FACTORS ASSOCIATED WITH ADHERENCE AMONG INDIVIDUALS WITH DIABETES MELLITUS: A LITERATURE REVIEW

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ABSTRACT

Background: Diabetes Mellitus (DM) is a condition that is characterised by an increase in the blood glycaemic level due to insufficient and defective insulin action in the body. The aim of this review was to examine the factors associated with adherence among individuals with DM.

Method: A literature review was conducted on published work related to the factors associated with adherence among individuals with DM by searching online databases.

Results: A total of 23 published studies that focused on the adherence to anti-diabetes drugs were reviewed. Fifteen cross-sectional studies identified several factors that were significantly associated with adherence, such as gender female (n=5), age (n=2), educational level (n=6), financial status (n=4), and knowledge or information about diabetes (n=4). Qualitative studies reported that family support and system-level facilitators were associated with adherence to the management of diabetes.

Conclusion: It is suggested that diabetes education plays an important role in adherence. Health care professional should focus on the educational interventions to increase adherence to treatment.

Keywords: adherence, diabetes mellitus
1.0 Introduction

Diabetes is a disease characterised by increased glycaemic level due to a defect in insulin secretion and insulin action. Diabetes mellitus (DM) is a term used to describe a series of complex and chronic heterogeneous metabolic disorders, which are characterized by symptomatic glucose intolerance as well as disordered lipid and protein metabolism (Inamdar et al., 2013). There are three types of DM. Type 1 or insulin-dependent Diabetes Mellitus (T1DM) is caused by a lack of insulin due to the destruction of insulin-producing beta cells in the pancreas of the body (NIDDK, 2016). Type 2 or insulin-independent Diabetes Mellitus (T2DM) is caused by insulin resistance that occurs in the body (WHO, 2003). The third type of DM, is known as Gestational Diabetes Mellitus (GDM), which is caused by intolerance to carbohydrates and results in hyperglycaemia with the onset or recognition of pregnancy (WHO, 2013). The conditions of DM can jeopardise the quality of life of the patient as more complications can develop. This condition can affect the execution of vocational, social, personal and general activities in one’s daily life (Lam, Zaim, Helmy, & Ramdhan, 2014; Mazlina, Shamsul, & Saini Jeffery, 2011). DM patients are usually required to consume the prescribed medicine on a long-term basis. However, despite the effectiveness of drug therapy in managing the condition of DM, a high rate of poor adherence persists (Mann, Ponieman, Leventhal, & Halm, 2009). According to the WHO (2003), DM patients require long-term treatment, and poor adherence to the treatment might contribute to the sub-optimal clinical benefits. Non-adherence to the treatment might lead to a reduction in benefit from the treatment, extra visits to the doctor, unnecessary hospitalisation, and decreased satisfaction with medical care, as well as further medication (Clark, 2004).

According to the WHO (2003), adherence to a long-term therapy is defined as “the extent to which a person’s behaviour-taking medicine, following a diet, and executing lifestyle changes, corresponds with the agreed recommendations from a healthcare provider.” The adherence to treatment does not simply refer to the act of taking medication, but also refers to how the person can manage their treatment, such as the doses, times, frequency as well as duration (Helena, Nermes, & Eluf-Neto, 2008). According to Wabe, Angoma, and Hussein (2011), the worldwide adherence rate for diabetes varies from 36% to 93%. In Malaysia, one study showed that more than half of the study population did not adhere to treatment (Mafauzy, Hessin, & Chan, 2008).

The treatment of diabetes mellitus is complex as it involves a modification of one’s lifestyle to optimize nutrition and physical activity as well as the addition of pharmacological therapy to provide the necessary physiologic support for insulin deficiency or insulin resistance. The ultimate goal of anti-diabetic medication is to avoid the acute osmotic symptoms of hyperglycaemia, to avoid instability in blood glucose over time, and delay as well as prevent the development of diabetes complications without affecting the quality of life (Inzucchi et al., 2012; Odegard & Capoccia, 2007). A position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) showed that highly motivated patients with HbA1c of less than 7.5% could be given the opportunity to engage in lifestyle changes for a period of three to six months before embarking on pharmacotherapy (Inzucchi et al., 2012). Lifestyle modification involves medical nutrition therapy and physical activity. In addition, in Malaysia, diabetes education has been highlighted the importance of lifestyle modification in recent published Clinical Practice Guidelines on Management Type 2 Diabetes Mellitus (2015). A recent systematic review also
demonstrated that engagement in diabetes education achieved statistically significant reductions in HbA1c levels (Chrvala, Sherr, & Lipman, 2015). Thus, diet, exercise, weight control, and education remain the foundation of any type 2 diabetes treatment programme (Inzucchi et al., 2012; Ministry of Health, 2015).

In addition to non-pharmacological therapy, pharmacological therapy should be given to those with moderate hyperglycaemia (≥7.5% HbA1c) or to those whose lifestyle changes are anticipated as being likely to be unsuccessful in reducing HbA1c (Inzucchi et al., 2012). Metformin, a biguanide, is the optimal first-line drug. The mechanism of metformin is that of decreasing the production of hepatic glucose and not stimulating insulin secretion; thus, on its own, it is not usually accompanied by hypoglycaemia (Lamanna, Monami, Marchionni, & Mannucci, 2011). Besides metformin, there are some pharmacologic options for diabetes mellitus treatment including oral agents, non-insulin injectable agents, and injected insulin. For the non-insulin pharmacological agents, the glucose-lowering effectiveness is high for metformin, sulphonylureas, thiazolidinediones (TZDs) and Glucagon-like peptide-1 (GLP-1) agonist, and is expected to result in a 1.0 to 1.5% HbA1c reduction (Bennett et al., 2011; Bolen, Feldman, Vassy, Wilson, & Yeh, 2007). If monotherapy alone does not achieve or maintain HbA1c for over three months, then the next step would be a combination therapy with the addition of one to two oral or injectable insulin agents or non-insulin agents, the aim of which, where possible, is to minimize any side effects (Nathan et al., 2009). Again, where possible, all treatment decisions should be made in conjunction with patient preferences and characteristics, and susceptibilities to side effects and hypoglycaemia should play a major role in drug selection (Inzucchi et al., 2012; Ismail-beigi et al., 2011).

The World Health Organization has recognized that many factors affect the adherence to treatment for diabetes, such as disease and treatment characteristics, and complexity, age, gender, self-esteem, stress, depression, quality of the relationship between patients and healthcare providers, social support and patients’ ability to remain adherent amidst changing circumstances in their daily life (Sabaté, 2003). It classifies these factors into five categories, which are socioeconomic factors, factors associated with the healthcare team and system in place, disease-related factors, therapy-related factors, and patient-related factors (Sabaté, 2003). In broader terms, these factors can be divided into three groups, which are patient factors, medication-related aspects, and social and medical support (Borgsteede et al., 2011; Heissam, Abuamer, & El-dahshan, 2015). Adherence to anti-diabetic medication can be seen as a multifactorial behaviour.

2.0 Materials and Methods

To identify research related to the adherence to diabetes mellitus treatment, as well as the factors associated with adherence and the strategies used to improve adherence, articles related to cross-sectional studies, cohort studies (prospective and retrospective studies), and trials (randomized clinical trials [RCT]) were selected. The review examines the factors that are associated with the adherence of individuals with diabetes mellitus to either pharmacological or non-pharmacological therapies. It also reviews the strategies/interventions used to improve adherence to the treatment of diabetes mellitus that healthcare professionals could consider using.
Published articles related to the adherence among individuals with diabetes mellitus were collected using online databases from the Library of University Putra Malaysia, and Pub Med based on the keywords. The keywords used were ‘compliance’, ‘adherence’, and ‘concordance’. A list of related journal articles related to the adherence of individuals with diabetes mellitus for the last ten years (2007-2016) was generated. References from the identified articles as well as relevant books on adherence were also included in the literature search. Relevant studies were identified based on the title and abstract for which the main topic of the study was adherence. In this review, adherence was defined as the extent to which a person’s behaviour in taking medicine, following a diet guideline, and performing lifestyle changes was according to the recommendations given by a healthcare professional (WHO, 2003).

Studies were included if they met the following inclusion criteria: the study involved targeted individuals with diabetes mellitus aged at least 18 years of age; the study was written in English; the study was an original study, the purpose of the study was related to adherence, and the measures of adherence were stated.

Studies were excluded if they were commentaries, editorials, letters, government reports, or practice guidelines; involved a specific target population, such as infants and children; were related to pregnant women (gestational diabetes mellitus); were related to symptoms/conditions other than diabetes mellitus; were not written in English; were case reports with a small sample size (e.g. one or two cases); or were a published work review/opinion paper. Then, each relevant study was reviewed and selected based on the inclusion criteria. A total of 23 journal articles met the inclusion criteria. The journal articles were grouped into two categories based on the study design; namely, quantitative group or qualitative group (see figure 1).

779 articles was generated by entering the key word in the searching list

249 articles was generated after filtering by using the exclusion criteria

65 articles was selected based on topic and abstracts

23 articles was used in the Literature Review

Figure 1: The article selection process
3.0 Result

3.1 Study Background

A total of 23 studies were reviewed and selected for further analysis. The studies were conducted in Malaysia (n=3), the USA (n=8), Taiwan (n=1), Australia (n=1), India (n=1), Pakistan (n=1), the UK (n=1), Nigeria (n=1), Korea (n=1), Africa (n=2), Saudi Arabia (n=2), and New York (n=1).

For the reviewed studies, respondents were recruited from outpatient medical centres, clinics, and general practitioners’ offices (n=20), community clinics (n=1), and the community (n=1).

Several types of study were reported, including cross-sectional study (n=15), cross-sectional and qualitative study (n=2), cohort study (n=3), retrospective study (n=1), retrospective and prospective study (n=1), and randomized-controlled trial (RCT) (n=1).

3.2 Reviewed studies

Table 1: Reviewed studies

<table>
<thead>
<tr>
<th>Authors (published year), country</th>
<th>Participants</th>
<th>Type of study</th>
<th>Data collection methods</th>
<th>Findings (factors associated with adherence)</th>
</tr>
</thead>
</table>
| Ahmad, Ramli, Islahudin, & Paraidthathu (2013), Malaysia | Patients with type 2 diabetes mellitus at Primary Health Clinics of the Ministry of Health | Cross-sectional | Medication compliance questionnaire | • Approximately 53% of patients in the study population were non-adherent.  
• Variables associated with non-adherence were age, medication knowledge, and comorbidities. |
| Alatawi, Kavookjian, Ekong, & Alrayees (2016), Saudi Arabia | Patients reporting a history of type 2 diabetes, over the age of 18, and who were on at least one prescribed diabetes medication (n = 222) | Cross-sectional | Questionnaire and interview | • Most reported taking the prescribed dose every time taken.  
• 60% not taking it the prescribed number of times per day.  
• 50% not taking at the prescribed time of day (interval).  
• ‘Forgetting to take medication(s)’ (29%) was the most common barrier among qualitative analyses for open-ended questions to |
take medication as prescribed. Other barriers included ‘travel’ (13%) and ‘work’ (10%).

- Patients who reported the most ready stage of change for global adherence measures were also most likely in the 6 or 7 days without missed doses category of the MTR-7, and were also in the high categories of adherence for all three of the MDAM sub-behaviours.

- The current result supports previous work that the total number of medications may influence medication adherence behaviour.

- Results showed that perceived susceptibility, perceived benefits, and self-efficacy most significantly influenced adherence behaviour.

<table>
<thead>
<tr>
<th>Study</th>
<th>Methodology</th>
<th>Patient Characteristics</th>
<th>Results</th>
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</table>
| Al-Qazaz, Sulaiman, Hassali (2011), Malaysia | Cross-sectional Interview and questionnaire | Patients diagnosed with type 2 diabetes for at least 1 year; treated for diabetes with oral medication for at least 1 year; age > 30 years old | • The median of Morisky Medication Adherence Scale (MMAS) was 6.5 (IQR, 4.75–7.75).  
• Significant difference in Morisky Medication Adherence Scale (MMAS) scores was found between educational levels, as those patients with higher educational level had better medication adherence (Kruskal-Wallis test).  
• Patients taking between 1 and 3 medications daily were found to have a higher score for MMAS compared to those taking more than 3 |
<table>
<thead>
<tr>
<th>Authors</th>
<th>Study Details</th>
<th>Methodology</th>
<th>Data Collection</th>
<th>Findings</th>
</tr>
</thead>
</table>
| Awodele, & Osuolale (2015), Nigeria | Patients with type 2 diabetes in Alimosho General hospital, Igando Lagos state | Retrospective & Prospective | Review of case notes, counselling and education of patients on medication adherence | • Proportion of females/males with T2DM was 69% and 31%, respectively.  
• 51.32% of the patients viewed their medications as being unaffordable.  
• 56.6% of the patients were aged 61 years old and above.  
• Significant relationship was found between age, gender and adherence to medication.  
• No significant association between education level and adherence. |
| Balley, Barner, Weems, Leckbee, Solis, Montemayor, & Pope (2012), US | Adults with diabetes who used a grocery store chain pharmacy or a community clinic for the underserved (n=59) | Cross-sectional | Self-administered anonymous survey | • Participants (52.6%) reported their health status as good or excellent and over one-half (56%) of the participants were non-adherent.  
• Factors were significantly related to non-adherence: cost, no refills, poor health status, fewer disease states, and any reason. |
| Currie Peyrot, Morgan, Poole, Jenkins-Jones, Rubin, Burton, & Evans (2012), UK | General practice records and included patients who had diagnostic codes indicative of type 2 diabetes or who had received a prescription for an oral antidiabetic agent and were treated with insulin | Retrospective | Records in the 30 months before the index date was inspected for clinical codes (recorded at consultation) indicating medication noncompliance or medical appointment | • Those identified as clinic non-attenders were more likely to be smokers, younger, have higher HbA1c, and have more prior primary care contacts and greater morbidity.  
• Those identified as medication non-compliers were more likely to be women, smokers, and have higher HbA1c, more prior |
<table>
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<tr>
<th>Study Authors</th>
<th>Study Details</th>
<th>Methodology</th>
<th>Results/Findings</th>
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</table>
| Fürthauer, Flamm, & Sönnichsen (2013), Australia | Patients with at least one of the target-diseases and checked the guideline conformity of treatment using nine quality indicators | Cross-sectional                      | • Non-adherence to guideline recommendations were present in 16.8% of all quality indicators.  
• In 61.5% of these cases, the treatment was wrongly judged as not recommended by the physicians.  
• In 10.2% physicians attributed non-adherence to patient’s non-compliance, and in 10.7% to an adverse drug event, whereas only 5.4% of non-adherence was related to an adverse drug event reported by the patients.  
• Patients were unaware regarding the reason for non-adherence to therapy in 64.4% of the quality indicators.  
• 20.0% patients regarded a drug as not needed. |
| Kalyango, Owino, & Nambuya (2008), Africa | Patients aged 18 years and above, had been taking diabetes treatment for at least one | Cross-sectional-based interview      | • Overall, the prevalence of diabetes treatment non-adherence was 28.9%.  
• Factors significantly associated with non- |
<p>| Month (n = 402) |  |  | Adherence were sex (female gender) (OR=2.83, CI=1.62-4.95), education level (none or primary) (OR=0.58, CI=0.36-0.92), patients self-rating of how much of the prescribed drugs they or their caretakers could usually afford (some or none) (OR=1.91, CI=1.22-2.98), number of health education sessions attended in the previous six months (none or one) (OR=0.51, CI=0.27-0.95), duration of time since last health education session attended (&gt; 7 months) (OR=1.73, CI=1.02-2.92), patients’ self-rating of how well they understood their drug regimens (a little/don’t understand) (OR=2.61, CI=1.19-5.71), and time since last visit to a health worker (&gt; 3 months) (OR=3.22, CI=1.85-5.59). |
| | | |
| | | • In multivariate analysis, factors independently associated with non-adherence were female gender (OR=2.95, CI=1.39-6.24), not understanding the drug regimen well (OR=4.06, CI=1.01-16.32), patients or their caretakers being able to afford only some or none of the prescribed anti-diabetic drugs (OR=3.70, CI=1.81-7.59), and longer time since last visit to a health worker (OR=7.26, CI=2.65-19.86). | • No significant association |</p>
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<tr>
<th>Study Authors</th>
<th>Study Design</th>
<th>Study Methods</th>
<th>Key Findings</th>
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</table>
| Kassahun, Gashe, Mulisa, & Rike (2016), Africa | Patients who were treated for diabetes with anti-diabetic medication (n = 285) | Cross-sectional Structured questionnaire and reviewed patients’ record card | - 31.2% non-adherence to anti-diabetic medication.  
- Significant association between medication’s side effect, education level, monthly income and presence of glucometer at home with adherence to anti-diabetic medication. |
| Khan, Lateef, Al Aithan, Khameen, Khn (2012), Saudi Arabia | Patients with at least a one-year history of Diabetes, and who were on a fixed drug therapy for the last six months, and who were getting medication on a regular basis (n = 468) | Cross-sectional Questionnaire-based interview | - More than half of the participants (57.5%, n = 289) did not adhere to the anti-diabetic medication as advised by the GP.  
- Similarly concerning the advice on exercise, where 62.6% (n = 293) did not follow the instructions given by the GP.  
- However, the instructions on diet were followed by 64.7% (n = 303) of the participants.  
- The non-compliance in the urban population was significantly higher than in the rural population (71.04 vs. 60.15%, P = .023).  
- Females were significantly more compliant (34.55 vs. 30.66%, P = .003).  
- Higher educational level of patients was found to be significantly associated |
The most important causes of non-compliance with clinic appointments were the non-availability of transport, followed by forgetfulness. Compliance was fairly high among those patients who had adequate information on the dose, duration of action, and side effects of the anti-diabetic medicines. Those patients who did not get adequate information on what to do in the event of their missing a dose, or if they experienced any side effects of the medicine, were more non-compliant. Those patients who agreed that the physician completely understood their health problem when they saw them on the day of appointment were also more compliant. The increased rate of therapeutic non-compliance in our study resulting from the multi-drug regimen (Metformin + Sulphonylurea) and insulin injection.

Mann, Ponieman, Leventhal, & Halm (2009), New York

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<tr>
<th>Study</th>
<th>Design</th>
<th>Method</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>History of Type 2 diabetes for at least six months who were prescribed diabetes medication (n=151)</td>
<td>Cross-sectional</td>
<td>Questionnaire-based interview</td>
<td>Approximately one-quarter (28%) of the patients reported poor adherence to their diabetes medication (Morisky&gt;1). Five variables predicted poor adherence in multivariable analysis:</td>
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have diabetes only when the glucose is high (disease belief), not taking medications when sugar normal.

- Patients holding sceptical beliefs were significantly more likely to be poorly adherent than those holding ambivalent ($p = .02$), indifferent ($p = .03$) or accepting beliefs ($p < .001$).

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study Design</th>
<th>Data Collection</th>
<th>Findings</th>
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<tbody>
<tr>
<td>Ngo-Metzger, Sorkin, Billimek, Greer, &amp; Kaplan (2011), U.S.</td>
<td>Patients with type 2 diabetes from seven outpatient clinics (N=1361)</td>
<td>Cross-sectional Questionnaire and review of medical record</td>
<td>Over half (53.2%) of Mexican Americans reported cost-related non-adherence compared to 27.2% of White and 27.6% of Vietnamese patients. Perceived financial burden was found to be associated with poor glucose control (HbA1c ≥8%), after adjusting for socio-demographic and health characteristics, but not when adjusting for non-adherence. There is a significant association between the presence of financial barriers and HbA1c. Being uninsured and non-adherent were each independently associated with HbA1c.</td>
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<td>Park, Kim, Kim, Kam, Kim, Ha, &amp; Hyun (2010), Korea</td>
<td>Patients older than 65 years who had been taking diabetes medication and who were treated at a tertiary hospital or either of two private internal</td>
<td>Cross-sectional Questionnaire-based interview</td>
<td>Medication adherence was 61.1% for tertiary hospital patients, which was significantly higher than 43.3% for private clinic patients. No significant relationship was found between the</td>
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medicine clinics for longer than six months (n = 265)

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<tr>
<th>Socio-demographics and adherence in tertiary hospital patients. Low financial level had a significantly higher adherence in private clinic patients.</th>
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<tbody>
<tr>
<td>- Regular meal habits had significantly higher adherence in private clinic patients.</td>
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<td>- Better storage conditions for drugs had significantly higher adherence in both tertiary hospital and private clinic patients.</td>
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<td>- Lower barrier to medical utilization had significantly higher adherence in tertiary hospital patients.</td>
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<td>- Higher perceived severity of diabetes complications had significantly higher adherence in private clinic patients.</td>
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<tr>
<td>- Higher self-efficacy of medication had significantly higher adherence in both tertiary hospital and private clinic patients.</td>
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<tr>
<td>- In multiple linear regression, better drug storage conditions and high self-efficacy had significantly high adherence in tertiary hospital patients. High perceived severity of diabetes complications, high efficacy, and low financial had significantly high adherence in private clinic patients.</td>
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<td>Study Authors</td>
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| Riaz, Basit, Fawwad, Ahmendani, & Rizvi (2014), Pakistan | Subjects with type 1 Diabetes Mellitus attending the Baqai Institute of Diabetology & Endocrinology (BIDE) and Diabetic Association of Pakistan (DAP), from July 2011 to June 2012 (n=194) | Cross-sectional | Clinical characteristics, anthropometric measurements, knowledge regarding type 1 diabetes along with adherence to dietary advice, physical activity and insulin were noted on a predesigned questionnaire | - One hundred and fourteen (58.5%) patients were non-adherent to dietary advice, 82 (42.3%) non-adherent to physical activity, while 88.1% respondents were non-adherent to their prescribed insulin regimen.  
- Factors associated with non-compliance were family type, occupation & educational level of respondent’s parents, duration of type 1 Diabetes Mellitus, family history of diabetes, frequency of visits to diabetic clinic, knowledge regarding diabetes, lack of family support and fear of hypoglycaemia. |
| Sankar, Lipska, Mini, Sarma, & Thankappan (2013), India | Patients aged 18 and above and diagnosed with diabetes by a modern medical practitioner with a written prescription of medication. (n=346) | Cross-sectional | Self-administered questionnaire                                         | - Prevalence of poor adherence was 74%  
- Multiple regression analysis showed that patients using oral hypoglycaemic agents, who had lower per capita monthly expenditure, those with irregular blood sugar monitoring, who received limited diabetes management instructions from health professionals, who resorted only symptomatic management, and those who did not receive family member’s help to remember medications were more likely to report poor adherence compared to their counterparts. |
<table>
<thead>
<tr>
<th>Study Authors</th>
<th>Study Details</th>
<th>Study Design</th>
<th>Data Collection Method</th>
<th>Key Findings</th>
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<tbody>
<tr>
<td>Spain, Wright, Hahn, Wivel, &amp; Martin (2016), U.S.</td>
<td>US residents ≥18 years of age diagnosed with type 2 diabetes who reported ever being prescribed at least 1 of 4 injectable medication types: exenatide once-weekly (QW), liraglutide, basal insulin, or prandial/premixed insulin</td>
<td>Cross-sectional</td>
<td>Internet-based survey</td>
<td>Among patients who delayed filling their prescription by 1 week, cost was a common reason for delay for refilling of liraglutide (63%) and exenatide QW (49%). The most commonly reported barrier to maintain injectable medication was injection concerns (42%), such as aversion to needles, pain, or needle size. Lack of perceived need was the most common reason for discontinuation for basal (47%) and prandial/premixed (44%) insulin. For liraglutide, the most common reason for discontinuation was experiencing an adverse event (33%); for exenatide QW, it was injection concerns (38%).</td>
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<td>Tan, Juliana, &amp; Sakinah (2011), Malaysia</td>
<td>Patients who had glycosylated haemoglobin (HbA1c) level of at least 6.5%, after attending a diet counselling session at the Outpatient Dietetic Clinic, HUSM, were enrolled (n=61)</td>
<td>Cross-sectional</td>
<td>Questionnaire-based interview. Anthropometric and biological measurement was taken.</td>
<td>Only 16.4% of the respondents adhered to the dietary regimen provided by dietitians. Among the 7 dietary self-care behaviours, item number 6 (eat lots of food high in dietary fibre, such as vegetable or oats) had the highest compliance rate (54.1%); whereas item number 3 (eat five or more servings of fruits and vegetables per day) had the lowest compliance rate (23.0%). There was a significant association between gender</td>
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<tr>
<td>Study (Year)</td>
<td>Participants</td>
<td>Study Type</td>
<td>Follow-up Duration</td>
<td>Findings</td>
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</table>
| Chen, Tseng, & Cheng (2013)      | Patients aged 18 years or above and who were first diagnosed with type 2 diabetes in 2002 | Cohort study                    | 7-year follow-up period from 2002 to 2009. | - Patients with high or intermediate Continuity of Care (COC) scores had higher adherence to medications than those with low COC.  
- Association between COC and healthcare outcomes was partly mediated by better medication adherence. |
| Kirman, Martin, Levin, Fanseca, Schmittdiel, Herman, & Aubert. (2015), U.S. | Patients aged 18 years and above, who were treated for diabetes with noninsulin medications in the second half of 2010 and had continuous prescription benefits eligibility through 2011 (n = 218,384) | Retrospective cohort study      | Extracted data from a large pharmacy claims database | - 69.0% of patients met the criteria for adherence using the modified definition.  
- Patients aged 65-74 years (OR=1.27, CI=1.23-1.30) and those aged 75 years and above (OR=1.41, CI=1.37-1.44) were more likely to be adherent than those aged 45-64 years old.  
- Patients who were male (OR=1.14, CI=1.12-1.16), completed graduate school (OR=1.41, CI=1.36, 1.46), and with annual income >$60,000 (OR=1.27, CI=1.23-1.30) were more likely to adherent.  
- Patients using the mail channel (OR=2.09, CI=2.04-2.13) and an additional pill a patient took per day (OR=1.22, CI=1.21-1.22) were more likely to be adherent.  
- Patients new to therapy (OR=0.39, CI=0.38-0.40), patient out-of-pocket costs for each additional $15 cost |
<table>
<thead>
<tr>
<th>Study Authors</th>
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<th>Study Details</th>
<th>Findings</th>
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<tbody>
<tr>
<td>Lee K., Muhamad Hanafiah Juni</td>
<td>Prospective Cohort</td>
<td>Review of the database from a large US-based healthcare claims company</td>
<td>Per month (OR=0.89, CI=0.89, 0.89), and patients with no endocrinologist specialist prescribers (OR=0.91, CI=0.89-0.94) were less likely to be adherent to diabetes medication.</td>
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<tr>
<td>Tunceli, Zhao, Davies, Brodovicz, Alexander, Iglay, &amp; Radican (2015), U.S.</td>
<td>Retrospective Cohort</td>
<td>Patients aged 18 years or older with a type 2 diabetes diagnosis received between 1 January 2007 and 31 March 2010 (N=133449)</td>
<td>Proportion of patients’ adherent to oral antihyperglycemic monotherapy was 59%. Results from the logistic regression demonstrate a significant increase in the likelihood of non-adherence for patients who were younger, new to therapy, on a twice-daily dose, female, or on fewer than three concomitant medications compared to their reference groups. Higher average daily out-of-pocket pharmacy expense was also significantly associated with an increased likelihood of non-adherence.</td>
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<tr>
<td>Mansyur, Rustveld, Nash, &amp; Jibaja-Weiss (2015), U.S.</td>
<td>RCT</td>
<td>Patients were randomized into the parent study, 123 to intervention and 125 to usual care</td>
<td>Compared to men, women were less likely to receive support, faced more barriers, reported less self-efficacy and had lower levels of self-care adherence. Perceived support was consistently correlated with better self-efficacy in women but not men, even though men reported higher levels of support.</td>
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Patients with diabetes, average age of 69 years (n = 45)

Cross-sectional qualitative study

Focus group discussion on system-level facilitators and system level barriers to adherence to oral hypoglycaemic agents (OHA)

- Of the 12 focus groups at five sites, 7 contained high-adherence patients.
- The system-level facilitators of OHA adherence were good overall pharmacy service, specific mechanisms for ordering and delivering medications (automated phone refill service, Web-based prescription ordering), and providing pillboxes and printed lists of current medications to patients.
- The system level barriers of OHA were poor pharmacy service quality and difficulty coordinating multiple prescriptions.

Mayberry & Osborn (2012), U.S.

Adult with type 2 diabetes (n=61) attending outpatient clinic.

Cross-sectional & Qualitative

Focus group discussion & survey

- Perceiving family members were more knowledgeable about the diabetes was associated with perceiving family members performed more diabetes-specific supportive behaviours.
- Family members’ non-supportive behaviours were associated with being less adherent to medication regimen.

### 3.3 Factors associated with the adherence among individuals with diabetes in cross-sectional study design

Fifteen studies used the cross-sectional study design to determine the factors associated with the adherence; two of these studies included the anthropometry and biological assessment in the study (Tan, Juliana, & Sakinah, 2011; Riaz Basit, Fawwad, Ahmendani, & Rizvi, 2014); four of these studies reviewed the medical record of the individual with diabetes (Ngo-Metzger, Sorkin, Billimek, Greer, & Kaplan, 2011; Currie et al., 2012; Awodele, & Osuolale, 2015). Interviews were conducted in nine of the studies to obtain information from individuals with diabetes. An Internet-based questionnaire was used in one of the studies.
(Spain, Wright, Hahn, Wivel, & Martin, 2016), and interviews were conducted with individuals with diabetes and general practitioners to understand the relationship of the individuals with diabetes and healthcare professionals (Fürthauer, Flamm, & Sönnichsen, 2013).

3.3.1 Factors associated with non-adherence

Four studies mentioned that gender was one of the factors associated with non-adherence to the management of diabetes (Tan, Juliana, & Sakinah, 2011; Awodele & Osuolale, 2015; Kalyango, Owino, & Nambuya, 2008; Currie et al., 2012), and one of the studies mentioned that females had better adherence compared to males (Khan et al., 2012). Two studies reported that increasing age was one of the factors associated with non-adherence (Ahmad et al., 2013; Awodele & Osuolale, 2015). Five studies found that educational level was associated with non-adherence among individuals with diabetes (Riaz et al., 2014; Kalyango, Owino & Nambuya, 2008; Kassahun et al., 2016; Khan et al., 2012; Al-Qazaz et al., 2011); however, one study indicated that educational level was not associated with adherence among individuals with diabetes (Awodele & Osuolale, 2015). Four studies proposed that financial status was associated with non-adherence among individuals with diabetes, as it posed a financial burden (Ngo-Metzger et al., 2011; Sankar et al., 2013; Park et al., 2010; Kassahun et al., 2016). Four studies found that insufficient knowledge or information was one of the factors associated with non-adherence among individuals with diabetes (Ahmad et al., 2013; Riaz et al., 2014; Kalyango et al., 2008; Khan et al., 2012).

3.4 Perspectives of factors associated with diabetic compliance among patients from longitudinal cohort study

Three studies reported the factors associated with diabetic compliance among individuals with diabetes. One of the studies was a seven year follow-up cohort study, while two other studies were retrospective cohort studies. Better continuity of care was associated with higher adherence to medication compared to their counterparts (Chen, Tseng, & Cheng, 2013). Two studies suggested that females were likely to be non-compliers compared to males (Currie et al., 2012; Tunceli et al., 2015). The study done by Currie et al. (2012) reported that smokers, or those having higher HbA1c, more prior primary care contacts and greater morbidity were more likely to be medication non-compliers. While the logistic regression showed that younger age, new to therapy, on a twice-daily dose, fewer than three concomitant medications, and financial burden were more likely to be non-adherents (Tunceli et al., 2015).

3.5 Intervention for the management of diabetes among patients in trials designs

The study conducted by Mansyur et al. (2015) randomized the individuals with diabetes into intervention groups that used an interactive educational programme for diabetes management containing culturally targeted video segments, educational modules and games. It was shown that females who had lower levels of self-care adherence, and received less social support, faced more obstacles, as well as less self-efficacy correlated with non-adherence (Mansyur et al., 2015). Although males were reported to receive higher levels of support, perceived support was correlated with higher self-efficacy adherence in females but not males (Mansyur et al., 2015).
3.6 Perspective of the management of diabetes among patients from qualitative research

Two studies reported the perspective of the management of diabetes strategies from individuals using focus group discussions and surveys. The study conducted by Mayberry and Osborn (2012) found that the supportive behaviour from the family was associated with higher adherence to the medication compared to those receiving less family support. Another study, conducted by Hsu et al. (2014), reported that system-level facilitators, such as good pharmacy service, specific mechanisms for ordering and delivering medications, and providing pillboxes, and printed lists of current medications to patients were associated with better adherence; however, poor pharmacy service quality and difficulty in coordinating multiple prescriptions were associated with poor adherence (Hsu et al., 2014).

4.0 Discussion

Herein, several studies found that insufficient knowledge and information on diabetes or the management of diabetes was associated with poor adherence among individuals with diabetes. This could be due to the limited diabetes information from healthcare professionals or less frequent visits to the diabetes clinics, which were the factors of poor adherence to treatment (Sankar et al., 2013; Riaz et al., 2014). This can result in poor control of the diabetes condition, which later, results in other complications (Rwegerera, 2014), and is likely to be associated with an increase in health costs (Salas et al., 2009). The result was supported by the cohort study done by Chen et al. (2013), in which individuals with diabetes who obtained a higher Continuity of Care (COC) score were more likely to have better adherence.

According to qualitative studies, individuals with diabetes perceived that social support was one of the factors associated with adherence. For example, supportive social behaviour, especially from family members, was associated with better adherence (Mayberry & Osborn, 2012). The result was supported by several cross-sectional studies that found that lack of family member support and absent of reminder from family members to take the medication were the factors associated with poor adherence (Sankar et al., 2013; Riaz et al., 2014). The study conducted by Khan et al. (2012) also mentioned that the relationship between the patient and the physician played an important role in the management of diabetes. The association was determined by the RCT conducted by Mansyur et al. (2015), who found that males were likely to receive higher perceived social support; however, perceived support was correlated with better self-care adherence among females. The results suggested that social support plays an important role among individuals with diabetes, and that a lack of adequate social support seems to be an obstacle to adherence.

4.1 Limitations

There are some limitations in this review. Firstly, this review only examined recent studies; thus, the long-term effects or trends might not be identified in the review. Second, all the studies in the review were identified through searching databases online, and, thus, it is possible that not all studies relating to the management of diabetes were included in the review. Third, most of the studies identified in the studies were cross-sectional studies, where
limited longitudinal or trials were included in the review; thus, the long-term effects or trends may not be identified in this review.

4.2 Clinical Implications

The management of diabetes provided by healthcare professionals especially emphasize providing adequate information about the management of diabetes to both those individuals with diabetes as well as their family members is needed. In addition, social support to individuals with diabetes is encouraged. Furthermore, the relationship between patients and healthcare professionals is one of the factors associated with adherence. Healthcare professionals should develop a good relationship as well as provide adequate education and support to improve adherence among individuals with diabetes.

5.0 Conclusion

Majority of the articles suggested that educational level plays an important role in maintaining the adherence of diabetic treatment. Intervention study also suggested that it is possible to increase the adherence to educational programme, especially interactive educational programme. At the same time, the supportive behaviour from the family and health care professionals also help in increasing adherence. Thus, it is suggested that health care professional should educate their patients to increase their awareness, as well as provide support to increase adherence. Future research should focus on the impact of education component, especially on the educational method use in increasing treatment adherence.

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Authors contribution

Author 1: review, writing and editing manuscript,

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