Exploratory Research in Clinical and Social Pharmacy 14 (2024) 100450

Contents lists available at ScienceDirect

Exploratory Research in Clinical and Social Pharmacy

journal homepage: www.elsevier.com/locate/rcsop

Adherence to Parkinson's disease medication: A case study to illustrate reasons for non-adherence, implications for practice and engaging under-represented participants in research

Delyth James [a,*], Joshua Smith [a], Emma Lane [b], Rhian Thomas [c], Sarah Brown [a], Heidi Seage [a]

[a] Department of Applied Psychology, Cardiff School of Health Sciences, Cardiff Metropolitan University, Llandaff Campus, 200 Western Avenue, Cardiff CF5 2YB, Wales, UK
[b] Cardiff School of Pharmacy & Pharmaceutical Sciences, Cardiff University, King Edward VIIth Avenue, Cardiff CF10 3NB, Wales, UK
[c] Swansea University Medical School, Swansea University, Grove Building, Singleton Park, Swansea, Wales SA2 8PP, UK

ARTICLE INFO

Keywords:
Parkinson's disease
Medication adherence
Patient perspectives
Self-management
Theoretical domain framework (TDF)
Case study
Representation in research

ABSTRACT

Parkinson's disease (PD) is a progressive neurodegenerative disease which primarily presents with the core symptoms of rigidity, postural instability, tremor, and bradykinesia. Non-adherence to prescribed PD treatments can have significant ramifications, such as poor symptom control and greater disease burden. Reasons for poor adherence are multifaceted, particularly when medication regimens are complex and often based on perceptual and practical barriers. Additionally, engaging fully non-adherent patients in research is challenging since they may have dropped out of service provision, yet their contribution is vital to fully understand the rationale for non-adherence.

This paper aims to present a case study on the perspectives of one person with PD, a participant in a previously published qualitative study investigating the barriers and facilitators to medication adherence in PD. In this paper, the participant's diagnostic journey is described, and experiences of medical consultations are summarised to explain their reasons for not adhering to any of the standard UK PD treatments prescribed. The participant's preferences for using Vitamin B1 (thiamine) injections to manage the symptoms are reported and the rationale for doing so is discussed. We consider the case through the lens of a behavioural science approach, drawing on health psychology theory, the Theoretical Domains Framework (TDF), to inform the review and the practical challenges faced when analysing the data for this participant. Implications for pharmacy practice, in particular, are also put forward with view to ensuring that patients such as Mr. Wilkinson are provided with the opportunity to discuss treatment choices and self-management of long-term conditions such as PD. We also discuss the importance of reaching under-represented members of the population in medication adherence research, which embraces the principles of equality, diversity, and inclusion in research.

1. Background

In this paper we present a case study of an individual who is non-adherent to Parkinson's medication and discuss the implications for pharmacy practice. We reflect on the challenges encountered when including fully non-adherent patients in qualitative data analysis and the importance of engaging under-represented participants such as this in research. The rationale for publishing this case study draws on the authors' experiences of conducting research to explore the barriers and facilitators to medication adherence in people with Parkinson's, where several methodological challenges were faced relating to data gathered from one 'fully non-adherent - outlier' participant. This case study emphasises the importance of recruiting fully non-adherent patients to research of this nature and highlights the fact that they are often not included in adherence studies due to recruitment difficulties.

Parkinson's disease (PD) is a progressive neurodegenerative disease, and second most common neurodegenerative disease in the UK following Alzheimer's disease.[1] PD presents primarily with the core symptoms of rigidity, postural instability tremor, and bradykinesia,[2] but also features a range of non-motor symptoms such as cognitive

* Corresponding author.
E-mail addresses: dhjames@cardiffmet.ac.uk (D. James), laneel@cardiff.ac.uk (E. Lane), Rhian.Thomas@swansea.ac.uk (R. Thomas), sabrown@cardiffmet.ac.uk (S. Brown), hseage@cardiffmet.ac.uk (H. Seage).

https://doi.org/10.1016/j.rcsop.2024.100450
Received 27 February 2024; Received in revised form 30 April 2024; Accepted 5 May 2024
Available online 7 May 2024

impairment, sleep disorders, psychological impairments, pain, and peripheral symptoms such as constipation.[3] The primary pathology is the progressive loss of the dopaminergic neurons of the substantia nigra which control motor function and as yet, there are no interventions that can modify the trajectory of the disease.[4] Unlike many other degenerative diseases there are however a range of symptomatic pharmacological and surgical treatments which can be offered at different stages of progression. The pharmacological treatments dominate in early-stage disease, largely focussing on restoring the lost dopaminergic neurotransmission and include the dopamine precursor L-DOPA and dopamine agonists.[5]

Pharmacological treatment guidelines for medication strategies in early PD are broadly consistent across different countries. United States (US), European and United Kingdom (UK) guidelines recommend the use of the dopamine precursor Levodopa, for patients in whom the motor symptoms are impacting on quality of life,[6] with additional options of dopamine agonists (if patients are less than 60 years of age), monoamine oxidase B inhibitors and catechol-*o*-methyl transferase inhibitors.[7] These medications are not without side effects, with dopamine agonists now well known for their propensity to induce impulse control disorders, whilst long term use of L-DOPA is associated with the development of motor complications. These manifest as 'on/off' fluctuations, in which periods of good motor function are fragmented by sudden unpredictable 'off' periods, when medication ceases to alleviate symptoms, and the onset of abnormal involuntary movements known as L-DOPA-induced dyskinesia.[8] It is these considerations and others that make careful consultation with the patient, ahead of initiating therapy, critical to their understanding of the risks and benefits that can be proffered.

In general, adherence to prescribed medication is remarkably low when considered across the population with only 10–20% of PD patients being fully adherent to their prescribed medication regimen.[9–13] For optimal management, PD medications should be taken at well-timed intervals through the day and may also include additional medications for the troublesome non-motor symptoms. Since the timing of doses is particularly important with PD medication, the definition of non-adherence in this population therefore relates to those who miss doses of medication as well as those who take all the necessary doses but at a different time of day to that agreed. The challenges of medicating in PD are compounded by it being a disease linked with ageing and thus higher rates of comorbidities, necessitating additional non-PD medications. Adherence to medication in PD is therefore consistent with populations with long-term conditions, with the potential significant ramifications of non-adherence including poor symptom control, greater disease burden, fatigue, and depression.[14,15]

Reasons for poor medication adherence often comprise a combination of perceptual and practical factors. Perceptual factors are often based on individuals' perceptions of the illness or beliefs about the medication. Illness perceptions have been found to predict patient self-management and adherence behaviours in a range of physical health conditions.[16] The Necessity-Concerns Framework (NCF), states that an individual's beliefs about a specific medication are influenced by the patients' perception of the necessity of taking their prescribed medication weighted against their perceived concerns about taking it.[17,18] It has been shown that sociodemographic and clinical factors were only able to explain a small amount of the variance in medication non-adherence, whereas illness perceptions and patient beliefs contributes to significant proportions of the variance in non-adherence and disease outcomes.[19,20] Factors associated with increased necessity beliefs for PD medications in a cross-sectional study were severity of illness, younger age at onset of PD and a longer time since starting the medication.[21] This highlights the importance of taking an approach to treatment which includes understanding the patient's perspectives of the condition and the benefits of medicine-taking.

The Theoretical Domains Framework (TDF) is a framework that can be used to understand medication adherence behaviour based on 14 domains.[22,23] Application of the TDF to medication taking behaviours is an effective approach to identifying the specific barriers and facilitators to adherence. The TDF was utilised in our previous study to identify the barriers and facilitators of medication adherence in PD, following interviews with twelve UK based patients who had been recruited from a PD charity and two social media groups.[24] The findings included the views and medication-taking behaviours of one participant who had disengaged with standard PD treatment and had chosen to self-medicate with Vitamin B1 (Thiamine) injections purchased online from a clinic in Italy. Whilst this produced some complex challenges for applying framework analysis to the data, it reinforces the importance of including outliers such as this participant in the reporting of medicines adherence research.

This paper aims to review the perspectives of one participant who took part in our previously published qualitative study[24] where the barriers and facilitators to medication adherence in PD were mapped to the TDF. This one participant presented medication-taking behaviours which were different to the other PD patients, yet it was essential to include these data in the results, and as such a different approach to analysis was required to identify the barriers and facilitators. The purpose of this paper is therefore to present the perspectives of this one participant as a case study to offer a deeper understanding of the rationale for non-adherence to PD medication. This case study also illustrates the challenges of engaging non-adherent patients in research and the importance of designing studies in such a way that recruitment strategies can reach under-represented members of the population can be reached in research.

2. Case presentation

This case study is based on data from one participant who was interviewed as part of our study to explore the barriers and facilitators to prescribed Parkinsonian treatment.[24] The semi-structured interview schedule used, based on the fourteen domains of the TDF, is presented in Appendix 1. A pseudonym has been used to maintain anonymity and steps taken during reporting of information to minimise the risk of the participant being identifiable. Ethical approval was provided by Cardiff Metropolitan University's ethics committee [Reference number PGT-4197].

Mr. Wilkinson is a white male first diagnosed with PD in March 2018 aged 62 years, three years before taking part in the study interview. At the time of the study (July 2021) Mr. Wilkinson was retired and residing in South Wales. He was physically active and participated in various sports (boxing, swimming, cycling and football). He had no other comorbidities and had been active throughout his life; however, he had increased his level of physical activity since the PD diagnosis.

2.1. History of diagnosis

The initial diagnosis following a consultation with a neurologist for tremor was not conclusive for PD. However, following the neurologist's request of a second opinion from a more senior consultant within the same clinic he was formally diagnosed with PD and was told that the tremor symptoms he was experiencing were early signs of the disease. Mr. Wilkinson was accepting of this diagnosis and was keen to find out about strategies to slow down disease progression.

2.2. Alternative treatments

In between the two consultation periods Mr. Wilkinson decided to research alternative management of PD and found information from a European clinic surrounding the use of vitamin B1 (Thiamine) injections to manage PD symptoms. He discovered an educational video providing information on the benefits of vitamin B1 treatment, showing improvements in symptoms for people with PD (i.e., the video showed someone who was unable to walk being able to walk following injections

with vitamin B1 treatment).

2.3. Follow-up consultation and prescribed treatment

The use of vitamin B1 treatment was discussed with the clinician at the neurology clinic who was not aware of its use to manage PD symptoms. Mr. Wilkinson was surprised that the neurologist did not know about B1 treatment or any other new areas of treatment for PD and this led to a lack of confidence in them. The consultant neurologist proceeded to initiate standard treatment for PD in line with UK guidelines[6] without providing any further opportunity for Mr. Wilkinson to feel involved in the decision about his treatment or any discussion about other possible self-management approaches for PD.

2.4. Adherence to PD treatment

Mr. Wilkinson chose not to take any of the medication regimen prescribed to him at the neurology clinic. Instead, he purchased vitamin B1 injection online from the European country where this research originated. He self-injected 2 ml (presumed to be 1 mg/ml) vitamin B1 intramuscularly (IM) on alternate weekdays (i.e. three times week), as per the dosing recommendations from the clinic. He also mentioned that he took a magnesium supplement tablet daily to help manage his PD, but further information about the rationale, formulation, and dosing of this was not explored further during the interview.

2.5. Rationale for B1 use and outcomes

Mr. Wilkinson perceived that injecting one dose of B1 on alternative days was easier compared to taking multiple PD tablets a day at specific times. He also believed that if he held off taking PD medication (as per UK guidelines), for as long as possible then he would gain more benefit in the future. The channels of communication between himself and the clinic in Italy were excellent where he knew that he could contact the nurse there at any time and get a timely response to his questions. The fact that this service was free instilled confidence in the prescriber, the clinic system as well as the perceived efficacy of the treatment.

At the time of the interview, Mr. Wilkinson had been self-treating with Vitamin B1 for nearly three years. He did not perceive that the B1 treatment helped with tremor in his left arm, however he believed that it had been successful in slowing down the progression of other PD related symptoms such as “stiffness”. At first, he continued to experience the PD symptoms of muscle cramps, fatigue, and stiffness, while using vitamin B1 treatment but these resolved when the dosage of Vitamin B1 (thiamine) was increased (as advised by the Italian Clinic). He no longer experienced physical aching or pain. He reported that his cognition had improved and that he had more “clarity” and less “mind fog”. His mood had improved, and he attributed these improvements to the treatment of B1. He is an active member of a PD support group and described his peers who are taking prescribed medication for PD as being “a lot worse off than him”. He felt that his peers were “dependent” on their medication and views his treatment regimen as allowing him to have more freedom compared to his peers with PD. He observed that members of his PD support group needed higher medication doses due to increased “off” and reduced “on” medication periods. Although he was aware that the vitamin B1 treatment was not going to cure his PD, he found living with his tremor manageable, as he was still able to do the things that he wanted to do, such as play football. He also felt that he was able to live independently and did not want to put pressure on his family to “look after him”. By engaging in physical activities such as this, he felt like he was able to achieve these goals.

2.6. Adherence to vitamin B1 treatment

He reported regularly taking one to two week breaks from using the vitamin B1 treatment. The rationale for stopping the vitamin B1 injections were related to his desire to test the efficacy of treatment. However, when he did so, he noticed that his symptoms returned and when he resumed the vitamin B1 treatment, the symptoms returned to baseline. Mr. Wilkinson explained that he was committed to using the vitamin B1 injections long-term, but that the threshold for stopping treatment would be reached when he no longer has the physical ability to continue to inject himself (i.e., when he reaches the stage when the tremor symptoms are too severe for him to be able to hold a needle).

2.7. Social support

He indicated that in the UK system he only had access to a PD nurse, whereas by going through the clinic in Europe he has direct access to a “specialist doctor” who responds to his e-mails within 24 h. This additional support did not cost anything and led to him comparing the two systems of care, which only worsened his dissatisfaction with the UK service.

2.8. Further reflections

Mr. Wilkinson’s approach to self-medicating with B1 injections stemmed from the fact that he was disillusioned with the UK’s approach to treating PD based on his early experiences of diagnosis and the lack of opportunities to discuss his treatment options. He felt as though there was “no hope” offered during his time visiting the UK based clinic, where he saw other people with more severe PD at later stages of the disease and did not want this for himself. During his initial consultations he would have liked more emphasis on living well with PD rather than symptom management. As a result of this Mr. Wilkinson has been lost to the NHS system in terms of PD and did not attend hospital monitoring appointments.

3. Mapping of participant findings to TDF

Table 1 present analysis of the codes for Mr. Wilkinson’s interview data relating to the facilitators for self-managing PD with Vitamin B1 (Thiamine) therapy compared to the facilitators for adhering to prescribed Parkinsonian medication. Data representing the facilitators for each of these specific behaviours have been categorised according to the fourteen domains of the TDF with supporting quotes to represent each domain where relevant.

The facilitators for taking the alternative Vitamin B1 far outweighed the facilitators for adhering to taking standard prescribed Parkinsonian treatment. The dominant domains in terms of facilitators for using vitamin B1 therapy were *Beliefs about Capability, Beliefs about Consequences and Reinforcement,* (where perceived positive effects seem to be reinforcing the behaviour of using alternative treatment over standard prescribed treatment).

Mr. Wilkinson’s interview data posed many challenges in terms of applying the process of framework analysis using the TDF,[25,26] as discussed in our previous paper.[24] The interview schedule and framework analysis applied in the original study[24] had been designed to capture data for people who were being prescribed antiparkinsonian medications. When a patient is not taking any of the prescribed medication, but instead chooses to use alternative treatment, albeit not fully adherent to it, (since he took ‘drug holidays’), application of the TDF and reporting of findings becomes more complex. The framework for data analysis was originally conceptualised for barriers and facilitators to standard UK PD medication, so it was challenging to use the same parameters when considering an individual who had chosen an alternative treatment pathway. Therefore, it was initially thought that Mr. Wilkinson’s data should be removed from analysis due to the level of non-adherence to Parkinsonian medication and non-engagement with the UK’s healthcare service for his PD. Further discussion with the research team led us to reconsider this decision, since it was recognised that his data could be applied to this framework, if Vitamin B1 treatment was

Table 1
Facilitators for self-managing with Vitamin B1 treatment and for adhering to prescribed treatment (Facilitator Codes and Quotes for Mr. Wilkinson).

TDF Domain	Facilitators for using Vitamin B1 treatment		Facilitators for using standard/prescribed PD treatment	
	Application of data to TDF framework	Supporting quotes	Application of data to TDF framework	Supporting quotes
1) Knowledge	Has seen videos of the benefits of B1 treatment on reducing motor symptoms in other people with PD.	"*and when you look at the YouTube videos online from (XXX) (.) you'll see the benefits of some of them who can hardly walk when he took them on board (.) and then they're walking (.) they're standing up right (.) their movement is a lot better (.) their balance is a lot better*" (p13.438–443).	Understands that B1 treatment won't influence tremor.	"*you know they they say (.) it won't treat tremor (.) which is one of the main indicators of Parkinson's*" (p13.443–444).
2) Skills	Organisation skills aids B1 treatment behaviour.	"*Umm (2) not really no no I haven't to be honest umm (2) I'm I'm usually quite organised sort of person so (XXX) it comes just quite easy for me (.) to to make sure I follow follow the regimen*" (p2.95–298).	N/A	N/A
4) Beliefs about Capabilities	Indicates that B1 treatment won't cure PD but they believe they are capable of living with their current level of tremor. Finds injecting B1 once every two days is much easier than taking PD medication daily.	"*It's not going to take it away completely but (.) I can live with it … the bit of the tremor that I have (.) and I can live with it the way I am at the moment so if that's the way it's got to be then that's the way it's going to be*" (p4.125–129). "*It's a lot of tablets (.) and I spoke to the doctor about that and he said the best way of doing it is to do two millilitres of injection three times a week (.) that's what I'm on (2) the regime that way is so much easier than taking eight tablets a day*" (p11.351–355).	N/A	N/A
5) Optimism	B1 treatment suggested to be successful.	"*Umm who was having some (.) really good success with it*" (p1.21).	N/A	N/A
6) Beliefs about Consequences	Believes that they do not require to take PD medication to function more normally/ control symptoms. Believes that the longer they withhold from taking PD medication the more they will benefit in the future.	"*For the moment (.) I'm able not to take prescribed medication*" (p14.454). "*Because if I can hold that off for as long as I possibly can I'll have more benefit in the future*" (p14.456–457).	Recognises that lapses in medication regimen can reduce quality of life and this indicates why you should follow treatment.	"*it's it depends on your quality of life because if your quality of life ain't good because you're not taking your medication (.) then take your medication*" (p8.251–254).
7) Reinforcement	B1 treatment has reduced or stopped aches & pains, diminished mental capacity and low mood. Unsure of what B1 treatment is doing but it appears to have reduced PD progression	"*So my aches and pains I used to have are not there anymore (.) umm my sort of clarity is a lot better (.) I don't have a lot mm f mind fog umm and my moods a lot better (.) umm so something is happening*" (p1.32–35). "*But I don't know what exactly what it's holding back (.) because I at the moment I'm not developing an awful lot which is good to see you know I'm glad to see*" (p2.37–39).	N/A	N/A
8) Intentions	Intends to start taking PD medication once they are unable to physically inject B1 treatment due to PD symptoms.	"*Which is Leva-dopa (.) uh so I will look at that but until I get to a point where (.) I can't inject because I've got to inject myself on alternative sides instead of the same place every time (.) I've got to be able to hold a needle as well (.) so if you can imagine holding a needle with a tremor*" (p5.166–170).	N/A	N/A
9) Goals	The goal is to stay on B1 treatment as long as the tremor and quality of life does not decrease.	"*I think my goal is to to as long as (.) I remain in a position I remain in I will continue with the medication (.) if my quality of life with my tremor changes (.) then I'll look at a prescribed medication for for tremors*" (p5.161–164).	N/A	N/A
10) Memory, Attention and Decision Processes	Has decided to take vitamin B1 thiamine and magnesium over prescribed PD medication.	"*At the moment I'm not on any prescribed medication but I do take alternative medication which is high dosage vitamin B1 thiamine (.) and magnesium*" (p1.13–15).	N/A	N/A
11) Environmental Content and Resources	Was surprised that UK specialists didn't know about B1 treatment/ new areas of treatment for PD.	"*I said have you heard about this vitamin B1 (.) and he went no I haven't (.) I said well I said (.) well why in (XXX) then (.) in in the (XXX) is that they all share information (.) is that these specialists in (.) are developing this regime with a high dosage vitamin B1 (.) yet you don't know anything about it (.) surely if you're in on (.) dealing with Parkinson's (.) you're always looking to see what is out there*	Costs of maintain the B1 supply (has become more expensive since the UK' exit from the European Union). Suggests that B1 treatment dosage strength can vary depending on the batch.	"*since the exit from theEuro it* [B1 treatment] *has become a bit more expensive*" (p3.91–92). "*sometimes with B1 you just don't get a exact (.) there's no exact dosage for whatever you are (.) so you've got to test it to see how far you benefit from it (.) sometimes you can be on a high dosage (.) sometimes you can be on a low dosage*" (p14–15.483-487).

(*continued on next page*)

Table 1 (*continued*)

TDF Domain	Facilitators for using Vitamin B1 treatment		Facilitators for using standard/prescribed PD treatment	
	Application of data to TDF framework	Supporting quotes	Application of data to TDF framework	Supporting quotes
		and peop what are people doing and developing" (p13.421–429).		
12) Social Influence	Colleagues with PD appear to be worse off than he is possibly because they are on PD medication.	"a lot of my colleagues I keep in touch with who are with a sort of Parkinson's group (.) umm are a lot more worse off then I am (.) but but they are on prescribed medication" (p2.39–43).	Considers taking Levodopa because their friends take it to manage their tremors.	"*…because I know there's a couple of friends who take (.) levodopa because their tremors too much for them*" (p9.306–307).
13) Emotion	Has positive feelings towards B1 treatment due to perception that it is benefitting them.	"*As long as I feel it's* [B1 treatment] *doing something (.) I'm very positive about it*" (p14.478–479).	N/A	N/A
14) Behavioural Regulation	They initially experimented with the B1 treatment dosages to find a suitable dose.	"*Different dosages have changed umm (.) experimenting to try and find the right dosage*" (p15.516–517).	N/A	N/A

established as the barrier to adhering to standard prescribed PD medication. The complexity of the data meant that discussions were needed to categorise the data into the most appropriate domains, as some codes did not clearly fit into TDF domains and others could be placed into more than one. Although this added additional complexity to the analysis, we considered the facilitators to his vitamin B1 treatment behaviour as a barrier to adherence to standard therapy and vice versa. The TDF-informed interview schedule enabled Mr. Wilkinson to share relevant information linking to the related behaviours, which in turn aided mapping to the TDF. To further illustrate this complexity, we have extracted the coding framework with supporting quotes for the facilitators and barriers to Parkinsonian medication for this participant (Appendix 2).

4. Discussion

This case study focuses on an individual's experience of self-managing PD symptoms using vitamin B1 which highlighted a number of interesting and important issues. Mr. Wilkinson was a participant in a previously published qualitative study which investigated the barriers and enablers to adherence to antiparkinsonian medications.[24] The inclusion of Mr. Wilkinson's interview data in the earlier full study and the presentation of his details in this case study has provided many interesting areas for discussion. This case study also offers healthcare professionals a unique insight into the management of PD as it captures the experiences of an underrepresented voice in pharmacy research – the non-adherent patient.

This case study used the TDF framework to identify factors that facilitated Mr. Wilkinson's alternative treatment choices as well as behaviours that created barriers to adherence to standard PD medication. *Beliefs about Capabilities* of administering vitamin B1 and *Beliefs about Consequences* of using this treatment were dominant factors for this individual as well as the effect of positive *Reinforcement* on symptom management gained from the effects of vitamin B1 therapy. These are illustrated by the following TDF descriptions and corresponding extracts of quotes as presented in Table 1 and summarised in Box 1 below.

Although *Beliefs about Consequences* arose as a dominant facilitator across the whole group researched in our previous study, on the whole *Beliefs about Capability* and *Reinforcement* did not feature as strong enablers to PD medication adherence.[24] This is somewhat surprising since taking a complex medication regimen, such as that prescribed for PD management needs a high degree of capability for good adherence. Similarly, it would be expected that the reinforcement gained from the control (or absence) of PD symptoms after taking prescribed medication would also act as an enabler to adherence, but this was not apparent across the data for the other eleven participants interviewed. Mr. Wilkinson's beliefs about his capability to manage a complex medication regime were likely to be influential in his decision to research and source an alternative PD treatment. It seems unlikely that he would have researched his preferred treatment if he had low capability beliefs and this behaviour suggests that he had high levels of health literacy which may contrast with the wider group of participants, although this was not

Box 1
Illustrative Quotes and Descriptions of Dominant TDF Domains for Mr. Wilkinson.

Beliefs about Capabilities
Mr. Wilkinson finds injecting vitamin B1 once every two days is much easier than taking PD medication daily:
"It's a lot of tablets (.) and I spoke to the doctor about that and he said the best way of doing it is to do two millilitres of injection three times a week (.) that's what I'm on (2) the regime that way is so much easier than taking eight tablets a day".

Beliefs about Consequences
Mr. Wilkinson believes that the longer they withhold from taking PD medication the more they will benefit in the future:
"Because if I can hold that off for as long as I possibly can I'll have more benefit in the future".

Reinforcement
Mr. Wilkinson believes that vitamin B1 treatment has reduced or stopped aches and pains, diminished mental capacity and low mood:
"So my aches and pains I used to have are not there anymore (.) umm my sort of clarity is a lot better (.) I don't have a lot mm f mind fog umm and my moods a lot better (.) umm so something is happening".
Mr. Wilkinson is unsure of what B1 treatment is doing but it appears to have reduced PD progression:
"*But I don't know what exactly what it's holding back (.) because I at the moment I'm not developing an awful lot which is good to see you know I'm glad to see*".

captured as part of this study.

Further quantitative research is needed to establish the prevalence of these barriers and enablers in a large sample of PD patients. We are in the process of developing a structured questionnaire to establish the prevalence of these barriers and facilitators to medication adherence in a large sample of PD patients. To date, medication non-adherence studies in PD have focused on patients who choose to take the treatment offered by the prescriber but might not be fully adherent to the mediation regimen,[27] rather than choosing not to take any of the medication. Further analysis of this one outlier (or deviant) participant offers great insight for clinical practice and added value for qualitative researchers by allowing different perspectives which are often missed, to be fully explored in a case study.[28] This research also demonstrates the need for recruitment strategies that support the inclusion of patients such as Mr. Wilkinson. Had we conducted this study in a clinical setting, this individual and those like him who do not take any of their prescribed treatment may not be in the system and as such would not have been recruited. Although non-adherent patients will still require monitoring and will be utilising the PD services to some extent. There is a need to continue to support patients who chose not to follow standard treatment to engage in research of this nature. Developing recruitment strategies that go beyond the clinical setting is one way of achieving this. For example, utilising social media, support groups and other innovative methods of recruitment offers the opportunity to engage those participants who would not necessarily take part in adherence research.

Several of the TDF domains were facilitators in Mr. Wilkinson's decision to manage PD symptoms via vitamin B1 injections. Knowledge of PD treatment and beliefs about the consequences of taking antiparkinsonian medicine underpinned Mr. Wilkinson's desire to source alternative treatment. Horne & Weinman's[17] Necessity-Concerns Framework can be used to understand how Mr. Wilkinson's medication beliefs influence adherence. He perceived that the benefit to postponing treatment with antiparkinsonian medications (i.e., that this would improve the medication's effectiveness long term) outweighed the risks of not taking the medication. He was also concerned that once he began taking antiparkinsonian medications, he would become dependent on the medication for symptom control. These beliefs about the consequences of taking antiparkinsonian medication contrast with those expressed by adherent PD participants who considered the medication to be essential for symptom control.[24]

Social comparison also played an important role in Mr. Wilkinson's treatment decisions; he is a member of PD support group and is in contact with people with different levels of disease progression. He measured the efficacy of B1 treatment by making comparisons between his own health status to others within this group; such downward social comparison (comparing oneself to those who have more pronounced symptoms or disability) reinforced Mr. Wilkinsons treatment decisions and led him to view the perceived side effects of taking antiparkinsonian medication as outweighing current benefits. It is interesting to note that whilst Mr. Wilkinson was fully non-adherent to prescribed PD medication, he occasionally took breaks from injecting the vitamin B1 treatment to gauge whether it was still working. This behaviour of taking a 'medication holiday' is well documented in the literature[29] and is captured by the Intentional Non-Adherence Scale (INAS) which measures the behaviour of 'testing treatment' where patients take less doses of medication than prescribed to see if it is still needed.[30,9]

Although there is some emerging evidence that vitamin B1 deficiency may influence the risk of developing PD[31,32,33] there is an absence of robust clinical evidence that symptoms of PD can be improved with B1 supplementation.[32,33,34] A series of small, case study reports by one Italian research clinic, implicate vitamin B1 as beneficial for a range of movement disorders and for post-stroke and multiple sclerosis related fatigue, with a similar small open label study in PD which was then extended into a larger series of patients.[35] A very recent correlative study (which was published later) also suggested that there was a relationship between vitamin B1 intake and lower levels of PD symptoms.[36] Although minimal clinical evidence exists, this sits on a broader base of preclinical literature that is more convincing. Mr. Wilkinson developed his understanding of the therapeutic benefits of B1 through online resources and health forums. Prior to being diagnosed with PD, he attended an online appointment with an Italian centre for PD treatment, which provided one-to-one advice and training on how to administer vitamin B1 injections. The internet is a common way to gain information about symptoms or health conditions, individuals report that they are more likely to look online for information about "new" symptoms than contact their healthcare providers. Health information is associated with a greater knowledge of treatment options[37] yet it can be challenging to navigate the complexity of healthcare information available to patients and to ascertain the validity of information that is presented about treatment options. However, more recently, the well-trusted Science of Parkinson's Blog (www.scienceofparkinsons.com) has been introduced for PD, which includes an entry on the use of Vitamin B1 (thiamine) (Be one with Vitamin B1 – The Science of Parkinson's (scienceofparkinsons.com). Furthermore, Parkinson's UK and the Michael J Fox foundation both have webpages about the use of vitamin B1 on their websites.

In terms of limitations, it is important to note that the qualitative study from which this case study derives, did not intend to explore the reasons for taking alternative treatments to the standard UK prescribing guidelines. In this sense, Mr. Wilkinson was adherent to vitamin B1 injections (bar a few medication holidays to check efficacy), but not adherent to the recommended treatment guidelines in the UK. An investigation of adherence to PD services in other parts of the world may have yielded different interpretations of the findings of framework analysis. Had this been the aim, we would have redesigned the interview schedule to explore the rationale and behaviours relating to the use of alternative and concomitant treatments (in this case vitamin B1 injections and magnesium supplements respectively) in more depth.

The authors of this paper do not endorse the use of vitamin B1 or magnesium supplements for the treatment of PD since these are not part of the UK prescribing guidelines. However, the general public is able to access a range of materials beyond the scientific literature and will form their own opinions on the evidence available, which may be at odds with the medical reality. For example, a lay person may interpret this preclinical data to be more clinically relevant than it is, and it is our responsibility as clinical practitioners to help patients put this information into context. As previously discussed, all the major Parkinson's organisations have summaries of the evidence for vitamin B1, but much of the material is also provided through blogs and books. The Italian clinic itself provides powerful videos extoling the benefits of vitamin B1 treatment, however, there is clearly a potential conflict of interest if patients are only receiving information from this source. Linking this back to the theoretical perspective of the Necessity-Concerns Framework, the availability of these resources creates a compelling reason for using alternative treatments by describing their benefits in this way. As healthcare practitioners, we need to be equipped to engage in conversations about the pros and cons of conventional treatments over newer ones, which may not yet have the evidence-base.

This case study raises a number of implications for pharmacy practice, in particular, the need to ensure that patients such as Mr. Wilkinson are provided with the opportunity to discuss treatment choices and self-management options for long-term conditions such as PD. Mr. Wilkinson is highly motivated to control his condition and perceives to be self-managing PD effectively, albeit with therapy that is outside the recommended UK guidelines. This highlights the need for healthcare professionals to explore, discuss and acknowledge the patient's beliefs, goals and preferences about their condition and its treatment. Mr. Wilkinson has indicated that he may return to the 'standard' medication in the future. The risk of not acknowledging the patient's views and their agency to take an alternative approach means that the opportunity for continued conversation/shared decision-making both at treatment initiation and throughout the course of the disease could be lost. To that

end, there is a need to keep the lines of communication open to allow that discussion to evolve over time and avoid patients dropping out of the system, particularly in the early stages where the patient tries to evaluate initial treatment decisions. Beliefs and illness perceptions may change over time, particularly as patients evaluate their treatment choices, illustrated by Mr. Wilkinson who takes 'drug holidays' and compares his progress to peers.

As healthcare providers we can learn from this case study by being aware of the breadth of unverified treatments being discussed, particularly online (including those in private UK clinics and overseas) so that we are able to support patients to make informed decisions about their self-management options, referring them to trusted, balanced sources of information. For this to happen, healthcare professionals need to keep themselves updated on new/alternative treatments, to enable an informed discussion about all available treatment options, whether within UK guidelines or not. In this case study, the prescriber's lack of knowledge of vitamin B1 as a potential treatment option was a pivotal point, after which Mr. Wilkinson lost confidence in the consultant as a credible source of information and potentially altered his perception of the support available within the system.

This case study has also highlighted the potential consequences when there is a perceived lack of support or dissatisfaction with the opportunities to discuss different treatment options within the clinical consultation which are essential for shared decision-making. When patients feel involved in the decision-making for their treatment, by engaging in discussions about treatment choices, they are more likely to follow the treatment plan.[38] Considering the patients' personal preferences, values and needs is important when discussing treatment options since these factors have a significant impact on perception of illness control, subsequent self-management behaviours and adherence to medication.[39–41]

To summarise, this case study offers healthcare professionals a unique insight into the management of PD as it captures the experiences of an underrepresented voice in pharmacy research – the non-adherent patient. The paper highlights the need within PD services to consider opportunities for how to support individuals who engage in treatments that are not offered within UK healthcare settings.

5. Conclusion

In conclusion, this paper presents interesting findings to Illustrate one case study's reasons for not taking standard PD medication and how the lack of a shared decision-making approach during initial consultations led to alternative PD treatment being sought. The importance of engaging under-represented participants in adherence research is also demonstrated along with the methodological and analytical challenges for dealing with 'outlier' cases such as this. Researchers who routinely analyse qualitative data through a behavioural science lens, may lead to a narrow view, since as highlighted in this paper, in many ways Mr. Wilkinson was adherent, just not adherent to the treatment offered in the UK. Finally, important implications for pharmacy practice are raised, in particular with regards to the need to recognise the influence that the patient's perspective has on self-management of symptoms and medication-taking behaviour and how these are addressed within the consultation. As part of clinical practice there is a need to consider opportunities for how cases such as Mr. Wilkinson could be supported through PD services, even if they are also receiving treatment elsewhere.

Funding

This research received no specific grant from any finding agency in the public, commercial, or not for profit sectors. The work was completed as part of a MSc in Health Psychology at Cardiff Metropolitan University which was self-funded by JS.

CRediT authorship contribution statement

Delyth James: Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Joshua Smith:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Emma Lane:** Writing – review & editing, Writing – original draft. **Rhian Thomas:** Writing – review & editing. **Sarah Brown:** Writing – review & editing. **Heidi Seage:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This paper and the research behind would not have been possible without the agreement and consent of the participant involved.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rcsop.2024.100450.

References

1. Rocca WA. The burden of Parkinson's disease: a worldwide perspective. *Lancet Neurol.* 2018;17(11):928–929. https://doi.org/10.1016/S1474-4422(18)30355-7.
2. Ball N, Teo WP, Chandra S, Chapman J. Parkinson's disease and the environment. *Front Neurol.* 2019;10:218. https://doi.org/10.3389/fneur.2019.00218.
3. Huang X, Ng SE, Chia NY, et al. Non-motor symptoms in early Parkin'on's disease with different motor subtypes and their associations with quality of life. *Eur J Neurol.* 2019;26(3):400–406. https://doi.org/10.1111/ene.13803.
4. Müller T. Drug therapy in patients with Parkinson's disease. *Transl Neurodegen.* 2012;1(1):1–13. https://doi.org/10.1186/2047-9158-1-10.
5. Segura-Aguilar J, Paris I, Muñoz P, Ferrari E, Zecca L, Zucca FA. Protective and toxic roles of dopamine in Parkin'on's disease. *J Neurochem.* 2014;129(6):898–915. https://doi.org/10.1111/jnc.12686.
6.. National Institute for Health and Care Excellence (NICE) Cited in Joint Formulary Committee, 2024, London BMJ Group and Pharmaceutical Press https://bnf.nice.org.uk/treatment-summaries/parkinsons-disease/.
7. Pringsheim T, Day TGS, Smith DB, et al. Dopaminergic therapy for motor symptoms in early Parkinson disease practice guideline summary: A report of the AAN guideline subcommittee. *Neurology.* 2021;97(20):942–957. https://doi.org/10.1212/WNL.0000000000012868 [Accessed 27/2/24].
8. Van Der Velden RM, Broen MP, Kuijf ML, Leentjens AF. Frequency of mood and anxiety fluctuations in Parkin'on's disease patients with motor fluctuations: a systematic review. *Mov Disord.* 2018;33(10):1521–1527. https://doi.org/10.1002/mds.27465.
9. Shin JY, Habermann B, Pretzer-Aboff I. Challenges and strategies of medication adherence in Parkin'on's disease: a qualitative study. *Geriatr Nurs.* 2015;36(3):192–196. https://doi.org/10.1016/j.gerinurse.2015.01.003.
10. Lakshminarayana R, Wang D, Burn D, et al. Using a smartphone-based self-management platform to support medication adherence and clinical consultation in Parkinson's disease. *NPJ Parkinon's Dis.* 2017;3(1):1–10. https://doi.org/10.1038/s41531-016-0003-z.
11. Leopold NA, Polansky M, Hurka MR. Drug adherence in Parkin'on's disease. *Mov Disord.* 2004;19(5):513–517. https://doi.org/10.1002/mds.20041.
12. Grosset KA, Bone I, Grosset DG. Suboptimal medication adherence in Parkin'on's disease. *Mov Disord.* 2005;20(11):1502–1507. https://doi.org/10.1002/mds.20602.
13. Kulkarni AS, Balkrishnan R, Anderson RT, Edin HM, Kirsch J, Stacy MA. Medication adherence and associated outcomes in medicare health maintenance organization-enrolled older adults with Parkin'on's disease. *Mov Disord.* 2008;23(3):359–365. https://doi.org/10.1002/mds.21831.
14. Malek N, Grosset DG. Medication adherence in patients with Parkinson's disease. *CNS Drugs.* 2015;29(1):47–53. https://doi.org/10.1007/s40263-014-0220-0.
15. Aloudah NM, Scott NW, Aljadhey HS, Araujo-Soares V, Alrubeaan KA, Watson MC. Medication adherence among patients with type 2 diabetes: a mixed methods study. *PLoS ONE.* 2018;13(12), e0207583. https://doi.org/10.1371/journal.pone.0207583.
16. Aujla N, Walker M, Sprigg N, Abrams K, Massey A, Vedhara K. Can illness beliefs, from the common-sense model, prospectively predict adherence to self-management

behaviours? A systematic review and meta-analysis. *Psychol Health*. 2016;31(8): 931–958. Available at: https://doi.org/10.1080/08870446.2016.1153640.
17. Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychol Health*. 1999;14(1):1–24. https://doi.org/10.1080/08870449908407311.
18. Clifford S, Barber N, Horne R. Understanding different beliefs held by adherers, unintentional nonadherers, and intentional nonadherers: application of the necessity–concerns framework. *J Psychosom Res*. 2008;64(1):41–46. https://doi.org/10.1016/j.jpsychores.2007.05.004.
19. Horne R, Weinman J. Self-regulation and self-management in asthma: exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. *Psychol Health*. 2002;17(1):17–32. https://doi.org/10.1080/08870440290001502.
20. Fleisher JE, Dahodwala NA, Xie SX, et al. Development and validation of the Parkinson's disease medication beliefs scale (PD-Rx). *J Parkinon's Dis*. 2016;6(2): 383–392. https://doi.org/10.3233/JPD-150765.
21. Kim SR, Kim JY, Kim HY, So HY, Chung SJ. Factors associated with medication beliefs in patients with Parkinson's disease: a cross-sectional study. *J Mov Disord*. 2021;14(2):133. https://doi.org/10.14802/jmd.20147.
22. Patton DE, Ryan C, Hughes CM. Enhancing community pharmacists' provision of medication adherence support to older adults: a mixed methods study using the theoretical domains framework. *Res Soc Adm Pharm*. 2021;17(2):406–418. https://doi.org/10.1016/j.sapharm.2020.03.004.
23. Prajapati AR, Dima AL, Clark AB, et al. Mapping of modifiable barriers and facilitators of medication adherence in bipolar disorder to the theoretical domains framework: a systematic review protocol. *BMJ Open*. 2019;9(2), e026980. https://doi.org/10.1016/j.sapharm.2020.03.004.
24. Smith J, Seage CH, Lane E, James DH. Using the theoretical domains framework to uncover the barriers and facilitators of medication adherence in Parkinson's disease. *Explor Res Clin Soc Pharm*. 2023;11, 100309. ISSN 2667-2766 Doi.org/10.1016/j.rcsop.2023.100309.
25. Pope C, Ziebland S, Mays N. Qualitative research in health care: analysing qualitative data. *Br Med J*. 2000;320(7227):114. https://doi.org/10.1136/bmj.320.7227.114.
26. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. *BMC Med Res Methodol*. 2013;13(1):1–8. https://doi.org/10.1186/1471-2288-13-117.
27. Fleisher JE, Stern MB. Medication nonadherence in Parkinson's disease. *Curr Neurol Neurosci Rep*. 2013;13(10):382. https://doi.org/10.1007/s11910-013-0382-z. PMID: 23954970; PMCID: PMC3808168.
28. Spencer L, Ritchie J, Lewis J, L.. *Dillon (National Centre for Social Research). Quality in Qualitative Evaluation: A Framework for Assessing Research Evidence*. Government Chief Social Researcher's Office.; 2003 [ISBN 07115044658.].
29. Hughes CM. Medication non-adherence in the elderly. *Drugs Aging*. 2004;21: 793–811. https://doi.org/10.2165/00002512-200421120-00004.
30. Weinman J, Graham S, Canfield M, et al. The intentional non-adherence scale (INAS): initial development and validation. *J Psychosom Res*. 2018;115:110–116. https://doi.org/10.1016/j.jpsychores.2018.10.010.
31. Sandeep, Sahu MR, Rani L, Kharat AS, Mondal AC. Could vitamins have a positive impact on the treatment of Parkinson's disease? *Brain Sci*. 2023;13(2):272. https://doi.org/10.3390/brainsci13020272.
32. Håglin L, Johansson LI, Forsgren L, Bäckman L. Intake of vitamin B before onset of Parkinson's disease and atypical parkinsonism and olfactory function at the time of diagnosis. *Eur J Clin Nutr*. 2017;71:97–102.
33.. Luong KVQ, Nguyen LTH. Thiamine and Parkinson's disease. *J Neurol Sci*. 2012;316 (1–2):1–8. ISSN 0022-510X https://doi.org/10.1016/j.jns.2012.02.008.
34. Costantini A, Pala MI, Compagnoni L, Colangeli M. High-dose thiamine as initial treatment for Parkinson's disease. *BMJ Case Rep*. 2013, bcr2013009289. https://doi.org/10.1136/bcr-2013-009289.
35. Anker AE, Reinhart AM, Feeley TH. Health information seeking: a review of measures and methods. *Patient Educ Couns*. 2011;82(3).
36. Costantini A, Fancellu R. An open-label pilot study with high-dose thiamine in Parkinson's disease. *Neural Regen Res*. 2016;11(3):406–407. https://doi.org/10.4103/1673-5374.179047.
37. Joosten EAG, DeFuentes-Merillas L, de Weert GH, Sensky T, van der Staak CPF, de Jong CAJ. Systematic review of the effects of shared decision-making on patient satisfaction, treatment adherence and health status. *Psychother Psychosom*. 2008;77 (4):219–226. https://doi.org/10.1159/000126073.
38. Costantini A, Pala MI, Grossi E, et al. Long-term treatment with high-dose thiamine in Parkinson disease: an open-label pilot study. *J Altern Complement Med*. 2015;21 (12):740–747. https://doi.org/10.1089/acm.2014.0353. Epub 2015 Oct 27. PMID: 26505466.
39. Leventhal H, Diefenbach M, Leventhal EA. Illness cognition: using common sense to understand treatment adherence and affect cognition interactions. *Cogn Ther Res*. 1992;16(2):143–163. https://doi.org/10.1007/BF01173486.
40. O'Connor SM, Jardine AG, Millar K. The prediction of self-care behaviors in end-stage renal disease patients using Leventhal's self-regulatory model. *J Psychosom Res*. 2008;65(2):191–200. https://doi.org/10.1016/j.jpsychores.2008.02.008.
41. Vallis M, Jin S, Klimek-Abercrombie A, et al. Understanding strategies to improve medication adherence among persons with type 2 diabetes: a scoping review. *Diabet Med*. 2023;40(1), e14941. https://doi.org/10.1111/dme.14941.