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Arden, M., Drabble, S.J. [orcid.org/0000-0001-7183-6321](https://orcid.org/0000-0001-7183-6321), O'Cathain, A. et al. (2 more authors) (2019) Adherence to medication in adults with Cystic Fibrosis: An investigation using objective adherence data and the Theoretical Domains Framework. *British Journal of Health Psychology*, 24 (2). pp. 357-380. ISSN 1359-107X

<https://doi.org/10.1111/bjhp.12357>

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# Adherence to medication in adults with Cystic Fibrosis: An investigation using objective adherence data and the Theoretical Domains Framework

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**Objectives.** Adherence to nebulizer treatment in adults with Cystic Fibrosis (CF) is poor, and interventions are needed. This research aimed to identify the factors affecting nebulizer adherence using the Theoretical Domains Framework (TDF) and to compare these for participants with different levels of adherence.

**Design.** Data-prompted interviews using the TDF.

**Methods.** Eighteen semi-structured interviews were conducted with adults with CF during which objectively measured adherence data were discussed. Framework analysis was used to code the data into TDF domains, and inductive qualitative content analysis was used to code different beliefs and experiences. Aspects of the TDF that differed between participants with different adherence levels were explored.

**Results.** Factors influencing adherence to treatment included all 14 domains of the TDF, 10 of which appeared to vary by adherence level: Skills; Memory and decision-making; and Behavioural regulation; Environmental context and resources; Social influences; Beliefs about consequences; Beliefs about capability; Reinforcement; Social role and identity; Intentions; Optimism; and Emotions.

**Conclusions.** This study is the first to use objectively measured adherence data in a data-prompted interview using the TDF framework to systematically assess the full range of factors potentially influencing adherence. The results highlighted that interventions need to consider issues of capability, opportunity, and motivation. Interventions that challenge dysfunctional beliefs about adherence and which support the development of routines or habits and problem-solving may be particularly useful for adults with CF.

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### Statement of contribution

#### **What is already known?**

- Adherence to medication in adults with cystic fibrosis is poor.
- Previous research has identified a range of contributing factors in relation to subjective reports of adherence.
- There is a wide discrepancy between self-reported adherence and objectively measured adherence.

#### **What this study adds**

- A data-prompted interview using objectively measured adherence data enabled the systematic assessment of potential factors that could be targeted in an intervention to increase adherence.
- There were some differences in the factors that were identified by high and low adherers.
- There is not one-size fits all intervention for adherence to medication in cystic fibrosis.

Cystic Fibrosis (CF) is a genetically inherited condition that affects approximately one in every 2,500 babies born (Cystic Fibrosis Trust, 2019). CF causes the lungs and digestive system to become clogged with thick sticky mucus (UK Cystic Fibrosis Registry Report, 2017) which results in recurrent lung infections, lung damage and ultimately, in over 80% of cases, respiratory failure (O'Sullivan & Freedman, 2009). The median predicted survival for a child born with CF is currently 47 years in the United Kingdom (UK Cystic Fibrosis Registry Report, 2017).

Effective self-management of CF requires a complex daily regimen of treatment (Sawicki, Sellers, & Robinson, 2009; Sawicki & Tiddens, 2012) including inhaled treatments, usually delivered via a nebulizer; antibiotics to reduce infections, and mucolytics (e.g., hypertonic saline and dornase alpha) to thin mucus and clear airways. However, consistent with adherence rates across a range of long-term conditions, adherence to nebulizer treatment in people with CF is low, ranging from 31% to 53% for inhaled antibiotics and 53%–79% for inhaled mucolytics (Eakin, Bilderback, Boyle, Mogayzel, & Riekert, 2011). Nebulizers such as I-neb<sup>®</sup> (Philips Respironics) that electronically record the time and frequency of nebulizations have shown a wide discrepancy between patient self-reported adherence to inhaled therapy (80%) and objective measurement of adherence (36%) (Daniels *et al.*, 2011).

A range of qualitative studies, which have mainly used a thematic approach to analysis, and reviews have attempted to understand the factors influencing adherence to treatment in CF for adolescents and adults (Abbott, Havermans, & Hart, 2009; Arias-Illoriente, García, & Martín, 2011; Foster *et al.*, 2001; George *et al.*, 2010; Hogan, Bonney, Brien, Karamy, & Aslani, 2015; Hoo, Boote, Wildman, Campbell, & Gardner, 2017; Horky, Sherman, Laura, Polvinen, & Rich, 2014; Lask, 1994; Macdonald *et al.*, 2016; Pakhale *et al.*, 2016; Sawicki, Heller, Demars, & Robinson, 2015). These have tended to find that adherence to treatment is reported to be influenced by the extent of treatment burden, having the time to do treatment, having a routine, forgetting to do treatment, a person's identity, perceptions of control, and social support. Knowledge and beliefs about the necessity of treatment, and concerns about its effectiveness have also been commonly identified, consistent with the Necessity–Concerns Framework that proposes that adherence to treatment occurs where necessity is perceived as high and concerns are low (Horne, Weinman, & Hankins, 1999). While these studies provide some insights, they may not be accessing the full range of factors that influence objectively measured adherence because subjective reports of adherence are inaccurate (Daniels *et al.*, 2011), and the factors affecting them may be

subject to recall (Kimmel, Lewis, Jaskowiak, Kishel, & Hennessy, 2003) and social desirability bias (Paulhus & Reid, 1991). Conversely, data-prompted interviews involve using sources of objective data, such as graphical representations of quantitative data (e.g., a graph showing objectively measured adherence), as a prompt for discussion in a qualitative interview (Kwasnicka, Dombrowski, White, & Sniehotta, 2015) to reduce problems of recall bias. The value of this methodology is that the data provide specific examples of (non) adherence that can stimulate reflection (Harper, 2002), and the relationships and any inconsistencies between the narratives and the objective data can be explored in depth (Kwasnicka *et al.*, 2015).

Psychological interventions have so far shown limited success in increasing adherence in people with CF (Goldbeck, Fidika, Herle, & Quittner, 2014), and this might be because the interventions are not targeting the most appropriate factors. For example, Quinn *et al.* (2004) delivered a motivational interview intervention via telephone to people with CF over a 3-month period but found no effect on adherence rates compared to a control group.

Fully understanding the factors affecting adherence is an important step in the process of developing effective evidence-based behaviour change interventions to support self-management of long-term conditions. Such understanding enables the design to be based on appropriate theories, and the components and effects to be specified and empirically tested (Craig *et al.*, 2015). There is evidence that interventions based on theory are more effective than those that are not (Michie & Prestwich, 2010). However, it can be difficult to identify which theories are most appropriate for a given behaviour, population, and context. Focusing on one theory may result in some key determinant(s) of the behaviour being missed (Patey, Islam, Francis, Bryson, & Grimshaw, 2012).

The behaviour change wheel (BCW) provides a comprehensive framework for intervention development established from a synthesis of other frameworks (Michie, Van Stralen, & West, 2011; Michie, Atkins, & West, 2014) at the centre of which sits the COM-B model that proposes that behaviour (B) arises when an individual has sufficient capability (C), opportunity (O), and motivation (M). The Theoretical Domains Framework (TDF; Cane, Connor, & Michie, 2012) was developed using a systematic consensus approach to identify and synthesize 14 key domains from 33 different behaviour change theories, each of which describes a construct that influences capability, opportunity, or motivation (Michie *et al.*, 2011; Michie, Atkins, & West, 2014). TDF domains that influence capability include the following: Knowledge (awareness); Skills (ability or competence); Memory, attention, and decision processes (ability to retain information and to focus); and Behavioural regulation (efforts to manage or change actions). Domains that influence opportunities include the following: Environmental Context and Resources (aspects of a person's situation or environment that impacts on behaviour) and Social influences (interpersonal influences that affect thoughts, feelings, or behaviours). Domains that impact on motivation include the following: Intentions (a decision to act in a certain way); Goals (end states that an individual wants to achieve); Beliefs about Capabilities (self-confidence and perceived behavioural control); Optimism (confidence that desired goals will be attained); Beliefs about consequences (outcome expectancies); Reinforcement (the response to a given stimulus – reward or punishment); Social/professional role and identity (set of behaviours or qualities displayed in a social or work setting); and Emotion (an individual's reaction to a matter or event). The TDF is recommended as a framework to inform interviews to identify the factors that influence a behaviour, within the BCW framework for intervention development (Michie, Atkins, & West, 2014).

The TDF has been used to identify factors relating to adherence to treatment for bronchiectasis by patients and health care professionals (McCullough *et al.*, 2015). Presseau *et al.* (2017) conducted and coded interviews using the TDF and identified Beliefs about consequences, Memory/Attention/Decision Processes, Behavioural Regulation, Social influence, and Social/Professional Role and Identity as being domains relevant to medication adherence following myocardial infarction. However, no studies to date have used the TDF to identify the factors affecting adherence in CF, and none have utilized feedback from objective measures of behaviour to provide a stimulus for discussion.

This study aimed to use the TDF to assess the factors affecting nebulizer adherence in adults with CF to inform the development of an intervention. This is the first study to use objective measures of adherence as a prompt to identify specific beliefs and experiences related to adherence and to compare these beliefs and experiences in adults with very low adherence (0%–25%), low adherence (25.1%–50%), moderate adherence (50.1%–75%), and high adherence (>75%).

## Method

Semi-structured interviews were conducted with adults with CF who used an I-Neb<sup>®</sup> nebulizer to deliver antibiotic and/or mucolytic treatment. The I-Neb<sup>®</sup> nebulizer electronically recorded all treatments from which data about date and time of nebulization were downloaded and presented in graphical form (date, day, or time on the  $y$ -axis and treatment taken on the  $x$ -axis). Interviews were conducted by a researcher unknown to the participants. During the interview, participants were shown charts of the last 6-month adherence data including overall percentage adherence, time of day of administration, and patterns of adherence across the days of the week. The charts were used as a prompt for discussion about the specific beliefs and experiences that affected their nebulizer treatment adherence. The topic guide (available as a Appendix S1) comprised open questions about the experience of adherence to treatment in CF (e.g., How easy or difficult is it to manage your CF?) as well as specific questions about nebulizer adherence informed by the COM-B and TDF (see Michie *et al.*, 2014; e.g., Do you have the skills to be able to use your nebuliser as prescribed?). Interviews were audio-recorded and transcribed verbatim.

Ethical approval for the study was obtained from [Hampshire A REC: 14/SC/1455].

## Participants

Participants were selected from the 110 adults (16 years +) with CF who attended a CF clinic in the United Kingdom and used at least one prescribed I-Neb<sup>®</sup> treatment per day, excluding those who were pregnant, post-transplant, on the active transplant list, or in the palliative phase of the disease. Selected participants were purposively sampled by age, gender, socio-economic status (estimated from postcode using the English indices of deprivation, 2015), and adherence rates (measured using the output from I-Neb<sup>®</sup> devices over the previous 6 months). Adherence rates were used to classify participants into groups of very low adherers (VL: 0%–25%), low adherers (L: 25.1%–50%), moderate adherers (M: 50.1%–75%), or high adherers (H: >75%). Participant characteristics are summarized in Table 1. Age and adherence has been described in categories to prevent the identification of participants, given the small population from which they were sampled. Twenty-one participants were selected and invited to take part in the study, from

**Table 1.** Participant characteristics

| Participant number | Gender | Age category (years) | Types of nebulized treatments taken (D, A, H <sup>a</sup> ) | Mean adherence category <sup>b</sup> | IMD deprivation quintile <sup>c</sup> |
|--------------------|--------|----------------------|---|--------------------------------------|---------------------------------------|
| 1                  | M      | 19–25                | D   | VL                                   | 4                                     |
| 2                  | M      | 16–18                | D   | VL                                   | 3                                     |
| 3                  | F      | 31+                  | D, A  | VL                                   | 3                                     |
| 4                  | F      | 31+                  | D, A, H   | VL                                   | 4                                     |
| 5                  | F      | 26–30                | D, A  | VL                                   | 5                                     |
| 6                  | F      | 16–18                | D, A  | L                                    | 4                                     |
| 7                  | M      | 19–25                | D, A  | L                                    | 5                                     |
| 8                  | M      | 19–25                | D, A  | L                                    | 4                                     |
| 9                  | M      | 26–30                | D, A  | L                                    | 4                                     |
| 10                 | M      | 26–30                | D, A, H   | L                                    | 2                                     |
| 11                 | M      | 31+                  | D, A, H   | M                                    | 2                                     |
| 12                 | M      | 19–25                | D, A  | M                                    | 3                                     |
| 13                 | M      | 31+                  | D, A, H   | M                                    | 4                                     |
| 14                 | M      | 16–18                | D, A, H   | M                                    | 3                                     |
| 15                 | M      | 16–18                | D, A  | H                                    | 2                                     |
| 16                 | F      | 31+                  | D, H  | H                                    | 3                                     |
| 17                 | M      | 31+                  | D, A  | H                                    | 2                                     |
| 18                 | M      | 19–25                | D, A, H   | H                                    | 4                                     |

Notes. <sup>a</sup>D = dornase alpha (mucolytic), A = antibiotic: either a single antibiotic, or two antibiotics taken in alternate months, H = hypertonic saline (mucolytic).

<sup>b</sup>Where very low adherers (VL) = 0%–25% mean adherence, low adherers (L) = 25.1%–50% mean adherence, moderate adherers (M) = 50.1%–75% mean adherence, and high adherers (H) = 75.1 + % mean adherence.

<sup>c</sup>IMD deprivation quintiles: 1 ≤ 8.49 (Least deprived), 2: 8.5–13.79, 3: 13.8–21.35, 4: 21.36–34.17, 5: ≥34.18 (Most deprived).

whom 20 consented, and 18 interviews were conducted (two participants were unavailable to interview).

### Analysis

Framework analysis was used to code the data (Ritchie & Spencer, 1994) using NVivo (version 10, QSR International). SD read and coded the transcripts and selected parts of the interview relating to nebulizer adherence which were analysed further. MA and SD independently coded the selected sections using the 14 TDF domains as a framework. Where text related strongly to more than one TDF domain, it was coded in both; otherwise, it was coded under the domain that best matched the content. The coders met to discuss and resolve any discrepancies and agree codes. The types of statements under each domain were then analysed using inductive content analysis (i.e., identifying themes arising from the data) to create sub-categories. The researchers met frequently to discuss and agree coding and category descriptions which indicated common beliefs, experiences, and perceived barriers and facilitators. Some categories were combined to form larger categories that could be described under a single heading. Consistent with established procedure (see Atkins *et al.*, 2017; Patey *et al.*, 2012), categories were retained if reviewers

agreed the following: The belief statements were mentioned by several respondents; there were conflicting beliefs, that is different participants reported opposing beliefs; or there was evidence of strong beliefs that may affect the target behaviour.

The researchers looked for aspects of the TDF that differed between participants with different adherence rates, such that belief categories were present in some adherence levels but not others, and that the frequency of participants reporting category beliefs between different adherence levels differed by two or more.

## Results

Table 2 shows all 14 TDF domains and categories identified during analysis with example quotes for the most frequently reported categories (for illustrative quotes in all categories, see Table S1). Quotations are annotated with the participant number and their adherence level (see Table 1).

### *Domains related to capability*

All of the TDF domains<sup>1</sup> related to capability featured strongly in the sample. The most commonly reported category beliefs were as follows: struggling to plan treatment; having knowledge about treatment-taking procedures; and having good nebulizer skills (see Table 2). Some of the categories of belief differed between participants with different levels of adherence (see Table 3).

Participants across all adherence groups reported having *knowledge* about their nebulizer treatment, what it does, how and when to take it, and why it is important; and the *skills* to do their nebulizer treatments, although there were a few specific difficulties noted around sterilizing by boiling and opening containers. Sometimes knowledge about the ‘rules’ of treatment taking were perceived to impact negatively on the ability to take treatment: ‘. . . I couldn’t take one now and then take one at teatime because there’s only 4 hours between it and you’ve got to have 8 hours between it’ (P11: M). These ‘rules’ often reflected ideas about optimal treatment taking, and sometimes, treatment was missed if it did not meet these rules.

*Memory* was identified such that some participants talked about forgetting their nebulizer treatments, and this was mentioned by both very low and high adherers. More commonly reported, particularly for very low, low, and moderate adherers, were participants ignoring reminders to do their treatment: ‘I think, I’ve tried alarms in the past and I tend to ignore those quite easily’ (P4: VL), suggesting that for some participants, ‘forgetting’ was a decision rather than an accident.

Participants spoke about using a wide range of *behavioural regulation* strategies. Treatment plans or routines were widely discussed. Some participants identified specific cues or prompts for treatment: ‘And you know I said about taking the DNase out of the fridge at night-time and putting it next to the bed in the morning so I didn’t have to move anywhere. It’s just there’. (P5: VL). Almost all participants talked about times and situations in which they struggled to plan treatments or where routines were disrupted: ‘we still struggle to get them all in to us on a daily basis . . . you know no matter, no matter what we do there’s always sometimes a distraction or something happens like the

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<sup>1</sup> TDF domain names are italicised.

**Table 2.** TDF domains and categories identified in relation to nebulizer adherence

| COM factor TDF domain                    | Category – factors related to adherence to nebulized treatment; <i>n</i> = number of participants reporting category out of 18 participants  | Illustrative quotes (see supplementary table for further examples)   |
|--|--|--|
| Capability                               |  |  |
| Knowledge                                | <ul style="list-style-type: none"> <li>• Having knowledge about treatment-taking procedures (<i>n</i> = 16)</li> <li>• Having knowledge about treatment action (how treatments work) (<i>n</i> = 11)</li> <li>• Having knowledge about the importance of nebulizer treatment (<i>n</i> = 7)</li> <li>• Having knowledge about treatment concerns (<i>n</i> = 3)</li> </ul> | <p>...you have to mix it up with like a liquid and then you have got to dissolve it, shake it, wait for it to settle and then pop it into the nebuliser (P10: L)</p> <p>DNase which is the stuff that thins out the mucus to be able to cough it up more easily... (P10: L)</p>                              |
| Skills                                   | <ul style="list-style-type: none"> <li>• Having good nebulizer skills (<i>n</i> = 14)</li> <li>• Being able to concentrating on treatment taking (<i>n</i> = 5)</li> <li>• Not having preparation or cleaning skills (<i>n</i> = 3)</li> </ul>   | <p>I can hold my breath and I can do it exactly and I am one of the shortest times to take it like it takes 1–3 min (P5: VL)</p> <p>Like if I were going to have it now sort of ... probably just, not saying I couldn't concentrate on other things but I just, I couldn't do it walking about (P18: H)</p> |
| Memory, attention and decision processes | <ul style="list-style-type: none"> <li>• Ignoring reminders to take treatment (<i>n</i> = 9)</li> <li>• Forgetting to take treatment (<i>n</i> = 7)</li> </ul>   | <p>I think, I've tried alarms in the past and I tend to ignore those quite easily. (P4: VL)</p> <p>Get home later and it will completely slip my mind and I just forget to do it all together. (P2: VL)</p>  |
| Behavioural regulation                   | <ul style="list-style-type: none"> <li>• Struggling to plan treatment (<i>n</i> = 17)</li> <li>• Having a plan for treatment or having a routine (<i>n</i> = 13)</li> <li>• Knowing that others are monitoring nebulizer adherence (<i>n</i> = 12)</li> <li>• Create prompts or cues for treatment (<i>n</i> = 9)</li> </ul>   | <p>we still struggle to get them all in to us on a daily basis ... there's always sometimes a distraction or something happens like the unexpected (P4: VL)</p> <p>and sort of planning out when you're going to take it and things like that. ...that's sort of the main thing for me (P12: M)</p>          |

Continued



**Table 2.** (Continued)

| COM factor TDF domain               | Category – factors related to adherence to nebulized treatment; <i>n</i> = number of participants reporting category out of 18 participants   | Illustrative quotes (see supplementary table for further examples)   |
|-------------------------------------|---|--|
| Opportunity                         | <ul style="list-style-type: none"> <li>● Self-monitoring nebulizer treatments (<i>n</i> = 6)</li> <li>● Treatment is automatic or habitual (<i>n</i> = 5)</li> <li>● Self-monitoring health outcomes/symptoms (<i>n</i> = 5)</li> <li>● Planning rewards for yourself for good adherence (<i>n</i> = 3)</li> </ul>  | They said at hospital it weren't that bad but I, I, to me it were bad. It were like 50%, probably less... (P8: L)  |
| Environmental context and resources | <ul style="list-style-type: none"> <li>● Having the time or capacity to do treatment (<i>n</i> = 16)</li> <li>● Having the equipment/resources for treatment taking (<i>n</i> = 14)</li> <li>● Weekends change the context for treatment (<i>n</i> = 13)</li> <li>● Having an active social life as a barrier for treatment (<i>n</i> = 11)</li> <li>● Holidays and travel as barriers to treatment (<i>n</i> = 11)</li> <li>● Being able and willing to take treatment away from home or not (<i>n</i> = 11)</li> <li>● The time of day can affect treatment (<i>n</i> = 10)</li> <li>● Stressful or unusual events which are a barrier to adherence (<i>n</i> = 6)</li> <li>● Multi-tasking while doing treatment (<i>n</i> = 6)</li> <li>● Hospital as a facilitator for treatment (<i>n</i> = 4)</li> <li>● Distractions and interruptions to treatment (<i>n</i> = 4)</li> </ul> | I'd say in the mornings is when I just do the Promixin because I haven't got time to do anything else (P10: L)<br>That's a pain. We were camping and it was really hard to clean my neb properly. (P16: H)<br>I do it but the circumstances of doing it like effect like my social life... (P7: M) |
| Social influences                   | <ul style="list-style-type: none"> <li>● Having support from family and others (<i>n</i> = 15)</li> <li>● Having support from health care professionals (<i>n</i> = 11)</li> </ul>  | Me friend when [name] comes she'll say 'have you done your nebulizers today?' just in a general chat (P3: VL)  |

Continued

**Table 2.** (Continued)

| COM factor TDF domain                 | Category – factors related to adherence to nebulized treatment; <i>n</i> = number of participants reporting category out of 18 participants   | Illustrative quotes (see supplementary table for further examples)  |
|---------------------------------------|---|---|
| Motivation                            | <ul style="list-style-type: none"> <li>● Making social comparisons with others who have CF (<i>n</i> = 9)</li> <li>● Experiencing conflict or nagging from others (<i>n</i> = 9)</li> <li>● Being willing to take treatment in front of others or not (<i>n</i> = 8)</li> <li>● Perceiving a lack of or limited support (<i>n</i> = 5)</li> <li>● Experiencing conflict with health professionals (<i>n</i> = 3)</li> <li>● Declining offers of support or avoiding support from others (<i>n</i> = 3)</li> </ul> | <p>As soon as they got it I went up t'hospital for a separate appointment with one of physios and she taught me through it all. (P3: VL)</p> <p>I think it's more a case of as I say I know that's there's people who take more medication and things than what I do so (P9: L)</p> |
| Social/Professional role and identity | <ul style="list-style-type: none"> <li>● Being organized or disorganized (<i>n</i> = 7)</li> <li>● Being obstinate or rebellious (<i>n</i> = 7)</li> <li>● Having control over treatment taking (<i>n</i> = 6)</li> <li>● Being a lazy person or not (<i>n</i> = 5)</li> <li>● Being the kind of person who takes their treatment (<i>n</i> = 3)</li> </ul>   | <p>...I've never really like planned things massively ahead so yeah I don't know... (P12: M)</p> <p>if I'm really stubborn about it then the more nagging the more it pushes me away... (P7: L)</p>   |
| Beliefs about Capabilities            | <ul style="list-style-type: none"> <li>● Adherence to treatment is difficult (<i>n</i> = 16)</li> <li>● Using a nebulizer is easy (<i>n</i> = 12)</li> <li>● Adherence to treatment is easier with a routine (<i>n</i> = 10)</li> <li>● Nebulizer treatment is an annoyance (<i>n</i> = 10)</li> <li>● Adherence to treatment is especially difficult when tired (<i>n</i> = 7)</li> </ul>  | <p>It's not that hard just blowing through a machine for 5 min before you go to bed, is it? (P18: H)</p> <p>Its physically making yourself do it...which is the thing (P7: L)</p>   |

Continued

**Table 2.** (Continued)

| COM factor TDF domain      | Category – factors related to adherence to nebulized treatment; <i>n</i> = number of participants reporting category out of 18 participants   | Illustrative quotes (see supplementary table for further examples)   |
|----------------------------|---|--|
| Optimism                   | <ul style="list-style-type: none"> <li>● Believing that complete (100%) adherence is unachievable (<i>n</i> = 8)</li> <li>● Believing that complete (100%) adherence is achievable (<i>n</i> = 5)</li> <li>● Being uncertain about whether 100% adherence is achievable (<i>n</i> = 4)</li> </ul>   | <p>It's just life. It's never going to be absolutely hundred percent is it? (P16: H)</p> <p>It is though, it is because it is necessary and there is no excuse not, so it is achievable 100%. . . because it's necessary cos it's for your life (P14: M)</p>   |
| Beliefs about consequences | <ul style="list-style-type: none"> <li>● Nebulizer treatments are effective (<i>n</i> = 12)</li> <li>● My health depends on me doing my nebulizer treatment (<i>n</i> = 12)</li> <li>● Nebulizer treatment are not (always) effective (<i>n</i> = 9)</li> <li>● Nebulizer treatments help my symptoms (<i>n</i> = 9)</li> <li>● Nebulizer treatment has long-term benefits (<i>n</i> = 7)</li> <li>● Nebulizers are not the most important part of my CF treatment (<i>n</i> = 6)</li> <li>● Occasional non-adherence is OK (<i>n</i> = 6)</li> <li>● Nebulizer treatment means I can avoid the need for IVs/Hospital stays (<i>n</i> = 5)</li> <li>● If I feel OK I don't need to do my treatment (<i>n</i> = 5)</li> <li>● Nebulizer treatments make me feel worse (<i>n</i> = 5)</li> <li>● Bugs can become resistant to treatment (<i>n</i> = 3)</li> </ul> | <p>I do definitely think that all the nebulizer stuff is is a really good a really good drug to to have and a necessary one I think (P3: VL)</p> <p>. . .as long as I do my treatment I know that in a few weeks' time you know 95% of the time I'm absolutely fine I can do whatever I like (P17: H)</p> <p>So it's like what's the point in taking all this medication if 6 months down the line let's say, it turns out that it's really done nothing, it's been a waste of time (P2: VL)</p> |
| Reinforcement              | <ul style="list-style-type: none"> <li>● Feeling better as a result of nebulizer treatment (<i>n</i> = 11)</li> <li>● Not feeling that the nebulizer is working (<i>n</i> = 10)</li> <li>● Experiencing negative effects of the nebulizer treatment (<i>n</i> = 8)</li> </ul>   | <p>After a couple of days of being on it, I will cough more up, it does feel a lot thinner and my lungs feel clearer (P13: M)</p> <p>well you don't straight away but say you have like a week off, you will feel awful and your chest will hurt all the time (P6: L)</p>  |

*Continued*

**Table 2.** (Continued)

| COM factor TDF domain | Category – factors related to adherence to nebulized treatment; <i>n</i> = number of participants reporting category out of 18 participants   | Illustrative quotes (see supplementary table for further examples)   |
|-----------------------|---|--|
| Intention             | <ul style="list-style-type: none"> <li>● Experiencing other rewards for adherence to treatment (e.g., improvements in lung function or praise from clinicians) (<i>n</i> = 5)</li> <li>● Feeling worse as a result of not doing nebulizer treatment (<i>n</i> = 4)</li> <li>● Experiencing negative consequences of non-adherence to treatment (<i>n</i> = 4)</li> </ul>                  | DNase doesn't – I don't even notice any difference. I don't know if it does anything or not (P16: H)   |
| Goals                 | <ul style="list-style-type: none"> <li>● Having an unstable intention for adherence or non-adherence (only some of the time) (<i>n</i> = 14)</li> <li>● Having a stable intention for adherence or non-adherence (<i>n</i> = 13)</li> <li>● Intending to change (improve) adherence (<i>n</i> = 11)</li> </ul>  | I do do it, whatever time I come in, and again, even if I'm drunk, which is very rare! (P16: H)<br>maybe if I'm sort of going round there to someone's house and I'm staying one night, I'll maybe say 'well I'll miss the night dose and I'll miss the morning dose' (P13: M)   |
| Emotion               | <ul style="list-style-type: none"> <li>● Having other life goals (<i>n</i> = 14)</li> <li>● Having goals for the amount of treatment taken (<i>n</i> = 13)</li> <li>● Having goals related to health outcomes (<i>n</i> = 13)</li> <li>● Having goals that conflict with the ability to take treatment (<i>n</i> = 12)</li> <li>● Not having or avoiding goals (<i>n</i> = 12)</li> </ul> | I think that having kids makes me think that I don't wanna be ill. . . cos I have to be alive for them and well for them. . . (P16: H)<br>Like if this time next year, if you can tell me it's still ninety five percent, I would be happy. You know what I mean? (P18: H)   |
| Emotion               | <ul style="list-style-type: none"> <li>● Experiencing low mood or depression (<i>n</i> = 8)</li> <li>● Feeling regret or anticipating feeling regret (<i>n</i> = 5)</li> <li>● Feeling fearful (<i>n</i> = 4)</li> <li>● Avoiding thinking about CF or treatment (<i>n</i> = 4)</li> </ul>  | But now I mean I am trying to take it every morning but it's just yeah I think a lot of my medication at the minute is actually depression related why I can't take it (P5: VL)<br>Because then because if I do get to that stage, which I've kind of accepted [I] am. . . I can, I can't look back and say I could have done better. (P15: H) |

**Table 3.** TDF domains associated with *capability* where there are different patterns of category beliefs between participants with different levels of adherence

| TDF domain                                | Category   | Adherence level  |                |                |                 |
|---|--|------------------|----------------|----------------|-----------------|
|   |  | V low<br>(n = 5) | Low<br>(n = 5) | Mod<br>(n = 4) | High<br>(n = 4) |
| Skills                                    | Not having preparation or cleaning skills        | 0                | 1/5            | 0              | 2/4             |
| Memory, attention, and decision processes | Forgetting to take treatment                     | 3/5              | 0              | 1/4            | 3/4             |
|   | Ignoring reminders to take treatment             | 3/5              | 4/5            | 2/4            | 0               |
| Behavioural regulation                    | Treatment is automatic or habitual               | 0                | 2/5            | 0              | 3/4             |
|   | Self-monitoring health outcomes/symptoms         | 0                | 2/5            | 1/4            | 2/4             |
|   | Planning rewards for yourself for good adherence | 1/5              | 2/5            | 0              | 0               |

Note. Light shading indicates <50% of participants; dark shading indicates  $\geq$ 50% of participants.

unexpected' (P4: VL). Lower adherers but not moderate or higher adherers reported planning rewards for themselves for adherence to treatment.

Some, mostly moderate or high adherers talked about some aspects of their treatment being automatic or habitual and requiring less effort: 'It definitely is a routine mindset... I don't even think about it in the morning particularly, if I'm going to work...' (P17: H).

Participants talked about self-monitoring their treatment taking by looking at the battery level on the nebulizer or the amount of medications used, and mostly moderate to high adherers talked about self-monitoring their health (e.g., lung function) or CF symptoms (e.g., coughing). Most participants spoke, and were positive about, health professionals monitoring their treatment using downloads from their I-Neb<sup>®</sup> nebulizer: 'It's nice to have the feedback'. (P7: M).

### **Domains related to opportunity**

Both of the TDF domains related to opportunity featured in the sample. The most commonly reported category beliefs were as follows: having the time or capacity to do treatment; having support from family or others; and having the equipment/resources for treatment taking (see Table 2). A proportion of the categories of belief differed between participants with different levels of adherence (see Table 4).

*Environmental contexts* relevant for adherence included temporal factors, locations, events, resources, and competing demands. A majority of environmental categories were identified by participants across the range of adherence categories. Some factors were consistently perceived as barriers including social life, holidays, and travel. Some participants found taking treatment away from home was not a barrier while others were unwilling to do so.

Some environmental factors were experienced differently across adherence categories. Very low adherers reported that being in hospital was a facilitator for treatment: 'I do it in hospital, come out, do it for about a week or so, and then after that, I'm back to

**Table 4.** TDF domains associated with *opportunity* where there are different patterns of category beliefs between participants with different levels of adherence

| TDF domain                          | Category   | Adherence level  |                |                |                 |
|-------------------------------------|--|------------------|----------------|----------------|-----------------|
|                                     |  | V low<br>(n = 5) | Low<br>(n = 5) | Mod<br>(n = 4) | High<br>(n = 4) |
| Environmental context and resources | Times of day help with treatment                     | 0                | 2/5            | 2/4            | 2/4             |
|                                     | Stressful or usual events are a barrier to treatment | 3/5              | 2/5            | 1/4            | 0               |
|                                     | Hospital is a facilitator for treatment              | 3/5              | 1/5            | 0              | 0               |
|                                     | Distractions and interruptions are a barrier         | 1/5              | 0              | 0              | 3/4             |
| Social influences                   | Conflict with health professionals                   | 3/5              | 0              | 0              | 0               |
|                                     | Declining/avoiding support from others               | 2/5              | 1/5            | 0              | 0               |
|                                     | Willing to take treatment in front of others         | 1/5              | 0              | 1/4            | 1/4             |
|                                     | Not willing to take treatment in front of others     | 1/5              | 2/5            | 0              | 3/4             |

Note. Light shading indicates <50% of participants; dark shading indicates  $\geq$ 50% of participants.

where I were. . .’ (P2:VL). Stressful or infrequent events (e.g., Christmas, moving house) were barriers for treatment for participants with low and moderate adherence but not for high adherers.

Some participants reported that they were able to engage in other tasks while doing treatment; however, for mostly high adherers, distractions were a barrier to treatment: ‘Sometimes, I don’t finish, you know when you start it, I then get busy with kids and don’t finish, then I have to start it again’. (P16:H)

*Social influences* included support from others, the impact of social situations on treatment, conflict with others, and social comparison. Willingness to take treatment in front of others was not necessarily a barrier to adherence given that most high adherers were not willing.

Almost all participants except the two lowest adherers spoke about the social support that they received from at least one source: from family, health care professionals, and others: ‘I don’t think I’d do it, if I didn’t have the motivation to get out my bed I wouldn’t do it, if [my mother] didn’t bring it upstairs’ (P6: M), although some participants reported receiving limited support, and some lower adherers reported declining or avoiding support-seeking: ‘I don’t like offloading stuff like that I don’t like [my partner]doing it but that’s just me’ (P3: VL). A number of participants reported that their adherence (or lack of) caused conflict with others, both family and health professionals. Notably, it was only very low adherers who reported conflict with health professionals, for example: ‘he were basically telling me off. . . in front of a load of other people . . .’. (P3: VL)

Participants across all adherence categories made social comparisons with others with CF in terms of how much treatment they needed to take, how they managed their adherence, factors affecting their ability to adhere, and the impact of this on their health.

### **Domains related to motivation**

All of the TDF domains related to motivation featured in the sample. The most commonly reported categories were as follows: that adherence to treatment is difficult; having other life goals; and having unstable intentions for adherence or non-adherence (see Table 2). A large proportion of the categories of belief differed between participants with different levels of adherence (see Table 5).

Participants talked about a range of personal qualities and *social identities* that influenced their adherence to nebulizer treatment in either positive or negative ways. Some of these qualities were perceived to be stable and consistent since childhood, or as a result of parental influence. Participants with higher adherence used different identity constructions (the kind of person who takes their treatment; being organized) while lower adherers talked about being obstinate or rebellious, or being 'lazy' or disorganized: 'And you can't turn stubborn off, you can't, if you're a stubborn person you're a stubborn person for life'. (P2: VL)

Almost all participants *believed that they were capable* such that nebulizer treatments were quick and easy to do, although most participants found them or the processes around them to be an annoyance, particularly cleaning and sterilizing nebulizers. Across all adherence groups, participants reported that adhering to nebulizer treatment was difficult. Specifically, tiredness was perceived to make adherence more difficult (although not for high adherers) and having a routine was perceived to make adherence easier: 'On the whole I'd say it's alright like majority of the time I feel like I manage it quite well but I think that sometimes I don't know I think more recently I've noticed it that like if I get out of a routine then it becomes difficult to manage. . .' (P12: M).

Participants with lower adherence tended to report being *optimistic* that 100% adherence was possible, while those with higher adherence reported being more pessimistic: 'It's just life. It's never going to be absolutely hundred percent is it?' (P18: H)

Participants discussed a wide range of necessity and concern *beliefs about* nebulizer treatments and the *consequences* of adherence and non-adherence. Across all adherence categories, participants reported that nebulizer treatments are effective, help with symptoms, are important to be able to remain well/avoid becoming ill, avoid the need for hospital stays, and have long-term benefits. Within this belief and across adherence categories, there was also an understanding that occasional non-adherence was acceptable to some.

Participants across all adherence categories believed that nebulizer treatments were not always effective although the extent of this lack of effectiveness varied, so that very low adherers believed that they may not be effective at all: 'a waste of time' (P2: VL) while higher adherers thought that there were some types of treatment that were not fully effective: '...because that is helping my chest, this keeps certain infections at bay, but every now and then one will creep through' (P14: M).

Participants' beliefs that nebulizers were not the most important part of CF treatment occurred across adherence categories. Some participants believed that IV antibiotic treatments (P1: VL, P5: VL, P9: L, P18:H) physiotherapy (P6:L) and exercise (P6: L; P17:H) were more important than nebulizers. The belief that treatment was not needed if participants felt well was held by low and very low adherers.

**Table 5.** TDF domains associated with motivation where there are different patterns of category beliefs between participants with different levels of adherence

| TDF domain                           | Category  | Adherence level  |                |                |                 |
|--------------------------------------|---|------------------|----------------|----------------|-----------------|
|                                      |   | V low<br>(n = 5) | Low<br>(n = 5) | Mod<br>(n = 4) | High<br>(n = 4) |
| Social role and identity             | Being the kind of person who takes their treatment            | 0                | 1/5            | 0              | 2/4             |
|                                      | Being lazy  | 1/5              | 2/5            | 1/4            | 0               |
|                                      | Not being lazy  | 0                | 0              | 0              | 1/4             |
|                                      | Being organized   | 0                | 1/5            | 0              | 2/4             |
|                                      | Being disorganized  | 2/5              | 0              | 2/4            | 0               |
|                                      | Being obstinate or rebellious                                 | 4/5              | 2/5            | 1/4            | 0               |
| Beliefs about capability<br>Optimism | Especially difficult when tired                               | 1/5              | 4/5            | 2/4            | 0               |
|                                      | Complete adherence is achievable                              | 2/5              | 1/5            | 2/4            | 0               |
|                                      | Complete adherence is unachievable                            | 0                | 3/5            | 2/4            | 3/4             |
| Beliefs about consequences           | Uncertain about whether adherence is achievable               | 2/5              | 0              | 2/4            | 0               |
|                                      | Nebulizers are not the most important part of my CF treatment | 2/5              | 3/5            | 0              | 3/4             |
|                                      | Nebulizer treatments make me feel worse                       | 3/5              | 1/5            | 1/4            | 0               |
|                                      | Bugs can become resistant to treatment                        | 0                | 0              | 2/4            | 1/4             |
| Reinforcement                        | Feeling worse as a result of not doing nebulizer treatment    | 1/5              | 2/5            | 0              | 1/4             |
|                                      | Other rewards for adherence to treatment                      | 2/5              | 0              | 0              | 3/4             |
| Intentions                           | Having stable intentions not to adhere                        | 2/5              | 2/5            | 0              | 0               |
|                                      | Having unstable intention to adhere                           | 3/5              | 4/5            | 2/4            | 0               |
| Emotions                             | Feeling regret or anticipated regret                          | 1/5              | 1/5            | 0              | 3/4             |
|                                      | Feeling fearful   | 0                | 1/5            | 0              | 3/4             |
|                                      | Avoiding thinking about CF or treatment                       | 2/5              | 1/5            | 0              | 0               |

Note. Light shading indicates <50% of participants; dark shading indicates ≥50% of participants.



Some participants in the very low and low adherence categories reported that their nebulizer treatment made them feel worse, often due to reported side effects. Some participants in the medium and high adherence categories reported beliefs about treatment resistance: 'I was told that [the bacteria] actually become acclimatised to it, and it would lose its effectiveness' (P13: M)

Participant's beliefs about *reinforcement* from treatment varied in part because of the different drugs that they were taking. Hypertonic saline (a mucolytic) was reported to have immediate noticeable effects on coughing and sputum levels: 'Yeah. Always do hypertonic saline first with salt water, so that makes me cough like mad, and that will get the easy stuff up as it were' (P13: M). Antibiotic treatments were perceived as the least likely to produce noticeable effects: 'Stuff that I've had like all my life, like Colomycin. It's like just an antibiotic that you take. My chest feels exactly the same whether I'm on that or not. And then some of the nebulisers and antibiotics, I've started on. . . I don't feel any different if I'm taking them or not'. (P18:H). Some participants had experienced negative effects of their treatments which included the following: feeling tight chested, wheezy, coughing, losing their voice, itching, 'the shakes', and unpleasant smell or taste.

Some participants spoke about receiving reinforcement from others for their adherence including receiving praise for efforts to adhere (lower adherers): 'I get enough praise when I go up to the hospital. It actually is really helping seeing the physios every two weeks'. (P5: VL); or very high levels of adherence or lung function (high adherers): 'When the physio printed out my nebuliser thing at my annual review a couple of years ago, she was like, Whoa! 98% compliance! Can I show this to other people!' (P16: H).

Reinforcement could also be through a negative outcome, for example being 'told off' for low adherence. This was more commonly reported by low-very low adherers but one high adherer (P15:H) also described a past experience that prompted an improvement in their adherence: '... And that's when it really kicked in when I saw my lung deteriorating and it were like I can do a lot more than what I have been doing. That's what really did it. Ever since then I would say I have been between 80-90%' (P15: H)

Patterns of *intention* between high and low adherers were difficult to discern because participants talked about different periods of adherence at different times. However, only low adherers reported stable intentions for non-adherence. Many participants, like P15 above, reported moments where they made a conscious decision to change, that is to increase their adherence or 'getting back on track. . .' (P14: M).

Most participants across all adherence groups reported occasional periods of intentional non-adherence. For some, there were particular occasions when treatment would be intentionally missed. While for others, intentional non-adherence was for some but not all daily prescribed treatments: '...and I was supposed to take it 4 times a day. Even, when I were proper on it I'd only take it 3 times a day' (P11: M)

Participants reported having a wide variety of *goals* related to adherence for treatment, their health, and their life generally, although some reported avoiding having goals. Those with low adherence tended to talk about more modest treatment goals: 'we are working on me trying to do the night time ones'. (P3: VL) while high adherers' treatment goals appeared more ambitious: 'Just take them all'. (P18: H).

Life goals were varied and included being well enough to go on holidays, get married, have and bring up children, and employment goals. Some goals were in conflict with adherence and included the following: wanting to be normal/have a normal life, family, or child-related goals, work and school goals, goals related to other treatments, social life and friends, and relaxation and sleep.

Participants expressed *emotions* in relation to how they felt about treatment adherence in relation to having CF and in terms of emotional factors that impacted on their ability to adhere. Participants expressed regret that they had experienced in relation to non-adherence, and about adherence as a way to avoid anticipated regret: ‘because then because if I do get to that stage, which I’ve kind of accepted [I] am. . . I can, I can’t look back and say I could have done better’. (P15: H). Fear was perceived to be a driver for adherence, particularly for the highest adherers: ‘Yeah, I’m a good girl, cos I’m terrified, I’m terrified of being ill. . .’ (P16: H). Conversely, some lower adherers, avoided thinking about CF and adherence: ‘I find other things to do, like to put me off it, like put it to the back of my mind. If I don’t think about it, I ain’t got to do it sort of thing’ (P2:VL).

Low mood was often used to explain periods of lower adherence; ‘It all depends on what kinda day I’ve had and how I feel on that day. . .’ (P3:VL) but this did not vary by adherence level. Sometimes lower adherence was in relation to day to day fluctuations in mood, periods of stress that resulted in low mood, or longer periods of depression.

## Discussion

This study aimed to use the TDF to assess the factors affecting nebulizer adherence in adults with CF to inform the development of an intervention. The TDF allowed for a thorough and systematic assessment of the factors influencing adherence in this sample of adults with the CF. Using objectively measured adherence data as a stimulus for discussion enabled a more thorough and realistic discussion of the beliefs and experiences affecting adherence (Kwasnicka *et al.*, 2015). All of the 14 TDF domains showed some variation across individuals, consistent with the view that a one-size fits all intervention is unlikely to be successful (Easthall & Barnett, 2017). Ten TDF domains showed apparent variation across adherence levels and might be particular targets for intervention (Skills; Memory, attentions and decision processes; Behavioural regulation; Environmental context and resources; Social influences; Social role and identify; Beliefs about capability; Optimism; Beliefs about consequences; Reinforcement; Intentions; and Emotions). These domains and the specific beliefs categories provide a basis for the next steps of intervention development using the BCW (Michie *et al.*, 2011).

Having access to objectively measured adherence data for each participant allowed us to make some tentative comparisons between higher and lower adherence in terms of the domains and belief categories that were reported to influence their nebulizer adherence. Many of the domains identified in this study as being relevant have been identified in previous qualitative studies (Macdonald *et al.*, 2016; Sawicki *et al.*, 2015). However, the objectively measured adherence data for the participants enabled greater insight about which of these factors might explain differences in adherence levels, and therefore, what might be the best factors to focus on in an intervention, as well as those that may be inappropriate.

Knowledge about treatment has regularly been identified as a theme in qualitative studies (Sawicki *et al.*, 2015). However, consistent with studies showing no relationship between knowledge and adherence (Lin, Kendrick, Wilcox, & Quon, 2017; Modi & Quittner, 2006), this study shows that most participants report that they have good levels of knowledge. This is consistent with a systematic review that showed that knowledge is necessary but not sufficient to promote medication adherence (Kahwati *et al.*, 2016). Likewise, having the time/capacity to do treatment was identified which is consistent with qualitative work identifying the importance of this factor (Sawicki *et al.*, 2015).

However, time was identified as important by both high and low adherers, and yet high adherers were able to overcome this challenge suggesting that there are other motivational or capability issues (see Michie *et al.*, 2011) that are more likely to explain adherence differences and hence be suitable targets for intervention.

Consistent with the necessities and concerns model (Horne *et al.*, 1999), and previous research into adherence in CF (e.g., Sawicki *et al.*, 2015), participants reported a wide range of different beliefs about the consequences of nebulizer adherence/non-adherence. Participants did not get direct positive reinforcement from most of their nebulized treatment, and this could lead to participants to question its effectiveness. Given the range of different beliefs expressed across different categories of adherence, interventions should seek to address specific dysfunctional beliefs relevant to the individual. This approach has been used successfully in an intervention to improve medication adherence in stroke survivors (O'Carroll, Chambers, Dennis, Sudlow, & Johnston, 2013).

Lower adherers in this study were more likely to report ignoring reminders to take their treatment. This 'purposeful forgetting' (George *et al.*, 2010) is consistent with the findings of a large randomized controlled trial which showed no effect of reminders on adherence (Choudhry *et al.*, 2017). Reminders are only likely to be effective (and serve to prevent 'forgetting') if the recipient has a strong intention to adhere. The finding that lower adherers reported intentional non-adherence highlights the need for interventions to increase motivation for those individuals.

Participants across the board reported that, at least on occasion, they struggled to plan to take nebulizers and most highlighted the importance of routines in being able to adhere. Action planning (Sniehotta, Schwarzer, Scholz, & Schütz, 2005) is therefore likely to be an important component and has been used successfully in interventions to increase adherence to medication in other conditions (de Bruin *et al.*, 2017; O'Carroll *et al.*, 2013).

The highest adherers commonly reported that they did their treatments automatically, indicating that it was habitual. This is consistent with recent research showing the importance of automatic motivation habits in adherence (Hoo *et al.*, 2019; Phillips, Cohen, Burns, Abrams, & Renninger, 2016), including evidence that adherence interventions that focus on habit formation are the most effective (Conn & Ruppap, 2017). Habits mean that adherence requires less cognitive effort (Gardner, de Bruijn, & Lally, 2011), and this means that habits can be maintained in circumstances that might make treatment taking more challenging (Gardner, 2015). This could explain why it was mostly low–moderate adherers and not high adherers that reported that stressful events were a barrier to adherence. People with strong habits may be able to take their treatment even in the context of stressful life events. Alternatively, experiencing stressful life events may lead to chaotic unpredictable lifestyles which have been found to be associated with lower adherence (Wong, Sarkisian, Davis, Kinsler, & Cunningham, 2007; Zullig *et al.*, 2013).

In addition to stressful events, participants reported a wide range of environmental factors which impacted on their ability to adhere. Being able to plan how to overcome these barriers or 'coping planning' (Sniehotta *et al.*, 2005) is also likely to be an important part of a successful intervention to improve adherence (de Bruin *et al.*, 2017).

Most high adherers reported experiencing fear as a factor that affected their adherence as has been reported previously (White, Miller, Smith, & McMahon, 2009). Conversely lower adherers reported avoidance consistent with previous research (Abbott, Dodd, Gee, & Webb, 2001). These emotions may reflect alternate responses to the perception of threat. Protection motivation theory (Rogers, 1975, 1983) suggests that a perceived threat is likely to result in fear (threat appraisal) that can be reduced either by behavioural action

(adherence) where individuals have the resources (i.e., capability and opportunity) to act (coping appraisal), or by avoidance where individuals lack those resources. Interventions should therefore focus on increasing the individual's capability and opportunity to act and to increase their confidence that they can cope.

### **Implications for interventions and clinical practice**

This study illustrates the wide range of factors affecting nebulizer adherence in adults with CF and emphasizes that different people have different issues affecting their adherence including issues of motivation, capability, and opportunity. There is not therefore a simple one-size fits all intervention that can be effective and clinicians need to be aware of these differences in order to tailor adherence support appropriately.

This study also highlights the importance of clinician access to objectively measured adherence data to inform discussions about adherence since time and date stamped data enable respondents to identify beliefs and experiences related to specific instances of documented behaviour. Concerns are often expressed about the use of objective adherence data within consultations because of fears of 'big brother watching' (Campbell, Eyal, Musiimenta, & Haberer, 2016); however, participants in this study were aware that health professionals were monitoring their adherence as part of their care and were positive about the role that this played in helping them to understand and support their adherence.

The role of health professionals was highlighted in a number of categories. Having social support from health professionals was identified as important but lower adherers were more likely to report conflict with health professionals. It may be that conflict had arisen as a result of low adherence, for example where health professionals have tried to impress, perhaps a little too forcefully, the importance of adherence. Or it could be that conflict with health professionals results in a lack of trust which results in lower adherence. In a complex disease such as CF, the relationship between patient and health professional is extremely important and should allow for good communication and mutual respect (Arias-Illoriente *et al.*, 2011; Sawicki *et al.*, 2015); thus, communication style is an important consideration in practice and intervention development (Hagger & Hardcastle, 2014).

### **Strengths and limitations**

This research enabled us to identify a wide range of beliefs and experiences about nebulizer adherence in adults with CF and to begin to understand how these beliefs might be related to objectively measured nebulizer adherence. This understanding enabled the identification of potential factors from the TDF to address in an intervention, across issues of capability, opportunity, and motivation.

Previous studies that have used the TDF approach have tended to identify fewer domains as being relevant for adherence (McCullough *et al.*, 2015; Pesseau *et al.*, 2017). Our greater yield might be the result of using objective adherence as a stimulus during the interview or that the investigators recognized more conflicting beliefs (Atkins *et al.*, 2017; Patey *et al.*, 2012) due to comparing participants with different adherence levels. The interview schedule also included prompts that related to TDF domains (as recommended by Michie *et al.*, 2014), and this may have resulted in participants commenting on a wider range of domains than they would have done without these prompts. However, our ability to use objective adherence data to interpret the potential importance of the domains has

enabled us to narrow down the category beliefs that might be particularly relevant for intervention development.

This research has a number of limitations. First, there were a relatively small number of purposively sampled participants interviewed and the comparisons made between participants with different categories of adherence must be tentative as a result. Future research should utilize a larger sample powered to detect a difference. Second, the sample is context specific and drawn from a single CF centre in the United Kingdom. There must be some caution in transferability of findings to CF outside this context and to other conditions (Morse, 2015). While the participants were purposively sampled to represent the range of characteristics of adults with CF, they were only sampled from the 110 patients who were willing to use an I-Neb<sup>®</sup> that enabled the tracking of treatment taking, and it is conceivable that the clinic practices, particularly the regular downloading and discussion of I-Neb<sup>®</sup> data, influenced the findings to some extent. Future research should explore the extent to which these findings are generalizable. Third, although we have identified some potentially important factors to target in an intervention, it is not possible from these data to determine how these factors might interact to influence adherence.

### **Conclusion**

This research study is the first to use objectively measured adherence data in a data-prompted interview using the TDF framework. This technique enabled the systematic assessment of participants' adherence-related beliefs and experiences and enabled comparisons between participants with different levels of adherence. The analysis enabled the identification of TDF factors related to capability (i.e., Skills; Memory and decision-making; and Behavioural regulation), opportunity (i.e., Environmental context and resources; and Social influences), and motivation (i.e., Beliefs about consequences; Beliefs about capability; Reinforcement; Social role and identify; Intentions; Optimism; and Emotions) that likely need to change in order to support adherence to nebulizer treatment, although there is unlikely to be a one-size fits all solution. These findings can be used to develop suitable interventions using the BCW (Michie *et al.*, 2014).

### **Acknowledgements**

This article summarizes independent research funded by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research Programme (Grant Reference Number RP-PG-1212-20015). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, or the Department of Health and Social Care.

### **Conflict of interest**

As the first author of this paper is an editor of this journal, they have been blinded throughout all stages of the submission and review process.

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Received 22 May 2018; revised version received 4 February 2019

### Supporting Information

The following supporting information may be found in the online edition of the article:

**Appendix S1** Adherence in Cystic Fibrosis Interview Topic guide

**Table S1** TDF domains and categories by participants' objectively measured adherence level with illustrative quotes