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'For me, it didn't seem as drastic a step as being controlled by insulin': A qualitative investigation of expectations and experiences of non-insulin injectable therapy among adults with type 2 diabetes

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Running Title: Expectations and experiences of non-insulin injectable use

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Conflicts of interest

EHT has undertaken research funded by an unrestricted educational grant from Abbott Diabetes Care, AstraZeneca, and Sanofi; received speaker fees from Novo Nordisk and Roche to Australian Centre for Behavioural Research in Diabetes (ACBRD); and served on an advisory board for AstraZeneca. JF has received unrestricted educational grants for research support from Roche, Sanofi, and Medtronic. EEH has undertaken research funded by Sanofi. JAMN has undertaken research funded by Sanofi and Eli Lilly/Boehringer Ingelheim. JES has received honoraria for advisory boards and lectures from AstraZeneca, Eli Lilly, Novo Nordisk, Sanofi, Mylan, Boehringer Engelheim, MSD, Abbott and Pfizer. TS serves on advisory boards for Novo Nordisk and Liva Health Care, and is

currently on a EIT Health research grant held jointly with Roche Diagnostics. JS has served on advisory boards for Medtronic, Roche Diabetes Care, and Sanofi Diabetes; her research group (Australian Centre for Behavioural Research in Diabetes [ACBRD]) has received honoraria for this advisory board participation and has also received unrestricted educational grants and in-kind support from Abbott Diabetes Care, AstraZeneca, Medtronic, Roche Diabetes Care, and Sanofi Diabetes. JS has also received sponsorship to attend educational meetings from Medtronic, Roche Diabetes Care, and Sanofi Diabetes, and consultancy income or speaker fees from Abbott Diabetes Care, AstraZeneca, Medtronic, Novo Nordisk, Roche Diabetes Care, and Sanofi Diabetes. All other authors have no conflicts of interest to declare.

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Authors contribution

EHT and JSp conceived of the study and designed the interview schedule with input from TD, JF, VH, JMN, JES, and TS. EHT and JSc conducted interviews and qualitative analysis. All co-authors reviewed example interview quotes and discussed the results. EHT prepared the first and subsequent drafts of the manuscript. All authors reviewed the manuscript, and approved the final version for submission.

Novelty statement

- Much research has examined oral and insulin treatment perceptions among adults with type 2 diabetes, and their role in timely treatment uptake and use. This novel qualitative study explored expectations and experiences of injectable GLP-1RA therapy among Australian adults.

- Concerns about injectable GLP-1RA therapy are similar to established salient psychological concerns about insulin, such as injections symbolising worsening health.
- Expected weight-related benefits and treatment convenience are key motivators of treatment uptake and continuation.
- GLP-1RA injectable experience may reduce concerns about injectable treatment in general, and provide opportunity for health professionals to address concerns about future insulin use.

Abstract

Background: This qualitative study aims to explore beliefs, attitudes, and experiences of injectable glucagon-like-peptide-1 receptor agonists (GLP-1RAs) use and discontinuation, as well as attitudes to further injectable treatment intensification, among adults with type 2 diabetes (T2D).

Methods: Nineteen in-depth semi-structured interviews lasting (mean±SD) 45±18 minutes were conducted, face-to-face (n=14) or via telephone (n=5). Transcripts were analysed using inductive template analyses. Eligible participants were English-speaking adults with T2D who had recently initiated (≤3 years) GLP-1RA treatment.

Results: Participants were aged 28-72 years, who predominantly lived in metropolitan areas (n=15), and had experience of daily (n=11) and/or once-weekly (n=13) GLP-1RA formulations. Six participants had discontinued treatment and seven had trialled two or more formulations. Expectations and experiences of GLP-1RA were related to the perceived: 1) symbolism and stigma of injectable diabetes treatment; 2) ease of injectable administration and device preferences; 3) treatment convenience and social impact; 4) treatment efficacy and benefits, and; 5) negative treatment side-effects. Some participants reported increased receptiveness to insulin therapy following their GLP-1RA experience, others emphasised unique concerns about insulin beyond injectable administration.

Conclusions: This study provides a novel understanding of expectations and experience of non-insulin injectables among Australian adults with T2D. Our data suggest expectations may be informed by attitudes to insulin therapy, while perceived treatment benefits (e.g. weight-related benefits, administration frequency) may motivate uptake and ongoing use despite concerns. Experience of GLP-1RA injections may impact receptiveness to future insulin use.

Keywords: type 2 diabetes, psychology, medication taking, injections, GLP-1RA

Introduction

Clinical guidelines for the management of type 2 diabetes (T2D) recommend person-centred care, with consideration of the individual's treatment perceptions, preferences, abilities and social context.^{1,2} Research has demonstrated an association between beliefs about medications, receptiveness to and timely intensification of medicines, as well as optimal self-management among adults with T2D.³ An awareness of common beliefs about and barriers to diabetes medication use may assist health professionals to support people with diabetes and facilitate treatment adjustment when indicated.

Beliefs about and experience of oral diabetes medications and insulin therapy have been extensively explored, while limited research has examined attitudes toward glucagon-like-peptide-1 receptor agonists (GLP-1RAs).³ GLP-1RAs are a newer class of medication, predominantly administered via injection. An oral GLP-1RA formulation (Semaglutide) has been developed recently, but is not yet globally available. GLP-1RAs are associated with glucose reductions, weight loss, cardiovascular benefits, and do not directly cause hypoglycaemia, although short-term gastrointestinal side-effects are common.^{1,4} The degree of beneficial and adverse effects differ between GLP-1RA formulations, as does administration frequency (once daily, twice daily, once weekly), timing (e.g. 30 minutes before meals, same time each administration), and injectable device features (e.g. needle size, preparation).⁴

Treatment satisfaction with injectable GLP-1RAs (across formulation types) has been demonstrated to be higher than, or at least equal to, comparator treatments in clinical trials⁵ and large observational studies.⁶⁻⁸ Quantitative research has identified (perceived or experienced) favourable treatment attributes, including treatment efficacy, potential for weight loss, lack of associated hypoglycaemic episodes, and convenience.⁹⁻¹⁴ While the most common reasons for discontinuing injectable GLP-1RA are a perceived lack of need, preference for oral medications, adverse gastrointestinal events, and lack of efficacy.¹⁴⁻¹⁶ In contrast, a study of UK physicians identified "patient fear of insulin" as a reason for GLP-1RA prescription.¹³ A large discrete choice experiment study among adults with T2D (N=875; 58% non-insulin treated) identified a preference for either once-weekly or once-daily injectable GLP-1RA treatment over insulin therapy.¹⁷ Nonetheless, hypothetical willingness to initiate a once-weekly injectable treatment, such as GLP-1RAs, is as low

as 31%,¹² suggesting similar 'psychological resistance' to that reported for insulin therapy.¹⁸ Salient psychological barriers to insulin use include, for example, perceived stigma, self-blame or feelings of failure associated with treatment progression.^{19,20} However, limited qualitative studies have explored potential psychological barriers to injectable GLP-1RAs.¹⁴ Research to date has largely used structured, pre-defined questions with fixed response options (e.g. questionnaires, discrete choice experiments) that provided no opportunity to elicit unknown barriers to, or experience with, injectable GLP-1RA treatment. One, recently published, interview study explored primary reasons for continuation or discontinuation of injectable GLP-1RA among 36 American adults.¹⁴ However, the largely quantitative data presented focuses on common facilitators and challenges of treatment, drawing on responses to a pre-determined list and open-ended questioning, rather than providing a rich narrative of the beliefs, attitudes and experiences of participants. Therefore, the aim of this study was to undertake an in-depth exploration of the expectations and experiences of adults with T2D regarding GLP-1RA use, and (dis)continuation, as well as attitudes toward further injectable treatment intensification.

Methods

A qualitative study with semi-structured face-to-face or telephone interviews were conducted with adults with T2D in Victoria, Australia. Ethics approval was obtained from Deakin University Human Research Ethics Committee (HEAG-H 86_2018). Participant recruitment and interviews took place between May to November 2018.

Participants and recruitment

Participants were eligible for this study if they were: English-speaking adults (aged 18+ years) living in the state of Victoria (Australia), who self-reported a diagnosis of T2D and that they had commenced (though not necessarily continued) GLP-1RA therapy in the past three years. This included twice daily (TD) and once weekly (OW) exenatide, dulaglutide (once weekly), and liraglutide (once daily), which were all approved and available in Australia during the study period. Australian blood glucose management guidance for T2D suggests consideration of GLP-1RA therapy as a second- or third-line approach when HbA1c remains above target.² Participants were recruited into the study via:

- 1) Diabetes Victoria and The Australian Centre for Behavioural Research in Diabetes (ACBRD) websites, social media (Twitter, Facebook) and e-newsletters.
- 2) an email sent to National Diabetes Services Scheme registrants who were listed as: consenting to being contacted via email for research opportunities, adults (≥ 18 years) living in Victoria,

diagnosis of T2D, prescribed treatment of 'non-insulin injectable medication' in the past three years (N=1,074; open rate: n=474, 44%).

- 3) a study flyer circulated to Victorian health professionals working directly with people with T2D via their professional organisations.

Potential participants were invited to contact the research team by telephone or email to obtain study information and undergo eligibility screening. During screening, participants were asked to confirm their current and prior diabetes medications and duration of use. We aimed to interview approximately 20 people, and purposively sampled eligible potential participants to achieve an approximate gender balance; representation across a broad age range, varying GLP-1RA formulations, metropolitan and non-metropolitan residence, and; inclusion of those who have discontinued use of GLP-1RAs.

Overall, 52 enquiries were received, including eight from potential participants who were deemed ineligible (started GLP-1RA treatment >3 years prior, n=7; participant in GLP-1RA clinical trial with blinded treatment allocation, N=1), five who declined to take part, and five who made no further contact during the study period. Recruitment concluded following interviews with 19 participants, at which time the interviewers deemed that saturation of identified themes had been achieved.

Interview schedule and procedure

A semi-structured schedule was developed to elicit a narrative from participants about their experience of diabetes. The final interview schedule is summarised in Table 1, including order of topics covered and an overview of specific prompts. The interview schedule was informed by our prior qualitative research examining attitudes to insulin initiation and use employing a narrative interview approach,²¹ as well as existing literature that explores GLP-1RA preferences (largely discrete choice experiments).

Prior to the interview, participants provided written informed consent. Interviews were conducted face-to-face in a private meeting room in a non-clinical setting or via telephone. All interviews were audio recorded. The mean interview duration was 45 minutes (range: 24-81 minutes). Interviews were conducted face-to-face (n=14) or via telephone (n=5). After the interview, participants completed a short demographic questionnaire. Participants were given a \$AUD20 e-gift voucher as a token of appreciation. Interviews were facilitated by either EHT (n=8), a research fellow with a PhD in health psychology and experience in qualitative methods, or JSc (n=11), a research assistant with a psychology honours undergraduate degree. EHT and JSc took turns to lead and observe the first seven interviews to provide opportunity for later discussion, critique and refinement of both the

interview schedule and facilitation approach in order to improve data quality and reduce interviewer variation.

Transcription and analysis

Audio recordings were transcribed verbatim by an Australian transcription service, checked for accuracy by JSc, and uploaded to QSR NVivo Version 12. Inductive (data-driven) template analysis was conducted by EHT and JSc²². An initial coding framework, reflecting potential themes and/or subthemes, was formulated, reviewed iteratively and revised by EHT and JSc. Initially, two interviews were coded independently by EHT and JSc to check for inter-coder agreement, identify disagreement and revise the framework accordingly. Following refinements, a further three interviews transcripts were coded independently resulting in a high level of coding consistency ($\kappa=0.84$, agreement: 99.5%). JSc coded all remaining interviews, with input from EHT as needed. Themes relevant to the current study aim were identified. All authors reviewed the final theme names, descriptions and illustrative quotes. Participant study ID, gender (W, M), years of age (y), and GLP-1RA treatment status (current or, discontinued) are provided for all quotes reported below.

Findings

Participant characteristics

Demographic and clinical characteristics are provided in Table 2. The 19 participants, including 10 women (53%), were aged 28 to 72 years (median=64), predominantly retired/not working ($n=15$; 79%), and born in Australia ($n=14$; 74%); other countries of birth were Canada, England, Greece, Italy, Northern Ireland, with migration pre-1986. Participants reported a median diabetes duration of 10 years (range: <1-26). At the time of interview, 13 (68%) participants were taking GLP-1RAs and six had discontinued use. The median duration of use (across all GLP-1RA formulations) was 15 months (range: 5-36) for those taking GLP-1RAs, and 5.5 months (range: 1-24) for those who had discontinued. Visual inspection suggests that those who had discontinued were more likely to be women ($n=4$, 67% vs $n=6$, 46%), with a longer diabetes duration (median: 13 vs 5 years), though similarly aged (median: 64 vs 66 years old), compared to participants who were currently taking GLP-1RAs. Self-reported reasons for discontinuation were a lack of initial or sustained benefit to blood glucose or weight outcomes (ID11, 12, 20, 22, 36), severe or prolonged side-effects including nausea and vomiting (ID9, 12), incompatibility with lifestyle (ID36), and/or upcoming weight loss surgery (ID20). Seven participants (ID2, 13, 22, 24, 25, 26, 27) reported having trialed two or more injectable GLP-1RA formulations, typically commencing with TD Exenatide and subsequently a weekly formulation (Dulaglutide or OW Exenatide). Five participants currently (ID2), or previously (ID 1, 8, 9, 20), managed their diabetes with insulin. Some participants self-reported discontinuing insulin due

to a lack of necessity after aggressive early treatment following diagnosis (ID20), substantial weight loss (ID1, 8), and suboptimal insulin-taking behaviour (ID9).

Expectations and experiences of GLP-1RA

Five broad themes relating to the expectations and experiences of GLP-1RA were identified: 1) symbolism and stigma of injectable diabetes treatment; 2) administration and device preferences; 3) treatment convenience and social impact; 4) treatment efficacy and benefits, and; 5) negative treatment side-effects.

Symbolism and stigma of injectable diabetes treatment

Prior to GLP-1RA prescription, most participants (n=14) reported being unaware of non-insulin injectables for T2D. Participants reported that their knowledge of insulin therapy (regardless of whether they had previously used insulin) influenced their expectations of injectable GLP-1RAs. Participants were concerned that GLP-1RA use could symbolise worsening of health or a more serious form of diabetes; related to their belief that insulin was a last resort diabetes treatment:

“I only knew about insulin and, you know, that once you're on insulin, you're on it for life. That's what I was told and you avoid it if you can. So again that was a barrier for me...it was concerning to me to start with but she explained that it was non-insulin...” (ID24, M, 66y, current)

As this quote illustrates, some participants reported greater receptiveness when they understood that GLP-1RA was not a form of insulin:

“For me, it didn't seem as a drastic step as being controlled by insulin... (ID36, W, 63y, discontinued)

Some participants described a stigma surrounding injectable diabetes treatments. They reported concern about the potential need to inject GLP-1RA in public, being mistaken for an illicit drug user, and that they and others might regard them as a ‘sick person’:

“I was a bit depressed because, I had to have injections, you know? It reminded me, like, of a type 1 diabetic... I felt like a sick person.... the stigma around it and the labelling and... people that get injections. It's like, ‘Well, you must be sick if you get injections.’” (ID20, W, 35y, discontinued)

Administration and device preferences

Participants described being concerned initially about self-administering injections. They reported nervousness, fear of injecting themselves and fear of pain, as well as a lack of confidence in their ability to physically administer injections correctly:

“I was a bit anxious about using an injection, a needle. I wasn’t sure whether I’d be able to cope with it or not. I mean, I’ve had a lot of health issues over my lifetime, but I’ve never had to inject myself.” (ID27, W, 67y, current).

Some participants became more comfortable with their injectable treatment shortly after initiation and reported that injections hurt less than they expected, while others stated ongoing difficulties:

“I have a hard time sticking myself. I do it but I sort of try and do it without looking.” (ID5, M, 54y, current)

Participants discussed attributes of administration devices they liked and disliked including device and needle size, ease of use, and temperature control. For some, the positives outweighed the negatives:

“It’s just the [OW Exenatide] needle itself is quite large, but...But, I’m used to it, it’s a small price to pay. (ID1, W, 72y, current)

Participants who transitioned between more than one formulation reflected on their device preferences. Notably, participants reported the once-weekly exenatide device and needle were large and that preparing the solution prior to injection was frustrating and inconvenient:

“The needle didn’t scare me. It was just the stupidity of this big syringe.... I found it quite a clumsy sort of treatment...very time consuming and fiddly.” (ID13, M, 66y, current)

Treatment convenience and social impact

Participants’ expectations and experiences surrounding the impact of GLP-1RA use on their daily routine and lifestyle related typically to administration frequency (e.g. weekly versus daily) and the potential reduction in the number of daily tablets required. Weekly injections were described as more convenient than daily injections, and daily injections more convenient than taking tablets multiple times per day:

"It would be a once a week, once off, mix it up, and I'm right, and then I can go. Like, it wouldn't impact my life like having to take something and then not being able to eat, you know." (ID28, W, 28y, current)

For some, timing requirements (in relation to meals) and storage needs (i.e refrigeration) negatively impacted on spontaneity, social outings, and ability to travel:

"I just find the whole idea of going out for dinner particularly inconvenient. You've got to eat within an hour and sometimes there's been times where I've injected [TD Exenatide] before I've left the house and we get delayed... I just find it has been an issue... getting the time right..." (ID2, M 52y, current)

Treatment efficacy and benefits

Expected benefits of GLP-1RA initiation included reduced blood glucose levels, appetite suppression and weight loss. One participant suggested she had an (unmet) expectation that this combination of benefits would be the "magic" diabetes bullet:

"I thought it would work like magic and that it would bring down my sugar [blood glucose] levels and then I would lose weight... I actually thought this is going to change me... this was going to be the answer to everything I wanted with diabetes" (ID36, W, 63y, discontinued)

Participants reported anticipated weight loss as a primary motivator for commencing GLP-1RA, one which helped them overcome some of the perceived negative treatment attributes (e.g. injections; gastro-intestinal side-effects):

"I didn't really like the injection side of thing and having to do it myself and all that but put that aside... she explained to me that [GLP-1RA] would help me lose weight. I'm like, right, that's enough motivation." (ID24, M, 66y, current)

Participants positively recalled initial weight loss, appetite suppression and associated blood glucose reduction. They indicated that these clinical outcomes led to other positive benefits, such as improved emotional wellbeing, a regained sense of personal control or self-efficacy, and increased motivation for further self-care. One man said:

"That motivated me, because not only was I seeing better blood glucose results, I was seeing weight loss...all of a sudden, my enthusiasm was back. It was like somebody had waved a magic wand." (ID8, M, 56y, current)

In contrast, other participants reported unmet expectations with regard to weight loss and/or blood glucose management, resulting in disappointment and, potentially, discontinuation of treatment:

“Neither of those things [glucose and weight reduction] really happened. So, that was a bit of a let-down... Maybe it was because I was just eating too much?... I thought, ‘It’s not working. Like, I’m a fail story... I’m not a success story.’” (ID20, W, 35y, discontinued.)

As indicated above, some participants attributed treatment inefficacy (or efficacy) as partially or fully due to their own behaviour. For example, a lack of weight loss, or reduction in blood glucose, resulting from their own perceived failings to implement dietary or physical activity changes. While others attributed treatment (in)efficacy to physiological factors, such as appetite suppression leading to weight loss, or that certain medications are unsuitable for some individuals.

Negative treatment side-effects

Few participants recalled concerns about perceived negative side-effects prior to commencing GLP-1RA, while two reported worries about hypoglycaemia and thyroid tumours. Actual experience of negative side-effects varied: some participants recalled they “didn’t feel any different” (ID36) or only temporarily “off-colour” (ID24); others described gastro-intestinal side-effects such as nausea, vomiting, change in bowel movements, and lumps, bruising and/or bleeding at injection sites. Most experienced at least partial resolution of side-effects after a few weeks:

“I would literally switch from frantically starving to within a click of fingers to horrendously nauseous and then back ... and this would just go on day and night, day and night for weeks. So that was kind of horrible and it started to calm down after about three weeks, but gee that was tough... It never totally went. (ID25, W, 62y, current)

Some participants perceived that their gastro-intestinal side-effects signalled the treatment was working or that such side-effects were the mechanism behind appetite suppression and weight loss. Participants reported these side-effects to be “manageable” and/or worth the potential discomfort for the associated weight loss benefits:

“I still get a little bit of nausea, which to me, is really good, because it does put me off eating all the time... As long as the weight comes off...I will put up with anything, as long as it goes.” (ID28, W, 28y, current)

Role of GLP-1RA in promoting receptiveness to insulin therapy

Participants not currently taking insulin therapy (n=18) were asked whether their experience with GLP-1RA injections had affected their views on potential future insulin use. While some reported that they had previously been willing to inject insulin if needed, others indicated that experience with GLP-1RA use (whether positive or negative overall) had assisted them to overcome injection-related anxiety, and they would now be more confident in trying insulin:

“If that’s as bad as it [injecting] gets, other than making a few calcs in the morning of what sugar levels are and what you should be taking, then that’s not really too much drama.” (ID22, M, 64y, discontinued).

In contrast, others discussed the perceived association with disease severity or the perception of insulin as an ‘end-stage’ treatment. For some participants the experience of GLP-1RA injectable treatment did not lessen their concerns about insulin use:

“It’s not about using a needle. It’s nothing to do about using the needle. It’s about the fact that I’m now insulin dependent... I don’t want it to get to that stage. I want to put it off for as long as possible.” (ID25, W, 62y, current)

Participants also perceived insulin therapy as more inconvenient and burdensome due to additional self-care activities, such as more frequent (and potentially public) injections, dose adjustments, glucose monitoring, and dietary changes, as well as the potential increased risk of hypoglycaemia:

“You have to monitor your blood glucose much more frequently and there's a significant risk of hypos.” (ID11, M, 72y, discontinued.)

Discussion

This in-depth qualitative study explored expectations and experience of injectable GLP-1RA use among Australian adults with T2D, including, for the first time, how this experience may impact attitudes to future insulin initiation. This qualitative study has identified several concerns regarding the use of GLP-1RA injectable therapy, including the belief that injectable treatments signal worse health, stigma related to illness perceptions and injection use, anxiety surrounding the administration of injections, inconvenience caused by treatment timing and storage requirements, as well as the negative impact of gastro-intestinal side effects. While perceived facilitators and/or benefits of GLP-1RA injectable treatment include the impact on glycaemic outcomes and weight loss, as well as frequency of administration. Findings also suggest that experience of GP1-RA injectable treatment may, for some, promote receptiveness to future insulin use.

Several of the concerns raised here about GLP-1RA use seem consistent with established salient psychological barriers to insulin use.^{19,20} We might consider whether psychological insulin resistance may be more accurately conceptualised as “psychological injectable resistance”. Indeed, initial concerns about GLP-1RA therapy in the current study largely related to the injectable administration of the treatment. As has also been observed following insulin initiation,^{23,-28} some participants reported overcoming concerns about performing injections following GLP-1RA initiation, as well as

feeling, hypothetically, more receptive to the prospect of insulin therapy. Thus, prior use of injectable GLP-1RA may support later acceptance of, and adjustment to, insulin among people with T2D; although, this was not a universal experience.

Similarities in perceptions of injectable GLP-1RA and insulin therapy may also be a consequence of individuals drawing on their knowledge and attitudes about insulin therapy to inform expectations about non-insulin injectable treatment. Indeed, participants reported minimal prior knowledge of GLP-1RA and some reported relief upon understanding that GLP-1RA injectables were not a form of insulin. Health professionals need be cautious not to inadvertently reinforce negative beliefs about insulin in their efforts to distinguish insulin from injectable GLP-1RA therapy. Instead, the introduction of GLP-1RA injectable treatment may provide a unique opportunity to identify and address concerns about injectable treatment in general, including insulin, which may support future treatment intensification. Reflecting the diverse expectations and experiences within themes, such discussion should also take a person-centred approach, tailored to the specific concerns or expectations raised by the individual.

Consistent with prior findings,^{14,29} potential for weight-loss and glucose reduction were reportedly drivers of GLP-1RA uptake / ongoing use, and (if realised) described as outweighing concerns about injectable treatment. Participants used emotive language (e.g. “magic” ID36, ID8, or “fail[ure]” ID20) in describing both their hopes for and experience of weight loss. Several participants attributed treatment inefficacy to a failing in their own self-care rather than of the medication. Average effect of GLP-1RA on weight observed across GLP-1RA formulations varies from an increase of 0.3 kilograms to a reduction of 6.5kgs.⁴ In clinical discussion of GLP-1RA therapy, realistic expectation setting with regard to treatment-related weight loss is essential. A data-driven and balanced approach to communicating treatment benefits and risks is needed.³ This is particularly important given the established prevalence of self-blame and internalised stigma associated with both type 2 diabetes and excess weight.³⁰

Overall, GLP-1RA injection administration was largely described by participants as convenient, particularly for weekly formulations. Though exceptions relating to the treatment features of specific formulations (e.g. storage, preparation requirements, administration timing in relation to meals) were reported by some. Conclusions regarding formulation preferences cannot be drawn from this small qualitative study, though these findings are consistent with prior research.⁴

A strength of this study is that purposive sampling was used to maximise variability in participants' demographic characteristics (i.e. age and gender) and GLP-1RA treatment experience (i.e. current/previous injectable GLP-1RA use; GLP-1RA formulations). However, this highly select small

sample is not (nor intended to be) representative of the broader Australian population with T2D or specific subgroups of people with T2D (e.g. those for whom English is a second language; young adults with T2D). Despite the multiple methods of recruitment, the sample likely reflects a highly engaged group and future research would benefit from recruitment via diabetes clinic lists.

Furthermore, quantitative research would provide opportunity to confirm the relevance of the identified themes, and the extent to which they are endorsed, in a large-scale, more diverse and representative sample. While experience may differ by GLP-1RA formulation, current treatment status, and other participant characteristics, direct comparisons cannot be made within the current study. Furthermore, the findings of the current study are specific to those with experience of taking *injectable* GLP-1RA therapy and should not be extrapolated to a) oral GLP-1RAs or b) the attitudes of those who declined GLP-1RA therapy. Additional qualitative research is needed to explore further the reasons for treatment refusal as well as experience of oral GLP-1RA use. Though experience with GLP-1RA initiation and use was relatively recent (i.e. ≤ 3 years prior) and a narrative interview style was used to explore expectations and experience over time, accuracy of recall is unknown.

Longitudinal qualitative research, tracking participants over the course of their treatment exposure (i.e. from recommendation to initiation, and through to ongoing use and/or discontinuation), could overcome this limitation in future research. Finally, the possibility of a researcher-based bias during qualitative data collection and analyses should also be acknowledged. Strategies to mitigate undue influence on interviews and data analyses included co-author (multidisciplinary) input on the interview schedule, final theme selection and description, and shared facilitation of interviews with a second team member (JSc), including observation of, and reflection on, early interviews.

The findings of this study suggest some consistency in expectations and experiences of GLP-1RA injectable treatment with salient psychological barriers to insulin use, e.g. stigma, negative symbolism, and administration anxiety associated with injectable treatment.^{19,20} Attitudes toward insulin may play an important role in shaping expectations, and perhaps receptiveness to, injectable GLP-1RA treatment. In turn, experience of GLP-1RA may inform receptiveness to future treatment intensification in the form of insulin therapy. Weight-loss and administration frequency, in particular, are viewed positively as unique treatment features which motivate uptake, and, if realised, ongoing use of GLP-1RA injections. Ensuring realistic and balanced setting of expectations within the clinical discussion of GLP-1RA may mitigate against the potential distress associated with unmet expectations.

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Table 1. Summary of interview schedule order, topics and prompts

Topic	Prompts
Background information	Self-introduction
	Brief diabetes history, including changes in treatment
Prior knowledge and expectations of GLP-1RA	Prior knowledge of “injectable medications”
	First learnings about GLP-1RA treatment
	Perceived reasons for GLP-1RA recommendation
	Expectations of GLP-1RA prior to starting: positive and negative
Decision making: support and informational needs	Information provided by health professional: benefits and side effects
	Additional support and information sought out
	Additional support and information wished for (i.e. ideal)

Treatment experience: initial weeks*	First GLP-RA injection experience and support received <u>Negative / positive aspects</u> of treatment, including weight-related
Treatment experience: ongoing/long-term (continuers only)	Current experience of GLP-1RA Impact on your diabetes goals New or ongoing negative / positive aspects Reasons for injection omission (if any)
Treatment disclosure	Treatment disclosure to family/friends; public injections
Discontinuation and/or change in formulation	Reasons for discontinuation / change in formulation How decision made, by who, and further support sought Reaction to / experience of stopping treatment
Attitudes about future injectable diabetes treatment	Attitudes to: change in GLP-1RA injection frequency (continuers); injectable diabetes medicine in general (discontinuers only); starting insulin (non-insulin-treated only) Impact of 'GLP-1' on attitudes toward insulin
Final comments	Recommendation of 'GLP-1' treatment for others Anything further to add

*questions repeated where multiple formulations had been initiated.

Table 2. Demographic and clinical characteristics of study participants (N=19)

Variable	N(%) or median (range)
Gender: women	10 (53)
Location: non-metropolitan	4 (21)
Age (years)	64 (28 – 72)
Place of birth: Australia	14 (74)
Employment status	
Employed full-time or part-time	4 (21)
Retired / disability pension	14 (74)
Unemployed	1 (5)
Relationship status: in a relationship	11 (58)
Highest qualification	
None / primary school	3 (16)

High school completion	5 (26)
Certificate / trade	4 (21)
University degree	7 (37)
Diabetes duration (years)	10 (1 – 26)
Insulin treatment	
Current	1 (5)
Prior	4 (21)
Current GLP-1RA treatment: total	13 (68)
Once daily Liraglutide	0 (0)
Twice daily Exenatide	3 (16)
Once weekly Exenatide	6 (31)
Once weekly Dulaglutide	4 (21)
Prior (discontinued or transitioned) GLP-1RA treatment	
Once daily Liraglutide	1 (0.5)
Twice daily Exenatide	8 (42)
Once weekly Exenatide	5 (26)
Once weekly Dulaglutide	0 (0)
GLP-1RA duration of use (months)	
Total *	12 (1 – 36)
Current/ongoing (n=13)	15 (5 – 36)
Discontinued (n=6)	5.5 (1 – 24)

Data are n(%) or median, range

*Includes both current and prior GLP-1RA use.