Commentary

Asthma management in the real world

The perils of simplicity

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More than 50% of asthma patients in Canada have uncontrolled asthma,[1] despite publication of several versions of treatment guidelines[2] and evidence derived from double-blind randomized controlled trials (DBRCTs). The factors contributing to these care gaps are not well understood, but part of the problem might be *how* data from different types of studies are interpreted and applied in primary care. In a recent editorial, McIvor and Sampalis[3] suggested that there was a discrepancy between efficacy results observed in DBRCTs and effectiveness observed in the real world in day-to-day clinical management.

McIvor and Sampalis' eloquent discussion underscored the benefits and limitations of DBRCTs and how data obtained in this setting might not reflect real-world practices.[3] As they pointed out, DBRCTs represent ideal situations that include carefully selected patients who adhere to strict protocol requirements. In DBRCT settings, issues related to care and compliance might not influence study outcomes. In contrast, in the real world, access to care and compliance with treatment can play vital roles in achieving therapeutic goals.

Get real

McIvor and Sampalis[3] suggested that there was a need for well designed postmarketing studies to generate data assessing real-world effectiveness of asthma treatments. This premise contributed to the motivation to conduct the SIMPLE (Singulair in Mild Asthma: Compliance and Effectiveness) trial.[4] In their editorial, they appropriately outlined differences between phase IV trials (postmarketing studies to obtain more information, including the risks, benefits, and optimal use of drugs) and postmarketing observational studies (PMOSs). In the latter approach, medication is acquired through the regular sources, including health care plans or out-of-pocket payment by patients. In PMOSs, factors such as accessibility of care, adherence to treatment guidelines, and compliance can affect the study outcomes.

As McIvor and Sampalis[3] suggested, the real-world clinical practice setting is better represented by PMOSs than by phase IV studies. Unfortunately, the SIMPLE trial was a phase IV study; and, as with many phase IV trials, it was fraught with limitations, including a lack of a control group, selection bias, and an open-label design,[5] rendering the results virtually impossible to interpret. (A more detailed examination of the trial's limitations can be found in the Critical Appraisal on **page 1019**.[5]) Furthermore, and perhaps more important, the strategy of switching patients whose asthma is uncontrolled or who are unsatisfied with low-dose inhaled corticosteroids (ICSs) to montelukast violates a fundamental premise of guideline-driven asthma management. It is a strategy that might serve to widen the care gaps that currently exist.[1] For example, the Canadian Asthma Consensus Guidelines and the Global Initiative for Asthma guidelines on asthma management recommend ICSs as first-line maintenance therapy for patients with persistent symptoms.[2,6] If asthma control remains suboptimal, factors that could be contributing to poor control should be assessed. If patients are not adherent to or are unsatisfied with their ICS therapy, this should be investigated thoroughly. If patients' asthma remains uncontrolled on low- to moderate-dose ICS therapy, addition of a long-acting β_2-agonist is recommended by national (Canadian Asthma Consensus Guidelines) and international (Global Initiative for Asthma) guidelines.[2,6]

Closing care gaps

It does not seem reasonable to substitute evidence from phase IV studies like the SIMPLE trial[4] for that from DBRCTs only because certain confounding variables in the real world present challenges to the implementation of data obtained from DBRCTs. In patients who are not adherent to or are unsatisfied with ICS therapy, knowledge translation (driven by guideline recommendations) about the benefits of ICS therapy will not be realized if these patients are simply switched to another therapy. A more appropriate strategy would be to identify and modify factors and barriers that influence patient behaviour (related to ICS use) and asthma outcomes, including inhaler technique, access to medication, and use of optimal doses of ICSs. Current guidelines[2,6] underscore the importance of patient education and partnership in care. For those patients who object to ICS therapy, selection of another medication is the obvious strategy.

Because the desired result of knowledge translation includes changes in behaviour and outcomes, it seems counterproductive to conduct SIMPLE-type studies that are

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designed to overlook real-world issues that might be contributing to care gaps and that emphasize simplicity over evidence-driven care. To better understand how montelukast compares with low-dose ICS treatment in mild asthma in the real-world setting, the authors should have carried out a PMOS. Having said that, the data from such a study might not bring us any closer to understanding how to overcome implementation barriers that exist in the real world, as many observational studies lack adequate control groups. The results of the SIMPLE trial send a conflicting message to primary care physicians that is not in keeping with current guidelines on asthma management.[2,6] An important advantage of DBRCTs, whether or not they are conducted in the real-world setting, relates to their prospective, comparative approach, which includes a control arm. In the SIMPLE trial[4] the authors use baseline data (representing the effect of previous treatment) as a control state, against which a prospective trial of montelukast is compared. This approach, unfortunately, violates important study design principles, rendering the results of the SIMPLE trial[1] impossible to interpret. Responses to treatment might be influenced by behaviour driven by participation in a clinical trial and by confounding factors related to medication use before the treatment phase.

Troublingly simple

Troublingly, the SIMPLE trial[4] seems to suggest that patients whose asthma is not controlled by ICSs or who are not adherent to ICS therapy should be switched to second-line anti-inflammatory therapy without consideration of the factors contributing to nonadherence and without the addition of a long-acting β_2-agonist (for adherent but uncontrolled patients), as recommended in many guidelines. This message could serve to confuse busy family physicians and to widen already broad care gaps.

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Competing interests

Dr D'Urzo has participated in many clinical trials studying the use of long-acting β_2-agonists and inhaled corticosteroids in asthma management that were funded by various pharmaceutical organizations.

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