oromotor dysfunction also have an increased risk of sleep-disordered breathing—though some do not present until well into adulthood, at which point such historical details are not usually sought clinically. Myofunctional therapy has recently come into focus as an important domain in the maintenance of long-term, stable improvements in craniofacial architecture and in sleep-disordered breathing, and seems one way to span both developmental and genetic aspects of sleep-disordered breathing.[10]

Recently the European Respiratory Society Task Force on the diagnosis and management of obstructive sleep-disordered breathing in childhood included orthodontic treatment in addition to adentonsillectomy and anti-inflammatory treatment for management of paediatric sleep-disordered breathing. It might be the first step of evolution toward a model of creating long-term stable improvements in craniofacial aberrancies that are present from childhood and that can lead to sleep-disordered breathing in adulthood. But challenges remain: visionary prevention of sleep-disordered breathing is hampered by the well guarded silos of the health-care system, topped by a healthy dollop of future discounting. Of course it can be said that prevention of all chronic diseases is subject to such vagaries, but for sleep-disordered breathing, not only must disparate specialties connect, but a truly joint medical and paediatric approach to the clinical syndrome is needed. Since few sleep centres see patients at all stages and ages of life, the experience and observations that might be learned by following members of three or even four generations of families might not materialise. What's more, such division produces the most dogged of handicaps; our own ignorance of what we do not know.

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Severe asthma: looking beyond the amount of medication

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In 2008[1] we proposed the concept of problematic severe asthma as an umbrella term for children referred to a specialist service who are not responding to high-dose asthma medications.[2] Problematic severe asthma comprised non-asthma-related conditions (ie, wrong diagnosis) and asthma-plus comorbidities (eg, obesity, rhinosinusitis, food allergies, and dysfunctional breathing; excluding gastro-oesophageal reflux).[3] After confirming the diagnosis, all children with problematic severe asthma referred to our severe asthma clinic undergo a detailed nurse-led assessment,[4] which considers airway disease in the context of comorbidities, and social and environmental factors,[5] before even considering assessment of airway pathology using bronchoscopy. As a result of this assessment, these children are either diagnosed with difficult asthma, in whom basic management steps needed to be correctly applied, or severe therapy-resistant asthma, for which children undergo detailed pathological phenotyping by bronchoscopy and are candidates for novel biologicals.[6] This classification is advantageous for research because the pathophysiology of severe therapy-resistant asthma is likely to differ substantially from moderate asthma in which children are not taking inhaled corticosteroids. However, has this classification adequately covered the needs of the clinician?

First, it is not logical to apply the term problematic severe asthma to children who might have a completely different diagnosis—eg, a vascular ring. Although cumbersome,

a more accurate term is asthma-treatment-resistant symptoms. Second, the division between so-called asthma plus, difficult asthma, and severe therapy-resistant asthma is not as clear cut. For example, obese asthmatic patients might have a different phenotype from those without obesity (eg, dysanaptic airway growth[7] and peripheral interleukin-6-driven inflammation)[8] and might also need invasive airway phenotyping, especially if they do not lose weight. Patients who are non-adherent to treatment might in fact have severe therapy-resistant asthma and become disillusioned with medications that do not work. Third, although many children with difficult asthma improve,[9] some continue to have asthma attacks. Finally, most asthma deaths are in patients with so-called mild but difficult asthma (surely a contradiction in terms).[10] Hence we propose developing our previous scheme to move beyond severity as a clinical concept being solely defined by level of medication.

In this scheme, the nurse-led assessment should come as soon as it is clear that the child has true problematic severe asthma and not an alternative diagnosis. As before, the initial but now provisional categorisation is difficult asthma, asthma plus, and severe therapy-resistant asthma; this last group is phenotyped as before.[6,11] We acknowledge that some children might have features of more than one category. Children with difficult asthma and asthma plus should be subsequently reassessed by the multidisciplinary team. In many cases, the issues will have been resolved and the child will have controlled asthma, and can be followed up in a regular asthma clinic with a focus on avoiding recurrence of problems such as poor adherence. Children who do not improve should be assigned to the categories of refractory difficult asthma and refractory asthma plus, respectively, the detailed management of which has been discussed in detail elsewhere.[12]

Refractory difficult asthma usually relates to ongoing poor adherence documented by electronic monitoring, preferably measuring inhalation rather than just actuation,[13] but also to patients with persistent adverse environmental exposures, such as pet allergens and tobacco. The distinction between refractory difficult asthma and people with severe therapy-resistant asthma who are disillusioned with medications, is made by directly observed therapy (DOT) during hospital admission or at school. The usual response is improvement of symptoms, and normalisation of spirometry and fraction of exhaled nitric oxide (FeNO). These patients need to be managed with DOT in the first instance, with ongoing psychological support to try and encourage behaviour modification. In some cases, this management process cannot be made to work—eg, if DOT is planned at school and school attendance is very poor—and alternative steps are needed. The same is true of children whose parents cannot or will not address environmental issues. The question needs to be posed as to whether these parental actions reach the stage in which child safeguarding has become a concern, and we certainly have a low threshold for discussing these concerns with the families and the safeguarding team. Also, is it ethical to give an injectable biological therapy, with all the fiscal cost and inconvenience this entails, to children whose parents will not follow the steps necessary to control their child's asthma? Since non-adherence to inhaled corticosteroids is a prominent cause of asthma death,[10] we argue that, in children, this treatment is justifiable; children should not be penalised for the behaviour of their parents. So we go on to phenotype the airway and treat children who meet the eligibility criteria for omalizumab or other biologicals, monitoring

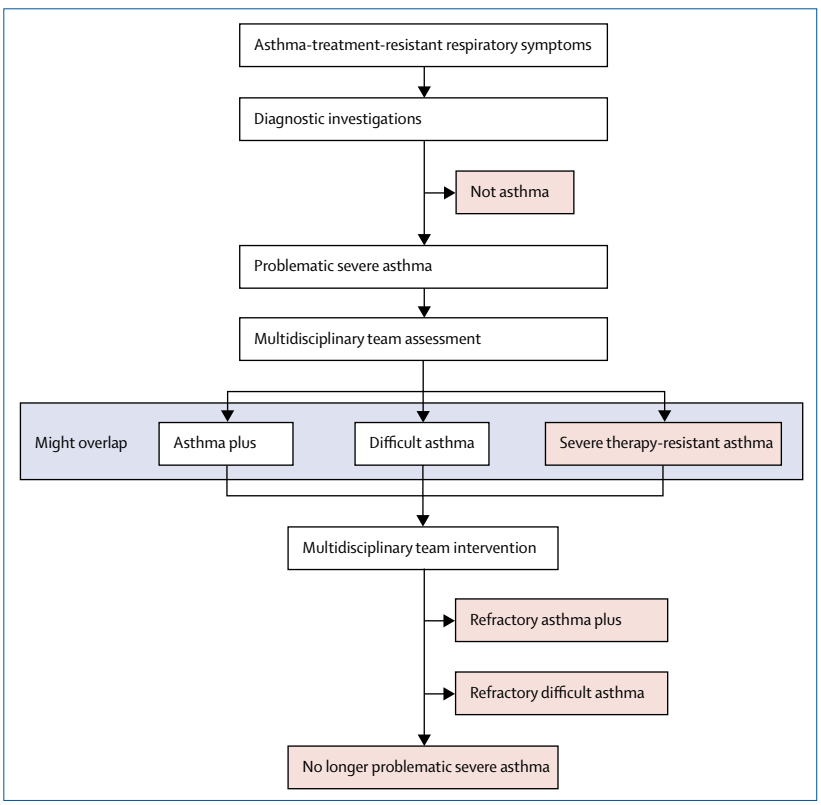

Figure: **Approach to children with asthma-treatment-resistant respiratory symptoms**

with FeNO and induced sputum. Ongoing psychosocial morbidity also might lead to refractory difficult asthma, and psychological, even psychiatric, support might be indicated.

Refractory asthma plus, which remains an issue, often means obesity-associated asthma. Weight loss, including bariatric surgery, is the best option,[14] but if that is not successful then the airway phenotype needs to be determined and appropriate medication prescribed. Specifically, if the symptoms are not related to ongoing and uncontrolled eosinophilic airway inflammation, escalation of the dose of inhaled corticosteroids is not justified. Other refractory comorbidities include exercise-induced laryngeal obstruction, for which surgery can be beneficial,[15] and rhinosinusitis.

The updated scheme is summarised in the figure, which highlights five categories into which a child referred with asthma-treatment-resistant symptoms might be placed. It acknowledges that severe asthma consists of more than just severe therapy-resistant asthma, and emphasises the National Review of Asthma Deaths' finding that many patients who have died of asthma indeed did not have severe therapy-resistant asthma.[10] Although research into mechanisms of severe asthma will not change with this update, hopefully it will usefully inform clinical practice in this challenging field.

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Aiming for zero tuberculosis transmission in low-burden countries

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The End TB Strategy, approved by the World Health Assembly in May 2014, proposes ambitious targets to reduce the global burden of tuberculosis (TB).[1] The strategy calls for all governments to show high-level political commitment, including those of high-income countries with a low burden of disease. The framework for TB elimination in low-incidence countries, launched at the World TB Conference in 2015, challenged low-burden countries to aim for TB elimination (defined as <1 incident case of TB per million population) by 2035 or earlier.[2] In low-incidence settings, most cases of TB occur among foreign-born individuals; thus, to achieve a substantial reduction in case numbers, meticulous premigration screening and an emphasis on the identification of active cases among often hard-to-reach populations, with treatment of both active and latent TB infection, is necessary.[3] Consideration will need to be given to risk–benefit analyses and the cost-effectiveness of these approaches, which might not always be feasible or ethically acceptable.

Despite these efforts, it seems unlikely that low-incidence countries will achieve TB elimination