Management of difficult-to-treat asthma in adolescence and young adults

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Managing a heterogeneous and chronic disease like asthma in young people can be challenging. Early multidisciplinary management and effective transition of young people with difficult-to-treat asthma from paediatric to adult services is important. https://bit.ly/3h67VgS

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Abstract

The period of adolescence and young adulthood (AYA) has been proposed to extend from 11 to 25 years of age as patients in this age group face similar challenges. AYA is a time of fast and great physiological and psychological growth, in which an individual transitions from a young dependent child to a mature independent adult. Behaviour patterns during adolescence, such as risk taking and desire for privacy, can challenge parents or healthcare professionals' (HCPs') ability to help adolescents to manage their asthma.

Asthma itself tends to remit, become milder or worsen into a severe variant during adolescence. The pre-pubertal male predominance of asthma switches to a female predominance in late teen years. ∼10% of AYA with asthma have "difficult-to-treat asthma (DTA)", characterised by poor asthma control despite treatment with inhaled corticosteroids (ICS) and other controller medications. DTA management in AYA requires a multidisciplinary team approach and systematic assessment that can address the key questions of objective confirmation of diagnosis, severity assessment, phenotyping, comorbidities, asthma mimickers or other drivers of poor control such as non-adherence to treatment.

A key task for HCPs is to establish the magnitude of the severe asthma component *versus* other non-asthma drivers of symptoms (*e.g.* inducible laryngeal obstruction or breathing pattern disorder). Severe asthma is a subset of DTA and is determined once asthma diagnosis and its severity have been confirmed and adherence to controller (ICS) treatment has been assured. Severe asthma is a heterogeneous disease and appropriate phenotyping is necessary for the management of treatable traits and consideration for biologic therapies.

Finally, an important part of successful management of DTA in the AYA group is the provision of an effective transition of asthma care from paediatric to adult asthma services through setting up a well-designed asthma transition pathway tailored to the individual patient needs.

Educational aims

- To understand the challenges and complexity of managing young people with difficult-to-treat asthma.
- To outline the systematic approach for management of young people with difficult-to-treat asthma.
- To discuss the importance of a robust transition programme for safe and effective care of young people in adult asthma services.

Definitions

The Global Initiative for Asthma (GINA) [1] defines uncontrolled asthma as the presence of poor symptom control and/or asthma exacerbations leading to use of oral corticosteroids (OCS) twice or more per year or one or more hospital admissions per year for severe asthma attacks. Difficult-to-treat asthma (DTA)

represents ~17% of all asthmatic patients [2], who have uncontrolled asthma despite treatment with medium-to-high dose inhaled corticosteroids (ICS) in combination with a second controller (in keeping with treatment at steps 4–5 of the GINA guidelines). Multiple modifiable factors often drive poor control in DTA patients, which include wrong diagnosis (treating the wrong disease), presence of asthma mimickers, comorbidities, and suboptimal treatment or non-adherence to ICS treatment. Severe asthma, which affects <5% of all asthmatic patients [3, 4], is a subset of uncontrolled asthma in which asthma remains poorly controlled despite management of modifiable factors or becomes uncontrolled after a step down of treatment to below step 4 of the GINA guidelines (figure 1) [1].

Natural history of asthma in adolescence and young adulthood

During adolescence, a child goes through significant physiological and psychological changes that impact on asthma prevalence, control and severity. The adolescence and young adulthood (AYA) age group (age 11–25 years) share similar challenges and require a similar health approach to manage chronic diseases such as bronchial asthma.

Asthma in adolescence is common and has been reported to afflict up to one in 7–12 people [5]. Risk of asthma morbidity including mortality in AYA is high. A review of asthma deaths in Australia demonstrated an increase in deaths in children up to the age of 17 years. Low socioeconomic status, poor follow-up care, poor adherence, lack of a personalised asthma action plan and tobacco smoking were identified to increase the risk of asthma deaths in this population [6]. However, in Finland the implementation of an integrated asthma programme improved asthma outcomes and reduced morbidity and mortality across all age groups including AYA [7], demonstrating that asthma outcomes can be improved if the correct approach is used.

Asthma can remit, or change to a mild or severe form during adolescence. Causes of remission or worsening of asthma in adolescence are not fully established. Reported predictors of asthma remission in adolescence include pre-pubertal mild disease, minor airway inflammation, absence of allergic sensitisation and male gender. Conversely, heredity, expression of high type 2 inflammation such as blood eosinophils, atopy, low lung function, smoking and pre-pubertal presence of severe asthma were all reported to predict asthma persistence and severity [8, 9]. Causes of the post-pubertal switch of asthma from male to female predominance are not known. Females are also more susceptible to develop severe asthma in their later teens. Genetics, sex hormones, pregnancy, immune responses and mechanical factors, such as airway size and lung growth, were all proposed to relate to the gender disparity of asthma prevalence in AYA [10]. In addition, obesity, environmental pollution and tobacco smoke exposure were reported to reduce responsiveness to ICS and accelerate loss of lung function and asthma severity [11].

Severe asthma is probably less common in children than adults, with a reported prevalence of 5% of all asthma at the age of 10 years [5, 12]. Despite this it disproportionately accounts for 60% of all asthma-related health cost, which is attributed to the disease and costs related to side-effects from excessive corticosteroids exposure [13].

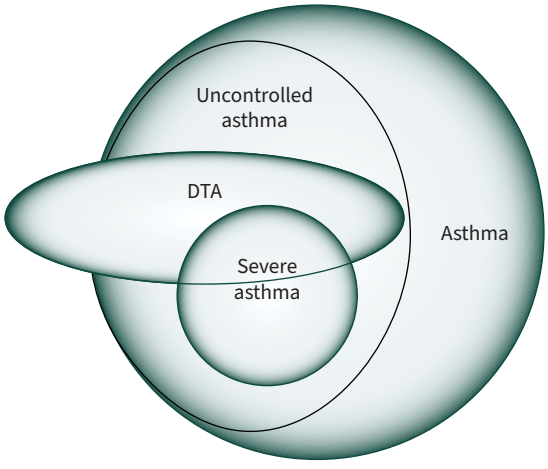


FIGURE 1 Asthma severity model. Uncontrolled asthma is often due to a lack of baseline treatment, but a minority will continue to have poor control despite treatment at steps 4–5 of the GINA guidelines and are labelled as difficult-to-treat asthma (DTA). A subset of DTA have severe asthma.

Psychological factors and asthma in AYA

During adolescence, the growing child will be seeking independence and builds relationship with their friends and peers whilst aiming to keep harmony with their family. Adolescents prefer learning from direct experience, respond to rewards, and are probably more tolerant to ambiguity and to adopting risk-taking behaviour [14]. Key life drivers during the adolescence include academic and sporting performance and forming relationships, which all can increase risk of stress, anxiety, depression, or other mental health issues [15]. Marijuana, alcohol and other illicit drug use can also confound mental health during AYA. Teenagers may deny illness leading to under diagnosis and treatment, or overexpress symptoms leading to over diagnosis and treatment. In the latter group, patient symptoms will be discordant to objective measures of asthma such as lung function. The potential detrimental impact of social media on young people's mental health has been well described [16].

Diagnostic algorithm for DTA in AYA

Asthma in adolescence is both under- and over-diagnosed and is associated with erratic adherence and poor self-management [17, 18]. The complexity of factors driving DTA in AYA warrants the adoption of a systematic approach for its assessment and management. This will be comprised of obtaining a focused and detailed history, physical examination and conduction of investigations for objective asthma diagnosis confirmation, as well as identification of triggers and co-morbidities and establishing drivers of poor control such as treatment non-adherence.

Systematic assessment of DTA in AYA

Structured history and examination

A focused and structured history followed by physical examination is vital for the assessment of DTA. The use of a purposely designed proforma can improve the efficiency of clinic review. Predesigned assessment proforma (table 1) could be completed electronically or on paper by the patient/parent prior to a clinic visit and made available to the healthcare professional (HCP) to form the basis of the clinic consultation.

Investigations

A stepwise investigations algorithm is needed to conduct the series of tests required to objectively assess asthma diagnosis, determine phenotype, severity, control and quality of life (table 2).

The high prevalence of non-adherence to treatment in DTA (~40–50%) mandates objective measurement of adherence [19, 20]. Reliance on patient accounts or HCPs impression were shown to be inaccurate [21], thus prompting the need for objective measures of adherence. Available tools to measure adherence include counting of prescription pick-up rate or prescription possession ratio, and use of dose counting chips attached to inhaler devices [22]. The presence of a high fraction of exhaled nitric oxide (F_{ENO}) despite treatment with high-dose ICS is often seen as a marker of non-adherence, which prompted the development of the F_{ENO} suppression test that measures the magnitude of F_{ENO} suppression following direct or virtual observation of ICS dosing (figure 2) [23]. Adherence to maintenance oral prednisolone/prednisone can be measured using a validated liquid chromatography–tandem mass spectrometry assay that can simultaneously measure prednisolone and cortisol. Adherent patients are expected to have detectable prednisolone and suppressed cortisol levels using spot testing [24]. AYA attitudes towards treatment adherence can also be evaluated using validated questionnaires which could facilitate initiation of a discussion to improve adherence [25].

Diagnostic outcomes and design of a management plan

The systematic assessment will lead to a series of outcomes related to asthma diagnosis confirmation, asthma control, severity, phenotyping, comorbidities and asthma mimickers. Particular consideration should be made to conditions that tend to be common in the AYA age group, such as anxiety, depression, exercise-induced dyspnoea (EID), breathing pattern disorders and hyperventilation syndromes, inducible laryngeal obstruction (ILO), underlying cardiac disease, congenital malformation and psychogenic cough [26]. Often talking to young people on their own may help the team in understanding their overall health needs. Multidisciplinary team discussion and an action plan will then need to be formulated to prioritise required steps of management and produce short- and long-term goals. Most AYA asthma patients should lead a normal life including fulfilling their academic and vocational aspirations whilst achieving good asthma control, which often means getting the basics right rather than reliance on expensive treatments. Unsuccessful DTA treatment in AYA is often due to failed medical care rather than due to patient-related factors.

Asthma treatment

Treatment of asthma in AYA would follow local, national and global guidelines, such as GINA [1]. Asthma guidelines are based on a step-wise treatment approach commencing from use of low-dose ICS

TABLE 1 Focused history and examination of a young person with difficult asthma

History or examination domain	Questions to elucidate asthma severity, phenotype and comorbidities
Age and mode of onset	Age of symptoms and asthma onset, any relation to puberty
Symptoms pattern	Dyspnoea pattern (episodic *versus* constant), presence and phase of wheeze (inspiratory/expiratory), cough, sputum production and colour, propensity for LRTI
Allergies and triggers	Rhinitis, hay fever, atopic dermatitis, food and aeroallergies, nonspecific triggers (*e.g.* strong smells, changing temperature), aspirin intolerance, perimenstrual exacerbation
Asthma control and severity measures	Frequency of OCS and antibiotic use, SABA use (inhaled or nebulised), emergency room visits, hospitalisation, high dependency and intensive care unit admission, and intubation history
Upper airways symptoms	History of rhinitis, polyps, blocked nose, post-nasal drip, and any features of ILO (*e.g.* throat level symptoms, sensation of strangulation, breathing through a straw, or difficulty to breathe in)
Breathing pattern disorder	Features of hyperventilation syndrome such as air hunger, perioral and extremities paraesthesia during attacks, constant dyspnoea, disproportionate level of exercise limitation
Past medical history	Obesity, sleep apnoea, metabolic syndrome, cardiac disease, congenital anomalies, *etc.*
Psychological factors	Childhood traumatic experience, schooling difficulties, panic, anxiety, depression, personality traits, home and family factors
Personal and social history	Home, number of people at home, indoor pollution (pets, moulds, dust), outdoor pollution, smoking (passive/active), alcohol and illicit drug use
School and occupational history	Schooling and sport performance and attendance, triggers at school or work
Physical examination	Height, weight, BMI, nose and throat assessment, breath sounds, presence of wheeze (polyphonic and variable *versus* monophonic and fixed), breathing pattern such as apical breathing, stigmata of other diseases including skin and any OCS-related side-effects

LRTI: lower respiratory tract infection; SABA: short acting β_2-agonist; OCS: oral corticosteroids; BMI: body mass index; ILO: inducible laryngeal obstruction.

TABLE 2 Investigations to be considered in a young person with difficult-to-treat asthma

Investigation	Specification and description
Asthma control and quality of life quantification	ACQ, AQLQ, HADS
Allergy tests	Specific IgE, total IgE, aeroallergen- and food-specific IgE, skin prick testing (guided by history)
Type 2 asthma biomarkers	F_{ENO}, blood eosinophils, sputum eosinophils
Screening for other diseases including metabolic screen	Connective disease screen, vasculitis, immunoglobulins, functional antibodies[#], vitamin D, cortisol assay, HbA1c, lipid profile
Lung function	Full set, loops, gas transfer, reversibility, peak flow records, bronchial provocation testing
Radiology	Chest radiography, bone density scan CT-scan of thorax (dynamic inspiratory and expiratory and lung parenchyma high-resolution scan) in cases of diagnostic uncertainty and suspicion of EDAC or TBM
CPET and nasendoscopy	CPET for unexplained breathlessness and BPD Nasendoscopy for suspected ILO
Bronchoscopy	Upper airway, TBM and EDAC, airway disease, BAL, biopsies

ACQ: Asthma Control Questionnaire; AQLQ: Asthma Quality Of Life Questionnaire; HADS: Hospital Anxiety and Depression Score; F_{ENO}: fraction exhaled nitric oxide; HbA1c: haemoglobin A1C; CT: computed tomography; EDAC: excessive dynamic airway collapse; TBM: tracheobronchomalacia; CPET: cardiopulmonary exercise test; BAL: bronchoalveolar lavage; BPD: breathing pattern disorder; ILO: inducible laryngeal obstruction. [#]: Functional antibodies refer to serum IgG antibodies to *Streptococcus pneumoniae* (pneumococcus) and *Haemophilus influenzae*.

ICS prescription refill count:

$$\text{MPR} = \frac{\text{Number of collected prescriptions in last 12 months}}{\text{Number of prescribed inhalers in last 12 months}} \times 100$$

Illustrative example: the MPR for a patient who collected 7 out of an expected 12 prescriptions=58% (which is under the accepted required adherence target of ≥70% [20])

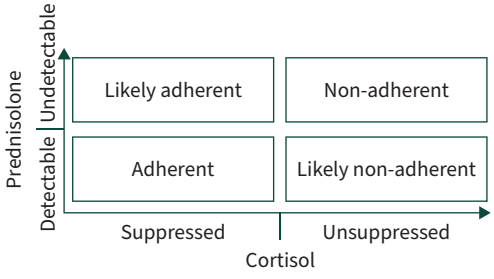
F_{ENO} suppression test: a test developed to measure magnitude of F_{ENO} suppression following observed (direct or virtual) administration of fixed doses of ICS [24].
Illustrative example: an 18-year-old female presented with poorly controlled asthma despite treatment with 1600μg of inhaled budesonide per day. Her F_{ENO} level remains consistently raised. Below is the result of 1 week of administration of an observed dose of 1000 μg of inhaled fluticasone daily

	Day 0	Day 7	Change %
F_{ENO} (ppb)	166	21	–87.4
Blood eosinophils (cells per μL)	650	450	–30.8
ACQ6 (0–6 scale)	2.6	1.2	–53.9

Despite using only 75% of the prescribed dose during the 7 days of the test, a strong suppression of F_{ENO} was observed (87% compared to the accepted cut of 42% that indicates positive suppression and likely non-adherence) alongside improved ACQ and reduced blood eosinophils.

Assessment of prednisolone or prednisone adherence in patients on maintenance treatment

Various studies demonstrated 40–50% non-adherence with maintenance oral prednisolone in patients with difficult-to-treat asthma [20]. Detection of prednisolone non-adherence is important for guiding management as those with confirmed non-adherence should have regular prescribing discontinued in contrast to adherent patients who are at risk of serious side-effects and would be in urgent need of alternative treatment initiation, such as biologic treatment. A spot test of prednisolone adherence has been developed, which relies on the use of liquid chromatography-tandem mass spectrometry to measure prednisolone alongside cortisol. An adherent patient demonstrates cortisol suppression and detectable serum prednisolone [25].



Suppressed cortisol=<100 nmol·L^{-1} [25]

Illustrative example: a patient presented with poorly controlled asthma despite treatment with high-dose ICS and 20 mg per day prednisolone. Her prednisolone/cortisol assay is shown:

	Test 1	Test 2
Prednisolone	<20 nmol·L^{-1}	<20 nmol·L^{-1}
Cortisol	203 nmol·L^{-1}	242 nmol·L^{-1}

This spot test was repeated twice and confirmed presence of unsuppressed cortisol and undetectable prednisolone in keeping with prednisolone non-adherence. Maintenance prednisolone prescribing was discontinued.

FIGURE 2 Methods of assessing adherence to asthma therapies in routine clinical practice. ICS: inhaled corticosteroids; MPR: medication possession ratio; F_{ENO}: fraction exhaled nitric oxide; ACQ: asthma control questionnaire.

and stepping up as guided by asthma control and exacerbation risk to add other controller treatments of leukotriene receptor antagonists, long-acting β_2-agonists (LABA), long-acting antimuscarinic agonists (LAMA) or theophylline. AYA asthma patients are prone to excessive reliance on short-acting β_2-agonist (SABA) relievers with consequent increased risk of poor control, exacerbation and mortality [27].

Patients with severe asthma require treatment at steps 4–5 of the GINA guidelines comprised of a moderate-to-high dose of ICS and other controllers and intermittent or regular use of OCS. Several effective biologic treatment options have become available for severe asthma. Frequent or regular OCS use

TABLE 3 Potential barriers to and proposed facilitators of adherence in adolescence and young adulthood

Adherence barriers	Adherence facilitators
Complex treatment regimen	Simplified treatment regimen: combination inhalers, once daily options
Fear of side-effects, bad taste of ICS	Asthma medicine education, inhaler technique optimisation, oral hygiene, alternative ICS options
Non-intentional, forgetfulness, busy schedule	Developing routines, smart inhalers, audio-visual reminders, mobile/web alerts, electronic monitors and feedback
Embarrassment, denial	Supporting relationships, family or peer-led interventions, CBT[#]
Low self-efficacy	Motivational interviewing
Cognitive difficulty	Literacy assessment[¶], simplified treatment regimen
Negative perception of HCPs	HCP team communication skills and motivational interviewing skills, non-judgemental with the aim to gain patient trust
Financial and social barriers, costs and affordability of treatment	Consideration of domestic and financial factors, treatment supply options, social services input
Maintaining adherence	Short- *versus* long-term adherence strategies, regular review by HCP

ICS: inhaled corticosteroids; HCP: healthcare professional; CBT: cognitive behaviour therapy. [#]: CBT is a psychological approach to change people's beliefs and behaviour; [¶]: health literacy represents the ability of an individual to obtain, read, understand and use healthcare information to make appropriate decisions and treatment plans.

should therefore become a treatment of last resort that should only be initiated under the guidance and monitoring of specialist centres. Prior to treatment step up, inhaler technique and adherence should be assessed and managed as described above. Table 3 presents potential barriers to adherence that are frequently encountered in AYA and proposed facilitators that can enhance and improve adherence.

Self-management

Self-management comprises gaining the knowledge and skills that allow AYA patients with asthma to develop into autonomous experts who can manage their asthma throughout their adult life to reach better health outcomes [28]. Self-management reduces dependency on HCPs, parents and carers.

Enabling AYA patients to self-manage their asthma should start in the early phase of the transition period. Adolescents vary markedly during their teens in their ability and maturation, including literacy skills [29]. These factors need to be considered during the development of a self-management plan. Core items of self-management plans should include asthma education, asthma natural history, triggers, exacerbation risk, how treatment works, what good control looks like, and how to achieve and maintain it. A well-constructed self-management plan should enable AYA patients to assess their asthma control, reduce reliance on SABA use, measure peak expiratory flow rate and design treatment step up/down as required. A self-management plan should include attaining specific development goals and focus on areas where the AYA patient is not confident (*e.g.* a goal to reduce severe exacerbations to zero, or reduce use of SABA to <3 times per week, improve adherence to ICS to >80% of the time, develop an understanding of why preventer treatment is necessary).

Virtual mobile/web-based self-management has been increasingly used and is likely to become the main way of applying self-management in this era of smartphone applications [29]. Peer-led interventions may prove useful in assisting AYA patients to self-manage. The developed personalised asthma management plan should include input from family, school, teachers, co-workers and managers, and facilitate shared decision making. Motivational interviewing skills of active listening, empathy, a non- judgmental approach, gaining the AYA patient's confidence and maintaining medical privacy can all aid the HCP to assist AYA patients to set their goals, change behaviour and enable self-management [30, 31].

Severe asthma treatable traits

Effective self-management and adherence leads to significant improvement in asthma and reduces the need to escalate treatment to OCS or biologics. However, a minority of patients will continue to have uncontrolled asthma despite treatment optimisation at GINA steps 4–5 (severe asthma) [4]. Severe asthma is a heterogeneous disease that requires systematic phenotyping to allow identification of treatable traits where treatment can be tailored. The treatable trait concept describes a clinical entity that responds well to specific treatment (figure 3).

Phenotype#	Management options
Allergic (raised total serum IgE and positive specific IgE)	Minimise allergen exposure, optimise allergy treatment, anti-IgE, anti-IL4R [32, 33]
T_2 high and eosinophilic Eosinophils ≥300 cells per μL and F_{ENO} 25 ppb	Corticosteroid response phenotype Treatment options: anti-IL5, anti-IL5R and anti-IL4R biologics [32, 33]
Fungal asthma (SAFS and ABPA)	Antifungal therapy and corticosteroids [34–36]
Infective asthma	Chronic bronchitis, underlying bronchiectasis • Prophylaxis antibiotics, long-term macrolide therapy [37, 38]

FIGURE 3 Treatable traits of severe asthma. Treatable traits relate to all asthma and are not necessarily specific to the AYA group of asthma patients. #: one or more phenotypes can exist in the same individual, concept of "the dominant phenotype". T_2: type 2; IL-5: interleukin 5; anti-IL-5R: anti-interleukin 5 receptor; anti-IL-4R: anti-interleukin 4 receptor; anti-TSLP: anti-thymic stromal lymphopoietin; SAFS: severe asthma with fungal sensitisation; ABPA: allergic bronchopulmonary aspergillosis.

In the clinic, these phenotypes are not mutually exclusive, with patients often presenting with multiple traits (*e.g.* allergic, eosinophilic and infective traits presenting in the same patient). Therefore, the clinician's task is to apply a tailored treatment approached prioritising the strongest or most dominant phenotype likely to drive the disease, but also would consider treating factors that can undermine treatment response such as the co-presence of an infective phenotype prior to commencing biologic treatment. A management strategy should therefore be formulated to include staged treatment trials, review and assessment of response, and continuation of treatment long-term in the event of a satisfactory response or discontinuation and consideration for treatment switch in the event of a negative treatment trial outcome.

Organisation and delivery care transition from children to adult services

Transition of asthma care from children's to adult services is a process of empowering the growing child to become an independent, competent and expert adult patient (figure 4). Starting from 11 to 13 years of age, transition should be individualised depending on mental and physical development, disease activity and health literacy. Questionnaire-based tools have been developed to aid in assessing and preparing the adolescent for transition (*e.g.* transition readiness assessment tool; Ready Steady GO [40, 41].

Transition should be AYA patient-centred and include progress tracking, identification of key areas of knowledge that need development and should culminate in production of a transition report for the adult asthma service which should also link with the AYA primary care team. A transition report should cover areas of past medical history, concurrent treatment, comorbidities, emergency management plans and other AYA-related factors such as schooling and work and psychological wellbeing (figure 4).

A well-designed transition service requires the close working of paediatric and adult severe asthma team members through regular, joint multidisciplinary team (MDT) meetings, use of shared protocols and assessment tools, effective communication to ensure that all involved in AYA care say the same thing, and include family to support AYA independence and self-management. The example of a transition model we follow in Birmingham, UK is described in figure 5.

The transition programme was developed following discussions between the paediatric and the adult MDT teams. The key elements of the pathway are the involvement of the respiratory nurses and a youth worker in preparing the young person for asthma care in the adult centre in line with their wishes. The pathway also provides equal emphasis on safe and effective transition of young people with significant comorbidities for continued MDT input and not just those on biologics.

The young person undergoes a transition-focused annual asthma assessment at 15 years of age. The asthma control, medications, comorbidities and investigations, like bone density scan or chest computed tomography, are reviewed. The paediatric severe asthma team attend the first appointment at the adult

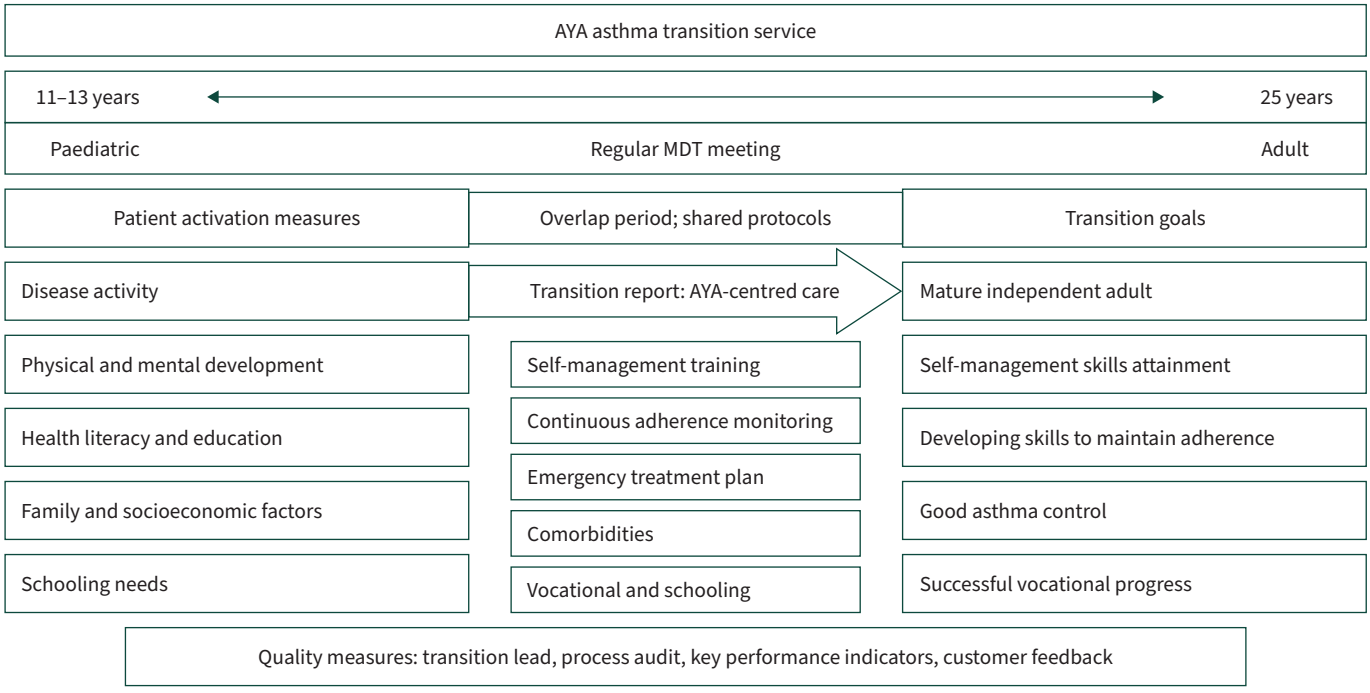


FIGURE 4 Example of a model of transition for adolescents and young adults with asthma from paediatric to adult services that specifies the key measures to activate transition, the overlap period and the ultimate transition goals to be achieved during adulthood. AYA: adolescent and young adult; MDT: multidisciplinary team.

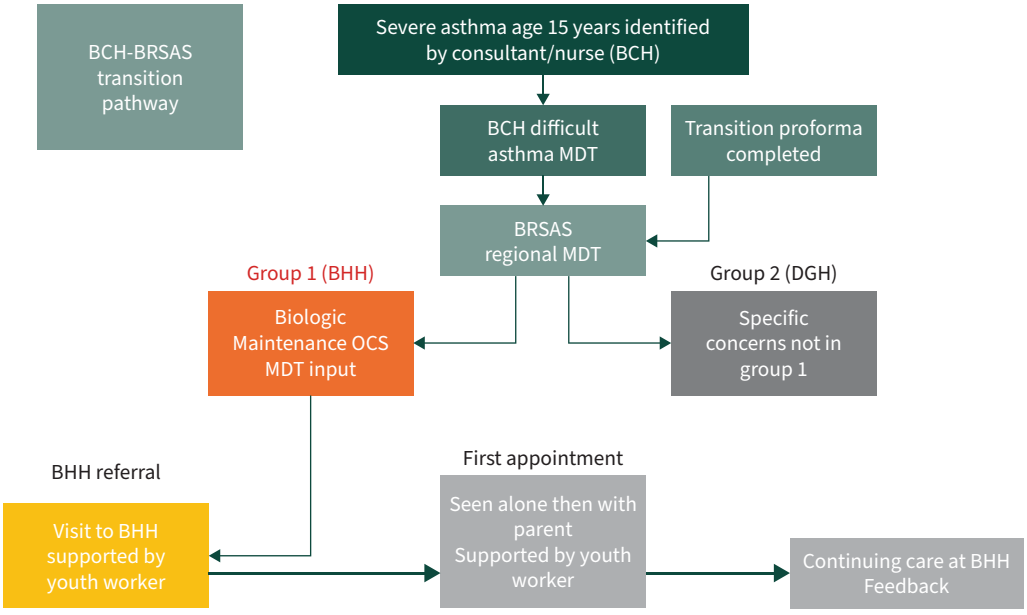


FIGURE 5 Severe asthma transition from paediatric to adult services pathway followed in Birmingham, UK. Using key transition triggers, patients are identified and assessed by the paediatric difficult asthma MDT and discussed at the adult MDT of the Birmingham Regional Severe Asthma Service (BRSAS). Patients with specific needs, such as biologic treatment, and those requiring specialised MDT input transition to the hub site in BRSAS, while others with no specific concerns transition to local spokes within the network. BCH: Birmingham Children's Hospital; MDT: multidisciplinary team; BHH: Birmingham Heartlands Hospital "hub"; DGH: district general hospital.

centre with the young person and the family following which the young person is formally discharged from paediatric services.

The process is reviewed regularly based on the feedback from the young person and the family. The establishment of a paediatric severe asthma MDT for effective management of comorbidities and the availability of new biologics have improved the care of young people. The unpublished data from our centre shows that of the 13 young people transitioned between 2019 and 2021, at a median age of 16.5 years, 11 (85%) were on biologics compared with eight out of 17 (47%) transitioned between 2016 and 2018. Moreover, the joint adult and paediatric work has resulted in a significant reduction in young people transitioned on maintenance OCS: 11 out of 17 (65%) to two out of 13 (15%) during the same time periods.

Conclusions

The management of DTA in adolescents and young adults is challenging but rewarding at the same time. Setting-up the correct service structure equipped with trained HCPs is essential to achieving successful outcomes for DTA management in AYA. Services should be patient centred with the ethos of forming healthy empowering and empathic relationships with the AYA patient to allow her/him to develop into a mature independent adult possessing lifelong knowledge and skills to self-manage their asthma and reduce dependency on family, carers and HCPs. Given the correct approach most AYA asthma patients should expect to lead a normal life, achieve best asthma outcomes, and reduce reliance on excessive use of SABA and OCS with its consequent serious side-effects. This article presents what would be considered an optimised model of care delivery that can be adapted for local use. Good asthma control is not necessarily the result of using the newest medicine, but about getting the best outcome with appropriate management.

Key points

- Assessment and management of asthma severity and comorbidities in young people is key to improve disease control and quality of life.
- A robust transition programme is required for supporting young people's asthma management.

Self-assessment questions

1. What is the difference between difficult asthma and severe asthma?
2. List any four treatable traits in severe asthma.
3. What are the known predictors of asthma remission in young adults?
4. Only children with severe asthma should be transitioned to the specialist adult severe asthma services. Is this statement true or false?

Conflict of interest: None declared.

References

1 Global Initiative for Asthma. Global strategy for asthma management and prevention, 2020. https://ginasthma.org/wp-content/uploads/2020/04/GINA-2020-full-report_-final-_wms.pdf
2 Barnes PJ, Woolcock AJ. Difficult asthma. *Eur Respir J* 1998; 12: 1209–1218.
3 Chung KF, Wenzel SE, Brozek JL, *et al.* International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014; 43: 343–373.
4 Hekking PW, Wener RR, Amelink M, *et al.* The prevalence of severe refractory asthma. *J Allergy Clin Immunol* 2015; 135: 896–902.
5 Dharmage SC, Perret JL, Custovic A. Epidemiology of asthma in children and adults. *Front Pediatr* 2019; 7: 246.
6 van Asperen P. Deaths from childhood asthma, 2004–2013: what lessons can we learn? *Med J Aust* 2015; 202: 125–126.
7 Haahtela T, Tuomisto LE, Pietinalho A, *et al.* A 10 year asthma programme in Finland: major change for the better. *Thorax* 2006; 61: 663–670.
8 Ross KR, Gupta R, DeBoer MD, *et al.* Severe asthma during childhood and adolescence: a longitudinal study. *J Allergy Clin Immunol* 2020; 145: 140–146.
9 Hovland V, Riiser A, Mowinckel P, *et al.* Early risk factors for pubertal asthma. *Clin Exp Allergy* 2015; 45: 164–176.
10 Liptzin DR, Landau LI, Taussig LM. Sex and the lung: observations, hypotheses, and future directions. *Pediatr Pulmonol* 2015; 50: 1159–1169.

11 Yoo S, Kim HB. Lee SY: Effect of active smoking on asthma symptoms, pulmonary function, and BHR in adolescents. *Pediatr Pulmonol* 2009; 44: 954–961.
12 Lang A, Carlsen KH, Haaland G. Severe asthma in childhood: assessed in 10 year olds in a birth cohort study. *Allergy* 2008; 63: 1054–1060.
13 Chen W, Safari A, FitzGerald JM, *et al.* Economic burden of multimorbidity in patients with severe asthma: a 20-year population-based study. *Thorax* 2019; 74: 1113–1119.
14 Sawyer SM, Afifi RA, Bearinger LH, *et al.* Adolescence: a foundation for future health. *Lancet* 2012; 379: 1630–1640.
15 Blakemore SJ. Adolescence and mental health. *Lancet* 2019; 393: 2030–2031.
16 Richards D, Caldwell PH, Go H. Impact of social media on the health of children and young people. *J Paediatr Child Health* 2015; 51: 1152–1157.
17 Merkus PJ, Pijnenburg MW. Diagnosing asthma in children or adolescents/young adults? It is time for a change! How timing is everything, also in clinical practice. *Eur Respir J* 2020; 56: 2002687.
18 Kaplan A, Price D. Treatment adherence in adolescents with asthma. *J Asthma Allergy* 2020; 13: 39–49.
19 Hassan M, Davies SE, Samuel P, *et al.* Prevalence and predictors of adherence to controller therapy in adult patients with severe/difficult-to-treat asthma: a systematic review and meta-analysis. *J Asthma* 2020; 57: 1379–1388.
20 Pearce CJ, Fleming L. Adherence to medication in children and adolescents with asthma: methods for monitoring and intervention. *Expert Rev Clin Immunol* 2018; 14: 1055–1063.
21 Jácome C, Pereira AM, Almeida R, *et al.* Patient-physician discordance in assessment of adherence to inhaled controller medication: a cross-sectional analysis of two cohorts. *BMJ Open* 2019; 9: e031732.
22 Boddy CE, Naveed S, Craner M, *et al.* Clinical outcomes in people with difficult-to-control asthma using electronic monitoring to support medication adherence. *J Allergy Clin Immunol Pract* 2021; 9: 1529–1538.
23 Heaney LG, Busby J, Bradding P, *et al.* Remotely monitored therapy and nitric oxide suppression identifies nonadherence in severe asthma. *Am J Respir Crit Care Med* 2019; 199: 454–464.
24 Mansur AH, Hassan M, Duffy J, *et al.* Development and clinical application of a prednisolone/cortisol assay to determine adherence to maintenance oral prednisolone in severe asthma. *Chest* 2020; 158: 901–912.
25 Toelle BG, Marks GB, Dunn SM. Validation of the inhaler adherence questionnaire. *BMC Psychol* 2020; 8: 95.
26 de Benedictis D, Bush A. Asthma in adolescence: is there any news? *Pediatr Pulmonol* 2017; 52: 129–138.
27 Kilford EJ, Garrett E, Blakemore SJ. The development of social cognition in adolescence: An integrated perspective. *Neurosci Biobehav Rev* 2016; 70: 106–120.
28 Holley S, Knibb R, Latter S, *et al.* Development and validation of the adolescent asthma self-efficacy questionnaire (AASEQ). *Eur Respir J* 2019; 54: 1801375.
29 Morrison D, Wyke S, Saunderson K, *et al.* Findings from a pilot randomised trial of an asthma internet self-management intervention (RAISIN). *BMJ Open* 2016; 6: e009254.
30 Holley S, Morris R, Knibb R, *et al.* Barriers and facilitators to asthma self-management in adolescents: a systematic review of qualitative and quantitative studies. *Pediatr Pulmonol* 2017; 52: 430–442.
31 Schaefer MR, Kavookjian J. The impact of motivational interviewing on adherence and symptom severity in adolescents and young adults with chronic illness: a systematic review. *Patient Educ Couns* 2017; 100: 2190–2199.
32 Agache I, Beltran J, Akdis C. Efficacy and safety of treatment with biologicals (benralizumab, dupilumab, mepolizumab, omalizumab and reslizumab) for severe eosinophilic asthma. A systematic review for the EAACI Guidelines – recommendations on the use of biologicals in severe asthma. *Allergy* 2020; 75: 1023–1042.
33 Agache I, Song Y, Rocha C, *et al.* Efficacy and safety of treatment with dupilumab for severe asthma: a systematic review of the EAACI guidelines–Recommendations on the use of biologicals in severe asthma. *Allergy* 2020; 75: 1058–1068.
34 Swaminathan N, Mansur A. P130 Prevalence and clinical outcomes of fungal sensitive asthma in a severe asthma population. *Thorax* 2016; 71: Suppl. 3, A154.
35 Moss RB. Treatment options in severe fungal asthma and allergic bronchopulmonary aspergillosis. *Eur Respir J* 2014; 43: 1487–1500.
36 Eraso IC, Sangiovanni S, Morales EI, *et al.* Use of monoclonal antibodies for allergic bronchopulmonary aspergillosis in patients with asthma and cystic fibrosis: literature review. *Ther Adv Respir Dis* 2020; 14: 1753466620961648.
37 Gibson PG, Yang IA, Upham JW, *et al.* Efficacy of azithromycin in severe asthma from the AMAZES randomised trial. *ERJ Open Res* 2019; 5: 00056-2019.
38 Ibrahim K, Mansur A. S66 Long-term azithromycin therapy improves clinical outcomes in an infective phenotype of severe asthma. *Thorax* 2017; 72: Suppl. 3, A41–A42.
39 Menzies-Gow A, Corren J, Bourdin A, *et al.* Tezepelumab in adults and adolescents with severe, uncontrolled asthma. *N Engl J Med* 2021; 384: 1800–1809.
40 Nagra A, McGinnity PM, Davis N, *et al.* Implementing transition: ready steady go. *Arch Dis Child Educ Pract Ed* 2015; 100: 313–320.

41 Ferris ME, Harward DH, Bickford K, *et al.* A clinical tool to measure the components of health-care transition from pediatric care to adult care: the UNC TR(x)ANSITION scale. *Ren Fail* 2012; 34: 744–753.

Suggested answers

1. Difficult asthma is an umbrella term referring to patients with uncontrolled asthma despite being prescribed appropriate medications. Correction of modifiable factors usually improves asthma control. Severe asthma is a subset of difficult asthma where the disease remains uncontrolled despite optimisation of care.
2. Infection, fungal sensitisation, type 2 (T2) high inflammation, allergic and eosinophilic asthma.
3. Pre-pubertal mild disease, minor airway inflammation, absence of allergic sensitisation and male gender.
4. False. Any young person with uncontrolled asthma should be transitioned to a specialist centre for multidisciplinary assessment of disease severity, management of comorbidities and access to specialist services like physiotherapy.