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Participants' experiences of intensifying insulin therapy during the Treating to Target in Type 2 Diabetes (4-T) trial: qualitative interview study

Running title: Participants' experiences of intensifying insulin therapy

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Abstract

Aim To explore participants' experiences of intensifying insulin therapy during the Treating to Target in Type 2 Diabetes (4-T) trial.

Methods In-depth interviews were conducted with 41 trial participants who had had their insulin therapy intensified during 4-T. Data were analysed using an inductive, thematic approach.

Results The vast majority of participants were receptive towards intensifying treatment. Whilst some were happy simply to follow health professionals' recommendations, others saw taking two types of insulin as a more effective way of controlling their diabetes. Post-intensification, participants sought to remember to take their additional injections by developing injection related strategies and daily routines. The need to inject insulin whilst in public often arose more frequently following intensification and was a consistent source of anxiety. Those who were worried about injecting in public sought to avoid having to do so; for example, by injecting in toilets or by advancing or delaying the timing of their injections.

Conclusions It was not increasing the number of daily injections per se which was problematic for 4-T participants who had agreed to have their insulin therapies intensified, but the increased likelihood of having to inject insulin in public. Addressing concerns about injecting in public places may help promote adherence to intensified insulin regimens.

Keywords: intensive therapy; adherence; patient experience; qualitative methods

List of abbreviations:

FBG	Fasting blood glucose
PPBG	Post-prandial blood glucose
4-T	Treating to Target in Type 2 Diabetes
OHA	Oral hypoglycaemic agents
SMBG	Self-monitoring blood glucose

Introduction

Achieving optimal levels of glycated haemoglobin (HbA_{1c}) requires control of both fasting blood glucose (FBG) and post-prandial blood glucose (PPBG). As endogenous meal-related insulin secretion declines, people with type 2 diabetes who are treated with long-acting insulin require the addition of rapid-acting insulin to improve glycaemic control, a process termed intensification of insulin therapy [1].

Whilst the intensification of insulin therapy is an important stage in the treatment process, the vast majority of research has focused on barriers to initiating insulin [1]. Several studies have highlighted that individuals may seek to avoid initiating insulin due, for example, to the perceived pain of injecting, the inconvenience of having to administer daily injections, and the belief that insulin signifies personal failure to self-manage their disease effectively [2, 3, 4, 5]. Few studies have sought to explore whether similar barriers exist when intensifying insulin therapies [1, 6, 7].

Elsewhere, we have described attitudes towards initiating insulin which were held by participants in the Treating to Target in Type 2 Diabetes (4-T) trial [8]. Here, we explore trial participants' accounts of having had their insulin therapies intensified during 4-T.

The 4-T trial

The 4-T trial was a large, three-year, multi-centre, open label trial conducted to compare the efficacy of three different insulin regimens when added to oral hypoglycaemic agents (OHA) in people with type 2 diabetes [9, 10]. The trial evaluated the impact of basal (insulin detemir), prandial (insulin aspart) and biphasic (insulin aspart 30) based insulin regimens in participants inadequately controlled on metformin and/or sulfonylurea therapy. The trial employed a treat-to-target approach (HbA_{1c} ≤ 6.5 %). In order to inform adjustments to daily insulin doses, participants were required to undertake regular self-monitoring of blood glucose (SMBG) and to provide trial staff with SMBG readings. Participants not achieving target glycaemic control in years two and three of 4-T had their sulfonylurea (if taken) discontinued (metformin, if taken, was continued) and a second insulin formulation added [Fig 1].

4-T data show that at the end of the first year of the trial, less than a quarter of all participants achieved target glycaemic control (biphasic 17%, prandial 24%, basal 8%). At the end of the trial, less than half achieved target glycaemic control (biphasic 32%, prandial 45%, basal 43%) [9, 10]. This interview study was undertaken to understand why the majority of participants did not achieve the glycaemic target. A key objective was to explore their views about having their insulin therapies intensified, their experiences of taking two types of insulin daily, and whether experiences of intensification impacted upon their perceived commitment and ability to adhere to their treatment regimens.

Methods

Qualitative approaches are recommended when little is known in advance about the area of investigation [11, 12]. In this study, we utilized single, in-depth interviews as these encourage participants to display their own understandings and meanings and permit (unanticipated) themes and hypotheses to be identified and explored [13]. The research was approved by the Hertfordshire Research Ethics Committee (ref: 08/H0311/98).

Sampling

Our sampling and recruitment methods have been reported elsewhere [8]. In brief, 11 of the 58 4-T centres were included in the study, which were selected to ensure diversity in centre size, geographical location and research profile. Trial participants were recruited using an opt-in procedure. To aid sampling, those who opted-in also permitted the research team to access their trial data. As the number of participants who opted-in to the study (n=68) was greater than that required to meet the study's sample size (n=45), purposive selection was used to recruit a final sample which included equal numbers from across the three treatment arms and which broadly reflected the wider trial population in terms of age, gender and variation in glycaemic control.

Data collection & analysis

Interviews were informed by a topic guide and conducted at a time and location convenient to participants. Interviews were conducted by a non-clinical researcher (NJ), lasted between 40 minutes and 2 hours, were tape recorded, and explored participants' experiences of taking part in and receiving care during 4-T (including their encounters with health professionals); their views and perceptions of insulin; their experiences of intensification and associated self-management practices; their reasons for adhering and not-adhering to insulin therapies (both pre and post intensification); and strategies for incorporating intensified insulin regimens into daily life.

The study was informed by the principles of grounded theory which involves concurrent data collection and analysis, together with efforts to check and refine developing categories of data by using the method of constant comparison. This method involves systematically comparing interview transcripts in order to identify cross-cutting themes and common experiences [13]. Themes and hypotheses identified in early interviews informed questions in later interviews. Team members independently reviewed data and regular meetings were held during and after data collection to explore participants' underlying reasoning, discuss deviant cases and reach agreement on recurrent themes and findings. QSR NVivo 2, a qualitative data-indexing package, was used to code the data. Interviews were coded to capture data relating to the areas explored in the topic guides as well as emerging findings.

Results

Participants were broadly representative of the 4-T trial population in relation to age, gender and glycaemic control, and included those with both high and low final HbA_{1c} results (range: 5.3 – 9.9%) [Table 1]. Out of the 45 4-T participants who took part in the study, 41 (91%) reported having had their insulin therapy intensified during the trial [Fig 1]. We draw upon these 41 participants' accounts in the remainder of this paper.

Receptiveness towards intensification

The vast majority of participants appeared to have been 'psychologically receptive' [8] towards intensifying their insulin therapies. The reasons participants gave for agreeing to intensify treatment broadly fell into one of two categories: 'doctor knows best' and 'to aid control'. Participants who appeared happy to follow health professionals' recommendations often seemed unsure, precisely, why the second insulin was being added, but felt that 'I'm no expert so if they told me I needed it then I accepted their word' (Pt24). In contrast, those who appeared to believe that intensification would aid control, tended to see the role of the additional insulin they had been asked to take as helping to either top-up or balance out the insulin they were already taking.

'Topping up' explanations appeared to be rooted in participants' experiences of undertaking SMBG during the trial and discussing their readings with 4-T staff. As a result of undertaking SMBG, some participants reported being able to observe how their blood sugar levels were either 'terrible in the morning' (Pt7) or 'going up in the evening' (Pt30), which in turn enabled them to see taking two types of insulin as a means to achieve consistent readings over a 24 hour period (Pt45, Box 1). Those participants who welcomed intensification as a means of 'balancing out' their insulin reported having become concerned that the doses of their initial insulin were too high. In this context, introducing a second type of insulin was perceived as a means of enabling doses of their initial insulin to be reduced to within more 'acceptable' limits (Pt13, Box 1).

Managing two types of insulin

In the majority of cases, participants appeared to have adapted effectively to managing their intensified insulin regimen. This is because, from early on in the trial, participants had usually established practices and routines which helped them to remember to administer their daily injections. Practices included: carrying insulin pens around in pockets and bags, keeping basal insulin next to the bed or prandial insulin in the kitchen, and receiving reminders to inject from friends and family members. These strategies served to make having to take insulin part of everyday life, 'like cleaning your teeth' (Pt37).

Intensification could result in participants having to develop and adapt their routines. Participants randomised to prandial insulin, for example, occasionally reported difficulties remembering to take their new (basal) insulin at a set time each night, as they were used to injecting insulin with meals

(Pt36, Box 1). However, increasing the frequency of daily injections tended not to be seen as problematic by these participants because, as patient Pt39 explained, 'I was already injecting three times a day [...] once more wasn't going to make any difference.'

For participants randomized to basal insulin, having their treatment intensified meant going from one or two daily injections of insulin to having to inject up to five times a day. This news was sometimes met with surprise and apprehension amongst participants who were unsure how they were going to fit the additional injections into their daily lives (Pt28, Box 1). As a result, their new injection regimen could require participants to make conscious and deliberate efforts to adapt daily practices, where 'You have to just think through the logistics; a little bit of when and where you take your medication' (Pt33). However, as participant Pt11 (Box 1) highlights, increasing the number of daily injections from once/twice to four/five times a day could help make injecting more routine and therefore a more normal aspect of everyday life.

Difficulties with injecting in public

Whilst the majority of participants had adjusted to intensification by adopting strategies which helped them to remember to take their injections, most disliked having to inject in public. All participants who had had their insulin therapies intensified were required to administer at least one daily injection of insulin with meals (Fig 1) and participants described mealtimes as occasions when they were most likely to have to inject outside their homes. Fear of others' (negative) reactions, such as putting them off their dinner (Pt42, Box 1) or being seen as either 'unclean' or a 'drug addict' (Pt31, Box 1) resulted in participants trying to avoid having to inject in restaurants and cafes. When dining out, therefore, participants frequently injected in the toilet (Pt26, Box 1). Toilets, however, were not always seen as ideal (or hygienic) places in which to inject (Pt1, Box 1). Hence participants who wished to avoid injecting in the toilet or at the table, described how they would take their insulin up to thirty minutes before or after their meal so that they could inject in the car en-route to the restaurant, or upon arriving home (Pt21, Box 1). These participants tended to see advancing or delaying mealtime insulin injections as falling within treatment parameters and thus saw themselves as adherent. Rather than alter the timing of their injections, other participants developed alternative strategies, such as avoiding eating out (Pt23, Box 1).

Discussion

Although it is often assumed that people with type 2 diabetes may be psychologically resistant to intensifying insulin therapy [1] we found that the majority of 4-T participants were willing to use an additional type of insulin. Their experiences of intensification suggest that it is not the increased frequency of injections per se which participants found most problematic, but rather the increased likelihood of having to inject insulin in public and, potentially, experience negative reactions from others.

The vast majority of participants were 'psychologically receptive' [8] towards the intensification of their insulin therapies. Deference to health professionals'

expertise, the potential to record more consistent SMBG readings, and to achieve reductions in doses of initial insulin post-intensification were all important factors promoting acceptance towards taking two types of insulin. Previous research has shown that patients may not always desire to be highly involved in making decisions about treatment and may instead prefer to defer such decisions to health professionals [14]. Whilst there is currently a dearth of qualitative studies that explore experiences of taking insulin amongst people with type 2 diabetes, research has shown that individuals may be keen to limit the amount of insulin they inject on a daily basis [15].

Making injections part of daily routines helped 4-T participants remember to take their different types of insulin at appropriate times of the day. This finding is consistent with previous research, which found that cultivating routines could help individuals with type 2 diabetes remember to take their OHA [16]. Qualitative studies of patient adherence to medications for other forms of chronic illness, such as epilepsy, have reported similar findings [17].

Whilst participants were willing to increase the number of daily injections, many were worried about taking their insulin in public, due to the stigma which they associated with injecting and their fears about how other people may react. In this context, the requirement to inject insulin with meals created difficulties for participants when eating out. Most reported trying to find ways of avoiding having to inject in front of others; for example, by injecting in toilets or by advancing or delaying the timing of their injections.

The potential for injections to induce feelings of social embarrassment is a recognised feature of 'psychological insulin resistance' [18]. Whilst we argue that the majority of our participants were receptive towards taking insulin, the fact that feelings of stigma appeared to lead some to advance the timing of their mealtime insulin injections is worrying, as this can increase the risk of hypoglycaemia, especially amongst those with tight glycaemic control. Similarly, delaying mealtime insulin injections can result in surges in post-prandial blood glucose levels and a rise in overall HbA_{1c}.

Sub-optimal injecting practices (such as injecting in toilets and altering the timing of injections) have been reported in other qualitative studies involving people with type 1 and type 2 diabetes [19]. Our findings highlight that whilst 4-T participants reported engaging in these practices they appeared not to view their actions as signs of treatment non-adherence. This finding is important, as it suggests individuals with type 2 diabetes may view feelings of stigma as personal difficulties, as opposed to treatment barriers which could, or should, be shared with health professionals.

Practice implications

Health professionals need to remember that some individuals with type 2 diabetes may be worried about injecting insulin in public. Concerns about injecting insulin in public should be fully addressed by health professionals. Individuals should be given clear and consistent advice regarding when to administer their injections and both patients and health professionals should work together to identify practical strategies for alleviating concerns about

injecting in public. Health professionals could also work with individuals who have type 2 diabetes, to identify and cultivate daily medication routines which may foster adherence to insulin therapies.

Whilst the role of SMBG in the care of individuals with type 2 diabetes is controversial, given the lack of evidence that it leads to clinical improvements [20], our findings suggest that encouraging SMBG at the point where intensification may shortly be needed could help foster receptiveness towards taking two types of insulin. Prior to intensification, individuals with type 2 diabetes could be supported to take regular SMBG readings over the course of the day, and encouraged to discuss the results with their designated health professionals. Drawing attention to high SMBG readings may help individuals in coming to view intensified insulin regimens as potentially offering a more effective approach to controlling their diabetes.

Strengths and limitations

This study provides an in-depth perspective on 4-T participants' experiences of intensifying three different insulin regimens, this being a highly under explored area. It is limited insofar as it is United Kingdom based, and the vast majority of interviewees were White-British, thus restricting the extent to which findings may be transferred to other health care systems and ethnic groups. By virtue of having agreed to take part in 4-T, participants may have held more positive views and beliefs about insulin than the wider population of people with type 2 diabetes. Finally, participants' retrospective accounts may be subject to recall bias, although it must be noted that purposive sampling meant the study included trial participants with high and low final HbA_{1c} results. Further research could usefully explore understandings and experiences of intensifying insulin therapies amongst individuals with type 2 diabetes receiving treatment in non-trial settings.

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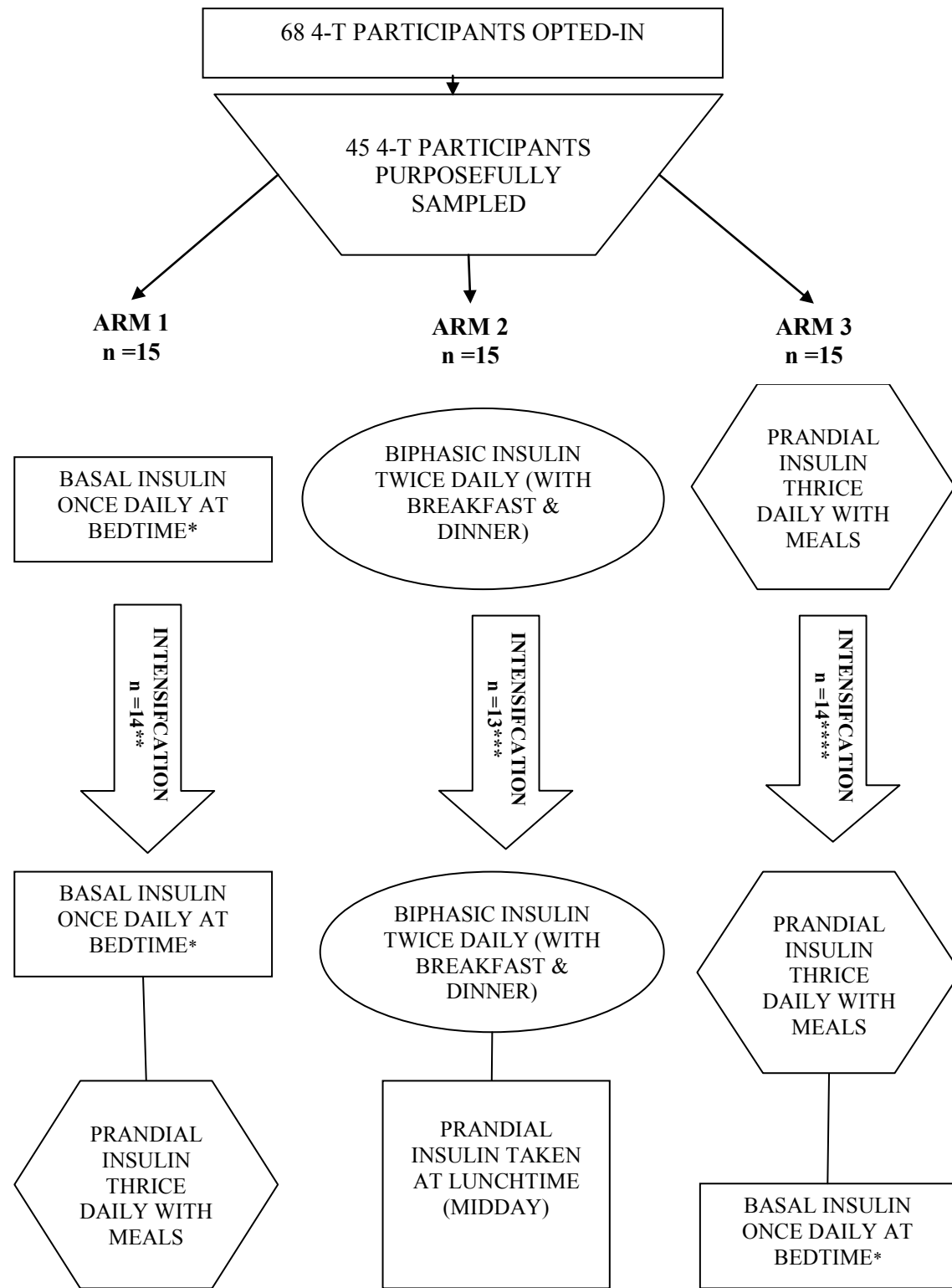
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Figure 1 Initial and intensified insulin regimens for 4-T participants



Notes

- * Twice a day if required
- ** One participant not intensified due to having achieved trial target
- *** One participant not intensified due to having achieved trial target. One participant not intensified as not considered clinically appropriate
- **** One participant not intensified due to having achieved trial target

Table 1 Participant characteristics

Participants	4-T (n=708)	Qualitative sample (n=45)
Age		
Mean age (\pm SD)	61.7 (\pm 9.8)*	64.7 (\pm 8.5) †
Sex		
Male (%)	454 (64)	29 (64)
Female (%)	254 (36)	16 (36)
Randomisation		
Biphasic (%)	235 (33)	15 (33)
Prandial (%)	239 (34)	15 (33)
Basal (%)	234 (33)	15 (33)
Glycated hemoglobin at Yr 3		
Median HbA _{1c}	6.9%	6.9%
Number (%) of participants with HbA _{1c} \leq 7%	425 (60)	26 (58)
Number (%) of participants with HbA _{1c} \leq 6.5%	283 (40)	19 (42)
Notes * Age at trial initiation † Age at interview ➤ Percentages have been rounded to the nearest whole number		

Box 1 Participant quotes

Receptiveness towards intensification

Pt45: 'I was always waking in the morning with it [blood sugar levels] very high [...]. So, they put me on this one which keeps it steady at night.'

Pt13: 'All of a sudden everything went soaring high and I had to up the aspart a great deal [...] So then they suggested I go for this [...] long acting one overnight [...] and that meant that I could knock right down the aspart.'

Managing two types of insulin

Pt36: 'What (name of nurse) said to me was to take it at bedtime. Which is fine except that I tend to go to bed very late and so we agreed that I would take the insulin at about 10 o'clock. Sometimes depending on what's happening and what I'm doing, sort of 10 o'clock's gone past and I haven't taken it and it might be 11 o'clock or half past 11 before I remember to take it.'

Pt28: 'In January of 0 seven they shocked me by saying, "Well, we're going to have to put you onto a different injection" and I thought what, *just* the different injection? And they said "No, no, as well, and by the way, up three times a day." So I then realised, five times a day!'

Pt11: 'And perversely having four injections a day has made it easier to do injections. It's more routine, it's more regular and like I say I don't actually think about it.'

Difficulties with injecting in public

Pt42: 'It didn't bother me about using a needle but if people are watching you [...] you don't know how they feel about seeing people inject themselves. So, normally, I try to do it in, like a private way.'

Pt31: 'I just don't think I would like to do anything like that (inject) in public, whether I did it in my stomach, on my arm or anywhere, no. No. They might think I'm a junkie!'

Pt26: 'If I go out with anybody I always go and do it (inject) in the toilet. I won't ever do it outside.'

Pt1: 'I used to hide myself away in the toilets and then I used to think, you know, this just isn't right. This is silly. I mean there's more germs in the toilet than there are on, you know, a good table cloth.'

Pt21: 'With this injection, aspart, you can do it twenty minutes beforehand and then it begins to get into the bloodstream or you can do it after your meal but I usually do it before because you have a meal out and then you don't want to dash home.'

Pt23: 'I wouldn't go out to lunch with them (friends) and in the end I had to tell them why. I said, "I can't. I have got to have insulin. And I am not going to go into a toilet".'