Two pathways, one patient; UK asthma guidelines

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The first widely disseminated 'asthma guideline' came out of Australia and New Zealand in 1989,[1] followed shortly by the British Thoracic Society (BTS) in 1990,[2] the United States National Heart, Lung, and Blood Institute Expert Panel Report in 1991[3] and the Global Initiative for Asthma (GINA) strategy document in 1995.[4] All have benefited from regular updates, the BTS collaborating with the Scottish Intercollegiate Guideline Network (SIGN) since 2003, most recently in 2016.[5] Each new iteration of the asthma guidelines was written by experts in the field and based on best available evidence. It is not known whether these guidelines (or any others) have improved the care of people with asthma; asthma prevalence has continued to rise (although it may now have plateaued), and deaths overall have not fallen, although this statistic is driven entirely by an ageing population, as deaths in England from asthma in the young have in fact dropped dramatically.[6] It is likely, however, that guidelines have reduced variation in diagnosis and treatment of this complex disease.

In 2013, the National Institute for Health and Clinical Excellence (NICE) joined the guideline party, with a new approach that included consideration of health economics as well as clinical effectiveness. Their rationale included concerns that deaths were not falling, drug costs were rising and over-diagnosis and under-diagnosis still a significant issue. While the strength of evidence for each of these points varies (drug costs are rising across all areas of medicine, and over-diagnosis rates of 30% have been demonstrated repeatedly, even in recently diagnosed individuals[7]), all healthcare professionals involved in the care of people with asthma would recognise that each of these issues do need careful consideration. However, what had not been established was whether these failures were due to the inadequacy of existing guidelines. If this were the hypothesis, then surely the rational approach would be to test current guidelines against a new proposed standard before development of the NICE guidelines? This has not happened; NICE have now published their guidance,[8] after three consultation periods and a feasibility study, and people with asthma and the healthcare community have no idea whether the new guidance performs better or is easier to implement than the BTS/SIGN version. This would not be important if the general messages in the NICE guidance were similar to those already proposed. They are not. Recently, White and colleagues (in *Thorax*),[9] the Primary Care Respiratory Society[10] and many others[11 12] have pointed out they give advice that is diametrically opposed to the BTS/SIGN guidance in many key areas.

For diagnosis, NICE insist that clinical history must be supported by objective testing, whereas BTS/SIGN support the clinical judgement of the doctor. In this, NICE are much more closely aligned to GINA, with the BTS/SIGN out of step with most national and international guidelines. Asthma is a disease defined by characteristic physiology, and as we know that the link between variable airflow obstruction and symptoms is minimal, relying on the diagnostic power of The Physician in isolation seems a curious approach. While we agree strongly that the diagnosis must be supported by objective testing, we find it harder to justify the emphasis NICE have placed on the measurement of exhaled nitric oxide (FeNO) in the diagnostic algorithm, with a proposed flat cut-off of 40 ppb (35 ppb for children); data from healthy (non-asthmatic) volunteers in Sweden suggest that the upper limit of normal (ULN) ranges from 30 ppb for a 30-year-old woman to 51 ppb for a 65-year-old man, with further adjustments required for atopy (atopic individuals having an ULN about 13 ppb higher than non-atopic) and smoking (current smokers ULN about 5 ppb lower than non-smokers).[13] The consequences of relying on an unadjusted cut-off in an untested algorithm are of course, unknown.

The BTS/SIGN diagnostic algorithm likewise does not make complete sense; the only route to a diagnosis of asthma, regardless of whether there was a high or intermediate clinical probability (in the opinion of The Physician), is via a positive response (which can be determined entirely on the basis of symptoms) to steroids. The potential for false negatives (through insensitive markers of response or through lack of adherence) and false positives (through placebo effect or natural variation in symptoms) is not considered, nor is the fact that not all asthma is responsive to low-dose inhaled corticosteroids, and not all steroid-responsive airway disease is asthma.

The truth probably lies somewhere between. Asthma is a clinical diagnosis, triggered by typical symptoms and supported by the demonstration of a variable and (partially) reversible airflow obstruction. However, the measurement of lung function and airway responsiveness in primary care is difficult, and FeNO is not useful for ruling in or ruling out a diagnosis of asthma. The determination of steroid responsiveness (along with other disease characteristics, treatable traits or phenotypes) should follow from that.

More contrasting guidance is given for management. NICE recommend that inhaled bronchodilators alone should be used first line, ignoring their own insistence that asthma diagnosis should be supported by evidence of airway inflammation and steroid responsiveness, via a raised FeNO—a true paradox.[14] BTS/SIGN have recently moved to recommending inhaled corticosteroids (ICS) as first line, possibly guided by the realisation that in many asthma deaths, over-reliance on short-acting bronchodilators and underuse of ICS play a significant role.[15 16] In the absence of good evidence to support either, the expert advisors on the committees (some of whom sat on both) have come to opposite conclusions.

The biggest controversy surrounds initial add-on therapy. NICE have recommended montelukast rather than addition of a long-acting beta-2 agonist (LABA), on the basis of significantly reduced cost, offset by a relatively small reduction in mean benefit. The implications of this change in a clinical environment, where combination ICS/LABA therapy has been the mainstay of management steps 3–5 for 15 years, have not

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been considered. An important benefit of ICS/LABA therapy over montelukast is the reduction of the risk of severe asthma exacerbations. Adherence to tablets for asthma may well be greater than for inhalers, so does this mean that patients may preferentially choose the tablet over the inhaled steroid? What is the likelihood that patients will take two different drugs that have no immediate efficacy feedback? Finally, two prescription fees will be paid by many, in contrast to those prescribed fixed ICS/LABA combinations.

Lastly, while both guidelines cover diagnosis and chronic disease pharmacotherapy, BTS/SIGN (like GINA) are far more comprehensive and include guidance on acute asthma, asthma in pregnancy and transitional care, among many other aspects.

NICE acknowledge the practical impossibility of fully implementing their guidance at this time: "…primary care services should implement what they can of the recommendations, using currently available approaches to diagnosis until the infrastructure for objective testing is in place", which makes us wonder why they have persevered with publishing them, rather than focusing their efforts on providing evidence to support this infrastructure. Although we recognise and support the need to scrutinise and renew guidelines regularly in the light of new evidence, having two sets of guidelines will only lead to confusion, worse outcomes and potentially higher cost.

Asthma management is already complicated and there are now more treatment options than ever before. What is required is not varying and contradictory guidance, but testing of both the evidence for and implementation of current guidelines, before changes can be recommended, in a joint effort that would catapult the UK to the global forefront of asthma healthcare research. Why BTS/SIGN and NICE have not decided that the best way forward for people with this life-threatening chronic disease is to work together (imagine the uproar if we had two sets of UK resuscitation guidelines) is unclear. This is must happen, and quickly, in the interests of patient safety.

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