

Individual, healthcare professional and system-level barriers and facilitators to initiation and adherence to injectable therapies for type 2 diabetes

Bryne, Jo; Willis, Andrew; Dunkley, Alison ; Fitzpatrick, Claire; Campbell, Sandra; Sidhu, Manni; Choudhary, Pratik; Davies, Melanie; Khunti, Kamlesh

DOI:

[10.1111/dme.14678](https://doi.org/10.1111/dme.14678)

License:

Other (please specify with Rights Statement)

Document Version

Peer reviewed version

Citation for published version (Harvard):

Bryne, J, Willis, A, Dunkley, A, Fitzpatrick, C, Campbell, S, Sidhu, M, Choudhary, P, Davies, M & Khunti, K 2021, 'Individual, healthcare professional and system-level barriers and facilitators to initiation and adherence to injectable therapies for type 2 diabetes: a systematic review and meta-ethnography', *Diabetic Medicine*, vol. 39, no. 1, e14678. <https://doi.org/10.1111/dme.14678>

[Link to publication on Research at Birmingham portal](#)

Publisher Rights Statement:

This is the peer reviewed version of the following article: Byrne, J. et al (2021), Individual, healthcare professional and system-level barriers and facilitators to initiation and adherence to injectable therapies for type 2 diabetes: A systematic review and meta-ethnography. *Diabet Med*, which has been published in final form at <https://doi.org/10.1111/dme.14678>. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Use of Self-Archived Versions. This article may not be enhanced, enriched or otherwise transformed into a derivative work, without express permission from Wiley or by statutory rights under applicable legislation. Copyright notices must not be removed, obscured or modified. The article must be linked to Wiley's version of record on Wiley Online Library and any embedding, framing or otherwise making available the article or pages thereof by third parties from platforms, services and websites other than Wiley Online Library must be prohibited.

General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

Individual, healthcare professional and system-level barriers and facilitators to initiation and adherence to injectable therapies for type 2 diabetes: A systematic review and meta-ethnography

Jo Byrne¹, Andrew Willis², Alison Dunkley², Claire Fitzpatrick², Sandra Campbell¹, Manbinder S Sidhu³, Pratik Choudhary², Melanie J Davies^{1,2}, Kamlesh Khunti²

¹ Leicester Diabetes Centre, University Hospitals of Leicester NHS Trust, Leicester, United Kingdom

² Leicester Research Centre, University of Leicester, Leicester, United Kingdom

³ Health Service Management Centre, University of Birmingham, Birmingham, United Kingdom

Corresponding author:

Dr Jo Byrne

jo.l.byrne@uhl-tr.nhs.uk

Manuscript word count: 4991/5000

Abstract word count: 247/250

Conflicts of interest: KK has served an advisor/consultant for: Amgen, AstraZeneca, Bayer, NAPP, Lilly, Merck Sharp & Dohme, Novartis, Novo Nordisk, Roche, Berlin-Chemie AG / Menarini Group, Boehringer-Ingelheim, Sanofi-Aventis and Servier. He has served as a speaker or a member of a speakers bureau for: Amgen, AstraZeneca, Bayer, NAPP, Lilly, Merck Sharp & Dohme, Novartis, Novo Nordisk, Roche, Berlin-Chemie AG / Menarini Group, Boehringer-Ingelheim, Sanofi-Aventis and Servier. Additionally, he has received grants in support of investigator and investigator initiated trials from AstraZeneca, Novartis, Novo Nordisk, Sanofi-Aventis, Lilly, Servier, Pfizer, Boehringer Ingelheim and Merck Sharp & Dohme. PC received personal fees and/or research support from Novo Nordisk, Lilly, Sanofi, Insulet, Medtronic, Dexcom and Abbott. MJD has acted as consultant, advisory board member and speaker for Novo Nordisk, Sanofi, Lilly and Boehringer Ingelheim, an advisory board member and speaker for AstraZeneca, an advisory board member for Janssen, Lexicon, Servier and Gilead Sciences Ltd and as a speaker for Napp Pharmaceuticals,

Mitsubishi Tanabe Pharma Corporation and Takeda Pharmaceuticals International Inc. Also, MJD has received grants in support of investigator and investigator initiated trials from Novo Nordisk, Sanofi-Aventis, Lilly, Boehringer Ingelheim, AstraZeneca and Janssen. All other authors report no conflicts of interest.

Novelty Statement

What is already known?

- Engagement with insulin treatment for type 2 diabetes affected by individual, healthcare professional and system-level barriers.
- Ethnicity, gender and age associated with delayed initiation and poor adherence.
- Glucagon-like peptide-1 (GLP-1) analogues overcome barriers such as hypoglycaemia, weight gain and injection frequency.

What has this study found?

- Explored diverse views (since the introduction of GLP-1 analogues) relating to barriers and facilitators across different social/cultural identities.
- New qualitative synthesis and conceptual evidence

What are the clinical implications of the study?

- Provides a model and clinical tool to help patients, health practitioners and policy makers identify barriers and facilitators.

Acknowledgements

This project is funded by/supported by the National Institute for Health Research (NIHR) Applied Research Collaboration East Midlands (ARC EM), previously known as Collaboration in Leadership in Applied Health Research and Care East Midlands (CLARHC-EM). The views expressed in this publication are those of the authors and not necessarily those of the National Institute for Health Research or the Department of Health and Social Care.

Abstract

Aims

To review and synthesise the contemporary qualitative evidence, relating to individual, healthcare professional (HCP) and system-level barriers and facilitators to injectable therapies in people with type 2 diabetes, and evaluate (using an intersectional approach to explore the diverse perspectives of different identities) whether views have changed with treatment and guideline advancements.

Methods

A meta-ethnography approach used. Eight databases searched from the years 2006 (GLP-1 analogues introduced) to February 2021. Study selection (using a pre-defined inclusion criteria), quality appraisal and data extraction, conducted independently by two reviewers.

Results

Screened 7143 abstracts, assessed 93 full text papers for eligibility and included 42 studies - using data from 818 individuals with type 2 diabetes and 160 HCPs. Studies covered a diverse range of views from HCPs and individuals, including those relating to older adults and people from ethnic migrant backgrounds, and 10 studies rated moderate to strong research value. Key themes abstracted: barriers (physical/psychological/social) and facilitators (motivation/ capability/opportunity).

Commented [MS(oAHR1): I would not use abbreviations in an abstract; unless the journal is happy with this.

Conclusions

The first synthesis of contemporary qualitative data to adopt an intersectionality approach and explore diverse views relating to barriers and facilitators that influence engagement with injectable treatments for type 2 diabetes. A model is presented to help patients, health practitioners and policy makers identify barriers and facilitators and understand the complex interplay of physical, psychological and social factors involved when prescribing injectable therapies. Despite advances in injectable treatments and guidelines, findings highlight the many barriers that still exist and show how strongly held culturally-specific health beliefs of people from diverse socio-economic and ethnic backgrounds can become substantial obstacles to treatment.

Key words

Type 2 diabetes, insulin, glucagon-like peptide-1, medication adherence, treatment refusal, attitude to health, attitude of health personnel, qualitative research.

Introduction

Qualitative evidence has highlighted individual, healthcare professional (HCP) and system-level barriers as reasons for delaying the initiation of insulin, to improve glycaemic control, in people with type 2 diabetes [1]. In addition, demographic factors associated with delayed initiation and poor adherence include age [2], gender [2, 3] and ethnicity [4, 5]. In recent years, glucagon-like peptide-1 (GLP-1) analogue injectable treatments for type 2 diabetes have been introduced to overcome some of the potential barriers associated with insulin initiation and adherence, such as weight gain, frequency of injections and hypoglycaemia.

Qualitative evidence reviews in this area have focused on insulin initiation [1] and medication adherence [6, 7]. However, to our knowledge, there has not been a specific qualitative evidence review which has explored barriers and facilitators to injectable therapies in type 2 diabetes since the implementation of the new GLP-1 analogue injectable treatments. Furthermore, there has been no such review that has explored the diverse views of different social groups and identities. Therefore, the aim of this review was to use a meta-ethnography approach to understand the complex processes involved with initiating and adhering to injectable therapies (exploring any differences between views on insulin and GLP-1 analogues) in people with type 2 diabetes, especially among specific ethnic, gender and socio-economic groups.

Commented [MS(oAHR2)]: Socio-economic groups?

Originally developed by Noblit and Hare [8], meta-ethnography is an increasingly used method for synthesising qualitative data [9-11]. It allows reviewers to reinterpret conceptual data (i.e. themes) created by authors of primary studies, in order to use the findings of individual studies to produce a new synthesis and conceptual evidence. Subsequently, this reinterpretation can be used to inform and shape future policy and guidance. Furthermore, this method allows, where possible, for an intersectional approach to be applied to identify diverse views and key differences on the same topic from the perspectives of individuals from different ethnic/social groups

Methods

The study has been reported in line with new meta-ethnography guidance [12] and involves a seven-phased iterative synthesis process (Fig. 1)

'Figure 1 to be inserted here'

Search strategy and processes

The Patient/Population, Intervention, Comparison, Outcomes, Study type (PICOS) search tool was used and a table of keywords, synonyms and medical subject headings (MeSH) was created to inform our search strategy (Table 1). In addition, a research filter was used: designed and validated to identify relevant qualitative studies from a variety of health topics while minimising the yield of false positives [13]. The strategy was adapted to conduct comprehensive searches of eight electronic databases (Web of Knowledge, MEDLINE, EMBASE, ASSIA, Science Direct, SCOPUS, CINAHL and APA PsycNET) for published, English language studies (qualitative or mixed methods reporting separate qualitative findings) from the years 2006 (introduction of GLP-1 analogues) to February 2021. The databases covered research literature from across clinical, nursing and social sciences. Title/abstract lists from the searches were imported into Endnote X7 and screened for duplicates to produce a master title/abstract list. In addition, a manual, supplementary search of the reference lists of relevant papers was done to identify any further citations. Grey literature was not searched as our aim was to find the key peer-reviewed studies that would offer a conceptual insight.

'Insert Table 1 here'

Selecting primary studies

Using inclusion/exclusion criteria (Table S1), two experienced reviewers (JB and CF) independently screened the master title/abstract list to select studies for full text review. Also, any study that presented an element of uncertainty, due to lack of detail in the abstract, was put forward to clarify its inclusion. The reviewers independently read the full texts in parallel to determine inclusion. Any discrepancies were resolved via discussion with a third reviewer (AD); no additional information was sought from authors of included papers.

Reading and data extraction approach

JB and CF independently extracted data from the selected studies. This was an iterative process whereby the papers were critically read and the following study information was extracted: bibliographical details (title, author/s, publication date); aims; setting; limitations/biases; theoretical background; sampling approach; participant characteristics (e.g. number, sex, age, ethnicity, socio-economic status, injectable therapy status); data collection methods; data analysis approach; quality assessment; key themes.

Identifying themes from the primary studies required close line-by-line reading from across the full paper. Schütz's notion of first- and second-order constructs was used to describe the thematic data extracted [14]. First-order constructs involved direct quotes from individuals and HCPs relating to the barriers and facilitators to initiation and/or adherence to injectable therapies for type 2 diabetes; second-order constructs involved the primary author's conceptual understanding of these first-order themes.

The papers were read in chronological order to help appreciate any subtle changes that may have occurred since the introduction of newer injectable therapies. In addition, the Critical Appraisal Skills Programme (CASP) checklist [15] was used to quality assess the studies. Data extraction and thematic coding were managed with NVivo 11 software and all data were added, independently by each reviewer, to two Excel spreadsheets: 1) study characteristics and, 2) first- and second-order constructs. The reviewers then compared this data for accuracy and reached an agreement on first- and second-order constructs, resolving any discrepancies via the third reviewer (AD).

Process for determining how studies are related

JB and CF compared studies to determine contexts, research design and participant characteristics. In particular, to identify intersectionality, they compared gender, age, ethnicity and socio-economic status. Also, the type of injectable therapy and stage of treatment (i.e. pre- or post- initiation) were considered. Themes were compared, regarding the views of individuals and HCPs, to identify similarities and differences, and to uncover possible relationships across the data. In addition, the time contexts, relating to the introduction of newer injectable therapies, were considered.

Three types of synthesis can be used in a meta-ethnography: a reciprocal translational analysis involves the 'translation' of similar themes from individual studies into one another to evolve overarching concepts; in contrast, a refutational synthesis involves exploring and explaining contradictions between individual studies; finally, a line-of-argument synthesis involves building up a whole contextual picture of the subject in question - putting an interpretative order on the similarities and differences arising from the studies [8]. All studies were considered, and a reciprocal translational analysis synthesis was determined because themes across the studies were similar and re-occurring despite the advances in treatments.

Process of translating studies

A draft matrix was created to act as a visual discussion aid and to explore (via a constant comparing and sorting process of the shared meaning of the themes identified from the primary studies) how the second-order constructs related to each other. JB and CF did this individually and then collaboratively using NVivo 11 to manage the process.

Synthesis process

To create third-order constructs (higher level interpretative findings) [14], JB drafted interpretative constructs based on the similarities between all the reviewed studies. This involved further re-reading of the original studies and matching the second-order constructs with their respective patient quotes (first-order constructs) to allow the findings to be re-conceptualised and to generate a new interpretation (line-of-argument). The line-of-argument synthesis involved building up a whole conceptual picture based on the findings from the individual studies, to develop a visual model to explain how barriers and facilitators to injectable therapies influence individuals' behaviour. All draft constructs were shared with other members of the review team (CF, AD, and AW), and collaboratively discussed until a consensus was reached on the interpretations. In addition, feedback was sought via our patient research groups and professional networks, from interested individuals with type 2 diabetes (7 individuals all on injectable therapies – 4 females; 2 South Asian and 5 white British; aged 62 - 78 years) and HCPs delivering diabetes care (3 general practitioners, 6 diabetes specialist nurses, 1 practice nurse, 1 pharmacist and 2 diabetologists) respectively. This allowed us to seek diverse perspectives and develop more nuanced interpretations for each of the first-, second- and third-order constructs identified, especially with regard to intersectionality.

Results

Figure 2 shows the results of the study selection process using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flowchart [16]. Table S2 details the references for all the included studies which are labelled [S1] to [S42].

'Figure 2 to be inserted here'

Characteristics of the studies included are presented in Table S3. A total of 7143 abstracts were screened, with 93 full text papers assessed for eligibility and 42 papers included in the review - using data from 818 individuals with type 2 diabetes and 160 HCPs. Globally, studies were conducted in primary (n=25) and/or secondary care (n=28) across six continents – Europe [S1-S16], North America [S11, S17-S23], South America [S20], Oceania [S24-S28], Asia [S27-S40] and Africa [S41-S42]. Four studies were delivered in more than one country [S11, S20, S28, S29]. The same participant cohorts were used in some individual studies reported by the same research teams. The majority of the studies (n=29) focused on individuals' views, seven on HCPs' views and three included both. Two studies included people being treated with a GLP-1 injectable therapy, but no views about this specific treatment were explored [S13, S16]; subsequently, only data relating to views about insulin therapy were available for analysis and synthesis. The studies covered a diverse range of views from both HCPs and individuals with type 2 diabetes, including those relating to older adults [S19] and people from African [S2, S7, S22], South Asian [S5, S9, S10, S14], Nepalese [S27, S28], Chinese [S18] and Hispanic [S21] migrant backgrounds. From an intersectionality perspective, four studies were identified which explored the views of people with type 2 diabetes belonging to an ethnic migrant group from a lower socio-economic background - Brown et al explored health beliefs of UK African-Caribbeans [S2]; Khan et al explored the refusal of insulin among UK Bangladeshis [S5]; Noakes explored perceptions about insulin among UK black Africans and African-Caribbeans [S7]; and, Hu et al looked at the meaning of insulin in Hispanic US immigrants [S21]. There were no papers exploring intersectionality which related to gender.

All studies collected data using either semi-structured interviews and/or focus groups. The CASP assessment revealed a general improvement in study quality from 2015 onwards, and the two reviewers (JB and CF) agreed that ten studies could be considered to have moderate to strong research value. Table S4 shows the outcome of the translation - the second-order themes translated from the original second-order constructs (i.e. the authors' explanations of key themes) and the reviewers' synthesised translations (third-order constructs). The interpretative findings of this translation (categorised as either individuals' or HCPs' views) and synthesis are presented below.

Third-order constructs

Commented [MS(oAHR3): Do we need to provide any examples of the range of HCPs in the sample?

The third-order constructs conceived from the data were categorised as either barriers or facilitators to insulin treatment, as there were no studies with views about GLP-1 injectable treatments to include in the synthesis. . A barrier was interpreted as something that prevented an individual or HCP from accepting the need for insulin treatment, and could occur within any of the following three contexts that influence behaviour: physical, psychological and social. A facilitator was something that helped an individual or HCP to overcome barriers in order to accept the necessity of starting and maintaining treatment, and involved competency, opportunity and motivation to bring about the desired behaviour.

Physical barriers

Individuals' views

Physical barriers were the perceived negative side-effects of injections and insulin treatment and the physical harms caused to individuals. These perceptions were driven by both the real and the imagined (often based on anecdotal evidence and/or knowing other people with diabetes) experiences of injectable treatments and were identified across all ethnic groups.

For many individuals, negative injection side-effects were a major barrier. Injections were associated with pain [S11, S12, S18, S20, S23, S26, S31, S35, S38] , skin-damage [S12, S17, S26, S32, S35, S41] and infection [S29, S33]. The pain caused by needles was a real concern for many individuals and difficult for them to accept. In addition, bruising and scarring could cause distress and anxieties about body-image. Moreover, the risk of infection and the further complications caused by this posed a significant threat for some. Alongside this issue, were the negative side-effects associated with insulin. The risks of hypoglycaemia [S5, S7, S11, S14, S15, S20, S21, S23, S25, S26, S29, S35, S36, S37, S41] and weight gain [S3, S5, S11, S14, S20, S21, S23, S29, S32, S37, S38] were the main anxieties expressed. In particular, the experience of having a 'hypo', or seeing someone else experiencing one, was a traumatic event that people wanted to avoid. Long-term insulin use was sometimes considered to cause organ damage [S21, S31, S32, S35, S40], especially kidney damage, and reduced male sexual activity (e.g. loss of libido and erectile dysfunction) was also linked to insulin injections [S17, S30].

HCPs' views

HCPs were aware of the many negative side-effects of injections and insulin. For some doctors, old age and the physical deterioration of health presented a complexity of problems that, from a professional perspective, often caused a barrier to treatment, with some questioning whether the benefits of initiating insulin would outweigh the risks in elderly patients with complex health needs [S1, S19, S30].

Psychological barriers

Individuals' views

The psychological burden of insulin treatment involved concepts such as fear, failure and loss of control and was consistently expressed across studies and across all ethnic groups. These accumulated in negative reactions often reinforced by poor communication from HCPs.

For many individuals, the fear of needles and injections was the greatest barrier to initiating insulin treatment. Many people reported extreme emotional responses and distress at having to inject themselves, and often felt completely overwhelmed [S1, S3, S5-S7, S11-S14, S20, S21, S23, S29, S31, S33, S35, S37, S39-S41]. Failure and loss of control were also a concern. The need for insulin treatment often led people to blame themselves due to a loss of control over their diets and a failure to follow the recommendations of their healthcare providers [S5, S22, S23, S26, S34]. This perceived failure and loss of control could manifest as guilt and cause much grief. Furthermore, such reactions were frequently confounded by unsympathetic and threatening reactions from others, such as family and doctors, who individuals felt blamed them for their condition [S5, S22, S32]. Another psychological barrier was fear of death. Insulin treatment signaled a 'last resort' for many people who believed, often due to limited knowledge and misconception, that their diabetes had reached a stage of severity in which no other options were available [S14, S20-S22, S25, S27, S29, S31, S40].

For some individuals, another psychological barrier was low self-efficacy and motivation which led to a lack of confidence to perform injections without any medical supervision. Self-injection was seen as a complex process and concerns were expressed about 'doing the right thing' [S35, S42]. For some, this low self-efficacy led to a lack of motivation to carry out the task properly, and a complacent response towards the necessity of taking insulin injections [S22]. Negative interactions with HCPs (both in primary and secondary care) could create a barrier of mistrust that affected a person's opinion about insulin treatment. This mistrust often stemmed from a negative interaction with a doctor that had upset an individual [S3, S36]. The initiation of insulin often accumulated in frustration and anger towards the doctor: some people were angry and denied that they even had a problem [S22], some wanted to blame the doctor for not acting sooner [S22] and others were critical of their doctor's over-reliance on medications [S23].

HCPs' views

Many HCPs recognised the concerns expressed by individuals, such as fear of needles and injections, loss of control and low self-efficacy. They also recognised emotional reactions, such as denial, which could cause a barrier to treatment [S29, S30, S34]. From their perspective, some doctors saw the considerable effort required to motivate and educate people to enable self-injection as a barrier [S19] and expressed feeling overwhelmed [S24]. Moreover, among some HCPs, there was recognition that some doctors themselves created a barrier to effective engagement with insulin treatment, by showing a lack of empathy with regard to their patients' emotional needs that led to mistrust [S4, S30].

Social barriers

Individuals' views

Social barriers to insulin treatment arose from the restrictions it placed on everyday life. For many, insulin treatment posed a significant threat and inconvenience to their daily work and leisure due to the frequency of injections. For those on insulin, activities such as socialising, exercise, travel and work could be restrictive, and careful forward planning was required to avoid problems from occurring when insulin was needed [S10-12, S14, S20, S23, S29, S31, S32, S37, S40, S41]. Moreover, in a Kuwait-based study, inconvenience and annoyance were experienced by insulin-pump users treated for type 2 diabetes, especially when it came to activities such as going through airport security, swimming, wearing clothes and sleeping [S38].

Social networks played a key role in how insulin treatment was perceived. The reaction of others was a fundamental barrier and the social embarrassment of injecting in public was voiced by many people across all ethnic groups [S6, S7, S10, S12, S14, S17, S20, S22, S23, S25-S27, S29, S31, S36]. However, this embarrassment was strengthened by the stigma of injections that was present in different ethnic cultures across countries. In non-Western cultures, such as South Asian [S9, S10], Chinese [S18], Afro-Caribbean [S7] and Hispanic [S21] cultures, injections were often negatively associated with dangerous diseases and drug taking, and taking insulin was often considered to bring dishonor and shame to a family. Moreover, this stigma was sometimes extended beyond insulin injections to a more general social stigma, which involved negative attitudes and mistrust towards Western medicine. This was often expressed through anecdotal arguments and narratives which claimed the health benefits of non-evidence based beliefs in such things as traditional herbal medicine in Chinese, Nepalese and African cultures [S18, S28, S32] and warmer climates in Afro-Caribbean cultures[S2].

Religious beliefs and practices (such as a strong belief in the power of prayer and religious fasting) presented as more barriers to insulin treatment. Religious beliefs could influence behaviours and attitudes towards insulin treatment. In particular, it was prevalent within some UK African/Afro-Caribbean communities where people would refuse insulin, choosing instead to believe in the power of prayer and deities [S7]. Also, the use of holy water, instead of medication, and fasting had impacted on adherence to treatment in an Ethiopian-based study [S42].

Starting insulin treatment and maintaining a regime sometimes required a level of dependency on others to support giving injections and monitoring blood sugars. Unfortunately, caregivers were not always available, which became another barrier to the initiation of insulin [S5, S22]. System-level barriers involving access and affordability were also a concern. In some countries like Malaysia and Ethiopia, financial constraints often affected people's ability to access and store treatment. Diabetes treatments were not always free or available and had to be privately purchased (often from unchecked suppliers), which became a significant financial burden [S32, S41, S42]. In addition, it was noted that some African-Caribbean people living in the Caribbean could not afford fridges for the proper storage of insulin [S7]. People from different countries and ethnic groups expressed frustration at the lack of information and education opportunities [S3, S7, S12, S21, S22, S40 S42], as well as the lack of continuity of care [S29]. Even when group education was available, a lack of educator skills, to address concerns and fears, was seen as a barrier by some participants in a UK-based study [S16]. Finally, time constraints on consultations with doctors were also viewed as a barrier to effective communication about treatments [S29].

HCPs' views

The powerful influence of 'others' beliefs about insulin and injections was seen as a barrier by HCPs, and was perceived as being accentuated in poorer ethnic communities where there was a high prevalence of diabetes. In a UK study, HCPs caring for South Asian communities felt their South Asian patients were more likely to be influenced by other people's views relating to the social stigma of insulin and injections [S9].

Dependency on others also concerned HCPs, especially doctors. Illiteracy and poor sight were highlighted problems that increased dependency [S1, S34]. Some doctors expressed anxiety about patients depending on them, and worried about their professional responsibility to ensure that these individuals could cope with their insulin treatment [S19].

HCPs across countries also felt that there were a number of barriers within their healthcare systems which prevented people accessing the necessary information and treatments. Both time and language constraints were perceived as a problem. Language often presented as a barrier to effective communication, with people from ethnic migrant groups not able to communicate effectively in the language of their host country. This was expressed by HCPs looking after ethnically diverse populations in the UK and Malayasia, and hindered effective engagement with their patients to explore barriers to treatment [S9, S30]. Some HCPs also felt there was a lack of appropriate professional guidance and training to support their patients effectively [S30].

Motivation/capability/opportunity facilitators

Individuals' views

For individuals, capability and opportunity were intrinsically related to each other in facilitating the perceived health benefits that would motivate them to engage with insulin treatment. In turn, motivated individuals were more willing to accept the identified barriers of injecting insulin and participate in self-management behaviour [S6, S17, S20].

Capability involved people acquiring the appropriate knowledge and developing the skills to be well informed about insulin treatment and know how to manage injections effectively. Globally, educational opportunities for improving capability varied considerably depending on the healthcare system and the resources available. Group support was viewed as a positive way to learn about insulin treatment and address some of the fears, concerns and misconceptions that people may have [S3, S7 S16, S24]. Sharing experiences with peers offered group participants a supportive environment to learn from each other [S16]. Individuals considered successful group education to be when the facilitators addressed negative insulin beliefs via practical demonstration and practice of injection technique [S16]. Also, some felt that the provision of printed information was useful to reinforce key messages [S13, S16], but did not want to be overburdened with leaflets [S16]. Moreover, the importance of strong facilitation skills to manage individuals' expectations within a group was highlighted [S16]. For people from ethnic migrant backgrounds, tailoring educational content (i.e. such as providing translated printed information) and ethnic concordance with facilitators, who were more relatable, were perceived as being beneficial components of group support [S7].

Another key opportunity for people to learn was through the support of their doctor. The doctor-patient relationship was considered to be a key factor for promoting the effective initiation of insulin treatment. A positive doctor-patient relationship was achieved through having continuity of care and a supportive and approachable doctor with strong communication skills [S17, S20, S21, S26, S29, S40, S41]. Individuals also pointed to their social network for opportunities to learn and be supported with their insulin treatment. For example, in South Asian communities, the involvement of family members was sometimes necessary because many people depended on them to support and help with decisions about their health [S10].

Individuals expressed an expectancy for non-injectable diabetes medications, like an insulin abletor patch, to make treatment less painful and more acceptable to them [S17,S20] . Participants with type 2 diabetes, who used insulin pumps, considered the pump to be a more acceptable delivery method as it was less painful than the injections and pens, and facilitated better self-monitoring of blood sugars [S38].

HCPs' views

Like their patients, HCPs were motivated to initiate insulin treatment when they were able to perceive and accept the health benefits it provided. For some, this meant a need for good clinical evidence before they were willing to initiate treatment [S19]. Diabetes specialist nurses were more likely to advocate the use of clinical guidelines to simplify the process of initiation, whereas doctors would take a more cautious approach to using guidelines when clinical evidence was limited [S24].

Some HCPs expressed the benefits of group education and the need to familiarise people with insulin injections prior to initiation [S4, S19]. When available in primary care, doctors spoke of the relief and benefit of having access to diabetes specialist nurses to carry out the initiation of insulin treatment with patients [S19]. Doctors were aware of their own reluctance to carry out this task, and the advantage of having a trained nurse meant more patients were been successfully started on insulin [S24].

For individuals from ethnic migrant backgrounds, some HCPs felt there was an advantage of using HCPs from the same ethnic origin to overcome language or other cultural barriers [S9]. In South Asian communities, the involvement of family members in the decision-making process was seen as being beneficial [S9]. Finally, in countries where insulin treatment was not always free, the need for government support to make it more affordable and accessible was highlighted as a system-level facilitator [S29,S40].

Line-of-argument synthesis

Figure 3 is a visual representation of the line-of-argument synthesis generated by the interpretative findings. It shows how the relationships between the third-order constructs influence engagement with an injectable treatment for type 2 diabetes. Our synthesis shows how an individual is affected by physical, psychological and social barriers which influence their capability and opportunity to engage. These barriers are not separate entities but interact with each other depending on the different circumstances of the individual. Similar barriers exist across different social groups, but some barriers, particularly among individuals from ethnic migrant backgrounds, result from deeply entrenched culturally-specific health beliefs that form part of an individual and their community's identity but conflict with the accepted beliefs of the dominant culture of their host country, leading to resistance and hesitancy. These culturally-specific beliefs are often accentuated in poorer communities due to the higher prevalence of diabetes which creates more opportunities for individuals to be influenced by the experience of others and develop misconceptions. To overcome these barriers, an individual requires capability and opportunity facilitators (often limited by the socio-economic status of an individual) that will work together to address potential barriers and, moreover, motivate them to engage in a mental evaluative process that will lead to the desired behaviour.

Commented [MS(oAHR4): ...who may be misinformed"
Misconceptions is too big a statement I feel.

'Figure 3 to be inserted here'

Discussion

Summary of the findings

We believe this is the first synthesis of qualitative data that has adopted an intersectionality approach to explore diverse views that influence engagement with injectable therapies for the treatment of type 2 diabetes. The synthesis identified individuals' and HCPs' perspectives relating to barriers and facilitators which influence engagement with insulin treatment, as despite a move towards using GPL-1 analogue injectable therapies for type 2 diabetes, no studies were found that explored views relating to these treatments. The synthesis shows that each individual's experience is shaped by various physical, psychological and social barriers, to a greater or lesser degree, depending on the individual's circumstances. To overcome these barriers and bring about optimum engagement with treatment, an individual needs knowledge, skills (capability) and opportunities facilitated by HCPs.

From an intersectional perspective, our findings illustrate that socio-economic status limits capability and opportunity to effectively address barriers, and globally between countries there is much variation in system-level facilitators. Moreover, individuals' experiences from diverse ethnic and socio-economic backgrounds are often shaped by strong culturally-specific health beliefs that are a key part of their communities and often conflict with the beliefs of Western evidence-based health systems. Against this background, our research suggests that a person-centered, workforce and system-level approach is needed, which seeks to address intersectionality and the burden of treatment to achieve more successful engagement with insulin and other injectable treatments. Our model identifies the interplay between specific barriers and facilitators involved in engaging people with insulin treatment, and fits well with the COM-B model of behaviour – a widely used non-specific model which identifies what needs to change in order for a behaviour change intervention to be effective [17]. Both models identify three factors that need to be present for any behaviour to occur: capability, opportunity and motivation. These factors are continually interacting and the target behaviour (optimising engagement with insulin treatment) is viewed as part of a dynamic system based on the various physical (e.g. adverse effects of insulin), psychological (e.g. fear of needles) and social barriers (e.g. public embarrassment), and the facilitators (e.g. access to group education) that an individual experiences.

The interplay between these barriers and facilitators also relate to the Necessity-Concerns Framework which argues that engagement with medication is a decision-making process driven by considering perceptions about the necessity of a medication against concerns about potential adverse effects [18]. Our findings show how cultural-specific beliefs, fears and practical concerns influenced individuals' perceptions and the decisions they made with regard to engaging with treatment.

The concept of ‘psychological insulin resistance’ has been well documented in the literature and has been defined as involving a range of multifactorial psychological and social issues that can be interrelated [19]. Our findings demonstrate the high incidence of this resistance across countries and diverse groups - with side-effects, fear of injections, fear of failure and death, daily inconvenience and stigma being pre-dominant barriers. In particular, our findings highlight how this resistance is often heightened in ethnic migrant communities with a high prevalence of diabetes, due to culturally-specific health beliefs which are not evidence-based. In the UK, this cultural resistance to Western medical treatment is currently being observed with COVID-19 vaccine hesitancy among people from ethnic migrant groups (highest among black and South Asian populations), and follows a historical trend of lower vaccine uptake in these groups [20].

Strengths, limitations and reflexivity

Our review has a number of strengths. It involved a multi-disciplinary team and looked at both individuals’ and HCPs’ views across a wide range of countries with findings that have international significance. In addition, the concept of intersectionality was also explored to find out how different identities contribute to the conceptual evidence base. The review used PRISMA [16] and eMERGE guidance [12] to ensure robust reporting, and a comprehensive search was carried out of key databases to identify papers, with a quality assessment (using the CASP checklist [15]) revealing a sufficient number of papers rated as having moderate to strong research value. Also, data extraction and theme translation were initially carried out by independent reviewers to improve transparency and trustworthiness of the findings.

All draft interpretations of the constructs were refined by sharing with the wider review team and a stakeholder group made up of professionals and individuals from ethnically and socio-economically diverse backgrounds. This was important to increase the credibility and relevance of the findings. Furthermore, stakeholder involvement helped counteract any unintentional bias which may have occurred as a result of the reviewers' backgrounds (both white, middle-class females educated to degree level and above in health disciplines). Additionally, some bias may have occurred with the interpretation of the data as the lead reviewers were already familiar with the COM-B model. All studies were included in the synthesis and contributed to the line-of-argument. However, several studies used the same patient cohort for different qualitative analyses, which limited the range of experiences. Also, from an intersectional perspective, important contextual data was often not attributed to individuals' quotes, and the impact of context on the findings was not always adequately described to explore differences between the participants within studies. Disappointedly, we found no studies which explored gender differences relating to views about injectable therapies. Moreover, despite the introduction of GLP-1 analogues, only two UK studies included people on this injectable therapy but did not explore views relating to this treatment. This lack of conceptual data for GLP-1 analogues is interesting and may be a reflection of the higher drug-acquisition costs that have prevented widespread global use in real-world clinical settings [21]. Since the introduction of the injectable GLP-1 analogue, , there is now an oral GLP-1 analogue available which could provide another option to treat type 2 diabetes without the need for injections [22]. The fear of injections and the expectancy for less invasive treatment options were both themes highlighted in our findings, which suggests the new oral GLP-1 may be more acceptable to many people.

Conclusion

This meta-ethnography provides a comprehensive insight into how barriers and facilitators affect engagement with insulin treatment. Our model provides a useful tool for individuals, HCPs and policy makers to identify barriers and facilitators, and understand the complex interplay of the physical, psychological and social factors involved when initiating and adhering to injectable therapies. In particular, our synthesis draws attention to the experiences of people from diverse socio-economic and ethnic migrant backgrounds and how strong cultural-specific health beliefs, especially in poorer communities, can be a substantial barrier to treatment. Moreover, it highlights the need for quality self-management education to address both general and culturally-specific barriers expressed by individuals. Regarding further research, there is still a paucity of qualitative conceptual evidence relating to GLP-1 analogue injectable therapies. Furthermore, now there is an oral GLP-1 available, more qualitative studies will be required to assess the impact of this new drug on the treatment of type 2 diabetes. Finally, research to offer further insight into the diverse views of individuals from varied social groups is needed to provide a richer data set of qualitative experiences including gender, age, ethnicity and socio-economic status.

References

1. Ng CJ, Lai PS, Lee YK, Azmi SA, Teo CH. Barriers and facilitators to starting insulin in patients with type 2 diabetes: a systematic review. *Int J Clin Pract.* 2015;69(10):1050-70.1
2. Egede LE, Gebregziabher M, Hunt KJ, Axon RN, Echols C, Gilbert GE, et al. Regional, Geographic, and Ethnic Differences in Medication Adherence Among Adults with Type 2 Diabetes. *Ann Pharmacother.* 2011;45(2):169-78.
3. Lerman I, Díaz JP, Iburguenoitia ME, Pérez FJ, Villa AR, Velasco ML, et al. Nonadherence to insulin therapy in low-income, type 2 diabetic patients. *Endocr Pract.* 2009;15(1):41-6.
4. Millett C, Gray J, Saxena S, Netuveli G, Khunti K, Majeed A. Ethnic disparities in diabetes management and pay-for-performance in the UK: the Wandsworth Prospective Diabetes Study. *PLoS Med.* 2007;4(6):e191.
5. James GD, Baker P, Badrick E, Mathur R, Hull S, Robson J. Ethnic and social disparity in glycaemic control in type 2 diabetes; cohort study in general practice 2004-9. *J R Soc Med.* 2012;105(7):300-8.
6. Brundisini F, Vanstone M, Hulan D, DeJean D, Giacomini M. Type 2 diabetes patients' and providers' differing perspectives on medication nonadherence: a qualitative meta-synthesis. *BMC Health Serv Res.* 2015;15:516.
7. Psarou A, Cooper H, Wilding JPH. Patients' Perspectives of Oral and Injectable Type 2 Diabetes Medicines, Their Body Weight and Medicine-Taking Behavior in the UK: A Systematic Review and Meta-Ethnography. *Diabetes Ther.* 2018;9(5):1791-810.
8. Noblit GW HR, Hare R. *Meta-ethnography: Synthesizing qualitative studies*: Sage; 1988.
9. Campbell R, Pound P, Morgan M, Daker-White G, Britten N, Pill R, et al. Evaluating meta-ethnography: systematic analysis and synthesis of qualitative research. *Health Technol Assess.* 2011;15(43):1-164.
10. Britten N, Campbell R, Pope C, Donovan J, Morgan M, Pill R. Using meta ethnography to synthesise qualitative research: a worked example. *J Health Serv Res Policy.* 2002;7(4):209-15.
11. Campbell R, Pound P, Pope C, Britten N, Pill R, Morgan M, et al. Evaluating meta-ethnography: a synthesis of qualitative research on lay experiences of diabetes and diabetes care. *Soc Sci Med.* 2003;56(4):671-84.

12. France EF, Cunningham M, Ring N, Uny I, Duncan EAS, Jepson RG, et al. Improving reporting of meta-ethnography: the eMERGe reporting guidance. *BMC Med Res Methodol.* 2019;19(1):25.
13. Sub-Group IIS. <https://sites.google.com/a/york.ac.uk/issg-search-filters-resource/home>
14. Schütz A. *Collected papers.* The Hague: Martinus Nijhoff; 1962.
15. CASP Appraisal Programme. CASP qualitative checklist 2018 [Available from: <https://casp-uk.net/wp-content/uploads/2018/01/CASP-Qualitative-Checklist-2018.pdf>].
16. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol.* 2009;62(10):1006-12.
17. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci.* 2011;6:42.
18. Horne R. *Representstions of medication and treatment: advances in theory and measurement.* Netherlands: Harwood Academic Publishers. 1997; 155-188.
19. Brod M, Kongsø JH, Lessard S, Christensen TL. Psychological insulin resistance: patient beliefs and implications for diabetes management. *Qual Life Res.* 2009 Feb;18(1):23-32.
20. Razai MS, Osama T, McKechnie DGJ, Majeed A. Covid-19 vaccine hesitancy among ethnic minority groups. *BMJ.* 2021 Feb 26;372:n513.
21. Scherthaner G, Shehadeh N, Ametov SV, Bazarova AV, Ebrahimi F et al. Worldwide inertia to the use of cardiorenal protective glucose-lowering drugs (SGLT2i and GLP-1 RA) in high-risk patients with type 2 diabetes. *Cardiovascular Diabetology.* 2020;23. 10.1186/s12933-020-01154-w.
22. Robinson J. First oral GLP-1 treatment for type 2 diabetes recommended by EMA. *The Pharmaceutical Journal*, February 2020;Online:DOI:10.1211/PJ.2020.20207658

Barriers and facilitators to injectable therapies

Table 1: Search strategy

Search criteria	Description	MeSH (Medline)	Keyword search terms (truncation or wildcard operators for each database will be used to allow for different spellings, alternative endings and placement of words)
Population	People with type 2 diabetes	exp DIABETES MELLITUS, TYPE 2/	Type two, type 2, type II, non-insulin dependent diabetes, DMT2
Intervention	Injectable therapies	exp Glucagon-Like Peptide 1/ad, tu exp Incretins/ad, tu exp INSULIN/ad, tu [ad = administration & dosage, tu = therapeutic Use]	Glucagon like peptide 1, GLP 1, exenatide, liraglutide, lixisenatide, dulaglutide, incretin, insulin (<u>combined with</u> treatment or therapy or administration or dose or human or analogue or biphasic or basal or protamine or isophane or injection or pen or delivery or devise, or system or pump or syringe or needle)
Comparison	NA	NA	NA
Outcomes	Patient and healthcare professionals beliefs/experiences with regard to the injectable therapy initiation and adherence	exp Medication Adherence/eh, px exp TREATMENT ADHERENCE AND COMPLIANCE/eh, px exp Treatment Refusal/eh, px exp Patient compliance/eh exp Treatment Refusal/eh exp ATTITUDE TO HEALTH/eh exp ATTITUDE/eh "ATTITUDE OF HEALTH PERSONNEL"/eh exp Health Knowledge, Attitudes, Practice/eh exp Health Behavior/eh (eh = ethnology, px = psychology)	Health professional, health personnel, doctor, medic, physician, nurse, patient, client people, individual (<u>combined with</u> experience or belief or attitude or perception or view or opinion or feelings or knowledge or concerns or barriers or obstacles or hurdles or triggers or facilitators or benefits or anxieties or problems or difficulties or limitations or deterrents or complications or motivation) Medication (<u>combined with</u> adherence or compliance, concordance or initiation)
Study type	Qualitative or mixed methods studies	exp QUALITATIVE RESEARCH/ exp INTERVIEW/ exp Nursing Methodology Research	ISSG research filter used [31, 32] Mixed methods

Legends

Figures

- Figure 1 The seven phrases of a meta-ethnography
- Figure 2 PRISMA flowchart
- Figure 3 A model of how barriers and facilitators influence engagement with injectable treatments in type 2 diabetes

Supplementary Tables

- Table S1 Inclusion/exclusion criteria
- Table S2 References for included studies
- Table S3 Characteristics of studies
- Table S4 Barriers and facilitators to injectable therapies thematic synthesis