Predictors of adherence to treatment in bronchiectasis

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KEYWORDS
Patient compliance (medication adherence); Bronchiectasis; Beliefs about medicines questionnaire; Quality of life questionnaire-bronchiectasis

Summary

Objectives: We aimed to determine if beliefs about treatment, clinical factors and quality of life predicted adherence to treatment in patients with bronchiectasis.

Methods: We recruited participants with confirmed bronchiectasis to a one-year study. We calculated adherence to treatment using medication possession ratios and self-report. Baseline Beliefs about Medicines, clinical, demographic and Quality of Life Questionnaire-Bronchiectasis data were collected. We used logistic regression to determine predictors of adherence to treatment during the subsequent year.

Results: Seventy-five participants were recruited. Beliefs about harm, age and total number of prescribed medications were predictors of adherence to inhaled antibiotics. Concerns about medication, age and Quality of Life Questionnaire-Bronchiectasis Treatment Burden were predictors of adherence to other respiratory medicines. Beliefs about necessity of airway clearance and age were predictors of adherence to airway clearance.

Conclusion: Beliefs about treatment, age, number of prescribed medications and perceived treatment burden predicted subsequent adherence in bronchiectasis, thereby, providing potential targets for future interventions in this population. Clinicians can use these data to
Introduction

Non-cystic fibrosis (CF) bronchiectasis, known as bronchiectasis, is a chronic respiratory disease associated with ‘persistent or recurrent bronchial sepsis’ [1]. Patients with this condition experience impaired health-related quality of life and recurrent pulmonary exacerbations, which may result in hospitalization [1]. The global prevalence and incidence of bronchiectasis is not known [2]. The most recent prevalence data is from the United States and shows that the prevalence of bronchiectasis is thought to be increasing, with an 8.7% increase in prevalence annually between 2000 and 2007 [3].

Patients with bronchiectasis who are infected with Pseudomonas aeruginosa have worse health outcomes than those without this bacteria [4,5]. They are also prescribed more burdensome treatments such as inhaled antibiotics and airway clearance, alongside other inhaled and oral medications which may make adherence more difficult. Recently reported data demonstrate that non-adherence to treatment is a significant issue for these patients [6,7], with approximately 50% of this patient group completing less than 80% of prescribed inhaled antibiotics, other medicines and airway clearance [7]. Non-adherence has negative health consequences for patients with bronchiectasis. Those who are non-adherent to inhaled antibiotics have a shorter time to first exacerbation [6] and also experience more frequent exacerbations, nearly twice as many in one year compared to those who are adherent [7]. Similar to reports from cystic fibrosis [8], treatment burden may increase as new treatments continue to become licensed for use [9–12] which may lead to adherence becoming an even more significant issue for this population.

To develop effective interventions to enhance adherence and improve health outcomes in bronchiectasis, we need to have an understanding of the predictors of adherence in this population. Many psychological theories explain adherence behavior [13–15]; common to many of these theories is the influence of patients’ perceptions or beliefs on such behavior. In asthma, chronic obstructive pulmonary disease (COPD) and CF, patients’ beliefs about necessity for treatment and concerns about side-effects and/or long term effects of treatment are predictors of adherence to both inhaled treatments [16,17] and airway clearance [18,19]. A recently published qualitative study we conducted found that beliefs about the necessity for treatment and concerns about the side-effects of treatment influenced patients’ decisions about adherence in bronchiectasis [20]. We also reported that other factors such as patients’ perceptions of disease, symptoms and quality of life affected adherence decisions [20]. Furthermore, the practicalities of treatment including treatment burden, particularly for younger people completing treatments around work or caring commitments, were barriers to adherence [20]. However, these factors were identified through qualitative interviews based on subjective reports of previous adherence behavior and predictors of adherence to treatment have not been quantitatively determined in bronchiectasis. Thus, the aim of this study was to determine if baseline beliefs about treatment, clinical factors and quality of life predicted adherence to treatment (inhaled antibiotics, other respiratory medicines and airway clearance) in patients with bronchiectasis in the subsequent year. We hypothesized that stronger beliefs in the necessity for treatment and fewer concerns about treatment would predict increased adherence to treatment.

Materials and methods

The following methods have been reported in detail previously: study design, subjects, clinical data and adherence measurement and thus, are only summarized below for convenience of the reader [7]. Methods for the collection, analysis and results of the Beliefs about Medicines Questionnaire (BMQ) and quantitative predictors of adherence have not been previously reported and are the main focus of this paper.

Study design

The study was a one-year prospective study.

Study subjects

Participants with a diagnosis of bronchiectasis confirmed by high-resolution computed tomography who were prescribed inhaled antibiotics (tobramycin or colistimethate sodium) for ≥6 weeks at baseline and who had a positive sputum culture for P. aeruginosa were recruited to a one-year prospective study from secondary care hospitals in Northern Ireland between June 2010–August 2011. People with cystic fibrosis were excluded. Ethical approval was received from the Office for Research Ethics Northern Ireland (10/NIR03/17). Written informed consent was obtained from all participants.

Procedures

Beliefs about medicines questionnaires (BMQ) were administered at the baseline study visit. Each participant completed four questionnaires: BMQ-Specific for inhaled antibiotics, BMQ-Specific for other respiratory medicines, BMQ-Specific for airway clearance and BMQ-General (included in Supplemental file 1). The BMQ-Specific is a validated, self-administered questionnaire developed to
provide a quantitative method of analyzing the cognitions which may affect patients’ decisions regarding medication-taking [13]. It has not been used in patients with bronchiectasis and approval was received from R. Horne (principal author of the BMQ) for it to be used in this study. The BMQ-Specific contains questions pertaining to the necessity of treatment (BMQ-Specific necessity) and concerns about treatment (BMQ-Specific concerns) [13], with domain scores ranging from 5 to 25 (higher scores indicating stronger beliefs). To ensure the statements of the BMQ-Specific were of relevance to airway clearance, two of the statements were adapted as described by Bucks et al. 2009 [18] (with agreement from R. Horne). The BMQ-Specific necessity-concerns differential was calculated by subtracting the BMQ-Specific concerns score from the BMQ-Specific necessity score [13], with scores ranging from −20 to 20 [13]. The BMQ-General has two subdomains: BMQ-harm and BMQ-overuse. BMQ-harm contains questions pertaining to the harm caused by medicines in general whilst the BMQ-overuse focuses on patients’ beliefs about the overuse of medicines [13]. Domains are scored from 4 to 20 (higher scores indicate stronger beliefs) [13]. Cronbach’s alpha scores for all domains of both BMQ questionnaires were all ≥0.7 in this study. There is no minimal clinically importance difference (MCID) for the BMQ-Specific or BMQ-General.

Clinical data including demographic data, disease history, spirometry and medication data, along with disease-specific quality of life data measured by the Quality of Life Questionnaire (QOL-B) [21], were obtained as previously described [7]. Adherence to inhaled antibiotics, other respiratory medicines and airway clearance data were collected using a modified version of the Self-reported Medication-taking Scale [22,23] and prescription refill data collected prospectively on a 3 monthly and 6 monthly basis, respectively [7]. Medication possession ratios (MPRs) were calculated for inhaled antibiotics and other respiratory medicines for year of the study as previously described [7,24]. Participants were categorized as adherent to inhaled antibiotics and other respiratory medicines if they had an MPR of ≥80% and adherent to airway clearance if they scored ≥80% in self-reported adherence at all study time points [7]. No optimum threshold for adherence exists; however, this cut-off has been used to define adherence in bronchiectasis clinical trials [9,10].

Analysis

Data were analyzed using SPSS for Windows, version 19. All data were analyzed up until study completion or withdrawal from the study. For comparisons between adherence groups, independent t-tests, Mann Whitney U and chi-square tests were performed. Comparisons were based on MPR adherence for inhaled antibiotics and other respiratory medicines and self-reported adherence for airway clearance. Logistic regression analysis using forward selection based on likelihood ratio statistic was completed with adherence to each treatment (inhaled antibiotics, other respiratory medicines and airway clearance) as the dependent variables. The following candidate independent variables were entered into the preliminary models: baseline BMQ-necessity, BMQ-concerns, BMQ-harm, BMQ-overuse, age, FEV1 % predicted, total number of prescribed medicines, QOL-B Physical Functioning, QOL-B Role Functioning, QOL-B Treatment Burden and QOL-B Respiratory Symptoms. Beliefs about treatment were the main factors of interest; therefore, the four BMQ domains were entered first (Block 1). The clinical and quality of life variables were entered second into the model (Block 2). These variables were chosen based on findings from the univariate analysis and data from a related qualitative study [7,20]. BMQ necessity-concerns differential scores were not entered into the models as they were highly correlated with BMQ-necessity and BMQ-concerns scores. Final models included only those variables that significantly contributed to the model (p ≤ 0.05).

Results

Study participants

Study participants have been described in detail previously [7]. Briefly, we approached 108 potential participants, 33 declined to participate and 75 were recruited. Four participants died and two participants withdrew during the study [7]. Participants were predominately female (51/75), mean ± SD aged 64 ± 8 and FEV1 % predicted of 61% ± 25. Participants had low QOL-B scores, with 6/8 domains having mean scores <50. Thirty-five out of 66 (53%) participants prescribed inhaled antibiotics were adherent to this treatment and 39/73 (53%) participants prescribed other respiratory medicines were adherent to this treatment. Only 31/75 (41%) of participants were adherent to airway clearance. Participants were prescribed a mean ± SD of 12 ± 5 medications for bronchiectasis and other co-morbidities. Baseline BMQ-Specific and General scores for all participants are outlined in Fig. 1.

Beliefs about treatment, clinical factors and quality of life for adherent and non-adherent participants

Beliefs about treatment, clinical factors and quality of life data for adherent and non-adherent participants are outlined in Fig. 1.
Concerns about medication, age (ORs based on a 10-year increase in age) and QOL-B Treatment Burden were independent predictors of adherence to other respiratory medicines. Higher BMQ-concerns and QOL-B Treatment Burden score were associated with decreased odds of being adherent.

Predictors of adherence to treatment

Preliminary models containing all of the candidate variables for adherence to each treatment are reported in Supplemental file 2. Final logistic regression models for predictors of adherence to inhaled antibiotics, other respiratory medicines and airway clearance are reported in Table 2.

Beliefs about harm, age (ORs based on a 10-year increase in age) and total number of prescribed medications were independent predictors of adherence to inhaled antibiotics. Higher BMQ-harm scores and older age were associated with increased odds of being adherent to inhaled antibiotics, whilst increased number of prescribed medications were associated with decreased odds of being adherent to this treatment (Table 2). BMQ-necessity, BMQ-concerns, BMQ-overuse, FEV1 % predicted, QOL-B Physical Functioning, QOL-B Role Functioning, QOL-B Treatment Burden and QOL-B Respiratory Symptoms did not independently predict adherence to inhaled antibiotics (Supplemental file 2, Table 1).

### Table 1 Beliefs about treatment, clinical factors and QOL-B domains for adherent and non-adherent participants.

<table>
<thead>
<tr>
<th></th>
<th>Adherent</th>
<th>Non-adherent</th>
<th>p</th>
<th>Adherent</th>
<th>Non-adherent</th>
<th>p</th>
<th>Adherent</th>
<th>Non-adherent</th>
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<tbody>
<tr>
<td>BMQ-necessity</td>
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<tr>
<td>n = 35</td>
<td>19 (18–21)</td>
<td>20 (17–23)</td>
<td>0.19</td>
<td>20 (19–24)</td>
<td>20 (18–23)</td>
<td>0.49</td>
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<td>BMQ-concerns</td>
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<td>n = 34</td>
<td>12 (11–16)</td>
<td>12 (11–15)</td>
<td>0.68</td>
<td>11 (9–14)</td>
<td>12 (10–14)</td>
<td>0.12</td>
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<td>BMQ-differential</td>
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<tr>
<td>n = 30</td>
<td>6 (2–10)</td>
<td>7 (4–13)</td>
<td>0.26</td>
<td>10 (4–15)</td>
<td>7 (4–12)</td>
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<td>BMQ-overuse</td>
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<tr>
<td>n = 30</td>
<td>11 (8–13)</td>
<td>9 (8–11)</td>
<td>0.09</td>
<td>9 (8–12)</td>
<td>10 (8–12)</td>
<td>0.58</td>
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<tr>
<td>BMQ-harm</td>
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<tr>
<td>n = 30</td>
<td>9 (8–11)</td>
<td>8 (6–10)</td>
<td>0.03*</td>
<td>8 (7–10)</td>
<td>9 (8–11)</td>
<td>0.15</td>
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<td>Age</td>
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<tr>
<td>n = 35</td>
<td>67 ± 6</td>
<td>62 ± 10</td>
<td>0.01*</td>
<td>66 ± 6</td>
<td>63 ± 10</td>
<td>0.06</td>
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<td>FEV1, % predicted [7]</td>
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<tr>
<td>n = 66</td>
<td>62 ± 26</td>
<td>54 ± 20</td>
<td>0.16</td>
<td>61 ± 27</td>
<td>60 ± 23</td>
<td>0.94</td>
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<td>Total medicines</td>
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<tr>
<td>n = 72</td>
<td>10 (7–15)</td>
<td>14 (10–17)</td>
<td>0.02*</td>
<td>13 (9–15)</td>
<td>11 (7–16)</td>
<td>0.21</td>
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<td>QOL-B physical functioning [7]</td>
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<td>n = 35</td>
<td>30 ± 28</td>
<td>27 ± 21</td>
<td>0.65</td>
<td>24 ± 22</td>
<td>36 ± 28</td>
<td>0.04*</td>
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<td>QOL-B role functioning [7]</td>
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<tr>
<td>n = 35</td>
<td>46 ± 30</td>
<td>39 ± 24</td>
<td>0.36</td>
<td>39 ± 26</td>
<td>52 ± 28</td>
<td>0.04*</td>
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<td>QOL-B treatment burden [7]</td>
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<tr>
<td>n = 35</td>
<td>52 ± 20</td>
<td>58 ± 18</td>
<td>0.27</td>
<td>53 ± 21</td>
<td>60 ± 18</td>
<td>0.11</td>
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<td>QOL-B respiratory symptoms [7]</td>
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<tr>
<td>n = 35</td>
<td>57 ± 21</td>
<td>48 ± 21</td>
<td>0.08</td>
<td>52 ± 22</td>
<td>52 ± 20</td>
<td>1.00</td>
<td></td>
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</tbody>
</table>

Data presented as mean ± SD or median (IQR), *p ≤ 0.05.

| a | n = 66: 1 withdrawal, 8 participants inadequate adherence data.
| b | n = 64: 3 incomplete questionnaires, 7 participants not prescribed treatment, 1 withdrawal.
| c | n = 72 (other respiratory medicines: 1 withdrawal, 1 not prescribed, 1 incomplete questionnaire), n = 74 (airway clearance: 1 incomplete BMQ-general questionnaire).

Table 2 Final logistic regression models of predictors of adherence to inhaled antibiotics, other respiratory medicines and airway clearance.

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Independent variable</th>
<th>Odds ratio 95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adherence to inhaled antibiotics</td>
<td>BMQ-harm</td>
<td>1.33 1.04–1.71</td>
<td>0.02*</td>
</tr>
<tr>
<td></td>
<td>Agec</td>
<td>2.97 2.74–3.25</td>
<td>0.02*</td>
</tr>
<tr>
<td></td>
<td>Total prescribed medications</td>
<td>0.88 0.77–1.00</td>
<td>0.05*</td>
</tr>
<tr>
<td>Adherence to other respiratory medicines</td>
<td>BMQ-concerns</td>
<td>0.68 0.53–0.88</td>
<td>0.00*</td>
</tr>
<tr>
<td></td>
<td>Agec</td>
<td>3.18 2.85–3.56</td>
<td>0.00*</td>
</tr>
<tr>
<td></td>
<td>QOL-B Treatment Burden</td>
<td>0.94 0.90–0.98</td>
<td>0.01*</td>
</tr>
<tr>
<td>Adherence to airway clearance</td>
<td>BMQ-necessity</td>
<td>1.30 1.10–1.53</td>
<td>0.00*</td>
</tr>
<tr>
<td></td>
<td>Agec</td>
<td>2.94 2.74–3.18</td>
<td>0.02*</td>
</tr>
</tbody>
</table>

BMQ: Beliefs about Medicines Questionnaire, QOL-B: Quality of Life Questionnaire-Bronchiectasis. *p ≤ 0.05.

| a | n = 65: 8 participants inadequate adherence data for inhaled antibiotics, 1 participant withdrawal, 1 incomplete BMQ-harm questionnaire.
| b | Based on 10 year difference in age.
| c | n = 64: 3 incomplete questionnaires, 7 participants not prescribed treatment, 1 withdrawal.
Predictors of adherence in bronchiectasis

This is the first study to determine independent predictors of adherence in bronchiectasis. We hypothesized that participants with stronger beliefs in the necessity for treatment and fewer concerns about treatment would be more likely to adhere to treatment. We present novel data which show that, similar to other respiratory conditions, participants who were concerned about treatments were less likely to adhere to other respiratory medicines [16,17] and those who believed that their airway clearance was necessary were more likely to adhere to that treatment [18,19]. This is a significant finding as beliefs about treatment are not assessed in clinical practice and therefore, are unlikely to be taken into account when prescribing and monitoring treatments for bronchiectasis. Beliefs about treatment were stronger predictors of adherence status than the factors that currently inform treatment decision-making in clinical practice e.g. FEV₁ % predicted and quality of life. As new treatments for bronchiectasis continue to be investigated [9–12], it will be important for clinicians to explore patients’ beliefs about these new treatments as well as beliefs about existing treatments as part of interventions to maximize adherence to ensure potential treatment benefits gained. Several potential methods of changing beliefs about treatment exist [25], e.g. providing information about adherence behavior and its consequences. However, the most effective ways of eliciting and changing beliefs about treatment in bronchiectasis are not known and further research is needed to determine the most effective ways to enhance adherence to treatment in this population.

Comparing the predictors of adherence to treatment across the three treatment types, it is clear there were different predictors for each treatment type and that different beliefs about treatment predicted adherence for each treatment. Stronger beliefs about harm were associated with increased probability of being adherent to inhaled antibiotics. These findings may appear counterintuitive but can be explained by our recent conceptual model of adherence in bronchiectasis. This model states that a single factor does not predict adherence, rather it is a ‘cost-benefit’ analysis of barriers and motivators [20]. We noted that the majority of patients had concerns about the development of antibiotic resistance as a consequence of using inhaled antibiotics but that they were adherent in spite of this, because the potential benefits of adherence were greater e.g. reduced risk of taking more harmful, oral or intravenous antibiotics and symptomatic relief [20]. Beliefs about harm did not predict adherence to airway clearance and this is not surprising as the questions focused on the harm caused by medicines rather than airway clearance. However, it is not clear why BMQ-harm did not predict adherence to other respiratory medicines.

Perceived necessity for treatment has been shown to be an independent predictor of adherence to airway clearance in this study. This is likely to reflect a belief that a lack of symptoms such as sputum production indicate that airway clearance is not necessary [20,26]. Perceived necessity was not a significant predictor of adherence to inhaled antibiotics or other respiratory medicines. It is perhaps surprising that perceived necessity was not a predictor of adherence to these treatments as it has been shown to be lower in non-adherent patients with chronic diseases including asthma [27,28].

Those who were concerned about other respiratory medications were less likely to adhere. This may be due to inhaled corticosteroids and oral antibiotics being widely prescribed in this patient group [7]. Patients’ concerns about the side-effects of these treatments have been well documented in asthma and recently reported in our qualitative study [20,29]. Based on our hypothesis, we would have expected those with fewer concerns to also be more adherent to inhaled antibiotics, particularly as patients with bronchiectasis have expressed concerns about antibiotic resistance [20].

Age was the only factor that predicted adherence to all three treatments in this study, with a 10 year increase in age associated with nearly three times the increase in odds of being adherent. This is similar to that previously reported in adults with COPD [30]. It could reflect differences in younger participants’ perceptions of their health, ageing and need for treatment or that younger participants may also have had more time commitments such as work and caring for family members (children and older parents), making adherence difficult.

Total number of prescribed medicines predicted adherence to inhaled antibiotics, with increasing numbers of prescribed medications associated with a decreased probability of being adherent, reflecting an increasing burden associated with additional treatments and poorer health status. It is likely that as new medications for bronchiectasis begin to be prescribed [9–12], that the overall number of treatments prescribed for this condition will increase.

This is the first study to explore the association between the QOL-B and adherence. QOL-B Treatment Burden score was the only QOL-B domain to predict adherence to other respiratory medicines, with higher Treatment Burden domain scores (lower burden) associated with a decreased probability of being adherent. Medicines grouped as ‘other respiratory medicines’ were mainly delivered via inhaler and orally [7]. Recent qualitative findings revealed that patients did not perceive using inhalers or taking oral medicines to be burdensome [20] and it makes sense that if
a patient is non-adherent to these treatments, they spend less time on treatment and perceive their treatments to be even less burdensome. However, these findings contrast with the CF literature [31,32], where a higher treatment burden has been linked with non-adherence. This could be due to most CF treatments being in nebulized form, which is known to be more burdensome [20].

The key strength of this study was the prospective collection of adherence data over a one-year follow-up period. In addition, the sample was representative of a bronchiectasis population infected with P. aeruginosa, as the sample was predominantly middle-aged females with moderate impairment in lung function. Two methods were used to measure adherence as recommended in the literature [33]. However, it is recognized that both methods used are likely to have over-estimated adherence to treatment in this population [33], making the findings of this study even more clinically relevant as adherence is likely to be an even bigger problem than stated here.

This study had several limitations. The first was the study sample size. To minimize the chance of Type 1 statistical error, the number of predictors tested was limited. The second limitation of this study was the dichotomization of participants into adherent and non-adherent; however, this cut-off is commonly used in clinical trials for new medications and in adherence studies [6,9,10,24] and offers the best balance between sensitivity and specificity [34]. With the exception of beliefs about inhaled antibiotics, beliefs about specific respiratory medicines were not analyzed but rather, were grouped together as ‘other respiratory medicines.’ This may have masked potential relationships between beliefs about specific medications such as inhaled corticosteroids and adherence. Although differences in BMQ scores between adherence groups were statistically significant, the actual differences in scores were small and no minimal clinical important differences exist. However, the differences are of a similar magnitude to those previously reported in those with long term conditions [20,27,35].

These findings have a number of implications for clinicians and researchers. Younger patients, those with lower necessity beliefs, high concerns about treatment and a high number of prescribed medicines may be at more risk of non-adherence. Clinicians can use these data to identify those at risk of non-adherence amongst their own patients. However, the best interventions to change adherence in this population are not known. Therefore, researchers could use these findings to inform the development of new interventions for bronchiectasis. Age is not a modifiable factor but suggests that younger patients may be suitable targets for future adherence interventions and that age-related barriers to adherence may exist which may need to be targeted as part of any developed intervention. Beliefs about treatment are modifiable and could be approached using theoretically based behavior change techniques such as persuasive communication, self-monitoring and feedback [25,36]. As different beliefs predict individual treatments, it is likely that strategies to change adherence will need to be tailored to the specific beliefs that are relevant for each treatment. Given that the number of prescribed medicines predicted adherence, the need for all of the treatments prescribed for both bronchiectasis and co-existing conditions should be rationalized and clinicians could work with patients to prioritize treatments to maximize adherence.

Conclusions

In summary, this is the first study to determine predictors of adherence to treatment in bronchiectasis. We have demonstrated that beliefs about treatment, age, number of prescribed medications and perceived treatment burden independently predicted subsequent adherence in bronchiectasis and therefore, provide potential targets for future interventions to enhance adherence in this population.

Acknowledgments

The authors would like to thank Dr Ian Bradbury from the University of Ulster for his assistance with statistical analysis. The authors would also like to thank Prof. Rob Horne for providing the BMQ and Dr Alexandra Quittner for providing the QOL-B questionnaire and for her expert advice on MPR. We would also like to thank staff at the Northern Ireland Clinical Research Network (Respiratory Health) and the bronchiectasis teams in the Belfast, South Eastern, Western, and Southern Health and Social Care Trusts for their assistance with recruitment to the study, in particular, Rosemary Hanna, Oonagh Hewitt, Diane Todd, Sharon Mills, and Dr Terence McManus and Dr Martin Kelly.

Author’s contributions

All authors contributed to the concept and design; data collection, analysis and interpretation of study findings; drafting and revising of manuscript; and, approval of final manuscript.

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Competing interests

Gilead Sciences, Novartis and Forest have paid consultancy fees to Queen’s University Belfast for consultancy work undertaken by JSE. No other competing interests.
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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.rmed.2015.04.011.

References
