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## **Anaphylaxis in adolescents: a potential tripartite management framework**

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## **Abstract**

*Purpose of the review:* The incidence of anaphylaxis is increasing across all ages, but the risk of morbidity and fatality is disproportionately high in adolescents. This may, at least in part, be a consequence of a constellation of potentially-modifiable psychosocial factors that tend to manifest during adolescence. This paper highlights the shortcomings in and barriers to effective management of anaphylaxis in adolescents and proposes an integrated tripartite framework that may help promote successful management.

*Recent findings:* Existing mainstay anaphylaxis self-management approaches – comprising of careful avoidance of triggers, recognition of early features indicative of anaphylaxis and prompt self-administration of intra-muscular adrenaline (epinephrine) – often fail in adolescents. Key barriers to successful management centre on the impact of the psychosocial environment during adolescents' developmental transition. As a result, risk-taking, poor judgement of actions during reactions, and non-compliance to management instructions are common.

*Summary:* To be successful, anaphylaxis management strategies require more multi-dimensional approaches among adolescents. We propose a tripartite management framework that emphasises integration of the following components: (1) better understanding of adolescence; (2) incorporation of the constituents of adolescents' social networks; and (3) adolescent-tailored healthcare perspectives. This theoretical framework now requires translation into an intervention, feasibility and pilot testing, and formal evaluation through randomised controlled trials.

Keywords: adolescents, adrenaline, anaphylaxis, auto-injector, management

## Introduction

Anaphylaxis can be defined as “a serious life-threatening generalised or systemic hypersensitivity reaction” [1,2,3,4\*\*], rapid in onset, presenting with a constellation of features, and can be fatal in some cases [1,2,3,4\*\*]. There are presently no reliable global estimates of the incidence, prevalence, morbidity, and mortality due to anaphylaxis, this in part being explained by variations in definition, under-recognition, under-diagnosis and under-coding in clinical practice [1]. However, across Europe, the population-based incidence rate of anaphylaxis ranges between 1.5 to 7.9 per 100 000 person-years, whereas the lifetime prevalence stands at about 0.3% [5]. In the United States (US), the incidence rate has been estimated at 50 per 100 000 person-years with a point prevalence of about 1.6% [6,7\*]. Whilst ingested foods are the most common triggers of anaphylaxis in children and adolescents, medications and insect stings are the most common triggers in middle-aged and elderly adults [1,5,6,7\*].

The incidence of anaphylaxis appears to be increasing over time [5]. In the United Kingdom (UK), the age-standardised incidence rate increased from 6.7 in 2001 to 7.9 in 2005 per 100 000 person-years while the prevalence increased from 50 to 76 per 100 000 population during the same period; prescription for adrenaline auto-injectors (epinephrine) increased by 97% over the same period [8]. Similarly, between 1990 and 2000 the incidence rate increased from 47 to 59 per 100 000 persons in the US [6]. Although from a public health perspective, anaphylaxis remains an uncommon cause of death, given the increasing disease burden, healthcare utilisation and the fact that potentially avoidable deaths often occur in young people, the development of strategies for prevention of recurrence, management, and avoidance of fatalities has emerged as a priority area for health systems in many parts of the world [1,2,3,4\*\*].

Disproportionately, the morbidity and fatality from anaphylaxis are greater in adolescents than in other age groups [9,10-13,14,15,16,17]. Adolescence represents a time of great transition in the life of the young person, with rapid occurrence of physical, cognitive, psychological, and social developments [10,11,13,16,17]. There is therefore an unavoidable shift from dependence to independence as transfer of responsibility takes place from parents to the young person [10,11,13,16,17]. Socialisation increases, with an increasing influence from peers, which sometimes can be negative, resulting in impaired decision-making and risk-taking. Risk-taking is common among adolescents with food allergy – even those with previous food-triggered anaphylaxis – such that they sometimes eat foods that may contain allergens to which they are known to be sensitive. Furthermore, they may on occasions also fail to: seek help when experiencing reactions; recognise symptoms of anaphylaxis; carry their adrenaline auto-injector; and inform their peers that they are at risk of anaphylaxis and/or what to do if a reaction occurs [9,10-13,14,15,16,17]. Given this constellation of – potentially modifiable – psychosocial factors, tailoring of services in young people is crucial to effective management. In this paper we describe existing anaphylaxis management strategies, highlight key barriers to successful management in adolescents, suggest a theoretical framework to improve management in adolescents, and finally recommend key steps for policy, practice, and in particular future research to promote improved outcomes in adolescents at risk of anaphylaxis.

## Existing management approaches to anaphylaxis

Effective management of anaphylaxis must include both acute/emergency treatment and longer-term considerations [1,2,3,4\*\*,18,19]. Acute anaphylaxis management focuses on aborting reactions and providing essential life-supporting measures in order to prevent fatality, whereas long-term management centres on preventing any recurrence of anaphylaxis episode and minimising the risks if subsequent reactions ensue [1,2,3,4\*\*,18\*\*,19\*\*]. While acute management of anaphylaxis focuses on biomedical

considerations, longer-term management needs to be much more concerned with the wider psycho-social dimensions of living with an unpredictable and potentially life-threatening condition [1,3,18-20]. International expert groups have recommended different management options for both acute and long-term management of anaphylaxis, as briefly described below [1,2,3,4\*\*,18\*\*,19\*\*,20].

### *Acute management*

Deaths can occur within minutes of onset of anaphylaxis and it is difficult to predict the onset and severity of a reaction [1,2,3,4\*\*, 18-20]. Therefore, in emergency situations, rapid initial steps are recommended to be taken immediately reactions occur. The mainstay and first-line treatment option for acute management of anaphylaxis is the prompt injection of adrenaline, preferably injected through the intramuscular route into the mid-anterolateral thigh [1,2,3,4\*\*,18\*\*,19\*\*,20,21]. Delay in administration of adrenaline increases the risk of death [1,2,3,4\*\*,18\*\*,19\*\*], but the risk is minimised if timely given, in appropriate doses, and administered through the recommended route [22]. Despite its potentially very important benefits in the acute management of anaphylaxis, adrenaline auto-injectors are under-utilised, especially by adolescents [9,11,14,15]. Other recommended strategies, known as second- or third-line interventions for acute management of anaphylaxis, include initiating immediate call for help, provision of high-flow oxygen if indicated, intravenous fluid and cardiopulmonary resuscitations, and administration of H<sub>1</sub>-antihistamines, H<sub>2</sub>-antihistamines, and glucocorticoids [1,2,3,4\*\*, 18-20].

### *Long-term management*

Long-term management of anaphylaxis constitutes the need for developing tailored self-management plans aimed at preventing future recurrences of reactions [1,2,3,4\*\*, 18], including detailed guidance on avoiding triggers, recognising reactions, preparing for reactions, and appropriate self-management of reactions if they occur [1-4,18\*\*,19\*\*]. To achieve these, at-risk individuals, together with their healthcare professionals, are recommended to develop personalised emergency action plans, carry their adrenaline auto-injectors regularly, develop appropriate skills to use auto-injectors, manage concomitant diseases – in particular asthma in those with food-triggered reactions – and engage in regular follow-up assessments with their physician [1,2,3,4\*\*, 18\*\*,19\*\*]. Accidental anaphylactic reactions become less common once recommended management plans are initiated, in particular if both clinical and psychosocial perspectives are incorporated into these plans [4\*\*]. Immunotherapy has been shown to play an important role in long-term management of anaphylaxis triggered by venom and this approach is also yielding encouraging research results in those with food-triggered reactions; further work is however needed in relation to establishing the long-term effectiveness and safety profile of food immunotherapy [4\*\*,19\*\*,23,24,25].

### **Barriers to effective long-term management of anaphylaxis in adolescents**

Although the various stages of long-term management are well characterised, optimising this approach in adolescents is however challenging [9,10-13,14,15,16,17]. As described above, adolescents need to deal with a range of psychosocial developmental factors, which in many cases predispose to sub-optimal decision making and which may result in increased risk of reaction, near fatal episodes and fatal reactions, although it must be emphasised that the latter outcome remains very uncommon [9,10-13,14,15,16,17]. Key recurring themes from previous studies investigating the barriers to successful management of anaphylaxis among adolescents include: not being adequately prepared (e.g. adrenaline auto-injector not carried, asthma poorly controlled, insufficient knowledge of risky situations, and inability to identify potential sources of reactions); involvement in situations that lead to risk-taking (e.g. anxiety and fear of embarrassment and social isolation from peers, inconvenience or

forgetfulness in carrying adrenaline auto-injector, and not checking food labels when eating out); not taking appropriate help-seeking behaviour when faced with a suspected reaction; and not self-administering adrenaline even if available [9,10-13,14,15,16,17,26,27\*].

In a Scottish qualitative study of 26 adolescents and 28 parents, the main barriers to managing anaphylaxis in adolescents were failure to recognise reactions, uncertainty about adrenaline administration techniques and appropriate timing of administration, and fear of using adrenaline auto-injector [14]. In the US [11] and UK [16], only two-thirds of adolescents always carry their auto-injectors [10], and only a fifth had ever used these; only 40% took steps to avoid the foods which they were allergic to [12]; all these representing risk-taking behaviours that may lead to reactions and poor outcomes in those experiencing anaphylaxis. In another Scottish study, some adolescents perceived their anaphylaxis as 'no big deal'; this was particularly the case in those who could not recall a reaction as this happened in early childhood [13]. Risk-taking appears to vary according to the immediate social circumstances adolescents face. For instance, adolescents appear to be more likely to carry their auto-injectors when traveling or in the restaurant and less likely during sports activities or when wearing tight clothes [11]. Frequent carriage of auto-injectors however does not always translate to usage during reactions [9,11,14,15].

### **Strategies for improving management of anaphylaxis in adolescents**

Given the barriers noted above that inhibit successful self-management of anaphylaxis among adolescents, most of which relate primarily to features of the psychosocial impact of adolescents' developmental transition, we suggest that a multidimensional management approach needs to be developed. This should be tailored to the needs of adolescents, with a particular focus on tackling the known barriers to effective self-care. One such tripartite management approach is illustrated in Figure 1, which emerged through integration of our previous anaphylaxis systematic reviews and series of qualitative studies [4\*\*,5,13,14,16,17,19\*\*]. The model suggests that successful management can be achieved through recognising the various avenues of barriers (namely: (1) challenges of adolescents' developmental transition; (2) shortcomings of current management strategies among adolescents; and (3) challenges of adolescents' social networks) and then integrating these into clinical management strategies. The framework proposes a tripartite link between each of these domains, showing that, in formulating a successful and holistic management strategy, both for acute self-management and long-term management, the three domains need to be integrated. Further modelling is needed to develop this framework into a practical intervention, but in going forward it will, we hope, provide a firm foundation from which to develop effective complex interventions to support adolescents self-manage their anaphylaxis.

According to the proposed framework, the first step to a successful anaphylaxis management in adolescence therefore starts with better understanding of adolescence, the features that characterise this developmental transition, and the respective worldviews held by adolescents. Such understanding presents a clear pathway to minimising the negative consequences of this transition [13]. Clearly, a better appreciation of this developmental transition and its characteristics should therefore translate into initiating both acute self-management and long-term management approaches that integrate the social networks of young people and tailoring of clinical strategies to meet the needs of adolescents. As this transition leads to greater independence, adolescents require commensurate education on and training in the skills required for risk avoidance, symptom recognition, regular possession of their adrenaline auto-injector, and prompt use of it during a reaction.

Achieving anticipated successes during this developmental transition will benefit from incorporating adolescents' social networks into management strategies, given that the

impending independence forecloses constant parental oversight [10,11,13,16,17]. Social networks, such as friends/peers, teachers, or other support groups, may therefore represent active alternative cues to action in managing anaphylaxis, and thereby replace some of the oversight lost as a result of reducing parental supervision. With adequate training, adolescents' social networks can serve as cues to risk avoidance, symptom recognition, better carriage and usage of auto-injectors, and call for help or administer adrenaline during emergency. A recent study from South East England showed that belonging to a patient support group, possessing a self-management plan, perceiving the severity of their risk, and less perceived barriers to management all resulted to better adherence [20]. Such groups are now present in some regions – for example, those run by the UK Anaphylaxis Campaign (<http://www.anaphylaxis.org.uk/>) and the US Food Allergy Research and Education (<http://www.foodallergy.org/>), which have been in the forefront of supporting those at risk or suffering from anaphylaxis. Such patient support groups can prove useful in not only providing personalised support for the at-risk adolescents, but also serving as a means of informal education, training, and practical support to family members, healthcare professionals, teachers, and peers of adolescents on the knowledge required to successfully manage the risks of living with anaphylaxis [16].

Furthermore, appreciation of the features of adolescents' developmental transition and their worldviews should also in due course translate into refining healthcare strategies for effective management. Such strategies will include: (1) developing decision support algorithms for symptom recognition and administration of adrenaline, possibly in electronic format that can be accessible via smartphone apps; (2) designing adrenaline auto-injectors that can be more conveniently carried - the Kaleó models being recent developments in this field (<http://www.kaleopharma.com/>); and (3) establishing helplines for real-time access to specialist advice - a strategy that has shown effective in improving self-rated food-specific quality of life of children at risk of anaphylaxis [28]. Although achieving these practical objectives may be challenging, unclear early warnings or threshold of symptoms that herald reactions may lead to poor recognition of anaphylaxis among adolescents [4\*\*,15]. Therefore, from the clinical perspective, providing decision support algorithms to assess specific symptoms will provide prompt clue to administer adrenaline, encourage prompt steps to seek treatment, and call for help during reactions [4\*\*,15]. In social engagements, young people prefer auto-injectors that are more convenient to carry and easy to use (like the emerging Kaleó models mentioned above) than the choices currently available [10,14,15].

### **Conclusions: recommendations for practice and further research**

Current anaphylaxis management strategies among adolescents have aspects of the approaches directed at parents of young children and those aimed at adults. What is now needed is a more tailored approach based on a better appreciation of young people and the challenges and priorities they grapple with on a day-to-day basis. As highlighted in this paper, adolescents require more tailored multidimensional and holistic management approaches that go beyond education about the need for regular carriage of auto-injectors, as these approaches in and of themselves have been shown to be inadequate. In particular, while frequent carriage of anaphylaxis is important, many adolescents do not use them when faced with reactions, even when they carry them. More fundamental barriers to successful anaphylaxis management in this age group therefore appear to relate to the various psychosocial factors encompassing adolescents' developmental transition. We have highlighted that successful anaphylaxis management among adolescents will be enhanced by an integrated approach that incorporates better understanding of the constellation of features of this developmental transition into current healthcare management strategies.

For clinical practice, anaphylaxis management among adolescents will benefit by involving adolescents' social networks, including family members, but more so their friends/peers, teachers, and relevant support groups given the increased independence and reduced parental oversight on adolescents. Well-designed education and training of each of these groups will be required on how to serve as cues to at-risk adolescents in avoiding potential triggers, on when and how to use auto-injectors, and when to call for help during the time of reactions. Furthermore, though challenging developing computerised decision support tools for symptom recognition and administration of adrenaline may be helpful. In addition, re-designing auto-injectors that appeal to adolescents, which are convenient to carry will enhance better usage; at the same time, establishing helpline access to specialist advice for support in emergency contexts will facilitate efforts to seek quick help in times of need.

Further research is now warranted to highlight how adolescents' developmental trajectories can influence anaphylaxis management, particularly consideration of the peak and lowest period of risk of morbidity and fatality during adolescent developmental transition. More research is also needed to identify how and what educational strategies are more effective to influence the psychosocial environments (families, friends/peers, teachers, patient support groups) of adolescents in providing active cues for better prevention. In this regard, an assessment of the role of social media in promoting such education and training in enhancing the anaphylaxis management skill-sets of these groups will help in advancing this evidence base. Finally, the framework proposed in this paper needs to be further simulated in order to assess its potentials in informing the development of the clearer theoretical bases for initiating complex interventions [29] for anaphylaxis management among adolescents.

## **Key Points**

- Compare to other age groups, the risk of morbidity and fatality from anaphylaxis is disproportionately higher in adolescents
- Existing anaphylaxis self-management strategies often fail among adolescents primarily because of the influence of the psychosocial environment surrounding developmental transition during adolescence
- Successful management of anaphylaxis among adolescents will therefore require better understanding of adolescence, the features that characterise this developmental transition, and the respective worldviews held by adolescents
- We have proposed an adolescent-tailored, multidimensional, and holistic self-management framework that emphasises incorporation of better understanding of adolescence into current healthcare management strategies
- This theoretical framework now requires further simulation and translation into an intervention, feasibility and pilot testing, and formal evaluation through randomised controlled trials



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No conflict of interest declared.

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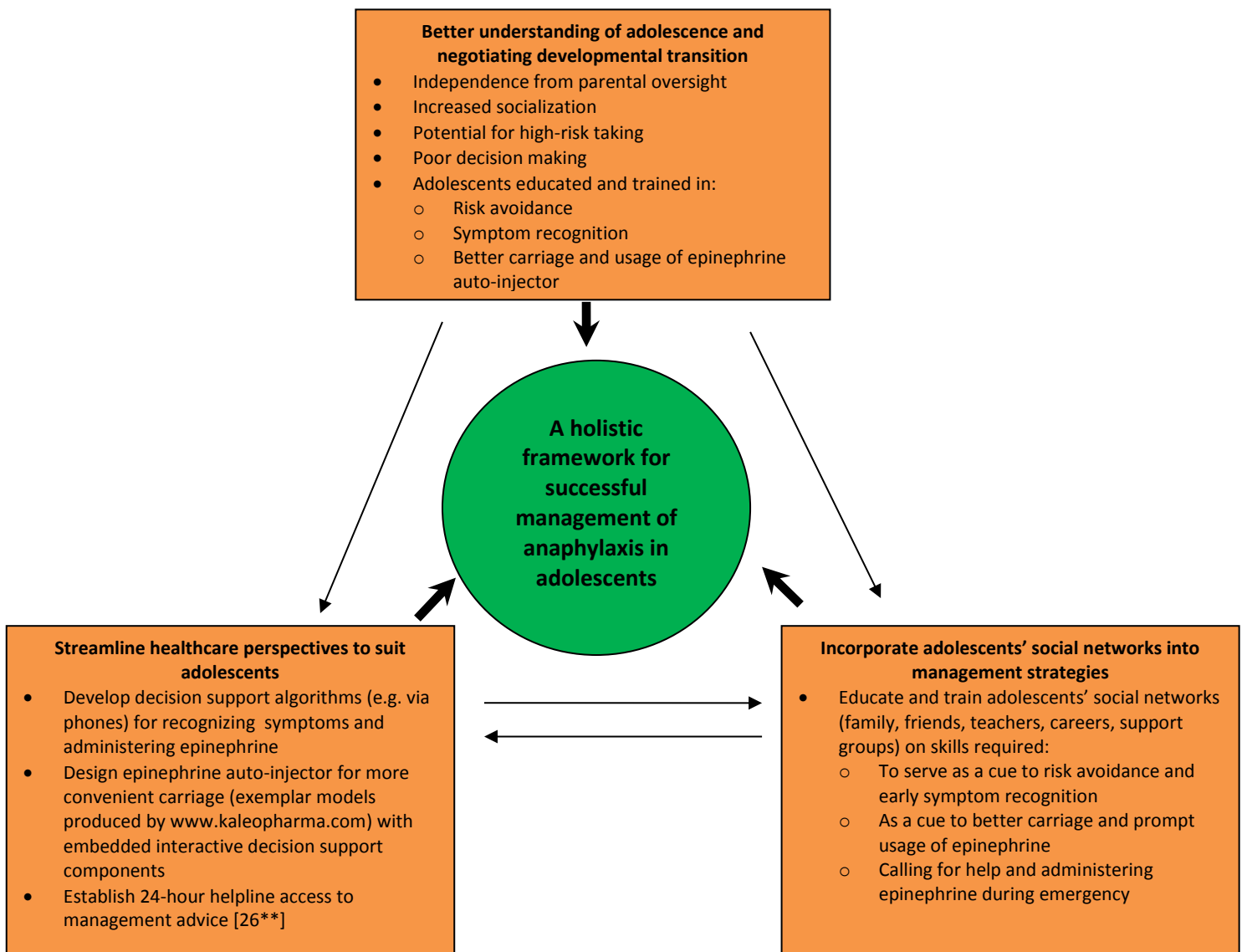
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**Figure 1** Depiction of a proposed holistic framework for the management of anaphylaxis in adolescents that integrates the different sources of barriers to success