

Adherence to aerosol therapy in young people with cystic fibrosis: patient and parent perspectives following electronic data capture.

Authors:

Daniel PH O'Toole^{1,2}, Gary J Latchford^{1,3}, Alistair AJ Duff^{1,3,4}, Rosemary Ball⁴, Pamela McCormack^{5,6}, Paul S McNamara⁵, Keith G Brownlee⁷, Kevin W Southern⁵

¹University of Leeds, Leeds, United Kingdom

²Imperial College Healthcare NHS Trust, London, United Kingdom

³St James's University Hospital, Leeds, United Kingdom

⁴Leeds Children's Hospital, Leeds, United Kingdom

⁵University of Liverpool, Liverpool, United Kingdom

⁶Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom

⁷Cystic Fibrosis Trust, London, United Kingdom

Corresponding author at:

Dr Daniel O'Toole, Community Cardio-Respiratory Service, Imperial College Healthcare NHS Trust, 5 North, Charing Cross Hospital, Fulham Palace Road, London, W6 8RF

Tel: +44 (0)20 3311 7161

Fax: +44 (0)20 3311 7044

Email: daniel.o'toole@nhs.net

Keywords: chronic illness and disease; respiratory disorders; cystic fibrosis; children, adolescents; psychology, psychological issues; health behavior; behavior change; adherence, compliance; qualitative; grounded theory; United Kingdom

Abstract

The benefits of improved treatments for cystic fibrosis (CF) depend on optimal adherence which remains problematic, particularly to aerosol therapy. In this study, we explored the process of adhering to aerosol therapy from the perspective of both adolescents with CF and their parents. Interviews were conducted individually with six adolescents and six parents, informed by accurate adherence data from an electronically chipped, aerosol device. Interview-transcripts from audio-recordings were analyzed using Grounded Theory Method (GTM). Major themes revealed differences in perspective between parent and adolescent, with this relationship mediating the cognitive and emotional processes that play a significant role in adherence behavior. These processes are further influenced by interactions with the aerosol therapy treatment regimen, device characteristics and the context in which adherence is taking place. Parents and adolescents have different views of treatment and how to manage it. Both need to be addressed if optimal adherence is to be achieved.

Background

Cystic fibrosis (CF) is a chronic, progressive, multi-system condition that primarily affects the respiratory, gastrointestinal and reproductive systems. CF places a substantial burden on people with the condition and their families and support systems, who need to manage the implications of CF in terms of symptoms, complications and prognosis, and the extraordinarily demanding treatment regimen (Abbott, & Hart, 2005).

It is the most common serious hereditary disease in Caucasians having a birth-prevalence of 1 in 2,000/2,500 (Macneil, 2016; Feuchtbaum, Carter, Dowray, Currier, & Lorey, 2012). Once seen as a pediatric condition because patients rarely survived into adulthood, progress in treatment over the past 20 years means that UK newborns with CF are now expected to live into their mid-50s and beyond (Dodge, Lewis, Stanton, & Wilsher, 2007), with a next generation of treatments based on genetic mutation class promising even further advances (MacKenzie et al. 2014; Ratjen et al. 2015). Despite this, progressive disease continues to lead to respiratory failure, prolonged periods of ill-health and reduced quality of life before death. Median age of death in the UK is 31 years (Cystic Fibrosis Trust, 2018) and maintaining good health requires people with CF to adhere to a time-consuming and demanding daily treatment regimen. One consequence of recent advances in care is that the burden of adherence has increased, with patients having to engage daily in a number of treatments including chest physiotherapy, enzyme replacement therapy, high-fat intake requirements and prophylactic antibiotics, mucolytics and vitamins. The median time spent daily on such treatments has been found to be 108 minutes (Sawicki, Sellers, & Robinson, 2008). People with CF also need to adhere to strict infection control guidelines which involves impeccable hygiene, avoiding other people with CF and being isolated in single-bed rooms when in hospital. The prevalence and impact of mental health problems on physical health outcomes in CF is becoming better understood (Quittner et al. 2014; Quittner et al.

2016). People with CF are thought to be at risk of depression and anxiety symptoms (Quittner, Goldbeck, et al., 2014) with the former in particular impacting on 5-year survival rates (Schechter, Ostrenga, Fink, Barker, & Quittner, 2017).

Over the last decade, investigations of treatment-specific adherence in CF care have shown different rates to different therapies (Quittner et al. 2014), with inhalation therapy being of particular interest due to its important role in preventing, eradicating and treating lung infection (Bodnár, Mészáros, Oláh, & Ágh, 2016). Although measuring adherence to inhalation therapy has benefitted significantly from Adaptive Aerosol Delivery™ (AAD) technology – which electronically records nebulizer use – the complex factors which influence the process of actually adhering remain largely elusive (McNamara, McCormack, McDonald, Heaf, & Southern, 2009). Variables known to be important in CF treatment adherence include age, beliefs about medication, and characteristics of the treatment (Duff, & Latchford, 2010). In general, maintaining adherence to a treatment regimen over the longer term is also dependent on developing habits as part of a daily routine (e.g., Yeh et al. 2018). For adolescents, these factors invariably include their parents or caregivers.

Sub-optimal adherence to CF treatments is the single biggest cause of treatment failure in CF (Quittner, Modi, Lemanek, Ievers-Landis, & Rapoff, 2008), and the most important factor in the accelerated deterioration in the condition reported in adolescents and young adults (Narayanan, Mainz, Gala, Tabori, & Grossoehme, 2017; Osterberg, & Blaschke, 2005). Poor adherence is linked to reduced lung-function and poorer health outcomes (Eakin, Bilderback, Boyle, Mogayzel, & Riekert, 2011), and associated with increased rates of exacerbation and need for intravenous antibiotic treatment (Briesacher et al. 2011; DiMatteo, Giordani, Lepper & Corghan, 2002; Arias Lorente, Bousono Garcia, & Diaz Martin, 2008). Many young people struggle to assimilate CF therapies into their daily routines and this has been reported to adversely affect psychological well-being and health-related quality of life

(Sawicki, & Goss, 2015). The transition to self-management of a long term condition by adolescents is a crucial stage, set against a background of shifting psycho-social processes (Giarelli, Bernhardt, Mack, & Pyeritz, 2008). Understanding and improving adherence is one of the most important contemporary challenges in CF, particularly since the advent of a new generation of treatments promising greatly increased efficacy. This is even more important for children and young people, where establishing good practice in adherence behavior has significant implications for later life (Abbott, & Bilton, 2015; Duff, & Oxley, 2016).

The aim of the current study was to elicit the perspectives of adolescent patients with CF and their parents on the process of adhering to inhalation therapy. It used a qualitative methodology enhanced by the provision to patients and parents of accurate adherence data as part of the semi-structured interviews. This innovative approach enabled us to prompt memory recall and ground the interviews in reality to open avenues of discussion that would not otherwise have been apparent.

Methods

Design

Ethical approval was granted for this study by the regional NHS National Research Ethics Service (ref: 11/YH/0284). Individual, semi-structured, face-to-face interviews were conducted with adolescents with CF and one of their parents in order to elicit experiences, understandings and perspectives of the process of adhering to inhalation therapy via the I-neb™ (Profile Pharma, Zambon SpA, Chichester, UK) device. The I-neb™ is used to take routine treatments such as bronchodilators (which make breathing easier) and occasional treatments for acute infection (antibiotics); *all* prescribed inhalation therapy via the I-neb™ was a target of interest in this study.

The I-neb™ uses vibrating mesh technology and an Adaptive Aerosol Delivery™ (AAD) system to deliver precise doses of aerosol into the inspiratory phase of the respiratory cycle. This technology has resulted in much quicker administration of treatment doses than previous types of nebulizer. Data about each treatment taken (including whether or not the dose has been administered fully) is recorded electronically enabling a ‘gold standard’ objective measure of adherence to nebulized therapy (McCormack, Southern, & McNamara, 2012). Adherence is calculated by dividing the actual number of doses taken by the expected (prescribed) doses, alongside the number of taken doses that were fully administered to give an overall percentage of adherence which is highly reliable and objective.

Adolescents were eligible for participation if they were 11–16 years of age, had a confirmed diagnosis of CF via sweat testing or CF-causing mutations and had been using the I-neb™ device for at least the last 12 months as part of their treatment regimen. Separate participant information sheets were developed for both the adolescent patients and the parents. This provided clear information about the study and invited participation. The parents and the adolescents were asked to sign a joint consent form in order to take part in the study. Participants were excluded if they were not deemed clinically stable (i.e., Forced Expiratory Volume in one second [FEV1] <50% in the preceding 12 months).

Sample

A convenience sample of six adolescents from two UK regional pediatric CF centers (Leeds and Liverpool) were recruited in order of attendance at routine out-patient appointments by their physiotherapist, resulting in a sample representative of adolescent patients seen in clinic, with variable adherence rates. They and one of their parents were interviewed separately, resulting in a total sample of 12. Those identified as the primary caregiver were invited to take part as we were keen to better understand the impact of this

important relationship on the process of adherence to aerosol therapy. The sample size enabled in-depth interviews to be conducted in order to facilitate this aim and to further explore participants' lived experience of aerosol therapy. The mean age of the adolescent participants was 13.2 years and the mean age of the parent participants was 42 years.

Procedure

Following recruitment, electronic diary data which is routinely downloaded from the I-neb™ at out-patient appointments by a physiotherapist was sent via secure e-mail to the chief investigator ahead of the semi-structured interviews. In order to anchor participants' experiences in real-life examples and prompt recall, part of the semi-structured interview was guided by a seven-day retrospective 'diary' based on an adapted printout of the electronic data downloaded from the I-neb™ device. This information was presented in an easy-to-understand table and discussed in addition to more general questions about the process of adhering to aerosol therapy.

Questions specifically relating to the I-neb™ data were incorporated into the interview schedule for both the adolescent patients and the parents in order to stimulate recall and prompt discussion of factors that may have influenced the process of adherence. The interview schedule enabled a similar structure for the adolescent and parent interviews but with a slightly different emphasis depending on the topic being discussed (e.g., "Looking at this information here, were there any days and times that you found it easier to take your aerosol therapy?" vs. "Looking at this information here, were there any days and times that you think your child found it easier to take their aerosol therapy?")

Participants were aware that the I-neb™ data would be used to inform the interview and the participant information sheets encouraged typical adherence behavior prior to the interviews by reassuring them that we were interested in their experiences of both adhering

and not adhering to their aerosol therapy. As I-neb™ data are commonly discussed with the adolescent patients and their parent as part of their routine clinic appointments, it was not thought that this would significantly influence adherence behavior prior to the research interview. Indeed, we were expecting similar experiences to those observed in routine clinics whereby a range of adherence rates are present regardless of the child and parent being aware that the I-neb™ data will be downloaded and discussed.

The semi-structured interviews were recorded and lasted approximately 90 minutes each. Over 500 pages of interview transcripts were produced and then analyzed separately using Grounded Theory Method (GTM).

Data analysis

The data analysis process was guided by the model of GTM proposed by Strauss and Corbin (1990) and Charmaz (2006). Analysis progressed from initial generation of open codes (whereby the transcripts were analyzed line-by-line with a code assigned to each), to refinement of higher order categories (axial coding stage one and two whereby open codes were grouped into a series of emerging categories) and finally the identification of core categories which became the basis for the theoretical formulation. Data analysis was supported by other techniques commonly used in GTM including constant comparison (by which new codes were constantly compared and modified alongside existing ones), memo writing (process notes on the analysis), and diagramming (a visual display that helped to conceptually map the process of analysis).

Efforts to ensure methodological rigor were focused on engaging in regular individual and group supervision (which consisted of members conducting qualitative research). Individual and group supervision sessions were facilitated by two senior academics who are experienced in using GTM. Supervision enabled the checking of line-by-line initial

codes, making comments and observations about axial codes and ensuring that the theoretical formulation could be further developed and refined. Minutes of the research supervision sessions were kept so as to provide a record of detailed discussions. This approach enabled the maintenance of an “audit trail” which Burns (1989) argues is a major factor in ensuring methodological and procedural rigor in qualitative research.

Results

Table 1 outlines demographic details of the child-parent dyad participants along with information relating to the adolescent child’s aerosol therapy regimen.

Table 1: Participant demographic information (N=12)

Participant	Gender	Parent	Aerosolized treatment(s) and daily dosage prescribed	Treatments taken	Doses administered fully	Overall 7 day adherence rate (%)
Child 1	Female	Mother	DNase ¹ (1 per day)	2 of 7	1 of 2	14.29
Child 2	Male	Mother	DNase ¹ (1 per day)	7 of 7	7 of 7	100
Child 3	Female	Mother	DNase ¹ (1 per day)	5 of 7	3 of 5	42.86
Child 4	Female	Father	DNase ¹ (1 per day) Promixin ² (1 per day)	14 of 14	13 of 14	92.86
Child 5	Male	Mother	Colomycin ² (2 per day)	12 of 14	12 of 12	85.71
Child 6	Male	Mother	Colomycin ² (1 per day) DNase ¹ (1 per day)	13 of 14	13 of 13	92.86

¹ bronchodilator; ² antibiotic

Analysis of the parent and adolescent data produced a series of initial open codes and higher order categories. Coding parent data produced 436 open codes and 112 higher order

categories, further revised to produce a theoretical formulation consisting of 9 core categories, and 42 subcategories. Adolescent data produced 362 open codes and 87 higher order categories, revised into 9 core categories, and 37 subcategories. The theoretical formulations for each group were represented visually and were broadly similar, each featuring nine core categories and four main processes (interaction with the aerosol therapy; internal cognitive, affective and behavioral processes; parent and adolescent interactions and experience of each other; the context of adherence), although each group had their own perspectives. A combined theoretical formulation is shown in Figure 1.

Figure 1: Combined theoretical formulation (INSERT FIGURE 1 HERE)

Qualitative themes

Parents and adolescents gave different but overlapping views of the aerosol regimen and the context in which adherence takes place. In particular, beliefs, emotional reactions and behavioral strategies connected to adherence were discernible in the accounts of both groups, and these interact with the parent and adolescent experience of one another, mediated largely by the strength of the relationship. The themes, example sub-themes and illustrative quotations from parent and adolescent perspectives are summarized in Figure 2 and then expanded upon further below.

Figure 2: Summary of main themes and examples of sub-themes, with illustrative quotations from parent and adolescent highlighting different viewpoints and perspectives (INSERT FIGURE 2 HERE)

Themes around the therapy

The process of adhering to aerosol therapy was experienced as only one part of a complex and demanding CF treatment regimen that places significant strains on the parents and young patients:

It is tough and I think when the doctors are saying you need to do this, this and this, they don't realize the day to day struggle of what it's really like to live with it. You know it's alright for them to sit there and say he needs this nebulizer every day, this tablet every day, that tablet every day, they're not dishing them up, administering all the medicine. (Parent)

The emphasis on the lack of immediate feedback (benefit) of the aerosol therapy was seen as a problematic barrier by some, but the feedback offered by the interactive features on the device itself was often experienced as a positive facilitator to adherence:

It buzzes and then I keep doing that until it like beeps once more and a smiley face comes on the screen. (Child, aged 12)

Sometimes if I haven't got the nebs in the right position it makes a little alarm. (Child, aged 13)

The I-neb™ was seen as less cumbersome and easier to use than other aerosol devices, which meant that many of the young patients were able to take responsibility for preparing the medication themselves. However, the specific instructions for cleaning and drying the device resulted in many of the parents doing this in practice and it was seen as onerous:

That's another thing, you have to boil the damn thing once a week, you have to boil it for about 10, 15 minutes. (Parent)

There were mixed views from both parents and young patients on using the data downloaded from the I-neb™ as a part of routine clinical practice, with some seeing it as motivating and others as punitive:

I think it does help, like 'cos you can see what it's really like, I mean I've never thought of it like that. I never really looked at it like this before. (Child, aged 13)

The downloaded information? This is where Big Brother looks at you and points the big finger! (Parent)

The most common theme expressed here concerned the way in which the data was communicated by the health care professional involved; with appropriate language (e.g., “I wonder if it would be ok to look at the feedback together?”), empathy and tactfulness seen as important motivators for adherence.

Cognitive, affective and behavioral processes of the adolescent and parent

The complex way in which salient thoughts and beliefs about aerosol therapy interact with feelings concerning adherence were seen as influencing the behavior of both the young people and the parents day by day. Sometimes families used strategies to increase adherence, with mixed success. Many young people, for example, knew about the serious consequences of not adhering to aerosol therapy. Whilst awareness of the consequences generated fear which was not pleasant, adolescents acknowledged that it probably encouraged adherence too:

At the end of the day if I don't take them I could die because I would become ill and that but it's keeping me alive...but I don't like doing them. (Child, aged 12)

Beliefs were not static however – with some adolescents and parents being aware of the potential consequences of non-adherence but expressing doubts about effectiveness:

I don't feel like it does much but I know like when I don't take it, I do notice that my chest feels a bit worse, but like for a day if I didn't take it then I wouldn't notice. I went through a phase of not taking it because I didn't think it was doing anything. (Child, aged 16)

I can understand why some parents would think 'stuff it, it's making no difference' because in some ways I feel like that. (Parent)

The interviews highlighted different perspectives on parent-child interactions related to adherence. Parents reported concern, for example, at the thought of relinquishing control as their child grows older; often causing significant anxiety and leading to increased daily reminders, and guilt if their child did not adhere. Adolescents, on the other hand, struggled to understand the parents' perspective; seeing parental frustration as a sign of not being understood and this in turn contributed to their own feeling of frustration and a sense of being different to others:

I like to know she's done it because if she hasn't done it I worry and again it's, she'll say I'm a control freak and I probably am a bit but having had all the years where I had complete control over her treatments to almost having no control at all now, erm yeah I like to remind her, just check in my own mind that she's done it. (Parent)

Cos it's like, no one else understands really. Like with my nebulizers it's like I know mum thinks it isn't much to do and I suppose it isn't but it's just another thing. (Child, aged 14)

The social context of adherence was discussed by several adolescents, who acknowledged thoughts about some treatments being easier (or less embarrassing) to do in front of peers – or family – than others:

You could go on the trampoline and that, you could do that with a mate but you couldn't take your nebulizer with a friend obviously. (Child, aged 11)

There was general awareness of a number of daily barriers to adherence (e.g., lack of time, feeling upset, tiredness and distractions) but the electronic diary data allowed participants to illustrate these with concrete examples:

I was really tired and just didn't do them. It depends what mood I'm in really. Erm sometimes when I'm tired, erm, or just don't feel like doing them. (Child, aged 12)

She wanted to watch 'I'm a celebrity' and I told her to get it done. (Parent)

Parent and adolescent interactions and experience of each other

Parents were sensitive to non-adherence, particularly as children took more responsibility themselves. This led to attempts by parents to prompt their child, and feelings of guilt and worry if they felt adherence was poor. Adolescents, on the other hand, generally resented parental reminders (often described as nagging) but paradoxically acknowledged that they often led to increased adherence:

I don't like being reminded but I know that if I don't get reminded then I won't do it.
(Child, aged 16)

The diary prompted concrete examples of the way in which language based on negotiation rather than challenge was more acceptable and felt to be more effective in prompting behavior:

I said 'while I'm in the shower, you make up your colomycin for me' so that's what he done. (Parent)

...after my dinner all my physio and I-neb and everything, after I've done all that, I can go back on my Xbox for like 10 or 20 minutes. (Child, aged 11)

Parent accounts suggested that they thought it important to accommodate specific treatment preferences, particularly around aerosol therapy, as a way of anticipating and managing potential problems and conflict:

I think his physio, he's more inclined not to want to do that than his aerosol therapy because he knows that's only going to take him a very short amount of time. (Parent)

In fact, the strength of the parent-adolescent relationship had the potential to act as a “buffer” and adolescents referred to ways in which practical and emotional support from parents had helped facilitate adherence and avoid conflict. However, the transition of responsibility with increasing age was a key theme. Although adolescents acknowledged this and felt that they needed to do more, in general parents continued to provide practical support – they ordered the medication and cleaned the device.

The context of adherence

Both groups discussed the way in which daily life influenced adherence – the diary prompted comments on the difficulties of attempting to fit multiple tasks into a limited amount of time. Aerosol therapy was seen as one part of a time consuming and burdensome treatment regimen. Some treatments were discussed as being interdependent, particularly aerosol therapy and physiotherapy, with the electronic diary data again prompting examples of how in practice the two treatments had to be planned so that there was a gap between them:

It can't be too close to his nebulizer either erm, if you're doing his physio it has to be at least an hour after his nebulizer. (Parent)

Particular times and events were seen as problematic, with holidays, school trips and sleepovers given as examples, partly because of pragmatic considerations such as cleaning the nebulizer. Parents and adolescents both commented on distractions which could lead to treatments being delayed or forgotten, especially social media and video games, and this was reinforced through several examples prompted by the electronic diary data:

I was probably on my computer, I might have been texting someone. If I'm on Facebook and I see something interesting, I'll put it down to type something and I'll forget about it. (Child, aged 14)

In general, both groups agreed that evening was better than morning because it was less busy, and weekends and school holidays were worse because there was less structure. Interestingly, for some participants busy lives were seen as a barrier to adherence, whereas for others, activities were used to increase motivation by acting as a reinforcing activity to be engaged in only after adherence.

Discussion

In this study, we qualitatively explored how the process of adhering to aerosol therapy in CF was experienced by both adolescent patients and their parent. The analysis revealed a complex interaction of cognitive, emotional and behavioral processes around adherence, with the parent and adolescent experience of one another at the core, and the parent and child relationship mediating the interactions. The above processes are further influenced by the interactions with the aerosol therapy treatment regimen, device characteristics and context in which adherence is taking place.

Participants were prompted by the electronic diary data downloaded from the I-neb™ device which provided a window into their lived experience and enabled rich and open accounts of the processes that influence adherence to aerosol therapy treatment. Parents and adolescents often compared aerosol therapy to other forms of treatment, with an internal hierarchy of preference often favoring those treatments that were quick and less intrusive. Although the overall theoretical formulation was very similar for adolescent and parent, the analysis highlighted the way in which the same phenomena could be experienced from different viewpoints and provided valuable insight into the process of adherence from both

perspectives. One interesting aspect that we were not adequately able to explore is whether the interactions between parent and child vary according to whether they were the same sex – i.e., our sample contained two mother-daughter dyads and four mixed dyads (three mother-son and one father-daughter). It is interesting to speculate on what difference same sex dyads may have made, though recruitment did ask to interview the primary caregiver, and the interviews showed that the parents were at least very involved in their child's care.

In this study, we provide further insight into the complex social context in which adherence is embedded and to which others have previously alluded (Dziuban, Saab-Abazeed, Chaudhry, Streetman, & Nasr, 2010). There is also support for the developmental, biopsychosocial model proposed by Barker and Quittner (Barker, & Quittner, 2010) with the current study identifying influences on adherence which may be seen as biological (i.e., therapy regimens that are dependent on disease management and progression), psychological (i.e., cognitive, emotional and behavioral processes alongside specific developmental challenges at different stages of adolescence in the parent-child relationship) and social (i.e., the environment in which adherence takes place and the demands of everyday life).

The results of the current study support and extend the conclusions from previous research on adherence in CF (e.g., Barker, & Quittner, 2010; Narayanan et al. 2017). In particular, it has highlighted the complexity involved, and the interactions which have a substantial influence on adherence – interactions between the different parts of the treatment regimen, interactions between the nebulizer and child and nebulizer and parent, interactions between children and their peers, and finally between child and parent. It has also placed adherence behavior in context – the internal context of the beliefs and emotions of the child and parent, and the exterior context of the busy and complicated lives led by them. It would appear that these interacting biopsychosocial processes make the prospect of consistent, 100 % adherence to aerosol therapy very unlikely.

Advances in AAD technology have resulted in devices that are more effective, easier to use and better able to provide useful feedback that can both encourage adherence and promote appropriate administration technique (e.g., cascading feedback system). However, the benefits of more advanced devices paradoxically create a number of associated issues. Ensuring that the device is appropriately maintained and cleaned creates an additional burden which was identified as a potential barrier by participants in the current study. Despite the device being much smaller and more portable than the previous generation of nebulizers, the negative impact that the above issue had on device portability and associated non-adherence was a relevant concern, particularly for the parents who were often tasked with cleaning and maintenance. In addition, some of the participants' saw the I-neb™ as fragile and expensive (and worried about losing or damaging the device) so were reluctant to take it away from home.

Appropriate stakeholders (i.e., patients, parents, clinicians, policymakers and manufacturers) may need to engage in a cost-benefit analysis that acknowledges the benefits of continued technological improvements alongside the unintended but associated consequences. In doing so, the rhetoric of continual advancement can be more appropriately situated in the context of everyday life.

There are a number of strengths associated with the current study. It enabled a detailed, more focused exploration of one part of the CF treatment regimen rather than CF treatment as a whole, as in much of the previous literature (e.g., George et al. 2010). It enabled both a patient and a parent perspective on adherence to be gained. The use of the electronic diary data was not only novel, but enabled adherence behavior to be explored *in situ*, as close as possible to its actual occurrence, grounded in reality as opposed to recollections (Reis, & Gable, 2000). A common criticism of qualitative methodologies is that they can only ever access information that the participant is consciously aware of. The fact

that the electronic diary data provided a prompt to participants about the actual rates of adherence and incidents which affected this suggested that the diary helped to bring into conscious awareness the multiple influences on adherence. Finally, the sample size enabled us to obtain detailed data on this process from a broad range of perspectives.

Conclusion

In this study, we describe a rich framework within which parents and their adolescent children negotiate patterns of adherence, balancing the needs of CF with the needs of emerging adulthood, and their competing and changing roles. Optimizing adherence is a key challenge for CF teams and it is essential that the different viewpoints of parents and adolescents are appreciated in order to optimize the opportunities for support.

There are a number of potential clinical implications arising from the current study. Health care professionals should demonstrate a continued overt awareness of the burden associated with aerosol therapy as only one part of an already complex, demanding and often inter-dependent treatment regimen. This burden is experienced differently by patients and parents and the use of the electronic diary data within routine clinical practice may allow this to be explored to enable clearer expectations being established collaboratively. Where increasing the number of aerosolized therapies is a necessity, exploring and advising on how the revised regimen may fit into their lives may help to motivate patients and parents, particularly where the beliefs in the benefits associated with the aerosol therapy are less strong. Indeed, evaluation strategies to simplify the burden of care has recently been cited as the top priority for research in CF care (Rowbotham et al. 2017).

The current study highlighted the complexity of adherence behavior, and the influence of the treatment (e.g., some are preferred over others), the overall regimen (e.g., treatments need to be timed relative to each other), the device (e.g., the I-nebTM is preferred but cleaning

is an issue), beliefs (e.g., about efficacy of treatment), emotions (e.g., anxiety about the consequences of non-adherence), behaviors (e.g., developing a routine) and the real life context (e.g., distractions such as Facebook or computer games). It also found many examples where parent and child had different perspectives on the same phenomena (e.g., the necessity of parental reminders or nagging). The electronic diary proved useful in obtaining many of these examples, with several participants commenting that they had forgotten about something until prompted by the diary in the interview. The diary may also therefore prove useful in assisting patients and parents in the identification of unhelpful influences on adherence and may help to target appropriate support, particularly for those whose problematic cognitions (e.g., a parent thinking that the aerosol therapy is not working) and emotions (e.g., a parent feeling anxiety and guilt) have the potential to result in less helpful behaviors (e.g., excessively reminding or “nagging” their child to take the aerosol therapy) that may negatively impact on the parent and child relationship. The importance of being clear with patients and parents that the therapy is an investment in long-term well-being and that the cumulative effect of missed doses is significant should be done alongside an empathic understanding of the complexities of adherence.

There was an emphasis within the current study that adherence to aerosol therapy does not exist in a psychosocial vacuum. The use of the electronic diary data within the semi-structured interviews enabled a number of lifestyle and environmental influences to be illustrated. Open discussion of these influences (using the electronic diary data appropriately) may help to identify specific commitments, times, events or situations which have the potential to negatively impact on the process of adhering to aerosol therapy. In this way the CF team can work in partnership with the patient and the parents to support overcoming these barriers to adherence.

References

Abbott, J., & Bilton, D. (2015). Adherence to Ivacaftor is suboptimal. *Journal of Cystic Fibrosis*, 14, 547–8. doi:10.1016/j.jcf.2015.08.001

Abbott J., & Hart, A. (2005). Measuring and reporting quality of life outcomes in clinical trials in cystic fibrosis: a critical review. *Health and Quality of Life Outcomes*, 3, 19. doi.org/10.1186/1477-7525-3-19

Arias Lorente, R.P., Bousono Garcia, C., & Diaz Martin, J.J. (2008). Treatment compliance in children and adults with cystic fibrosis. *Journal of Cystic Fibrosis*, 7, 359–67. doi:10.1016/j.jcf.2008.01.003

Barker, D., & Quittner, A.L. (2010). A biopsychosocial model of cystic fibrosis: social and emotional functioning, adherence, and quality of life. In: Allen, J.L., Panitch, H.B., & Rubenstein, R.C., (Eds). *Cystic Fibrosis*. (pp 468-481). New York: Informa Healthcare.

Bodnár, R., Mészáros, A., Oláh, M., & Ágh, T. (2016). Inhaled antibiotics for the treatment of chronic *Pseudomonas aeruginosa* infection in cystic fibrosis patients: challenges to treatment adherence and strategies to improve outcomes. *Patient Preference and Adherence*, 10, 183–93. doi:10.2147/ppa.s53653

Briesacher, B.A., Quittner, A.L., Saiman, L., Sacco, P., Fouayzi, H., & Quittell, L.M. (2011). Adherence with tobramycin inhaled solution and health care utilization. *BMC Pulmonary Medicine*, 11:5. doi:10.1186/1471-2466-11-5

Burns, N. (1989). Standards for qualitative research. *Nursing Science Quarterly*, 2, 44–52. doi:10.1177/089431848900200112

Charmaz, K. (2006). *Constructing grounded theory: A practical guide through qualitative analysis*. London and Thousand Oaks CA: Sage Publications.

Cystic Fibrosis Trust. (2018). *UK cystic fibrosis registry – Annual Data Report 2017*. London: Author.

DiMatteo, M.R., Giordani, P.J., Lepper, H.S., & Corghan, T.W. (2002). Patient adherence and medical treatment outcomes: a meta-analysis. *Medical Care*, 40, 794–811. doi:10.1097/00005650-200209000-00009

Dodge, J.A., Lewis, P.A., Stanton, M., & Wilsher, J. (2007). Cystic fibrosis mortality and survival in the UK: 1947–2003. *European Respiratory Journal*, 29, 522–6. doi:10.1183/09031936.00099506

Duff, A.J.A., & Latchford, G. (2010). Motivational Interviewing for adherence problems in cystic fibrosis: State of the art review. *Pediatric Pulmonology*, 45, 211–20. doi:10.1002/ppul.21103

Duff, A.J.A., & Oxley, H. (2016). Psychology. In: Bush, A., Bilton, D., & Hodson, M., (Eds). *Hodson and Geddes' Cystic Fibrosis*, 4th edition. (pp 582-597). Boca Raton, FL: Taylor and Francis.

Dziuban, E.J., Saab-Abazeed, L., Chaudhry, S.R., Streetman, D.S., & Nasr, S.Z. (2010). Identifying barriers to treatment adherence and related attitudinal patterns in adolescents with cystic fibrosis. *Pediatric Pulmonology*, 45, 450–8. doi:10.1002/ppul.21195

Eakin, M.N., Bilderback, A., Boyle, M.P., Mogayzel, P.J, & Riekert, K.A. (2011). Longitudinal association between medication adherence and lung health in people with cystic fibrosis. *Journal of Cystic Fibrosis*, 10, 258–64. doi:10.1016/j.jcf.2011.03.005

Feuchtbaum, L., Carter, J., Dowray, S., Currier, R.J., & Lorey, F. (2012). Birth prevalence of disorders detectable through newborn screening by race/ethnicity. *Genetics in Medicine*, 14, 937–45. doi:10.1038/gim.2012.76

George, M., Rand-Giovannetti, D., Eakin, M.N., Borrelli, B., Zettler, M., & Riekert, K.A. (2010). Perceptions of barriers and facilitators: self-management decisions by older adolescents and adults with CF. *Journal of Cystic Fibrosis*, 9, 425–32. doi:10.1016/j.jcf.2010.08.016

Giarelli, E., Bernhardt, B.A., Mack, R., & Pyeritz, R.E. (2008). Adolescents' transition to self-management of a chronic genetic disorder. *Qualitative Health Research*, 18, 441–57. doi.org/10.1177/1049732308314853

MacKenzie, T., Gifford, A.H., Sabadosa, K.A., Quinton, H.B., Knapp, E.A., Goss, C.H., & Marshall, B.C. (2014). Longevity of patients with cystic fibrosis in 2000 to 2010 and beyond: survival analysis of the Cystic Fibrosis Foundation patient registry. *Annals of Internal Medicine*, 161, 233–41. doi:10.7326/m13-0636

Macneil, S.J. (2016). Epidemiology of cystic fibrosis. In Bush A, Bilton D & Hodson M, (Eds). *Hodson and Geddes' Cystic Fibrosis*, 4th edition. (pp. 18-40). Boca Raton, FL: Taylor and Francis.

McCormack, P., Southern, K., & McNamara, P. (2012). New nebulizer technology to monitor adherence and nebulizer performance in Cystic Fibrosis. *Journal of Aerosol Medicine and Pulmonary Drug Delivery*, 25, 307–9. doi:10.1089/jamp.2011.0934

McNamara, P.S., McCormack, P., McDonald, A.J., Heaf, L., & Southern, K.W. (2009). Open adherence monitoring using routine data download from an adaptive aerosol delivery

nebuliser in children with cystic fibrosis. *Journal of Cystic Fibrosis*, 8, 258–63. doi:10.1016/j.jcf.2009.04.006

Narayanan, S., Mainz, J.G., Gala, S., Tabori, H., & Grossoehme, D. (2017). Adherence to therapies in cystic fibrosis: a targeted literature review. *Expert Review of Respiratory Medicine*, 11, 129–45. doi:10.1080/17476348.2017.1280399

Osterberg, L., & Blaschke, T. (2005). Adherence to medication. *New England Journal of Medicine*, 353, 487–97. doi:10.1056/nejmra050100

Quittner, A. L., Abbott, J., Georgiopoulos, A. M., Goldbeck, L., Smith, B., Hempstead, S. E., ...Elborn, S. (2016). International Committee on Mental Health in Cystic Fibrosis: Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus statements for screening and treating depression and anxiety. *Thorax*, 71, 26–34. doi.org/10.1136/thoraxjnl-2015-207488

Quittner, A.L., Goldbeck, L., Abott, J., Duff, A.J., Lambrecht, P., Sole, A., ...Tibosch, M. (2014). Prevalence of depression and anxiety in patients with cystic fibrosis and parent caregivers: Results of the International Depression Epidemiology Study (TIDES) across Nine Countries. *Thorax*, 69, 1090–1097. doi.org/10.1136/thoraxjnl-2014-205983

Quittner, A.L., Modi, A.C., Lemanek K.L., Ievers-Landis C.E., & Rapoff M.A. (2008). Evidence-based assessment of adherence to medical treatments in pediatric psychology. *Journal of Pediatric Psychology*, 33, 916–936. doi.org/10.1093/jpepsy/jsm064

Quittner, A.L., Zhang, J., Marynchenko, M., Chopra, P.A., Signorovitch, J., Yushkina, Y., & Riekert, K.A. (2014). Pulmonary medication adherence and health-care use in cystic fibrosis. *Chest*, 146, 142–51. doi:10.1378/chest.13-1926

Ratjen, F., Bell, S.C., Rowe, S.M., Goss, C.H., Quittner, A.L., & Bush, A. (2015). Cystic fibrosis. *Nature Reviews Disease Primers*, 1, 15010. doi:10.1038/nrdp.2015.10

Reis, H.T., & Gable, S.L. (2000) Event-sampling and other methods of studying everyday experiences. In: Reis, H.T., & Judd, C.M., (Eds). *Handbook of Research Methods in Social and Personality Psychology*. (pp 190–279). New York: Cambridge University Press.

Rowbotham, N.J., Smith, S., Leighton, P.A., Rayner, O.C., Gathercole, K., Elliott, Z.C., ...Smyth, A.R. (2017). The top 10 research priorities in cystic fibrosis developed by a partnership between people with CF and healthcare providers. *Thorax*. 73, 388–390. doi:10.1136/thoraxjnl-2017-210473

Sawicki, G.S., & Goss, C.H. (2015). Tackling the increasing complexity of CF care. *Pediatric Pulmonology*. 50, S74–S79. doi:10.1002/ppul.23244

Sawicki, G.S., Sellers, D.E., & Robinson, W.M. (2008). High treatment burden in adults with cystic fibrosis: challenges to disease self-management. *Journal of Cystic Fibrosis*, 8, 91–96. doi.org/10.1016/j.jcf.2008.09.007

Schechter, M., Ostrenga, J., Fink, A., Barker, D., & Quittner, A. (2017). Five year survival is decreased in CF patients who screen positive for depression, *Pediatric Pulmonology*, 52, S404–S505. doi.org/10.1002/ppul.v52.s47

Strauss, A.L., & Corbin, J. (1990). *Basics of Qualitative Research: Grounded Theory Procedures and Techniques*. Newbury Park CA: Sage Publications.

Yeh, E.A., Chiang, N., Darshan, B., Nejati, N., Grover, S.A., & Schwartz, C.E., ...Pediatric MS Adherence Study Group. (2018). Adherence in youth with multiple sclerosis: A qualitative assessment of habit formation, barriers, and facilitators. *Qualitative Health Research*. Advance online publication. doi:10.1177/1049732318779039

Author Biographies

Daniel O'Toole is a Principal Clinical Psychologist working in respiratory medicine for the Imperial College Healthcare NHS Trust in London.

Gary Latchford is a Consultant Clinical Psychologist working in adult CF at St James's University Hospital and Joint Director of the Clinical Psychology Doctoral Training Program at the University of Leeds.

Alistair Duff is a Consultant Clinical Psychologist working in pediatric CF and Honorary Clinical Associate Professor at the Institute of Health Sciences, University of Leeds. He is Head of the Department of Clinical and Health Psychology at the Leeds Teaching Hospital NHS Trust.

Rosemary Ball is a former Clinical Specialist Pediatric Physiotherapist for CF at the Leeds Children's Hospital.

Pamela McCormack is a Clinical Specialist Physiotherapist for CF at Alder Hey Children's NHS Foundation Trust.

Paul McNamara is a Professor in Child Health at the University of Liverpool, and Honorary Consultant in Pediatric Respiratory Medicine at Alder Hey Children's NHS Foundation Trust.

Keith Brownlee is Director of Policy, Programs and Support at the CF Trust. He is a former Consultant Pediatrician for children with respiratory conditions at the Leeds Children's Hospital.

Kevin Southern is a Professor in Child Health and the Deputy Head for the Department of Women's and Children's Health at the University of Liverpool.

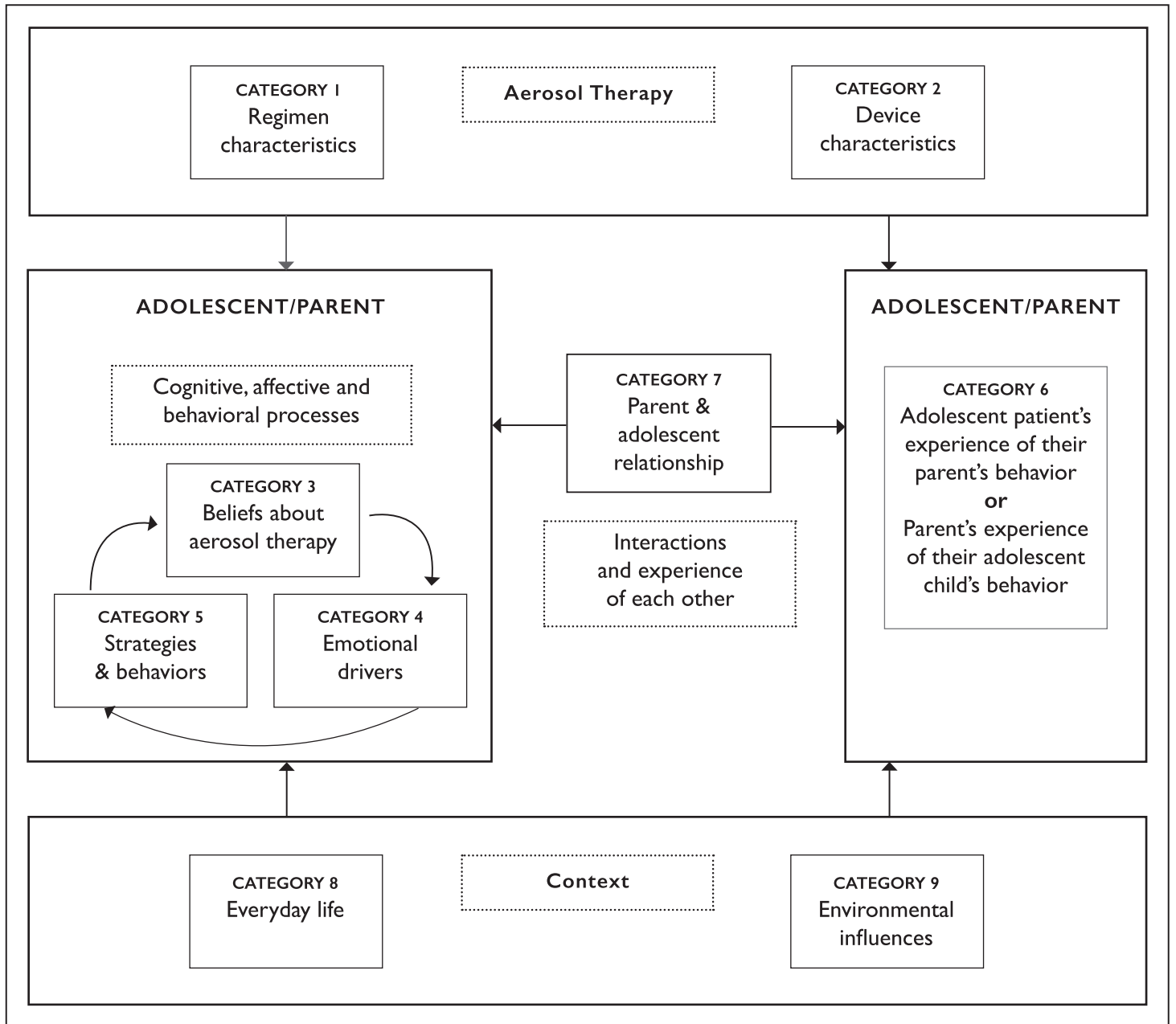


Figure 1: Combined Theoretical Formulation

Themes around the therapy

SUB-THEME	PARENT PERSPECTIVES	ADOLESCENT PERSPECTIVES
Multiple treatments	If you put the whole lot together it all gets too much sometimes	The nebuliser, it's just another thing to do
Feeling understood	The doctors are saying you need to do this, this and this, they don't realise the day to day struggle	Some days you get up and you have to do it but you just get bored of having to do them because you have to do so much like every day
The device: I-neb	The I-neb is, oh it's so much easier than what it was	Sometimes if I haven't got the nebs in the right position it makes a little alarm
Using downloaded data	It's really interesting actually because I just assume that she's done it and she's done it properly	I think I've done well and then you see it and I haven't done as well as I thought
Cleaning	You have to boil the damn thing once a week	Mum usually washes it

Cognitive, affective and behavioral processes of the adolescent and parent

SUB-THEME	PARENT PERSPECTIVES	ADOLESCENT PERSPECTIVES
Beliefs about effectiveness	Ever since she's been on the Neb she's never had a stay in hospital	I don't feel like it does much but I know like when I don't take it, I do notice that my chest feels a bit worse
Feelings of control	I like to know she's done it... she'll say I'm a control freak	I kinda like doing the neb on my terms when I'm ready
Feeling guilty	I feel really, really guilty if he doesn't have it	I sometimes feel bad if I forget to do me neb and stuff
Reminding	I should just record my voice and just play it continuously	I don't like being reminded but I know that if I don't get reminded then I won't do it
Rewarding and incentivizing	She'll have been doing it earlier here because she wanted to watch 'I'm a celebrity' and I told her to get it done	... after my dinner all my physio and I-neb and everything after I've done all that, I can go back on my Xbox for like 10 or 20 minutes

Parent and adolescent interactions and experience of each other

SUB-THEME	PARENT PERSPECTIVES	ADOLESCENT PERSPECTIVES
Forgetting	She does forget it sometimes	That's what Mum and Dad never understand they say 'How can you forget? You've been doing it all your life'. It's just I don't know, maybe it's 'cos of that I just forget
Feeling emotional	When she's upset, she will not do any of her medication	I just wouldn't do them, it depends what mood I'm in really
Responsibility	I think when they're younger, you have more control and that responsibility is then passed onto them	I've just got to remember, but most of the time my mum's in so I just do it when she gives it to me
The potential for conflict	The more you fight things the more she digs her heels in	My Mum like nags me. Like Mum says 'take your neb' and sometimes I like argue and say that I don't want to

The context of adherence

SUB-THEME	PARENT PERSPECTIVES	ADOLESCENT PERSPECTIVES
The juggling act	[Name of health professional] once asked us 'what gets in the way?' And we said 'life'	It kind of gets in the way of me playing on the computer endlessly or erm like if I'm going to my friends
School days vs. weekends	Weekdays are probably easier than weekends and school days are probably easier than when she's off school because you've got your routine	In the weekday I have much more of a routine
Mornings vs. evenings	We never do his I-neb in a morning. Because it's just too much	I was like missing registration so I'd have to go and explain why I was late
Staying over in a different house	He goes to his Dad's on a Saturday night... I don't let him take the I-neb with him 'Cos he'll forget to bring it back	I don't normally take me neb to me Dad's err I think like it's like a bit of a night off it

Figure 2: Summary of main themes and examples of sub-themes, with illustrative quotations from parent and adolescent highlighting different viewpoints and perspectives