Cystic fibrosis (CF) airways disease is unique, with chronic infection causing a localised but intense inflammatory process, acute in nature, but lasting for years. Prevention, eradication and suppression of airway infection have been the cornerstones of CF management, and success with these strategies has been a key factor in improving the outlook for people with CF. An armamentarium is available to achieve this goal, including a variety of aerosolised therapies. The evidence base to support these therapies ranges from good to poor. Individual patients respond uniquely, with therapeutic strategies working for some but not for others. It is complicated, and a team approach (including the patient) is essential to deliver the best regimen for each individual. What we do know with some certainty is that an aerosolised therapy does not work if it stays in the box or at the pharmacy.

Sustaining time-consuming treatments is a difficult challenge for people with CF. Recent innovations in aerosol delivery have provided some help. Devices that generate aerosol through mesh technology have reduced treatment times and improved deposition. Some devices, by monitoring inspiratory and expiratory flow, provide a pulsed delivery that synchronises with the respiratory cycle to optimise lower airway deposition. In a randomised controlled trial, we were able to show that the addition of a simple manoeuvre to guide breathing with such a device (a vibration at the end of inspiration) reduced treatment times to 3–4 min. Reduction in treatment time was associated with maintenance of adherence, which faltered in the control group.

A feature of these new types of adaptive aerosol delivery devices is that data can be downloaded that record the performance of the device. Electronic data capture (EDC) gives an insight into how often patients are taking their therapy and how long each treatment is taking. In a series of studies undertaken in an open and transparent manner, we have examined treatment behaviours in a large number of our young patients. We have found some surprising results, not the least of which is that most families are able to maintain this treatment burden for year upon year without any apparent diminution in maintenance of performance. Overall, we have shown that patients achieve adherence with approximately 60–70% of their aerosolised treatments, however, there is considerable variability in performance, with some intrasubject variability as well. These levels of adherence are probably better than sceptics expected, and in some cases, adherence is over 100%! We know from these studies and others that health professionals are not good at predicting compliance with prescribing hopes.

EDC has demonstrated some significant patterns in adherence; for instance, treatments are more likely to be missed in the mornings and, in school children, holiday adherence is poorer than term time. These insights can help us to work with patients to achieve concordance with therapies. Of particular interest is the finding that when prescribed two aerosol therapies a day, patients take, on average, 1.4 treatments a day, and when prescribed three therapies a day, they take on average 1.4 treatments a day. There is variance, but patients seem to be telling us that that taking more than two aerosol therapies a day is a tough ask. We need to take notice of these data, work in partnership with our patients to support them through the day-to-day drudgery of chronic suppressive antipseudomonal therapy, and be realistic as to what can be achieved on a long-term basis.

The CF community has followed the progress of dry powder inhalers (DPI) for the delivery of antipseudomonal antibiotics with considerable interest, particularly as many CF centres have recruited actively to clinical trials. After a long wait, two potential devices have become available one after the other. Is there still a place in clinical care for these devices, given the significant improvements in aerosol delivery over the past 10 years? The answer is probably ‘Yes’, as people with CF need access to a variety of antipseudomonal strategies to maintain well-being. However, these devices are expensive, and the UK National Institute for Clinical Excellence (NICE) has recently published a review, the preliminary findings of which do not support the use of a DPI for colistin (clinical trial published in this journal).

There are two main reasons for the NICE decision: (1) anxiety about the efficacy of DPI colistin compared with nebulised tobramycin and (2) the cost of DPI colistin compared with the cost of nebulised colistin (a relatively cheap intervention in the field of CF). Despite a limited evidence base, nebulised colistin is widely prescribed for CF, and represents standard therapy in most of the UK, and parts of Europe, Australasia and North America. Nebulised tobramycin is considerably more expensive, but has a more robust evidence base and, as such, is considered ‘standard therapy’ by regulatory authorities in Europe and the USA.

In the development of DPI colistin, comparison with nebulised tobramycin was requested by regulatory authorities. So, although significantly more expensive than nebulised colistin, this was the comparator for the DPI colistin study. In reviewing the results of the study published in this journal, CF physicians should be reassured that DPI colistin has acceptable efficacy over the 6-month study period, given that patients were established on long-term nebulised therapy (at least two cycles of nebulised tobramycin) prior to enrolment in this study. However, in their assessment of the trial data, NICE felt DPI colistin was inferior to nebulised tobramycin. Although this may be true statistically, it is not of clinical significance in the context of this intervention.

If in their final assessment, NICE does not support the use of DPI colistin, then where are we with respect to options for chronic suppressive therapies for *Pseudomonas aeruginosa* in the UK? NICE has approved the tobramycin dry powder device (the TOBI podhaler), on the basis that clinical trials demonstrate equivalence with nebulised tobramycin. Given that nebulised tobramycin is more expensive than nebulised colistin, they have proposed that the cost of DPI tobramycin is acceptable, by contrast with DPI colistin. It is difficult to follow the logic of this decision, in that NICE are comparing the efficacy of DPI colistin with nebulised tobramycin, yet making an economic comparison with nebulised colistin.

What does this mean for the patients? If the preliminary NICE decision stands, then UK physicians will be restricted to prescribing one DPI device to treat chronic CF airway infection. Previous experience

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**Editorial**

After a long wait, two arrive, one after the other!

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in the field suggests that the existence of a therapeutic monopoly is not in the best interest of patients or the health service. For example, the recent introduction of a second preparation of tobramycin for nebulisation resulted in considerable reductions in point-of-care costs. A similar competitive market would exist for both colistin and tobramycin dry powder devices. Patients and physicians are interested in these devices because they have their sights set on the long game, maintaining these therapies not just for months but for years. Not supporting DPI colistin appears to be a poor economic and clinical decision by NICE. If we are to support our patients in maintaining respiratory condition despite chronic airway infection, we require an assortment of tools, including a variety of inhaled antibiotic options.

People with CF are acutely aware of new developments in the field, some of which will potentially correct the underlying basic CF defect. They appreciate that they need to maintain condition in order to benefit from these emerging therapies, and we need to be able to support them in achieving these goals, and appreciate the reality that maintaining these long-term therapies is hard. New and more efficient aerosol devices have been an important step in that process, and dry powder antibiotics are another step on this challenging journey. It is important that these devices are available in an equitable manner to patients who need them.

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