

How Is Difficult Asthma managed?

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Abstract

Most patients with asthma can be easily treated. Some have *difficult* asthma; in some because the diagnosis is erroneous, in others because of co-morbidity or non-compliance. An ERS taskforce has called for an integrated approach for these patients; positive results have been reported using protocols. In the UK there is no overall understanding of the size of this problem, or how these patients are managed.

Method

Postal survey of 683 consultant members of the British Thoracic Society designed to elicit respondents' views on how they would manage four clinical scenarios.

Results

There was a 50.4% response rate. Few reported a uniform approach to the investigation of such patients. The availability of allied healthcare professionals was variable. The 21 consultant respiratory physicians reporting a special interest in difficult asthma were significantly more likely to objectively assess compliance, perform skin-prick tests, and to utilise a liaison psychiatrist, than those without expressed special interest in asthma. Many reported difficulty in accessing psychologists, liaison psychiatrists and social workers. Approaches to the diagnosis and management of "vocal cord dysfunction" were variable.

Conclusion

The results of this postal survey of specialist thoracic physicians in the UK suggests that a protocol for difficult asthma is not in widespread use and that access to necessary allied healthcare professionals is not uniform. Pulmonologists with a declared special interest in difficult asthma may have configured their services and approaches more in line with that proposed by the ERS task force.

Introduction

In 1998 an ERS taskforce on difficult/therapy-resistant asthma called for an integrated approach to define clinical phenotypes, evaluate risk factors, understand pathophysiology and find novel therapies [1]. Subsequently, the ENFUMOSA study group [2] have published details of 163 subjects with severe asthma, who have been carefully studied, and compared those with 158 milder-controlled patients with asthma, and the TENOR study has published similarly from the United States[3]. The ERS taskforce specifically recommended the use of a protocol for evaluating patients with difficult asthma, which recommended a number of assessments and investigations which should be undertaken on these patients, including, for example, psychological assessment. A protocolised approach had similarly been recommended from the United States as long ago as 1993 [4].

Subsequently, results from single centres of the value of a systematic assessment of these patients have shown the advantages of such an approach in detecting misdiagnosis, significant major psychiatric co-morbidity and high rates of non-adherence with oral steroid therapy [5]. Others have subsequently shown that such an approach reveals that only approximately half (46.5%) of cases had truly therapy-resistant asthma [6].

Most national and international guidelines on the management of asthma do not address the issue of difficult asthma, although one group have recently published specific recommendations [7]. The size of the problem is not known but the burden for the individual and healthcare system is likely to be considerable. Many patients requiring unscheduled healthcare do so in a repetitive manner[8] and resource utilisation is approximately three times higher in patients with poorly controlled severe asthma, compared with well controlled, persistent asthma [9] and these patients incur significant indirect costs due to time off work [10].

Within the group of people with difficult asthma, there will be some in whom there is significant co-morbidity, some in whom the diagnosis is erroneous, some who have significant psychological problems and some who fail to benefit from therapy as a result of non-compliance.

Methods

This was a postal questionnaire survey to 683 consultant members of the British Thoracic Society. Members known to be paediatricians, radiologists or thoracic surgeons were excluded. A covering letter stressed the anonymous nature of the survey and respondents were asked to complete the form themselves rather than pass it to colleague. If received inadvertently by a paediatrician or by someone not in clinical practice, they were asked to notify us and return the form uncompleted.

The questionnaire consisted of five parts. The first four parts concerned case histories of difficult asthma and a fifth section was designed to elicit information about the respondents place of work. (Appendix 1)

The case studies were based upon cases seen previously by the authors, but altered and anonymised.

The first case concerned a patient with multiple admissions and episodes of mechanical ventilation who was on maximal therapy. The respondent was asked to tick a list of investigations they would perform on the majority of patients of this type. Case 2 was designed to elicit the pattern of services available to patients with difficult asthma and concerned a student with asthma which had recently worsened despite maximal therapies. The respondent was asked to record which other health professionals would be physically present in their clinic at the time of referral and who would be easily available by onward referral within two or three weeks. Case 3 was designed to elicit a list of differential diagnoses and concerned a young man with asthma since early childhood, who had never been fully investigated because of severe anxiety and needle phobia. Respondents were asked to list five possible alternative diagnoses and also to list the three commonest misdiagnoses they see in patients attending with asthma. They were also asked to list the most unusual diagnosis they have ever made in somebody originally labelled as having difficult asthma. Case 4 concerned a young woman with asthma who had had frequent emergency department attendances, and was noted to have extremely variable spirometry and a glottic wheeze. Respondents were asked to state the likely diagnosis

and to list which investigations if any, they used to confirm the diagnosis and to describe who they would most involve in therapy in such a case.

The fifth section elicited information about the clinician completing the questionnaire, including their place of work and whether there was an asthma clinic or difficult asthma clinic in their hospital and if they were the clinical lead for that condition. They were also asked how many patients with difficult asthma they currently cared for.

Statistical analysis

SPSS 12.0 for Windows statistical software package was used throughout. Variables were treated non-parametrically and analysed using Mann Whitney U Test.

Results

344 questionnaires were returned, a (50.4% response rate). Three hundred and ten completed the questionnaire, but 34 were returned incomplete; 4 because the recipient had retired, 12 because the content was not perceived to be relevant to their speciality, 5 stated they were no longer in clinical practice and 7 did not see patients with asthma. One was from a locum who did not feel it appropriate to complete the form. Six were returned because the recipient was unknown at that address. Some forms were incomplete because for each of the case histories, the respondent could report that they would not usually see this sort of case, or that they would refer them to colleagues.

The investigations reported to be undertaken on those with difficult asthma are shown in Figure 1 and the availability of health professional colleagues in Figure 2. The five commonest differential diagnoses offered for Case 3 are shown in Figure 3 and the complete list of misdiagnoses reported by respondents to have mimicked difficult asthma is shown in Table 1.

233 respondents thought that the likely diagnosis for the clinical scenario outlined in Case 4 was that the patient had 'upper airway obstruction', 'vocal cord dysfunction', 'glottic wheezing', or similar words. 33 reported the problem to be psychological and 22 diagnosed the hyperventilation syndrome or dysfunctional breathing. A wide array of investigations were reported to be used in such cases 192 reporting that they used flow volume curves and spirometry; 113 requested an ENT opinion and 102 undertook a bronchoscopy and bronchoscopic examination of the vocal cords. 47 reported measuring bronchial hyperresponsiveness in such cases, 41 serial peak flow recording, 15 blood gas estimation and 13 CT scanning. There was a similarly diverse response to the question as to who respondents most involved in therapy for these patients and the commonest are listed in Figure 4.

Demographics of respondents

266/293 (90.8%) of respondents were Consultant Respiratory Physicians with the remainder being University senior lecturers, readers, professors or staff grade physicians. 140/294 worked at a District General Hospital, 94 in a teaching hospital, 42 in an associated University Hospital and 18 in a regional cardiothoracic centre.

Numbers of patients with difficult asthma

280 respondents reported caring currently for a mean of 25.1 patients. The total number of patients under the care of the 280 consultants is 7027; of whom approximately half (3635) were under the care of the 21 consultants who declared that they had a special interest in difficult asthma.

Specific clinics for those with asthma or difficult asthma

140/292 (48%) respondents said that in their hospital there was one consultant who leads on asthma of which 55/140 (39.3%) were the lead on asthma themselves. 122/293 (41.6%) had a specific clinic in their hospital mainly for people with asthma.

Only 65/287 (22.7%) had a specific clinic for those with difficult asthma in their hospital. 183 out of 284 respondents (64.4%) answered that there was someone in their Regional Centre with an interest in difficult asthma and 21 of those 183 (11.4%) were themselves the specialist for difficult asthma.

The responses of the 21 Respiratory specialists (Table 2), who reported having a special interest in difficult asthma, were compared with the 152 doctors who reported neither a specialist responsibility for asthma or for difficult asthma. Responses from the former showed a significantly higher use of liaison psychiatric opinion ($p=0.002$), prednisolone assays/cortisols ($p=0.028$) and use of skin prick tests for common inhaled allergens ($p=0.012$ /and fungi $p<0.001$). The most significant results are the increased ease of access from a difficult asthma clinic to a liaison psychiatrist ($p=0.001$). The 21 difficult asthma specialists also had a significantly increased

number of patients with difficult asthma 173.09 ± 232.7 (mean \pm SD) compared to the mean 10.43 ± 13.60 cared for by the remaining respiratory physicians.

Discussion

Seven years after an ERS taskforce recommended an integrated approach to the problem of difficult asthma[1] and 13 years after the value of a systematic approach was demonstrated to be helpful[5], within one European country at least, a systematic approach is not the approach of most pulmonologists. It is possible that the survey results were not representative, but a response rate of 50% from busy secondary care respiratory professionals in a country where the majority of patients with asthma are cared for in primary care is probably respectable. Furthermore the pattern of respiratory care in the UK is such that there is increasing sub-specialisation by respiratory specialists, some spending the majority of time caring for those with lung cancer, others mainly caring for those with sleep-related breathing disorders. It is thus possible that a large proportion of British respiratory physicians have only a minimal responsibility for the care of those with asthma and this may account for many not returning the questionnaire. This does not diminish the value of this report; we have sub-analysed our results according to whether our respondents reported having a specialist responsibility and interest in the care of those with difficult asthma, or a more partial responsibility. Differences in care were noted between these two groups and studies are needed elsewhere in Europe to determine whether the 1998 task force recommendations [1] are better implemented elsewhere.

This survey would suggest that if a patient with difficult asthma succeeds in seeing a respiratory specialist with a special interest in their condition, such a physician is more likely to have optimally configured their services. This is important when others [5,6] have shown high rates of non-adherence with oral steroid therapy and significant psychiatric co-morbidity in those with difficult asthma.

The 21 respondents in this study who reported that they had a special interest in difficult asthma were more like to undertake allergy testing, assess compliance with drug assays and utilise psychiatric opinions. Respondents who did not express a special interest in difficult asthma report that access to liaison psychiatrists, psychologists and social workers was poor. It seems unlikely that the complex psychological problems sometimes suffered by these patients, and the risks resulting from such co-morbidity [11] can be properly managed without good liaison

psychiatry and psychology services. Those with a specialist interest in difficult asthma are also far more likely to routinely perform skin-prick test reactions for fungi than the generalists and positive reactions to fungi have been reported to be more common amongst those with potentially fatal asthma [12], (although whether the process of identifying hypersensitivity to fungi affects outcomes is unclear). Even amongst those who report a special interest in difficult asthma it was only a minority who objectively tested patient compliance with medication.

In addition to the problems of non-compliance and psychological co-morbidity, the wide differential diagnosis of difficult asthma was also highlighted by this survey. The list of diseases that were reported as masquerading as difficult asthma also emphasises the importance of differentiating *localised* airway obstruction from *generalised* obstruction. Some examples of misdiagnosis reported in this survey were of fixed structural localised obstructions such as tumours or post-tracheostomy stenosis, but some were functional. The problem of vocal cord dysfunction (synonym glottic wheezing, synonym functional upper airway obstruction) was well recognised by respondents and the condition is common. In one emergency department study it was shown that 22% of patients attending with wheezing had vocal cord dysfunction[13]. However there seems to be little consensus on the optimal method of confirming the diagnosis, if such confirmation is needed, and even less consensus on management. This probably reflects omission of the subject from guidelines and none of the major national or international guidelines include the subject of vocal cord dysfunction. It is included in a European Respiratory monograph [14], which considered a number of diagnostic tests and suggested that direct examination of vocal cords is diagnostic revealing characteristic adduction of the vocal cords in association with wheezing. However, this may be present only intermittently. That monograph recognises that management consists of reassurance but that can be difficult, particularly when the condition co-exists with asthma. Psychiatric assessment is said to be necessary and speech therapy useful [14].

Our survey cannot reveal the size of the problem of difficult asthma, but 7,000 patients were reported as being under the care of British respiratory physicians with this diagnosis. This is likely to be an under-estimate. The full range of investigations and services necessary for these complex patients does not appear to be available in

every respiratory service, and there may be advantages in these patients being referred to a specific 'difficult asthma clinic'. This should permit better characterisation of these patients, an enhanced understanding and a more rational approach to the evaluation of therapies and interventions. We can then study whether such optimisation of the process of care is associated with improved outcomes. The subject of difficult asthma also needs to be specifically addressed within national and international guidelines; this would demonstrate the importance of the subject and highlight gaps in our evidence which should provide an added impetus for further research.

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Table 1 Commonest misdiagnoses for difficult asthma reported by respondents (Case 3)

Psychiatric Disease (212)
COPD (182)
Vocal cord dysfunction (111)
Bronchiectasis (72)
Cardiac disease (38),
But the respondents reported a long list of mistaken diagnoses of which the most commonly reported were tumours including lung cancer and carcinoid tumours, foreign bodies, cystic fibrosis, Churg Strauss syndrome, and lymphangioleiomyomatosis.

Table 2 Specialist versus non-specialist care for difficult asthma

	21 Specialists reporting a specialist interest in difficult asthma	152 non specialist respondents (Not the lead for asthma or difficult asthma)	
Would seek a liaison psychiatric opinion on the majority of patients (Case 1)	10/21 (47.6%)	16/123 (13%)	p=0.002
Prednisolone assays/cortisols	5/20 (25%)	17/127 (13.4%)	p=0.028
Skin prick testing for common inhaled allergens	18/21 (85.7%)	85/128 (66.4%)	p=0.012
Skin prick testing for fungi	20/21 (95.3%)	78/125 (62.4%)	p<0.001
Referral to liaison psychiatrist	15/21 (71.4%) easily available by referral, 6/21 (28.6%) difficult to access	47/142 (33.1%) easily available by referral, 94/142(66.1%) difficult to access	p=0.001
Difficult asthma patient load	173.09±232.7 (mean±SD)	10.43 ±13.60	p<0.001

Figure 1 Investigations frequently performed on the majority of patients with difficult asthma (Case 1)

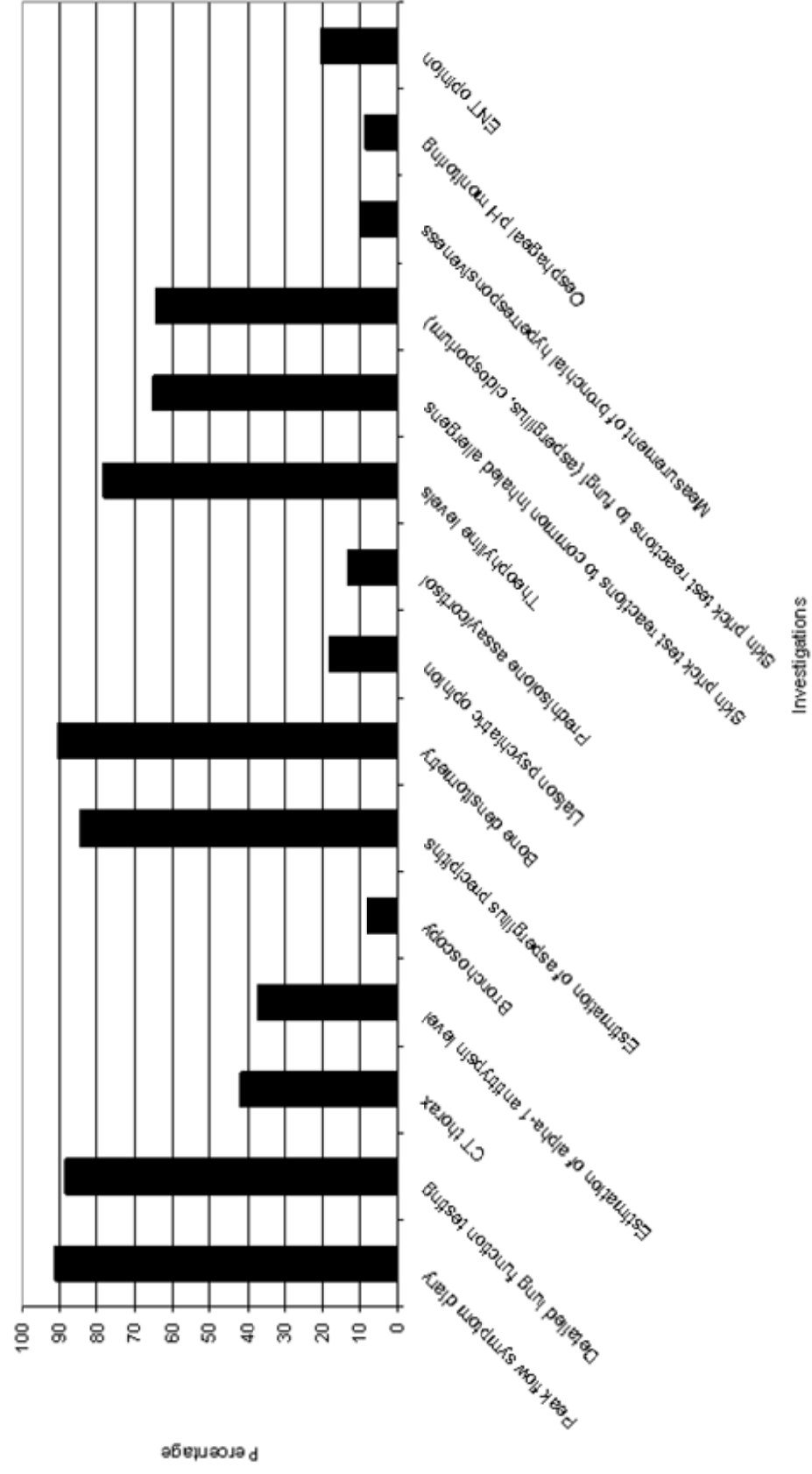
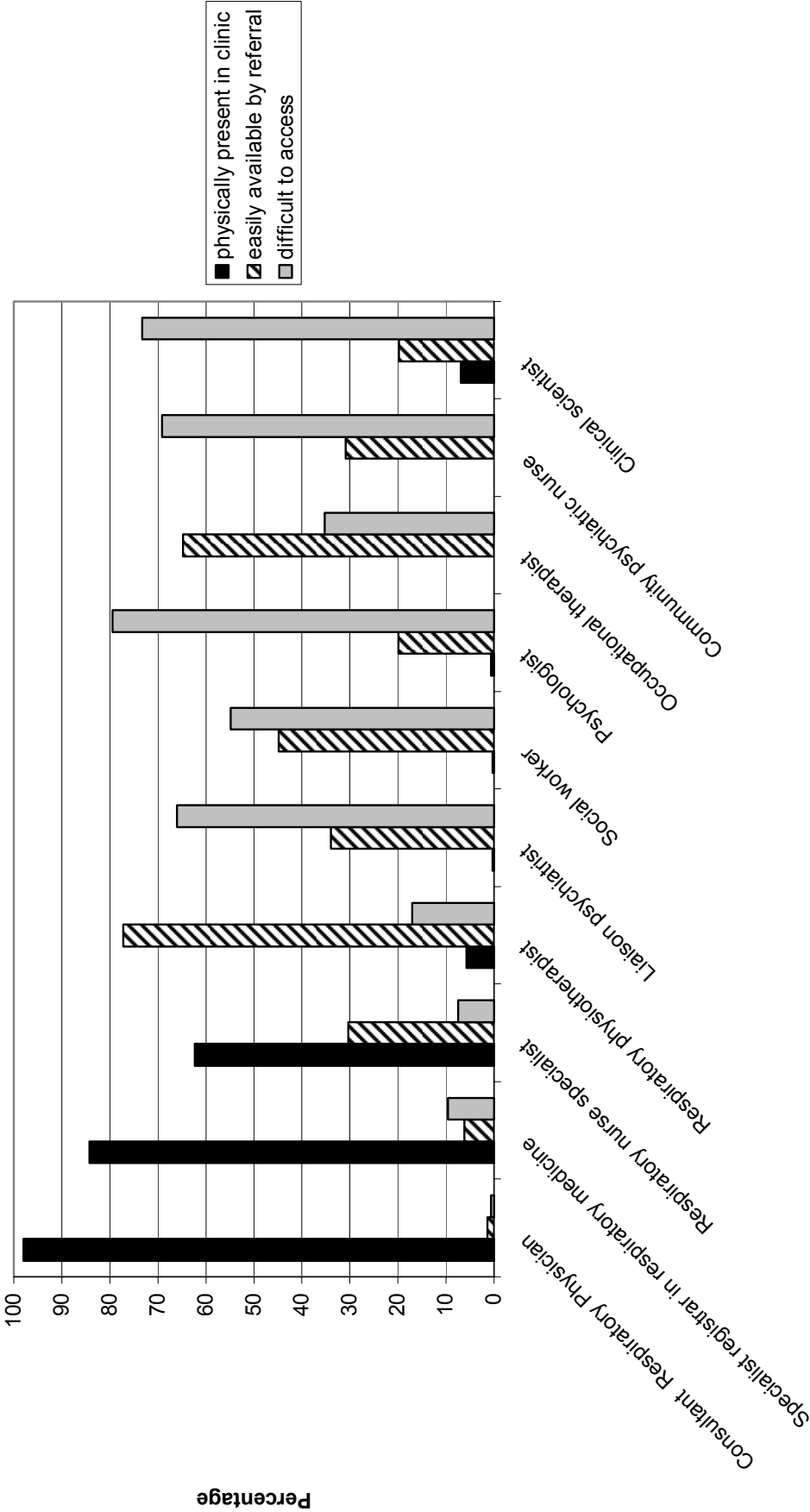
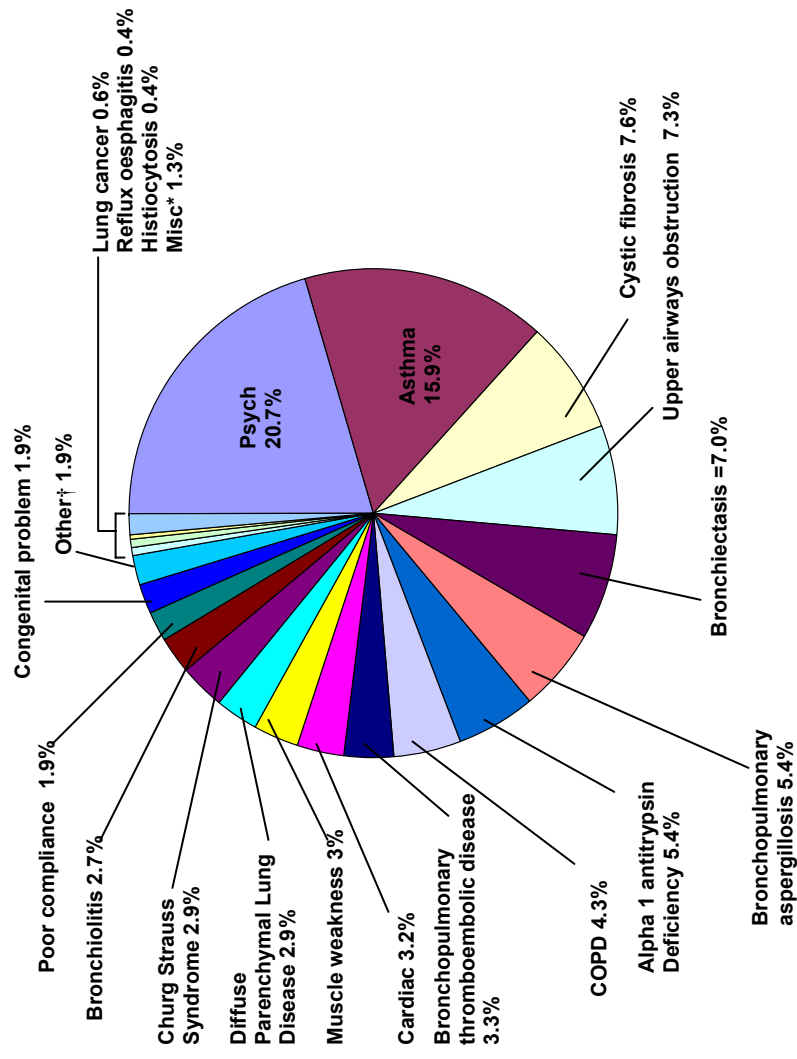


Figure 2 Availability of health professional colleagues

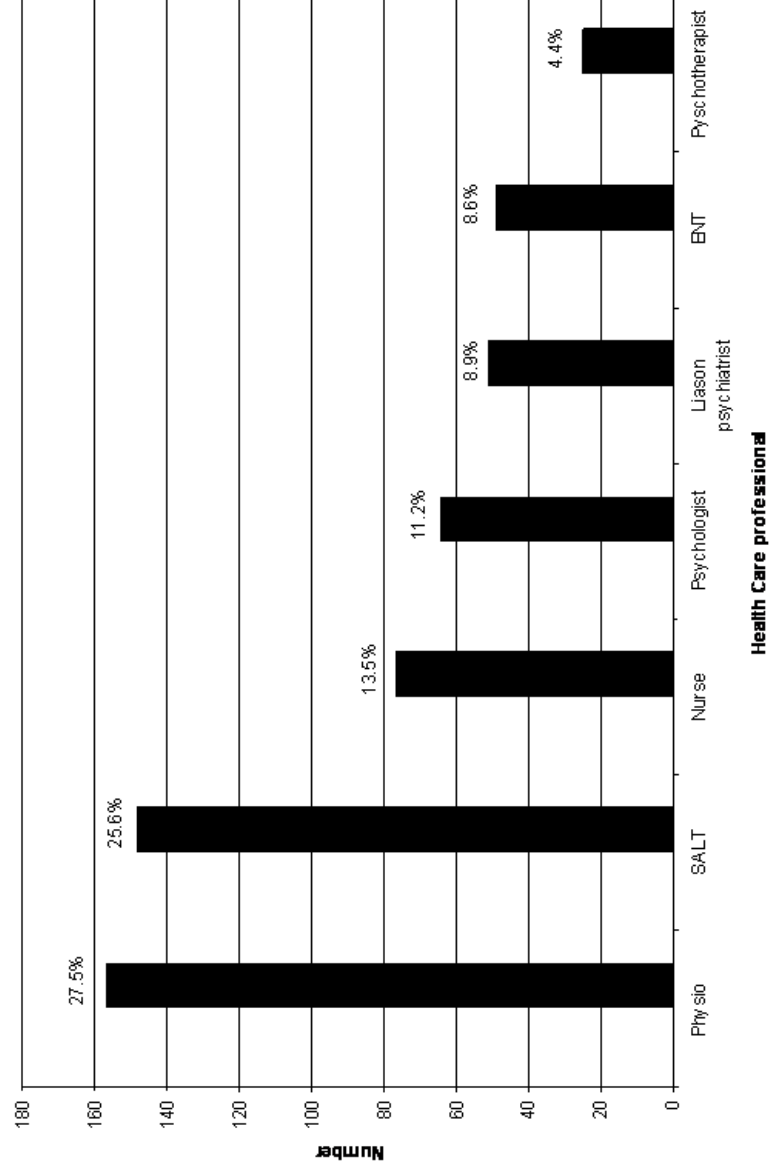




* Miscellaneous includes the following differential diagnoses, which less than 4 respondents had suggested - Obesity, chest wall deformity, sleep, systemic disorder, foreign body, occupational lung disease, pneumonia, Langerhans cell histiocytosis

† Other includes the following differential diagnoses in decreasing order of importance, allergic disease with allergen/allergic component, other respiratory disease, or rare condition, drug related illness, ENT and misdiagnosis of respiratory disorder.

Figure 4 Who is most involved with therapy of vocal cord dysfunction



SALT – Speech and Language therapy