

18.2.2008

# **Finnish Allergy Programme 2008-2018**

## **- time to act and change the course**

**Haahtela, T <sup>1)</sup>, von Hertzen L <sup>1)</sup>, Mäkelä M <sup>1)</sup>, Hannuksela M <sup>2)</sup>, and the Allergy Programme Working Group**

<sup>1)</sup> Skin and Allergy Hospital, Helsinki University Central Hospital

<sup>2)</sup> Allergy and Asthma Federation in Finland

### **Working group**

Tari Haahtela, Matti Hannuksela, Leena von Hertzen, Marina Erhola, Minna Kaila, Ritva Kauppinen, Lola Killström, Timo Klaukka, Krista Korhonen, Antti Lauerma, Jan Lindgren, Satu Lähteinen, Mika Mäkelä, Pertti Paakkinen, Juha Pekkanen, Anne Pietinalho, Anneli Pouta, Elina Toskala-Hannikainen, Outi Vaarala, Erkka Valovirta, Erkki Vartiainen, Petra Vidgren

---

Correspondence: Professor Tari Haahtela, Skin and Allergy Hospital, Helsinki University Central Hospital, P.O. Box 160, 00029 HUCH, Finland, e-mail: [tari.haahtela@hus.fi](mailto:tari.haahtela@hus.fi)

## **Abstract**

### **Background**

The prevalence of allergic diseases has grown in Finland, similarly to many other western countries. Although the origin of allergy remains unresolved, increasing body of evidence indicates that the modern man living in urban built environment is deprived from environmental protective factors (e.g. soil micro-organisms) that are fundamental for normal tolerance development. The current dogma of allergen avoidance has not proved effective in halting the “epidemic”, and it is the Finnish consensus that restoring and strengthening tolerance should more be in focus.

### **Aim**

The national 10-year programme is aimed to reduce burden of allergies. The main goals are to 1) prevent the development of allergic symptoms, 2) increase tolerance against allergens, 3) improve the diagnostics, 4) decrease work-related allergies, 5) allocate resources to manage and prevent exacerbations of severe allergies, and 6) decrease costs due to allergic diseases.

### **Methods**

For each goal, specific tasks, tools and evaluation methods are defined. Nationwide implementation acts through the network of local coordinators (primary care physicians, nurses, pharmacists). In addition, three non-governmental organisations (NGOs) take care of the programme implementation. The 21 central hospital districts carry out a three step educational process: i) health care personnel, ii) representatives and educators of NGOs, and iii) patients and the general population. For outcome evaluation, repeated surveys are performed and health care registers employed at the beginning, at 5 years, and at the end of the programme. The process will be evaluated by an independent external body.

### **Conclusion**

The Finnish initiative is a comprehensive plan to reduce burden of allergies. The aim is to increase immunological tolerance and change attitudes to support health instead of medicalizing common and mild allergy symptoms. It is time to act, when allergic individuals are becoming a majority of Western populations and their numbers are in rapid increase worldwide. The Programme is associated with the Global Alliance of Chronic Respiratory Diseases (GARD), WHO.

## Background

Allergy is frequently a lifelong immune dysfunction affecting the quality of life and causing a lot of visits to health care, hospitalisation days, work disability and use of medication. Allergic diseases are the most common chronic disorders of children and adolescents (1). Similarly to many other western countries, prevalences of allergic diseases in Finland are high (2) (Table 1), and have, except eczema, steadily increased since the 60s' (3). Although some countries have reported that the occurrence of atopy and atopic disease have levelled off, or even decreased (4), such reversing trends have not yet been discernible in Finland. In 2007, 9% of the adults living in Helsinki reported to have doctor-diagnosed asthma (The Finnish-Estonian-Swedish Study, unpublished). Sensitisation rates to common allergens (one or more positive skin prick test result) are approaching 50%; a population study in 2003 showed that 43% of school aged Finnish children were sensitised (5), and in 2006, that was true for 47% of the adults (6).

Unravelling the mechanisms in the development of tolerance has given an impetus for revisiting the current views and dogmas in allergy. Strategies that have been used for years have not been able to halt the “allergy epidemic” and reduce the burden due to allergies. In Finland, an exception is the benefits gained with the Asthma Programme discussed below. We have to enter a new era, from mere treatment of symptoms to prevention and preventive management. The novel data challenge many of those action models that have been adopted in the health care system and the society to counteract allergies. The need for a change in Finland was recognized already in 1998 in a consensus meeting (Allergic Population –a consensus statement 1998).

In allergy, there is no straightforward trend of worsening; mild symptoms often improve, even without treatment. Mild allergy symptoms are common and resolve often gradually and spontaneously, particularly in children. The available data show that majority of children with food allergies outgrow their disease (7,8). For mild allergy, guided self-management and follow-up are generally sufficient. Extensive diagnostic examinations should be performed only if the symptoms continue, become more severe and cause disability or marked inconvenience.

Due to the high occurrence of allergic diseases in western countries, even the numbers of

patients with severe symptoms are high; the health care system should allocate resources to manage these patients. Severe symptoms additionally cause the majority of costs; preventive and good control of the disease can thus considerably reduce these costs (**Fig 1**).

### **The Finnish Allergy Programme 2008-2018**

Experience from the Asthma Programme 1994-2004 has been used to facilitate also the Allergy Programme. The burden of a chronic disease can be decisively decreased. Although signs of reversing trends in asthma prevalence have not emerged in Finland, the programme has been a major success; hospitalisation days due to asthma have decreased by 70% in relation to the number of patients, and the absolute number of individuals with disability pensions due to asthma has shrunk 76% (9). In spite of increasing prevalence, the overall costs due to asthma have levelled off and are now decreasing, contrary to what was predicted. Even annual costs per patient attributable to asthma have been reduced by 50%. The overall costs of asthma in 1993 were circa € 285 million (loss of production also taken into account) and € 230 million in 2005. According to prediction, based on the 1993 trends, the 2005 costs would have been around € 800 million (Nordic Healthcare Group 2008, unpublished).

The Finnish Asthma Programme comprised both management guidelines and an action plan with *a priori* defined tools to achieve the goals. The process and outcomes were also evaluated. The Asthma Programme has served as a model for other programmes in Finland (e.g. COPD, tuberculosis, sleep apnoea) aimed at reducing the burden of chronic diseases.

Nonetheless, allergy is a multifaceted and more complex entity than asthma. The goals and foci of the novel Allergy Programme have to target the central problems and be pragmatic as well as achievable. The background of the programme stands, not only on the most recent scientific data, but also on long clinical experience, which are equally important in pursuing a change for the better.

In the programme, strategies are chosen, goals set, and tools and evaluation methods defined (**Fig 2**). Children and families are brought into focus more than in the Asthma Programme. Allergy Programme also revisits old dogmas and attitudes. In prevention and management, “avoidance and fear of all” is not the right strategy but can lead to isolation, actions that deteriorate daily living and in the worst case, to serious reactions if exposure

occurs unexpectedly (e.g. food exposure). Avoidance of allergens will always be important, but it must have justified and precise grounds and better defined time limits. Psychosocial factors should be better addressed as they play an important role in individuals' perception of symptom severity and create also "imagined allergy".

### **Implementation and collaboration**

The Allergy Programme is an educational action plan, which takes the advantage of the contact person network created during the Asthma Programme (10). In each municipal health care centre there are asthma contact persons (in 2008, 200 physicians and 580 nurses specifically trained in asthma). Similarly in pharmacies, 695 pharmacists have been educated as asthma contact persons (94% coverage of the pharmacies in Finland). These networks will be strengthened and a new one will be created in maternity and child health clinics.

National collaborators in the Allergy Programme are the Ministry of Social Affairs and Health, the National Public Health Institute, the Social Insurance Institution, the Finnish Institute of Occupational Health, the Associations of Finnish Pharmacies, specialist associations, the Finnish Lung Health Association FILHA, and the patient organisations, the Allergy and Asthma Federation and the Pulmonary Association HELI. The last three non-governmental organisations (NGOs) are responsible for the implementation of the programme.

The Finnish initiative joins the Global Alliance of Chronic Respiratory Diseases (GARD), WHO, a voluntary alliance of national and international organisations, institutions and agencies working towards the common goal of improving global lung health (1). The Allergy Programme will also benefit from the co-operation with the European Allergy Network (GA2LEN), and the essential global guidelines and action plans, such as the Global Initiative for Asthma (GINA), and the Allergic Rhinitis and its Impact on Asthma (ARIA) (11-13). The international dimension of the Programme may help others to create better models, while learning from the successes and failures of the Finnish initiative. Preventing the increase in allergies and asthma will be a particularly important topic in areas with developing national economy (14).

## Programme Goals

The general aim is to reduce the burden due to allergy in 2008-2018, and the Programme has 6 main goals. Baseline will be 2007-2009, depending on survey.

▶ ***To prevent the development of allergy symptoms***

Prevalence of asthma, allergic rhinitis, atopic eczema and contact dermatitis is decreased by 20%.

▶ ***To increase tolerance against allergens***

Numbers of subjects on elimination diets due to food allergy are decreased by 50%.

▶ ***To improve allergy diagnostics***

All patients are tested in quality certified allergy testing centres.

▶ ***To reduce work-related allergies***

Allergic diseases defined as occupational are decreased by 50%.

▶ ***To allocate resources to manage and prevent exacerbations of severe allergies***

“Allergy Control Cards” are in use in the whole country and emergency visits due to asthma are decreased by 40%.

▶ ***To decrease costs due to allergic diseases***

Predefined costs are reduced by 20%.

For each goal, specific tasks, tools and measures for evaluation have been defined. **Tasks** are the activities or targets in pursuing the goal. **Tools** are the means by which the tasks are carried out. **Measures** are the verification sources or methods to evaluate the outcome. In the following, each goal is considered separately and specific tasks, tools and measures are presented in some detail.

### **Goal 1. Development of allergy symptoms is prevented**

#### ***Allergy health is promoted by various methods***

There have been few, if any, methods available for promotion of allergy health. We introduce here the concept of “allergy health” to mean physical, psychological and social well-being irrespective of allergy. An individual can be healthy and functional, although allergic. Allergy is recognised as an individual feature rather than illness when the condition

is minor and relative. People must be encouraged to adopt such a way of living that promotes general health and immune balance. This is especially important in children and adolescents, whose development is endorsed by balanced diet, physical activity and a close connection with the natural environment, whether allergic or not. Anti-smoking advice and legislation must be improved. Exposure of children to environmental tobacco smoke is still a problem. Efficacy of asthma medication is poor in smoking patients, and asthma patients smoke as frequently as the population as a whole (9).

Tasks	Tools	Measures
Well-being and awareness of risk factors, natural history and outcomes of the disease among individuals with allergy are improved.	Public information, education, counselling  Internet-based Allergy Library for general public - Duodecim Health Library, allergy articles, <a href="http://www.terveyskirjasto.fi">www.terveyskirjasto.fi</a> , - Allergy & Asthma Book , includes self-management guidelines  Peer activities organised by the NGOs.	Knowledge measurement of personnel in the NGOs before-after the Programme.  Surveys of the quality of life, awareness and attitudes of allergic individuals before-after the Programme.

### ***Poor air quality increases symptoms***

Indoor air is in many dwellings and workplaces unacceptably poor. In Finland, indoor temperature is generally too high and air conditioning often defective, functions inadequately or brings pollutants and particles inside. Quality issues concerning buildings remain largely unresolved. There are too many dampness-associated indoor problems, and unacceptable building practices produces such problems ever more. The urban, ambient air in Helsinki and some other cities contains too high concentrations of small particles from increasing traffic and energy production. Small particles gain access deep into the respiratory tract and body increasing the risk of illness and worsening of symptoms.

<b>Tasks</b>	<b>Tools</b>	<b>Measures</b>
Overall exposure to passive smoking is reduced.	Education, counselling, possibly legislation.	Annual survey of smoke exposure at homes and in adults (National Institute of Public Health).
Exposure of children to passive smoking is reduced.	In maternity and child health clinics parents of small children are counselled to stop smoking (Current Care Guidelines).	Survey from the journals of maternity and child health clinics before-after Programme.
Problems of damp (mouldy) dwellings are taken seriously and actively reduced.	Information, counselling, large co-operation with public health authorities, building sector and health care specialists	Annual survey of visible signs of dampness and mouldy smell in dwellings (National Public Health Institute)
Exposure to ambient air small particles is reduced.	Information, counselling how to reduce diesel exhausts, improve wood burning, reduce spring dust in cities, affect traffic and air quality politics.  Local rules and national legislation	Ambient air PM2.5 ja PM10 concentrations in bigger cities are monitored and reported.

## **Goal 2. Tolerance against allergens in population is increased**

### ***a) Tolerance is actively strengthened and avoidance reduced***

Accumulating evidence supports the view that allergen avoidance alone does not prevent the development of allergic disease (15,16), although in single cases it is of importance.

Complete avoidance is virtually impossible and cannot provide long-lasting clinical benefits, except in certain specific cases (e.g. anaphylaxis). Even a governmental campaign of food allergen avoidance targeted to atopic pregnant and breast-feeding mothers and their infants has been unable to reduce allergy (17). Instead of allergen avoidance, tolerance to allergens in population must be improved by various means. Allergen avoidance is often necessary in acute occasions of severe symptoms, but as soon as the situation has resolved, other means that strengthen tolerance should be used.

<b>Tasks</b>	<b>Tools</b>	<b>Measures</b>
Tolerance to food and inhaled allergens is promoted.	Specific preventive diets are not used.  Instructions for preventive allergen avoidance are abandoned.	Surveys of the numbers of allergy diets in day care centres and schools before-after the Programme and at 5 years.  Surveys of the use of allergen avoidance methods by allergic persons before-after the Programme.
Prevalence of allergy symptoms and their severity are decreased.	The immune system is strengthened non-specifically (e.g. with pre-probiotic products), and specifically with allergen immunotherapy (SIT and SLIT).	Surveys of the use of probiotic products before-after the Programme.  Numbers of SITs and SLITs before-after the Programme (statistics of pharmaceutical industry)
Diagnostics of mild allergy symptoms is decreased.	The health care professionals evaluate the severity of symptoms by using an Allergy Barometer.	Use of Allergy Barometer in primary health care and in specialist services before-after the Programme.  Severity evaluation survey at pharmacies.

***b) Food allergy problems are reduced***

The entity “food allergy” comprises much imagined allergy and unnecessary avoidance of foods. Proportions of children on specific diets are too high, unnecessary avoidance of foods can even be deleterious as it may endanger the child’s intake of important nutrients and distort the child’s imagine of food and healthy eating.

<b>Tasks</b>	<b>Tools</b>	<b>Measures</b>
Symptom diary is systematically used in food challenge tests.	Symptom diary freely available at internet. “Food Allergy Control Card”.	Surveys of the numbers of allergy diets in day care centres and schools before-after the Programme.
At most 10% of all children with cow’s milk allergy uses amino acid -based formulas.	Education and self-management guidelines for the patient.	Registers of special reimbursements for cow’s milk allergy.  Sales statistics.
Diets of children starting school are evaluated.  Numbers of specific diets are reduced by 50%.	Health Library at internet.  Education and guidelines for nurses in child health clinics.  General information of parents.	Inquiries of diets to parents.  Inquiries to persons responsible for catering services in workplaces and schools before-after the Programme and at 5 years.

### **Goal 3. Diagnostics of allergy is improved**

Diagnostic practices vary greatly between different testing centres in the country. Allergy testing with allergens (skin prick tests, patch tests, challenge tests) will be centralised in large hospitals and in those private units which fulfil the quality requirements and in which an allergist is responsible for testing. In **Fig 3**, examples of reading keys of skin prick testing are depicted. Skin and Allergy Hospital, Helsinki University Central Hospital, together with the Finnish Dermatological Association, is in the key position in improving the quality of allergy testing.

GA2LEN audit for the Allergy Centre of Excellence was performed 1.2.2008 in Skin and Allergy Hospital and has promoted the quality of work.

Tasks	Tools	Measures
Quality of skin testing (skin prick tests, patch tests) and interpretation of the results are improved.	Standardised testing system. “Standard operating procedures” of uniform practices. Reading keys for the 30 most important inhalant and food allergens used in skin prick tests. Certification system in testing centres. Education of personnel in the key testing centres.	Auditing of testing centres in central hospitals and in private units.
Challenge testing is performed according to previously defined guidelines and is always guided by an allergist.	Guidelines available to all testing centres. Education.	Quantity and quality of allergen challenge tests before-after the Programme.

#### **Goal 4. Occurrence of work-related allergies is decreased**

Exposure to allergens and chemicals that cause rhinitis, asthma and contact dermatitis is still common in workplaces. Exposure, however, can be reduced in many ways. Dampness problems in workplaces cause morbidity and worsening of the work atmosphere. Buildings have been closed and even wrecked due to serious microbial problems (day care centres, schools, offices etc.). “Mouldy house diagnostics” does not work at the individual level. Occupational diseases need to be redefined medicolegally. Sensitisation to chemicals causing contact dermatitis still occurs and exposure must be reduced. Patch tests are interpreted non-uniformly, depending on the tester’s and interpreter’s expertise and education.

Contact dermatitis will often resolve spontaneously in a couple of years, but the chemical that has caused the problem is avoided for unnecessarily long periods of time.

<b>Tasks</b>	<b>Tools</b>	<b>Measures</b>
Exposure to allergens causing asthma, rhinitis and contact dermatitis is reduced.	Legislation concerning the safety of workplaces nationally and internationally (EU).  Improved working methods and safety to prevent occupational allergy.	Recorded and reported changes in legislation.  Statistics of Central Hospitals and the Finnish Institute of Occupational Health.  Statistics of occupational allergic diseases.
Diagnostics of occupational asthma, rhinitis and contact dermatitis is improved.	Standardised testing methods.  Evidence –based diagnostic practices.	Annual monitoring of test results and evaluation of allergens needed in testing.
Unnecessary avoidance of allergens is recognised and reduced.	Surveillance of patch- and other tests and their performance repeatedly (e.g. a couple of years' intervals).	Monitoring of test results.
Grounds for occupational diseases are clarified.	Cooperation between the Finnish Institute of Occupational Health, specialist services and insurance companies.	Surveys of occupational allergies before-after the Programme.

## **Goal 5. Resources are allocated to severe allergies and prevention of exacerbations**

### ***a) Treatment control of asthma and rhinitis is strengthened***

The good results from the Finnish Asthma Programme 1994-2004 are further improved.

Early detection, anti-inflammatory intervention and disease control are emphasised.

Treatment problems associated with severe asthma need specific attention. Exacerbations of asthma are still a major problem and their prevention is the key for reducing both suffering and costs. Majority of asthma patients suffers from concomitant rhinitis, which must be recognised and treated at an early stage. This improves also the control of asthma. Pollen

allergy is increasing in young population and new modes of specific immunotherapy (SIT) and sublingual immunotherapy (SLIT) are employed to improve access and adherence to treatment. Diagnosis of asthma in small children needs precision, and both under- and over-diagnosics are watched. The former causes unnecessary suffering and the latter overuse of drugs.

### Adult asthma and rhinitis

<b>Tasks</b>	<b>Tools</b>	<b>Measures</b>
Proportion of patients with chronic asthma (those entitled special reimbursement for asthma medication) is decreased by 5%.	Early intervention in asthma symptoms, rhinitis, smoking and indoor air problems.  Early detection and effective treatment of inflammation.	Asthma visits in central hospitals (registers).  Use of asthma medication (registers).
70% of adult asthma remains mild.	“Asthma Control Card”.  Guided self-management -medication -physical activity -avoidance of those allergens only that clearly worsen the symptoms	Asthma Barometer in pharmacies.  Exacerbations of asthma (emergency visits, registers) before-after the Programme.  Hospitalisation days (registers).  Disability pensions (registers).
Zero tolerance to asthma deaths	Good acute treatment in emergency units.	Surveys of the skills of the personnel before-after the Programme  Asthma deaths (statistics).
Rhinitis in asthma patients is treated.	Asking rhinitis symptoms in every asthma patient.  Lung function measurements in rhinitis patients at early stages.	Surveys of the management of rhinitis in patients with asthma before-after the Programme.
Allergic rhinitis is treated better.	“Rhinitis Control Card”.  Education of health care personnel.  Guided self-management.	Surveys of the number of untreated rhinitis patients, and impact of rhinitis on quality of life.

## Childhood asthma and rhinitis

Tasks	Tools	Measures
<p>The number of asthma diagnoses in infants and young children does not increase, regional variation is reduced.</p> <p>Asthma in infants and young children is treated more accurately according to real need.</p>	<p>Previously defined guidelines (The Finnish Current Care Guidelines) are used in asthma diagnosis.</p> <p>“Asthma Control Card for Young Children”.</p>	<p>Use of medication, special reimbursements (registers).</p>
<p>When asthma diagnosis is made, rhinitis is diagnosed and treated appropriately.</p>	<p>Inquiry of symptoms.</p> <p>Treatment of rhinitis in every patient with asthma.</p>	<p>Patient record surveys.</p> <p>A specific question to the Asthma Barometer.</p>
<p>Exposure of children to tobacco smoke is reduced.</p>	<p>Anti-smoking advice to young children’s parents at maternity clinics according to the Finnish Current Care Guidelines.</p>	<p>Surveys of the maternity clinic records before-after the Programme</p>

### ***b) Treatment control of atopic eczema is strengthened***

Marked symptoms should be treated like asthma and rhinitis: take the eczema into early control, find out in the long run what treatment is needed for maintenance, and prevent exacerbations.

Patient and his/her family, even health care professionals, do not recognize what is just dry skin and what eczema that should be treated with medication. The patients and their families have only a vague idea of the severity of eczema. Many families have incorrect perception of the causes of atopic eczema. Elimination allergy diets, that have been justified in infancy, are continued without medical need. Foods that do not cause symptoms are avoided unnecessarily. Topical corticosteroids are not used properly; too mild corticosteroids are

used, and the courses are too short and stopped abruptly. Many people are afraid of using topical corticosteroids in summer.

<b>Tasks</b>	<b>Tools</b>	<b>Measures</b>
Severity and exacerbations of atopic eczema are reduced.	The Finnish Current Care Guidelines (in process). “Atopic Eczema Control Card”	Use of medication, particularly for children prescribed topical corticosteroids, topical calcineurin inhibitors and emollients (registers).  Numbers of patients that have been allowed financial support for treatment (registers).
70% of the patients and 90% of health care personnel adopt the new treatment guidelines.	Education.	Surveys in pharmacies, specialist clinics, and child health clinics, how the new guidelines have been adopted.  Surveys to members of the patient organizations.

***c) Treatment of anaphylaxis is improved***

Anaphylaxis, a serious general allergic reaction, is not either recognised or treated properly.

<b>Tasks</b>	<b>Tools</b>	<b>Measures</b>
Recognition and treatment of anaphylaxis is improved.  Guided self-management of patients with anaphylaxis risk is improved.	Information to all health care units. A booklet and a video.  “Anaphylaxis Control Card”	Hospitalisation days (registers).  Deaths from anaphylaxis (statistics).  Numbers of im. adrenalin auto-injector prescriptions (industry).
Reporting is improved.	Internet-based notification form.  Cooperation with the National Agency of Medicines (register of drug adverse reactions ).	Quality and quantity of notifications to the National Anaphylaxis Register in Skin and Allergy Hospital /HUCH, Helsinki

## **Goal 6. Costs due to allergy are reduced**

Allergies cause relatively little hospital days and long-term work disability, but load strongly maternity and child health clinics, day care centres, schools, garrisons, primary health care and occupational health care. Allergies cause a lot of short absences from work, school and day care. Asthma and allergy drugs are major sectors of medical industry and pharmacies. Allergies affect markedly food industry, hotel and restaurant business, travelling and many authority activities, such as surveillance of medicines (hypersensitivity to drugs), and other products. Allergies are associated with building sector (indoor problems), surveillance of ambient air in communities (traffic exhausts, public sanitation) and with tobacco policy. Costs due to allergies have ramifications widely in the society and are not easily calculated. It must also be borne in mind that allergies benefit considerably different sectors of business (e.g. drugs, cosmetics, building and interior materials, household appliances).

Allergies are a problematic issue from another point of view of cost evaluation; allergies can manifest in the skin, nose, eyes, respiratory tract or gastrointestinal tract, and the symptoms are not always easily differentiated from symptoms caused by other diseases. Due to this, allergies and their treatment are often inaccurately reported. Direct costs due to asthma and allergies were nonetheless recently estimated (Tolerance and its improvement in allergy; National Public Health Institute Publications B 5/2007, in Finnish, English summary). Direct costs in 2005 were € 348 million per year (circa 3% of the overall costs of health care). According to the goal 6, direct costs will be reduced by 20% by the end of the year 2018.

Tasks	Tools	Measures
Indicators that identify changes in predefined allergy-associated costs are created.	Registers and statistics of different institutions.  Population surveys.	Use and sales of antihistamines and other drugs closely associated with allergies (registers).  Numbers and costs of primary health care visits and hospitalisation days due to asthma and allergies (specific survey, registers).  Economic value of work disabilities due to asthma and allergies.

## Key messages of the Allergy Programme

- *Endorse health, not allergy.*
- *Strengthen tolerance.*
- *Adopt a new attitude to allergy. Avoid allergens only if mandatory.*
- *Recognise and treat severe allergies early. Prevent exacerbations.*
- *Improve indoor air quality. Stop smoking.*

## Implementation of the Programme

The messages and principles of the Allergy Programme are targeted to the whole population, to patients with allergy and asthma and their families, to public health and patient organisations, to experts, authorities and legislators.

The primary target groups of education and publicity are

- health care professionals, authorities and persons responsible in day care centres, schools and other educational institutions,

- key persons and peer workers in patient organisations, and
- media.

The Finnish Lung Health Association FILHA, together with the Allergy and Asthma Federation and the Pulmonary Association HELI, is responsible for coordinating the implementation. Due to the cooperation between these three NGOs with a common project organisation, the programme targets the whole population in a short time and can be implemented cost-effectively in all parts of the country.

### ***Contact person network***

There are 5 university hospital districts and 21 hospital districts in Finland. Primary health care services are provided by circa 250 primary care centres or units of municipal federations, including at least a 3-fold number of maternity and child health clinics and circa 1000 units of occupational health. One-third of the last- mentioned units are private. The private sector is in general responsible for a growing part of all health care services.

In 2008, in hospital based specialist clinics (paediatrics, pulmonary medicine), primary health care, part of the occupational sector, and pharmacies there were circa 1 500 appointed asthma contact persons (doctors, nurses, pharmacists). For the Asthma Programme this network of skilled contact persons was the key to effective implementation. These contact persons will continue their invaluable work further in the Allergy Programme, and the network is additionally completed by nurses in maternity and child health clinics.

### ***Education of health care professionals***

Health care professionals are regionally educated by the hospital district, with the involvement of provincial governments. The NGO FILHA will coordinate this education, which is performed in 2008-2010 covering the whole country. Educators are mainly the specialists in each hospital district (allergists, dermatologists, pulmonologists, rhinolaryngologists, paediatrics and specialists in primary health care as well as nurses specifically trained in the area). Education will take place in own locales of the health care during the normal office hours as part of the regular educational programmes. External experts are used according to need.

### ***Other education***

Patient organisations arrange regional education to their key persons and peer workers. This education will be temporally linked to the education of health care personnel.

The Allergy and Asthma Federation and the Pulmonary Association HELI will organise annually circa 10 public events in different parts of the country, and educate personnel in regional offices during the first three years of the programme. The patient organisations produce the material needed

- publicity material for authorities, media and population
- education material to regional offices
- education material to population (general information) and to patients (self-management material)

After this first stage, education continues to gradually target key persons in pharmacies, in day care centres and schools (phase II). During the last tertile of the Programme (phase III), the messages and principles are reinforced, and finally, the process and outcome of the Programme evaluated.

### **Evaluation**

A plan to evaluate both the process and outcome of the Programme has been produced.

#### ***Outcome (effectiveness) evaluation***

The general and social outcome of the Programme will be evaluated. Understanding and adoption of the messages and principles of the Programme are clarified in health care as well as in organisations. In addition, changes in attitudes of the patients and the general population will be assessed. The focus, however, will be on the goals; how well the goals have been achieved? Have the chosen tools and measures been relevant in this respect?

The main methods to evaluate the outcomes are:

- **Surveys** before-after (and possibly in the mid of) the Programme targeting different groups, physicians, nurses in maternity clinics and schools, customers in pharmacies,

parents of allergic children etc. The surveys need resources, and not all of the mentioned surveys will be taken, and some others will come in addition or instead. Nevertheless, the list of surveys helps to target actions, which would be helpful while evaluating the progress and results of the Programme.

- **Inquiries** of the effectiveness of education and functioning of guidelines targeting the groups in question.
- **Hospitalisation days and emergency department visits** due to allergy and asthma in 2007-09 and in 2018 (registers).
- **Costs** due to allergy and asthma medication, daily allowances paid by sickness insurance for allergies and asthma, disability pensions and rehabilitation due to allergy and asthma in 2007-09 and 2018 (registers)
- **Monitoring of treatment costs** before-after the programme in randomly chosen units representing different types and sizes of health care units.

### ***Process evaluation***

Evaluation of the process will be performed by an independent external body (Helsinki University).

### ***Overall evaluation***

In the overall evaluation, the results from both process and outcome evaluation are considered. At the beginning of the Programme in 2008-09, a baseline clarification by interviewing the key persons in the Programme is performed to get a view of their expectations and thoughts concerning the Programme. In 2018, this interview is repeated. Effectiveness of publicity and education targeted to patients and the whole population will be additionally assessed using questionnaires.

## **Scientific background of the Programme**

### ***Tolerance***

In allergy, the key issue is the impaired tolerance against allergens and irritants due to defective immune regulatory mechanisms. At the population level, the role of and guidance for allergen avoidance has been debated, and inducing or restoring tolerance to allergens in one way or another has become a hot topic.

To develop normally, the mucosal immune system needs challenges which the modern sedentary lifestyle in urban built environment does not provide. Especially exposure to saprophytic micro-organisms/commensals via the skin, respiratory tract and, particularly the gut appears to be decisive for maintaining epithelial homeostasis and tolerance (18). Continuous exposure to saprophytes that have co-existed with man since ancient times does not elicit proinflammatory defence mechanisms, but instead, seems to induce the regulatory network associated with tolerance (19). Impaired function of this regulatory network may then lead to immune-mediated diseases including asthma, allergies, type 1 diabetes and inflammatory bowel disease. The regulatory network comprises most importantly regulatory T (T reg) cells and dendritic cells and the cytokines secreted by them (20-23). Data are accumulating that the balance between T reg cells and T effector cells has tottered in patients with allergies (24-26), or the function of T reg cells may be defective (25), implicating that the Treg cell function and/or Treg/T effector cell balance in these individuals must be restored by using novel innovative methods.

In addition to impaired physiological tolerance, even the psychological tolerance in population has been weakened. Fear of allergy or pseudoallergy, that are not uncommon today, must be dispelled.

### ***Strengthening or restoring of tolerance***

Tolerance can be strengthened, even restored, as shown by treating allergic individuals with specific immunotherapy (SIT) or, more recently, by sublingual immunotherapy SLIT, which target the regulatory network and restore the balance between T reg and T effector cells (27,28).

Crucial factors in the development of tolerance and in the responses produced via TLR activation in general are the dose and frequency of allergen exposure, the nature of allergen, and factors specific to host cells (29). As to the dose of allergen, a large body of data now show that in many cases, the dose-response relationship follows a bell-shaped curve (**Fig 4**); increasing exposure at relative low doses is associated with increasing frequency of symptoms/disease, whereas after a plateau, increasing exposure induces tolerance. Such a non-linear relationship has been found e.g. for bee venom allergen (30), cat, mite, rat,

mouse allergens (16, 31-33) and for endotoxin (34), suggesting that this bell-curve is a rather universal phenomenon for different allergens/bioparticles.

### *Continuous exposure to antigens is necessary*

The fundamental role of continuous exposure to commensals and saprophytes in the development and maintenance of tolerance has become increasingly clear. Rakoff-Nahoum et al. (18) were among the first to show that recognition of commensal flora by TLRs is necessary for the development and maintenance of mucosal homeostasis and tolerance, a finding that have been corroborated thereafter by others (35,36). Most recently, Hedl et al. (37) showed an important role for the breakdown product of peptidoglycan, muramyl dipeptide, and its receptor NOD2, in inducing non-specific tolerance in human intestinal macrophages. Much of the novel experimental data of mucosal homeostasis/tolerance and antigen exposure has indeed been obtained from studies exploring intestinal cells. The findings are evidently relevant also for inhalant allergens, as it has been shown that the majority of allergens after aerosol administration are found in the gut (38)

Other lines of evidence of the importance of continuous antigen stimulation in the development of tolerance come from epidemiology. Numerous studies of farm children consistently show that living in a microbe-rich environment confers protection against allergic disease (39). An analysis of house dusts in Finland and Russia using advanced methods showed that dust samples obtained from Russian Karelia, a microbe-rich area with low occurrence of atopic diseases, contained mostly gram-positive bacteria, whereas in Finland, majority of the dust bacteria were of the gram-negative lineage (Pakarinen, unpublished). This is in line with the concept that in soil and natural environment, gram-positive bacteria predominate (39,40).

Much attention has during the last few years been devoted to farm milk (41,42), as it has shown a particularly strong protective effect against allergies. The microbiota in fresh farm milk is similarly predominated by gram-positive bacteria (43). Moreover, in normal flora of the healthy skin and respiratory mucosa (44,45), even in the gut using advanced methods (46), gram-positive bacteria seem to predominate. Indeed, TLR2 and NOD2, the receptors of cell wall components rich in gram-positive bacteria (teichoic and lipoteichoic acids, peptidoglycan and its degradation fragments) have been particularly associated with the development of tolerance (37,47,48), in addition to TLR9, which also appears to be

important in this respect (36, 49). The question of a distinctive role of gram-positive bacteria in conferring protection against allergic diseases has been raised already in 2001 in a study of fecal flora of allergic and non-allergic children (50).

In sum, sustained adequate exposure to microbial antigens in terms of quantity, composition and diversity seems to be necessary for the normal development and maintenance of mucosal tolerance. This tolerance is apparently non-specific via the by-stander effect and actions of regulatory cytokines (22,51).

## References

1. Global surveillance, prevention and control of chronic respiratory disease: a comprehensive approach. Bousquet J, Khaltaev N (eds). Geneva: World Health Organization, 2007.
2. Allergia. Haahtela T, Hannuksela M, Mäkelä M, Terho EO (eds) (in Finnish). Jyväskylä: Duodecim, 2007.
3. Latvala J, von Hertzen L, Lindholm H, Haahtela T. Trends in prevalence of asthma and allergy in Finnish young men: a nationwide study from 1966 to 2003. *BMJ* 2005;330:1186-87.
4. von Hertzen L, Haahtela T. Reversing trends in the prevalence of asthma. *Allergy* 2005;60:283-92.
5. von Hertzen LC, Mäkelä MJ, Petäys T, Jousilahti P, Kosunen TU, Laatikainen T, Vartiainen E, Haahtela T. Growing disparities in atopy between the Finns and the Russians – a comparison of two generations. *J Allergy Clin Immunol* 2006;117:151-57.
6. Pallasaho P, Rönmark E, Haahtela T, Sovijärvi AR, Lundbäck B. Degree and clinical relevance of sensitization to common allergens among adults: a population study in Helsinki, Finland. *Clin Exp Allergy* 2006;36:503-09.
7. Bischoff SC, Mayer JH, Manns MP. Allergy and the gut. *Int Arch Allergy Immunol* 2000;121:270-83.
8. Brandtzaeg P. Current understanding of gastrointestinal immunoregulation and its relation to food allergy. *Ann NY Acad Sci* 2002;964:13-45.
9. Haahtela T, Tuomisto LE, Pietinalho A, Klaukka T, Erhola M, Kaila M, Nieminen MM, Kontula E, Laitinen LA. A 10 year asthma programme in Finland: a major change for the better. *Thorax* 2006;61:663-70.
10. Asthma Programme in Finland 1994-2004. Ministry of Social Affairs and Health. *Clin Exp Allergy* 1996;26 (suppl 1):1-24.
11. Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, FitzGerald M, Gibson P, Ohta K, O'Byrne P, Pedersen SE, Pizzichini E, Sullivan SD, Wenzel SE, Zar HJ. Global strategy for asthma management and prevention: GINA executive summary. *Eur Respir J* 2008;31:143-78.
12. Bousquet J, van Cauwenberge P, Khaltaev N; Aria Workshop Group; World Health Organisation. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001;108(5 Suppl):S147-334.
13. Cruz AA, Popov T, Pawankar R, Annesi-Maesano I, Fokkens W, Kemp J, Ohta K, Price D, Bousquet J; ARIA Initiative Scientific Committee. Common characteristics of upper and lower airways in rhinitis and asthma: ARIA update, in collaboration with GA(2)LEN. *Allergy*. 2007;62 Suppl 84:1-41.
14. Pearce N, Ait-Khaled N, Beasley R, Mallol J, Keil U, Mitchell E, Robertson C. Worldwide trends in the prevalence of asthma symptoms: phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2007;62:757-65.
15. Marks GB, Mhrshahi S, Kemp AS, Tovey ER, Webb K, Almquist C, Ampon RD, Crisafulli D, Belousova EG, Mellis CM, Peat JK, Leeder SR. Prevention of asthma during the first 5 years of life: A randomised controlled trial. *J Allergy Clin Immunol* 2006;118:53-61.
16. Cullinan P, MacNeill SJ, Harris JM, Moffat S, White C, Mills P, Newman Taylor AJ. Early allergen exposure, skin prick responses, and atopic wheeze at age 5 in English children: a cohort a study. *Thorax* 2004

17. Hourihane JO, Aiken R, Briggs R, Gudgeon LA, Grimshaw KE, DunnGalvin A, Roberts SR. The impact of government advice to pregnant mothers regarding peanut avoidance on the prevalence of peanut allergy in United Kingdom children at school entry. *J Allergy Clin Immunol* 2007;119:1197-202.
18. Rakoff-Nahoum S, Paglino J, Eslami-Varzaneh F, Edberg S, Medzhitov R. Recognition of commensal microflora by toll-like receptors is required for intestinal homeostasis. *Cell* 2004;118:229-41.
19. Rook GA, Adams V, Hunt J, Palmer R, Martinelli R, Rosa Brunet L. Mycobacteria and other environmental organisms as immunomodulators for immunoregulatory disorders. *Spinger Semin Immun* 2004;25:237-55.
20. Shevach EM. From vanilla to 28 flavors: multiple varieties of T regulatory cells. *Immunity* 2006;25:195-201.
21. Cools N, Ponsaerts P, Van Tendeloo VFI, Berneman ZN. Balancing between immunity and tolerance: an interplay between dendritic cells, regulatory T cells, and effector T cells. *J Leukoc Biol* 2007;82:1365-74.
22. Hubert P, Jacobs N, Caberg JH, Boniver J, Delvenne P. The cross-talk between dendritic and regulatory T cells: good or evil? *J Leukoc Biol* 2007;82:781-94.
23. Manke K, Johnson TS, Ring S, Enk AH. Tolerogenic dendritic cells and T reg cells: A two-way relationship. *J Dermatol Sci* 2007;46:159-67.
24. Akdis M, Verhagen J, Taylor A, Karamloo F, Karaginnidis C, Cramer R, Thunberg S, Deniz G, Valenta R, Fiebig H, Kegel C, Disch R, Schmidt-Weber CB, Blaser K, Akdis CA. Immune responses in healthy and allergic individuals are characterized by a fine balance between allergen-specific T regulatory 1 and T helper 2 cells. *J Exp Med* 2004;199:1567-75.
25. Hartl D, Koller B, Mehlhorn T, Reinhardt D, Nicolai T, Schendel D, Griese M, Krauss-Etschmann S. Quantitative and functional impairments of pulmonary CD4<sup>+</sup>CD25<sup>hi</sup> regulatory T cells in pediatric asthma. *J Allergy Clin Immunol* 2007;119:1258-66.
26. Ling EM, Smith T, Nguyen XD, Pridgeon C, Dallman M, Arbery J, Carr VA, Robinson DS. Relation of CD4<sup>+</sup>CD25<sup>+</sup> regulatory T cell suppression of allergen-driven T cell activation to atopic status and expression of allergic disease. *Lancet* 2004;363:608-15.
27. Akdis M, Akdis CA. Mechanisms of allergen-specific immunotherapy. *J Allergy Clin Immunol* 2007;119:780-89.
28. Schmidt-Weber C, Blaser K. New insights into the mechanisms of allergen-specific immunotherapy. *Curr Opin Allergy Immunol* 2005;5:525-30.
29. Kanzler H, Barrat FJ, Hessel EM, Coffman RI. Therapeutic targeting of innate immunity with Toll-like receptor agonists and antagonists. *Nat Med* 2007;13:552-559.
30. Müller UR. Bee venom allergy in beekeepers and their family members. *Curr Opin Allergy Clin Immunol* 2005;5:343-47.
31. Holt PG, Thomas WR. Sensitization to airborne environmental allergens: unresolved issues. *Nat Immunol* 2005;6:957-60.
32. Jeal H, Draper A, Harris J, Taylor AN, Cullinan P, Jones M. Modified Th2 responses at high-dose exposures to allergen – Using an occupational model. *Am J Respir Crit Care Med* 2006;174:21-25.
33. Matsui EC, Eggleston PA, Breyse PN, Rand PN, Diette GB. Mouse allergen-specific antibody responses in inner-city children with asthma. *J Allergy Clin Immunol* 2007;119:910-15.
34. Braun-Fahrlander C, Riedler J, Herz U, Eder W, Waser M, Grize L, Maisch S, Carr D, Gerlach F, Bufe A, Lauener R, Schierl R, Renz H, Nowak D, von Mutius E. Environmental exposure to endotoxin and its relation to asthma in school age children. *N Engl J Med* 2002;347:869-77.

35. Araki A, Kanai T, Ishikura T, Makita S, Uraushihara K, Iiyama R, Toysuka T, Takeda K, Akira S, Watanabe M. MyD88-deficient mice develop severe intestinal inflammation in dextran sodium sulfate colitis. *J Gastroenterol* 2005;40:16-23.
36. Rachmilewitz D, Katakura K, Karmeli F, Hayashi T, Reinus C, Rudensky B, Akira S, Takeda K, Lee J, Takabayashi K, Raz E.. Toll-like receptor 9 signaling mediates the anti-inflammatory effects of probiotics in murine experimental colitis. *Gastroenterology* 2004;126:520-28.
37. Hedl M, Li J, Cho JH, Abraham C. Chronic stimulation of NOD2 mediates tolerance to bacterial products. *Proc Natl Acad Sci* 2007;104:19440-45.
38. Willoughby JB, Willoughby WF. In vivo responses to inhaled proteins. I. Quantitative analysis of antigen uptake, fate and immunogenicity in a rabbit model system. *J Immunol* 1977;119:2137-46.
39. von Hertzen L, Haahtela T. Disconnection of man and the soil: implication for the asthma and allergy epidemics? *J Allergy Clin Immunol* 2006
40. Gisi U, Schkendel R, Schulin R, Standelmann F, Sticker H. *Bodenökologie*. Stuttgart: Georg Thieme Verlag, 1997
41. Waser M, Michels KB, Bieli C, Flöistrup H, Pershagen G, von Mutius E, Ege M, Riedler J, Schram-Bijkerk D, Brunekreef B, van Hage M, Lauener R, Braun-Fahrlander C. Inverse association of farm milk consumption with asthma and allergy in rural and suburban populations across Europe. *Clin Exp Allergy* 2007;37:661-70.
42. Perkin MR, Strachan DP. Which aspects of the farming lifestyle explain the inverse association with childhood allergy? *J Allergy Clin Immunol* 2006;117:1374-81.
43. Frank JF, Hassan AN. Micro-organisms associated with milk. In: *Encyclopedia of Dairy Sciences*. Roginski H, Fuquay JW, Fox PF (eds). San Diego:Academic Press, 2003, pp. 1786-96.
44. Tannock GW. *Normal microflora. An introduction to microbes inhabiting the human body*. London: Chapman & Hall, 1995.
45. Gao Z, Tseng C, Pei Z, Blaser M. Molecular analysis of human forearm superficial skin bacterial biota. *Proc Natl Acad Sci* 2007;104:2927-32.
46. Zoetendal EG, Vaughan EE, de Vos WM. A microbial world within us. *Molec Microbiol* 2006;59:1639-50.
47. Suttmuller RP, den Brok MHM, Kramer M, Bennink EJ, Toonen LW, Kullberg BJ, Joosten LA, Akira S, Netea MG, Adema GJ. Toll-like receptor 2 controls expansion and function of regulatory T cells. *J Clin Invest* 2006;116:486-94.
48. Taylor RC, Richmond P, Upham JW. Toll-like receptor 2 ligands inhibit Th2 responses to mite allergen. *J Allergy Clin Immunol* 2006;117:1148-54.
49. Moseman EA, Liang X, Dawson AJ, Panoskaltis-Mortari A, Krieg AM, Liu YJ, Blazar BR, Chen W. Human plasmacytoid dendritic cells activated by CpG oligodeoxynucleotides induce the generation of CD4+CD25+ regulatory T cells. *J Immunol* 2004;173:4433-32.
50. Kirjavainen P, Apostolou E, Arvola T, Salminen SJ, Gibson GR, Isolauri E. Characterizing the composition of intestinal microflora as a prospective treatment target in infant allergic disease. *FEMS Immunology and Medical Microbiology* 2001;32:1-7.
51. Botturi K, Vervloet D, Magnan A. T-cells and allergens relationship: are they that specific? *Clin Exp Allergy* 2007;37:1121-23.

Table 1. Estimated prevalences of allergic conditions in Finland in the 2000's (modified from ref 2). SPT= Skin Prick Test.

---

	%
Adult asthma	8-10
Childhood asthma	5
Asthma-like symptoms	5-10
Allergic rhinitis (seasonal and perennial)	30
Hay fever (pollen allergy)	20
Allergic conjunctivitis	15
Atopic eczema	10-20
Urticaria	7
Contact dermatitis	8-10
Food allergy (adults)	2-5
Food allergy (children)	5-10
Drug hypersensitivity	2
Insect hypersensitivity	2
Light hypersensitivity	15-20
Allergy to animals	15
At least one positive SPT result (adults)	47
Allergy in family	30
Use of asthma or allergy medication (past 12 mo)	35

---

## Legends for the figures

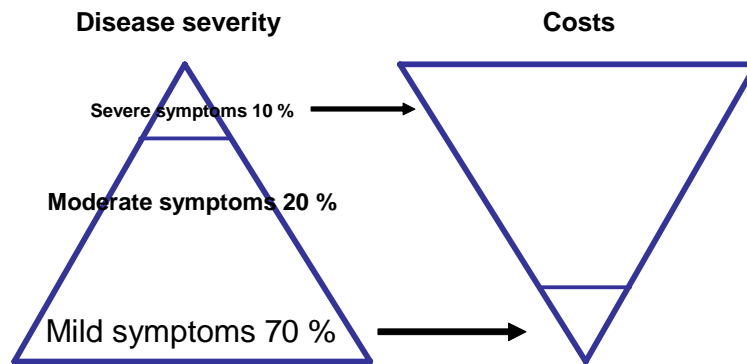
**Fig. 1.** The schematic allergy pyramid. Most of the allergy symptoms are mild and intermittent, but due to the high allergy prevalence, severe symptoms are also common and cause majority of the costs.

**Fig. 2.** The strategic planning of the Finnish Allergy Programme 2008-2018.

**Fig. 3.** Examples of the reading keys of skin prick tests. The wheal diameter is illustrated on the X-axis, and the percentage of subjects suffering from actual symptoms on the Y-axis. A positive skin prick test result does not equal to clinically significant allergy, it is a sign of exposure and IgE-associated sensitization, but must be related to symptoms history. The test does not make the patient allergic, e.g. foods should not be eliminated from the diet on the basis of the test result only.

**Fig. 4.** The bell-shaped curve for the dose-response relationship between occurrence of atopic diseases/symptoms and the dose of exposure to an allergen or bioparticle.

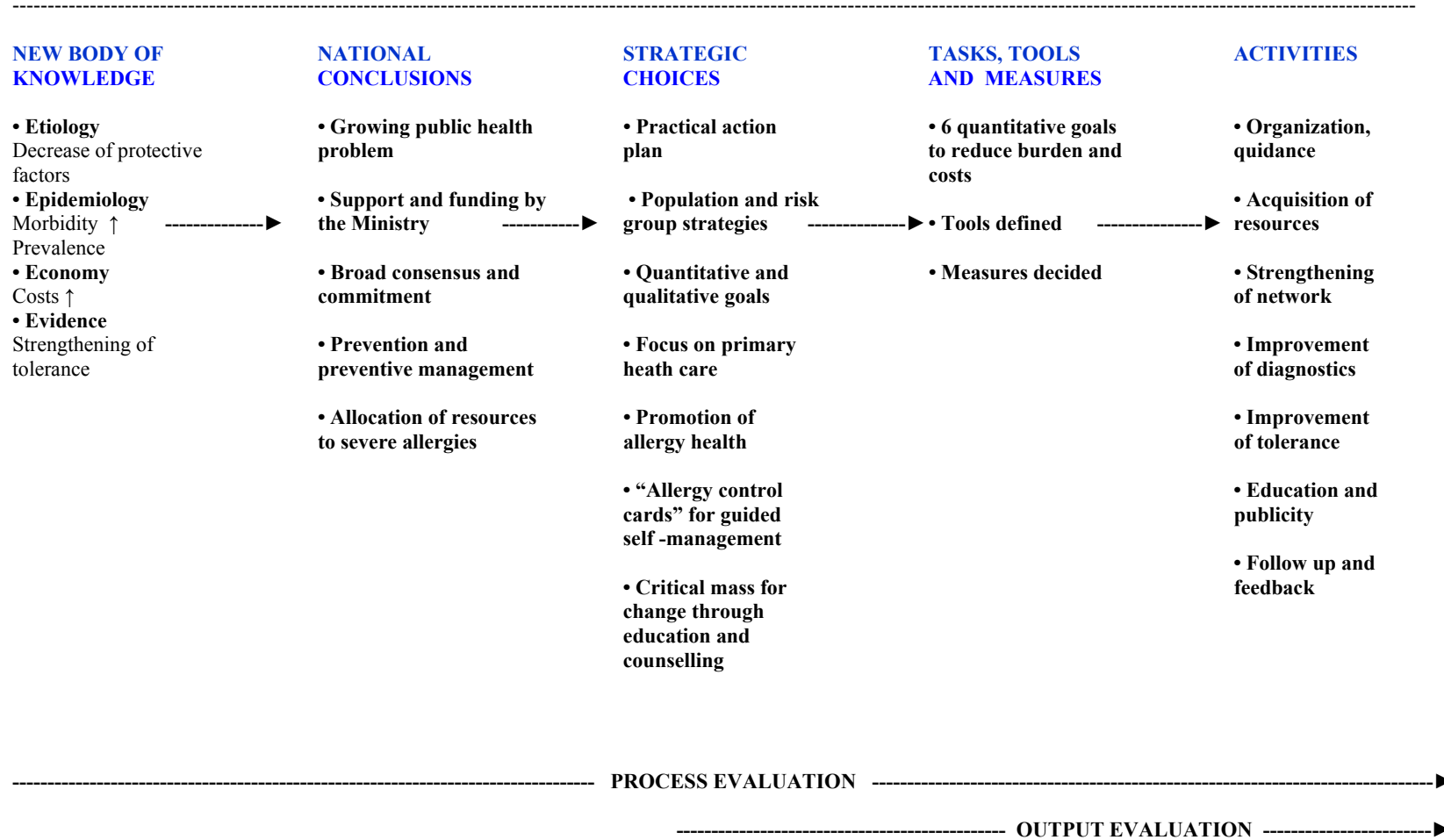
**Fig. 1.** The schematic allergy pyramid. Estimate of the relative severity of allergy symptoms and costs. Most of the symptoms are mild and intermittent, but due to the high allergy prevalence, severe symptoms are also common and cause majority of the costs.



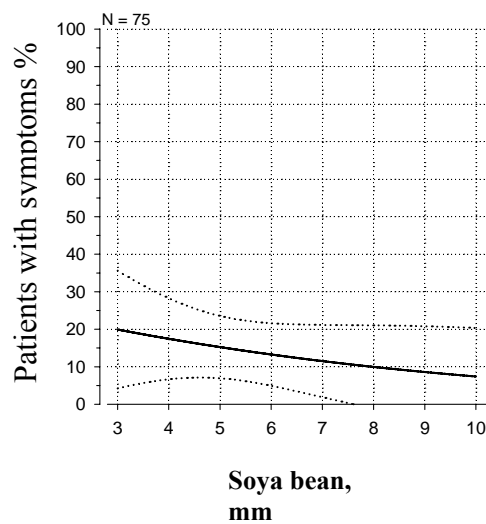
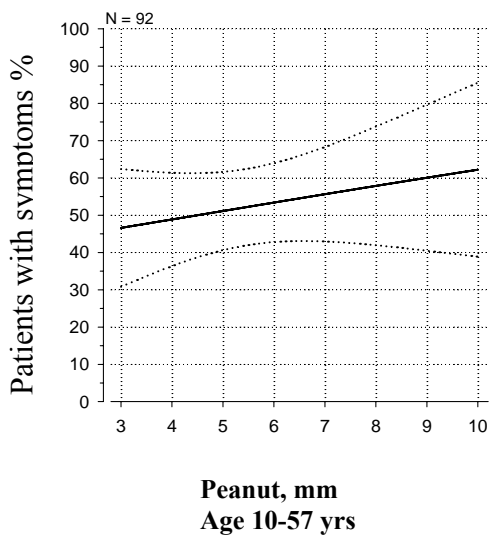
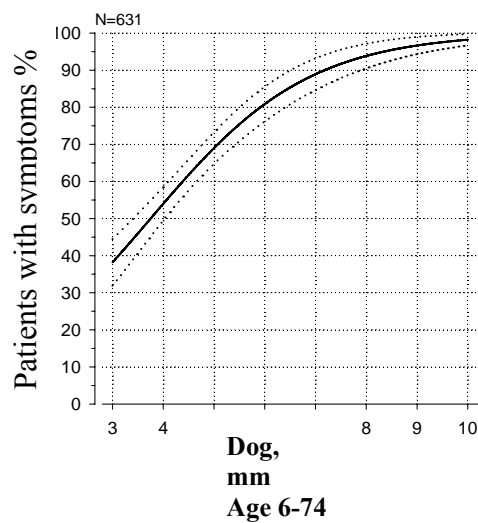
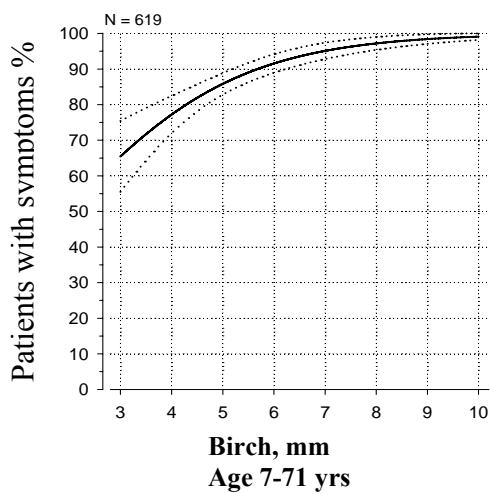
**Fig. 2.** The strategic planning of the Finnish Allergy Programme 2008-2018

**BACKGROUND**

**PROGRAMME**



**Fig. 3.** Examples of the reading keys of skin prick tests. The wheal diameter is illustrated on the X-axis, and the percentage of subjects suffering from actual symptoms on the Y-axis. A positive skin prick test result does not equal to clinically significant allergy, it is a sign of exposure and IgE-associated sensitization, but must be related to symptom history. The test does not make the patient allergic, e.g. foods should not be eliminated from the diet on the basis of the test result only.



**Fig. 4.** The bell-shaped curve for the dose-response relationship between occurrence of atopic diseases/symptoms and the dose of exposure to an allergen or bioparticle.

