
<th>Upper 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all willing vs. very willing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-0.27</td>
<td>2.25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SEIFA</td>
<td>-0.14</td>
<td>0.10</td>
<td>0.72</td>
<td>0.87</td>
<td>1.06</td>
</tr>
<tr>
<td>ITAS Negative Score**</td>
<td>0.12</td>
<td>0.04</td>
<td>1.05</td>
<td>1.13</td>
<td>1.21</td>
</tr>
<tr>
<td>ITAS Positive Score**</td>
<td>-0.43</td>
<td>0.12</td>
<td>0.51</td>
<td>0.65</td>
<td>0.83</td>
</tr>
<tr>
<td>Single Attitudinal Item Score***</td>
<td>2.28</td>
<td>0.43</td>
<td>4.27</td>
<td>9.82</td>
<td>22.57</td>
</tr>
<tr>
<td>Not very willing vs. very willing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-2.30</td>
<td>2.09</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SEIFA</td>
<td>-0.01</td>
<td>0.09</td>
<td>0.83</td>
<td>0.99</td>
<td>1.18</td>
</tr>
<tr>
<td>ITAS Negative Score**</td>
<td>0.11</td>
<td>0.03</td>
<td>1.05</td>
<td>1.12</td>
<td>1.19</td>
</tr>
<tr>
<td>ITAS Positive Score*</td>
<td>-0.22</td>
<td>0.11</td>
<td>0.65</td>
<td>0.80</td>
<td>0.99</td>
</tr>
<tr>
<td>Single Attitudinal Item Score***</td>
<td>1.83</td>
<td>0.38</td>
<td>2.94</td>
<td>6.22</td>
<td>13.17</td>
</tr>
<tr>
<td>Moderately willing vs. very willing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept**</td>
<td>-5.97</td>
<td>2.11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SEIFA</td>
<td>0.16</td>
<td>.09</td>
<td>1.00</td>
<td>1.17</td>
<td>1.39</td>
</tr>
<tr>
<td>ITAS Negative Score**</td>
<td>0.10</td>
<td>.03</td>
<td>1.04</td>
<td>1.11</td>
<td>1.18</td>
</tr>
<tr>
<td>ITAS Positive Score</td>
<td>0.04</td>
<td>.10</td>
<td>0.86</td>
<td>1.05</td>
<td>1.27</td>
</tr>
<tr>
<td>Single Attitudinal Item Score*</td>
<td>0.80</td>
<td>.38</td>
<td>1.06</td>
<td>2.21</td>
<td>4.63</td>
</tr>
</tbody>
</table>

\( R^2 = .44 \) (Cox & Snell), .47 (Nagalkerke). Model \( \chi^2 (12) 145.91, p<.001 \).

*p<.05, **p<.01, ***p<.001

ITAS = Insulin Treatment Appraisal Scale [26]; SEIFA = Socio-Economic Index For Areas [32].
4. Discussion

This study demonstrates that one in four adults with non-insulin-treated T2DM, for whom insulin is clinically indicated, are ‘not at all willing’ to begin insulin therapy, and only one in five are ‘very willing’. The strongest predictors of hypothetical willingness are attitudes towards insulin therapy, and this relationship is independent of demographics, clinical factors and emotional wellbeing. These findings emphasise the importance of identifying, and addressing attitudes towards insulin to enhance psychological receptiveness to this effective therapy.

Our finding that 22% were hypothetically ‘unwilling’ to initiate insulin is consistent with recent international data [18]. The most commonly endorsed negative insulin appraisal, across both measures, concerns the initiation of insulin being regarded as a sign of a worsening health, as similarly observed nationally and overseas [18], [26] and [27]. This appraisal may draw on the factual explanation of insulin initiation being necessitated, in most cases, by beta cell destruction, and has the potential to motivate treatment intensification. In contrast, this belief may be maladaptive if the individual delays uptake of insulin because they are not ready to accept this symbol of worsening of health or if they believe that initiating insulin will mean their health will deteriorate further. The second most commonly endorsed negative attitude concerns insulin initiation symbolising for the person a personal failure to manage their condition well enough to avoid the need for insulin.

The mean positive ITAS scores observed within this primary care setting are consistent with results from a national, population-based Australian dataset [27], whereby the majority of participants endorse the positive aspects of insulin therapy. However, mean ITAS negative scores are significantly less negative in this primary care setting. This may be a function of diabetes duration and progression. Compared
with the national population-based study, this clinical study included only those whose HbA1c was above target (≥7.5%; 58 mmol/mol) and who were using maximum OHAs. It may be that participants in the current study had previously discussed treatment intensification (i.e. insulin initiation) with their health professionals, acknowledging that more effective management of elevated glycaemic levels was needed, and thereby potentially reducing negative insulin appraisals. Similarly, a recent qualitative study of people with T2DM participating in an RCT concluded that they may be more receptive to insulin initiation and intensification than traditionally acknowledged [34] and [35]. Indeed, almost half of the current sample were at least ‘moderately willing’ to begin insulin, suggesting that insulin initiation in primary care, among those who would benefit most, would be acceptable for many adults with T2DM requiring treatment intensification.

In the current sample, diabetes-related distress and depressive symptoms were also less common in comparison to national Australian data [36]. It is also possible that the participants (who were recruited to a trial in which treatment intensification would be discussed) have comparatively better emotional well-being and less negative attitudes to insulin than those in the broader primary care setting. This would suggest that our findings potentially underestimate the scope of the problem.

Prior research has found women to be significantly less willing to initiate insulin than men [12], [15], [16] and [17] but, in the current study, the SEIFA IRSAD score was the only demographic characteristic that differentiated hypothetical willingness. Univariate statistics indicated a general trend of increasing willingness to initiate insulin among those living in more socio-economically advantaged areas. However, those ‘moderately willing’ lived in more advantaged areas than those who were ‘very willing’ suggesting a complexity to the relationship.
Further research is needed to clarify the role of socio-economic status in shaping attitudes to insulin initiation.

Interestingly, clinical factors such as HbA1c, co-morbidities and number of prescribed medications also did not differ significantly by willingness. While depressive symptoms and diabetes distress were associated significantly with both insulin appraisals and willingness, consistent with previous research [14], [16], [19], [23], [24], [26] and [37], neither general nor diabetes-specific emotional wellbeing added to the prediction of willingness. Assuming hypothetical willingness is an indicator of eventual insulin uptake, this is in keeping with previous longitudinal primary care research, which concluded that the presence of baseline depressive symptoms, but not anxiety, was not associated with insulin uptake or time to insulin initiation [38].

The relationship between insulin appraisals and willingness has been explored previously [14] and [19] but the proposed direction of the relationship, and subsequent analysis, was contradictory to well-established theories that attitudes predict behavioural intention and intention predicts behaviour [22]. Our findings indicate that the strongest known predictors of hypothetical willingness to initiate insulin are positive and negative attitudes towards insulin. Interestingly, the ITAS positive score added to the prediction of willingness over and above the ITAS negative subscale and the single attitudinal item. Previously, we have recommended limited use of the positive subscale [27] given its inability to discriminate between treatment groups (insulin vs. non-insulin) [26] and [27] or between those with more and less negative attitudes [37]. Our findings suggest that endorsement of positive insulin therapy appraisals are independent of negative attitudes, not merely the lack of negative attitudes, and may have utility in predicting future insulin uptake.
However, longitudinal research is needed to explore the role of attitudes towards insulin (positive and negative) in actual uptake of insulin.

Both the ITAS subscales and the single attitudinal item contributed independently to the prediction of hypothetical willingness, suggesting that they are not measuring precisely the same concepts. A chief advantage of the single item is its brevity and, perhaps, its narrow focus on commonly endorsed appraisals. However, its development has not been fully documented and it has not been psychometrically validated [18]. Our findings indicate that it has a weak relationship with the ITAS positive score and is only moderately correlated with the ITAS negative score, suggesting sub-optimal convergent validity with the longer ITAS. This may indicate that the single item does not provide comprehensive assessment of participant attitudes towards insulin or it may indicate some redundancy in the 20-item ITAS. Indeed, 8 of the 16 negative ITAS items were endorsed by ≤25% of the current sample suggesting that these items may not be relevant to many people. For example, the ITAS includes items about expected weight gain and hypoglycaemia which health professionals commonly perceive to be patient concerns, as shown in several qualitative studies [39], [40], [41] and [42]. However in the current sample, and in our national, cross-sectional data [23] and [27], we found that the majority of participants either disagreed (13%) or neither agreed nor disagreed (50.6%) that hypoglycaemia was a concern, and 76% of participants were unsure whether insulin causes weight gain. Further, responses to these items were not associated with hypothetical willingness. These data suggest that health professionals may overestimate the concerns of people with T2DM or perhaps misattribute their own concerns as those of their patients.
4.1. **Strengths and limitations**

The strengths of the current study include it being the first to explore and report factors associated with rates of hypothetical willingness to initiate insulin among Australians with non-insulin-treated T2DM; it is also among the first to explore these variables among people with T2DM for whom insulin therapy is clinically indicated: i.e. with sub-optimal HbA1c and already prescribed maximum doses of OHAs within a primary care setting. An additional strength of the current study is that it includes validated clinical data (e.g. HbA1c, co-morbid conditions and number of prescribed medications) as well as psychometrically robust psychosocial measures (e.g. ITAS, PHQ-9, PAID).

A limitation of the current study is that the sample may not be representative of the wider primary care population. The current sample reported lower rates of diabetes-related distress and depressive symptoms than found in a non-clinical national sample [36], and includes only English-speaking participants who self-selected to participate in a trial that may involve treatment intensification.

4.2. **Clinical implications and future directions**

The current data suggest a mismatch between receptiveness to initiate insulin among people with T2DM and actual insulin uptake in Australia. Approximately half of participants were, at least, moderately receptive to initiating insulin yet insulin initiation is frequently delayed in primary care [43]. Indeed, there are multiple causes of delays in treatment intensification, including not only psychological insulin resistance among people with diabetes but also physician reluctance (i.e. clinical inertia) and systemic barriers [44]. Interventions to increase the timely initiation of insulin within primary care are needed at both the practice/systems level (e.g. the
Stepping Up model of care [25]) and the patient level. Further, multifactorial research is needed to explore the interaction between patient, health professional and practice level barriers in the prediction of insulin uptake among adults with T2DM.

Our study shows the potential of modifying patient barriers to insulin initiation. For example, two thirds of participants believe that initiating insulin therapy means their diabetes has become worse while half interpret insulin use as a personal failure to manage their diabetes effectively. Both of these highly endorsed negative perceptions regarding insulin therapy might be prevented/minimised by health professionals educating people with T2DM that progressive beta cell destruction will necessitate regular review and intensification of management strategies aimed at maximising the patient's well-being in longer-term. For example, “Targets, Insulin, Management and Encouragement” is a practical guidance tool for use by health professionals that highlights readying the person with diabetes for insulin throughout the progression of their condition as well as monitoring emotional wellbeing and attitudes towards insulin [45]. Other recommendations highlight the importance of using sensitive, non-judgmental language when discussing treatment options and HbA1c targets to positively frame insulin therapy and foster receptiveness among people with T2DM [8], [46], [47], [48] and [49]. Despite a wealth of literature offering practical suggestions and recommendations for increasing receptiveness among people with T2DM for insulin initiation, few patient-level interventions have been evaluated. While additional research is needed to explore the predictive role of insulin therapy appraisals in relation to actual, real-world, insulin uptake, the relationship between insulin appraisals and hypothetical willingness observed in the current study suggests that interventions aimed at altering attitudes towards insulin among people with T2DM are also warranted.
5. Conclusion

The current study demonstrates that one quarter of Australians with non-insulin-treated T2DM and suboptimal HbA1c (despite maximal oral therapy) are ‘not at all willing’ to begin insulin therapy, if recommended by their GP, and only one in five are ‘very willing’. Demographics, clinical factors and emotional wellbeing have little explanatory value while attitudes to insulin therapy contribute significantly to hypothetical willingness to initiate insulin. Importantly, despite the majority endorsing positive appraisals of insulin, two thirds believe that insulin means their diabetes has become worse and half interpret insulin use as a personal failure to manage their diabetes effectively. These results emphasise the importance of GPs intervening early to counsel people with T2DM effectively to encourage psychological receptiveness towards insulin.

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Author contributions

JF, IB and DO conceived the Stepping Up Study and are chief investigators. JS is an associate investigator on the Stepping Up Study and EHT's PhD supervisor. JS and EHT advised on the psychosocial questionnaires included in the Stepping Up
Study. All authors were involved in the development of the Stepping Up Study protocol. EHT and JS conceived the research questions discussed in the current manuscript. EHT conducted data cleaning and analyses of the measures reported here and prepared the first and subsequent drafts of the manuscript. All authors reviewed, edited and approved the final manuscript.

Conflict of interest statement

EHT has no conflicts of interest to declare. JF has received unrestricted educational grants from Roche Diagnostics Australia, Medtronic and Sanofi Diabetes. IB has received unrestricted educational grants and in-kind support from Medtronic, Sanofi Diabetes and Roche Diagnostics. DNO has had various financial relationships with pharmaceutical industries outside the submitted work including consultancies, grants, lectures, educational activities and travel. JS is a member of the Accu-Check Advisory Board (Roche Diagnostics Australia). Her research group has received unrestricted educational grants from Medtronic and Sanofi Diabetes; sponsorship to host or attend educational meetings from Lilly, Medtronic, MSD, Novo Nordisk, Roche Diagnostics Australia, and Sanofi Diabetes; consultancy income from Abbott Diabetes Care, Roche Diagnostics Australia and Sanofi Diabetes.

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We would like to acknowledge the Stepping Up Study Investigators and research team, in particular Dr Jo-Anne Manski-Nankervis for managing the Stepping Up dataset. We also thank the health professionals and people with T2DM who participated in Stepping Up.
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[18] Polonsky WH, Hajos TRS, Dain MP, Snoek FJ. Are patients with type 2


Chapter 7: Predictors of Insulin Uptake among Adults with Type 2 Diabetes in the Stepping Up Study

Study 2b: Paper 4

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Highlights

- Comprehensive prospective study of predictors of insulin use for type 2 diabetes.
- Insulin uptake is predicted by baseline HbA1c and hypothetical willingness.
- The predictive model was independent of the model of care received.
- Negative, but not positive, insulin appraisals improved following insulin uptake.
Structured Abstract

Aims

We aimed to investigate predictors of insulin uptake, and change in insulin appraisals, among adults with type 2 diabetes mellitus (T2DM) who participated in the Stepping Up trial.

Methods

The Stepping Up model of care, supporting timely insulin initiation in primary care, was evaluated in a two-armed cluster-randomised controlled trial. Participants were 266 adults (mean±SD age 62±10 years; 39% women) with T2DM (median (IQR) duration 8.5 (5, 13) years) from 74 primary care practices (Stepping Up intervention: 57%, control 43%). At 12 months, 47% (n=126) had commenced insulin. Controlling for randomisation, logistic regression was used to explore baseline predictors of insulin uptake, including: demographic and clinical characteristics, emotional wellbeing (depressive symptoms and diabetes-related distress), insulin treatment appraisals, and, ‘willingness’ to initiate insulin. Two-way analysis of variance examined effects of, and interaction between, randomisation and insulin uptake on 12-month change in insulin appraisals.

Results

Participants using insulin at 12 months were more likely (all p<0.05) than those using tablets alone to report: lower socioeconomic status, higher baseline HbA1c (median Diff: 0.3%; 3mmol/mol), greater willingness to commence insulin (very willing: 27% vs 12%), and less negative and more positive insulin appraisals. All contributed significantly to the final model (χ²(8)=92.1, p<0.001) except insulin
appraisals. Regardless of trial allocation, those initiating insulin reported significantly greater reductions in negative insulin appraisals.

**Conclusions**

Controlling for randomisation, 12-month insulin use was predicted by higher baseline HbA1c and ‘willingness’ to use insulin if recommended. Negative insulin appraisals reduced following insulin initiation.

**Keywords**

Insulin therapy, Psychological insulin resistance, Attitudes, Primary care

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1. **Introduction**

Insulin therapy is recommended for people with type 2 diabetes mellitus (T2DM) with suboptimal glycated haemoglobin (HbA1c), typically greater than 5.7% (59 mmol/mol) using maximum oral hypoglycaemic agents (OHAs) [1,2]. Insulin is effective for lowering HbA1c [3,4], and preventing development or progression of diabetes-related complications [5]. However, insulin initiation is frequently delayed [6,7]. Reasons for delaying insulin initiation are multifaceted, including systemic healthcare, clinician, and patient barriers [6,8].

People with non-insulin-treated T2DM commonly report negative attitudes (appraisals) to insulin therapy [8-10], known as ‘psychological insulin resistance’. Such negative appraisals include, but are not limited to: concerns about daily injections, side effects, insulin symbolising their ‘failure’ to manage diabetes [8,11]. Negative insulin appraisals have shown to improve after insulin initiation [12,13]. Insulin appraisals can be measured using multi-item scales covering both negative and positive expectations about insulin use (for example: Insulin Treatment Appraisal Scale (ITAS) [14]). Insulin appraisals are predictive of hypothetical ‘willingness’ (intention) to begin insulin. For example, one in four Australians with T2DM requiring treatment intensification report being ‘not at all willing’ to begin insulin if recommended, and have more negative attitudes towards insulin than those who are ‘very willing’ [10], consistent with international findings [9]. Hypothetical (un)willingness has been used as a proxy measure of the proportion of people with T2DM who might delay insulin therapy [9], but, to our knowledge, it has not been established whether it predicts actual insulin uptake.

Research into predictors of actual insulin uptake have focused largely on the clinical characteristics (e.g. previous treatment, HbA1c) [7,15]. With regard to
psychological factors, studies have found no association between time to insulin uptake and depressive symptoms [16] or, after accounting for insulin appraisals, diabetes-specific distress [17]. A multi-clinic study in Japan concluded that those who commenced insulin therapy had a higher HbA1c and reported less negative, and more positive, insulin appraisals, at baseline, compared with those who remained on OHAs alone [12]. However, these findings have not been corroborated in a comprehensive, prospective investigation of demographic, clinical and psychological predictors of actual insulin uptake in adults with T2DM.

The Stepping Up model of care [18] was developed to reduce clinical inertia and systemic barriers [6] to timely insulin initiation in Australian primary care. The model involves training the in-practice team (i.e. General Practitioner (GP) and Practice Nurse (PN)) to enable insulin prescription, initiation and intensification within primary care, with support from diabetes specialists as necessary. A cluster-randomised controlled trial demonstrated that this model of care was successful in increasing insulin initiation (69.5% insulin uptake vs 21.7% in usual care) among adults with T2DM for whom insulin was clinically indicated [19].

The primary aim of the current study, using data collected in the Stepping Up study, was to investigate the role of the participants’ demographic profile, clinical characteristics, emotional well-being (diabetes-specific distress and depressive symptoms), insulin appraisals (positive and negative) and hypothetical willingness to initiate insulin in the prediction of actual insulin uptake, controlling for study randomisation. Our secondary aims were to investigate change in positive and negative insulin appraisals from baseline to 12-month follow-up, and examine the effects of, and interaction between, study arm (control vs intervention) and insulin uptake on 12-month change in insulin appraisals.
2. **Participants, Materials and Methods**

2.1. **Study design**

The current study used baseline data to predict insulin therapy use at 12 months in a two-armed, cluster-randomised controlled trial (RCT), which tested the ‘Stepping Up’ model versus usual care in general practices across the state of Victoria, Australia. The trial protocol, and primary outcome findings have been published elsewhere [18,19]. Participant data were collected between October 2012 and April 2015.

Ethical approval was received from the University of Melbourne Health Sciences Human Research Ethics Sub-committee (ID 123740) and Deakin University Human Research Ethics Committee (2012-108). The trial was registered with the Australian New Zealand Clinical Trial Registry (ACTRN12612001028897).

2.2. **Participants**

Primary care practices were eligible if they employed at least one consenting GP and PN and provided care to at least one eligible patient. 74 practices participated and their characteristics are described elsewhere [10,19].

Patients were eligible for inclusion in the study if they: were adults with T2DM, had HbA1c ≥ 7.5% (58 mmol/mol), had a prescription ≥2 OHAs at maximum tolerated doses or insulin initiation was considered clinically appropriate by the GP, had no previous insulin use. Patients were ineligible if they: were >80 years of age, unable to give consent, had unstable cardiovascular, or an existing debilitating medical, condition. Potential participants were identified by the practice (N=521) and sent a letter stating that they may benefit from clinical assessment and treatment intensification, which may include insulin therapy. A response was
received from 81% \((n=422)\) of those invited. Consenting participants completed the baseline questionnaire and gave a blood sample for HbA1c analysis. If HbA1c was <7.5% \((58 \text{ mmol/mol})\), they were excluded. The final sample included 266 participants.

### 2.3. Stepping Up Model

The Stepping Up model of care has been published elsewhere [18]. In brief, the model of care intervened at the practice level, providing GPs and PNs with training to enable timely insulin prescription, with support from the study Diabetes Nurse Educator (DNE) as required. The 1-2 hours group training focused on: evidence for timely insulin initiation; familiarisation with insulin delivery systems and titration tools; common patient barriers to insulin initiation and techniques to deal with them, including motivational interviewing training and goal setting strategies. Practices were supported by face-to-face, telephone and email contact from the study DNE during the 12-month follow-up period. The GP’s primary role was to discuss and prescribe insulin initiation, while the PN led insulin education, initiation and adjustment. If participants did not commence insulin at first, they continued to visit the PN and GP, as often as clinically appropriate.

Control practices were provided with a copy of the Royal Australian College of General Practitioners (RACGP) guidelines for the management of T2DM [2] and required to undertake a clinical review of, and consultation with, participants.

### 2.4. Measures

Participants’ medical records were accessed to extract demographic characteristics (age; gender; country of birth; primary language, and; postcode, used to determine the Index of Relative Socio-economic Advantage and Disadvantage
(IRSAD) decile [20]) and clinical characteristics (HbA1c; body mass index (BMI));
diabetes duration; number of co-morbid conditions [21], 12-month insulin uptake status). Psychological outcomes were collected at baseline and 12-months, with surveys completed in clinic or at home (and returned via post).

Depressive symptoms over the previous 2 weeks were assessed using the 9-item Patient Health Questionnaire (PHQ-9) [22]. Total scores range from 0 to 27, with higher scores indicating greater depressive symptoms, and scores ≥10 suggest at least moderate depressive symptoms [22]. Diabetes-specific distress was measured using the 20-item Problem Areas In Diabetes (PAID) scale [23]. Higher total scores (range: 0 to 100) indicate greater distress [23]. Scores ≥40 suggest severe diabetes-specific distress [24].

Attitudes to insulin were assessed using the 20-item ITAS [14], which includes 16 negative items (ITAS Negative, score range: 16 to 80) and four positive items (ITAS Positive, score range: 4 to 20). Higher scores indicate more negative/positive insulin appraisals. Hypothetical ‘willingness’ to initiate insulin was assessed using a single item asking individuals to indicate how willing they would be to take insulin if recommended by their doctor (responses: ‘very’, ‘moderately’, ‘not very’, ‘not at all’) [25].

2.5. Statistical analysis

Analysis was undertaken using SPSS version 22 (Chicago, USA). For the psychological measures, minimal (~10%) missing datapoints were replaced with the series mean. Where scale data were >10% missing, participant data were excluded from specific analyses as required. No independent variables of interest differed significantly by study randomisation at baseline (p>0.05). Students t-tests, Chi-
square, and Mann Whitney tests were used to investigate the relationships between insulin uptake (yes/no) at 12-months and baseline demographic, clinical, and psychological data. To identify predictors of insulin uptake, a hierarchical logistic regression was conducted including variables found to be significant in univariate analyses, controlling for randomisation. To check for cluster effects, this analysis was repeated using mixed-effects logistic regression in Stata 13 (StataCorp, TX, USA), with Practice entered as the random effect. The random effect was non-significant (data not reported).

Repeated measures t-tests were conducted to explore change in ITAS subscales from baseline to follow-up, overall. Two-way factorial Analysis of Variance (ANOVA) was conducted to investigate the main effects of insulin uptake (yes/no) and randomisation (control/intervention), and any interaction effect, on ITAS change scores. Results are reported as mean ± standard deviation, median (IQR), or % (n). All statistical tests were two-sided and differences were accepted as significant at $p<0.05$.

3. Results

Demographic, clinical and psychological characteristics of the sample (N=266), and by insulin uptake at 12 months, are shown in Table 1. Participants were men (61%, n=163), 62±10 years old and diagnosed with T2DM for 8.5 (5,13) years. Overall, 14% (n=37) reported moderate-to-severe depressive symptoms and 15% (n=39) reported severe diabetes-specific distress.

3.1. Factors associated with insulin uptake

Overall, 126 (47%) participants were using insulin therapy at 12-month follow-up. Those using insulin (compared to those not using insulin) were more likely to
have been randomised to the intervention arm implementing the Stepping Up model of care (81% vs 35%, $\chi^2 (1)=57.1, p<0.001$), reside in significantly less advantaged areas ($U=7489.0, p=0.032$), and have higher baseline HbA1c ($U=10757.5, p=0.002$). Insulin use at 12 months did not differ by other demographic or clinical characteristics. Baseline depressive symptomology and diabetes-specific distress did not differ between those who were and were not using insulin at 12 months (Table 1).

Among those using insulin at 12 months (compared to those not using insulin), baseline ITAS Negative scores were significantly lower ($t(258)=2.5, p=0.015$), and ITAS Positive scores were significantly higher ($t(259)=-2.8 p=0.006$) (Table 1). Similarly, insulin uptake also differed significantly by baseline hypothetical willingness ($\chi^2(3)14.9, p=0.002$). Of those using insulin at 12 months, the majority (59%, $n=72$) reported at baseline being ‘moderately’ or ‘very willing’ to begin insulin, in contrast with 39% ($n=54$) of those not using insulin.
Table 1

Baseline demographic, clinical and psychological characteristics for the whole sample and by insulin uptake at 12 months

<table>
<thead>
<tr>
<th></th>
<th>Total (N=266)</th>
<th>Not using insulin at 12 months (n=140)</th>
<th>Using insulin at 12 months (n=126)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomised to intervention</td>
<td>151 (56.8%)</td>
<td>49 (35.0%)</td>
<td>102 (81.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Demographic and clinical variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>61.8±10.1</td>
<td>62.3±10.5</td>
<td>61.3±9.6</td>
<td>0.455</td>
</tr>
<tr>
<td>Gender: women</td>
<td>103 (38.7%)</td>
<td>59 (42.1%)</td>
<td>44 (34.9%)</td>
<td>0.227</td>
</tr>
<tr>
<td>IRSAD decile</td>
<td>6 (4,8)</td>
<td>6.5 (4,8)</td>
<td>6 (4,7)</td>
<td>0.032</td>
</tr>
<tr>
<td>Country of birth: Australia</td>
<td>163 (61.3%)</td>
<td>85 (60.7%)</td>
<td>78 (61.9%)</td>
<td>0.842</td>
</tr>
<tr>
<td>Primary language: English</td>
<td>247 (91.9%)</td>
<td>132 (94.3%)</td>
<td>115 (91.3%)</td>
<td>0.340</td>
</tr>
<tr>
<td>Highest level of education:</td>
<td></td>
<td></td>
<td></td>
<td>0.634</td>
</tr>
<tr>
<td>Primary or less</td>
<td>26 (9.8%)</td>
<td>12 (8.6%)</td>
<td>14 (9.7%)</td>
<td></td>
</tr>
<tr>
<td>Secondary or trade</td>
<td>184 (69.2%)</td>
<td>96 (69.6%)</td>
<td>88 (68.5%)</td>
<td></td>
</tr>
<tr>
<td>Tertiary</td>
<td>56 (21.1%)</td>
<td>32 (22.9%)</td>
<td>24 (19.0%)</td>
<td></td>
</tr>
<tr>
<td>Employment status:</td>
<td></td>
<td></td>
<td></td>
<td>0.672</td>
</tr>
<tr>
<td>In paid work</td>
<td>117 (44.0%)</td>
<td>58 (41.4%)</td>
<td>59 (46.8%)</td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>35 (13.2%)</td>
<td>19 (13.6%)</td>
<td>16 (12.7%)</td>
<td></td>
</tr>
<tr>
<td>Unemployed in paid work</td>
<td>114 (42.9%)</td>
<td>63 (45.0%)</td>
<td>51 (40.5%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes duration, years</td>
<td>8.5 (5,13)</td>
<td>8 (5,13)</td>
<td>9 (5,13)</td>
<td>0.846</td>
</tr>
<tr>
<td>HbA1c: mmol/mol</td>
<td>70 (64,82)</td>
<td>69 (62,78)</td>
<td>72 (66,85)</td>
<td>0.002</td>
</tr>
<tr>
<td>%</td>
<td>8.6 (8.0,9.6)</td>
<td>8.4 (7.8,9.3)</td>
<td>8.7 (8.2,9.9)</td>
<td></td>
</tr>
<tr>
<td>Number of comorbidities</td>
<td>3 (2,5)</td>
<td>3 (2,5)</td>
<td>3 (2,5)</td>
<td>0.693</td>
</tr>
<tr>
<td>Body mass index</td>
<td>32.6±6.5</td>
<td>33.0±6.8</td>
<td>32.1±6.1</td>
<td>0.294</td>
</tr>
<tr>
<td>Psychological variables</td>
<td>Total (N=266)</td>
<td>Not using insulin at 12 months (n=140)</td>
<td>Using insulin at 12 months (n=126)</td>
<td>p value</td>
</tr>
<tr>
<td>--------------------------------------------------------------</td>
<td>---------------</td>
<td>----------------------------------------</td>
<td>-----------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td><strong>Depressive Symptoms:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHQ-9 total (scored: 0-27)</td>
<td>4.5±4.9</td>
<td>4.4±4.8</td>
<td>4.5±5.0</td>
<td>0.828</td>
</tr>
<tr>
<td>Moderate-to-severe (PHQ-9 ≥10)</td>
<td>37 (14.4%)</td>
<td>18 (13.2%)</td>
<td>15 (12.8%)</td>
<td>0.922</td>
</tr>
<tr>
<td><strong>Diabetes-specific distress:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAID total (scored: 0-100)</td>
<td>19.6±18.1</td>
<td>19.6±18.1</td>
<td>19.7±18.3</td>
<td>0.979</td>
</tr>
<tr>
<td>Severe (PAID ≥40)</td>
<td>39 (14.9%)</td>
<td>22 (15.8%)</td>
<td>17 (13.8%)</td>
<td>0.649</td>
</tr>
<tr>
<td><strong>Willingness to begin insulin:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all willing</td>
<td>59 (22.6%)</td>
<td>39 (28.1%)</td>
<td>20 (16.4%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Not very willing</td>
<td>76 (29.1%)</td>
<td>46 (33.1%)</td>
<td>30 (24.6%)</td>
<td></td>
</tr>
<tr>
<td>Moderately willing</td>
<td>76 (29.1%)</td>
<td>38 (27.3%)</td>
<td>38 (31.1%)</td>
<td></td>
</tr>
<tr>
<td>Very willing</td>
<td>50 (19.2%)</td>
<td>16 (11.5%)</td>
<td>34 (27.9%)</td>
<td></td>
</tr>
<tr>
<td><strong>ITAS Negative (scored: 16-80)</strong></td>
<td>46.8±7.5</td>
<td>48.1±8.1</td>
<td>45.5±8.8</td>
<td>0.015</td>
</tr>
<tr>
<td><strong>ITAS Positive (scored: 4-20)</strong></td>
<td>14.3±2.1</td>
<td>14.0±1.9</td>
<td>14.7±2.3</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Data are mean±SD, median (IQR), or n (%). Valid percentages reported due to missing data. ITAS = Insulin Treatment Appraisal Scale [14]; PAID = Problem Areas In Diabetes [23]; PHQ-9 = Patient Health Questionnaire [22]; IRSAD = Index of Relative Socio-economic Advantage and Disadvantage [20].
3.2. Predicting insulin uptake

In the hierarchical logistic regression socioeconomic status (step 1) did not significantly improve the base model, which accounted only for study arm (randomisation). At step 2, HbA1c added significantly to the model ($\beta=0.32$, $SE=0.12, p=0.008$). At step 3, both ITAS Negative ($\beta=-0.04, SE=0.02, p=0.016$) and Positive ($\beta=0.19, SE=0.08, p=0.014$) scores added significantly to the prediction of insulin use. However, at step 4, the independent contribution of ITAS scores was negated by intention (willingness) to begin insulin therapy. After accounting for randomisation status, the final model ($\chi^2(8)=92.1, p<0.001$) included independent contributions from socioeconomic status (IRSAD), HbA1c and hypothetical willingness (Table 2). Specifically, participants using insulin at 12 months were 9.5 times more likely to have been allocated to the intervention and, 5.6 times more likely to report being ‘very willing’ to begin insulin, compared to those using tablets alone. Every unit increase in HbA1c was associated with 1.4 times increase in the likelihood of 12-month insulin use. Confidences intervals suggest no meaningful association between IRSAD decile and insulin uptake, as such the independent contribution of socioeconomic status is not interpreted further.
Table 2

**Final model of hierarchical logistic regression predicting insulin uptake at 12 months**

<table>
<thead>
<tr>
<th></th>
<th>b</th>
<th>SE</th>
<th>Exp(B)</th>
<th>Lower, upper 95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intercept</strong></td>
<td>-5.9</td>
<td>1.9</td>
<td>0.003</td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Control variable: Randomisation</strong> (ref=control)</td>
<td>2.2</td>
<td>0.33</td>
<td>9.5</td>
<td>5.0, 18.1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Step 1: Demographics**
- IRSAD decile
  | -0.1 | 0.1 | 0.9 | 0.8, 1.0 | 0.048 |

**Step 2: Clinical characteristics**
- HbA1c
  | 0.4  | 0.1 | 1.4 | 1.1, 1.8 | 0.004 |

**Step 3: Insulin appraisals**
- ITAS Negative score
  | -0.0 | 0.0 | 1.0 | 0.9, 1.0 | 0.289 |
- ITAS Positive score
  | 0.1  | 0.1 | 1.2 | 1.0, 1.4 | 0.072 |

**Step 4: Intention to begin insulin**
- Willingness (ref=not at all)
  - Not very willing
    | 0.6  | 0.4 | 1.8 | 0.7, 4.2 | 0.189 |
  - Moderately willing
    | 0.6  | 0.5 | 1.9 | 0.7, 4.6 | 0.176 |
  - Very willing
    | 1.7  | 0.5 | 5.6 | 1.9, 16.3| 0.001 |

Log likelihood: -265.5
Model (df) \( \chi^2 \), p value: (8) 92.1, \( p <0.001 \)
Pseudo \( R^2 \): Cox and Snell; Nagelkerke 0.2998; 0.400

CI= Confidence Interval, SE= Standard Error, ITAS= Insulin Treatment Appraisal Scale [14], IRSAD= Index of Relative Socio-economic Advantage and Disadvantage [20].
3.3. Change in insulin appraisals

Overall, there was a significant reduction in ITAS Negative scores from baseline to 12-month follow-up (-4.3±10.1; t(214)=6.3, p<0.001). Two-way ANOVA revealed significant main effects of both randomisation (F(1,212)=7.7, p=0.006) and insulin uptake (F(2,212)=16.6, p<0.001) on change in ITAS Negative scores, where intervention participants reported greater mean reductions in scores compared to control arm participants (-7.3±10.5 vs -0.4±1.0, respectively), and initiating insulin resulted in a greater reduction in scores compared to those who were using tablets alone at 12 months (-8.3±9.6 vs -0.4±0.9, respectively). No significant interaction between randomisation and insulin uptake was observed, indicating that the reduction in ITAS Negative scores associated with insulin uptake was the same regardless of study arm allocation and vice versa.

Overall, ITAS Positive scores remained stable over time, with no significant difference from baseline to 12-month follow-up (0.1±2.69; t(215)= -0.4, p=0.724). Further, change in ITAS Positive scores, from baseline to 12-month follow-up, did not differ by randomisation (F(1,214)=0.8, p=0.363) or insulin uptake (F(2,214)=1.5, p=0.219).

4. Discussion

After accounting for the intervention (allocation to the Stepping Up model of care), our findings demonstrate that adults with T2DM, for whom insulin is clinically indicated, who have higher HbA1c and report ‘very willing’ to begin insulin are more likely to agree to insulin initiation. Further, insulin uptake is associated with a significant reduction in negative insulin appraisals, regardless of the model of care.
Consistent with prior research [12], higher baseline HbA1c was associated with greater likelihood of insulin uptake. Possible explanations for this relationship include people with T2DM perceiving their higher HbA1c, or hyperglycaemic symptoms, as indicating a greater need for insulin therapy [26]. Similarly, when a higher HbA1c is recorded, clinicians may be more convinced by the need for insulin, and the inefficacy of OHAs alone. This is consistent with evidence that clinicians prefer to delay insulin initiation until perceived to be absolutely necessary [27].

Consistent with previous research [16,17], both depressive symptoms and distress were unrelated to insulin uptake. As expected, baseline insulin appraisals were associated with 12-month insulin use. However, their predictive effect was negated in the regression model after the inclusion of hypothetical ‘willingness’. This suggests that asking adults with T2DM whether they are willing to consider insulin therapy is a useful first step in gauging readiness for and receptiveness to insulin. However, one in four are ‘not at all willing’, and understanding this position requires healthcare professionals to enquire about individuals’ attitudes to, understanding or expectations of insulin therapy. Our previous work has shown that attitudes towards insulin predict willingness [10]. Further, these findings should not be interpreted as meaning that those who report being ‘not at all willing’ will inevitably refuse insulin. Indeed, 41% (n=50) of those using insulin at 12 months had indicated being ‘not very’ or ‘not at all’ willing to begin insulin therapy at baseline. Of this group, the majority (data not shown above: 82%, n=41) were allocated to the intervention, highlighting the effectiveness of the Stepping Up model of care as an intervention to overcome psychological insulin resistance.

In the current study, those who initiated insulin reported significant reductions in negative insulin appraisals at 12 months compared with baseline, consistent with
previous longitudinal research [12,13], but no change in positive insulin appraisals. The ITAS Positive items focus on perceptions of the effectiveness of insulin for maintaining optimal blood glucose concentrations, improving energy, improving health in general, and preventing future complications. Thus, the relative lack of improvement in positive appraisals may relate to the ‘invisibility’ of improvements in health or prevention of complications in the short-term. Indeed, target HbA1c in the intervention arm was achieved by just 36% of participants [19]. Alternatively, the lack of change in positive appraisals may be due to questionnaire ceiling effects, caused by high endorsement of positive insulin appraisals at baseline.

Given the enhanced role of the PN in the Stepping Up model of care (i.e. insulin education, initiation and adjustment) compared with usual care, an interaction effect was expected between insulin uptake and randomisation on change in insulin appraisals, whereby those who initiated insulin and participated in the intervention would report the greatest change. While the Stepping Up model of care was effective at increasing insulin uptake [19], it offered no relative advantage over actual insulin uptake for reducing negative insulin appraisals. This may be because, while insulin was more likely to be initiated in the intervention arm, in the instances where insulin was initiated in the control arm, there was a similar level of clinician contact and counselling. Further, the main focus of the Stepping Up training was to reduce the primary care team’s clinical inertia. Thus, ongoing concerns about insulin post-initiation may not have been evaluated or tackled differently in the two arms. This suggests there is opportunity for further refinement of the Stepping Up model of care to engage more specifically, and perhaps directly with the person with T2DM, to improve insulin appraisals over time.
4.1. Strengths and limitations

This is the first study to undertake comprehensive investigation of the role of demographic, clinical and psychological factors associated with insulin uptake in a large, prospective primary care sample of adults with T2DM among whom insulin is clinically indicated. Further, this study includes validated clinical data (e.g. HbA1c, co-morbid conditions and number of prescribed medications) and psychometrically robust psychological measures (e.g. PHQ-9, PAID). To our knowledge, this is the first study to assess the predictive validity of the single-item measure of hypothetical ‘willingness’ to begin insulin.

As this study was conducted in a trial setting with clinical eligibility parameters and self-selection bias, the sample may not be representative of the wider Australian T2DM population. Specifically, we observed lower rates of diabetes-specific distress and depressive symptoms than found elsewhere [28], and included only those who were English speaking and self-selected to participate in a trial in which they would, potentially, undertake treatment intensification.

We investigated baseline predictors of insulin use at 12 months. However, it is possible that participants initiated and stopped using insulin between these time-points. Further, we were unable to assess willingness or attitudes immediately prior to insulin initiation. Thus, change in attitudes may have occurred before insulin use (influencing uptake) or after initiation (with experience influencing attitudes.)

5. Conclusion

This study demonstrates that willingness to begin insulin therapy is an independent predictor of actual insulin uptake, in addition to HbA1c, independent of the model of primary care. This highlights the need within primary care to assess
receptiveness to insulin, and understand reasons for lack of willingness, to encourage appropriate insulin uptake among people with T2DM for whom it is clinically indicated.

Acknowledgments

We acknowledge the Stepping Up Study Investigators and research team, in particular Dr Jo-Anne Manski-Nankervis for managing the Stepping Up dataset and Ms Alexandra Gorelik for providing statistical advice. We also thank the people with T2DM and healthcare professionals who participated in Stepping Up.

Funding

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EHT is supported by an Australian Postgraduate Award / Deakin University PhD scholarship. JF is supported by an NHMRC/PHCRED Career Development Fellowship. JS is supported by the core funding provided to The Australian Centre for Behavioural Research in Diabetes by Diabetes Victoria and Deakin University.

Author contributions

JF, IB and DO conceived the Stepping Up Study and are chief investigators. JS is an associate investigator on the Stepping Up Study and EHT’s PhD supervisor. JS and EHT advised on the psychosocial questionnaires included in the Stepping Up
Study. All authors were involved in the development of the Stepping Up Study protocol. EHT and JS conceived the research questions discussed in the current manuscript and formulated the analysis plan. EHT conducted data cleaning and analyses of the measures reported here. EHT prepared the first and subsequent drafts of the manuscript. All authors reviewed, edited and approved the final manuscript.

**Declaration of interests**

EHT has undertaken research funded by an unrestricted educational grant from Abbott Diabetes Care to The Australian Centre for Behavioural Research in Diabetes (ACBRD). JF has received unrestricted educational grants from Roche Diabetes Care, Medtronic and Sanofi Diabetes. IB has received unrestricted educational grants and in-kind support from Medtronic, Sanofi Diabetes and Roche Diabetes Care. DNO has had various financial relationships with pharmaceutical industries outside the submitted work including consultancies, grants, lectures, educational activities and travel. JS is a member of the Accu-Check Advisory Board (Roche Diabetes Care). Her research group (ACBRD) has received unrestricted educational grants from Abbott Diabetes Care, Medtronic and Sanofi Diabetes; sponsorship to host or attend educational meetings from Lilly, Medtronic, MSD, Novo Nordisk, Roche Diabetes Care, and Sanofi Diabetes; consultancy income from Abbott Diabetes Care, Janssen Pharmaceuticals, Roche Diabetes Care and Sanofi Diabetes.
References


Chapter 8: Negative Appraisals of Insulin Therapy are Common among Adults with Type 2 Diabetes Using Insulin: Results from Diabetes MILES – Australia Cross-Sectional Survey

Study 1c: Paper 5

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*Corresponding author

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7This manuscript was published in Diabetic Medicine, 32(10): 1297-1303. The formatting, structure, and referencing style is in accordance with the journal’s requirements. A statement of author contributions is provided in Appendix A. Journal permissions are presented in Appendix B.
Novelty Statement

- This is the first study to explicitly explore appraisals of insulin therapy among adults with Type 2 diabetes currently using insulin using validated measures.
- Despite insulin use, some people with Type 2 diabetes report negative appraisals of insulin therapy including physical and psychological barriers.
- Diabetes duration, years using insulin, injections and blood glucose checks per day do not differ between those with more and those with less negative appraisals of insulin therapy.
- Participants reporting more negative insulin appraisals also report poorer general and diabetes-specific emotional well-being, reduced diabetes-specific self-efficacy and satisfaction with blood glucose levels compared with those with more positive appraisals.
Abstract

Aims

To identify insulin therapy appraisals among adults with Type 2 diabetes using insulin and how negative appraisals relate to clinical, self-care and psychosocial outcomes.

Methods

Diabetes MILES – Australia 2011 was a national survey of adults with diabetes, focused on behavioural and psychosocial issues. Subgroup analyses were conducted on the responses of 273 adults with Type 2 diabetes using insulin (46% women; mean ± SD age: 59 ± 9 years; diabetes duration: 12 ± 7 years; years using insulin: 4 ± 4). They completed validated measures of insulin therapy appraisals (ITAS), depression (PHQ-9), anxiety (GAD-7), diabetes distress (PAID) and diabetes-specific self-efficacy (DES-SF).

Results

Insulin was perceived to be very important, and its benefits (e.g. improves health) were endorsed by most (82%). Fifty-one percent believed that taking insulin means their diabetes has become worse; 51% that insulin causes weight gain; 39% that they have ‘failed to manage’ their diabetes. Those with the greatest and least ‘ITAS Negative’ scores did not differ by diabetes duration or years using insulin, or by average number of insulin injections or blood glucose checks per day. Those with more negative insulin appraisals were significantly younger (Mean Diff. = 5 years, P <0.001), less satisfied with recent blood glucose levels (P <0.001, d = 0.63), had reduced diabetes-specific self-efficacy (P <0.001, d = 0.7), and were more likely to
report depressive symptoms, anxiety, or diabetes distress (all \( P < 0.001 \), \( d \) range = 0.65–1.1).

**Conclusions**

Negative insulin therapy appraisals are common among adults with Type 2 diabetes using insulin, and are associated with lower general and diabetes-specific emotional well-being, reduced diabetes-specific self-efficacy and satisfaction with blood glucose.

This article includes data presented at a scientific meeting: Holmes-Truscott E, Skinner TC, Pouwer F, Speight J. Psychological Insulin Resistance In Australians With Type 2 Diabetes Already Using Insulin: Results From Diabetes MILES – Australia. *Australian Diabetes Society – Australian Diabetes Educators Association (ADS-ADEA) 2012*, Gold Coast, Australia, 28-31 August 2012.
Introduction

Beta-cell failure generally occurs within 10 years for individuals with Type 2 diabetes mellitus [1]. Timely intensification of insulin therapy, and achieving and maintaining optimal HbA1c, significantly reduce the risk of developing or worsening of microvascular complications [2]. ‘Psychological insulin resistance’ describes the negative appraisal of insulin therapy, which may act as barrier to insulin initiation or use [3–5].

People with Type 2 diabetes using insulin report less negative insulin therapy appraisals compared with those not yet using insulin [6–9], leading some to suggest that the experience of insulin mitigates previously perceived barriers to insulin therapy [10]. However, research into insulin omission, or suboptimal insulin taking, suggest that psychological barriers continue to be of relevance for people with Type 2 diabetes using insulin [11,12]. For example, 20% of Americans with Type 2 diabetes skip their insulin injections ‘often’ or ‘sometimes’, and 46% change their daily activities to avoid additional injections [13]. Insulin omission is significantly associated with treatment dissatisfaction, pain and embarrassment, being younger and requiring a greater number of injections per day [12]. An international study reported common reasons for insulin omission, including stress or emotional problems, embarrassment of injecting in public and the challenge of taking insulin at regular times [11]. The above studies suggest that, for some, negative appraisals and barriers to insulin use persist beyond insulin initiation.

The Insulin Treatment Appraisal Scale (ITAS) [9] measures insulin therapy perceptions among those with Type 2 diabetes. For those already using insulin, it measures the lived experience of insulin therapy. Previous research with this measure has primarily focused on the insulin appraisals of those not yet using insulin [14,15];
and on the differences in scores between those using insulin and those not using insulin, with the former generally displaying significantly lower mean ITAS scores, indicating less negative appraisals [6–9,16]. However, the variance in ITAS scores commonly reported amongst adults with Type 2 diabetes using insulin suggests that a proportion have negative evaluations of insulin therapy equivalent to those of not using insulin.

Few studies have investigated the associations between insulin therapy appraisals and socio-demographic, clinical and psychosocial characteristics in adults with insulin-treated Type 2 diabetes. To our knowledge, only one study reports on the relationship between mode and duration of insulin injections and negative insulin appraisals using a validated measure [6], and although the association between emotional well-being and perceptions of insulin therapy has been more widely explored among those not using insulin, or where treatment is unspecified [9,14,15,17], no study has reported on these associations specifically among adults with Type 2 diabetes using insulin.

The aim of the current study is therefore to determine the extent to which adults with insulin-treated Type 2 diabetes experience positive and/or negative aspects of insulin therapy and to investigate whether those who report above average ITAS scores differ from those with lower scores in terms of other psychosocial factors, self-reported clinical factors and self-care behaviours.

Methods

The Diabetes MILES Study is an international collaborative exploring the psychosocial aspects of living with diabetes [18,19]. This study used a selection of data from the Diabetes MILES – Australia 2011 survey, a national cross-sectional
survey of adults with Type 1 diabetes or Type 2 diabetes. A detailed description of the methods and overall sample characteristics have been published elsewhere [18]. Diabetes MILES – Australia received ethics approval from the Deakin University Human Research Ethics committee (reference number: 2011-046).

Participants

Survey booklets were posted to a random sample of 15 000 National Diabetes Services Scheme registrants and the survey was also made available nationally online. In total, 3338 eligible respondents took part, including 1962 adults with Type 2 diabetes, of whom 724 (37%) were using insulin (49%, n = 953 female; age 59±9 years; diabetes duration 13±8 years). The survey included core measures, asked of all participants, and non-core questions asked in survey subsets to reduce respondent burden. This analysis includes participants who reported managing their Type 2 diabetes with insulin injections and completed questionnaires of interest (n = 279) (see below).

Measures

Self-reported demographic and clinical characteristics were collected from all participants: age, gender, relationship status, employment status, education level, BMI, diabetes duration, years using insulin and the presence of diabetes-related complications (yes/no).

Insulin therapy appraisals were measured with the 20-itemITAS [9]. The ITAS includes 16 negative and 4 positive statements against which respondents indicate their level of agreement (1 = strongly disagree to 5 = strongly agree). Scores are summed to provide an ITAS Negative score (16–80), an ITAS Positive score (5–20) and a total ITAS score (20–100). Our psychometric validation of the ITAS indicated
that the negative subscale score is the most robust [16] and, hence, the ‘ITAS Negative’ score is used here instead of the ITAS total score.

Depressed mood and anxiety were assessed using the nine-item Patient Health Questionnaire (PHQ–9) [20] and seven-item Generalized Anxiety Disorder (GAD–7) questionnaire [21]. For each measure, respondents rate symptom frequency over the past 2 weeks on a 4-point scale (0 = not at all to 3 = nearly every day). Item scores are summed to form a total score (0–27 for PHQ–9; 0–21 for GAD–7). For both, scores of ≥ 10 indicate moderate-to-severe symptoms.

Diabetes distress was measured using the 20-item Problem Areas in Diabetes Scale (PAID) [22]. Respondents rate the extent to which each issue is a problem for them on a 5-pointscale (0 = not a problem to 4 = serious problem). Item scores are summed and standardized to a score out of 100, where scores ≥ 40 indicate severe diabetes distress.

Diabetes-specific self-efficacy was measured using the eight-item Diabetes Empowerment Scale – short form (DES–SF) [23]. Respondents indicate the extent to which each item is true for them on a 5-point scale (1 = strongly disagree to 5 = strongly agree). A composite score (range 1–5) is calculated by summing item scores and dividing by eight.

Self-care behaviours and beliefs were assessed using single items from the Diabetes Self-Care Inventory-Revised (DSCI–R) [24]. Participants were asked to indicate the number of injections they require per day, whether they take the required number of injections (1 = never to 5 = always), their perceived importance (1 = not at all to 4 = very) and the burden associated with these injections (1 = not at all to 4 = a great burden). Because there was little variance in responses, these three categorical
variables were dummy coded to represent optimal versus suboptimal responses, with the former equating to ‘always’ taking insulin as recommended, considering it ‘very’ important, or ‘not at all’ a burden. Participants also recorded the average number of blood glucose checks performed per day, and satisfaction with their blood glucose levels (0 = very dissatisfied to 6 = very satisfied), over the past 2 weeks.

**Statistical analysis**

Participants with more than one missing value on the ITAS (*n* = 6) were excluded. According to scale guidance, missing data points were replaced with participants’ summed mean scores (for the PAID, if two or more items were missing, and for the ITAS, PHQ–9 and GAD–7, when only one item was missing). Missing data were not replaced for other variables. Valid percentage is used throughout.

Statistical analysis was undertaken using SPSS version 21 (Chicago, IL, USA). Univariate differences between groups were assessed by Student’s t–tests (for continuous variables) and chi-squared tests (for categorical variables). Participants who reported negative ITAS scores within the first or fourth quartile were compared on demographic, clinical, self-care and psychosocial variables. Results are reported as mean ± sd or % (*n*). All statistical tests were two-sided and differences were accepted as significant at *P* < 0.05.

**Results**

A sample of 273 adults with Type 2 diabetes using insulin injections completed the ITAS. Table 1 displays demographic, clinical and psychological characteristics of the sample.
Table 1

Demographics, clinical and psychosocial characteristics of the total sample and between group differences

<table>
<thead>
<tr>
<th>Variable (scoring range)</th>
<th>Total sample N=273</th>
<th>ITAS Negative score</th>
<th>Lower Quartile n=79</th>
<th>Upper Quartile n=71</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: years</td>
<td>58.7±8.7</td>
<td>60.3±8.2</td>
<td>55.0±10.2</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Gender: women</td>
<td>46.2% (126)</td>
<td>45.6% (36)</td>
<td>49.3% (35)</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Employment: in paid work</td>
<td>29.1% (67)</td>
<td>20.9% (14)</td>
<td>41.4% (24)</td>
<td>.013</td>
<td></td>
</tr>
<tr>
<td>Education: ≥ high school</td>
<td>70.6% (178)</td>
<td>67.1% (51)</td>
<td>73.5% (50)</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Relationship status: with partner / married</td>
<td>73.1% (196)</td>
<td>73.3% (55)</td>
<td>73.2% (52)</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Diabetes duration: years</td>
<td>12.5±7.5</td>
<td>11.9±6.9</td>
<td>11.5±6.7</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Years using insulin</td>
<td>4.1±4.2</td>
<td>4.1±3.6</td>
<td>3.6±4.3</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Diabetes-related complications: ≥1</td>
<td>54.6% (149)</td>
<td>55.7% (44)</td>
<td>43.7% (31)</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td>34.1±8.9</td>
<td>33.2±7.1</td>
<td>33.2±9.1</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Insulin injections: N per day</td>
<td>2.2±1.2</td>
<td>2.2±1.3</td>
<td>2.4±1.2</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Insulin injections: ‘(almost) always’ take required injections each day</td>
<td>77.7% (202)</td>
<td>69.7% (53)</td>
<td>85.9% (55)</td>
<td>.023</td>
<td></td>
</tr>
<tr>
<td>Insulin injections: considered ‘very important’</td>
<td>82.5% (217)</td>
<td>80.5% (62)</td>
<td>82.8% (53)</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Insulin injections: considered ‘not at all a burden’</td>
<td>61.6% (162)</td>
<td>87% (67)</td>
<td>30.8% (20)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Self-monitoring of blood glucose: average N checks per day over last 2 weeks (0-7+)</td>
<td>2.63±1.51</td>
<td>2.9±1.5</td>
<td>2.5±1.5</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Variable (scoring range)</td>
<td>Total sample</td>
<td>ITAS Negative score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>--------------</td>
<td>---------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$N=273$</td>
<td>Lower Quartile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upper Quartile</td>
<td>$p$ value</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Satisfaction with blood glucose levels over last 2 weeks</td>
<td>3.49±1.72</td>
<td>4.1±1.7</td>
<td>2.97±1.7</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>(0=very dissatisfied to 6=very satisfied)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin appraisal: ITAS negative score (16-80)</td>
<td>41.4±9.7</td>
<td>30.1±5.1</td>
<td>53.2±5.9</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Insulin appraisal: ITAS positive score (5-20)</td>
<td>14.9±2.6</td>
<td>4.9±3</td>
<td>14.4±2.6</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Depressive symptoms: PHQ-9 (0-27)</td>
<td>7.7±6.3</td>
<td>5.8±5.5</td>
<td>10.12±6.1</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Anxiety symptoms: GAD-7 (0-21)</td>
<td>5.1±5.2</td>
<td>3.8±4.5</td>
<td>7.0±5.3</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Diabetes distress: PAID (0-100)</td>
<td>24.9±20.5</td>
<td>15.3±15.5</td>
<td>36.3±22.4</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Diabetes self-efficacy: DES-SF (1-5)</td>
<td>3.7±0.7</td>
<td>3.9±0.6</td>
<td>3.5±0.6</td>
<td>&lt;.001</td>
<td></td>
</tr>
</tbody>
</table>

NB: data are M±SD or %(n). Valid percentages reported due to missing varied Ns for each questionnaire.

Complications count includes kidney damage, albuminuria, retinopathy, neuropathy, heart disease, stroke and vascular disease.

DES-SF= Diabetes Empowerment Scale – Short Form; GAD-7=Generalised Anxiety Disorder questionnaire; ITAS=Insulin Treatment Appraisal Scale; PAID=Problem Areas In Diabetes Questionnaire; PHQ-9=Patient Health Questionnaire.
The mean ITAS Positive score was high overall (14.9 ± 2.6), with three of the four positive items being endorsed (‘agree’ or ‘strongly agree’) by ≥ 75% of the sample. The mean ITAS Negative score was 41.4 ± 9.7. The mean number of negatively worded ITAS items endorsed by participants was 4 ± 3, with 27 (9.9%) participants endorsing no barriers and one individual endorsing all 16. The most commonly endorsed negative aspects of insulin use concerned weight gain and condition progression (n = 140, 51.3% for both).

To characterize how participants reporting most and least negative insulin appraisals differed, the upper quartile (UQ; ≥ 48) and lower quartile (LQ; ≤ 36) of ITAS Negative were examined. The mean ITAS Positive score did not significantly differ between groups.

Table 2 displays the total sample and percentage of participants in the UQ and LQ who agreed or strongly agreed with each ITAS item, ranked in descending order according to the UQ group. Table 2 also displays the percentage difference in item endorsement between groups, i.e. item discrimination. Each of the 16 negative items was more highly endorsed by the UQ group and each of the four positive items was more highly endorsed by the LQ group. Although the degree of endorsement is different between groups, similar trends in item rankings were apparent. For example, five of the top six most endorsed ITAS Negative items for each group were the same. ‘Insulin means my diabetes has become much worse’ was the most commonly endorsed ITAS Negative item among those in the UQ, while ‘Insulin causes weight gain’ was the most commonly endorsed ITAS Negative item among LQ respondents. The item that discriminates best between UQ and LQ is ‘insulin makes life less flexible’, with a 61% difference in endorsement between groups.
Table 2

**Endorsement of ITAS items overall and by quartile group in descending order according to the upper quartile**

<table>
<thead>
<tr>
<th>#</th>
<th>Question</th>
<th>Lower Quartile (%)</th>
<th>Upper Quartile (%)</th>
<th>Percentage Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITAS Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Taking insulin means my diabetes has become much worse</td>
<td>30.4</td>
<td>73.2</td>
<td>-42.8</td>
</tr>
<tr>
<td>5</td>
<td>Taking insulin makes life less flexible</td>
<td>5.1</td>
<td>66.2</td>
<td>-61.1</td>
</tr>
<tr>
<td>1</td>
<td>Taking insulin means I have failed to manage my diabetes with diet and tablets</td>
<td>24.1</td>
<td>59.2</td>
<td>-35.1</td>
</tr>
<tr>
<td>7</td>
<td>Taking insulin increases the risk of low blood glucose levels (hypoglycaemia)</td>
<td>17.7</td>
<td>59.2</td>
<td>-41.5</td>
</tr>
<tr>
<td>18</td>
<td>Being on insulin causes family and friends to be more concerned about me</td>
<td>15.2</td>
<td>57.7</td>
<td>-42.5</td>
</tr>
<tr>
<td>9</td>
<td>Insulin causes weight gain</td>
<td>44.3</td>
<td>56.3</td>
<td>-12.0</td>
</tr>
<tr>
<td>4</td>
<td>Taking insulin means other people see me as a sicker person</td>
<td>7.6</td>
<td>53.5</td>
<td>-45.9</td>
</tr>
<tr>
<td>20</td>
<td>Taking insulin makes me more dependent on my doctor</td>
<td>16.5</td>
<td>53.5</td>
<td>-3.0</td>
</tr>
<tr>
<td>13</td>
<td>Taking insulin is embarrassing</td>
<td>2.5</td>
<td>43.7</td>
<td>-41.2</td>
</tr>
<tr>
<td>14</td>
<td>Injecting insulin is painful</td>
<td>1.3</td>
<td>43.7</td>
<td>-42.4</td>
</tr>
<tr>
<td>10</td>
<td>Managing insulin injections takes a lot of time and energy</td>
<td>2.5</td>
<td>40.8</td>
<td>-38.3</td>
</tr>
<tr>
<td>15</td>
<td>It is difficult to inject the right amount of insulin correctly at the right time every day</td>
<td>3.8</td>
<td>31.0</td>
<td>-27.2</td>
</tr>
<tr>
<td>12</td>
<td>Taking insulin means my health with deteriorate</td>
<td>0</td>
<td>28.2</td>
<td>-28.2</td>
</tr>
<tr>
<td>6</td>
<td>I'm afraid of injecting myself with a needle</td>
<td>1.3</td>
<td>25.4</td>
<td>-24.1</td>
</tr>
<tr>
<td>#</td>
<td>Question</td>
<td>Lower Quartile (%)</td>
<td>Upper Quartile (%)</td>
<td>Percentage Difference</td>
</tr>
<tr>
<td>----</td>
<td>--------------------------------------------------------------------------</td>
<td>--------------------</td>
<td>--------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>16</td>
<td>Taking insulin makes it more difficult to fulfil my responsibilities (at work, at home)</td>
<td>0</td>
<td>21.2</td>
<td>-21.2</td>
</tr>
<tr>
<td>11</td>
<td>Taking insulin means I have to give up activities I enjoy</td>
<td>0</td>
<td>14.1</td>
<td>-14.1</td>
</tr>
<tr>
<td></td>
<td>ITAS Positive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Taking insulin helps to improve my health</td>
<td>77.2</td>
<td>73.2</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>Taking insulin helps to prevent complications of diabetes</td>
<td>78.5</td>
<td>70.4</td>
<td>8.1</td>
</tr>
<tr>
<td>17</td>
<td>Taking insulin helps to maintain good control of my blood glucose</td>
<td>82.3</td>
<td>70.4</td>
<td>11.9</td>
</tr>
<tr>
<td>19</td>
<td>Taking insulin help to improve my energy levels</td>
<td>36.7</td>
<td>23.9</td>
<td>12.8</td>
</tr>
</tbody>
</table>

NB: Endorsement is defined as selecting the 'agree' or 'strongly agree' response option. Percentage difference is defined as Lower Quartile minus Upper Quartile.
As seen in Table 1, UQ and LQ groups did not differ substantially on any demographic variables except age ($t(148) = 3.5, P = 0.001, d = 0.57$) and employment ($\chi^2(1) = 6.2, P = 0.013, d = 0.46$), where participants reporting more negative insulin appraisals were younger and more likely to be in paid employment.

Regardless of ITAS scores, participants injected insulin approximately twice per day and the majority felt that it was ‘very important’ to take all of their recommended daily injections. However, participants reporting greatest negative insulin appraisals (UQ) were significantly more likely to report taking their required daily insulin injections ($\chi^2(1) = 5.17, P = 0.023, d = 0.39$) and that taking these injections were at least somewhat of a burden ($\chi^2(1) = 46.99, P < 0.001, d = 1.4$) compared with the LQ group. Although there was no significant difference in duration of insulin use (years) between groups, more participants in the UQ group had been using insulin for $\leq 1$ year compared with the LQ group (39.6% vs. 16.4%; $\chi^2(1) = 7.40, P = 0.007, d = 0.54$). Participants reported a similar frequency of self-monitoring of blood glucose (SMBG) per day over the past 2 weeks, but the UQ group were significantly less satisfied with their blood glucose levels than the LQ group ($t(148) = 3.9, P < 0.001, d = 0.63$).

Participants reporting greatest ITAS Negative appraisals displayed significantly lower diabetes-specific self-efficacy than those in the LQ ($t(144) = 4.2, P < 0.001, d = 0.73$). The UQ reported significantly lower mean item scores, compared with those in the LQ ($P = 0.012$ to $< 0.001$; $d = 0.42 – 0.91$), except for item 1: ‘I know what parts of taking care of my diabetes I am dissatisfied with’ (Mean Diff. = -0.116, $t(144.41) = -0.597, P = 0.551$), and item 8: ‘I know enough about myself as a person to make diabetes care choices that are right for me’ (Mean Diff. = 0.2, $t(148) = 1.9, P = 0.056$).
Participants reporting more negative insulin appraisals (UQ) reported significantly more depressive symptoms ($t(144) = -4.5, P < 0.001, d = 0.74$) and anxiety symptoms ($t(143) = -4.0, P < 0.001, d = 0.66$) than those with the least negative appraisals (LQ). Half ($n = 40, 54.4\%$) of UQ participants reported moderate-to-severe depressive and/or anxiety symptoms compared with 28.6% ($n = 22$) in the LQ group. Participants in the UQ also reported significantly greater diabetes distress than those in the LQ ($t(112.5) = -6.4, P < 0.001, d = 1.07$). Of those participants in the UQ, 42.4% ($n = 28$) reported severe diabetes distress compared with 8.9% ($n = 7$) of those in the LQ.

**Discussion**

Our findings demonstrate that negative appraisals of insulin therapy are evident among adults with insulin-treated Type 2 diabetes. Furthermore, those who report more negative experiences of insulin therapy are also more likely to report poorer general emotional well-being, greater diabetes distress, lower diabetes-specific self-efficacy and less satisfaction with blood glucose levels. Consistent with other studies [6,7,9], our findings suggest that negative insulin therapy appraisals may persist beyond insulin initiation, and may need to be evaluated as part of ongoing holistic diabetes care, particularly where concerns exist regarding other diabetes outcomes.

Although, on average, people with Type 2 diabetes currently using insulin hold significantly less negative insulin appraisals than those not using insulin [6,7,9,16], only 10% of the current sample did not experience any barrier regarding insulin therapy. The most highly endorsed negative appraisals are similar between groups, with two exceptions. ‘Insulin causes weight gain’ (item 9) was the most endorsed negative aspect of insulin use among the LQ group. For the UQ group, four other aspects to insulin use were perceived to be more problematic than weight gain.
‘Insulin makes lifeless flexible’ (item 5), ranked second for the UQ group but eighth for the LQ group, making it the item that discriminated most strongly between the two groups. Given that UQ participants were younger and more likely to be in paid employment, it is unsurprising that insulin is perceived to be a greater inconvenience to these participants.

Previous studies have reported inconsistent results regarding the association of demographic characteristics and insulin appraisals among people with Type 2 diabetes. Where a significant association has been reported, those with greater negative appraisals were consistently more likely to be women [25–28] and less educated [6,29]. However, participants with greatest and least negative appraisals in the current study did not differ significantly by gender or education. Nor did the two groups differ according to clinical characteristics: BMI, diagnosis of diabetes-related complications, diabetes duration.

With regard to diabetes self-care, no significant between-group differences were apparent in the average number of years using insulin, number of insulin injections per day or frequency of SMBG per day over the past 2 weeks. When years using insulin therapy was categorized as ≤ 1 year or >1 year there was a significant difference between groups, with a greater number of UQ participants having started insulin therapy within the past year. This contrasts with the findings of a Chinese outpatient study [6]. Further, the majority of participants (regardless of ITAS quartile) had been using insulin for more than 1 year. This supports the idea that, for some, insulin therapy appraisals may not change radically after initiation of insulin therapy or may even increase with greater experience of using insulin.

Psychological barriers to insulin therapy have been reported as associated with, or a reason for, insulin omission [11,12], while optimal medication-taking
behaviours are reportedly associated with belief in the benefit of the medication [30]. By contrast, participants reporting the greatest negative appraisals of insulin therapy in the current study were actually more likely to report ‘always’ taking their injections as recommended, compared with those with less negative ITAS scores; and the vast majority of the sample reported that taking their insulin as recommend was very important and endorsed the benefits of insulin use. This suggests that negative insulin appraisals may be, at least in part, independent of beliefs in the benefits of insulin use [16]. Further, negative insulin appraisals alone do not appear to influence actual insulin-taking behaviour and investigation into the behavioural consequences of negative insulin appraisals is warranted.

Participants reporting the greatest negative appraisals of insulin (UQ) were significantly less satisfied with their blood glucose levels over the past 2 weeks. Furthermore, UQ participants reported lower diabetes-specific self-efficacy than those in the LQ but reported a similarly high belief that they knew which parts of their diabetes they were dissatisfied with (DES–SF item 1). It may be that participants with the greatest negative appraisals are less satisfied as a result of not seeing expected improvements in blood glucose levels following insulin initiation, and feel unrewarded for their efforts in undertaking a more demanding treatment regimen. The assessment of insulin appraisals may provide an indicator of whether the insulin type or dosage needs to be reconsidered to improve not only blood glucose levels but also treatment satisfaction. However, it is beyond the scope of the current study to assess the longitudinal relationship between insulin therapy appraisals and satisfaction with diabetes management, and we do not have HbA1c data with which to further examine this relationship.
Participants with greatest negative insulin appraisals (UQ) were also more likely to report depressive symptoms, anxiety symptoms and diabetes distress than participants in the LQ. One possible explanation for this is that those who generally have a more negative demeanour or mood may be more susceptible to negative beliefs, whether it be about insulin, blood glucose levels or life in general. Given the cross sectional nature of this study we are unable to make a determination and it is unclear whether poor emotional well-being (general or diabetes-related) preceded insulin use or may be more directly connected to the negative experience of insulin use. However, one third of participants with the greatest negative appraisals (UQ) did not report elevated levels of depressive symptoms, anxiety symptoms or diabetes distress. It is more likely that a combination of the above (i.e. the presence of emotional distress and dissatisfaction with blood glucose outcomes) is intertwined with this group’s lack of physical adjustment (to the side effects and inconvenience) and psychological adjustment (‘I’m sicker now’) to insulin use. Assessment of insulin appraisals and intervention may improve treatment satisfaction and indirectly improve diabetes-specific and general emotional well-being. Unlike depression, which may require referral to a mental health specialist, insulin therapy appraisals may be suitably assessed and addressed within the diabetes care setting by health care professionals.

The Diabetes MILES – Australia study has several limitations, which are detailed elsewhere [18]. Of particular relevance to the current analysis is the lack of HbA1c data, which would have been useful for investigating the impact of negative appraisals of insulin on an indicator of complication risk (i.e. diabetes outcome). Furthermore, the cross sectional nature of the study means that causality cannot be determined. In addition, the self-care data collected (e.g. insulin-taking behaviours)
were all uncorroborated self-report using single items from a new self-care measure (in development). Finally, to undertake a comparative analysis of those with greatest and least negative insulin appraisals, continuous ITAS Negative scores were categorized and only the extreme upper and lower quartiles were included, with half the sample ($n = 123$) discarded from analysis. This does not, however, appear to have diminished the power of our study nor artificially inflated relationships. Supplementary analysis (data not reported), using the whole sample, confirmed significant associations between ITAS Negative scores (as a continuous variable) and the demographic, clinical and psychosocial variables shown to be significant in Table 1.

**Conclusion**

Negative appraisals of insulin therapy are evident among adults with Type 2 diabetes currently using insulin. Previous research has focused on negative appraisals among people with non-insulin-treated Type 2 diabetes with an (unwritten) implication that insulin initiation represents overcoming those barriers. Our data suggest that this view is flawed. More negative appraisals of insulin are associated with poorer emotional well-being (general and diabetes-specific) and lower diabetes self-efficacy. Although greater negative appraisals do not appear to be related to sub-optimal insulin-taking behaviours, they are associated with reduced satisfaction with blood glucose levels, and this marker of disappointment with the efforts required by a more intensive diabetes treatment regimen needs to be further explored. Prospective studies are needed to examine the associations between negative appraisals of insulin before and after insulin initiation and the extent to which these may affect insulin-taking behaviours, HbA1c and emotional distress.
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Competing interests

EHT and TCS have no conflicts to declare. FP has acted as an advisory board member and speaker for Novo Nordisk, and as a speaker for Sanofi-Aventis. He has received a grant from Novo Nordisk to support research and he has received funding for travel and accommodation to attend DAWN2 (Diabetes Attitudes Wishes and Needs) International Publication Planning Committee meetings. The Australian Centre for Behavioural Research in Diabetes has received sponsorship for JS to host or attend educational meetings from Lilly, MSD, Novo Nordisk, Roche Diagnostics Australia and Sanofi Diabetes; and has received consultancy income from Roche Diagnostics Australia and Sanofi Diabetes. JS is a member of the Roche Diagnostics Australia Accu-Chek Advisory Board.
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Chapter 9: The Impact of Insulin Therapy and Attitudes
Towards Insulin Intensification among Adults with Type 2 Diabetes: A Qualitative Study*

Study 3: Paper 6

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Abstract

Background

As type 2 diabetes (T2DM) is a progressive chronic condition, regular clinical review and treatment intensification are critical for prevention of long-term complications. Our aim was to explore the personal impact of insulin therapy, both positive and negative consequences, and attitudes towards future insulin intensification.

Methods

Twenty face-to-face interviews were conducted, and transcripts were analysed using thematic inductive analysis. Eligible participants were adults with T2DM, using insulin injections for <4 years. Participants were mostly men (n=13, 65%), (median (range)) aged 65 (43-76) years, living with T2DM for 11.5 (2-27) years.

Results

Five themes emerged regarding the consequences (positive and negative) of insulin therapy, including: physical impact, personal control, emotional well-being, freedom / flexibility, (concerns about) others’ reactions. Increased inconvenience and the perceived seriousness of using fast-acting insulin were both reported as barriers to future insulin intensification, despite most participants being receptive to the idea of administering additional injections.

Conclusions

Positive and negative experiences of insulin therapy were reported by adults with T2DM and most were receptive to insulin intensification despite reported barriers. These findings may inform clinical interactions with people with T2DM and interventions to promote receptiveness to insulin initiation and intensification.
Keywords

Insulin therapy, Type 2 diabetes, Psychological insulin resistance, Treatment intensification, Attitudes.
1. **Introduction**

Type 2 diabetes mellitus (T2DM) is a progressive metabolic condition, which requires ongoing clinical review and responsive treatment intensification to avoid chronic hyperglycaemia, and the associated development of diabetes-related complications (Holman, Paul, Bethel, Matthews, & Neil, 2008; UKPDS, 1998). Early initiation and ongoing intensification of insulin therapy is recommended across international guidelines (Inzucchi et al., 2012; Nathan et al., 2009). However, among adults with T2DM, negative appraisals of insulin treatment, known as ‘psychological insulin resistance’, may lead to the delay of insulin initiation (Polonsky & Jackson, 2004). In addition, research exploring predictors of insulin omission suggests that psychological barriers may continue to be prevalent among people with T2DM post-insulin initiation (Peyrot, Rubin, Kruger, & Travis, 2010; Peyrot, Barnett, Meneghini, & Schumm-Draeger, 2012). However, little research has explored the lived experience of insulin use among adults with T2DM.

Most commonly, investigation of psychological insulin resistance post insulin initiation has been in quantitative, questionnaire-based research exploring differences in insulin appraisals amongst adults with non-insulin-treated T2DM versus those using insulin (Chen et al., 2011; Hermanns, Mahr, Kulzer, Skovlund, & Haak, 2010; Snoek, Skovlund, & Pouwer, 2007). Those using insulin generally report fewer negative attitudes to insulin overall compared with those who are not yet using insulin therapy (Chen et al., 2011; Hermanns et al., 2010; Holmes-Truscott, Pouwer, & Speight, 2014; Snoek et al., 2007), but they commonly endorse negative experiences in the form of side effects (e.g. hypoglycaemia and weight gain) (Holmes-Truscott et al., 2014; Snoek et al., 2007). For some, barriers to insulin use may persist beyond insulin initiation and are associated with greater impairment of
emotional wellbeing (Holmes-Truscott, Skinner, Pouwer, & Speight, 2015). However, quantitative assessments of insulin appraisals post-initiation have been conducted using questionnaires designed for those not using insulin, which may be inappropriate in content or emphasis, and may not fully capture the experience of those already using insulin (Polinski et al., 2012).

Qualitative research has explored attitudes towards insulin therapy among those not yet using insulin (Ho & James, 2006; Morris, Povey, & Street, 2005), as well as experiences, and retrospectively reported facilitators, of initiating insulin among those already using insulin (Abu Hassan et al., 2013; Jenkins, Hallowell, Farmer, Holman, & Lawton, 2010). However, there is a dearth of research exploring the experience of using insulin post-initiation. In one small-scale interview study (n = 8), participants reported that their experience of insulin therapy was less negative than anticipated, and resulted in increased self-reported diabetes knowledge and improved health (Phillips, 2007a). However, participants also reported increased anxiety about the possibility of experiencing hypoglycaemia and experiencing discrimination (within the workplace, and in regard to driving licensing and travel insurance) (Phillips, 2007a). Additional qualitative research is needed to corroborate this single study.

Insulin therapy may also need to be intensified over time, in response to diabetes progression, through increased dose, the addition of more injections per day and/or changes in insulin types (e.g. a single or twice-daily basal or mixed injection to a basal bolus regimen). However, international research suggests that there is a gap between the number of people with T2DM who would benefit from insulin intensification, and what actually occurs in clinical practice (Grant, Buse, & Meigs, 2005; Guler, Vaz, & Ligthelm, 2008). A few studies have offered limited insights
into attitudes to future insulin intensification: it has been reported that one third of participants with T2DM using insulin are troubled by (Zambanini, Newson, Maisey, & Feher, 1999), or not ‘motivated’ to consider (Martinez et al., 2007), the possibility of additional daily insulin injections, but reasons for this have not been identified. To our knowledge, only one qualitative study has explored attitudes towards insulin intensification (Jenkins, Hallowell, Farmer, Holman, & Lawton, 2011). Participants who had intensified their insulin therapy within a three-year insulin trial reported being generally receptive to insulin intensification. However, they reported concerns relating to the need to juggle their daily routine to make time for additional injections and wishing to avoid injecting in public. Further qualitative research is needed outside the trial setting to explore drivers of willingness to intensify insulin in the real world.

An understanding of the experience of insulin use post-initiation, and attitudes towards intensification, will assist researchers and clinicians in developing interventions and clinical strategies to optimise diabetes care and improve receptiveness to treatment intensification over time. In this paper, we report on the findings of a qualitative study exploring the lived experience of adults with T2DM already using insulin, including their perceptions of the consequences of insulin use, and of future insulin intensification.

2. Methods

We conducted semi-structured, face-to-face interviews with adults with T2DM currently using insulin therapy. Ethical approval was obtained from Deakin University Human Research Ethics Committee (2013-048).
2.1. Participants and recruitment

Participants were eligible if they were: English-speaking adults (aged 18+ years) with T2DM, using insulin therapy for less than four years, and able to attend an interview in Melbourne or Geelong (in the state of Victoria, Australia).

Participants were recruited through advertisements placed on the Diabetes Victoria and The Australian Centre for Behavioural Research in Diabetes (ACBRD) websites, social media (Twitter, Facebook) and e-newsletters from June 2013 to February 2014. Purposive sampling was used with the aim of achieving gender balance and a broad age range. We aimed to interview approximately 20 participants, with the possibility of conducting further interviews, if necessary, to achieve data saturation.

Potential participants were invited to contact the research team by telephone or email to obtain study information and undergo eligibility screening. Overall, 52 enquiries were received: 20 were ineligible, 12 declined or made no further contact after receiving study information, and 20 proceeded to interview.

2.2. Interview schedule and procedure

Informed by existing literature (Gherman et al., 2011; Snoek et al., 2007; Wang & Yeh, 2012), a semi-structured schedule was designed to elicit a narrative from participants about their lived experience of diabetes, insulin initiation and use (including perceived advantages and disadvantages) and attitudes to insulin intensification.

Prior to conducting face-to-face interviews, participants provided written informed consent. All interviews were conducted by EHT and audio-recorded in a private meeting room in a non-clinical setting. The mean interview duration was 42 minutes (range: 20-69 minutes). Post-interview, participants completed a short
demographic questionnaire. Participants were given a $AUD20 department store gift voucher as a token of appreciation.

2.3. Transcription and analysis

Audio recordings were transcribed verbatim, checked and uploaded to QSR NVivo Version 10. Inductive (data-driven) thematic analysis was conducted using a non-linear iterative process informed by Braun and Clarke’s (2006) six-phase process for undertaking thematic analysis. An initial coding framework was formulated, reviewed iteratively and revised by all authors. A sample of the transcripts was double-coded using the revised framework with a high level of coding consistency (mean inter-coder agreement rating = 99.5%). Themes relevant to the current study were identified. All authors reviewed the final themes to ensure they represented the data adequately and reflected the study aims.

3. Results

3.1. Sample characteristics

The sample included 20 participants, aged 43 to 76 years (median = 65, IQR = 58-69 years) with a median diabetes duration of 12 years (IQR = 7-16 years), 65% (n = 13) men. Median time since insulin initiation was two years (IQR = 9-36 months), with most participants (n = 17) taking ≤2 (range = 1-4) injections per day. Most participants (70%, n = 14) were born in Australia with six participants born elsewhere: five in the UK and one in Germany. The majority of participants (70%, n = 14) were retired/not working and 55% (n = 11) had a university degree.

3.2. Data saturation

Data saturation was achieved at participant #7, after which point no new themes emerged. However, purposive sampling continued until a reasonable
demographic spread was achieved. Due to an over-representative early response from male participants, women only were invited to participate from September 2013 onwards.

3.3. **Impact of insulin therapy use**

Five main themes emerged from participant discussion surrounding the perceived impacts or consequences of insulin therapy: physical impact, personal control, emotional well-being, freedom and flexibilities, and (concerns about) others' reactions.

3.3.1. **Physical impact**

The negative physical impact of insulin therapy concerned changes to diabetes symptoms or medical outcomes since insulin initiation, e.g. bruising/bleeding/pain at injection site, weight gain, and hypoglycaemia.

Injection pain was described as infrequent and surprising when it occurred. It was related sometimes to injecting cooled (refrigerated), rather than room temperature, insulin. Participants described occasional bruising and bleeding but these were not considered major problems.

“It still hurts sometimes. And that's a bit of a surprise when it hurts so much...the bruises are massive.” (#18, woman, age 54) “Sometimes it might bleed and bruise... but it's fine.” (#15, woman, age 65)

Some noted that their doctor had discussed the possibility of weight gain prior to them commencing insulin. Others were unsure of the direct relationship between insulin and weight gain but suspected insulin had caused or contributed to their weight gain.
“It piles weight on and I said to [my doctor] ‘there's something bizarre about this’.” (#03, man, age 67)

Participants discussed hypoglycaemia as a sign that they needed to reduce their insulin dose or increase their food intake at particular times of day. Some discussed the need to carefully consider their insulin dose, food intake, and blood glucose levels before exercising and some emphasised a preference to keep their blood glucose levels higher to avoid hypoglycaemia.

“I do have hypos and that was one of the things that alerted me to the fact that...I might've gone just a bit too far [with insulin dose].” (#03, man, age 67) “I'm not that happy to let it go below five. Because I just have an innate feeling it's probably not actually safe or proper... to let it drop too low because accidents happen.” (#08, man, age 68)

Physical benefits of insulin use were also reported: the most salient was a glycaemic improvement following insulin initiation, with 19/20 participants stating that their blood glucose levels, HbA1c, or “control” had improved or stabilised.

“I was taking my blood sugar several times a day to monitor it, quite excited about how I was controlling it, bringing it down very quickly.” (#01, man, age 57) “The greatest benefit would be it obviously controls my blood sugar levels.” (#10, man, age 69)

The physical benefits extended to perceived improvement in general health. For example, some participants reported “feeling healthier” (#20, woman, age 73) and “much more energetic” (#03, man, age 67). They also reported a belief that lowering their blood glucose would have positive effects on their future health, or help to prevent diabetes-related complications.
“Insulin is helping me control my diabetes. That is negating the harmful effects of having high sugar on my kidneys, on my eyes, on everything.”

(#05, man, age 45)

However, a minority offered vague comments suggesting they were uncertain or ambivalent about the broader beneficial health impacts.

“I don't think it improves your health... I suppose, if you didn't take it, you wouldn't last that long.” (#09, man, age 75) “I haven't seen any benefits personally.” (#05, man, age 45)

3.3.2. Personal control

Feeling “in control” psychologically was an important theme for participants. For some, initiating insulin was associated with a sense of loss of personal control over their diabetes management, and disappointment in their prior efforts to manage their diabetes. This disappointment extended to clinician titration of insulin doses, which was perceived to be an indicator of the condition worsening and their “failure” to manage diabetes appropriately. In some instances, participants reported that this feeling waned over time.

“You sort of felt, well, I guess, a sense of failure. That you couldn't control your blood sugars. That you needed that outside intervention.”

(#14, man, age 64) "Then it [insulin dose] went up to 40 [units] and with each increase I was defiant, saying ‘well, this is dreadful’. This is supposed to control my diabetes and at, at this rate, I'm going to be using a whole bloody pen just to kind of keep it under control... I thought rather naively that, you know, I'd get at least 10, 15 years on the tablets and I haven't.” (#05, man, age 45)
While insulin represented a loss of personal control for some, others reported an enhanced sense of control. They reported increased ownership over, or confidence in, their diabetes management as a result of being able to adjust their insulin dose to account for physical activity or hypoglycaemia – a benefit not afforded to them while taking oral medication alone.

"If I know for a week I'm not going to exercise, well, I just increase the insulin level to compensate. So I've got a lot of control over it." (#01, man, age 57)

This sense of greater personal control over diabetes led participants to self-regulate other daily diabetes self-management behaviours. For example, they reported more frequent blood glucose checking and paying more attention to food intake.

"I'm a lot more rigorous about my testing since I've been on insulin and, as a consequence of that, I tend to be a lot more rigorous about when and how much I eat.” (#01, man, age 57)

3.3.3. Emotional wellbeing

Participants reported that increased personal control over their diabetes management and/or improvements in their blood glucose levels left them feeling better emotionally, or more positive about life with diabetes.

"Mentally I've accepted the need for it. I realise the benefits and I can see the benefits so that's made me happier with the outcome." (#04, man, age 76) “I'm more satisfied that I'm doing everything I can to control the diabetes.” (#12, man, age 63)
The emotional impact of injections varied across participants. Participants recalled their initial fear of injections at insulin initiation and, for some, a sense of relief, followed when they experienced injections as surprisingly painless while others reported ongoing distress.

“I realised that it [injecting] wasn't the traumatic experience that I expected it to be. I was quite pleasantly surprised actually.” (#04, man, age 76) "You think, ‘I don't want to do this. I don't want to. Let's go. Suck it up. Let's do it. Get it over and done with. If it hurts it hurts but nothing you can do about it’." (#16, man, age 68)

3.3.4. Flexibility and freedom

Participants reported feeling that insulin made life less flexible or was inconvenient, which had broader negative impacts on their activities. Injections were perceived as burdensome, interfering with their ability to be spontaneous (e.g. go out for dinner, go to bed early) and required an increased level of daily structure and routine (e.g. scheduled mealtimes).

“Injecting at the correct time is very difficult because the demands on your lifestyle are not regimented...[they're] dictated by circumstances, which change every day.” (#08, man, age 68)

Participants felt that having to carry insulin and supplies when going out for the day was burdensome.

“You pack all your stuff together and, even just going out for dinner, it doesn't have to be overnight stay or anything...you've got to think ahead. It's like packing for an extra person.” (#18, woman, age 54)
Insulin was perceived as restricting opportunities, especially those involving travel. This included difficulty transporting insulin/supplies; needing refrigeration; carrying enough insulin to last a trip; obtaining travel insurance; obtaining letters from doctors to provide to airports or travel insurance; driving licensing; and travelling to places where healthcare and medications are accessible in case of emergency.

"That's probably the hardest part, going away, telling the tour directors of two different tours that I needed a fridge in every room ... making sure you've got letters on the plane... Travelling, yes, you wish you didn't have it then." (#15, woman, age 65)

In contrast to insulin use limiting participants’ freedoms, the increased sense of control over diabetes management (i.e. ability to adjust insulin) enabled, for some, a greater level of freedom. For example, being able to alter insulin dosage according to food intake.

“If ever I go out for lunch, I’m not going to say, ‘I’m not going to have that dessert’. In fact, actually, I will have that dessert because I know that I can have an extra few notches of insulin.” (#05, man, age 45)

3.3.5. (Concerns about) others’ reactions

Participants reported concern about other people’s negative reactions to their insulin use, which generally constituted family members expressing concern that insulin symbolised a worsening condition. Participants recognised that insulin therapy made their diabetes more visible to those around them compared with their previous tablet-only regimen. They believed that negative reactions were borne out
of well-intentioned concern for their health and wellbeing but, nonetheless, they experienced the reactions as unnecessary and frustrating.

"'Oh, he's on insulin. Oh, isn't that terrible!' And, you know, 'Oh God, you know, when's he going to die?' sort of thing... actually, it really annoys me. Yeah, I mean I suppose their heart's in the right place."

(#08, man, age 68)

Participants also reflected on the general public’s attitudes towards insulin. Some reported feeling that others may think of them differently because of their insulin use, and a minority discussed unwanted advice or interference.

"I was asked to disclose whether there were any illnesses that the company should be aware of and ...you would've thought that, you know, I said I'm a two-headed monster from Mars...because, all of a sudden, I'm appointed a buddy!"  (#03, man, age 67)  "You get a lot of good meaning, well-intentioned advice from other people that wouldn't know what an insulin pen looked like."

(#16, man, age 68)

Participants also expressed concern about having to inject insulin in public. Some participants felt embarrassed or self-conscious, and were uneasy that it may result in negative reactions / judgments, or upset others. Others simply wished to avoid undertaking what they perceived as a “private” activity in public. For some, this meant avoiding injecting outside the home except when absolutely necessary, seeking out private locations (e.g. bathrooms) and attempting to be discreet. Some reported becoming more comfortable with injecting in public over time.

“'If people didn’t understand what a diabetic was, why a diabetic has a pen, that sort of thing, [they might think] oh you know 'oh, she's shooting
up. ’ (#19, woman, age 69) “I sneak in... ‘I hope nobody comes, I'm not going into the toilet, I'm going to do it here. Hope nobody's coming, hope nobody's coming’ and I'm looking around and I quickly do it and get out.” (#17, woman, age 63) “I used to go to the ladies and then I thought, ‘hang on, it's silly’, I'll just do it like that and put it back in my bag.” (#15, woman, age 65)

3.4. Attitudes to future insulin intensification

Participants differed with regard to how they felt about the possibility of intensifying their insulin treatment in the future. Just over half (n=12) reported that the prospect of administering additional injections each day was not a major concern to them.

“It's just like anything, when I find out anything new, I get 'the sads’ for a couple of days and then I just get over it and do it.” (#06, woman, age 43) “What I know now, and the fact there's no pain, [means] there's no barrier to additional treatments if I had to.”(#04, man, age 76)

Others expressed a desire to avoid additional injections, indicating they would be more willing to increase the dose of existing injection(s) to avoid additional injections.

“That would p*** me off. Yeah, that would be concerning”(#13, man, age 56) “If it needed to be increased I'd increase it on the one dose, so I might go up to 40 [mmol/L] or something like that” (#07, man, age 59)
Two key barriers to insulin intensification were identified. First, participants felt that additional injections each day would be annoying, difficult to implement in their daily routine, and were concerned that they might forget to take them.

"It would be a nuisance because I think, I can forget, you know, I get into a routine...if I had to take more than one it would be the nuisance factor, the inconvenience rather than the actual injections." (#11, man, age 68)

"I would tend to resist that because...I'd have to organise to do it in the middle of the day and that would most likely be inconvenient most days." (#12, man, age 63)

Second, participants were concerned specifically about fast-acting insulin. They considered it to be particularly inconvenient and more serious, due to the need for pre-prandial injections and counting carbohydrates, and felt anxious about the associated increased risk of hypoglycaemia.

"The alternative was to change my insulin from a slow-acting insulin to a fast-acting insulin. Again, I was incredibly reluctant to do that because, with a slow-acting insulin, I feel I have more control. I know that I'm not necessarily going to go into a hypo." (#05, man, age 45)

"[It] was a scary prospect of like, carb counting, like the Type 1s do and that was scary." (#18, woman, age 54)

Finally, a minority of participants considered insulin intensification as a reflection on their diabetes self-management efforts.

"I'd probably feel disappointed... because I'd feel that maybe I hadn't paid enough attention to my diet. Or maybe I needed to exercise more."
(#20, woman, age 73) “I just want to stay on the two [injections]...so I’d 
better work a bit harder” (#15, woman, age 65)

4. Discussion

To our knowledge, this is the first in-depth qualitative investigation of the lived experience of insulin use among adult Australians with T2DM, and the first to qualitatively explore attitudes toward insulin intensification outside a trial setting. Our findings demonstrate that negative appraisals of insulin therapy persist after insulin initiation. Consistent with previous research (Guimarães et al., 2010; Hayes, Bowman, Monahan, Marrero, & McHorney, 2006; Tan et al., 2011), participants commonly reported negative physical side effects of insulin therapy, including: hypoglycaemia, weight gain and pain caused by or associated with insulin injections. In addition to these well-known physical impacts, the negative emotional impact of insulin therapy was also highlighted in our study. Similar to previous research (Abu Hassan et al., 2013; Furler, Spitzer, Young, & Best, 2011; Hayes et al., 2006; Jenkins et al., 2010; Morris et al., 2005; Noakes, 2010; Phillips, 2007a, b), some participants reported a sense of relief following their initial insulin injection. Others reported ongoing concern caused by daily injections and a wish to avoid adding extra injections to their regimen in the future. In addition, some participants reported that insulin use, and potential insulin intensification / dosage increases, signified for them a “failure” of their prior diabetes self-management and a further loss of “control” over their health. This “self-blame”, or the belief that personal failure to manage one’s health is an antecedent of treatment intensification has been reported elsewhere (Bogatean & Hâncu, 2004, Morris et al., 2005).
Participants reported a loss of freedom following insulin initiation, feeling that insulin therapy was an inflexible treatment option that impacted negatively on their ability to be spontaneous. The need to carry and administer insulin impacted on participants’ decisions to eat out and go on day trips. In particular, participants were concerned with the perceived difficulty of travelling (e.g. overseas holiday) as someone requiring insulin therapy. These findings reflect previous quantitative research, which has highlighted “insulin makes life less flexible” as a key discriminating item between those with most and least negative insulin appraisals (Holmes-Truscott et al., 2015), and the negative impact of insulin-treated diabetes on aspects of quality of life such as travel (Bradley & Speight, 2002).

The perceived inconvenience or inflexibility of insulin injections may be heightened for those who wish to avoid injecting in public. Attitudes towards public injections varied, with some participants wishing to avoid them entirely while others reported attempting to be discreet and seeking out some level of privacy. Participants reported feeling embarrassed about injecting in public and concern that others may think of them differently because of their insulin use. While not raised in the current study, fears about injecting in public may have consequences for optimal diabetes self-management. Previous research has reported people missing or delaying insulin doses due to social embarrassment (Brod, Kongsø, Lessard, & Christensen, 2009; Browne, Ventura, Mosely, & Speight, 2014; Jenkins et al., 2011; Shiu, Kwan, & Wong, 2003).

In addition to negative consequences of insulin therapy, participants raised a number of benefits, none more salient than direct improvements in blood glucose levels. For some, such improvement extended to indirect improvements in energy and health in general, and a belief that these improvements would reduce their risk of
developing long-term complications. This is consistent with our recent cross-sectional survey of Australians with insulin-treated T2DM where the majority of participants endorsed positive aspects of insulin therapy (Holmes-Truscott et al., 2015).

A certain satisfaction with insulin therapy was implied as participants reported that insulin therapy provided them with a greater a sense of personal “control”, and flexibility, over their diabetes management and this led them to feel more positive emotionally about their diabetes and blood glucose outcomes. For example, participants reported improved recognition of blood glucose patterns, self-regulating other diabetes self-management behaviours (e.g. food intake) and liking the ability to adjust insulin doses according to glucose patterns, food intake or physical activity. Similarly, other studies have shown that adults with insulin-treated T2DM report an increased understanding of their diabetes and its treatment following insulin initiation, improved diabetes self-management, and a greater sense of perceived control over their body and health (Morris et al., 2005; Phillips, 2007a; Vinter-Repalust, Petriček, & Katić, 2004).

A gap has been identified between the proportion of people with insulin-treated T2DM who would benefit from insulin intensification and actual clinical practice (Grant et al., 2005, Guler et al., 2008). Polonski et al. (2012) conducted a systematic review of studies exploring attitudes towards insulin intensification in people with T2DM concluding, from limited published research, that prior insulin experience was associated with increased acceptability of insulin intensification. Consistent with this, most participants in the current study reported being receptive to insulin intensification. Where barriers to additional injections were reported, participants discussed the ‘nuisance factor’. However, participants did not discuss inconvenience
in reference to injecting in public, as was a key finding elsewhere (Jenkins et al., 2011), but, rather, as an interruption to their routine and an increased likelihood of forgetting to inject. Changes in insulin type appeared to concern participants, who raised the increased risk of hypoglycaemic episodes and the need to carefully monitor blood glucose and carbohydrate intake as barriers to the use of fast-acting insulin.

4.1. Clinical implications and future directions

It is critical to the wellbeing and optimal self-management of people with T2DM that barriers to insulin initiation, maintenance, and intensification, are identified, acknowledged and used to guide patient education, counselling and/or regimen optimisation. Previously published recommendations suggest early education about the progressive nature of T2DM and the potential need for insulin initiation (Meneghini et al., 2010). The attitudes towards insulin intensification reported here, in particular with regard to concerns around fast-acting insulin, suggest that education and counselling about insulin therapy should not end at insulin prescription and initiation. Clinicians need to engage in ongoing discussions with people with T2DM about treatment intensification, including early discussion of the types of insulin available and the potential benefits and side effects of each type of insulin. Further, insulin regimen options need to be explored in the context of a person’s daily routine to support them to manage their diabetes optimally (e.g. through developing strategies for remembering to inject).

Attitudes towards insulin are not static. Indeed, a reduction in negative attitudes towards insulin has previously been observed after initiation (Hermanns et al., 2010) and, in the current study, some participants commented on their change in attitudes with greater insulin experience over time (e.g. becoming more comfortable
with injecting in public with experience). Similarly, it could be expected that participants’ attitudes towards intensified insulin regimens would change with experience. However, in this single timepoint study, it is not possible to observe actual change in attitudes towards insulin use, which might occur as a function of experience with, understanding and education about, and change in insulin regimen. To further understand how attitudes towards insulin change over time, and the mechanisms by which this occurs, longitudinal qualitative research is needed to investigate attitudes towards insulin pre- and post-initiation of insulin, and/or structured education or counselling about insulin therapy, and/or insulin intensification.

Despite reporting various negative consequences of insulin therapy, participants in our study also reported experiencing benefits. Namely, improvements in blood glucose outcomes leading to increased perceptions of personal control over the condition, flexibility and freedoms, suggesting at least some experienced greater satisfaction with treatment following insulin initiation. The perceived positive and negative impacts of insulin therapy, as reported here and elsewhere (Wang & Yeh, 2012) could be used to inform the development of evidence-based interventions and messaging to increase psychological receptiveness towards insulin initiation.

4.2. **Strengths and limitations**

The current study is one of the first in-depth explorations of the lived experience of people with T2DM using insulin, focusing on both the positive and negative aspects of insulin use, and on attitudes to insulin intensification in the real world. Purposive sampling was used to maximise variability in participants’ age and gender. Consistent with the average age of Australians with T2DM (National Diabetes Services Scheme, 2015), this study mainly included older, retired adults...
who had been living with diabetes for over a decade. As such, the findings of this study may not be representative of the experiences of younger adults with T2DM, an emerging group (Browne, Scibilia, & Speight, 2013). Further, this English-speaking participant group was predominately born in Australia or the UK and generally well educated. As such, the experiences of this group may not be representative of Australians with culturally and linguistically diverse backgrounds, and the current study was unable to explore insulin therapy experiences, which may be specific to different cultural groups within Australia. Further, participant recruitment was challenging, with just 50 people expressing an interest over an 8-month period, and over half of those being ineligible or not participating. This may suggest that those who did take part were more engaged in their diabetes self-care and diabetes issues than the general T2DM population.

5. Conclusions

This study demonstrates that people with T2DM experience several ongoing barriers to insulin use and have concerns regarding future insulin intensification. While certain concerns and negative experiences (e.g. injection anxiety, avoidance of public injections) lessened over time and with experience for some, other negative consequences are more persistent (e.g. impact on freedom and flexibility). Reported benefits of insulin therapy included perceived immediate improvements in blood glucose levels, energy and health, and increased satisfaction with diabetes management. Participants were mostly receptive to the possibility of future insulin intensification but cited inconvenience and perceived risk of hypoglycaemia as their greatest barriers to intensifying their regimen. These findings suggest that clinician counselling may be beneficial and evidence-based interventions are needed, in which
concerns about insulin are acknowledged, strategies for overcoming them identified, and benefits highlighted.

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**Conflict of interests**

EHT has undertaken research funded by an unrestricted educational grant from Abbott Diabetes Care to The Australian Centre for Behavioural Research in Diabetes (ACBRD). JB has served on a Sanofi Diabetes Advisory Board and the ACBRD has received honoraria in respect of this. She also has conducted research funded by unrestricted educational grants from Roche Diagnostics Australia and Sanofi Diabetes to the ACBRD, and has received consultancy income from both companies also. The ACBRD has also received sponsorship from AstraZeneca for meeting attendance by JB. JS is a member of the Accu-Chek Advisory Board (Roche Diagnostics Australia), and her research group (ACBRD) has received honoraria in respect of this. ACBRD has also received unrestricted educational grants from Medtronic and Sanofi; sponsorship to host or attend educational meetings from Eli Lilly, Medtronic, Merck Sharp & Dohme, Novo Nordisk, Roche Diagnostics Australia and Sanofi; consultancy income from Abbott Diabetes Care, Roche Diagnostics Australia, Janssen Pharmaceuticals and Sanofi; and speaker's honoraria...
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References


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Chapter 10: Discussion

10.1. Major Findings

The aim of this thesis was to undertake a program of research to investigate: a) the measurement of insulin appraisals among Australians with T2D, b) the occurrence of, and factors associated with, PIR and intention to begin insulin therapy among adults with non-insulin-treated T2D within national population level and clinical settings, c) the demographic, clinical and psychological predictors of actual insulin uptake, and d) attitudes toward insulin post-initiation, perceptions of benefits and consequences of insulin, and attitudes to further treatment intensification. The following sections summarise the findings of this thesis with reference to these four objectives.

10.1.1. Measuring insulin appraisals among Australians with T2D

As highlighted in Chapter 2, with the exception of a single interview study (Furler, Spitzer, Young, & Best, 2011) and the international DAWN study (Peyrot et al., 2005), which used unvalidated single items, there has been no research investigating attitudes towards insulin therapy among Australians with T2D and, thus the Australian perspective is largely unknown. Further to this, the acceptability, validity and reliability of insulin appraisal measures has not been explored among Australians with T2D. Therefore, the first objective of this thesis was to conduct psychometric validation of a commonly used measure of insulin appraisals, the ITAS (Snoek, Skovlund, & Pouwer, 2007), among Australians with T2D. In addition, validation was conducted separately by treatment type to ensure the scale demonstrated satisfactory psychometrics across both insulin-treated and non-insulin-treated populations. In the first Australian study employing the ITAS (see Chapter 4,
Study 1a), the measure was found to be acceptable and psychometrically sound among a national sample of adults with T2D. However, items in the Positive subscale did not load on a forced single factor, and the internal consistency of the single factor was low. Thus, computation of a Total scale score was not supported and the two ITAS subscales (Negative and Positive) were recommended for future use. Further analyses presented in this thesis used the two subscale scores in preference to the Total score, and where the Total score was used, the rationale was to enable comparison with international data.

10.1.2. Attitudes to and willingness to begin insulin therapy

The second objective of this thesis was to measure, and identify factors associated with PIR and receptiveness to insulin therapy among Australian adults with non-insulin-treated T2D. The mean Total and ITAS Negative scores among participants in Diabetes MILES – Australia (see Chapter 4; Study 1a) were similar to those reported internationally (Bahrmann et al., 2014; Chen et al., 2011; Hermanns, Mahr, Kulzer, Skovlund, & Haak, 2010; Snoek et al., 2007), whereby Total and Negative subscale scores were significantly higher, more negative, among those not yet using insulin in comparison to those using insulin. As observed elsewhere, positive insulin appraisals were highly endorsed among the non-insulin-treated sample (Chen et al., 2011; Larkin et al., 2008; Petrak et al., 2007; Snoek et al., 2007; Woudenberg, Lucas, Latour, & Scholte op Reimer, 2012). Among the current sample, the ITAS Positive subscale did not discriminate between treatment groups, and elsewhere results are inconsistent (Hermanns et al., 2010; Snoek et al., 2007).

The breadth and depth of the Diabetes MILES – Australia dataset (Study 1) provided the opportunity to contribute to existing knowledge through the comprehensive investigation of the psychosocial correlates of negative insulin
appraisals among those with non-insulin-treated T2D. Chapter 5 (Study 1b) investigated the independent contributions of general and diabetes-specific emotional wellbeing and beliefs about medication in predicting ITAS Negative subscale scores among adults with non-insulin treated T2D. Consistent with prior research (Makine et al., 2009), diabetes-related distress was found to be a stronger independent predictor of insulin appraisals than depressive symptoms. Similarly, despite anxiety disorder recently being reported as a predictor of actual insulin uptake (Iversen et al., 2015), anxiety symptoms did not contribute independently, after accounting for diabetes-related distress. This thesis examined, for the first time, the relationship between PIR and specific aspects of diabetes-related distress. The ‘emotional burden’ subscale of the Diabetes Distress Scale (Polonsky et al., 2005) was most strongly associated with negative insulin appraisals. ‘Regimen burden’ was moderately associated with the ITAS Negative, while a weak correlation was observed between ITAS Negative scores and ‘physician’ and ‘interpersonal’ distress. Beliefs about medications, in general, may play a role in attitudes to insulin therapy (Polonsky, Hajos, Dain, & Snoek, 2011), but the association had not previously been examined using validated measures, or measures that differentiate between general medication beliefs and diabetes-specific medication beliefs. In Study 1b, diabetes-specific, but not general, medication beliefs were independently associated with ITAS Negative. Greater diabetes-related ‘emotional burden’ and ‘concern’ about current diabetes medications was associated with greater negative insulin appraisals. These findings suggest that negative attitudes toward future insulin use may be an extension of negative perceptions/experiences of current diabetes medications (i.e. OHAs) and experience of the emotional burden of living with diabetes.
In Chapter 6, ‘hypothetical willingness’ to begin insulin therapy was investigated among adults with T2D for whom insulin was clinically indicated (the Stepping Up sample; Study 2b): 22% reported being, hypothetically, ‘not at all willing’, and just 19% reported being ‘very willing’, to begin insulin therapy if recommended. In a study of PIR across eight Western countries, not including Australia, the average proportion of participants reported as unwilling to begin insulin was slightly lower (at 17%), although there was considerable variation between countries (from 6% in Spain to 37% in Italy) (Polonsky, Hajos, et al., 2011).

Factors associated with hypothetical willingness to begin insulin were examined at the Stepping Up baseline using univariate analyses, which demonstrated no associations between willingness and: clinical variables (i.e. Hba1c, diabetes duration, number of co-morbidities, number of prescribed medications), current self-management behaviours (i.e. daily SMBG and diabetes medication-taking behaviours (MARS)). Further, with the exception of socioeconomic status, no association was observed between willingness and demographic variables (i.e. age, gender). Significant associations were observed between willingness and emotional wellbeing (i.e. depressive symptoms and diabetes-related distress) and insulin appraisals (i.e. ITAS Negative and Positive subscales and single attitudinal measure). In multivariate analysis, after accounting for socioeconomic status and insulin appraisals, neither depressive symptoms nor diabetes-related distress contributed independently to the prediction of hypothetical willingness to begin insulin. The multivariate analysis demonstrated that socioeconomic status and both negative and positive attitudes towards insulin therapy were predictive of being ‘very willing’ to begin insulin therapy among adults with T2D in primary care for whom insulin was clinically indicated. Thus, interventions to increase willingness to initiate insulin
therapy must tackle negative attitudes towards insulin therapy and improve positive insulin appraisals.

10.1.3. Individual-level predictors of actual insulin uptake

In Chapter 6, factors associated with ‘hypothetical willingness’ to begin insulin were identified, but whether this reflects actual refusal rates has not been verified previously. Furthermore, at the time of commencing this thesis, little prospective research had comprehensively explored the demographic, clinical and psychological factors associated with actual insulin uptake. Therefore, the third objective of this thesis was to identify demographic, clinical, and psychosocial predictors of actual insulin uptake among people with T2D for whom insulin was clinically indicated and assess the predictive validity of the ‘hypothetical willingness’ item (Chapter 7; Study 2b). Univariate analyses demonstrated that insulin use at 12 months among Stepping Up participants was associated with socioeconomic status and HbA1c at baseline. Consistent with recent studies, baseline ITAS Positive and Negative scores differentiated insulin users from non-insulin users at follow up (Keij, Ismail, & Winkley, 2016; Odawara, Ishii, Tajima, & Iwamoto, 2016), as did willingness to begin insulin. Depressive symptoms were not associated with insulin uptake, also consistent with prior research (Iversen et al., 2015; Nefs, Pop, Denollet, & Pouwer, 2013). In contrast to the only other study which has assessed the relationship between diabetes-related distress and insulin use (Keij et al., 2016), univariate analysis demonstrated no association between diabetes-related distress and insulin use at 12 months. Using a multilevel logistic regression model, after controlling for study arm allocation, willingness to begin insulin therapy was predictive of insulin use at 12 months, negating the contribution of negative and positive insulin appraisals. Those who were hypothetically ‘very willing’ to begin insulin were more
likely to have switched to insulin therapy at 12 months, compared to those who were ‘not at all’ willing. Higher baseline Hba1c was also an independent predictor of insulin use at 12 months. These results are consistent with a recent longitudinal study of Japanese adults with T2D, which identified that those who initiated insulin reported significantly higher HbA1c and less negative/more positive insulin appraisals, at baseline, compared with those who remained on OHAs (Odawara et al., 2016). However, in that study, insulin appraisals were assessed using a study-specific unvalidated measure and hypothetical willingness to begin insulin therapy was not measured.

10.1.4. Attitudes to insulin therapy after insulin initiation

The fourth aim of the current thesis was to examine attitudes towards insulin post-initiation. This included examination of: a) change in attitudes towards insulin after initiation, and among those with insulin-treated T2D, b) factors associated with negative attitudes towards insulin, and c) perceived benefits and consequences of insulin and attitudes towards future insulin intensification. Data from all three studies were relevant to this objective.

Participants in the Stepping Up trial (Study 2b) completed the ITAS at baseline and 12 months follow-up; enabling comparison of attitudes towards insulin over time as a function of insulin uptake and trial randomisation. The findings presented in Chapter 7 demonstrate a significant reduction in negative insulin appraisals overall at 12 months. Further, there was a significant main effect of insulin initiation, whereby those who initiated insulin therapy reported a significantly greater improvement in ITAS Negative scores at follow-up, compared to participants who remained on maximum daily OHAs. This is consistent with prior research (Hermanns et al., 2010). The Stepping Up study also provided the opportunity to compare change in
insulin appraisals by model of care received (usual care versus Stepping Up model of care) and identify any interaction effect with insulin uptake. A main effect of model of care was identified, whereby those in the intervention arm reported significantly greater improvements in ITAS Negative scores than those in the control arm, but no interaction was found. It is likely that the significant main effect of the study arm allocation is accounted for by the higher proportion of intervention participants who initiated insulin compared to the control arm, rather than any effect of the intervention itself. These results support the theory that uptake of and experience with insulin may mitigate negative perceptions of insulin therapy. In contrast to negative insulin appraisals, ITAS Positive scores did not change over time overall, or by insulin uptake. Elsewhere, the sensitivity of the ITAS Positive subscale to treatment change has varied (Hermanns et al., 2010; Liebl et al., 2013).

Despite average reductions in negative insulin appraisals, certain negative attitudes or consequences of insulin use may be endorsed after insulin initiation. Little research has explored the possible impact of ongoing PIR among adults with insulin-treated T2D. As shown in Chapter 8, in the Diabetes MILES –Australia sample (Study 1c), approximately half the participants with insulin-treated T2D endorsed negative ITAS statements relating to insulin symbolising disease progression, and causing weight gain. The negative ITAS item ‘insulin makes life less flexible’ discriminated most between those with lower and higher ITAS Negative scores. Those with more negative insulin appraisals were younger and more likely to be in paid work, which is consistent as this group are more likely to perceive the need for a treatment that fits into their lifestyle. In contrast to prior research (Chen et al., 2011), those with greater negative insulin appraisals were more likely to have been using insulin therapy for one year or less, compared to those with
less negative insulin appraisals. However, the majority of those with negative insulin appraisals had been using insulin for more than one year, indicating that negative attitudes towards or experience of insulin may be common regardless of insulin treatment duration.

Among Diabetes MILES – Australia participants, those with more negative insulin appraisals were more likely to perceive daily insulin injections as a greater burden, than those with less negative insulin appraisals, but they were injecting insulin a similar number of times per day and were also significantly more likely to report ‘always’ taking their insulin as prescribed, compared to those with less negative insulin appraisals. These results suggest that negative insulin appraisals alone are not associated with insulin omission; in fact, negative insulin appraisals may be the consequence of optimal, yet burdensome, insulin-taking behaviours.

Despite reporting always taking their insulin as recommended, participants with insulin-treated T2D with higher ITAS Negative scores reported significantly lower diabetes-specific self-efficacy and reported less satisfaction with their glucose levels over the previous two weeks in comparison to those with lower ITAS Negative scores. Similarly, perceived social acceptability of, and satisfaction with, insulin delivery and perceived glycaemic control over the previous 4 weeks has been found to be associated with self-efficacy with insulin therapy in a 36-week clinical trial of insulin initiation (Hayes et al., 2013). It may be that negative insulin appraisals among people with insulin-treated T2D are related to perceptions of insulin therapy as ineffective, as evident from less satisfaction with glucose levels, despite optimal insulin-taking behaviours. This may, in turn, reduce diabetes-specific self-efficacy and increase diabetes-related distress. Indeed, those with insulin-treated T2D and more negative insulin attitudes were also more likely to report diabetes-
related distress and increased depressive and anxiety symptoms. In contrast, an alternative explanation may be that those with a more negative outlook (evidenced by increased depression and diabetes-related distress) may be more susceptible to negative beliefs about their diabetes treatment and their ability to self-manage their condition effectively, and greater dissatisfaction with their treatment. Longitudinal studies are needed to more fully understand the nature of these relationships.

Thus, the results presented in Chapter 8 provide quantitative evidence that negative insulin appraisals persist among people with insulin-treated T2D, while Chapter 9 presented qualitative data from an in-depth interview study (Study 3) with adults with insulin-treated T2D. Participants discussed their perceptions of the negative impact of insulin therapy, including adverse physical effects (i.e. weight gain, hypoglycaemia, injection-related pain) and emotional wellbeing (i.e. injection-related fear or distress), personal control (i.e. sense of loss of control over treatment and health), lifestyle freedoms (i.e. having to consider insulin therapy when travelling and eating out, reduced sense of spontaneity), and other people’s perceptions of them (i.e. familial concerns, general public’s negative reactions to insulin therapy, injecting in public). The foremost-perceived benefit of insulin therapy was the observed improvement in glycaemic outcomes, which for some extended to more tangible improvements in general health. An additional identified benefit of insulin use, which is not covered within the ITAS but has been reported elsewhere (Morris, Povey, & Street, 2005; Phillips, 2007a), concerns an increase in perceived control over diabetes management and one’s health. This included better understanding of diabetes and control over outcomes and, in turn, for some it meant greater flexibility in their self-management (for example, ability to adjust insulin
doses according to glucose patterns, food intake or physical activity), with beneficial consequences for their quality of life.

In addition to investigating psychological receptiveness and resistance to insulin uptake and maintenance, this thesis set out to investigate these issues in relation to insulin intensification. A recent systematic review (Polinski et al., 2012) highlighted the lack of research examining rates of, attitudes towards, and factors associated with timely insulin intensification among those with T2D already using insulin therapy. In one of the only qualitative studies to explore attitudes toward insulin intensification to date, people with T2D were found to be largely receptive to insulin intensification (Jenkins, Hallowell, Farmer, Holman, & Lawton, 2011). Consistent with this, the qualitative findings presented in Chapter 9 indicate that people already using insulin are receptive to intensification. However, some reported a desire to avoid additional injections, appearing more receptive to increasing their current insulin dose(s). The main reported barrier to insulin intensification was the perceived inconvenience and inflexibility of additional injections (i.e. having to change daily routine). In addition, participants discussed the possible negative consequences of fast-acting insulin, such as increased risk of hypoglycaemia and the need for carbohydrate counting, as barriers to insulin intensification.

10.1.5. Summary

This thesis extends significantly on previous knowledge of the measurement, experience, and correlates, determinants and consequences of PIR and receptiveness among adults with T2D including among those currently, and not yet, using insulin therapy. Specifically, Study 1a (Chapter 4) confirmed the psychometric reliability and validity of the ITAS among those with insulin-treated and non-insulin-treated T2D separately. Chapter 5 (Study 1b) reported comprehensive cross-sectional
analyses of the demographic, clinical and psychosocial factors associated with negative insulin appraisals among a national sample of Australians with non-insulin-treated T2D; identifying diabetes-related distress and concerns about current diabetes medication as the strongest independent correlates. Chapters 6 and 7 reported on baseline and 12-month findings from a primary care sample of adults with T2D for whom insulin therapy is clinically indicated. Among this group, attitudes toward insulin therapy were associated with hypothetical willingness to begin insulin therapy (Study 2a, Chapter 6), and willingness, but not insulin appraisals, was associated with actual insulin uptake at 12 months (Study 2b, Chapter 7). Study 2b also demonstrated that change in negative, but not positive, insulin appraisals at 12-month follow-up was associated with insulin uptake. Chapters 8 and 9 confirmed the persistence of negative insulin appraisals following uptake of insulin therapy.

Among people with T2D already using insulin therapy, those with more negative insulin appraisals also reported worse emotional wellbeing and lower diabetes self-efficacy and satisfaction with blood glucose (Study 1c, Chapter 8). Finally, Chapter 9 (Study 3) reported on the experience of insulin use and identified receptiveness, and barriers to, future insulin intensification.

10.2. Implications for Assessment, Clinical Practice and Future Research

The following section discusses the implications of the studies presented in this thesis for the measurement of PIR and receptiveness, and for clinical practice, both before and after insulin initiation. Embedded in this discussion are implications of the findings in relation to theory, strategies for reducing negative insulin appraisals and improving receptiveness to insulin therapy initiation and intensification, and suggestions for further research.
10.2.1. Defining and measuring psychological insulin resistance and receptiveness

PIR and receptiveness were defined in this thesis as negative and positive attitudes to insulin therapy, which may act as barriers to or enablers of insulin initiation, ongoing insulin use and insulin intensification. These concepts were operationalised in this thesis through the measurement of insulin appraisals (negative and positive attitudes) (Polonsky, Hajos, et al., 2011; Snoek et al., 2007), as well as through the related measurement of ‘hypothetical willingness’ to begin (or intensify) insulin (intention) (Polonsky, Hajos, et al., 2011), and actual acceptance or refusal of insulin therapy (behaviour) (Jenkins, Hallowell, Farmer, Holman, & Lawton, 2010; Jenkins et al., 2011).

10.2.1.1. The value of measuring insulin appraisals

Refusal or acceptance of treatment intensification, as well as optimal use of any prescribed treatment, by people with T2D is of primary clinical importance due to the necessity of establishing and maintaining glycaemia within target and, in turn, preventing/delaying the development of diabetes-related complications (U.K. Prospective Diabetes Study Group, 1998). In Chapter 7 (Study 2b), it was demonstrated that actual insulin uptake was predicted by higher HbA1c, being allocated to the intervention arm (i.e. receiving the Stepping Up model of care), and importantly by intention to begin insulin, but not insulin appraisals. This poses the question of whether it is useful to assess insulin appraisals if intention (assessed with just a single question of ‘willingness’) is a better predictor of the desired behaviour. The stronger association between intention and behaviour, in comparison to attitudes, is likely due to intention encapsulating both negative and positive insulin appraisals (as shown in Chapter 6) as well as other unmeasured factors. For example, the
clinical decision-making dynamic suggests that some people with diabetes may accept their HCP’s authoritative recommendation regardless of their own reservations (Jenkins et al., 2011). However, to understand the reasoning behind intention, HCPs need to understand attitudes towards insulin therapy (in addition to other possible factors), including both negative insulin appraisals (PIR) and positive insulin appraisals (receptiveness). Furthermore, in clinical practice, it may be more appropriate to explore attitudes to guide ‘decisional balancing’ about the prospect of using insulin (Miller & Rollnick, 2002) rather than simply asking the potentially confronting and blunt question of willingness.

In addition to understanding attitudes that may lead to delays in insulin initiation, the measurement of insulin appraisals among those already using insulin therapy may also be used to identify new or ongoing barriers to insulin use, and explore their potential impact. For example, in Chapter 8 (Study 1c), negative insulin appraisals were identified among those already using insulin therapy, and this group also experienced worse general and diabetes-specific emotional wellbeing, lower diabetes self-efficacy and satisfaction with blood glucose levels compared to those with more positive insulin appraisals.

10.2.1.2. Measuring insulin appraisals over time or between treatment groups

As described in Chapter 2, several validated measures of insulin appraisals exist (Fu, Wong, Chin, & Luk, 2016; Martinez et al., 2007; Petrak et al., 2007; Snoek et al., 2007), in addition to other unvalidated measures (Odawara et al., 2016; Polonsky, Fisher, Dowe, & Edelman, 2003; Polonsky, Hajos, et al., 2011). When selected for use in this thesis, the ITAS was (and remains) the only measure to be developed and validated for use among both insulin and non-insulin using T2D populations (Snoek et al., 2007), and had demonstrated responsiveness (Hermanns et
Thus, if assessing PIR over time or between treatment groups (both done in this thesis), the ITAS may be the most relevant measure. However, the limitations of this scale need to be considered. First, as described in Chapter 4, 8% of the non-insulin-treated participants (but none with insulin-treated T2D) skipped the entire scale within the Diabetes MILES – Australia survey. The first sentence of the ITAS instructions reads, “The following questions are about your perceptions of taking insulin for your diabetes”, which may have prompted non-insulin-treated participants to skip the questionnaire entirely. After accounting for this, no particular items were skipped more commonly by either group, and all items appeared acceptable to both groups. Future researchers using the ITAS with non-insulin using participants might consider modifying the instructions to better emphasise the questionnaire’s relevance to maximise completions.

Second, as the ITAS was designed to be relevant to both insulin-treated and non-insulin-treated groups, it is possible that the items do not comprehensively capture the diversity of appraisals within both groups. In Chapter 9, a qualitative study identified negative experiences of insulin therapy among adults with insulin-treated T2D; some of which are not assessed within the ITAS. For example, participants reported the need to more carefully consider additional negative consequences, relating to their lifestyle (physical activity, dietary choices and meal times), and the nuisance of having to carry insulin/monitoring supplies. While the ITAS includes the statement ‘...insulin means my diabetes had become much worse’, people with T2D already using insulin also report increasing insulin dose(s) as an additional indicator of worsening health. Further, there are no items in the ITAS concerning attitudes towards insulin adjustment, different insulin regimens, or insulin intensification. Thus, the ITAS may have limited sensitivity to appraisal of
once-daily or biphasic insulin regimens compared with intensive insulin therapy (multiple daily injections or insulin pump). Future research should investigate differences in insulin appraisals among people with insulin-treated T2D using various insulin regimens. Among adults with insulin-treated T2D, negative experiences of insulin therapy may be better assessed through the use of a measure of insulin treatment satisfaction (e.g. Anderson et al., 2004) and/or experience (e.g. Moock, Hessel, Ziegeler, Kubiak, & Kohlmann, 2010) specifically designed for use among this treatment group. Future research needs to examine the overlap between the ITAS and measures of insulin treatment experience or satisfaction, and identify which are more strongly associated with insulin-taking behaviours (i.e. insulin omission) and willingness to intensify insulin regimen.

To protect the validity of ITAS for assessing change over time (and change in treatment), a balance must be struck between comprehensiveness and applicability across treatment groups. Indeed, items that require knowledge or experience of actual insulin therapy are of limited relevance to those not yet using insulin. This is evidenced by the inclusion of the item ‘insulin causes weight gain’, which, in both the original validation sample (Snoek et al., 2007) and in the Australian validation sample (Chapter 4), did not load on either the negative or the positive subscales (regardless of insulin use), and was the only negative item that was significantly more likely to be endorsed among the insulin-treated than the non-insulin-treated group. This suggests that people with non-insulin-treated T2D may be unaware of the association between insulin therapy and weight gain and, therefore, this item may not be relevant to this group. However, retaining the item may prompt HCPs to discuss this important potential side effect within care in the interests of informed decision making.
In contrast to the ITAS Negative, the ITAS Positive subscale scores did not discriminate between treatment groups cross-sectionally (Chapter 4) and did not change following insulin initiation (Chapter 7), consistent with prior research (Hermanns et al., 2010). This lack of sensitivity may be due to the ITAS Positive items referring mainly to knowledge of the physiological benefit of insulin use, which could be applied to any pharmacological treatment of diabetes, rather than to the consequences of insulin specifically. For example, items refer to insulin helping to ‘maintain good control of blood glucose’ and ‘prevent complications of diabetes’, which might be said of any glucose lowering agent when used appropriately. In Chapter 9, other benefits of insulin therapy were identified including: increased dietary flexibility due to the ability to adjust insulin, feeling more positive about health in general, relief over the ease of using insulin devices/injecting, and insulin use fostering personal control over diabetes. Thus, while it is recommended that the positive items of the ITAS are retained, this subscale may benefit from revision, with the development and testing of items referring to additional, and perhaps more immediately salient, benefits of insulin therapy.

10.2.1.3. Measuring psychological insulin receptiveness

The findings of this thesis suggest that PIR and receptiveness are not two ends of a single continuum, but may be parallel concepts. Statistically, the ITAS Positive perform quite differently to the ITAS Negative subscale: there was a weak association between subscales (rather than a strong negative correlation), positive items loaded weakly on the forced one-factor solution and reduced the internal consistency reliability of the Total ITAS score (Chapter 4). In Chapter 6, both Negative and Positive subscales were found to be independent predictors of intention to begin insulin therapy among Stepping Up participants. This suggests that the
initiation of, or intention to initiate, insulin would require the perceived necessity of insulin therapy (positive insulin appraisals) to outweigh the perceived concerns (negative insulin appraisals). This is consistent with the Necessity and Concerns framework (Horne, Weinman, & Hankins, 1999), which hypothesises that the decision to engage in treatment is based on both the perceived need for treatment (Necessity) and concerns about the consequences of the treatment (Concerns). While this framework has most commonly been applied to actual medication adherence in a range of chronic conditions (Horne et al., 2013), Patel and colleagues (2015) have recently suggested its relevance in predicting acceptance or refusal of insulin therapy among people with T2D. Therefore, it is recommended that both positive insulin appraisals (receptiveness) and negative insulin appraisals (PIR) are measured.

10.2.1.4. Short-form measures of insulin appraisals

Short-form measures of insulin appraisals may be preferred in clinical and research settings but the advantages (e.g. reduced participant burden) need to be weighed carefully against disadvantages (e.g. reduced validity). In Chapter 6, the ITAS was compared with a short, unvalidated measure of attitudes toward insulin, which asks participants to choose two of six statements (three positive and three negative) that best represent their feelings about insulin (Polonsky, Hajos, et al., 2011). There was a weak-to-moderate correlation between this single attitudinal measure and the ITAS Positive and Negative subscales, and it contributed independently, alongside ITAS subscales, to the prediction of willingness to begin insulin. This suggests that the single attitudinal measure assesses a concept related to, but not precisely the same as, that assessed by the ITAS. The 20-item ITAS provides a more complete profile of attitudes towards insulin therapy. However, it may also be that the predictive validity of the Total and Negative subscale scores is diluted by the
scale length, as items of less relevance or concern to the actual uptake of insulin may
be creating noise in the total scores. In contrast, responses to the single attitudinal
measure represent the two most salient attitudes to insulin within a short list of six,
though it is unclear whether these six items capture the most salient negative and
positive aspects of insulin therapy for all people with T2D. For example, the second
most highly endorsed negative ITAS item among Australians with T2D using OHAs
to manage their condition was ‘taking insulin makes life less flexible’ (65%). The
perceived impact of insulin therapy on lifestyle flexibility is not captured within the
single attitudinal measure. Thus, further work is needed before a short-form
instrument can be recommended.

10.2.2. Reducing psychological insulin resistance among adults not using
insulin therapy

Among people with non-insulin-treated T2D, this thesis has demonstrated the
correlational pathway between attitudes to intention (Chapter 6), and intention to
change in behaviour (Chapter 7), as proposed in the theory of planned behaviour
(Ajzen, 1991). Importantly, the association between intention to begin insulin
therapy and actual insulin uptake was independent of the model of care highlighting
that, in addition to successful practice-based/HCP level interventions to reduce
clinical inertia, interventions need to target change in attitudes towards insulin
therapy in order to increase intentions to begin insulin therapy among people with
T2D.

At the commencement of this thesis, many commentaries and perspectives on
PIR and techniques to reduce negative attitudes had been published (Clark, 2007;
Davis & Renda, 2006; Meece, 2006; Polonsky & Jackson, 2004). However, it is only
in more recent years that interventions have been developed specifically to reduce
negative insulin appraisals (Brod, Alolga, & Meneghini, 2014; Patel, Stone, Hadjiconstantinou, et al., 2015) and to improve understanding of insulin therapy as a treatment option (Hassali et al., 2013; Mathers et al., 2012). These interventions have been evaluated to varying degrees, but none, to the PhD candidate’s knowledge, in terms of their association with actual insulin uptake, which needs to be the focus of future research.

Patel and colleagues (2015) have developed an intervention for South Asian people with T2D living in the UK, which is designed to reduce myths and misconceptions about insulin therapy commonly reported among this community (Patel, Stone, Chauhan, Davies, & Khunti, 2012; Patel, Stone, McDonough, et al., 2015). The intervention is delivered via DVD, designed to be viewed by the person with T2D within clinic and followed by a discussion of the content with a HCP. Despite positive feedback regarding the DVD and associated resources, the time required to provide the intervention was perceived to be a limitation by the HCPs. This has implications for the feasibility of applying such an intervention within real-world care. It is already known that HCPs find insulin initiation a time-consuming exercise (Furler et al., 2011). If the DVD was found to be effective, an alternative implementation strategy may be required to extend the reach and acceptability of this intervention. Alternatively, the tool may be reformatted into a medium that could be viewed by people with T2D at home. For example, Brod et al (2014) recently developed an educational brochure that presents ten negative barriers to insulin therapy followed by an “unbiased, medically informative” response. This tool has undergone cognitive debriefing with people with T2D, but no further evaluation has been conducted. Thus, further research is needed to investigate whether this tool may be effective in reducing PIR or is associated with actual insulin uptake. Future
research needs also to the investigate the medium of delivery (i.e. DVD, brochure, website) within this context to identify the most acceptable, suitable, and effective way to challenge the insulin appraisals of people with T2D and increase intentions to use insulin when it is clinically indicated.

Patel and colleagues (2015) also reported difficulty engaging people with non-insulin-treated T2D to take part in the evaluation of their DVD. People with T2D were hesitant to take part due to their concern that consenting may mean that they would subsequently have to begin insulin therapy. As a consequence, the evaluation of this intervention was severely curtailed (N=3). Therefore, those with most negative attitudes towards insulin may be least inclined to engage with an intervention that explicitly aims to reduce negative attitudes towards insulin therapy. An alternative approach may be to re-frame the intervention as being more broadly about diabetes self-management, and present the strengths and weaknesses of various treatment options, rather than insulin in isolation. Mathers and colleagues (2012) have taken this approach in designing a decision aid tool, which provides evidence-based information about several treatment options (no change, lifestyle modifications, or insulin therapy) and aims to help adults with non-insulin-treated using T2D to make an informed decision about their treatment. The decision aid takes a “balanced approach”, highlighting both positive and negative aspects of insulin therapy and other treatment options (Ng, Mathers, Bradley, & Colwell, 2014). The decision aid was designed for completion by the person with T2D prior to consulting with the HCP, followed by in-practice discussion within usual consultation time constraints. Therefore, this type of tool may be more acceptable to HCPs employing the intervention and people with T2D experiencing PIR. The decision aid has shown encouraging results in reducing decisional conflict and
improving insulin knowledge and expectations, but did not demonstrate change in willingness to begin insulin therapy following the intervention (Mathers et al., 2012). This may be due to the decision aid’s focus, mainly on the practical aspects of insulin therapy, such as pain, weight gain, hypoglycaemia and risk of complications. Chapters 4-6 of this thesis highlight other salient negative attitudes towards insulin therapy among those with non-insulin-treated T2D, for example, those referring to the symbolism of insulin (‘insulin means I have failed…’) and inter-personal impact (‘insulin causes family and friends to be more concerned about me’). However, as insulin appraisals were not evaluated in the decision aid trial it is not possible to ascertain whether there was change in negative and positive insulin appraisals after completing the decision aid.

Each of the above-mentioned interventions were developed for use at the point of treatment intensification being required. Thus, interventions to reduce negative attitudes, and improve receptiveness, to insulin therapy have been designed typically to be reactive in nature. However, attitudes towards treatment progression may develop from diagnosis onwards (or may be formed pre-diagnosis). Indeed, the findings of this thesis indicate that insulin appraisals are not associated with diabetes duration among Australians with non-insulin-treated T2D (Chapters 5 and 6). Insulin initiation recommendations have highlighted the need for proactive within-care discussion of insulin therapy from diagnosis to increase awareness and acceptance of insulin therapy as a potential treatment option (Meneghini et al., 2010).

Attitudes towards insulin therapy are associated with other diabetes-specific psychosocial processes and outcomes. For example, in Chapter 5, it was identified that those with more negative attitudes toward insulin therapy also reported more negative beliefs, or ‘concerns’, about their current diabetes medications (OHAs) and
greater diabetes-related distress. Furthermore, diabetes-related distress and beliefs about medications have previously been shown to be associated with diabetes medication-taking behaviours (Aikens, 2012; Aikens & Piette, 2009), and diabetes-related distress is prospectively and positively associated with HbA1c (Fisher et al., 2010). Thus, proactively identifying and addressing negative beliefs about current diabetes medications and diabetes-related distress from an early point in the person’s journey with diabetes may help to improve their receptiveness to further treatment intensification, as well as current medication-taking behaviours, which, in turn, is likely to improve glycaemic outcomes (Aikens & Piette, 2013).

Recommendations for tackling PIR also highlight the need to reframe the need for insulin therapy through clarifying any inaccurate illness perceptions and misconceptions (e.g. Clark, 2007; Polonsky, 2007; Polonsky & Jackson, 2004; Reid, 2007). For example, the belief that ‘insulin means I have failed’ may be a consequence of a broader belief that they themselves are to blame, or at fault, for their diagnosis and/or their subsequent inability to maintain optimal blood glucose levels (Beverly et al., 2012; Broom & Whittaker, 2004; Browne, Ventura, Mosely, & Speight, 2013; Krall et al., 2014). Although not assessed in the current thesis, this suggests that attitudes towards insulin therapy may be, in part, a consequence of broader illness perceptions. Education received at diagnosis of diabetes, and reinforced thereafter, may play an important role in the development of illness perceptions and, consequently, medication beliefs and receptiveness to treatment progression. Indeed, illness perceptions have been found to be tenacious. A three-year follow up of the ‘DESMOND’ structured T2D education program delivered at diagnosis revealed benefits of the intervention were maintained in terms of illness perceptions but not in terms of bio-medical outcomes (Khunti et al., 2012). It would
be useful to examine attitudes towards current and future medications among the DESMOND participants (intervention versus control) to understand whether an intervention to improve diabetes education and illness perceptions at diagnosis may be effective, over the long-term, at minimising negative attitudes towards insulin therapy and improving receptiveness to treatment intensification.

The experience of hyperglycaemia, diabetes-related complications, and “engagement in disease progression” have been identified as facilitators of insulin receptiveness in qualitative research (Bogatean & Hâncu, 2004; Chin, Polonsky, Thomas, & Nerney, 2000; Jenkins et al., 2010; Phillips, 2007b). In addition, higher HbA1c is associated with insulin uptake in quantitative research (Odawara et al., 2016; Xiong et al., 2014). Thus, education provision to improve recognition and understanding of prolonged hyperglycaemia may be an avenue for future intervention development. Indeed, undertaking SMBG was reportedly associated with greater belief in the efficacy of insulin therapy in the DAWN study (Peyrot et al., 2005). Corroborating prior research, HbA1c was found to be an independent predictor of actual insulin use at 12 months among Stepping Up participants (Chapter 7). However, this finding should be interpreted with caution. A probable explanation for the association between baseline HbA1c and 12-month insulin use is that the likelihood of insulin prescription by HCPs increased as the perceived clinical need for insulin rose, regardless of study arm allocation. This is consistent with prior research that some HCPs prefer to delay insulin initiation until absolutely necessary (Peyrot et al., 2005). Neither baseline HbA1c, nor SMBG (at least once a day versus less than once per day), was found to be associated with willingness to begin insulin therapy among Stepping Up participants (Chapter 6), suggesting that engagement with disease progression was not a facilitator of receptiveness to insulin for people
with T2D. However, HCP-led discussion of out-of-target HbA1c (which occurred as a result of the intervention, or at the request of control clinics to undertake a clinical review of participants) may, in itself, have acted as an intervention to improve receptiveness to insulin therapy. Intention to begin insulin therapy was measured prior to this initial consultation. Therefore, the association between HbA1c and insulin uptake is unclear. Future research needs to examine whether an educational intervention to improve understanding of diabetes progression and, in particular, recognition and understanding of hyperglycaemia is associated with improved receptiveness to treatment intensification. The use of a ‘structured’ approach to SMBG has been shown to increase insulin uptake and reduce HbA1c compared to usual SMBG (Polonsky, Fisher, et al., 2011). A qualitative investigation would be of interest to examine how the structured approach to SMBG affects understanding and visibility of diabetes progression, and attitudes towards treatment intensification.

This thesis aimed to investigate factors associated with attitudes towards insulin and the relationship between insulin appraisals and intention to commence, or actual uptake of, insulin therapy among people with T2D. However, other factors, not investigated within this thesis, may also be relevant in the predicting intention or actual behaviour change. For example, according to the theory of planned behaviour, normative beliefs may add to the prediction of intention, or willingness, to begin insulin therapy (Ajzen, 1991) and it has been proposed that the most important determinant of intention to initiate insulin is the ‘subjective norm’ (Wolffenbuttel, Drossaert, & Visser, 1993). Indeed, qualitative literature (discussed in Chapter 2) has identified the role of others, including HCPs, family, friends and peers, in facilitating either PIR or receptiveness. Furthermore, HCPs may play a role in boosting diabetes-specific self-efficacy and improving experience of insulin therapy at the time of, and
beyond, insulin initiation (discussed in Section 10.2.3). However, none of the studies included in this thesis specifically examined the role of the others (HCPs, family, friends or peers) in the development of insulin appraisals, intention to begin insulin therapy, or actual insulin uptake. Thus, future research is needed to quantitatively examine the association between these variables.

A small number of longitudinal studies have reported change in insulin appraisals post insulin initiation, suggesting that uptake may be an effective intervention to reduce PIR in and of itself (Hermanns et al., 2010; Liebl et al., 2013; Odawara et al., 2016). Corroborating those findings, the results from this thesis showed that negative insulin appraisals were endorsed by significantly fewer adults with insulin-treated compared to non-insulin-treated T2D (Chapter 4), and significant reductions in negative insulin appraisals following insulin uptake (Chapter 7). Furthermore, in the qualitative study reported in Chapter 9, people with T2D reported their relief after injecting insulin for the first time, observed improvements in their blood glucose levels, and felt more satisfied that they were doing everything they could to manage their diabetes. Therefore, one way to improve attitudes towards insulin therapy may be an ‘insulin trial’, as previously suggested by Polonsky and Jackson (2004). This involves the individual trying an insulin injection in the safety of the clinic, or using insulin at home for a defined short-term period. This approach is clearly limited by the fact that the person with T2D must be willing to trial/use insulin therapy, which as evidenced by prior research (Polonsky, Hajos, et al., 2011) and in the current thesis, is not always the case. Thus, it is likely that various approaches are needed to reduce PIR and improve receptiveness to insulin therapy, as a ‘one size fit all’ approach will not work.
10.2.3. Psychological insulin resistance beyond insulin uptake

Experience of insulin therapy alone does not result in universal mitigation of negative attitudes, and negative experiences/consequences of actual insulin therapy may contribute to negative attitudes. The results presented in Chapter 8 highlight that negative insulin appraisals are reported among people with insulin-treated T2D, with only 10% not endorsing any negative aspect of insulin therapy. While ‘insulin causing weight gain’ was the only ITAS Negative item to be endorsed by significantly more insulin-treated participants than non-insulin-treated participants, symbolic and social consequences of insulin use were also commonly endorsed among those using insulin therapy (Chapter 4). Likewise, the in-depth qualitative interview study (Chapter 9) identified negative consequences of insulin therapy use in terms of perceptions of personal control, emotional well-being, lifestyle flexibility and others' (family, friends, general public) negative reactions, in addition to the physical impact of insulin therapy. Thus, despite insulin initiation, or experience, being associated with a reduction in negative insulin appraisals overall (Chapter 7), negative attitudes to insulin therapy may be salient for some people with T2D using insulin. However, to the PhD candidate’s knowledge, no intervention has been developed to date to reduce PIR among those with insulin-treated T2D.

This thesis (Chapter 8) demonstrated that negative attitudes towards insulin therapy are not associated with duration or intensity of insulin therapy, suggesting that additional familiarisation with, or experience of, insulin injections does not necessarily reduce negative attitudes towards insulin therapy or barriers to insulin intensification beyond initiation. Longitudinal research is needed to confirm this finding. In addition, negative attitudes towards insulin therapy (i.e. relating to inconvenience and perceived seriousness of using fast-acting insulin therapy) may be
barriers to insulin intensification among those using insulin therapy (Chapter 9) and, elsewhere, negative consequences of insulin therapy have been identified as barriers to self-titration (McBain, Begum, Rahman, & Mulligan, 2016). It is, therefore, important to consider the impact of negative attitudes toward, and experiences of, insulin therapy at all stages of care (i.e. prior to and after insulin initiation).

In addition to the actual physical experience of insulin administration and its consequences (e.g. reduction in blood glucose levels, reactions of others), it may be that education and support received from HCPs at the time of, and immediately following insulin initiation, partially accounts for the observed reduction in negative insulin appraisals after insulin initiation. Thus, enhanced education and support from HCPs may result in less negative insulin appraisals after insulin initiation. Prior research has demonstrated associations between insulin uptake and information provision from HCPs being perceived as adequate (Karter et al., 2010), and between patient-provider relationship/interactions and PIR, measured using the BIT questionnaire (Nam, Chesla, Stotts, Kroon, & Janson, 2010). The perceived patient-provider relationship, and its association with PIR, was not the focus of the current thesis. However, Study 2b (Chapter 7) examined the association of the model of care received (i.e. study arm allocation) on change in insulin appraisals among Stepping Up participants. The Stepping Up model of care was found to have no relative advantage in improving insulin appraisals over and above insulin uptake (experience) alone. This might be due to HCPs in the intervention arm providing limited additional support at the time of insulin initiation over and above HCPs who prescribed and initiated insulin therapy within usual care. Indeed, the main focus of the Stepping Up HCP training and specialist support was to reduce the primary care team’s clinical inertia, not necessarily to reduce PIR among patients. HCPs did not
receive comprehensive training in identifying and addressing concerns about insulin therapy (either before or after insulin uptake). It would be worthwhile to assess whether provision of comprehensive training in identifying and addressing barriers to insulin therapy for HCPs would be associated with a) improved insulin uptake, and b) further reductions in negative insulin appraisals among those who initiate insulin therapy, compared to the original Stepping Up model and usual care.

Nam et al. (2010) previously identified diabetes-specific self-efficacy as a mediator of the relationship between patient-provider relationship/interactions and PIR. Among Diabetes MILES – Australia participants with T2D already using insulin therapy, those with more negative insulin appraisals also reported lower diabetes self-efficacy (Chapter 8). Support and education received from the HCPs at the time of, and beyond, insulin initiation may help to reduce the negative experiences of insulin use through boosting diabetes self-efficacy. For example, those with insulin-treated T2D reporting more negative insulin appraisals, and lower diabetes self-efficacy, commonly endorsed that injecting insulin is painful, requires a lot of time and energy, and is difficult (Chapter 8). These types of negative experiences of insulin therapy or low insulin-related self-efficacy may suggest the need to trial a different insulin device or regimen, and/or review the person’s insulin administration technique. The association between diabetes self-efficacy and PIR may also relate to the perceived effectiveness of insulin therapy (Hayes et al., 2013). As discussed in Chapter 8, people with T2D whose blood glucose levels remain suboptimal despite using insulin therapy, or those experiencing hypoglycaemic episodes as a result of insulin therapy, may consequently feel that they are unable to manage their diabetes effectively (i.e. low diabetes self-efficacy). This highlights the need for timely titration or intensification of insulin therapy by the HCP. However,
large-scale cohort studies suggest that titration/intensification of insulin therapy, like insulin initiation, is also commonly delayed (Fulcher, Roberts, Sinha, & Proietto, 2015; Grant, Buse, & Meigs, 2005; Khunti et al., 2016; Polinski et al., 2014).

Consistent with clinical guidelines for the management of T2D, which advocate for person-centred care (Inzucchi et al., 2012; The Royal Australian College of General Practitioners and Diabetes Australia, 2014), identifying and addressing negative insulin appraisals or barriers to optimal insulin use should recognise the needs, concerns and context of the individual with T2D, providing an appropriate level of training, support and problem solving. For example, life stage and lifestyle may be related to barriers to optimal insulin use. Diabetes MILES – Australia participants with insulin-treated T2D who reported more negative attitudes to insulin therapy were typically younger and in paid employment, compared to those with less negative insulin appraisals, and the majority of the subgroup agreed that insulin made life less flexible (Chapter 8). Elsewhere, young adults (aged 18-39 years) with T2D have reported time constraints as a major barrier to optimal self-care (Browne, Scibilia, & Speight, 2013), and are significantly less likely to take their insulin injections as recommended compared to older adults with T2D (Browne, Nefs, Pouwer, & Speight, 2015). Furthermore, in another sub-analysis of Diabetes MILES – Australia participants with T2D, being employed was significantly associated with sub-optimal self-care (O'Neil et al., 2014). Younger people with insulin-treated T2D may have additional competing demands on their time, which need to be anticipated and acknowledged by clinicians.

Emotional wellbeing should also be considered. For example, Australians with T2D already using insulin therapy and reporting more negative insulin appraisals were almost twice as likely to report moderate-to-severe depressive and/or anxiety
symptoms, than those reporting less negative appraisals (Chapter 8). Elsewhere, the presence of depressive symptoms has been shown to be associated with requiring significantly more time, and visits, with HCPs to receive insulin administration training, compared to those without depressive symptoms (Dzida, Karnieli, Svendsen, Sølje, & Hermanns, 2015). Depressive symptoms are also associated with suboptimal medication-taking, including insulin omission among adults with T2D (Mashitani et al., 2015), and this relationship has been shown to be mediated by diabetes self-efficacy and diabetes-specific social support (including support received from HCPs) (Tovar, Rayens, Gokun, & Clark, 2015). Therefore, people with insulin-treated T2D who have concurrent depressive symptoms may require additional support and education from HCPs in order to bolster diabetes self-efficacy, reduce negative insulin appraisals, and consequently reduce the likelihood of insulin omission.

Quantitative research examining reasons for insulin omission has highlighted the role of negative insulin experiences and attitudes among adults with insulin-treated T2D (Davies et al., 2013; Farsaei, Radfar, Heydari, Abbasi, & Qorbani, 2014; Peyrot, Barnett, Meneghini, & Schumm-Draeger, 2012b; Peyrot, Rubin, Kruger, & Travis, 2010). In the current thesis, suboptimal insulin-taking behaviour (i.e. insulin omission) was not associated with PIR (Chapter 8). However, these findings are limited in that an unvalidated single-item measure of insulin-taking behaviours was used to quantify insulin-taking behaviours. Future research needs to explore the association between PIR and insulin omission using a more sensitive measure. For example, the MARS (used in the Stepping Up study), has been previously used in diabetes research (Barnes, Moss-Morris, & Kaufusi, 2004). The instructions normalise sub-optimal medication-taking behaviours in order to promote honest,
rather than socially desirable, responses. Another option is the recently published Morisky Insulin Adherence Scale, a validated measure designed specifically to assess insulin-taking behaviours among people with diabetes (Osborn & Gonzalez, 2016).

In addition to support from HCPs within usual care, people with T2D may benefit from insulin-specific structured education. The Global Guideline For Type 2 Diabetes (International Diabetes Federation, 2012) recommends that structured diabetes self-management education is an integral part of care from diagnosis and ongoing. However, the Diabetes MILES – Australia survey demonstrated that less than half of Australians with type 1 diabetes or T2D have received structured education, and the majority of those were offered education only at the time of diagnosis (Speight et al., 2011). In the Stepping Up study, the median diabetes duration of participants who initiated insulin was nine years and, thus, structured education received at baseline is unlikely to remain effective at the time of insulin uptake. Furthermore, initial structured diabetes education may not comprehensively cover insulin therapy use (e.g. insulin types, administration techniques, self-titration), let alone the psychosocial barriers to insulin initiation or intensification discussed in this thesis. However, such programs may be expanded to include treatment-specific modules. For example, the structured T2D self-management education program, DESMOND (Davies et al., 2008), was recently expanded to include the Injectable Therapy Toolkit, which includes core and topic-specific education sessions on insulin therapy. However, its effectiveness has not yet been published. Existing structured education programs that focus on insulin therapy have been developed to provide training in the skills needed for flexible, intensive insulin therapy, and are generally restricted to those with type 1 diabetes (i.e. Dose Adjustment For Normal
Eating program (DAFNE) (DAFNE Study Group, 2002)). However, the 4-day Newcastle Empowerment program, which combines the principles of DAFNE (flexible insulin management to enable dietary freedom) with an empowerment approach, is available to people with type 1 diabetes and those with insulin-treated T2D who are willing to engage in an intensive basal bolus insulin regimen (Lowe, Linjawi, Mensch, James, & Attia, 2008). Flexible insulin therapy structured education programs have demonstrated improvements at follow up in diabetes knowledge and diabetes self-efficacy (Lowe et al., 2008) as well as diabetes-related distress and general emotional well-being (Hopkins et al., 2012; Speight et al., 2016). However, this type of program may not be appropriate for those with T2D using ‘simple’ insulin therapy regimens recommended for first-step insulin initiation (i.e. once-daily basal or pre-mixed insulin injections) (The Royal Australian College of General Practitioners and Diabetes Australia, 2014). This suggests an existing gap in the availability of structured education for those with T2D using insulin. Furthermore, no structured education program for people with T2D has assessed the impact of the intervention on attitudes towards insulin therapy (i.e. PIR).

10.3. Limitations of the Research

The specific limitations of each of the six empirical research studies included in this thesis are described in Chapters 4-9. In addition, broad limitations of the Diabetes MILES – Australia study are published elsewhere (Speight, Browne, Holmes-Truscott, Hendrieckx, & Pouwer, 2012). The following section summarises limitations across the thesis as a whole, with reference to the design, the measures used, and the sample representativeness of each study (1: Diabetes MILES – Australia, 2: Stepping Up Study, 3: Qualitative Interview Study).
10.3.1. Study design

One objective of this thesis was to examine attitudes towards insulin therapy held by Australians with T2D longitudinally, and how attitudes differ by insulin use. Data collected from the Diabetes MILES – Australia 2011 national cross-sectional survey were used to compare insulin appraisals among adults with insulin-treated and non-insulin-treated T2D. A longitudinal follow-up survey of this national sample, allowing for the assessment of change in insulin appraisals over time, and treatment, would have been ideal. However, due to the small proportion of people with T2D initiating insulin at any given time-point and the potential loss to follow-up, it was not possible to guarantee in advance a sufficiently sized longitudinal sample who would initiate insulin within the require time period. This is supported by unpublished insights from the recently conducted (2015) second Diabetes MILES – Australia survey. In total, longitudinal data were collected from 168 participants with T2D who reported not using insulin therapy in 2011, of whom 16 reported now using insulin therapy. Thus, a prospective, observational, population-level study of change in insulin appraisals over time was not possible within this PhD.

The Stepping Up Study provided the opportunity to investigate change in insulin appraisals over time and after insulin initiation, with participants with T2D completing psychosocial survey booklets, including the ITAS, at baseline and 12-month follow-up (Furler et al., 2014). However, participants may have initiated insulin at any point within the 12-month trial period. Significant change in negative insulin appraisals was demonstrated among those who initiated insulin. However, it is unclear when the change in insulin appraisals occurred and whether it preceded insulin initiation or followed experience with insulin. This is because the study design did not allow for repeated measurement of insulin appraisals, or any other
psychosocial measures, throughout the follow-up period or even at the time of, or immediately after, insulin initiation. Such additional measurement would have increased participant burden and potentially increased attrition rates and, arguably, would have been an intervention in itself.

Study 3 provided opportunity for qualitative investigation of the impact of insulin therapy among those already using insulin. Instead of recruiting a separate sample, it may have been preferable to conduct a mixed-methods study, through the inclusion of qualitative interviews in the Diabetes MILES – Australia or Stepping Up studies. This may have reduced the recruitment period as well as enabling purposive sampling of participants with more and less negative insulin appraisals. However, this was not possible for the following reasons. First, Diabetes MILES – Australia participants had provided consent to participate in future research, but this was limited to a) completion of another similar survey in 4 or 5 years, and/or b) an interview or focus group within the next year. Study 3 was conducted in 2013-14, outside of the ethically approved time period for which consent to be contacted for an interview study was provided. The Stepping Up sample was also deemed unsuitable for the qualitative study. Interviews would need to have been conducted at the conclusion of the trial in order to capture those who had initiated, and ‘experienced’, insulin therapy, as well as avoiding contamination of the results of the RCT. The trial concluded in April 2015 and did not fit within the timeline of this PhD. Furthermore, the experience of insulin use among Stepping Up intervention participants may differ considerably from the experience of the general population of adults with T2D in primary care, and the control arm included only a small pool of participants. Therefore, the decision was made to recruit a separate sample to qualitatively explore the impact of insulin therapy use among people with T2D.
10.3.2. Representativeness and generalisability of the samples

A key limitation of this thesis concerns the representativeness, and therefore generalisability, of the study samples. The recruitment methods and actual response rates suggest the study samples are skewed towards more empowered participants, which may not represent the general Australian population with T2D. With regard to Diabetes MILES – Australia (Study 1), the majority of participants were recruited through invitations sent to a random sample of 15,000 NDSS registrants who had previously consented to being contacted about research opportunities (Speight et al., 2012). Approximately half of the one million NDSS registrants with T2D (National Diabetes Services Scheme, 2016) have indicated consent to be contacted about research participation opportunities. However, it is estimated that one in five Australians with T2D are undiagnosed and therefore not registered with the NDSS (Australian Bureau of Statistics, 2013). Furthermore, the response rate for this large-scale mail-out was just 18%. Online survey participation was also made available nationally to eligible Australians regardless of the NDSS registration, and attracted ~1000 participants. However, the study was advertised only through relevant diabetes media, including the NDSS and Diabetes Australia (national and state-based) websites, and a range of diabetes or health specific newsletter/e-newsletters, and therefore may not have been seen by individuals who do not regularly review or subscribe to such sites. This limitation applies also to Study 3, which similarly recruited participants through advertisements placed on websites, social media and e-newsletters of Diabetes Victoria and the Australian Centre for Behavioural Research in Diabetes.

It has been suggested that adults with T2D with negative insulin appraisals may be hesitant to participate in studies about insulin therapy due to concern that
they may subsequently have to use insulin (Patel, Stone, Hadjiconstantinou, et al., 2015). In the Stepping Up study, an invitation letter was sent to 521 potentially eligible adults with T2D, which stated that the aim of the study was to make sure that patients get the best available treatment which “may involve different or additional medicines or even starting insulin”. It may be that the 19% who did not respond to the study invitation (Furler et al., 2015) were more likely to report PIR or be less engaged in their health in general. Indeed, those who did participate displayed, on average, lower rates of diabetes-specific distress and depressive symptoms, and lower ITAS Negative scores at baseline (Chapter 6) compared with the Diabetes MILES – Australia 2011 sample (Chapter 4). Therefore, while the Stepping Up trial identified all eligible adults with T2D in the primary care practices for whom insulin was clinically indicated, it may under-represent those who are hypothetically unwilling to begin insulin therapy, and consequently the proportion of people with T2D who might refuse insulin therapy.

Finally, it is important to note the lack of cultural and linguistic diversity in the studies presented in this thesis. Given the nature of the sample, it is not possible to comment on the specific barriers to the insulin initiation and ongoing use faced by people from specific culturally and linguistically diverse backgrounds within Australia. All three studies required participants to be able to communicate in English. There was no funding to support the translation of study materials (i.e. survey booklets) or to provide translators for interactions with participants with T2D (i.e. Stepping Up consultations, qualitative interviews). While a small proportion of participants in Diabetes MILES – Australia (3%) and the Stepping Up (6%) studies reported a primary language other than English, this is considerably lower than the 19% of Australians who speak a language other than English at home (Australian
While linguistically concentrated among English-speaking participants, between 28% and 38% participants with T2D in the three studies included in this thesis report being born overseas, which is representative of the broader Australian population (Australian Bureau of Statistics, 2012). The rate of insulin-treated T2D is three times as higher among Indigenous Australians (i.e. of Aboriginal or Torres Strait islander descent) compared to non-indigenous Australians (Australian Institute of Health and Welfare, 2016). However, this group were under-represented in all three studies. As the study of PIR and receptiveness among Indigenous Australians was not the primary aim of this thesis, the included studies were not designed to capture issues of particular relevance to, or follow best practice principle for conducting research among (Jamieson et al., 2012), this community and therefore, Indigenous Australians were not recruited actively.

10.3.3. Measurement issues

The ITAS is the principal measure of insulin appraisals used within this thesis. The psychometric validation of the scale using national survey data (Study 1) confirmed that the measure was psychometrically robust and acceptable among Australian adults with T2D, although slightly less so for those not using insulin therapy (Chapter 4). However, the scale was developed for use in the USA and the exploratory work underpinning its development is not described in detail (Snoek et al., 2007). The scale has not undergone cognitive debriefing among its target population within Australia, beyond the general debriefing of the full Diabetes MILES – Australia questionnaire prior to the national survey (Speight et al., 2012). In the qualitative study with people using insulin, the negative and positive aspects of insulin use were explored beyond those included in the ITAS (Study 3). However, this thesis did not explore qualitatively whether the ITAS adequately identifies all
positive and negative aspects of insulin use among Australians with non-insulin-treated T2D.

Studies 1b and 1c (Chapters 5 and 8) both explored the association between insulin appraisals and diabetes-related distress in insulin-treated and non-insulin treated samples. However, different measures of diabetes-related distress were used in each study, and therefore the associations between diabetes-related distress and insulin appraisals are not comparable across treatment groups. Specifically, the DDS was completed by participants with the non-insulin-treated T2D, while the PAID was completed by insulin-treated participants. The reason for this is that two different diabetes-related distress measures, DDS and PAID, were included in alternate versions of the Diabetes MILES – Australia survey, with the broader aim to conduct a psychometric comparison of the established PAID with the novel DDS (reported elsewhere (Fenwick et al., 2016)). Appendix C (Methods) provides a detailed description of the measures included in each survey version.

Investigation of PIR was not the primary aim of the Diabetes MILES – Australia study, and the single item assessing hypothetical willingness to begin insulin was not included in the survey. Its inclusion in the survey would have characterised receptiveness to insulin therapy nationally and perhaps enabled a more concise exploration of the predictors of, and the association between, insulin appraisals and receptiveness within a single sample. Furthermore, it would have been useful to understand how those with non-insulin-treated T2D who skipped the ITAS questionnaire responded to the willingness item. It was hypothesised (in Chapter 4) that those who skipped the ITAS questionnaire completely did so because they thought it was irrelevant to them. Thus, it would be interesting to understand whether this group were more likely to also skip the willingness item or respond to it more
negatively (e.g. ‘not all willing’ to begin insulin therapy) in comparison to the rest of the non-insulin-treated sample, perhaps due to the perception of insulin as an inappropriate treatment option for them at this time. Finally, the inclusion of hypothetical willingness would have enabled the opportunity to examine receptiveness by treatment type among adults with non-insulin-treated T2D: lifestyle modifications only compared to those using OHAs. However, a key limitation of the Diabetes MILES – Australia data is the absence of objective clinical data (e.g. HbA1c, prescribed treatment doses), and therefore any sub-analysis by treatment type would be unable to differentiate between those using entry level versus maximum dose OHAs or identify those who would benefit clinically from insulin initiation, as was possible in Stepping Up (Study 2).

Study 1b and 1c findings, regarding the correlates of negative insulin appraisals, could not necessarily be followed up in the Stepping Up study. For example, beliefs about current diabetes medications were found to be predictive of insulin appraisals in Study 1b (Chapter 5), but were not assessed in the Stepping Up study. Therefore, we cannot determine whether current medication beliefs were predictive of insulin receptiveness or actual insulin uptake. The reasons for this were, first, the assessment of PIR and known correlates was of secondary importance in the trial and reducing participant burden was a study priority. Second, Stepping Up practices were recruited from October 2012 (Furler et al., 2014) and, therefore, the questionnaires included in the patient participant survey booklets were confirmed prior to completing the sub-analysis of correlates of negative insulin appraisals discussed in Studies 1b and 1c.

Study 3 offered the opportunity to undertake a qualitative exploration of attitudes towards insulin use and intensification among those already using insulin
therapy. Participants were asked how many injections they were currently taking, followed by enquiry about how they thought they would feel if they needed to take more injections each day (see Appendix C, Table 2). Participants discussed the possibility that additional injections might involve introducing fast-acting insulin into their treatment regimen, and the negative consequences of this (Chapter 9). However, participants were not specifically asked about the use of fast-acting insulins and, therefore, it is difficult to distinguish barriers to intensification associated with frequency of injections from type of insulin. Similarly, prior quantitative research has investigated attitudes to additional injections without exploring the influence of change in insulin type on responses (Martinez et al. 2007; Zambanini et al. 1999). Future research is needed to understand the barriers to increasing total daily insulin injections versus changing the type of insulin used among adults with T2D.

10.4. Strengths of the Research

This section summarises the key strengths of this thesis and its contribution to the current body of research in the area of PIR and receptiveness to insulin therapy among adults with T2D. The general strengths of the Diabetes MILES – Australia and Stepping Up studies are reported elsewhere (Furler et al., 2014; Speight et al., 2012), and strengths specific to each of the six empirical research studies included in this thesis are discussed in Chapters 4-9. Broadly, the strengths of this thesis lie in the fact that the research questions were addressed using a mixed-methods approach (including a large-scale national population-level survey, a fully powered, cluster randomised clinical trial in primary care, and a qualitative study in which data saturation was achieved), with comprehensive assessment of relevant psychological constructs using validated measures.
A broad definition of PIR and receptiveness was applied in this thesis, including psychological barriers to or enablers of insulin initiation, ongoing insulin use and insulin intensification. This definition facilitated a comprehensive program of research that investigated PIR and/or receptiveness throughout diabetes progression and treatment intensification. The ITAS was chosen to assess insulin treatment appraisals in Study 1 and Study 2 as it had been designed for use in non-insulin-treated and insulin-treated T2D. However, psychometric validation had not been conducted separately for each intended user group. In Study 1a (Chapter 4), data from the large-scale national survey were used to examine, for the first time, the psychometric properties of the ITAS in both insulin-treated and non-insulin treated T2D populations, with samples of sufficient size ($n=249$ and $n=499$) to enable appropriate subgroup analyses.

The extensive number of validated questionnaires, and study-specific clinical and self-care items, assessed in the Diabetes MILES – Australia study allowed for comprehensive investigation of factors associated with insulin appraisals among adults with non-insulin-treated T2D in Study 1b (Chapter 5). Factors investigated included both known correlates of insulin appraisals (i.e. diabetes-related distress (Makine et al., 2009)), as well as concepts not previously assessed in relation to PIR (i.e. anxiety symptoms, diabetes-related distress subscales), or those not previously measured using validated measures (i.e. beliefs about medications).

It has been suggested that PIR may not be as common as previously documented (Jeavons, Hungin, & Cornford, 2006), and that receptiveness may be a more common experience when insulin initiation is clinically indicated (Jenkins et al., 2010). However, research identifying hypothetical (un)willingness to begin insulin therapy has most commonly been undertaken in convenience samples of
adults with non-insulin-treated T2D with varying diabetes durations and treatment progressions. Thus, the Stepping Up study (Study 2a, Chapter 6) provided important and timely insight into rates of receptiveness and PIR, operationalised as hypothetical willingness, at a clinically relevant timepoint, as well as a comprehensive assessment of the factors associated with receptiveness to insulin therapy among this specific clinical cohort. Furthermore, for the first time, the predictive validity of the hypothetical willingness single item in determining actual insulin uptake among adults with T2D was examined (Study 2b, Chapter 7). The Stepping Up study also offered the opportunity to assess insulin appraisals, depressive symptoms and diabetes-related distress in the prediction of actual insulin uptake in a single prospective study. Previously these relationships have been examined separately (Iversen et al., 2015; Keij et al., 2016; Nefs et al., 2013).

Studies examining insulin omission show negative insulin appraisals among those with T2D already using insulin (Peyrot, Barnett, Meneghini, & Schumm-Draeger, 2012a; Peyrot et al., 2010). However, with the exception of one study (Chen et al., 2011), which examined the association between ITAS scores and insulin mode and duration, no previous quantitative research had explicitly investigated factors associated with negative insulin appraisals among adults with insulin-treated T2D. Using data from Diabetes MILES – Australia, Chapter 8 (Study 1c) presented the first comprehensive assessment of demographic, clinical, self-care and psychological factors associated with negative insulin appraisals among those with T2D already using insulin therapy. Extending on this work, the qualitative study (Study 3, Chapter 9) provided the opportunity to conduct an in-depth exploration of the perceived impact of insulin therapy use among adults with T2D, capturing any positive or negative insulin experiences that may not have been captured adequately.
in the quantitative assessment with the ITAS. Further, Study 3 responded to the call for additional research into receptiveness to insulin intensification (Polinski et al., 2012) and corroborated the findings of the few other qualitative studies undertaken to examine receptiveness to, and barriers of, insulin intensification among adults with insulin using T2D (Jenkins et al., 2011; Simon, Gude, Holleman, Hoekstra, & Peek, 2014).

In addition to contributing to the rapidly growing body of research globally, as described above, this thesis has advanced PIR and receptiveness research in Australia. Only two published studies had explicitly examined PIR among Australians with T2D at the commencement of this thesis: a multi-national survey using unvalidated items (Peyrot et al., 2005) and a qualitative investigation of barriers and enablers of insulin uptake among adults with T2D within Australian primary care (Furler et al., 2011). Thus, little was known about PIR and receptiveness within the Australian context. This thesis provides a comprehensive understanding of the barriers to insulin initiation, use, and intensification among Australians with T2D which may be used to inform strategies and interventions to reduce the impact of PIR and encourage receptiveness within the Australian context in the future.

10.5. Conclusion

The collective findings of this thesis extend significantly on previous knowledge of the measurement, experience, and correlates, determinants and consequences of PIR and receptiveness among adults with T2D throughout treatment progression.
The psychometric reliability and validity of the widely-used ITAS was confirmed among Australians with insulin-treated and non-insulin-treated T2D separately, and the use of the subscale scores were recommended in preference to the use of Total scale. The findings suggested that receptiveness to insulin therapy is not merely the absence of negative attitudes towards insulin therapy (PIR), but a parallel concept, and therefore both concepts need to be assessed. However, the ITAS Positive subscale may benefit from future review through the development and testing of additional items.

This thesis demonstrates the impact of PIR and receptiveness on actual insulin uptake: negative and positive attitudes to insulin therapy are associated with intention to begin insulin therapy and, in turn, intention was an independent predictor of actual insulin uptake. This suggests that interventions or strategies to increase timely insulin initiation for T2D should aim to reduce PIR and improve receptiveness to insulin initiation. In addition to assessing and addressing PIR at the time of insulin initiation, the findings from this thesis suggest that negative attitudes towards insulin therapy may develop early in diabetes duration and that concerns about oral diabetes medications and diabetes-related distress may contribute to their development. Therefore, identifying and addressing negative beliefs about diabetes medications and diabetes-related distress early, and in an ongoing manner throughout diabetes progression, may help to improve receptiveness to future treatment intensification. Future research needs to investigate the impact of interventions and structured education to promote appropriate beliefs about diabetes and medications and/or reduce diabetes-related distress on attitudes towards treatment progression.

Finally, the findings of this thesis corroborated previous research that actual insulin use is associated with a reduction in negative insulin appraisals but identified
the existence of negative insulin appraisals for some Australians using insulin therapy, and demonstrated that PIR among those already using insulin is associated with impaired emotional wellbeing, diabetes-specific self-efficacy and satisfaction with blood glucose. Furthermore, barriers to and enablers of insulin intensification were identified. These findings highlight the impact of PIR and receptiveness beyond insulin uptake and the need to identify ongoing, or new, concerns about insulin use beyond insulin initiation.
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clinical practice for the treatment of type 2 diabetes from four Australian

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their perceptions of computer-assisted self-management systems for insulin
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10.2196/jmir.3198.

the insulin treatment appraisal scale (ITAS) in patients with type 2 diabetes.

Speight, J., Browne, J. L., Holmes-Truscott, E., Hendrieckx, C., & Pouwer, F.
(2012). Diabetes MILES - Australia (Management and Impact for Long-term


Appendix A: Statement of Contributions

AUTHORSHIP STATEMENT

1. Details of publication and executive author

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<th>Title of Publication</th>
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<tbody>
<tr>
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<td><a href="mailto:holmest@deakin.edu.au">holmest@deakin.edu.au</a></td>
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<td>School of Psychology</td>
<td>Resistance and Receptiveness: Perceptions of Insulin use in Type 2 Diabetes</td>
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Project management of Diabetes MILES – Australia throughout 2011, including contributing to the design of the methodology and data collection. Identified research question. Data cleaning and analyses of the measures reported here and preparation of the first draft and subsequent drafts of the manuscript.

I declare that the above is an accurate description of my contribution to this paper, and the contributions of other authors are as described below.

Signature and date: [Signature] 5/2/2015

4. Description of all author contributions

<table>
<thead>
<tr>
<th>Name and affiliation of author</th>
<th>Contribution(s) (for example, conception of the project, design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)</th>
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<tbody>
<tr>
<td>Frans Pouwer, Department of Medical and Clinical Psychology, Centre of Research on Psychology in Somatic diseases (CoRPS), Tilburg University</td>
<td>Co-developer of The Diabetes MILES Study International Collaborative. Provided feedback on the interpretation of results, commented on manuscripts drafts, and approved the final manuscript.</td>
</tr>
<tr>
<td>Jane Speight, The Australian Centre for Behavioural Research in Diabetes, Diabetes Australia; School of Psychology, Deakin University</td>
<td>Conceived of The Diabetes MILES Study, and co-developed The Diabetes MILES Study International Collaborative. Principal investigator of Diabetes MILES – Australia. Provided guidance on the study aims and objectives and critically revised manuscript. Approved the final manuscript.</td>
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<tr>
<td>Professor Frans Pouwer</td>
<td></td>
<td>Febr 5th, 2015</td>
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<tr>
<td>Professor Jane Speight</td>
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<td>5th Feb 2015</td>
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<td>E Holmes-Truscott, TC Skinner, P Power, I Speight, Email or phone</td>
<td>Published online 3 July 2015, Primary Care Diabetes, doi:10.1016/j.pcd.2015.06.006</td>
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I declare that the above is an accurate description of my contribution to this paper, and the contributions of other authors are as described below. Signature and date: 7/12/2015

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<tbody>
<tr>
<td>Timothy C Skinner, School of Psychological and Clinical Sciences, Charles Darwin University, Darwin, Australia</td>
<td>Provided feedback on the interpretation of results, reviewed and commented on manuscripts drafts, and approved the final manuscript.</td>
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Provided feedback on the interpretation of results, reviewed and  
commented on manuscripts drafts, and approved the final manuscript.

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Diabetes Australia–Vic,  
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Deakin University, Burwood; AHP  
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MILES Study International Collaborative. Principle investigator of The  
Diabetes MILES Study – Australia 2011. Provided guidance on the study  
aims and objectives and critically revised the manuscript. Approved the  
final manuscript.

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<td>Dec 23, 2015</td>
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|                                                                            | 19/09/2016 |

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<tr>
<td>Irene Blackberry: Department of General Practice, The University of Melbourne, 200 Berkeley St, Carlton 3052, VIC, Australia; John Richards Initiative, Australian Institute of Primary Care and Ageing, La Trobe University, PO Box 021, Wodonga 3609, VIC,</td>
<td>Chief investigator; co-conceived the Stepping Up Study; involved in the development and review of the Stepping Up study protocol. Provided feedback on the interpretation of results, reviewed and commented on manuscripts drafts, and approved the final manuscript.</td>
</tr>
<tr>
<td>Australia.</td>
<td>David O’Neal: Department of Medicine, St Vincent’s Hospital, University of Melbourne, Fitzroy, 3065, VIC, Australia.</td>
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<td>John Purfier: Department of General Practice, The University of Melbourne, 200 Berkeley St, Carlton 3052, VIC, Australia.</td>
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<td>Jane Speight: The Australian Centre for Behavioural Research in Diabetes, Diabetes Victoria, 570 Elizabeth Street, Melbourne 3000, VIC, Australia; School of Psychology, Deakin University, 221 Burwood Highway, Burwood 3125, VIC, Australia; AHP Research, 16 Walden Way, Hornchurch RM11 2LB, United Kingdom.</td>
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<td>Predictors of insulin uptake among adults with type 2 diabetes in the Stepping Up Study</td>
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<td>John Furler, Department of General Practice, The University of Melbourne, 200 Berkeley St, Carlton 3052, VIC</td>
<td>Lead chief investigator; co-conceived the Stepping Up Study. Led the development of the Stepping Up study protocol. Reviewed, edited and approved the final manuscript.</td>
</tr>
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<td>Name</td>
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<td>E. Holmes-Truscott, TC Skinner, FPower J Speight. Published online 2 April 2015, DOI: 10.1111/dnoa.12729</td>
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Project management of Diabetes MILES – Australia throughout 2011, including contributing to the design of the methodology and data collection. Identified research question. Data cleaning and analyses of the measures reported here and preparation of the first draft and subsequent drafts of the manuscript.

I declare that the above is an accurate description of my contribution to this paper, and the contributions of other authors as described below. | Signature and date |
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<tr>
<td>Timothy C Skinner, School of Psychological and Clinical Sciences, Charles Darwin University, Darwin, Australia</td>
<td>Provided feedback on the interpretation of results, reviewed and commented on manuscripts drafts, and approved the final manuscript.</td>
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<tr>
<td>Frans Power, CIRP Center for Research on Psychology in Somatic diseases, Tilburg University, Tilburg, The Netherlands</td>
<td>Co-developer of The Diabetes MILES Study International Collaborative. Provided feedback on the interpretation of results, reviewed and commented on manuscripts drafts, and approved the final manuscript.</td>
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<tr>
<td>Jane Speight, The Australian Centre for</td>
<td>Conceived of The Diabetes MILES Study, and co-developed The Diabetes MILES Study International Collaborative. Principle Investigator of The</td>
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343
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Name of author | Signature | Date
--- | --- | ---
Timothy C Skinner |  | 
Fras Pauver |  | Dec 16, 2015
Jane Speight |

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Name and affiliation of contributor | Contribution | Signature* and date
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Signature and date: [Signature] 19/09/2016

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<td>Jessica L Browne: The Australian Centre for Behavioural Research in Diabetes, Diabetes Victoria, 570 Elizabeth Street,</td>
<td>Read and independently coded a selection of interview transcripts and collaboratively reviewed coding decisions with executive Author EHT. Reviewed and provided feedback on interpretation of identified themes and sub-themes. Reviewed and commented on manuscript drafts, and approved the final</td>
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<tr>
<td>Melbourne, 3000, VIC, Australia; School of Psychology, Deakin University, 221 Burwood Highway, Burwood, 3125, VIC, Australia</td>
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<td>Deakin University secure</td>
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Appendix C: Methods

Chapter 3 introduces the three studies from which data is analysed within this thesis, and the associated research questions. This appendix presents a detailed description of the methods for each study, as they relate to this thesis. Specific methods of each empirical paper are described in Chapters 4 to 9.

1. Diabetes MILES – Australia Study, 2011

1.1. Background

Diabetes MILES (Management and Impact for Long-term Empowerment and Success) is an international collaborative led by Professor Jane Speight (Deakin University, Australia) and Professor Frans Pouwer (Tilburg University, The Netherlands). Diabetes MILES explores the psychosocial and behavioural aspects of living with diabetes in a series of large-scale, cross-sectional national surveys. The first Diabetes MILES survey was undertaken in Australia in 2011 (Speight, Browne, Holmes-Truscott, Hendrieckx, & Pouwer, 2012), and others have been completed since in Australia (Hagger et al., 2016) and overseas (Nefs, Bot, Browne, Speight, & Pouwer, 2012).

1.2. Ethics approval

The Diabetes MILES – Australia (2011) study received ethics approval from the Deakin University Human Research Ethics Committee (ref number: 2011-046).

1.3. Research design

Diabetes MILES – Australia (2011) was a national cross-sectional survey of adults with type 1 diabetes or T2D, undertaken in July 2011. Detailed descriptions of
the study rationale, design, methods, and sample characteristics for the study have been published elsewhere, co-authored by this PhD candidate (Speight et al., 2012).

1.4. Participants

Eligibility criteria for the Diabetes MILES – Australia study included: living with type 1 diabetes or T2D, currently residing in Australia, aged between 18 and 70 years, and able to complete the survey without help from others. As it was not possible for the Diabetes MILES – Australia survey to be made available in other languages, participant eligibility included the ability to read and write in English. The final eligible sample consisted of 3,338 participants, including 1,962 (59%) adults with T2D (age 58.5±8.7 years; 49% women; T2D duration: 9±7 years) (Speight et al., 2012; Speight et al., 2011).

This thesis focused on data collected from those who self-reported a diagnosis of T2D and completed questionnaires of specific relevance to this thesis (see below). The participant group was further broken down to explore three overarching research questions, which are described in Chapter 3. Additional details regarding participant eligibility and demographics for each overarching research question are provided within the corresponding published manuscript (Chapters 4, 5 and 8).

1.5. Measures

A comprehensive list of all the measures included in the Diabetes MILES – Australia 2011 survey has been published (Speight et al., 2012). The primary questionnaire of relevance to this thesis is the Insulin Treatment Appraisal Scale (ITAS) (Snoek, Skovlund, & Pouwer, 2007), and several others are of secondary interest. These are described below.
1.5.1. **Attitudes towards insulin**

The ITAS (Snoek et al., 2007) was developed and validated in the US for use with people with T2D regardless of treatment type, enabling assessment of insulin appraisals both before and after insulin initiation. For people with T2D not yet using insulin therapy, the ITAS is used to explore participants’ beliefs and expectations regarding future insulin therapy use. For those already using insulin, the ITAS assesses the participants’ experience of insulin therapy.

The ITAS includes 20 items, which were generated through literature searches and informed by diabetes healthcare providers (Snoek et al., 2007). Respondents are asked to indicate their level of agreement with each statement on a five-point scale from ‘strongly disagree’ to ‘strongly agree’ (scores ranging from 1 to 5). The ITAS was conceptualised as two-dimensional, including a negative insulin treatment appraisal score (scored as the sum of 16 items) and a positive insulin treatment appraisal score (the sum of four items). Higher scores indicate more negative or positive insulin appraisals respectively. In addition, a single underlying construct (appraisal of insulin therapy) is computed by summing all 20 items after reverse scoring the positive items. Higher scores indicate more negative insulin appraisals overall.

The developers of the ITAS (Snoek et al., 2007) report that the scale has sound psychometric properties overall. Exploratory factor analysis supports a two-factor structure and good internal consistency reliability is demonstrated (Cronbach’s \( \alpha = 0.89, 0.90, 0.68 \) for the Total, Negative and Positive scales respectively), indicating homogeneity of the items within the total and subscales. Concurrent validity was also assessed, with low to moderate associations in the expected direction found between the ITAS Total score and measures of diabetes-related
distress (PAID scale: $r=0.35$) and general wellbeing (WHO-5 scale: $r=-0.14$). The ITAS has demonstrated sensitivity to change following insulin initiation (Hermanns, Mahr, Kulzer, Skovlund, & Haak, 2010). The psychometric properties of the ITAS in the current Australian sample were investigated as part of this thesis, and are reported in Chapter 4.

1.5.2. **Beliefs about oral medications**

For participants not using insulin, beliefs about current medications were assessed using the Beliefs about Medications Questionnaire (BMQ) General and Specific (Horne, Weinman, & Hankins, 1999). The BMQ Specific (11 items) includes two subscales representing the perceived ‘necessity’ (five items) of condition-specific medications in maintaining health, and ‘concerns’ (six items) associated with having to take those medications in the long term. The BMQ Specific items are tailored to the respondent group, in Diabetes MILES – Australia survey the questions referred to “your diabetes medicines”. The BMQ General (8 items) includes subscales addressing perceived ‘harm’ (four items) and ‘overuse’ (four items) of prescription medications in general.

All items are rated on a 5-point Likert scale from ‘strongly disagree’ to ‘strongly agree’ (scores ranging from 1 to 5). Subscale scores are calculated by summing item scores and dividing by the number of items. Higher scores indicate stronger beliefs in the subscale concept. For the BMQ Specific, a necessity-concerns differential score can be obtained by subtracting the ‘concerns’ score from the ‘necessity’ score, enabling assessment of whether concerns outweigh beliefs in the necessity of taking the medications (Horne & Weinman, 1999).
BMQ items were formulated through literature searches and interviews with people living with, and taking medications for, a chronic illness. The questionnaires were validated in a multi-condition sample, including a subsample (n=99) of adults living with diabetes (Horne et al., 1999). Each of the subscales in the General and Specific questionnaires were shown to have good internal consistency (ranging from $\alpha=0.66-0.80$).

In the current sample of Australian adults with non-insulin-treated T2D, the BMQ Specific subscales had satisfactory internal consistency reliability (‘necessity’ $\alpha=0.85$; ‘concern’ $\alpha=0.83$). Previously, an equally balanced (4-items per subscale) two factor structure was recommended for the BMQ General (Horne et al., 1999). However, Horne has since suggested (personal communication) that item four (“natural remedies are safer than medicines”) may perform better in the ‘harm’ subscale than the originally proposed ‘overuse’ subscale. To investigate scale structure, a forced two-factor solution with direct oblimin rotation exploratory factor analysis was conducted (Costello & Osborne, 2005). Consistent with Horne’s recommendation, the two-factor structure accounted for 64.5% of the total variance and, after rotation, a 3-item ‘overuse’ and five-item ‘harm’ scale was apparent, with all items loading >0.4 and no double loadings >0.3. Further, the three-item ‘overuse’ and 5-item ‘harm’ subscales produced better Cronbach’s alpha values (both $\alpha=0.82$) in comparison to the two four-item subscales ($\alpha=0.80$ and $\alpha=0.78$, respectively). As such, the current study utilises the modified BMQ General subscale structure.

1.5.3. Diabetes-related distress
At the time of undertaking Diabetes MILES – Australia 2011, two measures of diabetes-related distress, or the emotional distress associated with living with diabetes, were widely used clinically and in research, However, no study had directly
compared the scales. With the broader study aim of comparing the scales (Fenwick et al., 2016), both scales were included in the Diabetes MILES – Australia survey, in alternate versions, and both measures are of relevance to this thesis.

The Problem Areas In Diabetes (PAID) questionnaire (Polonsky et al., 1995) is a 20-item scale, in which respondents rate the extent to which each item, or issue, is a problem for them on a five-point scale (0=‘not a problem’ to 4=‘serious problem’). Item scores are summed and standardised to a score out of 100, where higher scores indicate greater distress and scores ≥40 indicate severe diabetes distress (Snoek et al., 2011). The PAID was developed through item generation by diabetes healthcare providers, focusing on their clinical experience with people living with diabetes (Polonsky et al., 1995). Early drafts of the questionnaire were piloted among people with diabetes using insulin and a psychometric validation was undertaken on the final 20-item version, demonstrating good internal reliability consistency (α=0.95) (Polonsky et al., 1995). The PAID has been translated into more than 20 languages, each shown to have satisfactory reliability and validity (Polonsky et al., 1995; Snoek, Pouwer, Welch, & Polonsky, 2000). Within the Diabetes MILES – Australia 2011 dataset, all 20 items of the PAID scale loaded well (>0.3) for participants with insulin and non-insulin treated T2D, and internal consistency reliability was strong (both samples α=0.96).

The Diabetes Distress Scale (DDS) is a 17-item scale that was developed in response to the reported limitations of the PAID (Polonsky, Fisher, Earles, et al., 2005). Perceived limitations included a lack of items addressing respondents’ feelings about healthcare providers, reported participant confusion over the exact meaning of some items, and the inability to differentiate between different types of diabetes-related distress (Polonsky, Fisher, Earles, et al., 2005). With these perceived
limitations in mind, the DDS was developed through discussion with people with diabetes, diabetes healthcare specialists and psychologists. A 50-item pool was developed and tested among people with diabetes, resulting in the deletion of items that were ambiguous or repetitive. Items were categorised into four distress domains, which were decided a-priori based on focus group findings. The final item reduction and scale validation resulted in a 17-item questionnaire. Respondents indicate the degree to which each item has been a problem for them over the past month on a 6-point scale (‘not a problem’=1, ‘very serious problem’=6). A composite score is derived by summing scores and dividing by the number of completed items. A score of ≥2 is considered indicative of moderate-to-high distress, and ≥3 indicative of high distress (Fisher, Hessler, Polonsky, & Mullan, 2012). The DDS also includes four subscales: emotional burden (5-items), physician-related distress (4-items), regimen-related distress (5-items), and diabetes-related interpersonal distress (3-items). Satisfactory internal consistency has been shown previously for the DDS total score (α=0.93) and the 4 subscales (α=0.88-0.90) (Polonsky, Fisher, Earles, et al., 2005). In the current sample of Australian adults with T2D, internal consistency reliability was satisfactory for participants who are insulin-treated (total score α=0.94, subscales α=0.89-0.91) and among those non-insulin-treated (total score α=0.93, subscales α=0.89-0.90).

1.5.4. General emotional wellbeing

The presence and severity of depressive and anxiety symptoms was assessed using the 9-item Patient Health Questionnaire (PHQ-9) (Kroenke, Spitzer, & Williams, 2001) and the 7-item General Anxiety Disorder (GAD-7) questionnaire (Spitzer, Kroenke, Williams, & Löwe, 2006). For each measure, respondents rate the frequency with which they have experienced symptoms over the past two weeks on a
4-point scale (‘not at all’=0 to ‘nearly every day’=3). Item scores are summed to form a total score (PHQ-9 range: 0-27; GAD-7 range: 0-21), where higher scores reflect greater depressive/anxiety symptoms and a cut-off score of ≥10 indicates moderate-to-severe symptoms.

Psychometric studies have demonstrated both scales to be valid and reliable in general population samples (Kroenke et al., 2001; Spitzer et al., 2006). The PHQ-9 and GAD-7 have both been validated in Australian samples (Carey, Boyes, Noble, Waller, & Inder, 2015; Dear et al., 2011; Reddy, Philpot, Ford, & Dunbar, 2010) and used with people living with diabetes, (Reddy et al., 2010; Stoop, Spek, Pop, & Pouwer, 2011; van Steenbergen-Weijenburg et al., 2010). In the current sample of Australian adults with T2D, both scales show good internal consistency, regardless of treatment regimen (PHQ-9 $\alpha=0.90$; GAD-7 $\alpha=0.93$). While these scales are not diagnostic tools, they can be used to identify the presence of depressive and anxiety symptoms (with follow-up clinical interview for those screening positively), as the scale items reflect the DSM criteria for Major Depression Disorder and General Anxiety Disorder (American Psychiatric Association, 2013). The PHQ-9 has also shown good psychometric properties against gold standard diagnostic Major Depressive Disorder tests (Gilbody, Richards, Brealey, & Hewitt, 2007). However, due to the nature of somatic depressive symptomology, the PHQ-9, like other depressive symptom questionnaires, may overestimate depressive symptom severity in people with T2D due somatic symptom overlap (Reddy et al., 2010). For example, changes in sleeping behaviours, energy and appetite, may be symptoms of both depression and T2D.
1.5.5. Diabetes-specific self-efficacy

Diabetes-specific self-efficacy was measured using the 8-item Diabetes Empowerment Scale – Short Form (DES-SF) (Anderson, Fitzgerald, Gruppen, Funnell, & Oh, 2003). The DES-SF was developed through the identification of items best representing each of the eight domains of the original scale (Anderson, Funnell, Fitzgerald, & Marrero, 2000), i.e. those with the highest item-total correlation (Anderson et al., 2003). Respondents indicate the extent to which they agree/disagree with each item on a 5-point scale (0='strongly disagree' to 5='strongly agree'). A composite score (range 0-5) is calculated by summing item scores and dividing by eight, where higher scores reflect greater diabetes-specific self-efficacy. The DES-SF is sensitive to change over time (Anderson et al., 2005), and has been shown to be valid and reliable (Anderson et al., 2003). In the current sample of Australian adults with T2D, all items loaded on a single scale (>0.30), which had satisfactory internal consistency reliability (insulin-treated: $\alpha=0.88$; non-insulin-treated: $\alpha=0.91$).

1.5.6. Self-management behaviours

The Diabetes MILES – Australia 2011 survey included a number of questionnaires exploring general and specific self-management behaviours. Of specific interest to this study were single items from the Diabetes Self Care Inventory-Revised (DSCI-R) (unpublished), regarding insulin injections, tablets, diet and exercise, the duration of insulin therapy, the number of injections taken per day, and the average number of blood glucose checks performed per day over the past two weeks and satisfaction with these checks (0='very dissatisfied' to 6='very satisfied'). Further to this, participants taking insulin injections were asked questions regarding whether they take their required number of injections (1='never' to 5='always'), the
perceived importance of taking their injections (1=‘not at all’ to 4=‘very’) and the burden associated with these injections (1=‘not at all’ to 4=‘a great burden’). The calculation of total scores is not recommended and item scores are used independently.

The DSCI-R was selected for inclusion in the 2011 Diabetes MILES – Australia survey in preference to previously validated self-care measures (e.g. Summary of Diabetes Self-Care Activities measure (Toobert, Hampson, & Glasgow, 2000)) for several reasons: due to the limitations and lack of responsiveness of other measures, due to the DSCI-R’s brevity, its relevance for participants with type 1 diabetes or T2D and, specifically, for its novel inclusion of importance and burdensomeness ratings for each self-care behaviour.

1.5.7. Socio-demographic and clinical characteristics

Socio-demographic and clinical characteristics were all self-reported by Diabetes MILES – Australia participants. Demographic data included: age; gender; relationship status (in relationship/single); employment status (employed/unemployed); education level (no formal qualifications, intermediate certificate/completed year 10, high school/year 12 completion certificate, trade/certificate/diploma, undergraduate university degree, higher university degree); and socioeconomic status (imputed based on participants post-code using published Socio Economic Index For Area - Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD) decile values designated by the Australia Bureau of Statistics (Australian Bureau of Statistics, 2011). Clinical data included: diabetes type (type 1 or type 2); diabetes duration (years); treatment type (insulin injections, insulin pump therapy, oral medications, diet and exercise, other: free-text response box); and treatment duration (years). After inspecting the ‘other’ free text responses, an
additional treatment regimen was included: non-insulin injectables (i.e. glucagon-like peptide-1 (GLP-1)). For the purposes of this thesis, treatment type was used to categorise and differentiate between participants with T2D who were using insulin and those not using insulin. Other clinical characteristics captured were Body Mass Index (BMI) (through the self-report of weight (kg) and height (cm)) and the presence of diabetes-related complications (including kidney damage, albuminuria, retinopathy, neuropathy, heart disease, stroke and vascular disease). Diabetes related-complications were summed (total possible score = 7) to allow for examination as a continuous variable.

1.6. Recruitment

Diabetes MILES – Australia survey booklets were posted to 15,000 randomly selected NDSS registrants with type 1 diabetes or T2D, aged 18-70 years who had previously consented to being contacted regarding diabetes research opportunities. The NDSS register includes 1.2 million Australians living with diabetes, of whom 86% have T2D (National Diabetes Services Scheme, 2016). The random sample of NDSS registrants contacted for the Diabetes MILES – Australia 2011 survey was stratified to ensure significant sub-samples of respondents with type 1 diabetes and insulin-treated T2D. Of interest to this thesis, 60% (N=9,000) of the NDSS

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9The NDSS is an initiative of the Australian Government administered with the assistance of Diabetes Australia. Registration enables people with diabetes to access subsidised products (e.g. blood glucose test strips, insulin pump consumables) and support services (e.g. structured education programs, telephone helpline). For a person to become registered with the NDSS, an accredited HCP must authorise a registration form on behalf of the person with diabetes, providing the individual’s contact details, date of birth, diabetes type and treatment, as well as whether they consent to receiving information about future research studies. Over time, personal and medication information should be updated to ensure subsidised access to relevant products and services.
registrants sampled had T2D and half of these were registered as using insulin to manage their condition.

In addition to the postal survey, the survey was also made available online and advertised nationally. Advertisements for the online study were promoted by Diabetes Australia and its associated state/territory member organisations via e-newsletters, websites and social media sites, as well as national, state and local e-newsletters administered by diabetes consumer groups (e.g. Type 1 Network), HCPs and community health (e.g. Primary Health Bulletin), and diabetes pharmaceutical/device companies (e.g. Medtronic, Sanofi).

1.7. Procedure and survey

In addition to the survey, the postal and online survey versions both included a plain language statement form (see Appendix D) and a contact details form. The contact details form provided participants with the opportunity to enter a prize draw and/or be contacted for participation in future research. The completion of this form was separate from the survey and was not linked to survey data. The hard copy differed from the online survey in that it also included a reply paid envelope for survey return.

In order to maximize the relevance of questions for particular subgroups and minimize respondent burden, six versions of the Diabetes MILES – Australia survey were developed (Speight et al., 2012). The surveys were categorised as specific to: type 1 diabetes, T2D using insulin, or T2D non-insulin. For each of these three participant groups, two survey versions (A/B) were developed (see below). NDSS registrants, who received a hard copy survey invitation, received a survey booklet matched to their recorded diabetes diagnosis and treatment (type 1 diabetes, T2D
using insulin, or T2D non-insulin). The appropriate survey version was allocated to online participants after they self-reported diabetes type and treatment.

All surveys included core measures and demographics, as well as questions specific to respondents’ diabetes type. In addition, questionnaires of secondary interest were included in either version A or B, to reduce overall respondent burden. Each of the survey versions was piloted with 20 Victorian adults (12 participants with type 1 diabetes and eight with T2D) followed by a cognitive debriefing interview to explore the relevance and suitability of content for the broader study population (Speight et al., 2012).

Several questionnaires of relevance to the current thesis were included in opposing A/B survey versions, or in a limited number of survey versions (see Table 1). Of particular relevance, the ITAS was included in opposing A/B versions: survey version A for those with non-insulin-treated T2D and survey version B for those with insulin-treated T2D. The inclusion of the ITAS in opposing A/B versions means that questionnaires of secondary interest to this thesis may not be available for both subsamples of interest in this thesis (adults with insulin-treated or non-insulin-treated T2D). For example, two measures of diabetes-related distress were used (see 1.5.3), with the DDS included in survey version A and the PAID included in survey version B. The BMQ General and Specific were included only in survey version A. A complete list of the questionnaires included in each Diabetes MILES – Australia survey version has been published elsewhere (Speight et al., 2012).
Table 1

_Inclusion of questionnaires of interest in T2D survey versions_

<table>
<thead>
<tr>
<th>Measure/variable</th>
<th>T2D participant group (survey version)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Insulin (A)</td>
</tr>
<tr>
<td>Insulin treatment appraisals: ITAS</td>
<td>X</td>
</tr>
<tr>
<td>Beliefs about medications: BMQ</td>
<td>X</td>
</tr>
<tr>
<td>General</td>
<td>X</td>
</tr>
<tr>
<td>Beliefs about medications: BMQ</td>
<td>X</td>
</tr>
<tr>
<td>Specific</td>
<td>X</td>
</tr>
<tr>
<td>Diabetes distress: PAID</td>
<td>X</td>
</tr>
<tr>
<td>Diabetes distress: DDS</td>
<td>X</td>
</tr>
<tr>
<td>Depressive symptoms: PHQ-9</td>
<td>X</td>
</tr>
<tr>
<td>Anxiety symptoms: GAD-7</td>
<td>X</td>
</tr>
<tr>
<td>Diabetes-specific self-efficacy: DES-SF</td>
<td>X</td>
</tr>
<tr>
<td>Self-management (study-specific items)</td>
<td>X</td>
</tr>
<tr>
<td>Demographics (study-specific items)</td>
<td>X</td>
</tr>
</tbody>
</table>

ITAS: Insulin Treatment Appraisals Scale (Snoek et al., 2007); BMQ: Beliefs about Medications Questionnaire (Horne et al., 1999); PAID: Problem Areas in Diabetes (Polonsky et al., 1995); DDS: Diabetes Distress Scale (Polonsky, Fisher, Earles, et al., 2005); PHQ-9: Patient Health Questionnaire (Kroenke et al., 2001); GAD-7: General Anxiety Disorder (Spitzer et al., 2006); DES-SF: Diabetes Empowerment Scale – Short Form (Anderson et al., 2003).
1.8. Response rate

Data collection took place over two months, starting from 1st July 2011. In total, 3,833 people responded to Diabetes MILES – Australia 2011. One quarter (N=987) of the surveys were completed online, including 220 participants who indicated that they had received the postal survey but instead opted to complete the survey online. A further 2,095 participants returned hard copy surveys. Thus, 2,351 invited NDSS registrants completed the survey, which equates to a 17% response rate. After adjusting for the 541 surveys returned to sender, the final response rate was 18% (Speight et al., 2012).

1.9. Data entry, cleaning and analysis

Upon receipt, completed surveys were de-identified and forwarded to a contract research organisation (CRO) for survey scanning and data entry. The data were then merged with the online survey data by the CRO. The CRO supplied a spreadsheet including all data (online and print survey), as well as scanned images of all hard copy surveys.

The data were transferred to Statistical Package for Social Sciences (SPSS) version 17.0 for data cleaning. Cleaning of the full Diabetes MILES – Australia 2011 dataset was co-performed by this PhD candidate and research fellow, Dr Jessica Browne. This included:

- confirmation of participants’ eligibility requirements; the data of 495 respondents were removed due to ineligibility (i.e. did not have type 1 diabetes or T2D, age outside the specified range, or self-reported that they completed the survey with assistance from others)
• validation of diabetes type and treatment against survey version and reported self-management characteristics

• inspection of hard copy surveys where the CRO was unable to decipher participant responses

• review and coding of qualitative responses

• missing data inspection and imputation, as appropriate, and computation of total or subscale scores to create a usable database for collaborative work going forward.

Data cleaning and analysis specific to the current studies was undertaken solely by this PhD candidate. Analysis of the Diabetes MILES–Australia dataset was driven by three overarching research questions (Chapter 3) and are presented as three empirical studies (Study 1a, 1b and 1c). These details can be found in relevant Chapters (4, 5 and 8).

2. Stepping Up Study

2.1. Background

The ‘Stepping Up’ study is a multidisciplinary research study, led by Professor John Furler (University of Melbourne), which trialled an intervention to facilitate insulin initiation in primary care for adults with non-insulin-treated T2D. The trial protocol was registered on the Australian and New Zealand Clinical trials registry (ACTRN12612001028897) and has been published elsewhere (co-authored by this PhD candidate) (Furler et al., 2014).
2.2. **Ethics approval**

The Stepping Up study obtained ethics approval from the University of Melbourne Human Research Ethics Committee (HREC 1237406). In addition, the Deakin University Human Research Ethics Committee provided ethics approval for the PhD candidate’s involvement within the study (2012-180).

2.3. **Research design**

Stepping Up is a two-armed, 12-month cluster randomised controlled trial testing a new model of care, compared to usual care, to facilitate timely and evidence-based initiation and up-titration of insulin in primary care for eligible adults with non-insulin-treated T2D. While the main unit of analysis was the individual with T2D, the complex nature of intervention (and potential for contamination) lent itself to cluster-randomisation at the practice-level. The Stepping Up intervention involves two key elements: a) supportive education for the general practitioner (GP) and practice nurse (PN), addressing inter-professional culture and clarifying roles and; b) practice systems change, tailored to meet the local practice and funding context and the needs of patients. The control arm practices were requested to provide usual care. Survey data were collected at baseline and at 12-month follow-up from participants (patients and health care professionals) and biomedical data were collected from all participants with T2D.

The primary outcome of Stepping Up was change in HbA1c at 12 months. The results of the primary analysis have been presented elsewhere (co-authored by this PhD candidate) (Furler et al., 2015; Furler et al., 2014). The primary outcomes for the purposes of this thesis were: a) hypothetical willingness to begin insulin (assessed at baseline), b) attitudes towards insulin therapy (at baseline and at 12
months), and c) the proportion of participants who were using insulin therapy (at the conclusion of the 12-month study).

2.4. Participants

Eligible Victorian primary care practices were those employing at least one consenting GP and one PN, and were able to identify at least one eligible patient with T2D. Patient eligibility requirements include: aged 18 to 80 years; diagnosed with T2D; non-insulin using; taking maximum oral hypoglycaemic agents; stability of current treatment for at least 3 months prior to enrolment; willingness to monitor blood glucose at least twice daily; and HbA1c ≥7.5% (58mmol/mol) in the past 6 months. In addition, a current HbA1c was assessed at baseline for all potential participants to confirm their eligibility for the study. Potential participants were excluded if they had previously used insulin, did not speak English or had any current physical or psychiatric condition that could impair their ability to inject insulin or monitor their blood glucose.

Sample size calculations, detailed elsewhere (Furler et al., 2014), were undertaken by the study statistician based on the Stepping Up study primary outcome: change in HbA1c. A minimum of 224 participants (an average of three participants per practice) from 74 general practices was required. The final sample consisted of 266 patients with T2D from 74 Victorian clinics. Clinics from metro, regional and rural areas of Victoria were represented, but the majority were located in major cities (64%). 162 GPs and 103 PNs took part and the median (IQR) number participating per clinic were 5 (4,9), and 2 (1,4), respectively. On average, the mean (SD) age of GPs was 49 (11) years, 62% (n=101) were male, and they had a median (IQR) of 20 (8,30) years clinical experience. All PNs were women with a mean (SD) age of 45 (10) years and median. The majority of participants with T2D were men.
(n=163, 61%), with a mean (SD) age of 62 (10) years and a median diabetes duration of 8.5 (5,13) years. This thesis focuses primarily on the data collected from participants with diabetes.

2.5. Measures

The Stepping Up study included a number of measures for each participant group, involving practice surveys, GP and PN surveys, and T2D participant surveys, as well as the collection of biomedical data.

Of relevance to this thesis were data collected from participants with T2D, at several timepoints in the trial. At baseline, the following data was collected from patient participant screening questionnaires and medical records: demographics (including: age; gender; country of birth; primary language; residential postcode), clinical data and medical history (including: BMI; diabetes duration; number of co-morbid conditions (Barnett et al., 2012); and current medications prescribed). Participants were also asked to report their frequency of blood glucose self-monitoring per day. In addition to the baseline assessment, HbA1c was assessed at 6 and 12 months follow-up. All HbA1c was assessed at DCCT-aligned\textsuperscript{10} pathology laboratories and communicated to clinicians and patients as part of routine clinical care; the data were retrieved from the clinic records or, with permissions in place, directly from pathology laboratory records.

Participants received a survey booklet for completion at baseline and at 12 months. The survey booklet included a number of scales relevant to the broader objectives of the Stepping Up study but not relevant to this thesis. Measures of

\textsuperscript{10}Pathology laboratories conduct DCCT-aligned HbA1c so that assays are standardised and an individual’s risk of complications can be inferred from the result.
relevance to the current study, and already described in Appendix C (Section 1.5), include: the ITAS (Snoek et al., 2007), PHQ-9 (Kroenke et al., 2001), and PAID (Polonsky et al., 1995). In addition, the following relevant measures are described below: the Medication Adherence Rating Scale (MARS) (Horne & Weinman, 1999), and single items assessing willingness to initiate insulin and attitudes towards insulin (Polonsky, 2007).

2.5.1. Medication Adherence Rating Scale

Medication-taking behaviour was assessed using the 6-item Medication Adherence Report Scale (MARS) (Horne & Weinman, 1999). Each item refers to a parameter relating to suboptimal medication-taking behaviour, and participants indicate the frequency with which they behaved accordingly on a 5-point scale (1 ‘always’, 2 ‘often’, 3 ‘sometimes’, 4 ‘rarely’, 5 ‘never’). The scale was designed to be specific to particular medical conditions with minimal modification (Horne & Weinman, 1999). Thus, with the developer’s permission, was adapted to refer to diabetes-specific medications. A total score (from 6 to 30) is calculated by summing all 6 item scores, with higher scores indicating more optimal medication-taking behaviours.

The MARS was developed by Horne and colleagues in response to the limitations of other self-report measures, which may overestimate medication-taking behaviours through self-presentational and recall biases (Horne & Weinman, 1999). The MARS does not ask participants to recall the exact number of days on which, or the time each day at which, they took their medications. Further, the design of the MARS attempts to normalise sub-optimal medication-taking behaviours by stating that the list of behaviours included “are some ways in which other people have said they use their diabetes medicines”, thus promoting a honest, rather than socially
desirable, response. The MARS has been used in samples of people with various conditions, including diabetes (Barnes, Moss-Morris, & Kaufusi, 2004). In the Stepping Up sample, the MARS had good internal consistency reliability ($\alpha=.86$).

2.5.2. Willingness to begin insulin

‘Hypothetical willingness’ to begin insulin therapy has been assessed to date using a single item to identify the proportion of people with T2D who are unwilling or willing to begin insulin therapy (Larkin et al., 2008; Nur Azmiah, Zulkarnain, & Tahir, 2011; Polonsky, Fisher, Guzman, Villa-Caballero, & Edelman, 2005; Polonsky, Hajos, Dain, & Snoek, 2011; Wong et al., 2011; Woudenberg, Lucas, Latour, & Scholte op Reimer, 2012). This question asks individuals to indicate their willingness (very, moderately, not very, not at all) to begin insulin if it was recommended by their HCP. This item has been scored inconsistently across prior research, including the use of all four categories or recoding to dichotomous or trichotomous variables using various cut points (Polonsky, Fisher, Guzman, et al., 2005; Polonsky et al., 2011). Given previous scoring inconsistencies, this thesis uses the original response options.

2.5.3. Attitudes toward insulin

Two measures of attitudes toward insulin were included to enable greater comparability of the insulin appraisals of the current sample to national samples (Chapter 4) and international samples (Larkin et al., 2008; Polonsky et al., 2011; Snoek et al., 2007; Woudenberg et al., 2012). In addition to the ITAS, described in Appendix C Section 1.5 (Snoek et al., 2007), a single question tool was used which asks respondents to identify two out of six statements that best match how they feel about the possibility of starting insulin (Polonsky et al., 2011). Half of these statements are positively worded (‘help to feel better’, ‘opportunity to have better
control’ and ‘logical next step in treatment’); and half are negatively worded
(‘feeling of personal failure’, ‘fear linked to injections’, and ‘feeling that the disease
is getting worse’). The number of positive and negative endorsements for each
participant was summed to provide a 3-point score, where 0=no negative
attitudes/two positive attitudes, 1=one positive and one negative attitude, 2=two
negative attitudes/no positive attitudes).

2.6. Recruitment

Potential clinics were identified through direct contact and promotion via
professional organisations (e.g. RACGP), University of Melbourne Department of
General Practice database (the VicREN practice-based Research Network), through
Medicare Locals,¹¹ and through ‘snowballing’ from key clinicians identified as
opinion leaders. Recruitment of patient participants began after clinic randomisation,
stratified by practice size and type.

Potentially eligible patients with T2D were identified through each practice’s
electronic medical records database. Upon identification, patients received a letter
from the clinic inviting them to participate and a follow up telephone call from the
GP and/or PN. The invitation letter stated that participants might benefit from
assessment and intensification of diabetes treatment, which may involve insulin
injection therapy. The invitation letter, plain language form and consent forms are
provided in Appendix D.

¹¹Medicare Locals were primary health care organisations established to coordinate
primary health care delivery. They were a key feature of the Australian
Government’s National Health Reform. From July 2015, they were replaced with
Primary Health Networks.
Recruitment of clinics and patients took place between October 2012 and January 2014 and was led by the University of Melbourne Stepping Up study team. Each participant was enrolled in the Stepping Up study for 12 months.

2.7. Procedure and intervention

The study protocol has been published elsewhere (Furler et al., 2014). Provided here is a brief description of the intervention, with emphasis on particular aspects considered relevant to this thesis.

Practices randomised to the intervention group received 1-2 hours training, and an accompanying educational booklet, delivered by the study team during a practice visit. The training included evidence for timely insulin initiation, common barriers to insulin initiation within primary care and how to deal with them, and familiarisation with insulin delivery systems and insulin titration tools. Of specific relevance to this thesis, the training included a brief outline of motivational interviewing and a list of eight common concerns about insulin therapy among people with T2D and how to respond to them. Participants received ‘Patient Packs’ including information and fact sheets about insulin therapy as well as a diary and phone record book for use in dose adjustment consultations. Practices were supported by practice visits, telephone and email contact from the study Diabetes Nurse Educator (DNE) as required during the 12-month follow-up period. Management options included referral to an endocrinologist, DNE or other HCP, if required.
Control arm practices were provided with a copy of the latest guidelines for the management of T2D (The Royal Australian College of General Practitioners and Diabetes Australia, 2014) and offered training in the Stepping Up model of care once the 12-month follow-up was completed. During the trial, control practices were asked to undertake clinical review of their eligible participating patients, as part of ongoing usual clinical care.

Following recruitment and baseline data collection, participants in the intervention arm were invited to attend their GP for a diabetes assessment. The GP discussed possible treatment intensification, recommended and prescribed insulin therapy commencement, and referred the participant to the PN. Immediately following this, the participant saw the PN for an insulin initiation assessment, during which time the PN worked through the patient pack with the participant. At this time, if the patient was agreeable, the PN gave the participant their first insulin injection. The Stepping Up study DNE attended the clinic to support the PN for the first participant at each intervention clinic. If insulin was initiated, the participants were asked to telephone the PN every three days to discuss blood glucose levels and adjust insulin dose and, after four weeks, attend an appointment for a clinical review. The role of the GP was to initiate and prescribe insulin, while the insulin adjustment was led primarily by PN and participating patient in discussion with the GP as necessary. If participants did not commence insulin at the first GP/PN visit, they continued to see the PN and GP as clinically appropriate with the aim of commencing insulin. GPs and PNs saw participants on as many occasions as was clinically necessary over the 12-month period.
2.8. Response and attrition rate

The recruitment period (from first to last practice/patient enrolment) took 16 months, during which 93 practices expressed interest in participation and identified 521 potentially eligible patients with T2D. After exclusion of non-responding potential participants with T2D ($n=99$) and those found to be ineligible at screening ($n=156$), the final eligible participating Stepping Up sample included 266 adults with T2D (51% of the potential population) across 74 practices. Of the total sample, 248 (93%) completed 12-month follow-up for the primary endpoint (HbA1c). As reported elsewhere (Furler et al., 2015), there were no differences in baseline characteristics observed between study completers and non-completers, except for gender, where women were more likely to be non-completers than men ($n=11$, 11% and $n=7$, 4%, respectively).

2.9. Data entry, cleaning and analysis

The completed demographic, baseline and follow-up questionnaires were checked for completeness before being scanned and processed by a CRO. Clinical data (e.g. HbA1c, medications and co-morbid conditions) were extracted from clinic records and entered by study research assistants. Pathology data were extracted, as required, by the study pathology provider. All data were uploaded into Stata 12 for further cleaning led by Dr Jo-Anne Manksi-Nankervis (project manager), with advice from the Stepping Up data management team (including this PhD candidate). Syntax was written to enable ongoing automated assessment of missing data and questionnaire scoring, following monthly update of databases by the CRO. The PhD candidate advised on the scoring (Appendix C, Section 2.5) and data management expectations, and reviewed the relevant syntax, for all questionnaires and measurements included in the current study.
Upon baseline and follow up database closure the PhD candidate exported the patient de-identified data into SPSS version 22. The raw and scored data were then reviewed, missing data identified and scale scores re-calculated to ensure accuracy. Using baseline and 12-month data, the PhD candidate created change scores for the ITAS.

Analysis of the Stepping Up baseline and follow up datasets was driven by two overarching research questions (Chapter 3) and are presented as two empirical studies (Study 2a and 2b). Data cleaning and statistical analysis undertaken for each study are detailed in Chapters 6 and 7 respectively.

3. Qualitative Study of Insulin Appraisals among Adults with Insulin-Treated Type 2 Diabetes

3.1. Background

A qualitative interview study was conducted with the broad aim of eliciting an in-depth narrative of the experience of diabetes and treatment progression among people with T2D using insulin therapy, from diagnosis to present day. This thesis examines a subset of the collected data with reference to the lived experience of adults with T2D already using insulin, including perceived consequences of insulin use and attitudes towards future insulin intensification (e.g. additional insulin injections).
3.2. Ethics approval

The qualitative study received ethics approval from the Deakin University Human Research Ethics Committee (ref number: 2013-048).

3.3. Research design

A semi-structured face-to-face interview study was conducted. A semi-structured approach was used to ensure interviews included discussion of the predefined objective or study focus, while allowing participants to express themselves freely “to offer new meaning to the study focus” (Galetta, 2013).

3.4. Participants

Eligible participants included English-speaking Australian adults (18+ years of age) with T2D who had been using insulin therapy for no more than three years. They needed to be able to attend a face-to-face interview in Melbourne or in Geelong (Victoria). The participant group is detailed in Chapter 9.

3.5. Materials

The semi-structured interview schedule was developed by the PhD candidate, in conjunction with the primary supervisor. The schedule was designed to elicit a narrative from participants about their lived experience of diabetes and attitudes to treatment intensification, and was informed by existing literature (Gherman et al., 2011; Snoek et al., 2007; Wang & Yeh, 2012). The schedule included a series of open-ended questions regarding the participant’s experiences and feelings at various stages or their diabetes duration, ordered by approximate chronological timing from diagnosis, to insulin initiation, to current day. A series of follow-up questions or prompts were developed to obtain further details following the main questions if the interviewee had not elaborated sufficiently. In addition to the interview questions,
the interviewer (this PhD candidate) read aloud items from the Insulin Treatment Appraisal Scale (ITAS) (Snoek et al., 2007) and interviewees were asked to reflect on whether each item was true for them now or in the past. The ITAS was not scored, but rather individual items were used to prompt discussion of concerns and perceived benefits of insulin therapy prior to initiation and the extent to which these concerns were alleviated or persisted. The tool was introduced mid-interview, after participants were given the opportunity to freely express (unprompted) specific barriers and benefits to going on to insulin. The focus of this thesis is the experience of insulin use and attitudes towards insulin intensification. Table 2 presents the questions from the interview schedule that are most relevant to the current study.
<table>
<thead>
<tr>
<th>Topic</th>
<th>Interview questions</th>
</tr>
</thead>
</table>
| Experience of insulin initiation | 1) How long after being recommended insulin did you begin using insulin?  
2) What was it like the first time you/your GP/nurse injected insulin?  
3) How did you feel about using insulin to manage your diabetes, at first?  
4) What did your family and friends think about the idea of you using insulin? |
| Satisfaction with and consequences of insulin therapy use | 1) Now that you’ve been using insulin for X years/months, how do you feel about using insulin to manage your diabetes?  
2) Do you feel insulin has made any difference to:  
   a) your diabetes outcomes overall?  
   b) how you manage your diabetes? (e.g. lifestyle changes, glucose monitoring)  
   c) how you feel? (e.g. more/less energy?)  
3) Compared to before insulin therapy, are you more or less satisfied with your diabetes management now?  
4) For you, what is/are the greatest benefit(s) of using insulin?  
5) Are there any negative aspects of using insulin?  
   a) How do these negative aspects of insulin use make you feel?  
   b) Do these negative aspects interfere with your ability to manage your diabetes?  
6) Do these negative aspects interfere with any other aspects of your life? |
### Interview questions

#### Insulin taking behaviours

1) Some people with diabetes miss an insulin injection or change their dosage of insulin. Do you ever miss or skip an insulin injection?
   a) How often do you miss injections? What are your reasons for missing a dose?

2) Do you ever take a reduced dose of insulin?
   a) How often do you reduce your insulin dose? What are your reasons for reducing your dose?

#### Insulin treatment intensification

1) How many injections do you take each day?

2) Has this changed over time, if so how have you felt about this change?

3) How do you think you would feel if you needed to take more injections each day?

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Each participant also completed a one-page demographics questionnaire (see Appendix E). Questions included gender, age, country of birth, primary language, education level, employment status, diabetes duration, insulin treatment duration, and HbA1c (%).

### 3.6. Recruitment

Participants were recruited through volunteer sampling using study advertisements placed on the Diabetes Victoria and The Australian Centre for Behavioural Research in Diabetes (ACBRD) websites, social media sites (Twitter, Facebook) and e-newsletters from June 2013 to February 2014. The study flyer/advertisement promoted the study as an interview study “to understand how people with T2D think about managing their diabetes and cope with beginning new
and more advanced treatments”. The flyer invited participants to attend a one-hour interview in Melbourne or Geelong, indicating that participants would receive a $20 gift voucher as a token of appreciation for their participation. Interested potential participants were invited to contact the research team by phone or email to obtain detailed information about the study and confirm eligibility.

Purposive sampling was used with the aim of achieving an approximately equal gender split and a broad range of ages. The aim was to interview a minimum of 20 participants with the possibility of conducting further interviews, if necessary, to achieve data saturation. Guidelines for qualitative research propose minimum sample sizes from as few as five to hundreds of participants depending on the theoretical framework underpinning the research, the research topic, the objective of the study (i.e. is it a comparative study), as well as the homogeneity of the sample (Guest, Bunce, & Johnson, 2006). Despite inconsistent sample size recommendations, guidelines consistently recommend that data saturation be reached. This can be demonstrated through a lack of new insights on the research topic emerging in later interviews, and therefore the collection of additional data, through increased sample size, would not provide novel data on the topic of interest.

Overall, 52 participants enquired about the study: 20 were ineligible (e.g. not insulin-treated or using insulin for more than 4 years), 12 declined the invitation or made no further contact after receiving study information, and 20 proceeded to interview. Due to an over-representative initial response from male participants, more men than women took part in the study overall, and in order to achieve a reasonable data-split, men were excluded from taking part from September 2013.
3.7. Procedure

Upon contacting the PhD candidate, via phone or email, potential participants were asked to provide their first name, contact details, diabetes type, treatment and treatment duration, age, gender, and preferred interview location for screening purposes. These data were stored separately from participant interview recordings and transcripts. Eligible participants were sent a plain language statement (PLS) and consent form (Appendix D) via email or post, according to their preference. Eligible participants were asked to read the PLS and contact the PhD candidate if they wished to proceed with an interview or had any further questions. An appointment time was made at a convenient time to the participant.

All interviews were undertaken in a meeting room in a non-clinical setting (Deakin University or Diabetes Victoria) between June 2013 and February 2014. Interviews lasted on average 42 minutes (range: 20-69 minutes). Upon consent, the interviews commenced and were audio-recorded for transcription and analysis. Immediately following the interview, participants were asked to complete the demographic questionnaire and were provided with a $20 department store gift voucher.

3.8. Data Entry

On completion of the interviews, the first 10% ($n=2$) were transcribed verbatim by the PhD candidate. The remaining 90% ($n=18$), the audio-files were sent to a professional and confidential transcribing company where they were transcribed verbatim. All transcripts were then checked against the audio recording by the PhD candidate and loaded into QSR NVivo Version 10, a qualitative data analysis software package.
3.9. **Data Analysis**

Inductive thematic analysis was undertaken to identify themes relevant to the general aim of the current study. Thematic analysis is a broad and flexible method used to identify, analyse, interpret and report patterns stemming from the original data (Braun & Clarke, 2006). Thematic analyses may be undertaken from a theoretical or inductive context. Inductive analysis refers to the analysis of themes being driven by the data rather than by a priori hypotheses, theory, or an existing coding framework (Braun & Clarke, 2006). A non-linear iterative process informed by Braun and Clarke’s (2006) six-phase process for undertaking thematic analysis was used to guide analysis. The PhD candidate (EHT), primary supervisor (JS) and another health psychology researcher with experience in diabetes and qualitative research (co-author JB), were all involved in analysis, enabling reflective analysis involving multiple revisions of the coding framework, double coding a portion of transcripts and checking for inter-coder agreement, and broad theme agreement amongst the team.

EHT read and re-read all transcripts, meanwhile generating initial data codes and categories from a subset of transcripts. The coding framework, along with coding definitions and rules, were reviewed by the full authorship team, and minor iterative revisions were made. Following this, EHT and JB independently coded two transcripts, and collaboratively reviewed their coding decisions and reflected upon when and how the coding framework was and was not adequate. Upon revising the framework so that it better reflected the data, EHT and JB then independently coded five transcripts using the revised coding framework. Inter-coder agreement for each code was assessed by summing the percentage of content in each code identified by both coders. A mean agreement rating (average percentage across codes) of 99.5%
was reached, indicating a high level of consistency in coding. The remaining transcripts were coded by EHT.

The data analysis was undertaken for the entire dataset generated by the interviews (not reported here). The final stage of thematic analysis was guided by the specific research questions of Study 3 (Chapter 3), and is described in Chapter 9.
4. References


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doi: 10.1186/1477-7525-8-113


Nur Azmiah, Z., Zulkarnain, A. K., & Tahir, A. (2011). Psychological insulin resistance (PIR) among type 2 diabetes patients at public health clinics in
federal territory of Malaysia. *International Medical Journal Malaysia, 10*(2), 7-12.


Melbourne: The Royal Australian College of General Practitioners and Diabetes Australia and Diabetes Australia.


Appendix D: Information Statements, Consent and Withdrawal

Forms

Dear NDSS Registrant,

You are invited to take part in the largest ever Australian survey about what it’s like to live with diabetes. The Diabetes MILES Study explores the Management and Emotional Impact of diabetes for Long-term Empowerment and Success of adults with type 1 or type 2 diabetes. By taking part in this study, you will help to increase awareness about what it’s like to live with diabetes in Australia. The results of this study will inform improvements of services and facilities for supporting people with diabetes.

Why have I been invited to take part?

You have been invited to take part because you have expressed an interest in receiving research opportunities on your NDSS registration form. The mailing of this survey is administered by the Victorian NDSS Agent, Diabetes Australia — Victoria. The Diabetes MILES research team do not have access to your personal information.

Who is conducting the survey? The Diabetes MILES Study is conducted by the Australian Centre for Behavioural Research in Diabetes (ACBRD), a partnership for better health between Diabetes Australia - Victoria and Deakin University. The Diabetes MILES Study is funded by a National Diabetes Services Scheme (NDSS) Strategic Development Grant. The NDSS is an initiative of the Australian Government administered by Diabetes Australia. We have also received sponsorship from sanofi-aventis (a pharmaceutical company) to enable us to build a website for the study and send the survey out to a larger number of people. Other sponsorships may be secured over the course of this research. This will not result in any alterations to the participant rights as outlined in this form. Professor Jane Speight (Director, ACBRD) is the principle investigator and takes responsibility for this study (e: jspeight.acbrd.org.au, t: (03) 8648 1850).

Who can take part?

To take part in this study you must live in Australia, have type 1 or type 2 diabetes and be able to read and write English without assistance. If you are unable to complete this survey without assistance, you may like to express your interest in completing the survey in coming years in another language or with assistance (if it was to become available) by completing the enclosed form and posting it back to the ACBRD research team in the reply-paid envelope provided.

Can I withdraw at any time?

Yes, you are free to decide not to participate or to withdraw from the study at any time without giving any reason. Doing so will not affect your relationship with the ACBRD, the NDSS, Deakin University, Diabetes Australia or sanofi-aventis. If you wish to be eligible to withdraw from this study later on, it is important that you provide either your contact details or NDSS Diabetes Services Scheme (NDSS) registration number (when asked during the survey) so we can identify your survey responses. If you do not provide either piece of identifiable information, your data will be completely anonymous and we will not be able to locate and remove your data. If you wish to have your data withdrawn from the study after you have returned the survey please complete and return the Withdrawal of Consent form (attached) or contact the ACBRD (e: DiabetesMILES@acbrd.org.au, t: (03) 8648 1844).

The Diabetes MILES Study is conducted by the Australian Centre for Behavioural Research in Diabetes, a partnership for better health between Diabetes Australia Victoria and Deakin University. It is funded by a National Diabetes Services Scheme (NDSS) Strategic Development Grant. The NDSS is an initiative of the Australian Government administered by Diabetes Australia.
What does the study involve?

Taking part in this study involves completing a questionnaire booklet. We expect this to take approximately one hour. This survey invites you to have your say and reflect on your experiences of living with diabetes. You can take part in this study by completing the enclosed questionnaire booklet and posting it back to the ADBRD in the enclosed reply-paid envelope. Or, you might prefer to complete the survey online at www.diabetesmiles.com.au.

Completion and return of the survey confirms that you have read this Plain Language Statement form and agree freely to take part in this study. The Plain Language Statement form is for you to keep.

Are there any benefits for me personally?

People take part in surveys like this for many reasons:

1) Some people find the questions interesting. Taking part offers an opportunity to think about diabetes, your health and how these affect your well-being
2) Others just want to take part in research that will help us to help other people with diabetes.

There are no specific benefits to you. However, as we appreciate that the questionnaire booklet is very long, as a token of our appreciation, every completed questionnaire booklet received by 31st of July 2011 will be entered into a prize draw, with a chance to win one of five $100 gift vouchers (which can be used at a range of Australian stores nationwide). To be eligible to receive a gift voucher please provide your contact details using the enclosed contact details form.

Are there any risks to me?

No foreseeable risks are associated with taking part in this study. Some questions ask about sensitive and/or personal information. We do not expect that these questions to cause you any distress. However, if you do feel distress or are upset as a result of these questions, we encourage you to contact Lifeline on 131114 (local call).

There will be no medical or blood testing involved in the study. By taking part you will be involved in research that will help us to understand more about how diabetes affects people’s lives.

Does the survey ask for contact or personal details?

The Diabetes MILES survey gives those persons taking part in the survey the option of providing contact details. However, choosing not to give your contact details will not affect your initial participation in any way. You are asked to provide your contact details to ensure the researchers are able to get in contact with you if you consent to any of the following opportunities:

1) Taking part in future research: the Diabetes MILES Study may continue beyond 2011 and we would like you to be involved. With your consent, you will be invited to take part in a similar survey in 4-5 years time which will further add to our knowledge about what it is like to live with diabetes as time goes on.
2) A chance to win one of five $100 gift vouchers: every complete questionnaire returned by 31st of July 2011 goes into a draw, with a chance to win one of five $100 gift vouchers to be used at a range of stores in Australia.
3) Withdrawing your data at a later stage: to be eligible to withdraw from this study later on, it is important that you provide either your contact details or NDSS number so we can identify your survey responses. If you do not provide either piece of information, your data will be completely anonymous and we will not be able to locate or remove your data.
Providing your contact details does not affect the confidentiality of your responses, as your contact details will be kept separate from your survey information and will not be shared with anyone outside the research team. Your contact details will not be used for any purpose other than that which you have indicated.

What will happen to my information?

Questionnaire booklets returned by post will be sent to the ACBRD office where all identifying material will be removed. The anonymous surveys will then be sent on to a data management company who will scan the surveys. All survey data will then be sent (in computer files) to the ACBRD office, where the information will be stored. These computer files will be accessible only by the research team. The anonymous paper surveys will be archived securely at Deakin University. In accordance with government requirements, all data and surveys will be kept for a minimum of six years after the completion of the Diabetes MILES Study and then disposed of by erasing of electronic files and shredding of paper copies.

Your responses will be analysed along with those from other people taking part in the Diabetes MILES Study. Your responses may also be used in the future to compare with future studies. Before future studies go ahead, we will apply for ethics approval. Any data made available to external research parties will be de-identified, meaning that no-one will be able to identify you from the information. Your personal details, such as NDSS registration details, will be kept in a separate ACBRD password-protected file which will never be made available to anyone outside the research team.

The overall results of the Diabetes MILES Study will be published or presented on the Diabetes MILES website (www.diabetesmiles.org.au), academic journals, at conferences, and in diabetes magazines and newsletters. No-one will be able to identify you from any of the information we publish or present. We will take great care to protect your identity. Your privacy is very important to us.

Has this study been approved by an Ethics Committee?

Approval to undertake this study has been given by the Human Research Ethics Committee of Deakin University (research project number: 2011-046).

Who can I contact about this study?

If you have any complaints about any aspect of the project, the way it is being conducted, or any questions about your rights as a research participant, then you may contact: The Manager, Office of Research Integrity, Deakin University, 221 Bunyip Highway, Burwood Victoria 3125, Telephone: (03) 9251 7129, Facsimile: (03) 9244 6581; research-ethics@deakin.edu.au

If you would like further information or have any questions about the study, please contact the ACBRD (e: DiabetesMILES@acbrd.org.au, t: (03) 8648 1844)

You may also like to visit the Diabetes MILES study website: www.diabetesmiles.org.au, or write to us at: The Diabetes MILES Study: The Australian Centre for Behaviour Research in Diabetes, 570 Elizabeth St, Melbourne Vic 3000

Sincerely,

Prof Jane Speight MSc PhD CPsychol AFBPsS
Principle Investigator

Dr Jessica Browne PhD MAPS
Associate Researcher

The Diabetes MILES Study is conducted by the Australian Centre for Behavioural Research in Diabetes, a partnership for better health between Diabetes Australia-Vic and Deakin University. It is funded by a National Diabetes Services Scheme (NDSS) Strategic Development Grant. The NDSS is an initiative of the Australian Government administered by Diabetes Australia.
Withdrawal of Consent

Complete this form only if you wish to withdraw from the Diabetes MILES Study.

To: Participant
Date: May 2011

Full Project Title: The Diabetes MILES Study (Management and Impact for Long-term Empowerment and Success) for Australian adults with type 1 or type 2 diabetes
Phase 2: Survey
Principal Researcher: Professor Jane Speight
Associate Researcher: Dr Jessica Browne

Please tick each box to indicate your agreement with each statement.

☐ I wish to WITHDRAW my data (responses) from the Diabetes MILES Study.
☐ I do not want my data to be used in any analysis or study publications.
☐ I understand that such withdrawal WILL NOT jeopardise my relationship with Deakin University, Diabetes Australia, the Australian Centre for Behavioural Research in Diabetes or the National Diabetes Services Scheme (NDSS).
☐ I understand that my withdrawal will not affect the care or treatment I receive from my health professionals.

By printing your name, signing and dating this form, you confirm that you withdraw your data from the Diabetes MILES Study.

Participant’s Name (printed) ..........................................................

Signature ..................................................................................
Date ..........................................................................

Please mail or fax this form to:

The Diabetes MILES Study
The Australian Centre for Behavioural Research in Diabetes
570 Elizabeth St
Melbourne
Vic 3000
T: +61 (0)3 8648 1844
F: +61 (0)3 9997 1778

The Diabetes MILES Study is conducted by the Australian Centre for Behavioural Research in Diabetes, a partnership for better health between Diabetes Australia-Vic and Deakin University. It is funded by a National Diabetes Services Scheme (NDSS) Strategic Development Grant. The NDSS is an initiative of the Australian Government administered by Diabetes Australia.
Patient invitation letter

Stepping Up Study

Dear patient,

Our practice is participating in a study run by the University of Melbourne to re-organise diabetes care in general practice to involve the Practice Nurse more. The aim of this study is to make sure that patients with diabetes get the best available treatment when they need it to control their blood sugar. This can involve different or additional medicines or even starting insulin.

We are inviting our patients with type 2 diabetes to take part in this important study.

Participation in this study is voluntary and there is no cost associated with participating. Whether you decide to participate or not will not affect your future medical care with us in any way and you are free to withdraw at any time. We respect your privacy and therefore have not passed on your information to the Stepping Up Study team.

What to do next:
To be involved, please

- read the enclosed Plain Language Statement,
- fill out the consent form and Brief Demographic Questionnaire and
- return them in the reply paid envelope as soon as possible.

Please also arrange to have the fasting blood and urine tests using the pathology slip enclosed at your local pathology provider.

Regardless of whether you decide to take part or not, please complete the Brief Demographic Questionnaire and return it in the reply paid envelope provided.

Your Practice Nurse will call you in the next week. Meanwhile if you have any questions or would like more information, please feel free to call our practice or call the Stepping Up Study team on 83443373.

Signed GP and PN

Study investigators:
Dr John Furler, Prof Dora Young, Prof James Bast, Prof Elizabeth Patterson, Dr Irene Blackberry, A/Prof David O’Neal from the University of Melbourne, Prof Danny Liew from Melbourne Health, Prof Leonie Segal from University of South Australia, Prof Jane Speight from Diabetes Australia Victoria and Prof Carl May from University of Southampton, UK

PhD Students:
Dr Jo-Anne Manski-Nankervis and Ms Elizabeth Holmes-Truscott

HREC-1237406.1 Patient invitation letter; 14 March 2012
Stepping Up Study

What is the Stepping Up Study?
This study is about re-organising care for diabetes in general practice to involve the Practice Nurse (PN) more. Our aim is to make sure that patients get the best available treatment when they need it to control their blood sugar. This can involve different or additional medicines or even starting insulin. The focus of this study is having your General Practitioner (GP) and PN take a lead in working closely as a team to ensure that your sugar control is better. While we will be supported by a team of diabetes nurse educator and diabetes specialists, your care will still be provided through our local practice. The study will compare the outcome of this enhanced GP and PN team with current general practice care.

The majority of the funding for the study came from the National Health and Medical Research Council. Roche Diagnostics and Sanofi-Aventis contributed the time for a Study Diabetes Nurse Educator (DNE), blood glucose meters and insulin.

Why is the Stepping Up Study important?
Type 2 diabetes is a progressive condition. As the pancreas runs out of insulin, so treatment with insulin is eventually needed by most people with type 2 diabetes. This is a normal part of the natural history of diabetes. Starting insulin can in fact slow the progression of diabetes and often makes patients feel better. Our proposal aims to help GP and PN support patients to change to insulin in a way that suits the patient. In this way the patient themselves can be in control.

What will taking part involve?
Taking part in this study simply involves making a time to see your GP to discuss your diabetes management, having some blood and urine tests and completing a study questionnaire at the start of the study and 12 months later. The questionnaire will take approximately 30 minutes to complete and will collect information such as your quality of life, mental health, how you feel about diabetes and its management and about the care you receive from your GP and PN. We will also arrange a diabetes blood test after 6 months. As part of the study evaluation, we will be inviting patients and PNs to audio record some consultations and may ask to interview you about your experience with the study. This is optional.

A study nurse will collect information about your use of health services, medicines you are on, and any diabetes complications you may have from your medical records. This helps us to measure the cost and the benefit of the study.

There is a 50:50 chance that your GP and PN will be allocated into the intervention group.

If your practice is allocated into the intervention group, your GP and PN will receive training to enhance GP and PN team at the start of the study. In addition to the usual GP care, you will also be asked to make a time to see your PN. You will be asked to monitor and record your blood glucose level using the blood glucose meter provided at the start of the study. The PN (working closely with your GP) will discuss with you the possibility of introducing insulin as a medicine for your diabetes. This would only be done if you wish to do so. You will receive $75 reimbursement towards the time and cost involved in

HREC 1237406.1 Patient Plain Language Statement; 9 May 2012
Plain Language Statement for Patients

the study. The benefits of your involvement in the study include the potential for improvement in your sugar control, receiving a new blood glucose monitor and having increased contact with your PN to assist you in the management of your diabetes.

If your practice is allocated into the control group, you will receive care as usual from your GP throughout your participation in the study. General practices that are allocated into the control group will receive the same training as the practices in the intervention group, however this training will be conducted 12 months after. The benefits of your involvement in the study include you being provided with a blood glucose meter and a reimbursement of $75 to cover time and cost involved after you have completed the 12 months follow-up whilst you receive the care your GP would usually provide.

Potential risks associated with involvement in the study may include need for increased visits to the GP, risk of hypoglycaemia (low blood sugar) with some diabetes treatments and distress associated with completion of the questionnaire.

There will be no financial costs associated with your participation in the study.

Your participation is voluntary and you are free to withdraw from the study at any time. Whether you choose not to participate or not will have no effect on your ongoing care at your general practice.

How will my privacy be protected?

All clinical data will remain in your practice. Any research data collected on you will be kept confidential subject to legal requirements and maintained in accordance with the University of Melbourne guidelines for the conduct of research. All information provided will be kept secure, in locked storage at The Department of General Practice, The University of Melbourne. The de-identified research data will be kept by the research team for 15 years, as stated in the NHMRC ethical guidelines, and then destroyed. You will not be identified in any publications of the study findings.

Who can I talk to about this study?

If you would like further information about the study please contact Dr Irene Blackberry on (03) 8344 3373 or email i.blackberry@unimelb.edu.au

This phase of the study has received approval from the Human Research Ethics Committee of the University of Melbourne. If you have any concerns about the conduct of this study please contact the Executive Officer, Human Research Ethics, University of Melbourne, VIC 3010, Ph 8344 2073, Fax 9347 6739.

Thank you for taking the time to read this information.

Study investigators:
Dr John Futter, Prof Doris Young, Prof James Beil, Prof Elizabeth Patterson, Dr Irene Blackberry, A/Prof David O’Neil from the University of Melbourne, Prof Dennis Liew from Melbourne Health, Prof Vivian Sage from University of South Australia, Prof Jane Spight from Diabetes Australia Victoria and Deakin University and Prof Carl May from University of Southampton, UK

PhD Students:
Dr Jo-Anne Manski-Nankervis and Ms Elizabeth Holmes-Truscott

HREC 1237406.1 Patient Plain Language Statement, 9 May 2012
Patient consent form for research project

Stepping Up Study

Patients Name: ____________________

Name of investigator(s): Dr John Furler, Prof Doris Young, Prof James Best, Prof Elizabeth Patterson, Dr Irene Blackberry, A/Prof David O’Neal, Prof Danny Liew, Prof Leonie Segal, Prof Jane Speight, Prof Carl May

Name of PhD students: Dr Jo-Anne Manski-Nankervis and Ms Elizabeth Holmes-Truscott

1. I consent to participate in the project named above the details of which have been explained to me.

2. I have read the Plain Language Statement provided to me and a written copy of the Plain Language Statement relating to the project has been given to me to keep, and I understand what is included in it.

3. I acknowledge that:
   - I have been informed that I am free to withdraw from the project at any time without explanation or prejudice and to withdraw any data previously supplied;
   - The project is for the purpose of research;
   - I have been informed that the confidentiality of the information I provide will be safeguarded subject to any legal requirements.

Signature ____________________ Date ____________________
(Patient)

This form is to be retained by the Stepping Up Study
HREC 1237405.1 Consent Form 14 March 2012
Patient revocation of consent form
Stepping Up Study

Patients Name: __________________________

Name of investigator(s): Dr John Furler, Prof Doris Young, Prof James Best, Prof Elizabeth Patterson, Dr Irene Blackberry, A/Prof David O’Neal, Prof Danny Liew, Prof Leone Segal, Prof Jane Speight, Prof Carl May

Name of PhD students: Dr Jo-Anne Manski-Nankervis and Ms Elizabeth Holmes-Truscott

I hereby wish to WITHDRAW my consent to participate in the project described above and understand that such withdrawal WILL NOT jeopardise any treatment I receive from my GP or my relationship with him/her.

Name: ____________________________________

Signature: _____________________________ Date: _____________________________

-----------------------------------------------------------------------

The section for revocation of consent should be forwarded to:

Dr Irene Blackberry,
Email: i.blackberry@unimelb.edu.au
Department of General Practice, University of Melbourne,
200 Berkeley St., Carlton VIC 3053, Ph 03 8344 3373 Fax 03 9347 6136

This form is to be retained by the Stepping Up Study
HREC 1237/001 Consent Form 14 March 2012


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Plain Language Statement

Date: May 2013

Full Project Title: Experience of beginning insulin therapy among people with type 2 diabetes: a qualitative investigation

Principal investigator: Prof Jane Speight
Student Investigator: Elizabeth Holmes-Truscott

Thank you for expressing interest in this study.

You are invited to take part in this interview study because you have type 2 diabetes and are currently using insulin to manage your diabetes. Taking part in this study will involve talking with a researcher about your experience of managing diabetes including the different medications you have used and how you feel about each of these treatments. By taking part in this study you will be helping us to develop a better understanding of how people with type 2 diabetes think about managing their diabetes and beginning new and more advanced treatments. In addition, your responses may be used to inform future research and develop the content of an program intervention to assist other people with type 2 diabetes beginning insulin.

Who is conducting this interview study?

The study is conducted by The Australian Centre for Behavioural Research in Diabtes (ACBRD), a partnership for better health between Diabetes Australia - Victoria and Deakin University. This study is managed by Elizabeth Holmes-Truscott and will form part of her PhD thesis. Professor Jane Speight, the director of the Centre and one of the Principal Investigators, takes overall responsibility for this study (e: jspeight.acbrd.org.au, t: 03 8648 1850).

Who can take part?

People with type 2 diabetes, aged 18 years or older, who are currently using insulin to manage their diabetes, can take part in this study. In this interview, participants will need to be able to talk about what it was like when they started using insulin. So, we expect participants to have begun insulin no more than 3 years ago. As the interview will be conducted in English, volunteers must be able to speak fluent English.

Can I withdraw at any time?

Yes. You are free to decide not to participate in this study. If you choose to take part, you can stop the interview at any time after it has started. Deciding not to participate (or to withdraw) will not affect your relationship with the ACBRD, Deakin University, or Diabetes Australia – Victoria. If you withdraw from the study during the interview, we can remove any information you have shared to that point from any analysis. However, once we have finished the interview and the data has been de-identified, you will not be able to withdraw the information you shared because we will not know which recording was yours. De-identification will occur within one day of the interview.
What does the study involve?

This study involves taking part in an interview (60 – 90 minutes long) about your experiences of living with and managing type 2 diabetes. In particular, participants will be asked to talk about the different treatments they have used to manage their diabetes, and how they felt about the transition to more advanced treatments. Participants will also be asked to indicate their beliefs about insulin now and prior to beginning insulin in a short 1 pages questionnaire.

The interview will take place at the Diabetes Australia – Victoria offices in Melbourne CBD, or if you prefer, at one of the Deskin University campuses (Burwood, Geelong Waterfront or Geelong Waurn Ponds). The interview will be conducted by Elizabeth Holmes-Truscott. All interviews will be audio recorded, and the recordings will be transcribed (typed in full).

At the completion of the interview you will be asked to complete a one page ‘About You’ form which will ask you to provide some personal details, e.g. age, gender, how long you have had diabetes. This information will be used to help us understand more about who took part in the interviews and to describe the participant group, e.g. how many men and women took part. None of the information will be used to identify you.

At the completion of the interview you may be invited by the investigator to assist the Centre in developing resources for other people with type 2 diabetes. This is completely voluntary and will not affect your participation in the current study or relationship with the research team.

Are there any benefits for me personally?

People take part in studies like this for many reasons, such as:

- Some people find the questions interesting. Taking part offers an opportunity to think about your diabetes and reflect on your experiences;
- Some people like to take part in research that will help us to help other people with diabetes.

As a token of our appreciation, each person taking part will receive a $20 department store gift voucher after the interview.

Are there any risks to me?

No, we do not anticipate that this study will pose any risks to you. By taking part you will be involved in research that will help us to understand more about how people with type 2 diabetes think about managing their diabetes and beginning new and more advanced treatments. We do not expect the questions to cause you any distress. However, if you should become distressed while answering the questions we would advise you to discuss this with the researcher. You have the right to refuse to answer any question that makes you uncomfortable, and you can ask to stop the interview at any time.

What will happen to my information?

Any information you share with us will remain strictly confidential. Your information will only be made available to the research team involved in the study. The audio recording of your interview will be held on file at the ACIRO (to enable transcription and double-checking of data) and will be accessible only by the research team. Audio recording file names, transcripts and notes will not include any identifying
Information about participants. The information you provide in the demographics form will be anonymous. All the information you share with us will be stored in a locked filing cabinet and/or electronically (on a computer) in a password protected file. In accordance with government requirements, your data will be stored for six years and then disposed of by erasing of electronic files and shredding of paper copies. The information that you supply will not affect the diabetes care that you receive or your legal rights.

Any details you share about yourself (e.g. surname, contact details) with the research team for the purposes of making arrangements to attend the interview will be destroyed (electronic files to be deleted, no paper documents of this information will be made) after the interview has taken place.

The overall results of the interview study will be presented in the student investigator’s PhD thesis and may also be published or presented in academic journals, at conferences, and in diabetes magazines and newsletters. Participants will be able to access any publications or reports resulting from the study on the ACBRD website (www.acbrd.org.au).

The principal investigators and/or the ACBRD may use your de-identified information in a closely related or an extension of the current research project. No-one will be able to identify you from any of the information we publish or present. We will take great care to protect your identity. Your privacy is very important to us.

Has this study been approved by an Ethics committee?

Yes. Approval to undertake this study has been given by the Human Research Ethics Committee of Deakin University (research project number: 2013-048).

Who can I contact about this study?

If you would like further information or have any questions about the study, please contact Elizabeth Holmes-Truscott at the ACBRD (e: elizabeth.holmes@acbrd.org.au, t: telephone 03 8648 1881) or write us at:

Elizabeth Holmes-Truscott
The Australian Centre of Behavioural Research in Diabetes
570 Elizabeth St
Melbourne
Vic 3000
T: +61 (0)3 8648 1845
F: +61 (0)3 9667 3778

You may also contact Professor Speight (e: jspeight@acbrd.org.au, t: (03) 8648 1850), who takes overall responsibility for this study. To find out more about the study and the work of The Australian Centre for Behavioural Research in Diabetes, you may also like to visit the ACBRD website: www.acbrd.org.au.

If you have any complaints about any aspect of the project (ID: 2013-xxx), the way it is being conducted or any questions about your rights as a research participant, then you may contact: The Manager, Office of Research Integrity, Deakin University, 221 Burwood Highway, Burwood Victoria 3125, Telephone: (03) 9224 7125, Facsimile: (03) 9224 0584; Email: research-ethics@deakin.edu.au.
Consent Form

Complete this form to participate in this project.

To: Participant
Date: May 2013
Full Project Title: Experience of beginning insulin therapy among people with type 2 diabetes: a qualitative investigation
Principal Investigator: Prof Jane Speight
Student Investigator: Elizabeth Holmes-Truscott

Please tick each box to indicate your agreement with each statement.

☐ I have read and I understand the attached Plain Language Statement.
☐ I freely agree to participate in this project according to the conditions in the Plain Language Statement.
☐ I have been given a copy of the Plain Language Statement and Withdrawal of Consent form to keep.
☐ I understand and consent to the interview being audio-recorded.
☐ I understand that the research team will not reveal my identity or personal details to anyone outside the research team, including where information is published or presented in any public form about this research study.
☐ I understand that the research team may use the information I share in a closely related or an extension of the current research project and that this information will be de-identified.

By printing your name, signing and dating this form, you confirm that you consent to take part in the study.

Participant’s Name (printed) .................................................................
Signature  ................................................ Date  ..........................

The Australian Centre of Behavioural Research in Diabetes
570 Elizabeth St
Melbourne
Vic 3000
T: +61 (0)3 8648 1844
F: +61 (0)3 5667 1778

Plain Language Statement & Consent Form to Participants  [2013-048]: version 1: 20/03/13
"Experience of beginning insulin therapy among people with type 2 diabetes: a qualitative investigation"

**********IMPORTANT**********

Complete this form and return it to us only if you decide to WITHDRAW from the above-named study.

I wish to withdraw from participating in the study entitled 'Experience of beginning insulin therapy among people with type 2 diabetes: a qualitative investigation' I do not want to take part in any additional study activities and I do not want the information I have already provided to be included in any analysis or study publications. I understand that withdrawing the information I have already provided will not be possible after completion of the interview. I understand that withdrawing from the study will not adversely affect my relationship with any of the organisations conducting this study. I understand that withdrawing from the study will not affect the care or treatment I receive from any health professionals.

Participant’s name (please print) ........................................................................................................................................

Participant’s signature....................................................................................................................................................

Date.............................................................................................................................................................................

Please hand this form to your researcher or mail or fax this form to:

Elizabeth Holmes-Truscott
The Australian Centre of Behavioural Research in Diabetes
570 Elizabeth St
Melbourne
Vic 3000
F: +61 (0)3 9667 1778

Plain Language Statement & Consent Form to Participants [2013-048]: version 1: 20/03/13
Appendix E: Interview Study Demographics Questionnaire

ABOUT YOU

Below are some questions about you. Answering these questions will help us understand a little more about who took part in the interviews.

1. What is your age? __ __ __ __
2. Are you: □ Male □ Female
3. What is your postcode? __ __ __ __
4. In which country were you born? □ Australia □ Other: ______________
4a. If other, in what year did you first arrive in Australia to live here? __ __ __ __
5. What is the main language you speak at home? □ English □ Other:___________
6. How old were you when your type 2 diabetes was diagnosed? __ __ years old
7. How do you treat your diabetes currently and how long have you been using this treatment?
   □ Insulin injections __ __ years
   □ Blood glucose-lowering tablets __ __ years
   □ Diet & physical activity (lifestyle changes) __ __ years
   □ Complementary and alternative medicines __ __ years
   □ Other: __________________________ __ __ years
8. What was your HbA1c the last time it was checked? ________ %
9. What is the highest qualification you have completed?
   □ No formal qualifications □ Certificate / diploma
   □ Primary school or intermediate certificate □ University degree
   □ High school or leaving certificate □ Higher University degree
   (e.g. Grad Dip, PhD)
10. Which of the following best describes your current employment?
    □ Full time work □ Retired
    □ Part time work □ Not working for another reason: ______________

THANK YOU FOR TAKING PART IN THIS STUDY