Patient involvement in agenda setting for respiratory research in the Netherlands

To the Editors:

Would it be beneficial to actively involve people with a respiratory condition in identifying and setting respiratory research priorities? Research priorities are traditionally set by medical and scientific experts, and it is often argued that this should remain unchanged since it gave rise to the development of high-quality knowledge, medical innovations and the improvement of quality of life [1]. Patients are often considered subjective, knowing little about health research. Furthermore, patient involvement would cost additional time and money [1]. So why would one consider giving patients a voice in setting research priorities? Different arguments are described in a growing body of literature addressing patient participation. First, there are indications that research priorities from experts differ from those of patients [2–4]. To become more responsive to patients' needs, it would be vital to involve patients in identifying priorities. Patients' ''experiential knowledge'', can complement scientific or medical knowledge [3, 5, 6]. Secondly, the process itself becomes more democratic [2, 5]. Furthermore, patient involvement in decision making can lead to better acceptance of these decisions and outcomes. These arguments have inspired a growing number of funding agencies, including the European Union, to involve patients in research.

A pioneer in involving patients research is the Netherlands Asthma Foundation (NAF). To be more democratic, responsive to patients' needs and to improve societal relevance of their research agenda, NAF involved in 2004, besides scientific and medical experts, people with asthma and/or COPD in setting their research agenda [7, 8]. In a facilitated process, patients articulated needs and prioritised research topics in a well-argued way. Patients did not, as was expected by some experts, just prioritise care research, social research or focus only on their own problems, they also prioritised (bio)medical research topics and thought of future generations [7]. In 2009, the NAF research agenda was updated and extended, including rare lung diseases: pulmonary fibrosis (IPF), pulmonary arterial hypertension (PAH) and the respiratory aspects of cystic fibrosis (CF) and sarcoidosis. Patients and medical and scientific experts were again involved because new diseases were included for which the patients' perspectives were not known and perspectives might have shifted. A project team was established, responsible for agenda setting, consisting of two employees of the NAF scientific department, a patient, an external researcher and an external advisor for the participatory process. Based on the ''dialogue model'', which describes a methodological design for patient participation in research agenda setting [9], a concise process was developed. The process had to meet the following criteria: 1) patients' and experts' perspectives should be recognisable in the agenda; 2) participation should be realised on the level of consultation [10], whereby patients' and experts' input should be equally weighted; 3) the process should not exceed available resources (time, budget); and 4) the agenda should highlight state-of-the-art research.

The agenda-setting process comprised three phases: consultation, prioritisation and integration. Experts and patients were consulted separately. Patients were invited by patient organisations *via* advertisements on their websites, email and oral invitation by regional consultants. Patients all differed from those involved in 2004 and none was refused. Patients were consulted in three heterogeneous focus groups (n=31) to identify research themes and topics. Issues encountered in daily life due to their diseases were identified. Some issues, *e.g.* regarding organisation of care and communication, were discarded being beyond the ''research'' focus. The identified issues were ranked and discussed by patients to gain insight in which issues were considered important and why. Differences and similarities between the people with different respiratory conditions were discussed. A broad range of issues were identified, *e.g.* the relationship between aetiology and genetic, environmental or lifestyle factors, interaction of multiple drugs and psychosocial effects. Noteworthy was the attention for children with a respiratory condition while children were not consulted. After three focus groups, saturation was reached. Data regarding CF was retrieved from the Dutch Cystic Fibrosis Foundation who had already established their own research agenda in 2007.

Experts were consulted using two routes. Members of the scientific advisory board (SAB) of NAF (n=20) indicated in a survey which topics of the former agenda should be kept, refined, removed or added. Secondly, research topics for rare lung diseases were obtained by seven semi-structured interviews. Respondents were selected on the basis of maximum variation sampling with respect to disciplinary background, disease and affiliation. Important research developments in their field, relevant knowledge gaps and often heard but unaddressed complaints from patients were discussed. Focus groups and interviews were transcribed and summaries were sent back for member check. Data were analysed to gain insight in important themes and topics according to patients and experts.

A session with SAB resulted in a list of research priorities from experts. For patients, a questionnaire was developed to validate and prioritise the identified 30 research topics, clustered in seven research themes. The link to the questionnaire was sent by email to members of relevant patient organisations. A paper version was provided for those without e-mail. From 201 returned questionnaires, 169 were filled in correctly and analysed using SPSS-10. This resulted in a list of research priorities from patients. No new topics were brought up in the questionnaire. Patients prioritised research on (genetic) origins, improvement of diagnostic tools and co-morbidity highly. Patients prioritised research topics specifically relevant for their condition as well as general topics like disease causes and development. For example, people suffering from IPF prioritised reduction of side-effects of prednisone highly, while

people suffering from PAH prioritised the improvement of the method for administering medication.

The project team integrated priorities. On the main research themes there was broad consensus, but priorities differed in the details (table 1). Issues highly prioritised by both patients and experts were taken up. Unique topics of patients or experts, which were highly ranked, were also included in the agenda. The overlap between priorities of experts and patients was substantial with respect to basic, translational and applied care research. For example, both identified genetic and environmental factors as well as early diagnosis as important research topics. This indicates that patients and experts have similar thoughts on which issues are important to address in respiratory research. Differences were also noted. Comorbidities and drug interactions were prioritised by patients (not experts), while smoking interventions were prioritised by experts (not patients). Topics exclusively introduced by patients were side-effects of drugs, unpleasant administering techniques and specific drugs for children. Two research agendas, with considerable overlap, were formulated; one for asthma/COPD and one for the defined rare lung diseases (table 1).

Development and execution of the approach was realised in 5 months with limited resources. The approach for updating and extending the research agenda proved useful for involvement of experts and patients and elicit their priorities. According to SAB, the research agendas were feasible, based on patients' perspectives and state-of-the-art science. Patients were satisfied with this approach and considered focus groups a useful method to gain insight in their experiential knowledge.

Recruitment of patients took place by convenience sampling. This entails the risk of a non-representative (biased) sample. However, we have no indication that there is a serious bias apart from the fact that, in focus groups, children and severely ill patients did not take part. Though, using two approaches (focus groups, questionnaire) increases the opportunity to become involved. The fact that no new topics arrived from the questionnaire indicated that saturation had been achieved. The facilitators were competent, using non-steering inquiry methods and had a neutral position [9].

Patients identified and prioritised research topics that were previously not the research focus in the Netherlands, such as co-morbidity, fatigue and effects of psychological problems (*e.g.* stress, depression) on the development of asthma or COPD. The input of patients largely reproduced the previous research agenda from 2004 [8, 9], though ''fatigue'' which was newly introduced. This issue is currently getting more attention in several disease domains. It indicates that patients are becoming aware of fatigue as a symptom of their disease.

Although there is much overlap between priorities of experts and patients on broader themes, in details they differ and bring different and challenging perspective and issues to the table. Ideally, a dialogue would have taken place between experts and patients to discuss differences and to increase mutual understanding [9]. However, different perspectives do not have to be reconciled when the topics are complementary and not contradictory. Nevertheless, if topics are only considered

TABLE 1 Themes in the research agenda for asthma and chronic obstructive pulmonary disease (COPD) and for rare lung diseases

Themes	Prioritised by
For asthma and COPD	
Development and mechanisms	
a. Genetic aetiological factors of asthma and COPD	E/P
b. The mechanism of increase or decrease of symptoms of asthma and COPD	E/P
c. The processes of asthma and COPD during life and their mechanisms	E
i. Comorbidity/multimorbidity	P
ii. Fatigue	P
d. Factors (environmental and psychosocial) and lifestyles affecting the development asthma and COPD	E/P
i. Air pollution, climate	E/P
ii. Fear, depression, physical stress	P
Care and treatment	
a. The earliest stages of asthma and COPD and methods to ascertain these stages	E/P
b. Possibilities to improve the treatment of asthma and COPD based on individual disease characteristics	P
i. Compliance to treatment	E
ii. Self-management	P
Prevention	
a. Interventions to prevent the development or progression of asthma and COPD	E/P
i. Physical activity/physical therapy	E/P
ii. Human smoking behaviour	E
iii. Intervention to affect starting or stopping smoking	E
For rare lung diseases	
Development and mechanisms	
a. Aetiological factors	E/P
i. Genetic factors	E/P
b. The process of chronic lung disease during life and their mechanisms	E/P
i. Prognosis	P
ii. Fatigue	P
iii Airway infection in cystic fibrosis	E/P
iv Biomarkers for prognoses and progression	E/P
c. Factors (environmental and psychosocial) and lifestyles affecting the development of chronic lung diseases	E/P
Care and treatment	
a. The earliest stages of lung disease and methods to ascertain these stages	P
b. Possibilities to improve the treatment of lung disease	E/P
i. Compliance to treatment	E
ii. Target finding for therapeutic interventions	E/P
iii. Airway infections in cystic fibrosis	E/P
iv. Physical activity/physical therapy	E/P
Prevention	
a. Prevention of development or progression of chronic lung diseases	E/P

E: experts; P: patients.

important by patients, not by experts, it entails the risk that experts will not submit research proposals on these topics. This shows once more, the importance to consider patient participation in research agenda setting as a mutual learning process for patients, experts and policymakers.

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Viral infections trigger exacerbations of cystic fibrosis in adults and children

To the Editors:

Cystic fibrosis (CF) is the most common autosomal recessive condition causing disease in western societies, and despite important advances in understanding the disease, patients with CF develop progressive lung disease with recurrent endobronchial infection, eventually becoming chronically colonised with resistant organisms such as *Pseudomonas aeruginosa*. The clinical course is punctuated by periods of acute worsening of CF lung disease that increase with age and declining lung function, while the frequency of exacerbations is also an independent predictor for decline in lung function and mortality [1]. How and why exacerbations of CF occur is poorly understood. Recent data suggest that exacerbations are not associated with an acquisition of new strains of bacteria, but rather clonal expansion of existing strains [2]. The factors that lead to this imbalance between chronic bacterial infection and host immune response, which then results in CF exacerbations, are unclear. Viral infection may be an important factor that triggers these events. In children with CF, viral respiratory tract infections are associated with exacerbations [3, 4]. In CF a respiratory virus infection superimposed upon chronic bacterial infection potentially could enhance inflammation and shift the balance to favour infection with chronic bacterial pathogens.

The aims of this study were to assess the prevalence and aetiology of viral respiratory tract infection in an adult population with CF, compare this to a group of children with CF and assess the impact of this on acute exacerbations of lung disease.

We recruited 17 adults (age greater than 17 yrs) and nine children (6–17 yrs) from the CF clinic at John Hunter Hospital, New Lambton, Australia with CF diagnosed by a positive sweat test and CF genotyping. Participants were assessed at baseline and reviewed every 3 months for 1 yr, from 2007 to 2009. Participants were advised to contact investigators as soon as they developed symptoms of a cold or a worsening of their chest disease and reviewed in 48 h. Acute exacerbations were defined when any four of the 12 items of the Fuchs' criteria were present [5]. At each visit, spontaneous sputum was sent for quantitative microbiology [6] and two throat swabs were performed using a semi-nested PCR for influenza A and B, respiratory syncytial virus (RSV), rhinovirus (RV), coronavirus, human metapneumovirus, parainfluenza 1, 2 and 3, and adenovirus [7] and RV were sequenced [8]. When data were normally distributed, differences were analysed using a non-paired t-test and, when not normally distributed, a non-parametric equivalent. Multivariate linear regression analysis was performed to determine risk for acute exacerbation, risk for exacerbation