



Psychological Insulin Resistance in Adults with Type 2 Diabetes Mellitus

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Abstract

Introduction: This systematic review explores Psychological Insulin Resistance (PIR) in adults with Type 2 Diabetes (T2DM). It examines patient's perceptions of the barriers to insulin therapy initialization, and restrictions on activities of daily-living and patient perception of its relationship to disease severity.

Materials and Methods: Six online electronic databases, PubMed NCBI, CINAHL, Cochrane, EMBASE, Wiley and Ovid, were systematically searched using keyword terminology and the PICOS tool focused on the Population, Intervention, Comparison, Outcomes and Study type to identify suitable primary research studies to be included. The quality of the included literature was appraised using the Critical Appraisal Skills Program (CASP) framework for eligibility. Selected studies were reviewed, and themes were identified as appropriate areas of exploration.

Results: A total of 3,764 records were identified through database searching and 487 studies screened for inclusion consideration. Of these, 54 studies were appraised using a critical appraisal system, where 10 papers were selected for inclusion. Within these 10 studies, three main themes were identified: 1) Injection anxiety and associated pain, 2) Restrictions to daily activities and 3) Patient perceptions of disease severity.

Conclusion: Causal factors for PIR in adults with Type 2 Diabetes Mellitus were investigated. Measuring and quantifying PIR took the form of qualitative, cross-sectional, editorial and review based studies. The presentation of patient perceptions of injection fear and anxiety, restrictions to daily life and disease severity were identified as common recurring themes within the selected studies.

OPEN ACCESS

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Received Date: 18 Nov 2020

Accepted Date: 11 Jan 2021

Published Date: 18 Jan 2021

Citation:

Keeler B, Meal A, Jiwani SI, Gyasi-Antwi P, Adams GG. Psychological Insulin Resistance in Adults with Type 2 Diabetes Mellitus. *Ann Clin Diabetes Endocrinol.* 2021; 4(1): 1021.

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Keywords: Psychological Insulin Resistance (PIR); Type 2 diabetes; Insulin; Hypoglycemia

Introduction

As of 2014, there was an estimated global prevalence of 422 million adults living with diabetes [1,2]. Management of T2DM is recommended to involve lifestyle and dietary advice and structured intensifications of Oral Hypoglycemic medication Agents (OHA's) dependent upon patient symptoms, HbA1c levels, contra-indications to medication, patient tolerance and patient choice [3,4]. For patients who are unable to maintain normal blood glucose levels, are symptomatically hyperglycemic or who have not achieved an individually assigned target HbA1c whilst on second or third intensifications of OHA's, or are intolerant to oral or non-insulin based injectable hypoglycemic agents, insulin therapy should be considered unless occupational implications or obesity related co-morbidities are apparent [5,6].

Exogenous injectable insulin refers to animal or synthetic insulin administration, which is subcutaneously injected or infused. Injectable insulin is produced within a laboratory environment either through animal extraction (historically) or through recombinant DNA techniques to construct 'Human' Insulin or 'Human' Insulin analogues [7-10]. Human insulin has the same amino acid sequence as endogenous insulin whereas human insulin analogues have modified amino acid structures to result in modified characteristics [11-13]. Non-animal sourced injectable insulin can be categorized into short, intermediate and long-acting insulin based on their characteristic action profiles [14].

Psychological insulin resistance (PIR)

'Psychological Insulin Resistance' (PIR) refers to a range of barriers to insulin therapy [15]. It has a presentation of 61% of T2DM patients [16] with 40% of patients initially unwilling to use

insulin therapy resulting in a delay of 2 years of appropriate insulin therapy [17]. PIR can be divided into 3 categories: patient-related, Healthcare Professional (HCP) and societal/system factors [18].

In this research, we evaluated the causal factors for Psychological Insulin Resistance (PIR) in adults with T2DM across several health systems [19].

Materials and Methods

A three-step search strategy was applied in this review and aimed at identifying all eligible published studies. First, PubMed NCBI, CINAHL, Cochrane, EMBASE, Wiley and Ovid were searched by one of the research team. An initial limited search was first undertaken to identify articles on the topic. The text words contained in the titles and abstracts of relevant articles, and the index terms used to describe the articles were then used to develop a full search strategy for the report. The search strategy, including all identified keywords and index terms, were adapted for each included information source.

The search strategy, including all identified keywords and index terms, were adapted for each included information source. Initial keywords used in this review were: Type 2 AND/OR Type 2 Diabetes AND/OR Insulin AND/OR refusal AND/OR psychological and resistance. Second, a process of screening, supplementary search parameters were used to ensure relevance to the topic, duplicate articles and those not relevant to 'PIR' were removed (n=1002). Following abstract review, studies were excluded if they were not primary research, unrelated to Type 2 diabetes, excluded human participants, non-English language and did not have full text availability for the review [20-25].

Finally, the full text of selected citations was assessed in detail against the inclusion criteria by two independent reviewers. Reasons for exclusion of full text studies that did not meet the inclusion criteria was recorded and reported in the systematic review. Disagreements between the reviewers at each stage of the study selection process were all resolved through discussion, and by including a third reviewer if required. The results of the search were reported in full in the final systematic review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram [26]. Of the 3,764 papers generated using the keywords, a final 10 papers were included for analysis [27].

Quality appraisal

The PICOS tool focused on the Population, Intervention, Comparison, Outcomes and Study type was used to identify components of clinical evidence for systematic reviews in evidence-based medicine to facilitate a rigorous searching system [28].

Study quality was assessed and scored independently by two of the reviewers, using standardized critical appraisal instruments from the critical appraisal skills program framework tool, which enabled appraisal validity and relevance [29,30].

Results and Discussion

Within this systematic review, 10 studies were identified with three main themes: 1) Injection anxiety and associated pain, 2) Restrictions to daily activities and 3) Patient perceptions of disease severity.

Theme 1 – Injection anxiety and associated pain

Patients should be encouraged to express their feelings and

fears when starting injectable therapy and Healthcare Professionals (HCPs) should recognize signs of needle phobia and offer strategies to help manage this TREND [31-34].

Subcutaneous insulin delivery is the standard method of exogenous insulin administration, however it is commonly associated with needle phobia (Trypanophobia) and injection pain and is a predominant factor of 'PIR' in diabetes, although studies have identified that most subcutaneous injectable therapies cause only mild pain and bleeding [35,36].

Trypanophobia exists upon a spectrum from none to very severe and the resulting non-concordance with medical advice can lead to severe detrimental outcomes to patient health. Limitations to belief are that 'true' lifetime phobia diagnosis had a presentation of 3% to 4.5% whereas needle fear without diagnosis showed 10% for adult sampling [37]. Yavuz et al. [38] estimated that physicians often over estimated patient fear of pain and in turn delay insulin initialization.

Every included study presented evidence that pain and the associated fear of injection as a common causal factor in the prevalence of PIR in adults with T2DM, which correlates with previous published data [18,39-41].

In a study by Lee [19], 84.4% (399 participants) were identified with fear of pain, a reason for PIR. This correlates with other studies where 78.2% (1110), [42], 68.8% of (148) Raghavendran et al. [43], 65.5% of (29) Taylor et al. [44], 50.8% of (1,267) Polonsky et al. [45], 44% of (402) Hussein et al. [46], 43.7% of (400) Ghadiri-Anari et al. [47], 38.8% of (234) Allen et al. [16], 14% of (2,168) Kim et al. [48] and 8.1% of (461) Tan et al. [49] respectively had the same reason for PIR development.

Fear of injection and its associated pain is considered a crucial barrier to insulin initiation and previous studies identified this as the most prevalent barrier to insulin therapy in relation to demographic factors of age, sex, educational level and those with diabetic complications [50-53]. However, from the studies included within this review, there appeared to be no direct correlation between geographical location, population, ethnicity, gender and age.

Populations within this review included Indian, Iranian, American, South Korean, Malaysian, Hongkongers, Pacific Islanders and Saudi-Arabian. Studies from the Middle East presented data on fear of injection/pain ranging from 43.7% (400 participants) Ghadiri-Anari et al. [47] to 78.2% (1,110) Mostafavian et al. [42], whereas studies from South-East Asia ranged from 8.1% (461) Tan et al. [49] to 68.8% (148) Raghavendran et al. [43] and from the USA and Australian Pacific islands ranging from 38.8% (234) Allen et al. [16], to 65.5% (29) Taylor et al. [30].

The mean age from 49 years of age Raghavendran et al. [43] with 68.8% (148) participants reporting fear of pain to 67 years of age Lee [19] with 84.4% (399) regards to gender, the highest reporting study Lee [19] 84.5% (399) had a female value of 60.8% (399) and the lowest reporting study [49], 8.1% (461) had a higher female predominance of 70.3% (461).

Limitations are evident in correlating demographic data on educational level and employment status with regards to theme 1 as the selected literature, due to its broad cross-sectional nature, explores these causal factors in varying educational and employment bandings. Further regressive data analysis would be required to explore this further [54,55].

Table 1: Characteristics of included studies.

Author	Country	Type of Study	Study Setting	Sample	Results
Raghavendran et al. [43]	India	Cross-Sectional (Semi-Structured Interview and Questionnaire)	Community Hospital	Participants	Causes of Psychological Insulin Resistance
				148 via consecutive sampling	· 74.3% - Financial constraints
				Inclusion Criteria	· 68.9% - Afraid of pain
				HbA1c 9%>	· 57.4% - Fear of dependency
				One or more OHA's	· 51.4% - Unable to convince someone to administer Insulin for them
				T2DM	· 45.9% - Previously witnessed Insulin
				Demographics	· 42.6% - Social stigma
				68.9% Female, 31.1% Male	· 40% - Felt Insulin shouldn't be taken until end-stage of disease
				Mean Age 49.3 years	· 35% - Self-blame for deterioration in condition
				Majority - Muslim Faith	· Female more afraid of pain than men (82.8% to 39.1%)
				89.9% Living w/ Families	· Women perceived more social stigma than men (55.9% to 13%)
				77% Dependent financially on Families	· Homemakers perceived more social stigma than counterpart (63.5% to 27.1%)
				75.7% w/ multiple Co-morbidities.	· Those with illness duration more than 10 years perceived more social stigma than counterparts (54.4% to 32.5%)
40% - Home Makers	· No associated correlation between perception of dependency				
Hussein et al. [69]	Saudi-Arabia	Cross-Sectional (Semi-Structured Interview and Questionnaire)	Primary Care Clinic	Participants	Causes of Psychological Insulin Resistance
				402 via inclusion criteria invitation	· 74.1% - Using Insulin means end stage disease
				Inclusion Criteria	· 47% - Injections require the help of others
				T2DM	· 44% - Injections are painful
				Over 30 years of age	· 29% - Insulin restricts daily activities
				Demographics	· 22% - Insulin treatment is not necessary
				62.2% Female, 37.8% Male	· 19% - OHA compliance means I don't need insulin
				37.8% 51-60 years of age	· 17% - Using insulin means a failure to self-care
				32.1% Uneducated	· 17% - Insulin causes anxiety due to complexity
				76.1% HbA1c 7%>	· 12% - Insulin increases body weight
					· 9% - Insulin can cause health problems
					· 8% - Using Insulin means addiction for life
					· 7% - Using insulin makes you different to others
	· 4% - Insulin causes hypoglycaemia				
Mostafavian et al. [42]	Iran	Cross-Sectional (Semi-Structured Interview and Questionnaire)	Outpatient Clinic	Participants	Causes of Psychological Insulin Resistance
				1110 clinic attendees	· 78.2% - Taking Insulin is painful
				Inclusion Criteria	· 74.4% - I am afraid of using a needle
				T2DM	· 34.5% - Insulin is expensive
				18 > years of age	· 30% - Will have to give up activities
				Non-Insulin therapy	· 21.8% - Increased risk of hypoglycaemia
				Demographics	· 18.2% - I will be more dependent on my Doctor
				77.3% Female, 22.7% Male	· 18.2% - My family will be more concerned about me
				Mean age – 56.1 years of age	· 17.3% - My health will deteriorate
				95.5% married	· 16.4% - Difficulty injecting right amount at the right time.
				82.7% Diagnoses 10> years	· 14.5% - Insulin means I have failed to self-care
				73.6% Family history of Diabetes	· 11.8% - Insulin decreases my self confidence
				68.2% Primary level or no formal education	· 11.8% - Insulin causes blindness and Renal failure
	· 9.1% Insulin is embarrassing				
	· 34.5% - Insulin is expensive				
	· 7.3% - Insulin will cause weight gain				
	· 7.3% - People will see me as a sick person				
	· 5.5% - Unable to fulfil my responsibilities				
	· 5.5% - Insulin will take up a lot of time				

				Participants	Causes of Psychological Insulin Resistance
Kim et al. [48]	South Korea	Observational (Questionnaire Secondary analysis of medical data)	Multi-Centre Hospitals	2168 clinic attendees	Patient Factors
				Inclusion Criteria	· 51.6% - Inconvenience
				T2DM	· 48.2% - Fear of Injection
				20> years of age	· 31.1% - Think 'it is the end of life'
				2 or more OHA's	· 14.0% - Concern about injection pain
				HbA1c 8% > (in last 6 months)	· 7.2% - No confidence in glucose control
				Demographics	· 2.9% Concern about hypoglycaemia
				67.3% Male , 32.7% Female	· 1.5% - Concern about weight gain
				Mean age – 57 years of age	· 1.5% - Prefer oral drugs
					· 1.2% - Prefer diet and exercise
					· 1.0% - Inability to self-inject
					Physician Factors
					· 33.6% - Patient refusal
					· 26.5% - Concern about compliance
					· 14.2% - Concern about hypoglycaemia
					· 12.2% - Controllable with oral therapies
					· 6.0% - Patients lack Diabetes knowledge
	· 3.9% - Need to follow up before initiation				
	· 3.0% Lost patient to follow up				
	· 2.6% - Diet change is needed				
	· 2.3% - Lack of time to explain				
	· 2.1% Concern about weight gain				
	· 1.6% - Lack of efficacy				
	· 1.2% - Comorbidity concerns				
	· 0.7% - Physicians decision				
	· 0.6% - Lack of patients will				
Allen et al. [16]	USA	Cross-Sectional (Questionnaire, Secondary Data analysis and 4 Diabetes Education focus groups)	Hospital	Participants	Causes of Psychological Insulin Resistance
				234 hospital attendees	· 89.6% - Want to try other options first
				Inclusion Criteria	· 83.6% - Would mean my diabetes has got worse
				30-70 years of age	· 43.4% - Reluctancy to inject in public
				HbA1c 7.5% >	· 38.8% - I would be scared of needle pain
				Able to speak and write in English	· 38.8% - Worried about weight gain
				Demographics	· 35.8% - Worried about hypoglycaemia
				Mean Age 56.6 years of age	· 22.4% - I don't think I could learn the technique
				Mean duration of disease – 8.4 years	· 20.7% - Too busy to add another demand
				Mean Body Mass Index – 34.5	· 16.4% - Financial difficulties/ Health Insurance complications
				Mean HbA1c – 8.8%	· 11.9% - I have seen others get serious complications
				Female 58% , Male 42%	
				80.1% Caucasian	
				10.1% Hispanic	
				59.7% - Married	
				40.3% - High School Education or below	

Taylor et al. [44]	Torres Islands (Australia)	Cross-Sectional (Questionnaire, Interview, and Secondary Data Analysis)	Primary Care Clinic	Participants	Causes of Psychological Insulin Resistance as Insulin Treatment Appraisal Tool (ITAS)- ITAS
				197 from disease registry	· 86.2% - People see me as a sicker person
				Inclusion Criteria	· 79.3% - Injecting insulin is embarrassing
				Those contained on the Torres Island T2DM register.	· 75.9% - Taking Insulin means me diabetes is worse
				197 participants for Data Analysis	· 75.9% Failure to manage diabetes with OHA's and diet
				29 participants (Insulin Naïve) Interviewed	· 65.5% - Injecting insulin is painful
				Demographics	· 62.1% - Taking Insulin means my health will deteriorate
				Female – 60.8 female,	· 58.6% - Afraid of injecting with a needle
				Male – 39.2%	· 44.8% - difficult to inject the right amount
				Mean Age – 60.6%	· 37.9% - taking insulin helps prevent complications
				Mean BMI – 32.5	· 34.5% - Taking insulin makes my life less flexible
				Mean duration of disease – 8.87 years	· 34.5% - I would have to give up enjoyed activities
					· 31.0% - Insulin improves my energy levels
	· 27.6% - Managing insulin takes up time and energy				
	· 27.6% - Insulin helps maintain blood glucose level				
	· 27.6% Insulin makes me more dependent on my doctor				
Lee et al. [18]	Hong Kong	Cross-Sectional (Questionnaire)	Outpatient Clinic	Participants	Causes of Psychological Insulin Resistance using ITAS tool (Insulin Users to Insulin Naïve)
				· 399 clinic attendees	· 89.4% to 75.8% - Helps to control blood glucose
				Inclusion Criteria	· 66% to 85.2% - Insulin indicates Diabetes has gotten worse
				· T2DM as per WHO classification for more than 6 months	· 46.8% to 66.8% - More dependent on Doctor
				· Over 30 years of age	· 44.7% to 73.3% - Life is less flexible on Insulin
				· Chinese Ethnicity	· 38.3% to 75.7% - Risk of hypoglycaemia
				· Canton or Mandarin Speaker	· 36.2% to 71.8% - Insulin causes weight gain
				· Mental Capacity	· 31.9% to 67.2% - My health will deteriorate
				Demographics	· 29.8% to 51.3% - Injecting is embarrassing
				· Female 60.8%, Male – 39.1%	· 27.7% to 74.9% - Difficult to inject correctly
				· Mean Age – 67.7 years of age	· 19.1% to 65.3% - Takes time and energy
				· 71% up to Primary School level education	· 17% to 51.1% - Giving up activities I enjoy
				· 4.9% Tertiary level education or above	· 10.6% to 61% - Difficult to fulfil responsibilities
Tan et al. [49]	Malaysia	Cross-Sectional (Questionnaire)	Public Health Clinic	Participants	Causes of Psychological Insulin Resistance using
				· 461 systematic random sampling	· 85.4% - Lack of confidence
				Inclusion Criteria	· 72.2% - Belief that Insulin causes blindness or renal complications
				· T2DM	· 72.2% - Restrictive to daily and work-life balance
				· Managed under Kubang Pasu Public Hospital Clinic Care	· 70.8% - Insulin would mean Diabetes now 'serious'
				Demographics	· 69% - sense of failure to manage condition independently
				· Female 70.3%, Male – 29.7%	· 68.1% - Fear of pain from injection
				· Mean Age – 56 years of age	· 59.6% - Fear of hypoglycaemia
				· Mean duration of disease – 5.3 years	· 58.8% - Cost of Insulin
				· Mean HbA1c – 8.79%	· 49.4% - Lack of family support to administer
				· Malay National – 94.6%	· 36.3% - Insulin causes vision problems
				· Unemployed – 65.1%	· 21.6% - Fear of skin scarring from injection
				· Primary or no formal education	· 17.5% - Embarrassing to inject in public
	· 54.2%				

				Participants	Causes of Psychological Insulin Resistance using
Ghadiri-Anari et al. [47]	Iran	Cross-Sectional (Questionnaire)	Hospital	· 400 clinic attendees	· 43.7% - Fear of injection
				Inclusion Criteria	· 14.2% - Hardship from insulin injection
				· T2DM 1 year or more	· 7.4% - Cost of insulin
				· 18 years of age or over	· 6.4% - Continuous dependency to insulin
				· HbA1c – 8% or more	· 5.4% - Fear of hypoglycaemia
				· Participant on maximum tolerated OHA's	· 5.4% - Limitation of daily works
				· Insulin deemed necessary	· 3.8% - Fear of social stigma
					· 3.8% - Fear of weight gain
				Demographics	
				· Female 69.3%, Male – 30.7%	
· Mean Age – 57.9 years of age					
· Mean duration of disease – 10.0 years					
Polonsky et al. [45]	USA	Cross-Sectional (Questionnaire, Interview, and Secondary Data Analysis)	Diabetes Conference	Participants	Causes of Psychological Insulin Resistance using (Unwilling to Willing Insulin users)
				· 1267 conference attendees	· 58.1% to 39.7% - I'm not confident I can handle the demands of Insulin therapy
				Inclusion Criteria	· 56.1% to 41.6% - Insulin would restrict my life, harder to travel and eat out.
				· T2DM	· 55% to 33.6% - Insulin therapy would mean I have failed
				· Attending Diabetes Conference on 'Taking Control of your Diabetes'	· 53.1% to 42.6% - Once you start Insulin you can never quit.
				Demographics	· 50.8% to 30.2% - It would be too painful
				· Female 65.8%, Male – 34.2%	· 49.3% to 37.9% - Insulin might cause hypoglycaemia
				· Mean Age – 57.4 years of age	· 46.7% to 35.4% - Taking insulin means my diabetes will become more serious
				· Mean duration of disease – 6.9 years	· 41.5% to 21.9% - It wouldn't be fair; I've done everything I was supposed to.
					· 16.7% to 8% - Insulin can cause problems like blindness

Key: Y = YES; CT = CANNOT TELL; N = NO

In a study by (Kruger et al. 2015), ways of reducing the perceived perception of fear and anxiety in patients were identified. Firstly, through identifying patients likely to exhibit avoidance behaviors and reporting previous negative experiences with needles through employment of open-ended questioning and the use of tools such as 'diabetes fear of injecting' and 'self-testing questionnaires' during the data gathering phase of consultation. Secondly identifying appropriate needle selection, involving the patient within the clinical rationale for the decision and finally provision of improved education, practical simulation and monitoring self-injectors on a regular basis [56-58].

Theme 2 – Restrictions to daily life

Insulin replacement therapies should support a flexible lifestyle with minimal restrictions Silver et al. [59] the flexibility of which is defined by the lowest requirement of EBG level monitoring and HCP consultations and the ability to vary injection preparation, dose and frequency as determined by shared decision making Kalra et al. [60].

Previous studies identified a range of negative patient attitudes towards insulin therapy in relation to personal and social consequences with regards to perceived inflexibility, unfeasibility, impracticality and unacceptability. An example of this being the perceived loss of personal freedom and enjoyed activities, set prandial and injection times, increased responsibility and reduced confidentiality of disease as determinants of PIR [18,40,41].

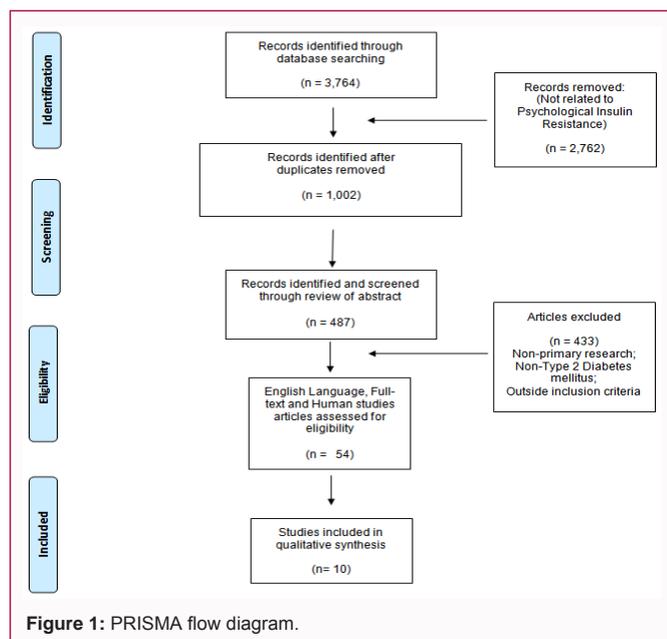
Each of the selected studies presented evidence of perceived negative attitudes towards insulin therapy on participant daily-living. It was therefore decided to thematically present these into general

personal restrictions to daily routines and the dependency on others as a result of insulin initiation [61-63].

Only a small number of studies reported time management specifically as a barrier to insulin initiation. This includes Taylor et al. [30], Allen et al. [16] and Mostafavian et al. [42] with study population 27.6% of 29, 20.7% of 234 and 5.5% of 1110, respectively. Previous studies established that lack of time was the biggest determinant in PIR prevalence with patients unable to manage an injectable insulin regime in their daily routine NG et al. [18].

The restriction towards personal and work-life and the surrender of enjoyed pastimes were reported in studies by Tan et al. [49] 72.2% of 461 , Polonsky et al. [45] 56.1% of 1,267, Kim et al. [48] 51.5% of 2,168, Lee et al. [19] 39% of 399, Taylor et al. [30] 34.5% of 29, Mostafavian et al. [42] 30% of 1,110, Hussein et al. [46] 29% of 402 and Ghadiri-Anari et al. [47] 5.4% of 400. Anecdotal evidence indicated that perceived lifestyle changes would be more impactful than the time management factors, with the ongoing prevalence of pen devices as opposed to cartridges and vial/syringe systems [64].

With regards to study population, the three studies located in the Middle East presented the lowest reporting of insulin therapy impacting and restricting daily life but had a high reporting of fear of dependency upon family members to support insulin administration, Raghavendran et al. [43] (50% of 148 participants), Hussein et al. [46] 47% of 402, (Mostafavian et al. [42] 18.2% of 1,110. The exception to this was Taylor et al. [30] and Lee [19] identifying perceived increases in dependency on HCP's respectively 46.8% of 399 and 27.6% of 67,



respectively.

The selected studies identified no correlation between gender and perceived restrictions to daily-living, Tan et al. [49] being the highest reported result being 70.3% female (461) and Kim et al. [48] reporting 3rd highest result being 67.3% male (2,168). However, in relation to reported perception of increased dependency on others (relative or HCP) the highest resulting studies all had higher proportion of predominantly female samples [42,43,46].

With regards to age, the studies with the highest and lowest reported perceptions of the impact of insulin on daily-living were from studies all sharing the same mean age Tan et al. [49] and Ghadiri-Anari et al. [47] of 57 years of age implying no definitive correlation. However, with regards to perceived dependency on HCP's, studies with the older mean ages Lee et al. [19] (67 years of age) and Taylor et al. [30] (60 years of age) reported high levels of dependency on HCP's upon initiating insulin whereas the youngest mean age of 49 years Raghavendran et al. [43] reported the highest levels of dependency upon relatives ('nearly half').

Reducing these negative perceptions is important in promoting adherence to advised therapies and by promoting flexible insulin regimes matched to the lifestyle of patients as part of a wider program of person-centered care, HCPs can achieve useful management aims [60,65].

Theme 3 – Patient perceptions of disease severity

Gherman et al. [41] indicated 47% of participants in one study expressed a view that their conditions were not severe at present and insulin therapy was not indicated [66]. A recurring theme from previous published data and selected studies here was that the initiation of insulin was indicative in deterioration in participants' condition and that this had connotations with end-of-life, self-blame and a sense of failure upon the participant with regards to pre-insulin and oral hypoglycemic treatments [67]. Insulin was historically seen as 'last resort' therapy and therefore restrictive lifestyles and disease progression [42,68].

All selected studies here, reported a sense that participants

perceived their disease had 'worsened' or that their health would 'deteriorate' from insulin initiation or that injecting insulin would indicate 'end of life' and that it should only be initiated at the 'end of life'.

This was reflected in the high reporting of these beliefs across most of the selected studies: Allen et al. [16] 83.6% of 234, Taylor et al. [44] 75.4% of 29, Tan et al. [49] 70.8% of 461, Hussein et al. [46] 74.1% of 402, Lee [18] 64.8% of 399, Polonsky et al. [45] 46.7%, Raghavendran et al. [43] 40.0% of 148, Kim et al. [48] 31.1%, Mostafavian et al. [42] 17.3%, Ghadiri-Anari et al. [47] 6.4% of 400.

There is a potential for some correlation with regards to study population samples, as 3 of the 4 lowest reporting perceptions for this theme are located in the Middle East. However, this does not correlate with previous themes in conjunction with higher female gender sampling [42,43,47].

Although not definitive, correlation between population, age or gender demographics studies included in this review, the highest reporting studies included data collection and secondary analysis of medical records in a predominantly female, middle aged samples [1,16] (Table 1).

Participants relayed first-hand accounts from previous encounters with a relative who was prescribed insulin but then died shortly afterwards. Relatives and friends who associated the initiation of insulin with increased diabetes severity and likelihood of death and perceptions that from HCP statements and diabetes medication pathways that insulin was used as a 'last resort' Tan et al. [70] thereby reinforcing this assumption [52,69,70].

Conclusion

This systematic review explored the causal factors for Psychological Insulin Resistance (PIR) in adults with Type 2 Diabetes Mellitus. Measuring and quantifying PIR took the form of qualitative, cross-sectional, editorial and review based studies. The presentation of patient perceptions of injection fear and anxiety, restrictions to daily life and disease severity were identified as common re-occurring themes within the selected studies. All studies used 'Insulin Treatment Appraisal' (ITAS) and 'Barriers to Insulin Treatment Questionnaire' (BITQ) tools or modified versions to gather data from participants exclusively, or in addition to further secondary data analysis. Further studies using longitudinal methodologies and consideration of HCP aspects of PIR would allow for comprehensive exploration of the topic.

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