

Review

Measuring adherence to therapy in airways disease

Non-adherence to medication is one of the most significant issues in all airways disease and can have a major impact on disease control as well as on unscheduled healthcare utilisation. It is vital that clinicians can accurately determine a patient's level of adherence in order to ensure they are gaining the maximal benefit from their therapy and also to avoid any potential for unnecessary increases in therapy. It is essential that measurements of adherence are interpreted alongside biomarkers of mechanistic pathways to identify if improvements in medication adherence can influence disease control.

In this review, the most common methods of measuring adherence are discussed. These include patient self-report, prescription record checks, canister weighing, dose counting, monitoring drug levels and electronic monitoring. We describe the uses and benefits of each method as well as potential shortcomings. The practical use of adherence measures with measurable markers of disease control is also discussed.

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Educational aims

- To understand the various methods available to measure adherence in airways disease.
- To learn how to apply these adherence measures in conjunction with clinical biomarkers in routine clinical care.

Introduction

Sub-optimal adherence to medication is a major issue in all airways disease that can have a significant impact on the use of unscheduled healthcare and overall costs to the health service [1]. The ability

to accurately measure adherence to medication is crucial in order to determine if lack of disease control is a result of ineffective treatment regimens or if medications are not being taken as prescribed. Assessing adherence as part of a patient's routine clinical care regime can therefore ensure that

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Measuring adherence in line with clinical biomarkers is essential to ensure that clinically relevant and appropriate treatment decisions are being made. <https://bit.ly/3yaPTO6>



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patients are gaining the maximum benefit from their medications and can potentially avoid unnecessary escalations in therapy. Conversely, a patient with objectively proven good adherence to prescribed treatments can provide clinicians with confidence that any increase in treatment is justified and necessary.

Other reviews in this issue of *Breathe* discuss the clinical impact of non-adherence in asthma and COPD and focus on interventions to address non-adherence [2, 3]. However, a critical first step is to identify that poor adherence is present and more importantly that better adherence is likely to substantially address the clinical problem. In this review, we present an overview of methods of measuring adherence to prescribed therapies.

Why do patients not take prescribed medication?

The term “adherence” refers to the extent to which the recommendations made by a healthcare provider regarding medications are accepted and followed by the patient [4]. This term recognises the patient’s right to choose whether or not they engage with this advice and removes the concept of blame [5]. The term “concordance” describes the concept of an agreement between the patient and healthcare provider on the decisions around their therapies that acknowledges their thoughts and views [6].

Adherence to medications can either be described as either intentional or unintentional. Intentional non-adherence usually reflects a scenario where a patient actively makes a decision to not follow the advice of their clinical team or does not take their prescribed medications. This usually follows a period of rational thinking where a patient considers the pros and cons in line with their own beliefs before making a decision [7]. Patients may have reservations about a certain treatment strategy after reviewing the potential side-effects or they may simply lack the required motivation to comply with treatment advice [8]. It is therefore essential that effective communication is established between a patient and their healthcare team to address any potential issues and to provide motivation to patients to take an active approach to managing their disease.

Unintentional non-adherence refers to behaviour that is less associated with beliefs and cognitions and relates more strongly to demographics and clinical variables [7]. The reasons for this type of non-adherence are often a result of patients either not remembering to take their treatment or not understanding how to use their medications [8, 9], it is therefore a more passive form of non-adherence. To address this issue, clinical teams may need to work to simplify medication regimens where possible or provide patients with feedback mechanisms, which will be discussed later in

this review, to provide reminders for taking their treatment and which have been consistently shown to improve adherence [10].

Measuring and targeting non-adherence in the right patients

Multiple studies have shown that poor adherence is generally associated with a poor clinical outcome in various patient populations, including poor disease control [11–13], increased healthcare utilisation [12–16] and mortality [17, 18]. However, it is important to note that, at an individual patient level, non-adherence is not always associated with poor disease control or outcome and by extension, that better adherence will not always be associated with better outcome. This is because the identification of non-adherence in isolation is not in itself very useful and must be aligned with identification of a mechanistic pathway that will respond to improved adherence to specific therapies. A simple example is fractional exhaled nitric oxide (F_{ENO}) which is a biomarker of type-2 cytokine driven airways inflammation and is prognostic for severe exacerbation in asthma and is also very predictive of response to inhaled corticosteroids (ICS) in all severities of asthma [19–22]. Consider two clinical scenarios where a symptomatic patient is identified as having poor adherence to ICS treatment: if one patient has a history of recent severe exacerbation requiring rescue prednisolone and a F_{ENO} of 80 ppb, and another patient with the same level of poor adherence has never had a severe exacerbation, and has a F_{ENO} of 12 ppb (and blood eosinophil count of $100 \text{ cells} \cdot \mu\text{L}^{-1}$), improving the poor adherence in the first patient is likely to be substantially more beneficial. Indeed, the latter patient may have identified that “taking the treatment” is not beneficial or indeed causes troublesome side-effects, and the emergent non-adherence may be a very logical thing for the patient to do. By extension, trying to “improve” adherence to ICS in this patient is unlikely to yield an improved clinical outcome, may introduce difficulties in the healthcare provider/patient interaction and a more appropriate clinical strategy would be to try and identify the precise mechanism of the patient’s symptoms. A similar strategy might reasonably be applied in COPD, where the benefits from ICS are seen in patients with a history of severe exacerbation and elevated blood eosinophil count above $150 \text{ cells} \cdot \mu\text{L}^{-1}$, with greatest benefit in those above $300 \text{ cells} \cdot \mu\text{L}^{-1}$ [23], whereas optimising bronchodilator treatment, pulmonary rehabilitation or other interventions may be a more appropriate strategy in relatively non-eosinophilic patients. Thus, like all other aspects of precision treatment in clinical medicine, non-adherence should move to a personalised and targeted approach to ensure maximal benefits.

Inappropriate escalation of treatment

An important clinical consequence of not identifying poor adherence as the predominant clinical problem is inappropriate escalation of treatment, particularly in those with a difficult to manage asthma. This may include unnecessary progression to oral corticosteroids or increasingly to biologic therapy. Indeed, there is already evidence that this is happening with biologic therapy, with substantial unnecessary expense to healthcare systems. In a study of a US prescribing database [24], examining 7658 prevalent and 3399 incident omalizumab users, medication possession ratio (MPR) for ICSs and/or ICS/long-acting β_2 -agonist (LABA) in the past 12 months before omalizumab initiation was low (defined as $\text{MPR} \leq 0.75$) in 72.5% and very low in 48.6% ($\text{MPR} \leq 0.5$). The mean number of exacerbations in the 12 months before incident use ranged from 1.50 to 2.11 per year and poor asthma control (defined as ≥ 3 rescue inhalers dispensed) ranged from 54% to 67%. Thus, many patients prescribed omalizumab had very poor adherence rates for ICSs and/or ICS/LABA prior to omalizumab initiation and it seems likely that many would have been adequately controlled with better adherence to inhaled treatment.

The point where patients with severe asthma potentially transition to biologic therapy is an obvious critical point where adherence should be part of multidisciplinary assessment. We and others have previously described poor adherence rates in this population, with patients displaying poor asthma control, frequent hospital admissions and frequent rescue steroids, with as many as 35% having an $\text{MPR} < 0.5$ [11, 13, 25]. It seems completely counterintuitive that some might suggest that non-adherence of this level might be treated with long-term biologic therapy without any attempt to identify or address the relevant clinical problem. Indeed, the Pro/Con debate [26, 27], in this issue of *Breathe*, may not be addressing a relevant clinical problem as: 1) it suggests that treatment should be withheld when non-adherence is identified but cannot be adequately addressed; and 2) implies that biologic therapy will fix adherence and prevent adverse outcomes. In terms of 1), a more relevant clinical strategy is to identify patients who are non-adherent with inhaled treatment, measure if their type-2 inflammation can be suppressed with high-dose ICS and then try to improve adherence with the often simple interventions that have been demonstrated to consistently improve adherence [10]. However, most clinicians would accept that if best efforts to improve adherence do not deliver an improved clinical outcome and the patient remains at risk, then a trial of biologic therapy may be appropriate. However, in terms of 2), evidence from other disease areas would suggest that adherence and persistence with biologic therapy is not good;

for example, biologic adherence rates in rheumatoid arthritis and psoriasis in the USA demonstrated rates with etanercept of 16–73%, adalimumab of 21–70% and infliximab of 38–81%, and identified that younger age, female sex, higher out-of-pocket costs, greater disease severity and more comorbidities were associated with lower adherence rates [28]. The authors concluded: “...Despite the efficacy that biologics have on the outcomes of RA, PsO, and PsA patients, adherence and persistence rates to these medications were low, presenting significant opportunity for improvement...” [28]. Thus, the assumption that non-adherence with inhaled treatment will be addressed by giving biologic therapy may be flawed and may simply move the poor adherence to another therapy area. Biologic therapy may only work if this treatment is supervised, and if ongoing treatment supervision is what is actually required, then this can be facilitated with inhaled treatments using SMART (single maintenance and reliever therapy) inhaler strategies. It is also important to note that current biologic therapy homecare packages have been supported by the pharmaceutical industry (at least in the UK) and incorporate both nurse-delivered treatment and pharmacy-to-home drug delivery. These are effectively adherence interventions and supports, and if these were to be removed in future, many of the benefits of the biologic treatment may be lost due to emergent poor adherence with treatment.

Measuring and identifying non-adherence

Adherence can be assessed by a number of methods. It is important to note that when reviewing results of observational studies and interventional clinical trials, it is important to identify if patients were aware that they were being monitored, as adherence is likely to transiently improve (known as the “Hawthorne effect” [29]). A common approach to measuring adherence is to estimate the amount of a medication which should be used over a set period of time (*e.g.* over 6 or 12 months) as prescribed by the healthcare provider, and compare this to the amount of medication actually used, using the various measurement methods discussed later in this review [30]. While there is no universally agreed threshold to define good adherence, a value of 80% has often been used to dichotomise non-adherent and adherent patients [31].

Patient self-report

Patient self-report is one of the most commonly used adherence measurements due to the low associated cost and ease of use and application within a clinical setting. Measures can range from patients being verbally asked about their adherence during the normal consultation process to data

being obtained through completion of a patient diary or questionnaires that can range from single-item questions to more complicated and detailed assessments [32]. When compared with objective measures, such as weighing inhalers or using electric dose counters, patients have been shown to overestimate their adherence when asked to self-report [33, 34].

A recent systematic review of patient-reported outcome instruments to evaluate adherence in adults with asthma concluded the evidence was mixed or unknown regarding the reliability and validity of currently available tools, but that there was no evidence of the responsiveness of any available instrument, and no recommendation could be made regarding the use of a particular tool in routine care or in research settings [35].

Specifically, in patients with severe asthma, one such questionnaire, the Medication Adherence Report Scale (MARS), was used in the U-BIOPRED severe asthma cohort to explore alignment with objective measurement of prednisolone in urine. The correlation was poor with adherence detection not matching between methods in 53%, suggesting that self-report using MARS is not effective at identifying poor adherence in this population [36]. Self-report tools to assess adherence have also been used in COPD [37], but it seems likely that the same limitations will be relevant in assessing individual patient adherence in routine clinical care using these tools.

Prescription records

Adherence can be estimated by comparing the prescribed amount of a medication over a set period of time (*e.g.* over 6 or 12 months) with the actual prescription refill date. This is usually expressed as a ratio or percentage of actual prescribed (or dispensed) medication/expected medication if it were taken as prescribed, over a fixed time period, which is usually 12 months and is often termed the medicine possession ratio (MPR) [11]. The main advantage of this method is that it is relatively simple to obtain and has no influence on the patient's current behaviours as the data is collected retrospectively. It is superior to self-report in difficult to control asthma; for example, in a Belfast study, 63 of 182 patients (35%) had filled <50% of prescriptions for inhaled combination therapy and 57 (88%) admitted low adherence after initial denial [13], with similar data subsequently demonstrated in another UK Specialist Centre [10]. Similarly, in a study from the Netherlands, 17% of patients had "difficult to control" asthma, but many had poor prescription filling and sub-optimal inhaler technique, reducing the proportion of those patients fulfilling the criteria for severe refractory asthma to 3.7% [38]. A further study assessing patients with COPD identified an average adherence rate of 43.3% (using prescription refill dates), which reduced as the frequency of dosing increased (*i.e.* twice daily

versus four times daily) [39]. This study also showed that increased medication adherence was associated with reduced healthcare utilisation and a reduction in expenditure. However, whilst use of prescription/dispensing records identifies patients who are not collecting medication and by extension, cannot be taking it, in those collecting medication, there is no information on whether the patient is taking their medication regularly, simply "stockpiling" medication or even taking the medication correctly, which is a specifically relevant issue for inhaled medication, where inhaler technique is critical.

Canister weighing

When investigating adherence, inhalers can be weighed when returned after a set period of time and the remaining doses can be calculated. However, this method has been shown to overestimate adherence when compared with electronic dose counters [34, 40–42]. This may, in part, be due to "test puffs" and "dumping", in which the inhaler is discharged several times into the air at one sitting in order to give the impression of an improved adherence [34, 40, 42]. One study attempted to address this by omitting the electronic data from the first and last days of the study period as it was felt that these would be the days in which dumping was most likely to occur [34]. In another study (in which 13.7% of all participants had at least one dumping episode during the 4-month study period, defined as more than 100 actuations in a 3 h period), the overestimation of adherence obtained by canister weighing was attributed to actuations discharged in a non-prescribed manner, as only two of several actuations at any one sitting would be counted by the electronic device [40]. Another study found a similar overestimation, and again ascribed this to intermittent over-usage (in this study patients overused medication on 22% of study days) [42]. This method does not lend itself to use in routine care or for more prolonged periods of monitoring.

Dose counting

Many inhalers have an integrated dose counter, these are primarily designed to advise patients when the inhaler is coming to an end so it can be replaced but can also be used in a limited way to monitor use. They have the advantage over electronic measures in that they have no battery that can become exhausted, nor are they prone to electronic malfunction [43, 44]. However, they give no information about date or time of use, nor if a metered dose inhaler was simply discharged into the air (because actuation of the inhaler advances the counter mechanism) leaving adherence assessments prone to error or manipulation by dumping or test puffs. Similarly, in breath-activated dry-powder inhaler devices, the dose counter continues to advance each time the device is "primed," regardless of whether or

not the medication is subsequently inhaled. If the device is primed twice without an intervening inhalation, the first primed dose of medication is lost. Therefore, dumping can occur with breath-activated devices. It is worth noting that in some dry-powder devices, *e.g.* Nexthaler (Chiesi), advance of the counter mechanism requires inhalation which adds greater validity to the use of inhaler counting and can facilitate assessment of use over short-term periods, but in general the use of inhaler dose counters is laborious and difficult to interpret in a routine clinical setting.

Oral medication use can also be monitored by counting the number of pills returned at the end of a set time period, but again this is not easy to implement in routine clinical care. A study which compared Zafirlukast pill counts with an electronic measure of pill dispensing found that mean adherence was higher when measured by pill count (89% *versus* 80%) [45]. Another study which used the same device to monitor oral corticosteroids adherence noted a larger difference (mean adherence *via* pill count 102.0%; electronic measure 66.1%) [41]. Pill counting as a method of adherence is open to the same problems as inhaler weights and dose counters: no information is given about when tablets were taken and how many tablets were taken, or if they were not taken and simply “dumped” [41, 45].

Drug levels

Serum levels of theophylline will reveal whether or not the patient is at least intermittently adherent with treatment. Prednisolone and cortisol serum levels can identify not only if prednisolone has been taken that day, but also if it is being taken regularly enough to completely suppress endogenous cortisol levels [13, 46]. Recent data has identified consistent thresholds for prednisolone and cortisol measurements to identify poor adherence [47, 48]. The detection of adherence status with prednisolone is particularly important in interpreting peripheral blood eosinophil counts, and in a patient with severe asthma, the identification of a blood eosinophil count in the “normal range” with a simultaneous detectable prednisolone level is generally consistent with eosinophilic disease [48]. Bioassays are frequently developed during drug development to assess systemic bioavailability, but these have not been used in routine care and the role of other novel methods such as estimating drug residues of inhaled medication in hair samples remains to be established [49–51].

Electronic dose counting

Clinicians now have the ability to attach electronic dose counters to inhalers that can record the number of doses a patient has taken in addition to

the date and time of use. This data can subsequently be downloaded by the patient’s healthcare team, analysed and interpreted to detect non-adherence with inhaled treatment over longer periods of clinical observation. However, many dose counters may not be a reliable indicator of adherence as they do not give accurate information as to whether doses were actually inhaled rather than simply being expelled. In one study, it was reported that some participants were using their inhalers without the monitoring device attached [52]. There have also been issues reported with failure to download recordings either due to device failure or battery issues [53]. Despite these potential issues, electronic monitoring devices still have the ability to detect objective evidence of non-adherence where adherence might be assumed when considering prescription refill rates or self-reported adherence [54].

Recent advances in electronic monitoring devices have provided some solutions to the issues experienced with their predecessors. While older electronic inhaler monitors were able to accurately assess the time and date of doses taken, they provided no information on inhaler technique or quality of inhalation. More recently the use of audio-based monitoring systems have shown the acoustic signal produced while a patient uses their inhaler and this can provide important information relating to adherence, technique and drug delivery [55]. These monitoring systems can be attached to inhaler devices and consist of a system of audio acquisition (*via* a recording which is initiated when the patient primes their inhaler for use) followed by the use of audio analysis algorithms to assess user technique and adherence [55]. One study using this monitoring technique in patients with COPD reported that actual adherence to ICS inhalers was only 22.6% of the expected amount if doses were taken correctly and at the right frequency [56]. This study was also able to identify a proportion of patients (25%) who, despite having high recorded inhaler usage, had a high error rate in their technique when using their inhaler.

Electronic monitors can also be used to assess adherence to oral medications, such as oral corticosteroids, by recording the opening and closing of pill bottles [44, 57]. However, this is of minimal use as it provides no information as to the number of pills removed at any time of opening or whether the pill was taken.

With the incorporation of digital support technologies aligned with electronic monitors on inhalers, *i.e.*, a connected inhaler system (CIS), there is the opportunity to not only identify poor adherence, but also to use the connected technology to provide ongoing support to patients to improve adherence using audio-visual reminders, and allows for direct patient engagement, patient self-management and the collection of real-time health data [58–60]. This mechanism of monitoring also allows clinicians to interpret whether changes in a patient’s condition are likely to be as a result

Self-evaluation questions

- The most reliable method of assessing adherence to inhaled treatment is:
 - Using a patient adherence questionnaire
 - Using an electronic connected inhaler system
 - Asking the patient during the consultation process
 - Counting the remaining doses in an inhaler after a set period of time
- A patient with asthma presents with poor asthma control while being prescribed a moderate dose of ICS. Upon assessment you find that their prescription pickup rate over the previous 12 months is 50%. The next step in management should be to:
 - Increase the dose of ICS
 - Attempt to improve adherence alone
 - Attempt to improve adherence while monitoring clinical biomarkers to assess response to medication
 - Immediately progress the patient to biologic therapies for safety purposes
- You are asked to assess a patient who is suspected to have low adherence to their medications. When speaking to the patient, they admit that they often forget to take their inhalers. They do not feel symptomatic at present but have had deteriorations in their condition in the past year requiring rescue prednisolone. F_{ENO} is 96 ppb and blood eosinophil count is 440 cells per μL . Ideally, you should:
 - Provide the patient with a CIS to monitor adherence while encouraging them to take their medications
 - Make no changes as the patient is currently not symptomatic
 - Increase their dose of ICS in an attempt to reduce future deteriorations in their condition
 - Add oral corticosteroids as they struggle to take inhaled medication
- A patient with COPD presents with persistent breathlessness on minimal exertion. Blood eosinophil count at the clinic is 96 cells per μL and forced expiratory volume in 1 s (FEV_1) is 66% predicted and FEV_1 /forced vital capacity ratio 54%. They assure you that they are adherent to their low-dose ICS/LABA treatment, but when you check their prescription records the pickup rate is 30% with none collected in the past 2 months. At the clinic, inhaler technique is good. Would you:
 - Increase to high-dose ICS/LABA and assume adherence is likely to remain at the same low level going forward
 - Challenge the patient about their adherence and try and increase adherence with current ICS/LABA
 - Consider stopping ICS treatment and using LABA/long-acting muscarinic antagonist treatment
 - Make no changes to their medication and assess them again in 4 weeks

of sub-optimal adherence rather than disease progression [14], facilitating a quick response to either address adherence issues or make therapeutic changes before an extended period of loss of disease control.

Not only does a CIS allow for the measurement of inhalation actuations but it can also provide audio-visual reminders to support patients and allows them to take more control of their disease

management. It has previously been shown that a patient's capability in managing their disease can be improved by involving them in the process of monitoring their symptoms [61]. A recent study, conducted in patients with uncontrolled asthma [62], showed that a patient group who were provided a CIS which provided feedback on maintenance inhaler use to both patients and healthcare professionals (HCPs) had significantly higher adherence rates *versus* a control group where no electronic sensors were provided. This study also compared the control group with the use of a CIS in three other groups that provided data on: 1) maintenance inhaler feedback to participants only; 2) maintenance and reliever inhaler feedback to patients and HCPs; and 3) the maintenance and reliever inhaler feedback to patients only. All three CIS groups showed greater levels of adherence when compared with controls. Additionally, the inclusion of feedback for rescue medication use also resulted in more rescue-free days when compared with the control group, but did not improve overall asthma control [62]. In fact, even when comparing two groups of patients both using electronic monitoring systems, the inclusion of a connected feedback system can still provide additional increases in adherence [63]. However, as with many controlled clinical trials, which have consistently shown improved adherence, the failure to identify the correct patient population (see above) and to specifically identify patients with targetable mechanistic pathways (type-2 airways inflammation for ICS or airflow obstruction for long-acting bronchodilators) means improved adherence will not necessarily translate into better outcomes.

F_{ENO} suppression with directly observed ICS: the F_{ENO} suppression test

As discussed previously, adherence to treatment is only one side of an important clinical equation and ideally should be aligned with measurements that identify those patients where better adherence is likely to improve clinical outcomes. Most patients with asthma, and certainly those with severe disease, have underlying type-2 cytokine eosinophilic asthma and we are in the fortunate position of having excellent biomarkers which are both prognostic for risk and therapeutic response to targeted treatments (F_{ENO} and peripheral blood eosinophil count).

A number of years ago, in a proof-of-concept study, patients with difficult asthma and poor adherence by prescription records, and a F_{ENO} >45 ppb, had 7 days of directly observed high-dose ICS with daily F_{ENO} measurements [64]. This demonstrated that non-adherent patients had significantly greater reductions in F_{ENO} when compared with those who were previously identified as adherent [64], which was evident at

day 5. This formed the basis of the F_{ENO} suppression test ($F_{\text{ENO}}\text{SuppT}$). In a follow-up study, $F_{\text{ENO}}\text{SuppT}$ was delivered using digital technology (home F_{ENO} monitoring and directly observed inhaled corticosteroid (DOICS) therapy using the INCA device, Vitalograph Inc.), which confirmed that this test can identify prior poor high-dose ICS adherence, but additionally could be used to estimate the “optimised” F_{ENO} and blood eosinophil count, when the patient was adherent with monitored high-dose ICS/LABA therapy [65]. This has obvious clinical utility as it can quickly identify those patients who are unlikely to achieve control of type-2 inflammation using inhaled treatment alone and could progress quickly to biologic therapy, but in parallel it can identify those patients where the clinical focus needs to be on better adherence with inhaled treatment. A recent systematic literature review [66] examining the assessment of adherence to corticosteroids in asthma by drug monitoring or F_{ENO} supports this use of $F_{\text{ENO}}\text{SuppT}$ as well as outcome data from small single centre studies [67, 68]. Additionally, this was further supported by the largest case series from the RASP-UK programme which demonstrated that a positive $F_{\text{ENO}}\text{SuppT}$ was associated with significantly fewer patients progressing to biologic therapy and a significantly greater chance of being discharged from hospital [69]. Scaling this approach is now feasible with the advent of CIS systems and is currently being tested in patients being assessed for biologic therapy in UK severe asthma centres.

Summary

Measuring adherence in airways disease is a vital part of a patient’s clinical assessment and management. The ability to gain an accurate insight into a patient’s medication adherence ensures that they are gaining the maximal benefit from their prescribed therapies and can potentially avoid unnecessary increases in therapy. It is critically important to align adherence measurement with biomarkers of mechanistic pathways that will respond to improved adherence to specific therapies, which identifies those patients where improvement in adherence will result in maximal clinical benefit. Conversely, confirming good adherence with prescribed treatment, in conjunction with poor disease control and a targetable disease mechanism, justifies the clinical decision to progress to more advanced treatment options, which is particularly relevant with biologic therapies in severe asthma. There are a number of methods available to clinical teams to monitor adherence in airways disease and recent advances allow collection of adherence data in real time with a connected system to encourage and promote adherence simultaneously. However, the importance of interpreting adherence data in conjunction with relevant clinical biomarkers is essential and there is a need to move towards a more integrated and personalised approach to ensure that clinically relevant and appropriate treatment decisions are being made.

Key points

- The identification of non-adherence in isolation is not in itself very useful and should be used in conjunction with clinical biomarkers.
- Patient self-reported adherence tends to be an overestimate. Other objective measures such as dose counters and inhaler canister weighing can also yield overestimations of adherence due to test doses and “dumping,” which is when the inhaler is discharged into the air deliberately.
- Prescription records can be useful, but are also prone to measurement error.
- The use of a CIS gives the opportunity to not only identify poor adherence, but also for direct patient engagement to encourage adherence to inhaled therapies.

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Conflict of interest

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Suggested answers

1. b
2. c
3. a
4. b

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