

# Adherence to Asthma Treatments

## An Audit of a Warehouse of Data

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Whether it is because they do not like to, do not remember to, or cannot afford to, it is an undeniable fact that people do not take their medications as well as they should. For many clinicians, this problem is partially hidden because patients do not like to, do not remember to, or do not admit to missing their medications.<sup>1-3</sup> For health-care systems, poor medication adherence leads to downstream costs through complications of partially or incompletely treated conditions. It is estimated that poor medication adherence, through the direct effect of untreated conditions and the additional cost of additional add-on treatment, costs over USD 500 million per annum.<sup>4</sup>

In respiratory medicine, adherence to inhaler therapy is a particularly problematic area. A systematic review of 51 observational studies by Dima and colleagues<sup>5</sup> indicated that adherence to inhaled corticosteroids (ICS), a crucial medication in the management of asthma, was less than 50%.<sup>5</sup> Their study also highlighted consistent links between adherence and stronger inhaler-necessity beliefs.

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At the time of their review, ICS were in effect the only available treatment for persistent asthma, leaving clinicians with the only potential solution to poor adherence being adherence-promoting interventions around the theme of necessity. Since Dima and colleagues completed their systematic review, a variety of effective but expensive asthma biologic therapies have become available. This raises the question of whether poor adherence to ICS is also true for asthma biologics. And if so, what cost implications do these incur?

In this issue of *CHEST*, Maddux and colleagues<sup>6</sup> report on the relationship of adherence to ICS to that of asthma biologic therapies among patients with severe persistent asthma.<sup>6</sup> To do this, they examined an anonymous database of 200 million US patients with private health insurance. They examined the pharmacy refill rates and persistence of refill rates, using a metric called the PDC (prescription days covered). This measure is an established effective way to quantify medication adherence. They also addressed outcomes with the biologic therapies and how this was affected by prior treatment adherence.

After careful refinement of the data, they reported on 5,319 people who started any asthma biologic therapy and compared the mean PDCs for ICS in the 6 months before and after starting treatment. The mean PDCs for any asthma biologic therapy was 0.76 (95% CI, 0.75-0.77), whereas the mean PDC for ICS was much lower. In the 6 months before starting the asthma biologic therapy, adherence to ICS was 0.44 (95% CI, 0.43-0.45) and was 0.40 (95% CI, 0.39-0.40) in the 6 months after a biologic therapy was started. In short, people treated with asthma biologic therapy were often not previously adherent to ICS. Good adherence to ICS before index biologic use was associated both with continued PDC for asthma biologic therapy and for ICS during the first 6 months of biologic use (OR = 9.93; 95% CI, 8.55-11.53). Hence, a clear takeaway of this study is that adherence to ICS is generally poor but adherence to asthma biologic therapy is reasonable.

In context, a recent paper by van Boven et al<sup>7</sup> examining treatment adherence in a large Australian database identified a strong relationship between poor ICS treatment and subsequent use of step-up asthma treatment. By using group-based trajectory modeling to

estimate medication adherence patterns, the authors identified that 80% of patients were nonadherent or intermittently adherent. These data suggest, as do the findings in the current study, that frequently, patients poorly adherent to ICS end up being prescribed add-on asthma biologic treatment. If done unwittingly this does seem to be an expensive oversight, given the cost of asthma biologic therapy at USD 20,000 to USD 50,000 per annum.<sup>8</sup> A follow-up study describing the patterns of adherence would be a welcome additional analysis of these data.

Maddux et al<sup>6</sup> also described the effect of asthma biologic therapy. Using a number of measures, including hospital and ED visits as well as rescue oral corticosteroids, they found that high asthma biologic PDC was associated with a nonsignificant reduction in asthma exacerbations during the first 6 months of therapy. This finding is surprising given that even in observational, real-world studies these agents are effective in controlling exacerbations. One reason could be that poor adherence to ICS prevents optimal effects of the biologic therapy. In context, in a large single-center retrospective cohort study from the United Kingdom by d'Ancona et al,<sup>9</sup> 20% of patients had adherence to ICS of less than 0.5 while on an asthma biologic therapy. Furthermore, these patients had more exacerbations and less reduction in oral corticosteroid use while on asthma biologic therapy. However, these data, like the current study, is not mechanistic. Nevertheless, both suggest that a future study addressing the complimentary role of ICS (with good adherence) in patients treated with asthma biologics is needed. Thus, the current study raises several themes around the need for ICS and targeted asthma biologic therapy.

There are several strengths to this study, most uniquely in how the authors compare the predictive nature of adherence of one medication to another. That they find only a small overlap is not too surprising given that one treatment is a once or twice daily at home treatment, whereas the other is a regularly scheduled provider-delivered treatment. The authors conclude that, because

efforts to “fix” adherence are not particularly good, adding an asthma biologic could be a potential solution to poor ICS adherence. It is our view that, given the cost of a typical asthma biologic therapy, everyone—clinicians, patients, and payers—should be fully aware of an individual's prior ICS adherence before adding this additional treatment.

Medication adherence is a big problem, but fortunately for us, this is a big problem that can be assessed with big data. Unfortunately, databases do not tell the story of why people do not take ICS but are willing to take an injection, nor do they give opinions on the rights and wrongs of treating poor adherence with step-up treatments. Skilled experts, such as the readers of this Journal, are placed to answer these questions and so are encouraged to look at the details of this paper, because it contains some unique perspectives that can inform practice and future thinking.

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