

Integrated Allergy and Asthma Prevention and Care: Report of the MeDALL/AIRWAYS ICPs Meeting at the Ministry of Health and Care Services, Oslo, Norway

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Key Words

Allergy · Asthma · EIP on AHA · MeDALL · AIRWAYS ICPs · GARD

Abstract

Allergic diseases and asthma are increasing in prevalence globally. They can start early in life and many persist. It is important to prevent, detect and control these diseases early on and throughout life, so as to promote active and healthy ageing. The translational activities of MeDALL (Mechanisms of the Development of Allergy; EU FP7) are of great importance and include the deployment of successful allergy programmes.

The Finnish Allergy Plan is a prototype for the prevention and control of severe allergic diseases. It has been considered for deployment to Norway by the Ministry of Health and Care Services in the frame of AIRWAYS ICPs (Integrated Care Pathways for Airway Diseases), a programme of Action Plan B3 of the EIP on AHA (European Innovation Partnership on Active and Healthy Ageing). Deployment of the Finnish and Norwegian Plans will make use of the scaling-up strategy of the EIP on AHA in regions in the European Union, and the WHO GARD (Global Alliance against Chronic Respiratory Diseases) globally. The regional deployment in Norway serves as a model of a national plan for the use of the EIP on AHA scaling-up strategy in other regions.

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Introduction

Allergic diseases are increasing in prevalence and severity globally. They start early in life and many persist throughout the life cycle. They include rhinitis, asthma, atopic eczema and diseases associated with food allergy. Although control has been achieved with many patients, there are needs that have not yet been met including the prevention and the management of severe disease [1]. Moreover, allergic diseases should be diagnosed and managed early in childhood in order to promote active and healthy ageing [2]. The concept that health and disease can be influenced by factors that often start early in childhood and manifest at various periods throughout the life cycle has an important bearing on the management of allergic diseases.

Since 2008, 'a new day has begun' [3] because an innovative Allergy Plan was endorsed by the Finnish Ministry of Social Welfare and Health following the successful Asthma Plan, designed to shift the paradigm of allergic diseases by focussing on the prevention and control of severe diseases [4]. This integrated programme has been operative in Finland and the first results, allowing a proof-of-concept, are encouraging enough to promote its deployment to other countries [5]. The MeDALL (Mechanisms of the Development of Allergy) Work Package 10 proposed the deployment of the Finnish Allergy Plan to other countries [6].

We report here on a meeting organized at the Ministry of Health and Care Services, Oslo, Norway, at which the following issues were discussed: (1) how the Finnish Allergy Plan can be deployed in Norway as part of the Norwegian Public Health Programme and (2) how this expertise can be used to scale up the programme with AIRWAYS ICPs (Integrated Care Pathways for Airway Diseases) [7] and the EIP on AHA (European Innovation Partnership on Active and Healthy Ageing) [8] in Europe, and the WHO GARD (Global Alliance against Chronic Respiratory Diseases) [9] globally. The meeting was co-organised by MeDALL and AIRWAYS ICPs.

MeDALL

MeDALL (EU FP7-CP-IP; project No. 261357; 2010–2015) was launched to generate novel knowledge on the mechanisms of the initiation of allergy in early childhood to young adulthood, in order to propose early prediction, diagnosis, prevention and targets for therapy [6, 10]. The

MeDALL design was based on a novel, step-wise, large-scale and integrative approach led by experts in the fields of allergy, epidemiology, allergen biochemistry, immunology, molecular biology, epigenetics and genomics, functional genomics, bioinformatics and computational and systems biology. It has combined the strengths of previous and ongoing projects in the European Union, and linked epidemiological and clinical research [11] with experimental and animal models. The MeDALL study population includes about 44,000 children from 14 birth cohorts spread across Europe, making this study unique, in terms of the geographical variability and a wealth of prospectively collected data on phenotypes, lifestyles and exposures in the first 2 decades of life. The MeDALL project was organized as 12 work packages developed by a consortium encompassing 23 public and private institutions and including 3 European small and medium enterprises.

The main achievements of MeDALL include (1) the description of the inter-relationships between asthma, rhinitis and eczema and comorbidity [12], with these phenotypes being defined according to MeDALL-agreed, expert-based definitions and (2) the classification of these entities into novel phenotypes by means of unsupervised cluster analysis. A major MeDALL effort has been a harmonized follow-up of all the participating birth cohorts [11, 13], with this follow-up and historical databases being integrated in knowledge-based management. The latter also integrates the results of the experimental work packages which used samples from the birth cohorts. The characterization of IgE and IgG responses in children from birth to adolescence is being performed with the MeDALL chip which contains more than 170 allergens [14]. This analysis holds great promise for the identification of the components predictive of disease severity or prognosis [15]. To further understand the mechanisms explaining the distribution of allergic diseases from birth to adolescence, MeDALL is performing epigenetic, proteomic and transcriptomic studies on the birth cohort samples. Initial findings in the discovery-based phase are currently being replicated in a large number of samples. Analytical strategies to integrate the different omics studies are being explored. To complement mechanistic experimental studies on children, MeDALL has included *in vitro* studies and *in vivo* animal studies. Relevant ethical and societal issues on allergic diseases are being internationally debated within MeDALL. Ultimately aiming to improve the health of European citizens, MeDALL includes a translational work package to reinforce its impact.

Public Health Policy in Norway

The public health policy in Norway is determined by the Public Health Act and the Public Health Report which are updated every 2 years (e.g. 2013 and 2015) [16] and include several principles of public health:

- Health equities which arise for the societal conditions in which people are born, grow, live and age. Levelling up the gradient of health inequities throughout society by acting on social determinants of health is a core public objective in order to distribute fairly limited resources.
- Health in all policies: equitable health systems are important to public health, but health inequities arise from societal factors beyond health care. The impact on health should be considered when policies and actions are developed and implemented in all sectors.
- Joined-up governance and inter-sectoral actions are vital for the reduction of health inequities.
- Sustainable development meets the needs of the present without compromising the ability of future generations to meet their own needs. Public health work is based on a long-term perspective.
- Precautionary principles need to be enforced if an action or policy has a suspected risk of causing harm to the public or the environment. The absence of scientific consensus that the action is harmful cannot justify postponing action to prevent such harm.
- Participation: public health work should be transparent and inclusive of process with participation by multiple stakeholders. The promotion of civil society participation is a key factor for good public health policy development.

The Public Health Report has stratified the responsibilities to local (municipality), regional (county) and national levels. Municipalities and counties are key stakeholders, but the responsibility to support them on a national level is clear. The responsibility of public health work has been moved from the Health Services sector to the municipalities. A regulation passed in June 28, 2012, emphasized that municipalities are to have a continuous overview of the health status of their populations and the determinants of health. They are to define public health challenges and strategies as well as implementing measures to fulfil these.

Local health reports, available to the public and updated once every 4 years, are collected by the Public Health Institute. Annual systematic planning with the municipalities proposes concrete goals and adjusts plans according to local challenges and opportunity structures.

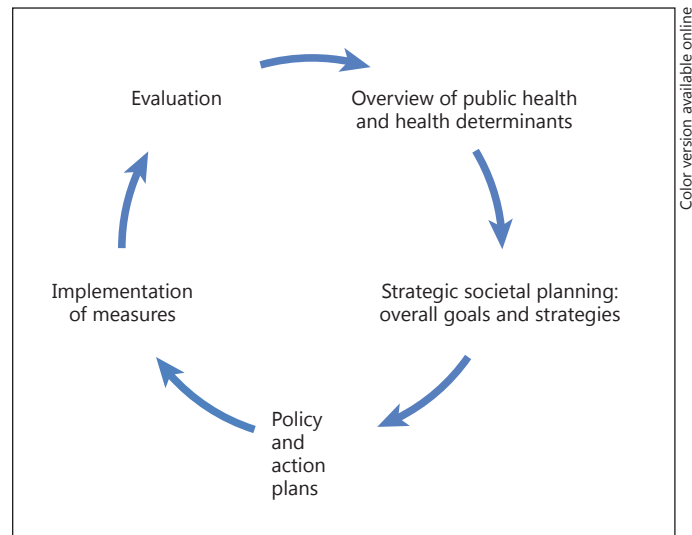


Fig. 1. Systematic public health work.

Measures should address social determinants (including housing, education, employment and income), social and physical environmental issues and health-related behaviours.

An evaluation of stated goals, strategies and efforts should be conducted for each planning period as part of the internal quality assessment. An annual review of all public health efforts should be undertaken by the elected municipal council (fig. 1).

The Public Health Report has developed a National Burden of Disease Evaluation based on data obtained across the country, in order to (1) facilitate a more systematic use of public health economies and (2) develop performance targets and indicators to be able to monitor the objectives of the public health policy and present a white paper to Parliament every year (fig. 2). The 2013 Public Health Report took developing environments and communities, environment and active and healthy ageing into consideration.

Rationale and First Results of the Finnish Allergy Plan

The asthma death epidemic of the 1980s has abated and, in most, but not all, European countries, death rates due to asthma (1,164 deaths in 2012) are quite low (European short list: cause of death statistics; source: www.gbe-bund.de). A similar trend of a reduction in hospitalisations due to asthma can be observed. Certain national

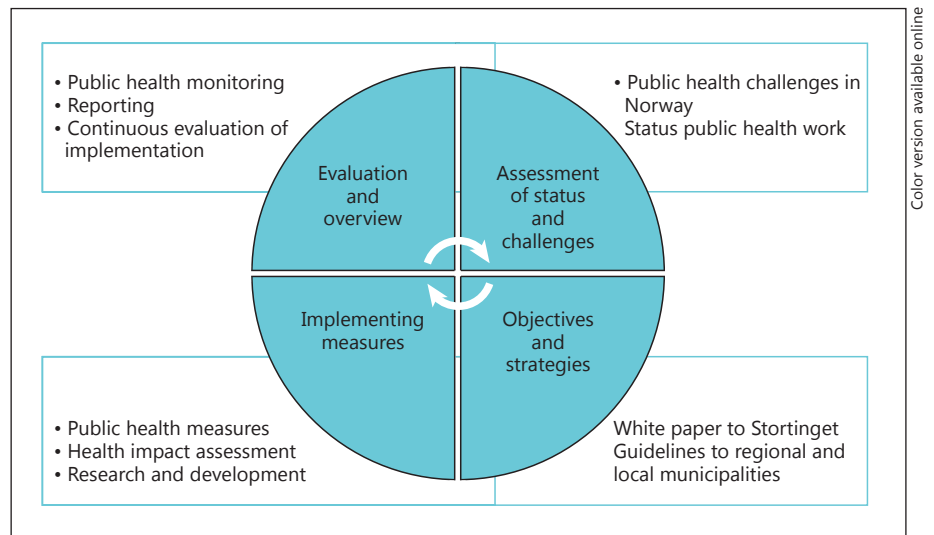


Fig. 2. White paper.

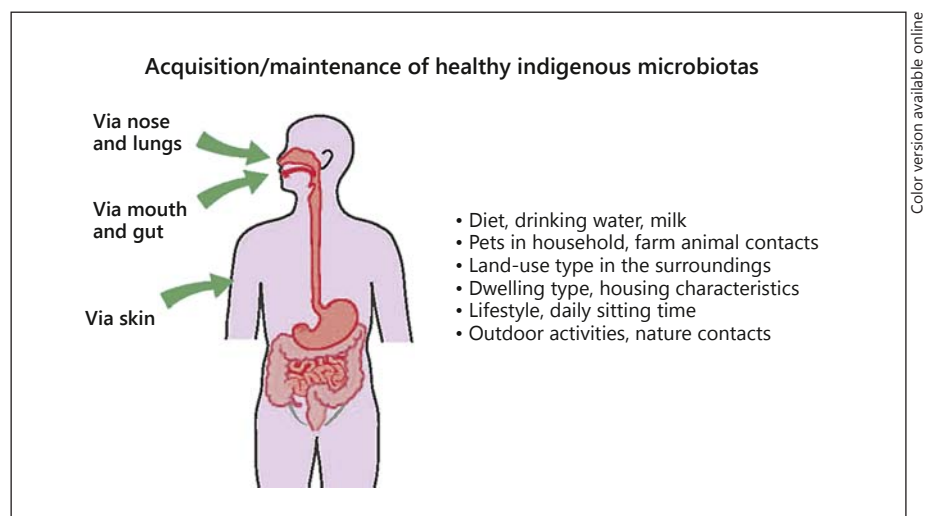


Fig. 3. Acquisition/maintenance of healthy indigenous microbiotas. Printed with permission [21].

plans such as the Finnish Asthma Plan (1994–2004) [17] have been found to be cost-effective but are insufficiently deployed, even in Europe. Thus, there are still many patients suffering from severe disease. An efficient strategy for the large-scale prevention of allergy and asthma has not yet been demonstrated as being effective or feasible. However, there is sufficient evidence to support changes in habits that have the potential to be effective at a low cost and with a low risk of harm.

The ongoing Finnish Allergy Plan (2008–2018) was developed in order to reduce the severity of allergic diseases and as an attempt to prevent them. The plan was based on studies showing that environmental factors may promote or reduce the onset of allergy. The example of

Karelia is worthy of note [18]. In the Russian Karelia, allergy has not increased in the past 50 years, but in Finland, it has boomed. Although the reasons for the differences are not fully understood, they may be related to biodiversity [19]. Along the same lines, it has been established that green areas around homes reduce allergic sensitization [20]. There is greater biodiversity in the Russian Karelia, both at the macro- and micro-level, than in the Finnish part. Microbiome studies suggest that IgE sensitization is associated with a decrease in microbial abundance and diversity [21]. These data propose that environmental biodiversity, human microbiota and allergy are inter-related [22]. Constant exposure to ‘non-danger’ signals (commensals) leads to making the difference between

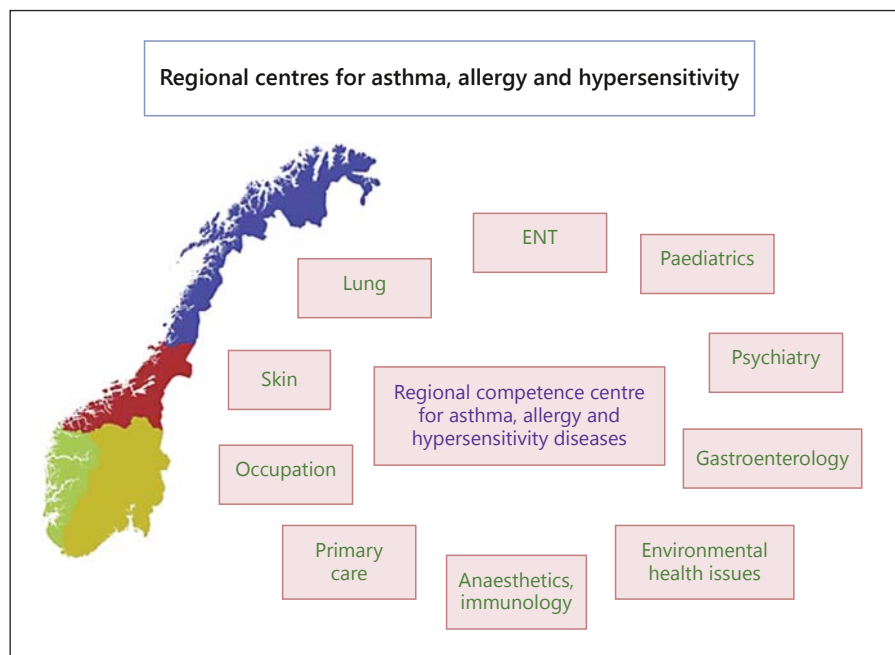


Fig. 4. Regional competence network for the implementation of the Norwegian Allergy Plan. ENT = Ear, nose and throat.

good and bad (danger vs. non-danger, self and non-self), preventing inappropriate inflammatory responses. The causes of allergy appear to be complex, but the solutions may prove to be simpler (fig. 3) [21].

The Finnish Allergy Plan is based on 5 key messages: (1) endorse health not allergy, (2) strengthen tolerance, (3) adopt a new attitude towards allergy and only avoid allergens if mandatory, (4) recognize and treat severe allergies early and (5) improve air quality and stop smoking [23].

The Finnish Allergy Plan (2008–2018) includes simple prevention measures, and has been widely disseminated in Finland at all levels, including to the lay public. The first results show that the severity of asthma (according to data on emergency visits, hospitalisations and self-reported severity) has been reduced and that prevention measures are meeting many of the proposed targets [5].

Deployment of the Finnish Allergy Plan to Norway

Asthma and allergic diseases represent a national challenge in Norway. Goals have been set by a 2015–2024 national plan. The Finnish Allergy Plan serves as a background to this plan, which includes issues like tolerance, exposure, improved diagnosis and control and, importantly, prevention, as well as acknowledging the need for more research to be able to achieve these goals.

Table 1. Goals of the Norwegian Asthma and Allergy Plan

- A shift in the paradigm of allergic diseases
- Challenge the myths
- Promote health (despite disease)
- Reduce the burden
- Prevent disease
- Stimulate tolerance
- Understand mechanisms
- Implement new knowledge in relevant health care
- Learn from others (Finnish Allergy Plan)
- Scale up the lessons learned using the EIP on AHA strategy

The Norwegian Asthma and Allergy Plan has several goals (table 1). These are to be attained through an integrated programme which will include all stakeholders (health care professionals, social workers, citizens, public health, local authorities, patients' organisations), who will function within networks coordinated by the *Helse-direktoratet* (Norwegian Directory of Health) on all levels of health care.

Specific goals include the increased knowledge of allergic diseases (from research), the assessment of baseline data and improved diagnosis, treatment and prevention (table 2).

The plan will be implemented through networks, including the regional competence centres in all 4 health regions of Norway (fig. 4).

Table 2. Specific goals of the Norwegian Asthma and Allergy Plan*Diagnosis and treatment*

- A 20% reduction in subjects with allergic diseases/hypersensitivity
- Improve diagnostic work-up
- Optimize treatment of severe allergic reactions and reduce hospitalisations by 40%
- Focus on severe allergic reactions to reduce exacerbations and hospitalisations

Prevention

- No tobacco exposure to children
- Improve preventive advice on the population level
- A 50% reduction in children with allergen diets
- A 50% reduction in subjects with work-related allergies

Table 3. Dissemination strategy of the Norwegian Asthma and Allergy Plan

- The public at large
- Patients and their families
- Primary care and community health care
- Strengthen disease ‘schools’ including new technology
- Pollen counts
- Allergy sentinel network
- Inform educational institutions about allergic diseases
- Competence in ‘allergology’ (not specialty)
- Dissemination to other European countries and regions (AIRWAYS ICPs)

Table 4. Strategy of the Norwegian Asthma and Allergy Plan (2015–2024)

- (1) Collect, improve and spread competence
- (2) Increase knowledge (research)
- (3) Work in networks coordinated by the Norwegian Directory of Health
- (4) Work at all levels of health care

Correct and relevant information are to be disseminated to all stakeholders (table 3).

The plan will be implemented by means of the 4 main strategies outlined in table 4. In particular, it will focus on (1) improving competence throughout the health care system as well as that of patients and the public and (2) improving knowledge by strengthening research and extensive collaborative work throughout the country.

Research will focus particularly on reducing the burden of disease and improving treatment and collaborative

Table 5. Goals of AIRWAYS ICPs

- (1) Propose a common framework of care pathways for chronic respiratory diseases which will facilitate comparability and transnational initiatives
- (2) Propose plans that target all populations according to culture, health systems and income
- (3) Develop a strategy based on WHO PEN and the essential list of drugs for low- and middle-income countries
- (4) Provide information about the development of cost-effective policies, in particular strengthening policies on smoking and environmental exposure
- (5) Aid risk stratification of chronic disease patients by means of a common strategy
- (6) Build a sentinel network for allergic diseases and asthma
- (7) Have a significant impact on the health of citizens in the short term (reduce morbidity, improve the education of children and work of adults) and the long term (promote healthy ageing)
- (8) Tackle chronic diseases throughout the life cycle
- (9) Define active and healthy ageing
- (10) Ultimately reduce the health care burden (i.e. emergency visits, avoidable hospitalisations, disability and costs) while improving quality of life and promoting active and healthy ageing. In the longer term, the incidence of disease can be reduced by innovative prevention strategies

WHO PEN = WHO Package of Essential Non-Communicable Diseases Interventions.

and multi-disciplinary care. These are to be achieved by: (1) prevention, (2) understanding gene-environment complexity, (3) basic mechanism research, (4) clinical research (diagnosis, treatment and health care/resources) and (5) the evaluation and implementation of research results.

Integration of the National Asthma and Allergy Plan into AIRWAYS ICPs

AIRWAYS ICPs is the model of chronic diseases of Area 5 of Action Plan B3 of the EIP on AHA (DG Sanco and DG Connect) [7] according to disease burden, mortality and comorbidities [24]. It was launched by the NHS in England (Newcastle, February 2014) and has been endorsed by the EIP on AHA Reference Site Network. The goals of AIRWAYS ICPs are to launch a collaboration to develop multi-sectoral care pathways for chronic respiratory diseases in European countries and regions (as part of the EIP on AHA), and to scale up globally with a WHO GARD demonstration research project [9]. AIRWAYS ICPs has strategic relevance for the European Union

Health Strategy and the WHO Action Plan for Non-Communicable Diseases (2013–2020), adding value to existing public health knowledge (table 5).

The Finnish Allergy Plan focuses on all allergic conditions, including asthma, and is generic enough to be used as a model for all chronic respiratory diseases. Several AIRWAYS ICPs goals are in line with the Finnish/Norwegian Allergy Plans, including Actions 4, 5, 7, 8 and 10.

The Finnish and Norwegian Allergy Plans have been endorsed by AIRWAYS ICPs and will be promoted across all regions of Europe and beyond.

Recommendations from the Meeting

The meeting highlighted opportunities within and outside of Europe to deploy national plans for combatting allergic diseases and reducing the burden on the individual and societal levels. The Finnish Asthma Plan, Finnish Allergy Plan and Norwegian Asthma and Allergy Plan can serve as templates for other countries and be adjusted to local limitations and national health care systems.

Furthermore, thanks to the MeDALL project, it has become clear that there is a need to improve our understanding of the mechanisms as well as the optimal management of co-existing allergic diseases in a smaller, but important, proportion of patients with allergic disease. Several recent papers from Oslo and by the MeDALL consortium suggest the likelihood that children and adults with asthma, allergic rhinitis and atopic eczema may constitute particular phenotypes that require specific attention, in research as well as in care. The results of the MeDALL project will be further embedded in the national plans. More comprehensive management plans for these selected at-risk patients is called for.

The meeting in Oslo thus led to a new initiative within the MeDALL consortium to enhance our understanding

of the developmental trajectories of these complex allergic phenotypes [12, 15, 25–28]. We will combine longitudinal data from birth to young adulthood, including lung function development and gene-environment interactions, particularly in subjects with ≥ 2 allergic diseases. The findings will be complemented by mechanistic studies. This initiative will hopefully bring us closer to understanding the mechanisms involved, and may lead to the identification of potential new targets for personalised treatment.

The link with AIRWAYS ICPs [7] is of importance, as chronic respiratory and allergic diseases must be taken into consideration throughout the lives of sufferers, in order to promote active and healthy ageing [29, 30]. Deployment of the Finnish and Norwegian Plans in other regions of the European Union will be carried out in collaboration with the EIP on AHA and the Collaborative Reference Network using the scaling up strategy of the EIP on AHA [Bousquet, in prep.], and globally with WHO GARD. The plans will be presented during the AIRWAYS ICPs meeting scheduled to take place at the Ministry of Health in Portugal (July 1–2, 2015) and in collaboration with WHO GARD. One further impact will be the regional deployment in Norway, which can serve as a model of a national plan for the deployment of the EIP on AHA scaling-up strategy in other regions. For the Finnish and Norwegian Plans, follow-up and evaluation are already built in. No local or national plan should be started without an organized evaluation process. Both the process itself and the outcomes should be evaluated in order to learn for the future. It is already clear that a systematic approach to tackle the asthma and allergy burden works in different societies. The Finnish and Norwegian Plans can be adjusted and implemented locally in variable health care environments. Simple common goals and educational tools to do the job pave the way for improved public allergy health.

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