DECISION MAKING IN ASTHMA MANAGEMENT : THE CONTRIBUTION OF ECONOMICS

GLAXOWELLCOME EUROPEAN ROUNDTABLE MEETING

Combining Clinical and Economic Factors to Design and Implement a Disease Management Programme (Example from France)

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INTRODUCTION

Many effective treatment measures are available nowadays for certain chronic disorders. In everyday practice, the effectiveness of these treatment measures appears to be limited by inadequate patient education: improved patient education should improve compliance and knowledge about the disorders and their treatments. In parallel, the increasingly rapid development of both diagnostic and therapeutic measures available places a heavy demand on physicians so that they can understand the best diagnostic and therapeutic options available. This cannot be achieved without suitable continuing professional education.

Asthma is one of the specific disorders, which may be managed in a co-ordinated care network. It is a chronic respiratory disorder which affects all ages and for which we are currently seeing an increase in morbidity and mortality [CREDES 97]. This deteriorating scenario is explained largely by poor understanding about the disease and the use of inappropriate treatments [Bartal M 91]. Poor compliance with treatment is still a major problem. Management via co-ordinated care networks should therefore enable patients' state of health to be improved and the costs of managing the disorder to be reduced. The co-ordinated care network management solution which has been proposed combines computerisation of medical files, communication via a computerised network, patient education, training of health professionals (doctors, pharmacists and paramedics) and establishing reference medical strategies.

1. JUSTIFICATION FOR THE STUDY

The choice of the disorder asthma was made on the basis that this is a common disorder for which measures exist to improve quality of management and therefore the patients' state of health. The following assumptions would appear to be reasonable for asthma:

1.1. Asthma is a common and sometimes serious disorder

Two types of prevalence are generally cited; cumulative prevalence (patients who have suffered from asthma during their lives) and the current prevalence of asthma (clinical manifestations treatment during the last 12 months). The current

prevalence of asthma is estimated to be 3.1% in France. This estimate has been confirmed by the CREDES study, which followed a permanent sample of subscribers to the social security system during the period 1988 to 1992 [CREDES 94] and from a study published in 1995 which found the prevalence of asthma to be between 2.7% and 4.1% in young adults [Liard 95]. The cumulative prevalence, however, is in the region of 7.4 to 9.4% [Liard 95]. There are, therefore, more than 2 million asthmatic people in France at present.

Asthma is a chronic disorder involving acute episodes, which may result in hospital admission. From an analysis of the data in the Medical Information Systems Programme (Programme Médicalisé des Systèmes d'Information) published in the CREDES report in France, there are 108,500 short stay hospital admissions in France every year due to asthma, representing a total of 604,000 hospital admission days per year, or between 1.4 and 1.6 billion francs expenditure per annum. In addition to this, there are a further 236,000 medium stay hospital admission days [CREDES 97].

The large number of annual hospital admissions for asthma and the annual mortality rate due to asthma (3.5 per 100,000, or 2,000 deaths per annum) demonstrate the importance of asthma as a public health issue [CREDES 97].

1.2. Measures do exist to improve the state of health of asthmatic patients

Interest in the management of patients suffering from asthma has justifiably increased during the 1980s. Treatments are available for asthma which have a high level of effectiveness compared to side effects (the inhaled anti-inflammatory agents). In parallel, the recent consensus recommendations have standardised treatment administration [International Consensus Report 1982, Global Initiative for Asthma, 1995].

Several problems have been identified arising from a lack of information available to asthmatic patients. Poor use of measured-dose spray inhalers has long been recognised and has been identified in almost half of the patients who use them. A quarter of the 1,500 asthmatic patients questioned in a recent survey did not understand the need for regular preventative treatment. More than 10% considered that inhaled corticosteroids could be taken at the time when they had respiratory problems. Studies using inhalation counters attached to inhalers have found compliance to be poor (little more than 50%) [Cochrane GM 92].

These observations have not unreasonably led to more general management approaches, which fall into two categories: community and individual. The Swedish programme entitled "Asthma year in the pharmacies" is an example of an ambitious community project [Lisper B 96]. In this project, information about asthma was widely displayed in dispensing pharmacies and through the media over a one year period. A parallel increase was seen in prescriptions and reduction in deaths from asthma. On an individual level, we see the education programmes. These have been developed particularly in northern European countries, the United States, England and Australia. Different forms of management have been used, depending on the social context and specific features of the health care systems involved. There are many possible schemes.

A large number of hospital admissions, emergency consultations and time lost from work could be avoided by better patient management. There are many published arguments which support this hypothesis. The evidence offered however, is variable

in quality and some findings are biased [Pauley 95, Mayo 96]. These must therefore be removed from the reference strategies used. Amongst the studies selected, some produced good results, although results were very variable [Trautner 93, Sondergaard 92, Zeiger 91, Osman 94, Mayo 90, Lahdensuo 96]: others evaluated programmes which were too different to be considered with those in the project [Drummond 94].

Results from the various randomised trials are extremely variable (Table II). One randomised trial [Sondergaard 92] over a 6 month follow up period found no difference in hospital admissions and a significant 39% fall in the number of days lost from work in patients who had been specifically educated. The failure to identify any difference in hospital admissions was undoubtedly due to the limited follow up period. This is an important factor when we are evaluating the effectiveness of an intervention, particularly in terms of its impact on hospital admissions. The German study conducted by Trautner [Trautner 93] illustrated this phenomenon well after an intensive 5-day education programme; the average number of hospital admission days per patient per year fell from 10 to 7 after one year, and then to 3 days after 2 years, i.e. a reduction of 30% during the first year and 70% during the second. This non-randomised trial ("before-after" trial without a control group) is interesting in that it illustrates the time required for an intervention to have maximum effect. Another randomised trial, which used a follow up period of one year, compared a group of patients which had undergone an education programme with a group of patients managed conventionally and found a 54% reduction in the number of hospital admissions for severe asthma in the group which had received the education programme [Osman 94].

The Mayo study [Mayo 90] found a significant 67% fall in hospital admission rates; all of the patients studied had been admitted to hospital at least twice during the 12 months before the trial or had been seen on an emergency basis at least 5 times during the previous 24 months. The Bailey study demonstrated improved compliance and control of asthma.

Taken together, all but one of these studies demonstrated that education has a beneficial effect on various indicators of morbidity, using criteria which varied depending on the trial: clinical control of the asthma, number of symptom-free days, reduced drug consumption, improved functional indices or improved quality of life. One exception was the Jones study; the programme used consisted of an action plan but this was not particularly directed towards improving knowledge about the disorder. The recent work by Côté [Côté 97] attempted to distinguish between the effects of education *per se* from those of the maintenance treatment. In order to do this, anti-asthmatic treatments were adjusted during a pre-inclusion phase to optimise control of the asthma. In this situation, the effects of education were less obvious in patients who were well controlled; their knowledge and compliance improved, although no detectable differences in morbidity could be found. This study, clearly, has left the field of normal conditions of patient management. Reductions in the hospital admission rates were not always found; because the frequency of this indicator is relatively low, in order for it to be sensitive, the studies have to be more powerful, either by concentrating on asthma patients who require frequent hospital admissions, or by conducting studies on larger numbers of patients.

Author	Patients (nbr)	Person performing intervention and Methods	Follow up period (months)	Results
Mayo 1990	47/57	Individual consultations with nurse and respiratory physicians	8	67% relative reduction in hospital admission rate $p < 0.004$
Bailey 1990	124/101	Non-doctor educator (document and peak flow meter) and group sessions	12	Comparable hospital admission rates Improved compliance and control of asthma
Wilson 1993	164/146	Two sub-groups followed up by a nurse: individual education versus group sessions	12	Greater number of symptom-free days in the two sub-groups
Osman 1994	397/404	Documents sent by post	12	Relative reduction in hospital admission rates (54% reduction in the most severe patients, $p < 0.05$)
Kotses 1995	36/30	Group sessions with an educator (document and peak flow meter)	6	Reduced number of attacks of asthma and drug consumption
Allen 1995	47/45	Group sessions (± family) with educator and doctor (document and peak flow meter)	12	Improved knowledge and compliance Comparable morbidity
Jones 1995	33/39	General practitioner (document and peak flow meter)	6	Comparable morbidity
Ingacio-Garcia 1995	35/35	Respiratory physician (document and peak flow meter)	6	Improved clinical and respiratory function indices
Lahdensuo 1996	56/59	Individual consultations with a nurse (document and peak flow meter)	12	Significant reduction in emergency appointments (53%), and in loss of work Improved quality of life
Côté 1997	95/54	Individual consultations with a pharmacist (document and/or peak flow meter)	12	Improved knowledge and compliance No differences in terms of morbidity
Sondergaard 1992	30/28	Education from doctor, nurse and pharmacist. Individual and by group	6	No difference in hospital admissions 39% reduction in absenteeism

Table II: Randomised trials which have evaluated the effectiveness of an education programme.

These conclusions argue in favour of the development of overall management programmes which include both improvement in knowledge, adjusting emergency and daily treatment by means of action plans and behavioural changes.

1.3. Improvement in patients' state of health leads to a reduction in cost

Few studies have been performed in France on the costs of asthma. In 1994, CREDES published the results of the first four years of the Health and Social Protection survey, conducted on the permanent sample of subscribers to the Assurance Maladie social insurance funds for salaried employees. This survey enables us to identify the distribution of the different sectors of outpatient expenditure; FF 1,678 per patient per annum expenditure for medical appointments and visits (Francs 1991), FF 1,700 for medicinal products, FF 222 for laboratory investigations and FF 322 for auxiliary medical procedures [CREDES 94]. The total annual costs of managing an asthmatic patient were estimated in another French study to be FF 20,000, FF 8,832 of which were due to direct medical expenditure and FF 11,784 of which were due to loss in production. Hospital admissions represented 20% of the direct medical costs, i.e. FF 1,692 per patient per annum [Lebrun 94]; this study is not representative of all asthmatic patients and relates particularly to patients with persistent asthma (FEV_1 between 50% and 90%). An earlier study, published in 1989 [Sansonetti 89] found the total costs to be even higher, from FF 5,770 to FF 118,911 for asthmatic patients followed up at hospital. Hospital admissions alone represented between 50 and 80% of this total. Hospital costs for the more serious cases were in excess of FF 95,000, a figure explained mostly by admissions to intensive care units. The national survey into hospital admissions conducted by CREDES between 1991 and 1992 estimated the average cost of a hospital admission to be FF 12,000 and that hospital admissions overall were responsible for an annual expenditure of 1.3 to 1.4 billion francs.

Sector of medical expenditure	Percentage of expenditure	Costs
Outpatient care (outpatient appointments and visits)	15%	FF 1,890
Paramedical care (physiotherapists and nursing staff)	9%	FF 1,134
Investigations (laboratory, radiology, respiratory function tests)	20%	FF 2,526
Medicinal products	25%	FF 3,213
Hospital admissions	19%	FF 2,423
Cures (thermal etc.)	12%	FF 1,461
Total	100%	FF 12,647

Table III: Distribution of costs of managing an asthmatic patient (1991 data adjusted for costs in 1997 by applying an annual increase of 5% per annum).

Management of an asthmatic patient within a co-ordinated care network should reduce the cost of managing the disorder as indicated from the literature review, although any cost estimates must include the costs of the education programmes and training themselves [Windsor 90, Bolton 91]. The financial returns of care networks have been reported in many articles published in this field, which have described cost-benefit ratios of between 0.7 and 11 [Trautner 93, Sondergaard 92, Fireman 81, Lewis 84, Clark 86, Kotses 95].

The data shown in Table IV enable us to develop a financial hypothesis to optimise medical management costs in asthma, which will need, however, to be confirmed by a medico-economic evaluation of the programme which is set up.

Sector of medical expenditure	Changes in expenditure	Source
Outpatient care	=	
Paramedical care	=	
Investigations (laboratory, radiology, respiratory function tests	= or ↓	
Specific medicinal products for asthma	+ 39%	Sondergaard 92
Other medicinal products	↓	
Hospital admissions	- 30% to - 67%	Mayo 90, Trautner 93, Osman 94
Cures (thermal etc.)	= or ↓	
Absenteeism	- 29%	Sondergaard 92

Table IV: Hypothesis on the impact of the co-ordinated care network on the medical management costs of patients with asthma

2. EVALUATION OF THE EXPERIMENTATION

The aim of this study is to perform a comparative evaluation of two ways of managing asthma in a patient population in order to be able to extrapolate the results obtained to the whole (pre-defined) population. In order for such a process to be valid, it is important that the nature of the intervention has been clearly defined and standardised, that the population used is as large as possible and that the data which are collected are collected under conditions which are as close as possible to everyday practice.

2.1 DESCRIPTION OF THE INTERVENTION

The network experiment is based on 5 major projects providing co-ordinated patient management:

- computerising medical consulting rooms,
- exchange of medical information between professionals (medical records and medical knowledge),
- introducing reference medical strategies for standardised patient management,
- medical training for doctors and other health professionals involved,
- patient education.

Continuous interventions:

- registration of all medical information about patients seen in each consultation by each doctor into his computer, in a structured medical computer file with a specific part dedicated to asthma,
- centralising and linking information about asthmatic patients obtained from doctors, the education centre, the hospital and the Assurance Maladie insurance funds,
- exchange of information between doctors using the network,
- setting up of an education centre for patients,
- provision of a personal activity table for each doctor to allow him to evaluate his own practice. A working group will be set up containing the doctors taking part in the experiment. The results obtained will be considered in a peer group environment in order to enable the practices to be evaluated and any new recommendations to be developed.

Intermittent interventions for all doctors:

- computer training
- training in medical reference strategies for the management of asthmatic patients
- training in medico-economic evaluations
- sensitisation to the education process

Intermittent interventions for patients:

- education and information sessions (several groups, planned to take place over 2 months), the frequency of which will be adjusted as a function of the reference medical strategy and as a function of the patients themselves.

2.2 DEFINITION OF THE SAMPLED POPULATION

The inclusion criteria must be sufficiently broad to enable the individuals recruited to be representative of the patients treated routinely in primary care. The standards which apply to applications for accreditation submitted by bodies belonging to the Assurance Maladie (as stated in article 2 of decree number 96-789 dated 11 September 1996) stress the fact that "experimentation must be based on the principle that it is voluntary on the part of the patients and doctors; the doctors must not undertake any form of patient selection other than that which represents the objective of the project".

The population will consist of adults and children over 10 years old who are suffering from asthma. We chose to exclude children 10 years old or less because of the practical difficulties associated with including this age group (different education materials, less precise therapeutic recommendations etc.). The recent consensus [International Consensus 92] and the "Global Initiative for Asthma" report from the National Heart, Lung and Blood Institute/WHO working party (1995) on the diagnosis and management of asthmatic patients defined four grades of severity of the disorder (intermittent, mild persistent, moderate persistent, severe persistent). These grades are based on clinical criteria and function tests. All of these grades must be included in a before-after study, as any patient selection with respect to the severity risks of the disorder introducing a major source of bias due to regression towards the mean.

Inclusion criteria

- patients followed up by a doctor who has agreed to take part in the study,
  adults and children more than 10 years old,
- patients with asthma, all grades combined,
- patients who reside in Eure and who do not intend to leave the region within a period of 18 months,

- patients who have given their informed consent and undertake to attend the educational sessions offered.

Non-inclusion criteria

- patients who would be impossible to follow up
- children 10 years old or less
- patients who refuse to take part in the network study

2.3 CHOICE OF A DESIGN

There were three possible options for the design of the study: a randomised trial on two parallel groups, a non-randomised cohort with a control group and a before-after study. A randomised trial on two parallel groups provides the most convincing level of evidence, although it appears to be difficult to perform in practice in the setting of this study. Randomisation may be applied either to the patients or to the doctors; in the former situation, in order for the randomisation procedure to achieve its aim, the doctors would have to operate a split type of behaviour and provide different care for different patients on their list, depending on which arm of the trial the patients had been randomised to. It is difficult to imagine this type of dissociated treatment strategy in a programme which is designed to alter medical behaviour. In the latter situation, the presence of two sub-groups of health professionals on the same site (one of which had undergone a training programme, whereas the other was only responsible for routine follow up visits) would be a potential source of conflict in the worse case scenario, or in the best situation would end in informal communication between the doctors. Regardless of the final outcome, the study would be subject to bias. In addition, this type of study would require computer investment for both groups, which is not provided for in its budget.

We could have considered a study using two cohorts on two different sites, in order to minimise the possibility of communication between investigators. In this situation, the intervention would only take place on one of the two sites. Recruiting patients with the same severity of disease at two similar sites should produce two matched patient populations. This solution was not chosen for cost and logistical reasons.

Two other "before-after" study designs were also possible:

- The first possible option would have involved monitoring results obtained prospectively before and after introducing the intervention. The time series compared would be equivalent with respect to the quality and content of the information gathered. On the other hand, the time taken to complete the study would be twice that required in the cohort protocol using a control group.
- The second possible option would have been to use retrospective information before the intervention was started, and prospective information thereafter. This study plan was broadly criticised by experts for three main reasons: memory bias with respect to the frequencies of morbidity events and medical resources used, the fact that it would not be correct to extrapolate the efficacy and quality of life data retrospectively and the lack of any control for confounding variables in the causal relationship between result and intervention.

These before-after study protocols without a control group do not, however, allow us to exclude the influence of confounding variables (epidemics of viral infection, pollution etc.), which would make the results uninterpretable. For this reason, they were not chosen.

The study design should therefore interfere as little as possible with daily practices and should be as pragmatic as possible, whilst still permitting results to be interpreted to an adequate level of certainty. The best suited model is the pragmatic quasi-experimental study.

2.4 PLAN OF THE STUDY

The study design takes into account the specific features of the disorder being studied and methodological requirements to ensure that results are credible [Bouyer J 95, ANDEM 95, Ravaud 97]. This is based principally on a before-after study with a control group. This process allows the influence of confounding variables to be removed and at the same time reduces the costs of conducting the study.

The type of study chosen is a before-after study. Two measures will be taken in order to control for bias in this type of study:

- all patients are to be included, regardless of the severity of asthma, in order to minimise bias due to regression towards the mean
- a national study will be conducted on a parallel control group in order to identify spontaneous trends in consumption of health care in the disorder, in the absence of any intervention in France.

This is therefore a "before-after" quasi-experimental study with a control group.

2.4.1. "Before" phase of the before-after study

For feasibility reasons, and for reasons due to the time required to conduct the study, the before phase will be conducted in part retrospectively and in part prospectively.

- the prospective period will be 5 months and will enable medical practices and current consumption of medical care to be determined precisely.
- the short follow up period requires a 7 month retrospective period to be added in order to provide sufficient data on hospital admissions, use of emergency care and loss of work, where memory bias is low.

This will be used as the reference period to evaluate the impact of the programme, as it reflects the conventional management of asthmatic patients.

This period will be examined in order to define the number of subjects required more precisely, depending on the results obtained.

2.4.2. "After" phase of the before-after study

An "after" study will be conducted 6 months later, after the project has been set up, in order to measure the impact of the programme on a one year period initially and then on an additional period of one year thereafter.

2.4.3. Parallel postal survey

The postal survey on medical management practices and details of the treatments used in asthmatic patients will be conducted in parallel on doctors who are not practising at the site where the study is performed, using a "before" phase and an "after" phase in the same way as the model for the study conducted on site. In the absence of a site with a similar prevalence of asthma to the town of Evreux, the whole population of France will be used as the reference population.

This parallel survey will act as the control group in the before-after study to confirm that the improvement seen in the results obtained on the study site and the reduction in costs associated with this is explained by the

intervention programme which has been introduced and not by spontaneous national changes in management practice for asthmatic patients throughout the medical profession.

Computerisation
Intervention to be evaluated
Retrospective data
Prospective data
Prospective data
Prospective data
Study on the experimental site
D0
BEFORE PHASE
AFTER PHASE
Parallel postal survey
Retrospective data
Prospective data
Prospective data
Prospective data

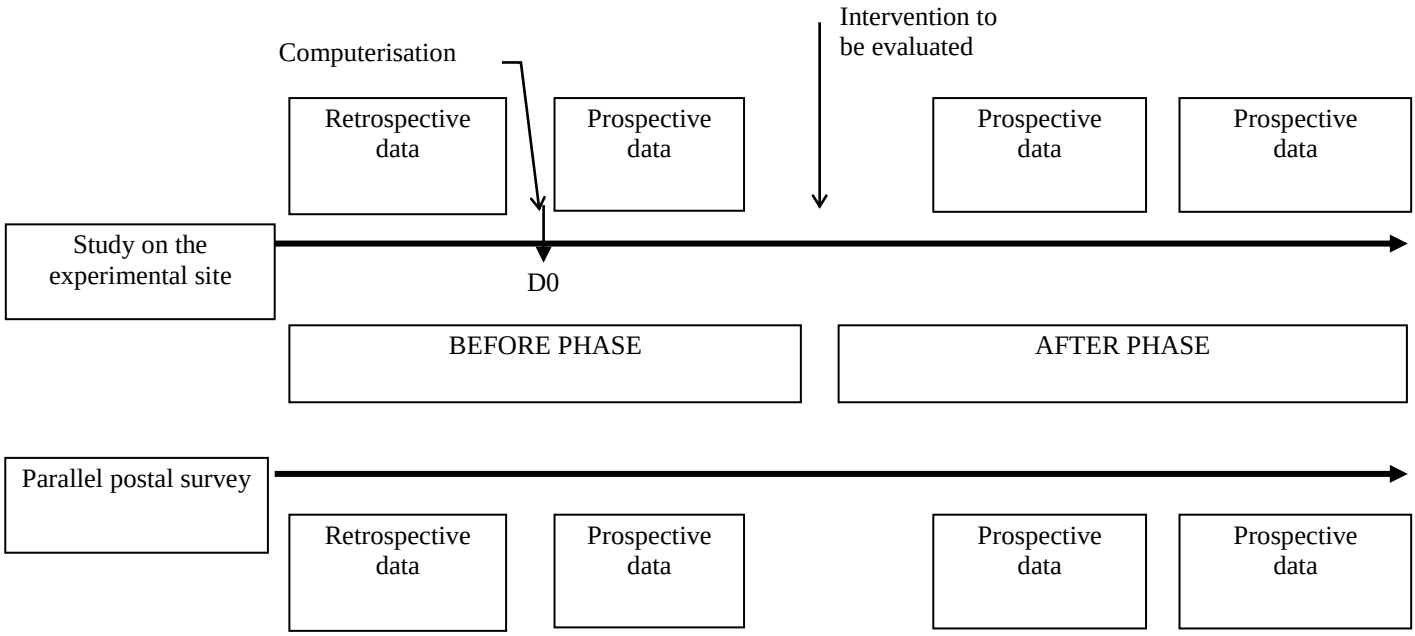

Figure 1: Plan of the study

5.2. Justification for the choice of study

6. DEFINITION OF THE TARGET POPULATION

7. LOCATION OF THE REFERENCE SITE

7.1. Justification of choice

There was an opportunity to form an agreement between ALLIANCE MEDICA and the Evreux CPAM to establish a care network based on the terms of reference of the decree dated September 1996. This is a medium sized town outside of the major city conurbations, providing stability in the population and in particular in the doctor-patient relationship.

The town of Evreux was chosen as the major pre-requisite of the study is that the health professionals are motivated by the experiment and wish to see it succeed. Evreux CPAM is also involved in research into care network experiments and is one of the voluntary sites for the experiment on the Vitale 2 chart; a number of doctors are highly motivated by a new means of organising the social delivery of medicine. All of these points are positive factors towards the success of the project.

7.2. Description of the reference site

The *département* (region) of Eure has approximately 550,000 inhabitants, 50 to 60,000 of whom live in the town of Evreux. The hospital centres identified in the *département* which have involvement in the treatment of asthma are the La MUSSE Medical and Surgical Centre (St Sébastien de Morsant), which has a follow up and rehabilitation department, Evreux General Hospital (departments of respiratory medicine, paediatrics, medicine and intensive care), and Vernon, Gisors, Pont-Audemer, Verneuil sur Ayre, Bernay and Louviers Hospitals. Most patient are admitted to these establishments, as the Assurance Maladie requires patients to be admitted to the nearest hospital.

There were 452 general practitioners and 243 specialists in the department in 1996 (Source: CREDES Eco Santé Software); 20% of doctors were computerised.

The medical department can identify the diagnosis of patients classified as suffering from a "chronic disease"; the disorder asthma is coded CIM 9 [code 493]. The only possible file interrogation which may be performed is a count of the number of patients suffering from asthma. The average number of new asthmatic patients registered in the chronic diseases database is 300 per annum. There were 252 short stay hospital admissions with a major diagnosis of asthma in Eure in 1995.

8. CHOICE OF PARTICIPATING DOCTORS

Doctors in Eure who take part in the experiment will be selected primarily on the basis of those who volunteer to take part. All general practitioners and respiratory physicians in Eure will be asked if they wish to take part. If however, too many doctors volunteer, geographical criteria may be used in the selection process (restricting the experiment to one town or geographical region of Eure).

9. CHOICE OF INDICATORS

Three major types of indicators were chosen; indicators used to measure the quality of care, indicators used to assess the management costs of asthmatic patients and indicators used to establish the extent to which the intervention has been introduced.

9.1. For medical practices

These indicators will be constructed after we have examined the differences between observed practices and the standards laid down, taken from the recommendations made by national and international consensus conferences and, retrospectively, from peak flow results and from an expert panel which has re-examined individual patient files.

With the exception of the first criterion relating to the validity of the diagnosis of asthma, the other criteria will be measured before and after the planned interventions. The indicators of good practice are as follows:

- the validity of the initial diagnosis of asthma made by the general practitioner, based on the final diagnosis made by the expert panel,
- evaluation of the grade of severity of the disorder by the general practitioner based on clinical and paraclinical criteria, compared to the final diagnosis made by the expert panel,
- treatment offered as a function of the severity of the disorder,
- actual patient follow up: frequency, follow up investigations etc. compared to reference medical strategies,
- education provided to patients, compared to the reference medical strategies.

9.2. For clinical results

9.2.1. Major end point for efficacy

As this study will be conducted under "real", pragmatic conditions, there must be no question of the process of collecting the treatment effectiveness data imposing additional costs or significant changes to the doctors' practice. For this reason, the effectiveness criteria which are conventionally used in a

clinical trial (follow up chart, FEV_1, PC 20 etc.) do not appear to be well suited, as they are demanding and introduce additional costs when used on a large scale in a large population of asthmatic patients.

Peak flow measurement is a reproducible measure which correlates closely with the extent of bronchial obstruction. It is easy to perform in a general practitioner's consulting room, although, in order to be interpreted, patients and doctors have to be correctly trained. This will not necessarily be the case at the start of the experiment before the patient education sessions have been provided and before the general practitioners have been trained. For this reason, the peak flow will not be used as the major end point.

The daily symptom diary requires close follow up, good compliance and patient involvement. It is a widely used tool in clinical trials, although its use on a large scale by doctors who have not been specifically trained, (as will apply to the first part of our experiment), carries a risk that there will be large amounts of missing or inappropriate entries. For these reasons, the major end point will be measurement of an asthma symptom score, which will be based on the frequency of symptoms due to asthma. This symptom score will be measured using a questionnaire relating to the week before the day on which any appointment takes place. A mean score will therefore be calculated during the before and after periods and for the parallel survey.

9.2.2. Secondary end points

* Assessment of control of asthma by the patient
* Mean daily frequency of use of rapid acting bronchodilators by the patient because of symptoms
* The best of the last three peak flow measurements in the doctor's consulting room

9.3. For quality of life

Quality of life scales may be generic (non-specific) or specific to a disorder. Use of a generic scale which has been validated in different languages has the advantage of enabling quality of life comparisons to be made not only between patients suffering from the same disorder, but also between patients of different cultures and patients with different disorders.

Generic indicators attempt to measure all of the important aspects of quality of life and are designed to be applicable to all diseases. They enable the dimensions of quality to be assessed as a single score without using multiple measurement scales.

The best known are the Sickness Impact Profile (SIP) [Berger 81], the Nottingham Health Profile (NHP) [Hunt 86] and the SF-36 [Ware 89]. The first of these consists of 136 questions grouped in two dimensions: physical functioning and psychological state, and into five specific, independent categories, all of which combine to produce a global score. The second uses a two part questionnaire: the

first consists of 38 questions to which the patient answers either yes or no. This refers to six domains: sleep, physical mobility, pain, mood changes, social isolation and emotional reactions. The second part brings together seven independent variables: paid work, domestic chores, interpersonal relationships, social life, family life, sex life, hobbies and holidays.

Finally, the SF-36 uses 36 questions to explore eight dimensions: mobility and physical performance, limitation in acts of daily living, social integration, restriction in normal occupation, either due to physical problems or to psychological difficulties, psychological distress, vitality and perceived health. To date, the SF-36 appears to be the best suited to our study amongst the generic questionnaires.

Using specific questionnaires consisting only of items which are specific to asthma will probably improve the sensitivity of the process. Several specific quality of life scales for asthma have been published for adults: the "Living with Asthma Questionnaire" [Hyland 91], the "Asthma Quality of Life Questionnaire" by Juniper [Juniper 92], the "Life Activities Questionnaire for Adult" [Creer 92], the "Asthma Quality of Life Questionnaire" by Marks [Marks 93], the "Asthma Brother Profile" [Hyland 95] and the "Air Index" [Letrait 96]. There are three specific questionnaires for children: the "Childhood Asthma Questionnaire" [Christie 93], the "Life Activities Questionnaire for Asthma" [Creer 93] and the "Pediatric Asthma Quality of Life Questionnaire" [Juniper 95].

From the specific questionnaires we chose the Juniper "Asthma Quality of Life Questionnaire" for Adults and the Juniper "Pediatric Asthma Quality of Life Questionnaire" for children.

9.4. For patient satisfaction

The concept being evaluated is the patient's satisfaction with the care which is provided to him. This is a complementary domain to the domains which have been described above, as consumer satisfaction may or may not correlate with the quality of care received. It relates principally to the quality of the interpersonal relationships between the patient and the doctor providing the care, and to the reception facilities provided by the various organisations concerned.

The arguments for and against the inclusion of this type of parameter are summarised in the table below:

Arguments against	Arguments for
• Patients responses say more about their personality than the quality of care	• The patient's opinion is a good indicator of his trust
• The patient tends to confuse quantity of care with quality of care	• It is not necessary to be a knowledgeable technician to provide a clear opinion about the quality of care

• The patient's point of view often contradicts that of the health professionals	• Gathering information from patients is inexpensive
• The patient's opinion is more of a reflection of the doctor's ability to listen than the doctor's technical ability	• The patient is an irreplaceable source of information which can only be obtained with his assistance

Insofar as patient satisfaction plays a considerable role in compliance with treatment we recommend that the self-completed questionnaire developed by Nguyen T.D., Attkinsson C.C. and Steigner B.I. [Tuan 83] is used to provide a measure of this.

9.5. For the level of training of health professionals

The network doctors will complete a questionnaire about their medical knowledge, before and after the training sessions

9.6. Understanding and level of education of patients about asthma

A quantitative and qualitative study will be conducted using tests, decision-making simulations and in-depth interviews with patients.

9.7. To evaluate the extent to which the intervention has been introduced

The use of indicators will enable us to evaluate the extent to which the education and training interventions which are offered are introduced and used.

9.8. Outpatient costs

Costs will be calculated from the point of view of the Assurance Maladie. Non-medical costs which fall directly on the family budget (patient contributions; statutory and actual) and loss of production to society will be excluded from the analysis. The only costs which will be included will be service payments (direct medical costs) and benefit allowances paid by the Assurance Maladie (social transfers).

9.8.1. Consultations

These costs will include:

* general practitioner appointments and visits,
* appointments with primary care specialists,
* hospital appointments: planned appointments and emergency consultations. For emergency consultations we will distinguish

between: patients discharged home after a single consultation, patients discharged home after a consultation and investigations, and patients admitted to hospital,

* home visits considered to be emergency (public holidays, night visits etc.)
* annual review appointments.

These will be allocated values from the Nomenclature Générale des Actes Profesionnels (NGAP) scales (procedure tariff scale) and from the reimbursement rates in force at the time of the study.

9.8.2. Prescriptions for paramedical procedures

These costs will include:

* physiotherapy procedures
* nursing procedures

These will be allocated values from the Nomenclature Générale des Actes Profesionnels (NGAP) scales (procedure tariff scale) and from the reimbursement rates in force at the time of the study.

9.8.3. Prescriptions for paraclinical investigations

These costs will include:

* assorted laboratory procedures performed
* assorted radiology procedures performed
* assorted functional investigation tests performed

These will be allocated values from the Nomenclature Générale des Actes de Biologie (NGAB) (laboratory procedures tariff scale), the Nomenclature Générale des Actes Profesionnels (NGAP) scales (procedure tariff scale) and from the reimbursement rates in force at the time of the study.

9.8.4. Drug prescriptions

The cost of drug prescriptions will be assessed using public tariffs, excluding VAT, as a function of the reimbursement rates in force at the time of the study. The costs of medical treatment will be calculated using the daily dosage and duration of treatment.

9.8.5. Health related transport

The cost of health related transport will be calculated from kilometre tariff rates depending on the type of transport used, (non-emergency patient transport, ambulance or private car).

9.8.6. Thermal cures

These costs will be calculated from the reimbursement rates by the Assurance Maladie.

9.9. For hospital costs

9.9.1. Short stay hospital admissions in the public sector

These will be all of the short stay hospital admissions to medicine or surgery, into a public institution or into an institution taking part in the public hospital service.

Costs will be calculated from the Programme de Médicalisation des Systèmes d'Information (PMSI), medico-economic database. The PMSI is currently in general use in the public sector for short stay hospitals containing 100 beds or more and operates in 139 private clinics.

Each short stay hospital admission will be allocated a diagnostic reference group using the PMSI rules, taking into account the major diagnosis (the disorder which consumed most resources), and associated diagnoses (co-morbidities), age and classified procedures, i.e. procedures which enable the admission to be classified into a surgical DRG or, failing this, the admission will be classified as a function of the diagnoses.

The DRG for asthma are as follows:

136: bronchitis, asthma, age 18 to 69 years old, without CMA
137: bronchitis, asthma, age >69 years old, with CMA
138: bronchitis, asthma, age <18 years old

The results of a national survey on the costs of medical activities within institutions taking part in the public hospital service (public or non-profit making private institutions) are published in two forms:

* a scale of costs by DRG (in points) used in the budget allocation reforms,
* total reference costs by DRG in francs, divided into 17 major categories of expenditure used for internal management purposes (cost centres).

Costs per DRG may therefore be allocated values by:

* either multiplying each DRG by the ISA point value (Indices Synthétiques d'Activité - Combined Activity Index) using the following equation: DRG numbers multiplied by the number of ISA points for the DRG, multiplied by the point unit value. The higher the number of points, the more expensive the DRG. The value of the ISA point varies depending on the region.
* or, by multiplying each of the 14 sections into which the cost of a DRG is broken down by cost accounting, by the corresponding numbers. This format provides a fine distinction between direct and indirect costs, by treatment or department, and between fixed and variable costs. This method therefore provides more than the tariff approach and provides information on the real cost of care in terms of the resources consumed.

Note: the daily allowance tariff will also be incorporated for hospital admissions, which may also be allocated values as a function of the length of the hospital admission and the hospital department involvement (general medicine, respiratory medicine, intensive care). The cost of a hospital admission will therefore be given by the length of the admission multiplied by the daily allowance rate for the type of department.

9.9.2. Short stay hospital admissions in private institutions

There are no private institutions within Eure, although patients may access care outside of the *département*.

In private, non-profit making institutions, costs per DRG will be calculated on the basis of historical invoiced costs using data provided by the invoice form 615, the means by which charges are reimbursed by the statutory authorities to the institution. Only those costs which are reimbursed by the statutory authorities, excluding certain invoice lines which represent supplementary hotel charges (television, telephone, private room not on medical prescription) will be excluded, as will fee supplements which may be added by the practitioners themselves. These latter charges may, however, be reintegrated into the cost.

Form 615 is divided into two parts:

* The first relates to admission charges which are sub-divided into several lines referred to by letter codes: FSO: operating theatre charges, which are proportional to the number of procedures, which are themselves graded in code letters K or Kc on the second part of the form; PHJ: daily pharmacy charges, to which must be added a specific reimbursement for pharmaceutical products which are used in anti-cancer chemotherapy, especially: PJ: the daily cost; SNG and TSNG: blood products and blood product transport etc.).

* The second relates to "fees" for surgical and anaesthetic procedures, morphological diagnostic procedures (radiography) or functional diagnostic procedures, laboratory investigations (histology, biochemistry) and procedures performed by paramedical staff (nurses, physiotherapists). Each line is described by a code letter (K or Kc for surgeons, physicians and anaesthetists, C, CS, CNPSY for consultations with assorted specialists, B for biological (laboratory) investigations, P for pathology (histology investigations), Z for radiology and related investigations, AMI for nursing procedures and AMM for physiotherapy procedures etc).

Using the same principles as cost calculation by cost accounting, the mean historical price may be calculated by DRG using the geometrical mean of the observed prices for all of the admissions classified into a given DRG.

9.9.3. Medium stay hospital admissions

Costs will be calculated from the PMSI database and the daily tariff cost.

9.10. Daily allowances

As the basis chosen to calculate costs is that of the Assurance Maladie, this should include cash payments made to asthmatic patients due to loss of work after the statutory exemption period if the patient is not ALD.

9.11. Costs of interventions performed within the co-ordinated care plan

Establishing a co-ordinated care network with a continuing medical education programme designed for doctors and educational activities for patients will inevitably lead to expenditure which must be counted in the overall costing of the project.

9.11.1. Costs of training on the management of asthma

* Payment to doctors taking part in training,
* Payment of trainers taking part,
* Materials required,
* Logistics.

9.11.2. Costs of the education centre

* Infrastructure costs (electricity, telephone etc.),
* Payment of staff (doctors, nurses),
* Payment of staff providing the patient education,
* Logistics,
* Educational materials,
* Other materials.

9.11.3. Costs of dispensatory measures

* Payment for the annual review outpatient appointment with the general practitioner.
* Educational payments for the general practitioner to provide the education session.
* The ability for the specialist to incorporate the respiratory function tests and consultation to the review appointments.

10. NUMBER OF SUBJECTS

The number of subjects required is calculated as a function of the major end point, based on the smallest clinically significant difference in result, variability in results (obtained from previous studies), the alpha risk (the risk of incorrectly concluding that a difference is present when it is not) and the beta risk (the risk of incorrectly rejecting a difference which is present).

Our aim is to identify a difference over two periods. Each patient will act as his own control and the statistical test used will therefore be the T test on paired series.

If we take the criterion used by Lahdensuo, the total number of incidents over a year, (where these incidents are represented by the sum of the consultations, days lost from work, days of antibiotic therapy or corticosteroid therapy), and using published figures (a difference in the mean number of incidents of 1.5, with a standard deviation of 0.6) 400 subjects will be required per group to demonstrate this difference to a statistical probability, alpha of 5% and beta of 10%.

The numbers required for the postal survey are determined on the same basis. The statistical power of the study requires that the same number of statistical units are present in the intervention group and in the parallel group, i.e. 400 patients. Assuming a response rate of approximately 10%, with two or more patients included per doctor, this will require a total of 2,000 questionnaires to be sent out. If more than 400 questionnaires are returned, these may be randomised in order to limit the number of statistical units studied to the number calculated. A delay to inclusion of one month and follow up period of 3 months should be allowed for. If an intervention occurs in one of the collection sites, such as EPU or adopting local medical standards, the data collected from this site should be excluded in order to avoid bias. Respondents will be voluntary (doctors), who will have to be remunerated.

11. CONDUCT OF THE STUDY

11.1 Before-after study performed in the Eure *département*

11.1.1. Recruitment of physicians

* Proposal to doctors in the Eure *département* to take part in the information meetings about the mailing section of the network project,
* Information meetings and recruitment,
* Obtaining consent (with repeat recruitment where necessary) and contract signing (4 copies: AM, doctor, CPAM, "blinding" third party),
* Doctors in the network will complete a "doctor" questionnaire.

11.1.2. Computerising the doctors'; surgeries

* Computerisation (on M0),
* Initial computer training (on M0).

This stage will take place over 3 months in three one month phases (M0, M1, M2).

11.1.3. Retrospective survey

One on-site visit by the CRA one month after the doctor's computer equipment has been installed (M1 to M3) will be arranged in order to inform the doctor about practical details required to conduct the study and to provide them with the following documents.

* information documents on the study,
* a register to record patients' questions and their opinions,
* "patient consent" forms,
* "patient inclusion" questionnaires,

* "retrospective study" questionnaires,
* "consultation" questionnaires for the doctor to be completed at each consultation (if computer records are not available) and for the patient if he consults a doctor outside of the network.

For the retrospective survey, the network doctors (general practitioners and primary care specialists) should:

* ask all asthmatic patients whom they see in consultations over a period of three months if they will take part in an epidemiological survey before the care network for asthma is set up. The doctor will record the names of the patients asked and their responses on a register.
* complete the computerised retrospective questionnaire at the consultation, for those patients who accept.
* ask patients for their agreement to use anonymised medical findings relating to them, which will be recorded in their computerised medical notes, for the next two years in an epidemiological study.
* return the questionnaires at the second CRA visit.

A second CRA visit will be arranged for three months later, on M4, in order to recover the questionnaires and for quality control of the information which has been collected.

11.1.4. Follow up phase for the "before" period

Between the first consultation, during which the retrospective survey is performed (M1 to M3) and the continuing medical education is received by the doctor. Patients will be followed:

* If the patient consults the doctor during this period, data from the consultation will be collected for the follow up period.
* If the patient consults a doctor who is not taking part in the network, the patient should ask the doctor to complete a consultation questionnaire.
* For emergency consultations or hospital admissions, a supplementary search will be performed to establish the detailed findings.

An on site study will be performed at the end of the follow up period to recover information about hospital admissions and use of emergency centres in hospitals and at the Evreux CPAM.

11.1.5. Continuing medical education

A two day medical training session will be organised on asthma and education, in several groups on M0.

11.1.6. Opening the education centre

The education centre will be opened on M7. This centre will provide education and follow up for patients. The patients will follow a "common pathway" of 2 x 2h educational meetings. The centre staff will then offer

the patients individualised educational support, depending on a patient's own level of knowledge and the profile of the patient. A computerised report will be sent to the doctor treating the patient (general practitioner), at the end of each session.

11.1.7. Including the patient in the experiment

During the first consultation which takes part after the doctor has received the continuing medical education, the doctors will ask those patients who have agreed to take part in the epidemiological survey if they will take part in the network:

* Patients must then sign a consent form and complete an initial questionnaire (M4)
* The co-ordinating doctor will confirm the inclusion criteria and register the questionnaire findings. He will provide the patient with *an envelope* containing: the patient's *personal network card* showing the patient's registration number, a *health diary* and a *personal batch of visit report forms* for visits relating to his asthma. An *explanatory booklet* will be provided together with the envelope (M5).
* The Evreux CPAM database will then be interrogated to recover information available from outpatient data (sums reimbursed, loss of work and paper prescriptions) and hospital data (hospital admissions, duration and data from the RSA files) (M5).
* The doctor will prescribe management by the education centre for persistent asthmatic patients in these consultations.

11.1.8. "After" prospective follow up

The patients will be followed up between the first consultation after the doctors' medical education (M7) and the end of the study (M31):

* If the patient consults the doctor during this period, the data from the consultation will be recorded for the follow up period.
* If the patient sees a doctor who is not taking part in the network, the patient should ask this doctor to complete a consultation questionnaire.
* For emergency consultations or hospital admissions, a supplementary survey will be performed to obtain the detailed findings from these episodes.

At the end of the follow up period, an on site survey will be performed to recover information about hospital admissions and use of emergency services in the hospitals and at the Evreux CPAM.

11.2. Parallel study on a national control group

11.2.1. Practical details

A database of 2,000 representative doctors in France will be used to send out a mailing at the same time as the before phase is started.

Obtaining consent (with repeat recruitment as necessary).

The following are to be given to the doctors by the CRA or sent by post:

* a questionnaire for the doctors
* a register to record all patients approached and any reasons given for refusal
* questionnaires for patients
* patient consent forms
* information documents about the study

11.2.2. Timing

This study should take place in parallel with the before-after study in two waves; the first to be performed at the start of the before phase and then a second to be performed one year later, during the after phase.

12. STATISTICAL ANALYSIS

12.1. Description of physicians' and patients' characters

A descriptive analysis will be prepared firstly for doctors and patients in the before-after study and secondly for the control group. This analysis will assess:

- general characteristics of the doctors
- socio-demographic and clinical characteristics of the patients

12.2. Analysis in the before-after study of the impact of the intervention performed in the town of Evreux:

Tests will be performed on paired series.
The tests used will be:

- for medical practices; the Chi-squared test,
- for clinical findings; the Student test,
- for quality of life; the non-parametric Wilcoxon test,
- for resources consumed; the non-parametric Wilcoxon test,
- for costs; the non-parametric Wilcoxon test.

12.3. Comparative analysis of results from the two parallel waves of the study

Tests will be performed on paired series.
The tests used will be:

- for medical practices; the Chi-squared test,
- for clinical findings; the Student test,
- for quality of life; the non-parametric Wilcoxon test,
- for resources consumed; the non-parametric Wilcoxon test,

- for costs; the non-parametric Wilcoxon test.

12.4. Inclusion of results and comparison of results of the before-after study with the parallel survey

If any significant differences are found within the control group, analysis of variance will be performed to examine the interaction, in order to take the change observed in the control group into account in the before-after study comparison.

12.5. Multiple linear regression and logistic regression

Multiple linear regression or logistic regression analysis will be used to identify factors responsible for the observed costs.

12.6. Identifying patient "responder" groups

Either by sub-group analysis, by age and by grade of severity, or by performing factorial analysis.

12.7. Evaluation of the specific impact of patient education

In order to isolate the impact of education from that of the other planned interventions (training health professionals, use of reference management strategies, use of specialists etc.), we have to clearly identify a patient population in which any improvement in the health indicators used can only be attributed to education. This population will consist of patients which the expert panel considers has received appropriate drug prescription from the start of the experiment and throughout its length. Any observed improvement in these patients could not result from changes in drug management due to improved training of the doctor concerned, or to specialist advice, or to use of reference medical strategies. Only education as undertaken within the framework of the network will produce any spontaneous change in the clinical course of the asthma in these patients. A comparison of changes in patients within the network and those in the parallel survey should therefore isolate the specific role of education.
Two sub-groups will therefore be established:

- those in which the expert panel decides that the treatment prescribed was appropriate at the start of the study and remains so throughout the study, from criteria laid down by the panel
- those in whom treatment was not appropriate by the criteria laid down by the panel, at a given time in the experiment, or in whom treatment is changed

Results from the first sub-group will be compared to the same sub-group of patients in the parallel survey to evaluate the role played by patient education and that due to the other planned interventions within the network.

In addition, in order to obtain better information about the role of education, a qualitative survey will be undertaken using questionnaires administered before and

after the intervention to examine the patients' knowledge about the disorder, treatments and action to be taken in specified situations likely to occur during the course of the asthma. This survey should provide information about the role of education, if the previous evaluation was not sufficiently powerful to produce any conclusion.

12.8. Analysis of the cost of the interventions

The return from the network is extremely sensitive to volume (the number of patients managed) and time (certain savings will only become apparent after several years). The more patients there are within the network the lower will be the operational costs (although there will, however, be stepwise increases as additional resources are required for patient follow up, e.g. additional staff etc). For the time effect, effectiveness appears to be relatively sustained during the first few years and even to improve after the first year [Trautner 93]. This has direct consequences on long term savings, which will, in this case, be greater.

13. PROVISIONAL CALENDAR

(Graph)
Task to be performed
Computerisation
1st CRA visit
Retrospective survey
Follow up
2nd CRA visit
Quality control of data
Continuing medical education
Opening education centre
CPAM and hospital survey
First analysis
"After" intervention follow up
"After" follow up
Interim analysis
Hospital and CPAM survey
Final analysis
Report

14. BIBLIOGRAPHY

ANDEM - Canger Octobre à October 1995.

TRANSLATOR'S NOTES:

En général, peu de commentaires, sauf abbreviations à verifier. Qqs termes à discuter car j'oublie s'il y a un terme standard pour ceux-ci.
Malgré les braves efforts de votre sectretaire, on n'a pas arriver à ouvrir la version 6.0, donc pour finir il faudra:
1. Inserer la bibliographie
2. Reinserer les qqs graphiques et remplacer les mots
3. Verifier les abbrebiations ci dessous et remplacer si necessaire.

PC20, page 18 please clarify abbreviation
ALD, please clarify abbreviation, page 24
p4 ? delete filiale de groupe ....
p9 les intervenants. Phrase removed.
p25 please clarify abbreviation EPU
p27 RSA please clarify abbreviation
RSA p27 please clarify abbreviation
p25 ISA - please check my translation. ?Other accepted term.
p25 CMA please clarify abbreviation

Je serai dans mon bureau pendant la journée (44 1388 454064) pour discuter les abbreviations.

Par ailleurs, merci- on n'a rien pris mais nous avons passé une excellente semaine. Mais elle passe si vite!

Amicalement,

Stuart