**If it’s “only” asthma, why are children still dying?**

Carroll WD1, Clayton S1, Frost S2, Gupta A3, Holmes S4, Nagakumar P2, Levy M5.

**Affiliations:**

1. Department of Respiratory Paediatrics, University Hospital of the North Midlands, Stoke-on-Trent, ST4 6QG, UK.

2. Department of Paediatric Respiratory Medicine and Cystic Fibrosis, Birmingham Women's and Children's Hospital, Birmingham, UK.

3. Department of Paediatric Respiratory Medicine, King’s College Hospital, Denmark Hill, London SE5 9RS, UK.

4. General Practitioner, Cannards Grave Road, Shepton Mallet, Somerset, UK.

5. Sessional General Practitioner, London, UK; Clinical Lead for the UK National Review of Asthma Deaths (2011-2014) ; Executive Board Member Global Initiative on Asthma (GINA).

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**Abbreviations:** ACQ: asthma control questionnaire, ACT: asthma control test, ATS: American Thoracic Society, BDP: beclomethasone dipropionate, BTS: British Thoracic Society, c-ACT: childhood asthma control test, CYP: children and young people, ERS: European Respiratory Society, FeNO: Fractional excretion of nitric oxide, GINA: Global Initiative for Asthma, ICS: inhaled corticosteroid, LABA: long-acting beta-2 agonist, LTRA: leukotriene receptor antagonist, OCS: oral corticosteroids, SABA: short-acting beta-2 agonist, SIGN: Scottish Intercollegiate Guidelines Network.

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Dr Will Carroll reports personal fees for lecturing and advisory board work from GlaxoSmithKline, Trudell Medical International, Orion Medical and Novartis Pharmaceuticals.

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Mrs Sue Frost has received funding from Novartis and is co-treasurer of the Severe Asthma Nurses Network which organizes conferences for professional development.

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Dr Steve Holmes works as a GP, he is funded for 1/2 session per week as a clinical commissioner, has received funding from Astra Zeneca, Beximco, Boehringer Ingelheim, Chiesi, Glaxo Smith Kline, Johnson and Johnson, Mylan, Napp, Novartis, Nutricia, Orion, Pfizer, Sandoz, Teva and Trudell Medical International.

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**What is known about this subject**

The UK has the highest rate of asthma deaths for children and young people aged 10-24 years in Europe.

A confidential review of asthma deaths in 2014 identified avoidable factors in almost all cases involving children and young people.

Asthma outcomes are better in adults and children who have specialist care.

**What this paper adds**

This commentary summarizes the advice from available national and international asthma guidelines highlighting where evidence exists.

It describes how self-reported thresholds for referral in primary and secondary care deviate from existing guidelines.

It describes the potential benefits of referring high risk children for specialist care.

In 2014 the National Review of Asthma Deaths (NRAD) carefully reviewed the care that had been received by individuals in the UK who had died from asthma. It highlighted the need for improvements, particularly in the care of children and young people aged 0-19 years (CYP) with asthma. The review concluded that there were potentially avoidable factors in 27 out of 28 of the cases involving CYP for whom records were available.1 Worryingly, despite NRAD being a confidential enquiry, the records for a further 8 CYP who died from asthma in the year of the study were not returned by their doctors.2

NRAD also highlighted an apparent complacency in the care of young people with asthma. Poor recognition of the risk status was found to be an important avoidable factor in 78% (22/28) of and in almost a third (5/16) of the CYP in primary and secondary care respectively.1

In summarizing the NRAD findings five years later, Asthma UK highlighted the ongoing poor quality of care for children with asthma in the UK. Aspects of care were well below the expected standard for about a quarter of the cases reviewed and almost half of CYP.3 This report should have been a ‘wake-up call’ to everyone caring for CYP with asthma in the UK. However, preventable asthma deaths in CYP have continued unabated and this has led to calls for national action to fully implement the NRAD recommendations.4,5

The recently published (2019) Nuffield Report found that the UK still has the highest asthma mortality rate among young people aged 10-24 in the European countries included in the comparison. The asthma mortality rate for the UK was approximately twice as high as that of the next worst European country.6 This is despite access to numerous evidence-based guidelines and treatment options.7,8

**Why are we letting children down so badly?**

Several factors could account for these poor outcomes. These include a significant variability in the quality of healthcare provided,1 failure to recognize risk of poor outcome or to implement guidelines. Recent coronial reviews have also identified a lack of continuity of care with failure of one person taking overall responsibility for CYP with severe or difficult to treat asthma with some children and young people suffering from a lack of basic care provision,3 coupled with a poor understanding of symptoms by CYP, parents and healthcare providers.9,10 Three separate Coroner’s Regulation 28 notices concerning asthma deaths in CYP have been issued in the last 4 years.11

Not all asthma is the same. Although deaths from asthma in CYP were seen across all asthma severities, it was most common in those with severe asthma with more than half (58%) of deaths in CYP occurring in this group.2 Whilst population estimates vary severe asthma is likely to occur in 5% or less of CYP with asthma.12-14 Studies show that subspecialist care is associated with improved outcomes15 for CYP with asthma. However, the observational evidence from NRAD and population studies show that a significant proportion of CYP with persistent poor control are not referred onwards, with barriers existing between primary, secondary and tertiary care.1,16 There is now a body of evidence summarized in the new GINA strategy document that individuals with ‘so called’ mild asthma are also at risk of poor outcomes. This is largely due to the adverse effects of regular use of SABAs and insufficient prescription of or adherence to inhaled corticosteroids which has resulted in fundamental changes to the international recommendations for the treatment of asthma.6,17

**What is severe asthma?**

Part of the problem that exists is that there is variation in the definition of severe asthma which is currently defined retrospectively based on the amount of treatment required to maintain control (see Box 1).7,18

CYP with poor symptom control despite being prescribed high dose asthma medication do not always have severe asthma. Some have alternate diagnoses and others will have modifiable factors such as nonadherence. These individuals have difficult asthma.7,18 Difficult asthma is at least twice as common as severe asthma.12

Whilst severe asthma currently accounts for up to 50% of asthma-related health care costs19 the treatment landscape for CYP with severe asthma is changing as newer drugs become available.14

**It is not just adults who are slipping through the net**

A recent interview study involving 219 healthcare professionals in the UK revealed that referral thresholds for CYP with asthma remain high.20 The results of self-reported referral thresholds for participants in primary (n=79) and non-subspecialist secondary care clinicians (n=47) are summarized in Table 1. The results are remarkably similar to those seen in the recent asthma UK report ‘Slipping through the net’ which described the experience of healthcare professionals working in adult asthma services.21 Primary care health care professionals (GPs and asthma nurses) report referring on to secondary care clinics (general paediatricians) when CYP with asthma have received a median of 3 courses of oral steroids, or had 2 A&E attendances or when a CYP has had 21 days off school in a year. Once in secondary care and under the care of a general paediatrician the referral thresholds to tertiary services (specialist difficult asthma clinics) are even higher; with children needing to have a median of 4 asthma attacks, 4 courses of oral steroids, 3 A&E attendances or hospital admissions, or more than 30 days off school in a single year before being referred. Moreover, a significant proportion of generalists reported uncertainty about what the referral threshold should be. An inquest in the matter of the preventable asthma death of a 10 year old girl heard that despite having 48 attacks, including 10 with life threatening features, she was never referred to a respiratory paediatrician.11

More than half of GPs and almost three-quarters of general paediatricians who answered self-reported adopting a higher threshold than the recommendations of NRAD which suggested specialist review if there had been three or more courses of oral steroids, two or more visits to accident and emergency or an admission to hospital.1

A delayed specialist referral pathway is not simply putting CYP with severe asthma at increased risk. Caring for people who experience an asthma attack costs over 3.5 times more than for those whose asthma is well managed, and the estimated annual cost of treating a child with asthma is higher than the cost for an adult. In 2007-08, 38% of emergency admissions for asthma were children aged under 15 and admissions per head of population were over twice as high for children as for adults.22 Most importantly, many newer treatments are only available to children who are seen in specialist clinics.23

Children, parents and healthcare providers seem to be willing to accept this situation, consistently reporting suboptimal control in population studies.9,24,25 It is disappointing that, despite access to high quality asthma guidelines, education and treatments, children’s asthma care remains so poor in the UK.6

**What can we do about it?**

The evidence suggests that we should adopt a zero tolerance approach to exacerbations, which are arguably best described as asthma attacks. Asthma attacks are not acceptable or “to be expected”. They are a signal that something serious has gone wrong and should always be followed up and investigated.1 A recent large population survey using general practice records showed that less than 6% of UK children aged 12-17 years has an asthma attack in a 12 month period.26 Subsequent assessment in primary or secondary care should include a careful review of treatment (particularly excess SABA and insufficient ICS prescriptions), inhaler technique, adherence, asthma control and lung function (in those old enough to perform it).1,7,8 CYP who are then found to have difficult to treat or severe asthma (see Box 1) should be referred to a subspecialist or severe asthma service.1,7,18 The available national and international guidelines all have slightly different definitions of what constitutes severe asthma in CYP, however all agree that severe asthma only exists when there is a confirmed diagnosis of asthma and the symptoms or attacks persist despite optimized treatment (see Box 1 for the definition used by the two paediatric asthma centres in the Midlands).

**How should severe asthma be managed in children and young people?**

CYP with poor asthma control are at increased risk for asthma attacks and death, 1,27 and if severe may be eligible for treatment with newer biological agents. In many cases, asthma control can be improved by addressing adherence issues, by increasing the treatment offered or reducing exposure to triggers.8 This can be done in any setting but requires training, time and tenacity. Recent international guidance stresses the importance of referral to specialist care in individuals who continue to have asthma attacks or whose asthma symptoms persist despite higher treatment levels (see Box 2).7

In the UK, the definition of an asthma specialist is rather blurred. In some centres, this role has been fulfilled by general paediatricians with an interest in respiratory disease. Many referrals from primary care to a paediatric department will assume the patient has been picked up by a paediatrician with a more specialist interest. However, only a small proportion of paediatricians have access to the full range of multidisciplinary expertise, investigations and treatments that are required to both diagnose and treat severe asthma. This includes access to dedicated asthma nurses, adherence monitors e.g. Smarthaler® devices or similar, lung function testing including spirometry and fractional exhaled nitric oxide measures, flexible bronchoscopy, cardiopulmonary exercise testing, specialised imaging as well as having an understanding of and access to newer biologic agents. The GINA 2019 booklet on severe and difficult to treat asthma provides guidance at all levels of care for diagnosing and managing these individuals.6 The ability of the asthma nurse specialist to perform a home visit is also considered vital28 (see Box 3) as is access to a dedicated multi-disciplinary team.

**Learning from recent experience in adults with severe asthma**

There is strong emerging evidence that adults with severe asthma do better when seen and assessed in severe asthma centres. In the Netherlands, a single day review has been shown to have a long-term impact on asthma control, quality of life and healthcare utilization.29 The emergence of newer technologies for measuring adherence and the advent of biological therapies for those who remain poorly controlled have been incorporated into the new NHS England guidance for adult asthma services.23,30 Adults with severe asthma now benefit from the expertise of severe asthma centres.30,31 These have been developed using a ‘hub and spoke’ model, with care being coordinated from a central hub. This has significantly improved access to specialist support and to emerging and novel therapeutics for adults with severe asthma. National data are not available, however in the North West alone, the adult severe asthma hub has recommended initiation of biologics in 790 adults with severe asthma between 2015-8 which are now licensed for use in children.14 Without changes in behaviour from primary and secondary care, CYP with asthma will be denied the same opportunities.

**Suggested referral pathway**

Whilst one size will never fit all, pathways for referral have been developed for use in the UK. An example of one is given in Figure 1 (below). This can be used to guide referrals. Nonetheless, there may be circumstances where referral is merited ‘off pathway’ before all criteria are fulfilled, for instance when diagnostic doubt exists and/or when there have been life-threatening events such as paediatric intensive care admission.

**Advice for referring teams**

When referring to a specialist multidisciplinary team it is useful to include as much information about the child and any test results or treatments they may have received as possible. This can include date of confirmed asthma diagnosis, confirmation of adherence and inhaler technique checks, current treatments and doses, copies from records of all asthma prescriptions issued in the previous 12 months, results from any tests performed e.g. lung function (spirometry, best annual PEFR, FeNO), skin prick or serum eosinophil count, any social/safeguarding concerns (such as not being brought for review in practice or hospital) or family history that should be taken into consideration and any comorbidities that are present. It could also involve relevant historic medication prescribed print outs, previous hospital admission and A&E correspondence, and information relating to family and carer belief systems relating to asthma and the medications used.

**Conclusion**

The Nuffield report has provided us with a stark reminder, five years after NRAD, that the UK still has much more to do to improve the care of children and young people with severe asthma. All too often asthma attacks in children are treated as isolated acute incidents by a variety of different healthcare professionals in different settings including paediatric emergency departments and out of hours services. Referral to specialist multidisciplinary care recognizes and addresses the chronic nature of the disease and ensures the consistency of care that these children deserve.

Conflicting guidelines and a lack of clear referral pathways for CYP with severe asthma mean we are destined to repeat our failures. These result in significant delays in referral which must be overcome if we are to tackle the poor outcomes seen for UK children with asthma.

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**Table 1:** Self-reported thresholds for referral onwards of healthcare professionals (all values reported as medians (interquartile range))

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Number in year before referral? | Exacerbations | Courses or oral steroids | A&E attendances | Hospital admissions | Days off school |
| Primary care (n=79) | 3 (2) | 3 (2) | 2 (1) | 1 (1) | 15 (12) |
| GPs (n=49) | 4 (2) | 3 (2) | 2 (1) | 2 (1) | 18 (15) |
| ‘Not sure’ [n(%)] | 7 (14%) | 9 (18%) | 7 (14%) | 4 (8%) | 20 (41%) |
| Practice nurses (n=30) | 2 (1) | 3 (1) | 2 (1) | 1 (1) | 15 (12) |
| ‘Not sure’ [n(%)] | 4 (13%) | 3 (10%) | 2 (7%) | 3 (10%) | 10 (38%) |
| General paediatricians (n=47) | 4 (1) | 4 (1) | 3 (1) | 3 (2) | 30 (21) |
| ‘Not sure’ [n(%)] | 9 (19%) | 8 (17%) | 14 (30%) | 9 (19%) | 18 (38%) |

**Box 1: Working definition of severe asthma in children and young adults\***

**Confirmed asthma diagnosis with:**

**Optimised treatment**

* Higher dose ICS (≥ 800mcg BDP equivalent daily for children 6-12 years, ≥ 1600mcg BDP equivalent daily for children > 12 years)
* ± LABA, ± LTRA (if appropriate)
* Adherence and inhaler technique checked and verified

**AND**

**Uncontrolled symptoms**

* Assessed using c-ACT (children 4-11) and ACT (children ≥12). ACQ or similar could also be used

**OR**

**Asthma attacks**

* ≥ 2 courses of OCS for 3 or more days in the last 12 months
* Any hospital admission for asthma attack in the last 12 months
* Any previous ICU admission or mechanical ventilation ever

\*Definition based upon combination of GINA guidelines 2019, SIGN/BTS guidelines 2019 for treatment of asthma and international ERS/ATS guidelines on definition, evaluation and treatment of severe asthma 2014.

**Box 2: When to refer to specialist care (red flags for referral)\*\***

\*\*Definition based upon GINA guidelines 2019 and SIGN/BTS 2019 guidelines for treatment of asthma

**Any child presenting to secondary care with a diagnosis of severe or difficult-to-treat asthma or who has:**

* Had ≥ 2 courses of OCS for 3 or more days in the last 12 months

**OR**

* Had more than 1 hospital admission (inpatient or A&E) in the last 12 months

**OR**

* Ever had a PICU admission requiring ventilatory support (mechanical/non-invasive)

**OR**

* Persistent poor control or unclear diagnosis for ≥ 3 months

**OR**

* Has a requirement for long-term (≥ 1 month) OCS maintenance therapy

**OR**

* Has other factors that increase the risk of death from asthma e.g.
* IgE mediated food allergy anaphylaxis
* Heavy use of SABA (≥ 1 canister/200 doses per month)
* Adverse behavioural or psychosocial factors

**Box 3:** Proposed requirements for CYP severe asthma service

**A specialist multidisciplinary paediatric asthma service that has:**

* At least 2 respiratory paediatricians with specific asthma training and expertise
* Asthma nurse specialist(s)

And direct access to other specialty services, such as:

* Flexible bronchoscopy
* Lung function lab with certified spirometry specialists
* Lung physiology
* Physiotherapy
* Pharmacist
* Clinical Psychologist
* Mental health services
* Social worker/safe guarding lead
* ENT
* Speech and language therapy