

Editorials

Recent Changes in International Asthma Guidelines May Be Influenced by Pharmaceutical Industry Conflicts of Interest

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As highlighted in this month's issue of *American Family Physician*, asthma treatment recommendations have recently changed.¹ Global Initiative for Asthma (GINA) guidelines now recommend the combination of an inhaled corticosteroid (ICS) and formoterol as the preferred as-needed therapy for asthma in adults and adolescents 12 years and older.² The National Asthma Education and Prevention Program (NAEPP) takes a different approach and suggests a combined rescue strategy as only an option for patients with mild asthma and conditionally recommends combination therapy as needed in patients with additional symptoms.³ This treatment approach is called single maintenance and reliever therapy (SMART). These recommendations and the randomized controlled trials (RCTs) of SMART were heavily influenced by the pharmaceutical industry.

Drs. Raymond, Peterson, and Coulter state that, "Most RCTs evaluating SMART used budesonide/formoterol (Symbicort)."¹ Budesonide/formoterol is marketed by AstraZeneca under the brand name Symbicort in the United States. AstraZeneca reported more than \$2.5 billion in sales of Symbicort worldwide in 2021.⁴

The GINA board of directors and scientific committee members have substantial financial conflicts of interest. Twelve of 17 members, including both chairs, have received personal fees from AstraZeneca.⁵ The NAEPP guideline has fewer members with similar conflicts of interest, and members with conflicts of interest recuse themselves from discussions on related topics.³ This difference aligns with how SMART is presented in the guidelines, with GINA recommending SMART as the preferred option, whereas the NAEPP recommends including SMART as the preferred approach for a smaller subset of patients.

The research base used to create these guidelines is substantially influenced by industry. A 2021 Cochrane review evaluated a single combined inhaler (fast-acting beta₂ agonist plus an ICS) used as rescue therapy in people with mild asthma.⁶ The review found six studies and used five for the meta-analysis. Four of the studies were funded by

AstraZeneca, and some authors in the studies were employees of AstraZeneca. Other authors received personal payments from AstraZeneca.⁷⁻¹⁰

A 2018 systematic review of SMART for persistent asthma found 16 RCTs, and 15 of those evaluated SMART as a combination therapy with budesonide and formoterol in a dry-powder inhaler.¹¹ Fourteen of the 15 studies were funded by AstraZeneca, had an AstraZeneca employee as a coauthor, or had authors who received honoraria or fees from AstraZeneca.¹²⁻²⁷ Many of the studies have a high or unclear risk of bias, especially in blinding of participants and outcome assessment and in selective reporting.¹¹

Conflicts of interest can influence health care decisions.²⁸ Industry influence may lead to more favorable recommendations in guidelines.²⁹ Most organizational guidelines still permit conflicts of interest and many do not follow the National Academy of Medicine (formerly the Institute of Medicine) conflict-of-interest recommendations for guideline creation.³⁰ The National Academy of Medicine recommends that guideline development group members should have no conflicts of interest whenever possible, members with conflicts of interest should not represent more than a minority of the guideline development group, and the chair or coauthors should not have a conflict of interest.²⁸ GINA does not follow these recommendations.

Trial design, results, and conclusions can be influenced by industry. Industry-sponsored studies have more favorable results and conclusions than studies sponsored by other sources,³¹ and financial ties between principal investigators and industry are associated with positive trial results.³² Industry funding may lead to overly positive spin when reporting results, physicians choosing inferior comparators, and commercially driven research agendas.³³ Research funded by governmental organizations may lead to less biased results. However, the pharmaceutical industry is involved in a large proportion of publications in high-impact journals.³⁴

The choice of rescue medication in patients with asthma affects health outcomes and health care costs. Our colleagues and patients should be able to make this decision

with guidelines and RCTs that are not unduly influenced by the industry.

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