Theme Foreword

Respiratory Medication Adherence: Toward a Common Language and a Shared Vision

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The World Health Organization highlights the importance of optimizing chronic respiratory disease (CRD) medication adherence with a view to improving clinical outcomes and alleviating ever-increasing pressures on the world's health care resources.[1,2] The Global Initiative for Asthma also advocates for optimized adherence, recommending that asthma symptoms and risk be optimized on the lowest dose of therapy appropriate and that high-cost add-on therapies only be considered in patients with severe disease who have persistent symptoms and/or exacerbations despite optimized treatment with high-dose controller medications and treatment of modifiable risk factors.[2] This requirement for optimized therapy as a prerequisite to asthma treatment escalations is of increasing relevance as evermore high-cost biological therapies with narrow therapeutic margins are expected to be licensed for CRD. Use of such novel therapies must be targeted at patients with true unmet need to maximize their cost-effectiveness.

Yet it is too simplistic to simply call for "good adherence" in all patients across all therapies. Once the benefit-risk ratio of a treatment is shown to be positive, the ultimate goal of the health care professional, payer, and patient should be to achieve "efficient use" of treatment, that is, use that maximizes treatment benefit while minimizing any potential risk of harm. Efficient use will vary between patients (eg, depending on their phenotype) and between therapies (eg, depending on their pharmacokinetic profile). Moreover, there is a wide range of real-life factors that can impair efficient use of therapy and resultant clinical outcomes.[3] Such issues include limited comprehension or recognition (among patients and/or their health care professionals) of the importance and value of efficient use,[4-6] medication beliefs and side-effect concerns, stigma around inhalers, particularly in CRD where inhaled therapies make up the backbone of licensed treatment, and device usage challenges.[7-9] Thus, interventions targeting "efficient use" of therapies must optimize adherence within the context of its indicated use, prescribed use, and tailored to the characteristics and requirements of the target patient. They must also furnish patients with the information they require to make appropriate decisions about their use of therapy, in a context of shared decision making (SDM). With reference to the physician-patient encounter, SDM has been defined as being "interactional" in nature.[10] It is a process of 2-way information exchange and has the defining characteristic of deliberation at its core (ie, between the physician and the patient or potential others). Both/all parties involved work toward reaching an agreement and have an investment in the ultimate decision made. Thus, the SDM philosophy emphasizes shared patient-physician participation at every step of the decision-making process. When fully realized in clinical practice, SDM can notably reduce patients' anxiety and decisional conflict, and improve satisfaction and medication adherence.[11]

An important prerequisite to the development of successful, scalable adherence interventions is the definition of clear adherence concepts and evaluation tools such that adherence behaviors can be accurately defined and characterized, and opportunities to intervene identified. In turn, this requires development, documentation, and use of standardized adherence definitions and

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methodologies for research and clinical practice. The tradition of combining distinct adherence behaviors (initiation of medication, implementation of the prescribed regimen and persistence with it) under one encompassing term has resulted in barriers to synthesizing adherence evidence and replicating and validating previous studies and substantial research inefficiencies. In the absence of a consensus vocabulary to ensure specificity of the adherence research question, selection of appropriate research methodologies, and clear reporting within adherence research, pooling evidence across the research community and identifying gaps in the evidence base has been a longstanding challenge. The Ascertaining Barriers to Compliance taxonomy developed by Vrijens et al[12] is an important step toward this, distinguishing between major concepts in adherence and standardizing terminology, such that common approaches, definitions, and outcomes can be consistently applied across studies and health programs, with greater comparability and efficiency.

Five articles[13-17] within this themed issue derive from a 1-day adherence expert panel meeting held by the Respiratory Effectiveness Group at the time of the 2015 European Asthma Allergy and Clinical Immunology Annual Congress. For more information about the Respiratory Effectiveness Group, visit their Web site at www.effectivenessevaluation.org. The meeting brought together world experts in asthma and chronic obstructive pulmonary disease (COPD) and in adherence and outcomes research. The multidisciplinary group set out to explore the following: what is meant by adherence in respiratory medicine, how it is currently measured, and how it can be positively affected. Through an examination of a number of wide-ranging and complex adherence-related issues and concepts—macro- (eg, health care system), meso- (eg, physician/practice), micro- (individual patient), and their interaction and mediators—the attendees (here coauthors) provide a snapshot of current knowledge in respiratory adherence and point to future needs to enable the field to progress in a unified and efficient manner.

Vrijens et al's article, "What we mean when we talk about adherence in respiratory medicine," revisits the authors' Ascertaining Barriers to Compliance taxonomy, which defines a temporal sequence of steps a patient must undertake to be defined as "adherent to treatment": initiation, implementation, and persistence.[13] In this instance, the steps are considered in the context of asthma and COPD. Behavioral determinants of adherence are considered across these steps as are measurement and assessment methods. The authors also touch on the clinical realities of treatment interruptions and variations in drug exposure that occur in real-world CRD management. Although epidemiological research has traditionally used concepts of "treatment episodes" and "treatment gaps" to reflect such clinical realities, in variable conditions such as asthma (where symptoms often drive the use of therapy) there is a need to reach consensus on clinically meaningful definitions of treatment gaps to help differentiate periods of nonimplementation from nonpersistence and to model outcomes accordingly.

Dima et al's article, "Mapping the asthma care process: implications for research and practice," outlines an asthma care model developed by the ASTRO-LAB research group following rigorous literature reviews and qualitative interviews.[14] The model offers a novel theoretical contribution to asthma management, mapping for the first time the sequence of treatment events, from diagnosis to treatment prescription, drug exposure, asthma trigger exposure, and health outcomes. It also includes the relationships between these components and moderators, including patient behaviors (medication adherence, symptom monitoring, managing triggers, and exacerbations) and health care professional behaviors (medical care and self-management support). The model details the major care events that affect adherence and, in its visual depiction of the relationships between these events, identifies targets for effective adherence interventions. In this issue, it is also used by Braido et al,[15] Costello et al,[16] and van Boven et al[17] to highlight the focus of their respective articles—each a more concentrated examination of a particular element within the macro-level care management model.

Braido et al's article, "'Trying, but failing' - the role of inhaler technique and mode of delivery in respiratory medication adherence" isolates the moderator "Adherence—regular and correct inhaler use" within the patient/carer domain of the model.[15] The authors focus on how modes of medication delivery can affect medication adherence, particularly adherence to inhaled therapies that are the backbone to asthma and COPD management. Through their review of the challenges posed by different inhaler device types, multiple devices, and mixed device use (for reliever and controller therapies), the authors illustrate the myriad of research challenges and opportunities that key elements of the asthma care model represent as well as the many management considerations clinicians face (eg, device selection, training, and education) when seeking to promote best use of available therapies to their patients.

Focusing on "Determinants of patient behaviors" in the asthma care model, Costello et al's article, "The seven stages of man: the role of developmental stage on medication adherence in respiratory diseases," skillfully illustrates the wide-ranging implications that just one (time-varying) patient characteristic can have on adherence.[16] The authors consider adherence determinants in both the lower and upper ends of the age spectrum, from young patients with pediatric asthma to elderly patients with COPD and possible cognitive impairment. In particular, the authors call for greater research into the adherence determinants and interventions in adolescents and elderly patients, noting the frequent gaps in access to effective adherence support in elderly patients in light of cognitive and developmental changes and the potential disruption in care continuity faced by children transitioning to adult services.

Finally, van Boven et al's article, "Enhancing respiratory medication adherence: the role of health care professionals and cost-effectiveness considerations," considers determinants of respiratory medication adherence from the perspective of health care professionals and payers.[17] The authors provide practical suggestions for clinicians and pharmacists to intervene to improve medication adherence in asthma and COPD. Examples of effective primary care interventions are shared and standard approaches to health economic evaluations of such interventions are explained, highlighting inherent differences in model assumptions for asthma versus COPD. The authors also outline some mechanisms (eg, intervention targeting) by which cost-effectiveness ratios for different interventions can be optimized to improve the probability of positive reimbursement decisions, system-wide implementation, and resultant health benefits.

Optimized medication adherence is a central pillar of effective CRD management. It equates to efficient use of available therapies such that outcomes are maximized and risks

minimized. The articles in this issue only begin to touch on the wide range of adherence determinants that exist within real-life CRD management. Within this complex mix of determinants and moderators of adherence behaviors there exist great opportunities to adopt and implement standardized research approaches to improve shared knowledge and understanding in the field. In clinical practice there is also a wealth of opportunities for health care professionals to intervene to optimize patients' adherence behaviors by taking time to ask targeted questions, try to understand the challenges (real or perceived) they face when prescribed CRD therapies, and work closely with patients across the adherence pathway to address barriers or concerns. Like all clinical fields, adherence research and clinical practice interventions continue to evolve and now face an era of increasing access to digital monitoring and technology-based solutions that will offer opportunities to monitor and characterize existing adherence behaviors and to prompt and promote beneficial changes.[18] The optimum role of such tools is yet to be determined, and is likely to change between patients, diseases, and disease stages, but they will be an addition to the clinician's armamentarium. Irrespective, considerate and tailored use of available adherence interventions (whether high-, low-, or no-cost; digital or human) will remain the key to their successful implementation and realization of their full benefit for patients, health care professionals, and health systems alike.

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