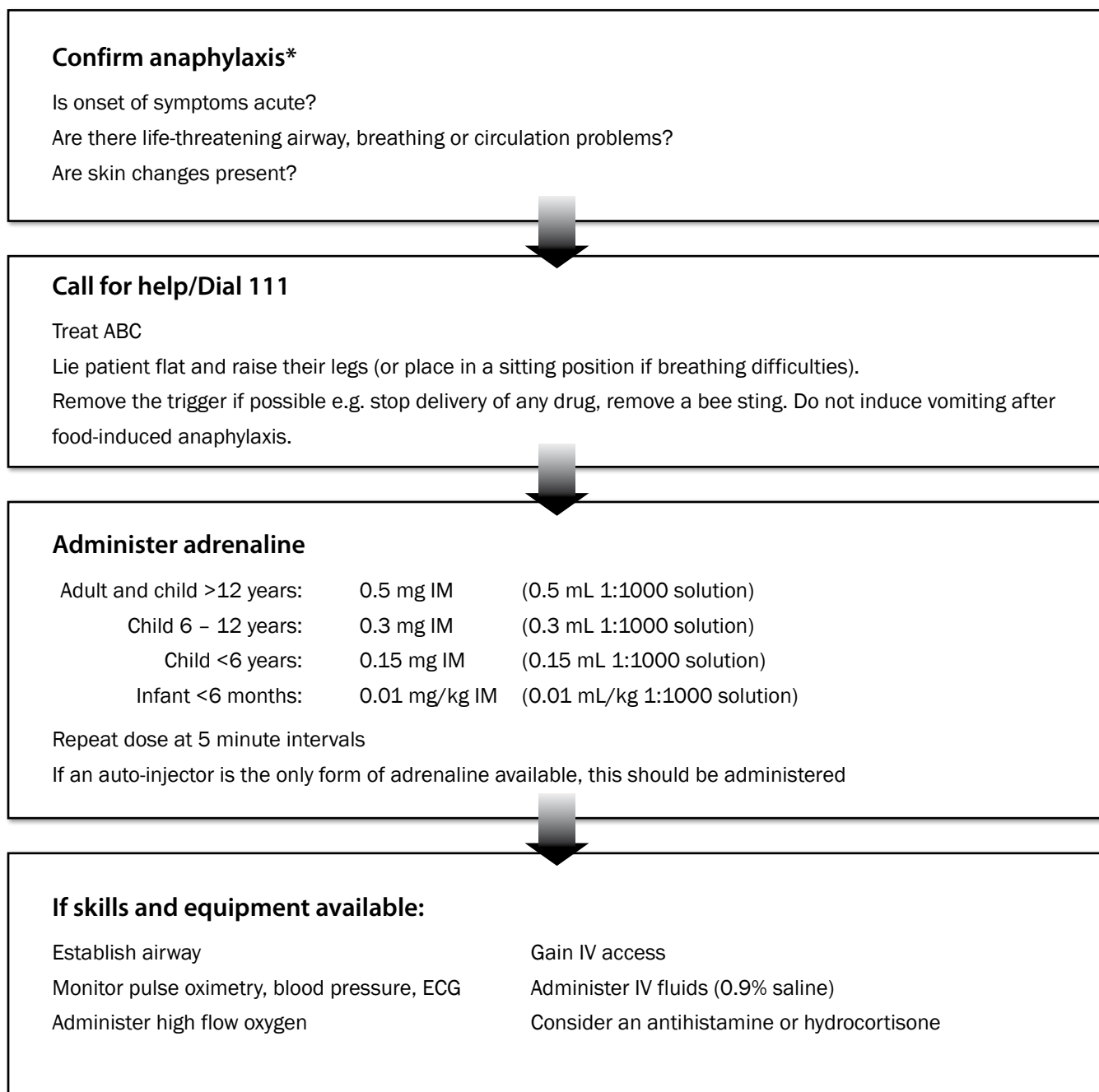


The management of **ANAPHYLAXIS** in primary care

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Anaphylaxis treatment algorithm



Adapted from the UK Working Group of the Resuscitation Council¹

*Anaphylaxis is a severe allergic reaction. Patients with signs and symptoms indicative of a mild to moderate allergic reaction (swelling of lips, face or eyes, hives or welts, tingling mouth, abdominal pain or vomiting) should be closely observed for deterioration and treated symptomatically.

Recognising anaphylaxis

Anaphylaxis is a potentially fatal hypersensitivity reaction, characterised by rapid onset of life-threatening respiratory and cardiovascular symptoms. Most episodes are triggered by an allergen interaction with immunoglobulin E (IgE), however reactions may occur in the absence of any obvious trigger (idiopathic anaphylaxis).²

Anaphylactoid reactions are distinguished from true anaphylaxis as they are not IgE mediated, but this distinction is not clinically relevant for treatment as both types of reaction cause the same symptoms and are treated in the same way.²

Allergic triggers in anaphylaxis

Food – egg, cows' milk (and dairy foods), peanuts, tree nuts, seeds (e.g. sesame), seafood, fruit (e.g. kiwifruit, banana). Sensitivity to food additives rarely causes anaphylaxis.

Insect venom – bees, wasps.

Medication – antibiotics (e.g. penicillin), aspirin/NSAIDs, muscle relaxants, herbal products.

Other – latex (e.g. balloons, gloves, condoms), blood products, radio contrast media, storage mite (found in stored grains e.g. flour), exercise, exposure to cold air or water.

Signs and symptoms of anaphylaxis may vary

Symptoms, severity and time of onset may vary between patients and from one episode of anaphylaxis to another.³ Symptoms usually occur within five to 30 minutes after exposure to a trigger, however reactions can occur up to several hours later, or symptoms can build up over time, beginning as a mild allergic reaction. Exposure to an

intravenous trigger usually results in a more rapid onset of symptoms, followed by stings, then orally ingested allergens.¹

If untreated, anaphylaxis can cause death within minutes due to cardiovascular collapse (more common in adults) or respiratory tract obstruction (more common in children).^{2,4}

Risk factors for mortality include;

- Age – adolescents and younger adults are at the highest risk for fatal anaphylaxis from foods, especially peanuts. Venom-induced deaths are more frequent in middle-aged adults and older adults account for most cases of fatal medication-induced anaphylaxis.
- Asthma – especially if not well controlled
- Cardiopulmonary disease
- Delayed or no administration of adrenaline

Diagnosing anaphylaxis

Diagnosis is based on history and observations at the time of the event and may be difficult due to the range of signs and symptoms that can occur. However, anaphylaxis is more likely when a certain combination of factors are present.¹

Criteria for suspecting anaphylaxis¹

Anaphylaxis is likely when all three of the following criteria are met:

1. Sudden onset and rapid progression of symptoms
2. Life threatening airway, breathing or circulatory problems
3. Skin and/or mucosal changes

Exposure to a known allergen supports the diagnosis.

Note that:

- Skin or mucosal changes alone are not a sign of anaphylactic reaction
- Skin or mucosal changes can be subtle or absent in some reactions (approximately 12%)
- Gastrointestinal symptoms may also be present

Differential diagnosis

Other conditions which may mimic the signs and symptoms of anaphylaxis include:¹

- Life threatening asthma, especially in children
- Septic shock – hypotension, petechial or purpuric rash
- Vasovagal episode (faint) e.g. after immunisation
- Panic attack – may occur in people who have had a previous anaphylactic reaction, if they think they have been exposed to the same trigger
- Breath-holding in children
- Idiopathic urticaria or angioedema
- Foreign body in the airway
- Reaction to MSG or sulphites
- Flushing due to menopause or drug reactions (e.g. vancomycin)

Signs and symptoms of anaphylaxis

Life-threatening symptoms:

Airway – pharyngeal or laryngeal oedema, hoarse voice, stridor, swallowing difficulties.

Breathing – dyspnoea, increased respiratory rate, wheeze, bronchospasm, hypoxia, pulmonary oedema, cyanosis and respiratory arrest.

Circulation – shock (pale, clammy), tachycardia, hypotension, dizziness, collapse, deterioration when sitting or standing, decreased consciousness, myocardial ischaemia, ECG changes, cardiac arrest.¹

Other symptoms:

Skin – erythema, urticaria, flushing, itching, angioedema.

Gastrointestinal – abdominal pain, cramps, vomiting, diarrhoea.

Nervous system – anxiousness, confusion, agitation.

Treating anaphylaxis

Adrenaline is the core treatment

Adrenaline (also called epinephrine) should be given immediately to all patients with life threatening features of anaphylaxis.² Adrenaline prevents and relieves laryngeal oedema and circulatory collapse, provides bronchodilation and reduces the release of histamine and other mediators.

It is important not to give adrenaline inappropriately e.g. for allergic reactions just involving the skin, vasovagal reactions or panic attacks.¹ However many cases of fatal anaphylaxis are caused as a result of the reaction not being recognised and adrenaline not delivered promptly enough or not used at all.¹

Intramuscular injection is used in most cases

Intramuscular (IM) injection of adrenaline is usually the most appropriate method of delivery in a primary care setting.⁵ The best site for IM injection is the anterolateral aspect of the middle third of the thigh, ensuring that the needle is long enough to reach the thigh muscle. IM adrenaline is not recommended after cardiac arrest has occurred.¹

Intravenous (IV) use of adrenaline is usually reserved for the hospital setting for those experienced in its use. IV injection can be administered when there is no response to IM adrenaline and when cardiovascular collapse is impending. This should be given by controlled infusion rather than a bolus.²

Subcutaneous injection of adrenaline is not recommended as absorption is slow and unreliable.⁵ Inhaled adrenaline is also not recommended as there is insufficient delivery for treating anaphylaxis.¹

Recommended adrenaline dose¹


Age group	IM adrenaline dose	mL of 1:1000 adrenaline
Adults and children >12 years	0.5 mg	0.5 mL
6 – 12 years	0.3 mg	0.3 mL
6 months – 6 years	0.15 mg	0.15 mL
<6 months	0.01 mg/kg	0.01 mL/kg

The dose should be repeated at five minutes if there is no improvement. Further doses can be given at five to ten minute intervals according to response.¹

Beta blockers reduce the efficacy of adrenaline. Patients using beta blockers may need IV glucagon or atropine in addition to adrenaline.

Use of adrenaline should not be withheld because of adverse effects

Transient palpitations, tremor and pallor may occur after injection of adrenaline.⁶ More serious cardiovascular effects (arrhythmia, myocardial infarction) may occur with adrenaline overdose, an inadequately diluted dose or a too rapid rate of infusion. Elderly people and people with hypertension, arteriopathies or ischaemic heart disease have the highest risk of adverse effects. Adrenaline should not be withheld but these groups of people should be monitored more closely for cardiac effects. Note that anaphylaxis itself also causes adverse cardiac events.²

 Adrenaline in New Zealand is available in 1 in 1000 (1 mL) or 1 in 10000 (10 mL) injection strengths. It should be stored in a cool, dark place, but should not be refrigerated.

Other treatments for anaphylaxis

Fluids are given IV (adult 500-1000 mL, child 20 mL/kg). They can be given rapidly but monitor response. Give further doses as necessary. A 0.9% saline solution is appropriate.

Oxygen is given using the highest concentration possible and at a high flow ($> 10 \text{ L/min}^{-1}$).^{1,4}

H1-antihistamines (e.g. loratadine or cetirizine) are sometimes used for anaphylaxis to down-regulate the allergic response and minimise the clinical impact of histamine release.⁴ H1-antihistamines may relieve itching, hives, other cutaneous symptoms and rhinorrhoea. After oral administration, onset of action is one to two hours. First generation sedating antihistamines (e.g. promethazine) should be avoided. IM preparations are not generally used.

Corticosteroids may help to shorten reactions. Recommended dose: Inject hydrocortisone slowly IV or IM. Adults 200 mg, children 6 – 12 years 100 mg, children 6 months to 6 years 50 mg, children less than 6 months 25 mg.¹

Bronchodilators such as salbutamol (inhaled or IV), ipratropium (inhaled) or aminophylline (IV) can be considered for people with severe breathing difficulties.¹

H2-receptor antagonists (e.g. ranitidine) are also sometimes used in anaphylaxis, however there is little evidence to support their effectiveness.^{1,4}

Signs and symptoms of mild to moderate allergic reaction

Swelling of lips, face or eyes

Hives or welts

Tingling mouth

Abdominal pain, vomiting

Mild to moderate allergic reaction

If life-threatening respiratory and cardiovascular features of anaphylaxis are not present, but there are other features of a systemic allergic reaction (e.g. skin changes, abdominal pain or vomiting), the patient should be closely observed for deterioration and given symptomatic treatment such as oral antihistamines and if clinically indicated, oral steroids (e.g. prednisone 20 mg).

Refer all patients with anaphylaxis to hospital care

All patients who have had an anaphylactic reaction should be referred to hospital care and monitored and observed for up to 24 hours.¹

Situations in which the risk of recurrence of symptoms (biphasic reaction) is higher include:¹

- Severe reactions which were slow in onset after exposure to the trigger
- Reactions in people who have severe asthma or with a severe asthmatic component
- Reactions in which the allergen may continue to be absorbed
- Previous history of biphasic reactions

Antihistamines and oral steroid therapy may be given for up to three days after an anaphylactic reaction. This is useful for treating any remaining symptoms (e.g. urticaria) and may decrease the chance of further reaction.¹ Long-term use of antihistamines does not prevent anaphylaxis.

Risk reduction

After any anaphylactic reaction, consider referral for identification of the trigger and implementation of a plan to reduce the risk of future reactions.¹ There are only a small number of allergy specialists and clinical immunologists available via the public or private health systems in New Zealand. In areas where allergy clinics or specialists are not available, patients can be referred to paediatric, medical or dermatology specialists. A list of allergy specialists can be found at www.allergy.org.nz

Principles of long-term management:⁷

- Refer to a specialist for identification of triggers – this may include allergy testing or food/drug challenge.
- Provide education about avoiding triggers – avoidance is the only means of prevention for many causes of anaphylaxis.
- Assess the risk of a recurrent reaction – implement risk reduction measures.
- Write up an emergency anaphylaxis action plan – essential for first aid management.
- Reassess regularly – determine whether the allergy is still present and review prevention strategies and first aid plans.

Identifying triggers


An allergy specialist or clinical immunologist may perform tests for allergen specific IgE (skin or blood tests) to help confirm or exclude a trigger. Other methods of allergy testing (e.g. hair analysis) are not recommended and may provide unreliable or misleading results.⁷

Education about avoiding triggers

Education about avoiding triggers is essential as this is often the only effective measure to prevent an allergy.⁷ It is important that concerns and anxieties about anaphylaxis

are also addressed. Having an allergy can be debilitating and restrictive and can affect well-being and quality of life.⁹

GPs may also be asked to work with parents to help educate the child's teachers or carers and provide relevant medical information.

 Information and practical suggestions for avoiding triggers, especially for food allergies, can be found online at the Australasian Society for Clinical Immunology and Allergy website (click on “anaphylaxis resources”): www.allergy.org.au

Assessing and reducing risk

In some cases people may be able to easily avoid the trigger that puts them at risk of anaphylaxis e.g. a specific drug or easily identifiable food such as shellfish. For others, reducing their risk is not as easy.

When the risk of anaphylaxis is not able to be easily managed, safety measures such as carrying an **adrenaline auto-injector** should be considered. An adrenaline auto-injector is recommended for:

- People with a history of idiopathic reaction
- People with continued risk from food or venom related reactions which are difficult to avoid
- People with known allergy who have concurrent asthma or ischaemic heart disease (increases risk of severe reaction)
- People who live in remote areas

EpiPen is the only type of auto-injector available in New Zealand and is not funded.* In comes in 0.3 mg (for adults and children over 20 kg) and 0.15 mg doses (for children 10 kg – 20 kg) and can be ordered directly from a distributor by the GP, purchased by the patient from a pharmacy, or ordered over the internet. It is essential

* Funding may be available from ACC for people with anaphylaxis due to insect stings or bites

that patients and their families are shown how to use the device correctly. Practice auto-injectors may be useful – these devices do not contain adrenaline or a needle and are usually available wherever auto-injectors are sold.

A **Medical Alert bracelet** or emblem should also be considered, especially for allergies to medicines and latex that need to be avoided in an emergency medical situation.


For drug allergies, patient details should be submitted to the Centre for Adverse Reactions Monitoring (CARM) so information can be entered into the national patient alert system.

Further risk reduction can be achieved by identifying patients who have a food allergy and also have **asthma** and ensuring that their asthma is well controlled.

Any patient who has had a systemic reaction to insect venom should be referred to a specialist who may recommend **venom immunotherapy** (desensitisation), which reduces the risk of anaphylaxis with subsequent exposure.

Anaphylaxis action plan

An anaphylaxis emergency action plan is a written document completed by the GP that includes information on allergic triggers, family contact details, signs and symptoms, and indicating when to call for medical assistance or use an adrenaline auto-injector if available. As symptoms of anaphylaxis often vary, it is important to have individual action plans with specific instructions. Copies of action plans should be kept by the patient, GP, allergy specialist and school/workplace.

 Action plans for anaphylaxis that can be completed by doctors for their patients are available online from the Australasian Society for Clinical Immunology and Allergy (click on “anaphylaxis resources”): www.allergy.org.au

Regular review

Some food allergies can resolve with age e.g. allergy to dairy products, soy, wheat and egg, so children should be reviewed regularly by a specialist to determine whether the allergy is still present. This also includes people who may have been incorrectly diagnosed. Unnecessary food avoidance can adversely affect nutrition, particularly in children.⁷

Severe allergies to multiple foods and allergies to tree nuts, peanuts or seeds are less likely to resolve. Allergy to seafood, insect venom and medications is usually a lifelong problem.⁷ However it is important that any allergy is properly diagnosed.

GPs should regularly review action plans and provide re-education on adrenaline auto-injector use, also checking with the patient that the medication has not expired.

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Unusual cases of anaphylaxis in New Zealand

Contributed by Dr Richard Steele

“Pancake” anaphylaxis

Storage mites, of which multiple species are present in New Zealand, are microscopic insects that are found in stored grains (e.g. wheat and corn). Sensitisation to these mites is associated with worsening symptoms of asthma, eczema and rhinitis as well as anaphylaxis.¹ Sensitisation is most common in people living in humid environments and living near or working in grain storage facilities due to increased exposure to the mite.

Anaphylaxis to storage mite is also called “pancake” anaphylaxis, as it usually presents in patients who have eaten homemade baked goods made of flour that has been stored at home for a prolonged period of time.² Most patients have a history of atopy.³ Skin prick test or specific IgE to house dust mite is an important clue as most patients are positive due to the high cross-reactivity between storage and house dust mite. Many of the patients are also sensitive to aspirin.³ The mites can be identified through microscopic examination of the ingredient in question, although experience is required to do this and is limited in New Zealand.

Management can be problematic and is not evidence based. Patients are usually counselled to avoid homemade food containing flour.³ They are also advised to eat foods from commercial sources where the turnover of ingredients is much shorter and ingredients are less likely to become contaminated with mites. All grains and flour stored at home should be kept in sealed containers in the fridge and for a short period of time.

Anisakis in the South Pacific

Anisakis simplex is a parasite found in many New Zealand fish species and is able to infect humans.⁴ The main risk factor for infection is eating raw or partially cooked fish.⁵ Occupational exposure in fish workers has also been documented. The acute illness is usually self limiting with severe abdominal pain, vomiting and diarrhoea.⁵

In New Zealand, allergic reactions to *Anisakis* are predominantly seen in those of Pacific Island origin. The patient usually presents with acute reaction (urticaria, angioedema and anaphylaxis) after eating infected seafood. Skin and specific IgE testing to seafood is usually negative. Specific IgE to *Anisakis* is available in New Zealand, and this is usually positive. Confusion can arise as the reaction after ingestion of *Anisakis* tends to be more delayed compared to other reactions to food.

Management is essentially similar to other forms of anaphylaxis. Patients should be advised to avoid all fish and cephalopods (e.g. octopus, squid). Crustaceans (e.g. prawns, shrimps) and shellfish can usually be eaten. Avoidance is problematic as the reactions to fish usually only occur intermittently depending upon whether there is infestation. Eating fish may be an important part of life for the patient and therefore education and negotiation is very important. If the patient elects to eat fish, the risks are likely to be reduced by suggesting that only the flesh (muscle) of the fish be eaten. Whole fish and the abdominal contents of the fish should be avoided. Fish should be obtained from fresh sources, and should be gutted quickly to avoid contamination of the muscle. Heating the fish to 60°C or freezing to -20°C (for at least 48 hours) is also recommended. Although the dead parasites remain allergenic after freezing this process is likely to reduce the risk of anaphylaxis.⁶ Fresh water fish are much less likely to be parasitized unless they have been fed untreated fish waste. Injectable adrenaline should be offered to those at risk of further exposure.

Food dependant exercise induced anaphylaxis (FDEIA)

FDEIA is another form of anaphylaxis that can easily be missed. It requires two triggers; the ingestion of foods or drugs followed by some form of exercise. The symptoms can vary from mild rhinitis/urticaria to severe anaphylaxis. The history of exercise can be missed, as it can be triggered, for example, by a vigorous walk. It is more common in children, and men are affected more than women. About 40% of cases have atopy.⁷ The mechanisms for FDEIA are unknown but may involve release of mediators during exercise which reduce the threshold of mast cells to activate and increased absorption of allergens from the GI tract.⁸

The most common food trigger is wheat⁹ but a variety of other food allergens have also been implicated. Skin and specific IgE testing can be helpful in giving a clue to the suspected allergen, however the gold standard test is to ingest the food in question and exercise under medical supervision. This is clearly not without risk and in practice in New Zealand this is usually not performed. In addition, challenge tests are resource intensive and can only confirm the diagnosis of FDEIA in up to 70% of patients.

More recently it has been shown that a combination of foods, drugs and other factors maybe required to precipitate a reaction. The most important groups of drugs to consider

are NSAIDs, particularly aspirin.¹⁰ COX-2 inhibitors have been reported not to lower the threshold for anaphylaxis.¹⁰ Other reported triggers included the strength/duration/type of exercise, timing after food ingestion, alcohol, atmospheric/seasonal conditions, fatigue, sleep, infection, stress, house dust mite ingestion¹¹ and menstruation.

Management focuses on patient education. If a particular food can be pinpointed, then it should be avoided between four to six hours prior to any exercise. In many cases the combination of factors cannot be fully elucidated and some patients will react regardless of the food eaten. In this situation all food should be avoided four to six hours prior to exercise. This may not be possible for a particular patient and therefore fitting this advice into a particular lifestyle and clinical presentation is needed. Patients should be advised to carry both injectable adrenaline and antihistamines. Antihistamines are potentially useful as a prophylactic measure or to treat non-life-threatening problems such as urticaria and angioedema, but should not take the place of adrenaline in the event of anaphylaxis. Patients should also be encouraged to exercise with others and in areas where medical help is accessible. It is important to stress that most of these patients can be managed effectively and should be encouraged to exercise as part of a healthy lifestyle.

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