Responding effectively to people with long term breathlessness

Introduction, Methodology, Scope and Definitions

This programme of work from IMPRESS includes:

- Impressions Blog 31: breathlessness
- The Introduction
- Methodology, Scope and Definitions
- Breathlessness prevalence modelling for COPD, heart failure, anxiety, obesity and anaemia
- The algorithm
- Breathlessness IMPRESS Tips BITs for clinicians
- Breathlessness IMPRESS Tips BITs for patients
- Breathlessness IMPRESS Tips BITs for commissioners
- Breathlessness IMPRESS Tips BITs for researchers

All the documents are available at http://www.impressresp.com/index.php?option=com_docman&task=cat_view&Itemid=82

Introduction

Following on from our groundbreaking work that analysed the relative value of interventions for a COPD population, IMPRESS decided to take on a new project. It decided to work with the London School of Economics again to apply the same STAR methodology to identify the relative value of interventions for a common symptom that matters to patients. We hypothesised that a symptom-based approach would:

- Be a more patient-focused approach than a disease-based approach
- Be more aligned to a holistic patient-centred approach

• Introduce multiple morbidities into the discussions
• Engage a wider range of clinicians from more than one specialty
• Take everyone “out of the box” and therefore potentially lead to innovative thinking about how best to practise population medicine and achieve the greatest health gain/improvement in health outcomes
• Answer some of the questions that commissioners are already asking about the right balance of generic and disease-specific services for people with long term conditions and how best to address the issues of comorbidities where, for example, it has been estimated only 14-18% of people with COPD only have COPD and when actively assessed for co-morbidities it may be as low as 3%.  

There were a number of common respiratory symptoms that we could have chosen, but we decided that the one that is a high priority on patient agendas, is closest to our previous work and sufficiently prevalent in the population to warrant a service, was chronic breathlessness in adults.

The few epidemiological studies available seem to point in the direction that chronic breathlessness affects about 10% of the general population, but the magnitude of the problem is greater in specific groups of the population, such as the elderly with about 30% of them being breathless. Despite these significant prevalence rates, breathlessness is mentioned as a reason for encounter in primary care in about 1% of the recorded consultations in general practice. Whether this figures is affected by coding behaviour in primary care or under-reporting of the symptom by patients is for discussion.

It has been an intellectually challenging piece of work. The cost-effectiveness evidence-base that we found for COPD does not exist for chronic and disabling breathlessness and therefore there is significant uncertainty. We needed to agree on a definition of breathlessness, identify the main underlying causes and bring together prevalence and incidence data for these causes: COPD, uncontrolled asthma, heart failure, anaemia, and obesity, singly or in combination and with or without anxiety, and distinguish between chronic and acute breathlessness. It seems as though some basic truths have been “blind-spots” in the research literature. For example, most patients and clinicians would say that breathlessness is a relatively common symptom for obese people (a belief also confirmed by the epidemiological data available, which show that about 50% of obese patients are breathless and up to 70% of obese elderly complain of some

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degree of breathlessness) and yet the recent excellent Royal College of Physicians Action on Obesity report has one mention and no discussion of breathlessness.\textsuperscript{10} In heart failure breathlessness may not be the cardinal symptom, which might be tiredness, however, the literature suggests up to 93\% of people with heart failure, mainly elderly, suffer from breathlessness. The sensation may be perceived by the individual as part of their normal ageing process. We had many debates about when breathlessness is disabling and warrants an intervention and what that intervention should be.

The interaction between breathlessness and anxiety is complex and so this is another reason why this project has been worth doing, because it forces discussions about the interaction between mental and physical health and highlights the need for healthcare professionals to have skills to promote both. For example, panic disorder is ten times more common in the population with COPD than in the general population.\textsuperscript{11} However, anxiety is under-diagnosed and under-treated in primary care despite strong evidence of the effectiveness of talking therapies.\textsuperscript{12 13 14}

There are few straightforward answers when you combine general practice, community and hospital clinicians from different specialties and disciplines to reach consensus about coding, symptom-scoring, patient and population interventions though much learning. It is also challenging when you bring together literature from medicine, psychology, and public health. There are also few examples of symptom-based services in operation and even fewer examples of how these are commissioned; that is, how they are paid for or monitored. However, we have reached some conclusions that could make a difference today to people with chronic and disabling breathlessness. We also have a reasonably long list of research questions that we encourage academic health science networks to investigate. We see this as the beginning of a debate about how to best set up a breathlessness service for a population. We welcome feedback, examples of good practice, and case studies and urge those setting up services to evaluate their cost and their outcomes, and to publish their findings.

One of our conclusions is that local breathlessness services and pathways will need to grow from what already exists provided by health and local authorities, and also will depend on the local populations' needs and health status. Disabling breathlessness is more common in deprived populations. Therefore we would encourage the local stakeholders involved in developing, approving and implementing joint strategic needs assessments to use our work as the basis for a local (and ultimately electronic) version.

What is certain is that the service will need to integrate mental and physical health pathways and services, and a common and consistent approach to behaviour change across a number of health specialties and public health. It is also certain that the normal consultation arrangements are not fit for purpose to assess a breathless person. We strongly recommend that services review the tests of change that a number of areas are undertaking to provide longer appointments in long term conditions in both primary and out-patients settings. We also want to reinforce the power of taking time with the patient.

\textsuperscript{14} Tyrer P et al Clinical and cost-effectiveness of cognitive behaviour therapy for health anxiety in medical patients: a multicentre randomised controlled trial. The Lancet, Available online 18 October 2013
to take a full history, once the immediate decision about whether to admit a patient has been made. At an individual level, always be mindful of three dimensions: the person’s mental health, their social context as well as their physical health, remember that breathlessness is not always caused by one single factor and that all breathlessness is stressful to some extent; the question is to what extent.

How these resources are organized

This is the introduction and methodology in which we review the definitions for breathlessness, and the main causes of breathlessness including COPD, heart failure, obesity, anxiety and anaemia, which are the terms around which we developed our work, as well as an exploration of the association between obesity and asthma.

We also propose an algorithm and Breathlessness IMPRESS Tips (BITs) organized for four main groups of stakeholders: patients, clinicians, commissioners and researchers. For each BIT, we give the rationale for suggesting it and reference the claim with currently available evidence.

We have taken a symptom-based approach, therefore our focus was not on asymptomatic patients but on finding and treating people with symptoms in an integrated way that increase value. However, it would be irresponsible to ignore primary prevention at either a population or individual level. Therefore we recommend that NICE public health guidance is followed about smoking, physical activity and weight management (see Appendix for a full list).

Method

We worked with a team from the London School of Economics including two academics from the School of Management who are experts in decision-making, a director of public health and the programme lead for the North West London Integrated Care Pilot. We invited our multi-disciplinary IMPRESS Implementation Group that had worked on our Relative Value work and represents general practice, community and hospital services and supplemented their knowledge and expertise with key informants from other specialties:

- Two primary care cardiovascular experts
- Two consultant cardiologists
- One Royal College of Physicians nominee from the Action on Obesity programme
- One health psychologist

The full list of contributors is available here.

The first task was to review the literature in order to complete a grid of the cost-effectiveness literature on interventions for breathlessness. Whilst this had to be abandoned due to the lack of evidence, it did create helpful dialogue about definitions, the scope of the work and what might be possible and meaningful.

Following substantial email debate between sub-groups looking at different causes of breathlessness, we organised a one-day workshop with key informants to debate the evidence that was available, using case studies to tease out different approaches and clinical behaviours to diagnose and manage chronic disabling breathlessness.
Subsequently, we created a web platform and email exchange to collect further evidence, refine the claims and agree on the content of this report.

Limitations of the methodology

The review of the literature for the collection of evidence available on breathlessness has not been systematic. We rather embraced a less structured and more opportunistic approach which anyway highlighted some main problems in the literature about breathlessness.

To start with, we faced problems around how breathlessness can be defined and assessed, as different scales have been used. Data on epidemiology of breathlessness is scarce, suggesting that a common and noticeable problem felt by a significant number of a local population is somehow under the radar of researchers. In the attempt of overcoming the lack of data on the epidemiology of breathlessness, we developed an algorithm for extracting these data from the electronic systems currently used in primary care. This attempt confirmed that coding of breathlessness in primary care is inconsistent.

We did not perform the same analysis on hospital data as coding in secondary care is driven by diagnosis and so was only helpful insofar as it described the impact of COPD and heart failure on hospital services. Similarly, if we look at QOF data\textsuperscript{15}, we cannot discover the prevalence of breathlessness, but only the prevalence of relevant conditions that may be associated with breathlessness in general practice.

Also the prevalence of breathlessness as a symptom reported by patients already diagnosed with a particular condition seems to be unevenly studied. For COPD and HF data are fairly available, but for other conditions (eg anxiety and anaemia) knowledge appears scarce. This affects whether and how the symptom is managed and treated in different conditions.

Scope of the work, definitions

In the literature, there are a number of words that are used for referring to breathlessness, such as shortness of breath, dyspnoea (literally “disordered breathing”)\textsuperscript{16}. There is no one definition of breathlessness from the patient or clinician perspective because patients use an array of terms to describe their breathing sensation and the term can represent a number of qualitatively distinct sensations\textsuperscript{17,18,19,20}

“I just feel I can’t get my breath”

“I never seem to have any breath when I try and do things”

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\textsuperscript{15} 2011-12 GP QOF submissions www.gpcontract.co.uk


\textsuperscript{17} Sarkar S, Amelung P J. Evaluation of the dyspneic patient in the office. Primary care. 2006;33:643–57.

\textsuperscript{18} Ambrosino N, Serradori M. Determining the cause of dyspnoea: linguistic and biological descriptors. Chronic Respiratory Disease. 2006;3:117.


“No matter how big a breath I take, it doesn’t feel enough”
“I can never catch my breath”
“It feels as if there is no air in the room”
“I feel as though I am so breathless I will die”
“It makes you very frightened”

These different sensations will depend on personally-felt interactions between physiological, psychological, social and environmental factors. Breathlessness can also be described by the individual in terms of time course, frequency and triggers, its intensity and the distress it evokes and impact on function, psychological, social and spiritual well-being. Qualitative studies on the experience of breathlessness show that the range of descriptors used by patients varies across the underlying conditions causing their breathlessness.

According to the American Thoracic Society breathlessness is a “subjective experience of breathing discomfort that derives from interactions among multiple physiological, psychological, social, and environmental factors, that may induce secondary physiological and behavioural responses”. (...)

breathlessness.\textsuperscript{32} Virtually all people will feel breathless on relatively mild exertion when at altitude so environment makes a difference.

The American College of Chest Physicians defines breathlessness as a complex sensation with a wide range of factors that can generate and sustain it\textsuperscript{33}. The efferent drive to breathe is mediated through the phrenic nerves and nerves supplying the intercostal muscles. When these pathways are stimulated out of proportion to their ability to respond by afferent signals from chemo- and mechano-receptors, the mismatch between the two systems generates the feeling of breathlessness.

Therefore to exclude shortness of breath caused by an acute condition and the normal – and healthy - feeling of being out of breath after physical activity, we chose to limit our scope to long-term or chronic breathlessness that develops over weeks or months and that might or might not have a physiological basis. How long “chronic” is, it is subjective.

**Assessing breathlessness to determine its impact and guide intervention**

As with other symptoms like pain, breathlessness can and should be measured to assess it adequately. There have been many efforts to develop and validate measures and instruments over the last few years. Some of these come from the respiratory community, and others from the cardiovascular community and they are not the same. For example, the first response from a cardiology colleague might be to use the New York Heart Association (NYHA) functional classification which includes breathlessness, whereas the first response from a respiratory colleague might be to use the Medical Research Council (MRC) dyspnoea scale which is also a functional classification and limited to breathlessness. They are very similar although not validated against each other in other conditions. There are also a number of versions of the MRC scale, which is important particularly at Grade 3 because this is currently used as the threshold for referral to pulmonary rehabilitation.

**Table 1 - Medical Research Council dyspnoea scale\textsuperscript{34}**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Degree of breathlessness related to activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Not troubled by breathlessness except on strenuous exercise</td>
</tr>
<tr>
<td>2</td>
<td>Short of breath when hurrying or walking up a slight hill</td>
</tr>
<tr>
<td>3</td>
<td>Walks slower than contemporaries on level ground because of breathlessness, or has to stop for breath when walking at own pace</td>
</tr>
<tr>
<td>4</td>
<td>Stops for breath after walking about 100m or after a few minutes on level ground</td>
</tr>
<tr>
<td>5</td>
<td>Too breathless to leave the house, or breathless when dressing or undressing</td>
</tr>
</tbody>
</table>

In order to determine the best course of therapy, physicians often assess the stage of heart failure according to the New York Heart Association (NYHA) functional


classification system. This system relates symptoms to everyday activities and the patient's quality of life.

Table 2 - NYHA Classification - The symptoms of Heart Failure

<table>
<thead>
<tr>
<th>Class</th>
<th>Patient Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I (Mild)</td>
<td>No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea (shortness of breath).</td>
</tr>
<tr>
<td>Class II (Mild)</td>
<td>Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea.</td>
</tr>
<tr>
<td>Class III (Moderate)</td>
<td>Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea.</td>
</tr>
<tr>
<td>Class IV (Severe)</td>
<td>Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.</td>
</tr>
</tbody>
</table>

Instruments may ask what breathing feels like (as with the Borg Scale or its modified version\(^{36}\)), whereas others may ask how distressing it is (eg. the Medical Research Council dyspnoea scale\(^{37}\), and its modified version\(^{36}\), the numerical Rating Scale (NRS)\(^{38}\) or how it impacts performance (such as the Baseline Dyspnea Index (BDI) - Transitional Dyspnea Index (TDI)\(^{40,41}\) or quality of life (eg, the Chronic Respiratory Disease Questionnaire (CRQ)\(^ {42} - 44\), the rating task (i.e., what patients or research subjects are instructed to rate), and whether measurements are real-time or involve recall of a specific episode, some defined interval, or how things usually are. Some measures are unidimensional (i.e. measuring the severity of breathlessness), others are multidimensional, and of these some are breathlessness-specific and others disease-

\(^{35}\) http://www.abouthf.org/questions_stages.htm accessed 25 July 2013


specific. Reviews on instruments for breathlessness assessment can be found in and.

Therefore our conclusion, confirmed by many, is that no single measure of breathlessness covers all its possible domains, and there is no reason not to use the NYHA or MRC scales as long as their purpose and how to use them is understood to increase inter-rater reliability and reproducibility (see Appendix).

We have also proposed an IMPRESS definition:

**Proposed IMPRESS definition**

Breathlessness is the sensation of not getting enough air, and may be the result of anything that interferes with the extraction of oxygen from air and its delivery to the tissues. Therefore any of: altitude, asthma, rib fracture, COPD, heart failure, exercise or anaemia may be the cause. It can also be caused, or contributed to, by anxiety.

Long-term or chronic breathlessness is experienced by an individual over a period of months and may develop without them noticing.

**Diagnosis associated with breathlessness**

The underlying causes of long-term breathlessness can be manifold. In the case of chronic breathlessness, the condition is most often due to respiratory or cardiac problems, such as

- Asthma
- COPD
- Heart arrhythmias
- Heart failure
- Lung cancer
- Pleurisy
- Pulmonary fibrosis
- Sarcoidosis
- Cardiomyopathy
- Croup
- Heart dysfunction
- Interstitial lung disease
- Pericarditis
- Pulmonary oedema
- Pulmonary hypertension
- Tuberculosis

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In addition to these cardio-respiratory causes (which represent two thirds of patients with breathlessness\textsuperscript{52}), other possible conditions associated with breathlessness are\textsuperscript{53,54}:

- Anaemia
- Obesity
- Chest wall pathology
- Broken ribs
- Foreign object inhaled: First aid
- Thromboembolic disease
- Gastroesophageal reflux disease
- Liver cirrhosis
- Neuromuscular disorders (myasthenia gravis, amyotrophic lateral sclerosis)
- Upper airway obstruction (laryngeal disease, tracheal stenosis)
- Hyperthyroidism
- Deconditioning
- Neuromuscular disease
- Epiglottitis
- Guillain-Barre syndrome
- Psychogenic causes (GAD, PTSD, panic disorders)
- Metabolic conditions (acidosis, uremia)
- Thyroid disease
- Chest wall deformities (kyphoscoliosis)
- Mental health problems

Breathlessness can be caused by a single underlying condition or by the interaction of two or more underlying conditions (complex multi-morbidity breathlessness).

In some cases the diagnosis or contribution of various components to the breathlessness remains uncertain, if not unexplained. A study of a sample of 72 patients referred because unexplained breathlessness had been present for more than 1 month, a definite diagnosis could be established only in 81\%.\textsuperscript{55}

It is worth mentioning also that diagnosing breathlessness can be difficult. The concordance between the clinical diagnosis on referral and the final diagnosis at the breathlessness clinic was found in less than 40\% of the patients studied by Nelson and colleagues in their study of 284 breathless patients referred from the GPs to a hospital-based breathlessness clinic.\textsuperscript{56} A slightly higher rate of accurate first diagnosis was reported by Pratter and colleagues. According to this study, physicians' predictions following history and physical examination were accurate 55\% of the time compared with final diagnoses. When results of pulmonary function tests were added, accuracy increased to 72\%.\textsuperscript{57}

The brief account made by Mustchin and Tiwari about the emergency admissions in which breathlessness was recorded as a prominent presenting symptom showed that in only 8\% of the cases there was a discrepancy between the admission and the final


\textsuperscript{53} http://www.mayoclinic.com/health/shortness-of-breath/MY00119/DSECTION=causes


diagnosis or no diagnosis was made during the hospital stay.\(^{58}\) In some cases it is not the presenting symptom.

Identifying the underlying aetiology of breathlessness is essential in determining its management and the most appropriate treatment for the patient. This may require the coordinated intervention of a number of experts. However, in some people, particularly frail elderly people, it may not be appropriate to make a diagnosis: the point of tests and diagnosis being to plan interventions.

Besides being affected by a physical problem and/or a particular psychological state, breathlessness can be shaped by an individual's particular life situation. Therefore in addition to other causal factors, sex, ageing, pregnancy, menopause have been reported to be often associated with breathlessness.\(^{59}\)

**Prevalence and incidence of breathlessness**

There are only a few large scale epidemiological studies on breathlessness. In addition, comparability across them is not straightforward because of the heterogeneity of definitions and measurements of breathlessness used, study populations included, time horizons and study designs adopted. In this section we briefly review and compare the results of the studies on breathlessness which have been realized in different settings: in the general population, in primary care, in ED departments, among the elderly, and among end-of-life patients.

**General population**

Two community-based Australian studies are available using data collected in two editions of the South Australian Health Omnibus. Currow found an overall prevalence of 8.9% in a population of 5,473 participants over 15 years in South Australia using 2006/2007 survey data. More marked impairment from breathlessness (MRC 3-5) was seen in 2.6% of the total population. The results by age group show that prevalence rates increase with age: 6.7% in people aged less than 35, 4.9% in people aged 35-49, 9.8% in those aged 50-64, 16.9% in those aged 65 or above.\(^{60}\)

In a similar sample of 5,331 participants from the 2007-2008 survey, there was an increase. Overall 11.1% of the population sampled reported breathlessness and 3.4% of them had an MRC score between 2 and 4. Prevalence was reported in 15% of the respondents aged 50 years or over\(^{61}\).

In a general population sample (2,306 participants) in Sweden, breathlessness, defined as grade 2, was reported by 20.5% of women and 12% of men, giving an overall prevalence rate of 16.4%.\(^{62}\)

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The Vlagtwedde/Vlaardingen study based in the Netherlands on a general population cohort of 7,360 exclusively Caucasian individuals of Dutch descent found moderate and severe breathlessness respectively in 5% and 1% of the study sample.\(^{63}\)

**Primary care**

Prevalence has been studied more extensively in primary care settings, as it appears to be a common symptom in general practice.\(^{64}\)

Jolly reported an annual incidence and an annual prevalence of 7.3 and 15.4 per 1,000 patients at risk per year\(^{65}\) in a sample of 121 patients in Canada in 1974-1975.

In a larger sample of a thousand patients over a 3-year period (1984-1987) in the USA, Kroenke estimated a three-year incidence of 3.7%.\(^{66}\)

More recently, Charles used the data available through the BEACH program, a national study of general practice activity in Australia from April 1998 to March 2004, to conclude that in 5,215 encounters the patient gave breathlessness as one of their reasons for the encounter, that is 0.9 per 100 encounters.\(^{67}\)

**Older people**

Breathlessness is a common experience for older people and therefore it is often associated not only with specific conditions but more in general with the process of ageing.

Abramson studied self-reported breathlessness measured by the MRC scale in a random sample of 4,276 adults aged between 45 and 69 years drawn from electoral rolls for Melbourne, Australia. The prevalence rate of exertional breathlessness was estimated at about 27%.\(^{68}\) A similar prevalence rate (24%) was found in a random sample of 210 55-year and older subjects in the Netherlands with a Borg score higher than 0\(^{69}\).

In a group of 152 patients with MRC grade > 1 and aged 60-79 living at home, 31% had breathlessness confirmed at examination.\(^{70}\)

In a large community-based study performed in France in a sample of more than 4,000 residents aged 65 and over, breathlessness was found in about 60% of them, with women reporting higher rates than men (63.8% vs 58.3%).\(^{71}\)

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In a UK-based study, 32.3% of the study population of 1,169 subjects aged 70 and over living at home in Barry, South Wales interviewed by Ho and colleagues had breathlessness (MRC grades 3-5) confirmed\textsuperscript{72}. As the only UK study we found, it is important to have these data but it is not certain to what we might attribute these higher rates.

Another European study among 114 patients over 70 found a higher prevalence rate of breathlessness (55%): 32% (n = 27) had mild breathlessness complaints (MRC 1 or 2) and moderate to severe symptoms (MRC > 3) were reported by 23% of the respondents. In the subsample that completed the BDI interview, 37% reported moderate to severe breathlessness. According to the Authors of the study discrepancies between these two figures may reflect differences in the two instruments and the mode of administration (questionnaire versus interview), the interval of approximately three months between the two assessments, and differences in the composition of the sample due to exclusion or drop-out in that interval.\textsuperscript{73}

**People with advanced disease**

A recent comparison of symptom prevalence among people with five advanced, life-limiting diseases found that breathlessness is one of the core symptoms which are particularly persistent and frequent towards the end of life. Breathlessness is a symptom which affects patients with many conditions. It is very common in patients with advanced cancer of any primary site, occurring in 78% of patients with lung cancer\textsuperscript{74} and 50-70% of all cancer patients.\textsuperscript{75} It affects up to 95% of chronic obstructive pulmonary disease (COPD) patients\textsuperscript{76} and 88% cardiac failure patients.\textsuperscript{77}

Usually it is associated with a great level of distress – Edmonds et al. (2001) reported that 60% of breathless patients with lung cancer described it as “very distressing”).\textsuperscript{78}

It can also be a major factor in causing emergency hospital admissions. Escalante et al. found that 7% of a sample of cancer patients was admitted to the ED with a complaint of


breathlessness. Its incidence increases in the last six weeks of life and is associated with a poor prognosis.

Some studies report that breathlessness is a contributing factor to the need for palliative sedation at the end of life. For example, Mercadante found that in 25 patients out of 77 terminally ill patients breathlessness was the indication for sedation. In a multicentre observational study investigating the efficacy of palliative sedation for end-of-life patients, the Authors found that almost 60% of the study population reported intolerable dyspnoea requiring sedation.

**Emergency Department (ED)**

Sudden shortness of breath, or breathing difficulty, is the most common reason for visiting ED. Breathlessness has been examined across diagnoses in a general ED in the United States, revealing a prevalence of 2.7% of all visits. In a UK-based study the prevalence of breathlessness resulted much higher rate as was found in 25% of all patients admitted as medical emergencies. Mustchin reported a similar rate: according to his results, in 21% of all emergency admissions breathlessness was recorded as the prominent presenting symptom.

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89 Pearson SB. The diagnosis and management of patients admitted to hospital with acute breathlessness. Postgraduate medical journal. 1981;57(669):419.

Conclusion

To conclude, the epidemiology of breathlessness seems to be an under-researched area of study. When studies are available, methodological differences compromise any possible direct comparisons. There are substantial differences between studies in the general population, primary care the elderly and end-of-life patients, and ED. Community studies by Currow in South Australia quantified breathlessness prevalence rates between 9 and 11%. Breathlessness as a reason for an encounter is reported in 1-4% of the patients attending primary care. A 4% three-year incidence rate is reported in one study and another one found an annual incidence of 7.3 per 1,000 patients at risk. Calculations of prevalence rates of breathlessness in older people vary between 24 and 32%.

Breathlessness is one of the core symptoms which are persistent and frequent towards the end of life. Depending on the underlying conditions it can affect up to the whole population of the end-of-life patients.

Sudden shortness of breath, or breathing difficulty, is the most common reason for visiting an ED – 25% of all patients admitted as medical emergencies reported also breathlessness.

Therefore breathlessness is a problem that would benefit from a population approach as well as a consistent approach by clinicians in general practice, community and hospital settings.

Breathlessness in different conditions

In this section we now review the epidemiology of breathlessness in different conditions. We consider heart failure, COPD, obesity, anaemia and anxiety which are responsible for about 50% of the burden of disease associated with breathlessness.  

For each of this condition we investigate (i) how often patients presenting with breathlessness are diagnosed with a specific condition and (ii) how often patients who already have been diagnosed with that condition complain of breathlessness. This is supported by detailed modelling, available at http://www.impressresp.com/index.php?option=com_content&view=article&id=172:impressions-31-breathlessness&catid=11:impressions&Itemid=3.

These data allow us to start describing who the breathless patients are and how the breathless population as a whole looks like. In order to do so, for each condition we have chosen data available from studies realized in the general population, when available, or in primary care. Therefore we have deliberately not included results from studies performed in special groups, such as the elderly or patients admitted to the hospital, or in particular settings, eg tertiary care centres, as not representative of the general population.

Available prevalence rates have been used to estimate the expected number of patients with breathlessness and of breathless patients with a specific condition already diagnosed both at the CCG level (under the assumption that there the median number of

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patients in a CCG is 251,700, of whom about 173,000 adults\(^{92}\) and for a GP (assuming an average list size of 1,520 patients, of whom 1,140 adults\(^{93}\)).

**Heart failure**

Heart failure (HF) is a complex clinical syndrome of symptoms and signs that suggest impairment of the heart as a pump supporting physiological circulation. It is caused by structural or functional abnormalities of the heart. The demonstration of objective evidence of these cardiac abnormalities is necessary for the diagnosis of heart failure to be made. The symptoms most commonly encountered are breathlessness, fatigue and ankle swelling.\(^{94}\)

Heart failure can be classified according to New York Heart Association criteria, where class I (i.e. no symptoms) is the mildest grade and class IV (symptoms of cardiac insufficiency at rest) is the most severe grade.\(^{95}\) The American College of Cardiology/American Heart Association (ACC/AHA) has proposed an alternative staged heart failure classification, listed from stage A identifying the patient who is at high risk for developing heart failure but has no structural disorder of the heart to stage D designating the patient with end-stage disease who requires specialized treatment strategies such as mechanical circulatory support, cardiac transplantation, or hospice care.\(^{96}\)

The prevalence of heart failure has been estimated at 1-2% of the adult population and approximately 6-10% in the elderly\(^{97}\), and the incidence approaches 5-10 per 1000 persons per year.\(^{98,99}\) According to the QOF statistical bulletin, in 2011-12 in England the prevalence of diagnosed HF was 0.7%.\(^{100}\)

Breathlessness is a hallmark symptom of HF, common and distressing for patients.\(^{101}\)

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\(^{95}\) [http://www.abouthf.org/questions_stages.htm](http://www.abouthf.org/questions_stages.htm)


\(^{99}\) For a review of epidemiological studies on heart failure see McMurray J, Stewart S. Epidemiology, aetiology, and prognosis of heart failure. Heart; 2000;83:596-602.


Studies on the prevalence of symptoms in HF patients have been realized in different settings (primary care vs secondary care vs ED), including a variety of study populations (eg. the community, the elderly and end-of-life patients), with methods which varied from medical records reviews to surveys to interviews. A comparative analysis of these studies is therefore quite challenging.

Studies performed in patients of every ages living in the community found prevalence of breathlessness of 57%, whereas among the hospitalized this rate was about 76-100%. These data are also confirmed by the latest National Heart Failure Audit on about 44,000 hospital admissions for acute heart failure across England and Wales. According to this audit about 80% of patients on first admission and 84% of those readmitted were breathless on minimal exertion or at rest, hence confirming the findings from previous audits.

Among the elderly breathlessness was reported in 54 to 66% of the HF patients recruited in the community, a prevalence rate lower when compared to elderly patients hospitalized among whom breathlessness was reported in 89-95% of the cases studied.

The results of the Olmsted County study which reported breathlessness in 93% of the 216 new cases of definite HF mainly among elderly patients living in the community seems to be an outlier when compared to this stream of research, which may be partially explained by the high proportion (49%) of patients over 80.

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A large US-based study of emergency visits for cardiorespiratory disease found that 62% out of 320 HF patients reported breathlessness as primary reason for the ED visit.\textsuperscript{113}

Another group of studies looked at patients with advanced HF, finding breathlessness in 45 to 85% of the study samples.\textsuperscript{114 115 116}

The last group of studies investigated symptoms prevalence in hospitalized end of life patients. A systematic review of studies on patients with end-stage chronic organ failure found that 42-79% (median 62%) HF patients at the terminal stage of their disease (eg in the last 2 weeks of life, the last week, the last 3 days, the last 24 hours) experienced breathlessness. Among those not at the terminal stage the same symptom was assessed in the range of 18-88% (median 72%)\textsuperscript{117}. Also Solano and colleagues who reviewed 64 original studies reporting the prevalence of 11 common symptoms among end-stage patients, including HF patients in whom breathlessness was reported in the range of 60-88%\textsuperscript{118}. The variability in the results of both these reviews reflects the heterogeneity in methodology used across studies.

In addition to these systematic reviews, we retrieved a few large population-based studies that measured the prevalence of breathlessness in HF patients near the end of life between 60 and 80%.\textsuperscript{119 120 121 122}

Reported prevalence rates of breathlessness with heart failure as underlying cause vary between 4 and 27% depending on the characteristics of the study populations.

In a study aiming at understanding the patient-perceived causes of breathlessness, people in the community reporting being breathless were directly asked to what they attributed their breathlessness. 17% of the respondents (more than 2,800 Australians) self-reported that the daily experienced of this symptom for at least 3 months within the last 6 months was caused by HF.\textsuperscript{123}

\textsuperscript{122} Zambroski CH, Moser DK, Roser LP, Heo S, Chung ML. Symptoms Experienced by Heart Failure Patients in Hospice Care. Am Heart J. 2005 Mar;149(3):558-64.
According to the data collected through the BEACH program, a continuous national study of general practice activity in Australia, 18.2% encounters at which the patient gave breathlessness as one of their reasons for encounter received a diagnosis of HF.\textsuperscript{124} Studies performed in specialist clinics found controversial results. In a study of 123 patients with a chief complaint of breathlessness of unknown cause present for >8 weeks referred to a university pulmonary practice, 6% received a final diagnosis of heart failure/ cardiomyopathy (includes diastolic dysfunction, systolic dysfunction, and ischemic heart disease).\textsuperscript{125} In a similar study performed in a sample of 284 consecutive patients referred from general practice to hospital with breathlessness, heart failure was found to be the final diagnosis in 27% of them, a much higher proportion.\textsuperscript{126}

Finally, a study realized in an Emergency Department in the US hospital reported that 26% of 162 patients who gave breathlessness as primary complaint for visiting the ED was then diagnosed with HF.\textsuperscript{127}

It is worth mentioning also a couple of studies about cardiac diagnoses in general which have been found associated with breathlessness. The first one is the study by Jolly on 50 primary care patients newly presenting with breathlessness which found that cardiovascular disorders was found in 16.7% of males and 31.3% of females.\textsuperscript{128} The second study aimed at testing a diagnostic algorithm for evaluating breathlessness in 152 elderly patients recruited from general practice and 21% of them were diagnosed with heart disease.

The prevalence rates collected from published studies allow thus to estimate that in an English CCG we would expect about 5,800 patients suffering from CF, half of them above the age of 65. Of the HF patients, about 3,750 would complain of some level of breathlessness (almost 2,100 in the older age group). The number of patients presenting with breathlessness and in whom HF would be found as the cause of their symptom would be about 3,400.

Table 3 – Estimate of the burden of disease of breathlessness associated with HF in a CCG

<table>
<thead>
<tr>
<th>Baseline population</th>
<th>No. patients per CCG</th>
<th>Prevalence rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIN</td>
<td>MAX</td>
</tr>
<tr>
<td>Median CCG population</td>
<td>251,700</td>
<td></td>
</tr>
<tr>
<td>Median CCG population (total adult)</td>
<td>172,730</td>
<td></td>
</tr>
<tr>
<td>Median CCG population – adult 18-65</td>
<td>135,454</td>
<td></td>
</tr>
<tr>
<td>Median CCG population – elderly 65+</td>
<td>35,411</td>
<td></td>
</tr>
<tr>
<td>Prevalence of HF - adult 18-65</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


\textsuperscript{128} Jolly DT. Dyspnea In Primary Care. Can Fam Physician. 1978 October; 24:983-984.
Prevalence of HF - elderly 65+

<table>
<thead>
<tr>
<th></th>
<th>MIN</th>
<th>MAX</th>
<th>AVG</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF cases – total</td>
<td>2,125</td>
<td>3,541</td>
<td>2,833</td>
</tr>
<tr>
<td>QOF diagnosed prevalence for HF</td>
<td>1,209</td>
<td>0.7%</td>
<td></td>
</tr>
</tbody>
</table>

Breathless patients in the general population

<table>
<thead>
<tr>
<th></th>
<th>MIN</th>
<th>MAX</th>
<th>AVG</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF patients diagnosed with HF</td>
<td>15,373</td>
<td>19,173</td>
<td>17,273</td>
</tr>
</tbody>
</table>

Breathless patients diagnosed with HF

<table>
<thead>
<tr>
<th></th>
<th>MIN</th>
<th>MAX</th>
<th>AVG</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF patients complaining of breathlessness - adult 18-65</td>
<td>772</td>
<td>1,544</td>
<td>1,158</td>
</tr>
</tbody>
</table>

HF patients complaining of breathlessness - elderly 65+

<table>
<thead>
<tr>
<th></th>
<th>MIN</th>
<th>MAX</th>
<th>AVG</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF patients complaining of breathlessness – total</td>
<td>1,919</td>
<td>4,837</td>
<td>3,240</td>
</tr>
</tbody>
</table>

Similarly, we can estimate that a GP with a patient list of 1,140 adult patients would have 32 patients with HF in total [23-41] and the majority of them will be elderly. More than 70% of them would complain of breathlessness, and again the elderly will be the most affected by it. This GP would see in total 114 patients complaining of breathlessness [101-127] and in 21 [13-32] of them HF will be found as the underlying cause for their breathlessness.

Table 4 – Estimate of the burden of disease of breathlessness associated with HF at the GP level

<table>
<thead>
<tr>
<th>Population baseline</th>
<th>No. patients per GP</th>
<th>Prevalence rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIN</td>
<td>MAX</td>
</tr>
<tr>
<td>Average patients list per GP in England (adult only)</td>
<td>1,140</td>
<td></td>
</tr>
<tr>
<td>Average GP population - adult 20-65</td>
<td>912</td>
<td></td>
</tr>
<tr>
<td>Average GP population – elderly 65+</td>
<td>228</td>
<td></td>
</tr>
<tr>
<td>Prevalence of HF - adult 20-65</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>Prevalence of HF - elderly 65+</td>
<td>14</td>
<td>23</td>
</tr>
<tr>
<td>Cases of HF – total</td>
<td>23</td>
<td>41</td>
</tr>
<tr>
<td>QOF diagnosed prevalence for HF</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Breathless patients in the general population</td>
<td>101</td>
<td>127</td>
</tr>
<tr>
<td>Breathless patients diagnosed with HF</td>
<td>18</td>
<td>23</td>
</tr>
<tr>
<td>HF patients complaining of breathlessness - adult 15-65</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>HF patients complaining of breathlessness - elderly 65+</td>
<td>7</td>
<td>21</td>
</tr>
<tr>
<td>HF patients complaining of breathlessness – total</td>
<td>13</td>
<td>32</td>
</tr>
</tbody>
</table>
COPD

Chronic obstructive pulmonary disease (COPD) is an umbrella term for chronic lung diseases. It is now the preferred term for the conditions in patients with airflow obstruction who were previously diagnosed as having chronic bronchitis or emphysema.

COPD is characterised by airflow obstruction that is not fully reversible. The airflow obstruction does not change markedly over several months and is usually progressive in the long term. COPD is predominantly caused by smoking. Other factors, particularly occupational exposures, may also contribute to the development of COPD. Smoking or inhaled dust leads to blockage or narrowing of the airways. COPD symptoms include breathlessness and a chronic cough. As the disease progresses over time, patients experience poorer lung health, worse breathlessness and more frequent exacerbations of their condition, where there is a rapid and sustained worsening of symptoms beyond normal day-to-day variations. This often leads to emergency hospital admissions.

COPD produces symptoms, which may respond to pharmacological and other therapies (eg pulmonary rehabilitation) that have limited or no impact on the airflow obstruction.

COPD is increasingly recognised as an important long-term lung condition with a high burden for patients in terms of disability and impaired quality of life and a large cost to the healthcare systems.

The complexity of the disease calls for a multidimensional assessment: several aspects of the clinical presentation of the disease, such as symptom perception, limitation in physical activity, lung function, and exacerbations, interrelate to configure the final disease expression. There is no single diagnostic test for COPD. Making a diagnosis relies on clinical judgement based on a combination of history, physical examination and confirmation of the presence of airflow obstruction using spirometry. Spirometry is required to diagnose COPD patients according to international guidelines.

The working definition of COPD, as noted in the 2013 update of the Global Initiative for Obstructive Lung Disease (GOLD) guidelines, goes as follows “COPD is a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients”.

This classification, which has been used in many studies and publications on COPD in the last year, has been now updated with a new classification system (A-D) based on symptoms, airflow obstruction, and exacerbation history. Symptom burden is measured by either the modified Medical Research Council questionnaire (mMRC) or the COPD


130 http://www.hta.ac.uk/project/2569.asp accessed on 24th September 2013

131 http://www.hta.ac.uk/project/2569.asp accessed on 24th September 2013


assessment test (CAT). The assessment starts with categorization by symptom burden, and then is refined by “risk” evaluation using FEV1 and/or exacerbation history. Patients can be categorized into the higher risk groups (C and D) by either low FEV1 or frequent exacerbations, or both.

This approach reflects the complexity of COPD better than the unidimensional analysis of airflow limitation assessed with spirometry previously used for staging the disease.

Despite the importance of this disease, the general perception is that the prevalence of COPD is not well measured. Potential sources of inter-study variation that could affect reported prevalence estimates have been identified.\textsuperscript{135}

It is currently estimated that in the UK over 3 million people have the disease and that an estimated 2 million have undiagnosed COPD (“the missing millions”) and data available seem to show that the problem in England, analyzed in this paragraph, is even more serious.

The study by Shahab and colleagues found out that spirometry-defined COPD was present in 13.3% of 8,200 adults over the age of 35 who participated in the Health Survey for England. Over 80% of them reported no respiratory diagnosis. Even among people with severe or very severe COPD by spirometric assessment, only 46.8% reported any diagnosed respiratory disease.\textsuperscript{136}

According to the Quality Outcome Framework (QOF) statistical bulletin approximately 939,000 out of 55 million people in England have been diagnosed with COPD in 2011-12, for a diagnosed prevalence of 1.7%.\textsuperscript{137} In 2004/2005 there were 717,000 patients diagnosed with COPD, and prevalence was about 1.4%.\textsuperscript{138}

Approximately 1 person in 59 has received a diagnosis of COPD at some point in their lives. In the most socio-economically deprived quintile, 1 in 32 patients was diagnosed with COPD, compared with 1 in 98 patients in the most affluent quintile. Most deprived patients represent about the 30% of the COPD patients, whereas the most affluent ones are about the 15%.\textsuperscript{139}

According to the NHS Atlas of Variation, respiratory disease is the third leading cause of death in England after circulatory disease and cancer. In England, around 23,000 people die from COPD each year. Acute exacerbation of COPD is itself a high-mortality condition: 1 in 12 patients will die during an emergency admission; 1 in 6 will die within 3 months.\textsuperscript{140} COPD is the second most common reason for emergency admission to hospital, accounting for 1 in 8 non-elective admissions. Local audit data suggests that a third of patients admitted for the first time with acute exacerbations of COPD have


\textsuperscript{137} The Health and Social Care Information Centre, Prescribing Support Unit, http://www.hscic.gov.uk/catalogue/PUB08661 accessed on 10th September 2013

\textsuperscript{138} The Health and Social Care Information Centre, Prescribing Support Unit, http://www.hscic.gov.uk/catalogue/PUB05951 accessed on 10th September 2013


severe disease and have had no prior diagnosis.\textsuperscript{141} Re-admissions are a substantial problem in the treatment of patients with COPD. Of all emergency re-admissions to hospital, COPD is the fifth most common cause. At any one time, around one-third of all people admitted as an emergency with COPD have been treated in hospital for the same condition within the preceding 30 days.

Mortality from COPD in England shows a strong urban/rural gradient: lower mortality rates were seen in rural and mixed areas, while higher event ratios were seen in conurbations. The same analysis showed a north/south divide, with higher COPD rates seen in northern areas of England.\textsuperscript{142}

Smoking accounts for approximately 80\% of COPD cases and is the cause of 85\% of all deaths from COPD.\textsuperscript{143} COPD is an important co-morbidity in those dying from other smoking related diseases, most commonly ischaemic heart disease and lung cancer Bill 4 and yet smoking is rarely cited on death certificates, even in cases where the causal link with smoking is very strong.

Prevalence of current smokers among COPD-diagnosed patients has been found at 35\% in the study realized by Shahab and colleagues. 29.5\% of patients were diagnosed with mild COPD, 38.3\% with moderate COPD and 40.5\% with severe/very severe COPD. A similar rate of smoking was found in a group of 307 patients with COPD enrolled in a London-bases study (32.9\%).\textsuperscript{145} Among the ever-smokers Shahab’s figures increase dramatically. 70.5\% of the ever smokers received a diagnosis of COPD, of whom 60.4\% of mild, 75.8\% moderate and 83.5\% severe/very severe COPD.\textsuperscript{146}

Interestingly, more recent avenues of research have started bringing into question the myth that COPD is only for smokers and showed that the burden of COPD in non-smokers is much higher than supposed. It is now recognized that never smokers may account for between one-fourth and one-third of all COPD cases.\textsuperscript{147}

The most common symptoms for COPD are breathlessness, chronic cough and chronic sputum production. COPD symptoms are often under-reported by patients.\textsuperscript{148 149 150 151}


\textsuperscript{147} For a review of studies on COPD in nonsmokers, see Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. Lancet. 2009 Aug 29;374(9691):733-43.


and not recognized by physicians, especially in the early stage of the disease.\textsuperscript{152, 153, 154} As a consequence, COPD is largely undiagnosed. Halbert et al. estimated that the ratio of true COPD cases to self-reported diagnoses ranged from approximately 1.5 to 4.\textsuperscript{155}

In addition to problems of under-diagnosis, there might be also problems with misdiagnosis. A review of the diagnoses or suspected diagnoses of the patients referred for spirometry in primary care showed that more than half of the patients referred for asthma or COPD or both, had no evidence of airway obstruction on testing. In 6 of them with BMI of more than 30, obesity seemed to rather be the cause for their breathing problems.\textsuperscript{156}

Breathlessness represents the most disabling symptom of COPD and its prevalence increases with the severity of COPD.\textsuperscript{157}

A number of studies have been performed in order to estimate the prevalence of breathlessness among COPD patients. Comparability across studies is undermined by the heterogeneity of study populations included and criteria adopted for assessing breathlessness. A number of studies investigated the prevalence of breathlessness (any level) in patients with COPD, finding rates between 3.8 and 53%. Moderate or severe level of breathlessness have been reported in 7-61% of patients with any severity of COPD.

We retrieved a couple of studies investigating the prevalence of breathlessness in the outpatient setting. In the study by Viejo-Bañuelos, out of almost 12,000 patients with a previous diagnosis of COPD - confirmed by history and spirometry – 54% of patients presented with breathlessness as reason for consultation.\textsuperscript{158} Another study performed in the US, including patients at least 60 years old with a primary diagnosis of COPD or HF, found that 74 out of a total sample of 133 COPD patients reported shortness of breath.\textsuperscript{159}

In a US-based study of emergency visits for cardiorespiratory disease found that 78.2% out of 239 COPD patients reported breathlessness as main presenting symptom for the

\textsuperscript{153} Rabe K. Outcome measures in COPD. Primary care respiratory journal. 2004;13(4):177.
\textsuperscript{157} Steuten LM, Creutzberg EC, Vrijhof HJ, Wouters EF. COPD as a multicomponent disease: inventory of dyspnoea, underweight, obesity and fat free mass depletion in primary care, Prim Care Respir J. 2006 Apr;15(2):84-91.
ED visit. Among patients with COPD, breathless patients were nearly twice as likely to be admitted as those who were not.\textsuperscript{160}

The prevalence of breathlessness caused by COPD has been reported in a few studies performed both in primary, in secondary care and in ED. Results showed some degree of variation, depending on the characteristics of the populations studied: high rates were found in primary care (19-36\%) and lower rates in secondary care (9-14\%) and ED (14-17\%).

In a study aiming at understanding the patient-perceived causes of breathlessness, people in the community reporting being breathless were directly asked to what they attributed the cause of their breathlessness. 64\% of the sample (more than 4,000 Australians) self-reported that the daily experienced of this symptom for at least 3 months within the last 6 months was caused by COPD.\textsuperscript{161}

According to the data collected through the BEACH program, a continuous national study of general practice activity in Australia, among the 602,100 encounters recorded from April 1998 to March 2004, there were 5215 at which the patient gave shortness of breath as one of their reasons for encounter (RFE), therefore presenting at a rate of 0.9 per 100 encounters. Of these, 19.2\% received a diagnosis of COPD.\textsuperscript{162}

It is worth mentioning also the study by Jolly on 50 primary care patients newly presenting with breathlessness which found that respiratory disorders (not specifically COPD) was found in 39\% of males and 35\% of females (aggregated 36\%).\textsuperscript{163}

A couple of study realized in specialist clinics reported prevalence rates in the range of 9-14\%. In order to test diagnostic approach based on objective confirmation of suspected diagnoses, Pratter et al. prospectively studied 85 patients with a primary complaint of breathlessness seen in a pulmonary subspecialty clinic and found that 14\% of the study sample was diagnosed with COPD.\textsuperscript{164}

In another study, Pratter analysed data from a group of 123 patients with a chief complaint of breathlessness of unknown cause present for >8 weeks referred to a university pulmonary practice. Patients underwent an algorithmic approach to breathlessness which was treated at any time that data supported a treatable diagnosis. Whenever possible, accuracy of diagnosis was confirmed with an improvement in breathlessness after therapy. 9\% of patients enrolled received a final diagnosis of COPD.\textsuperscript{165}

Similar rates have been found in a study realized in an Emergency Department in the US: 14\% of 162 patients who gave breathlessness as primary complaint for visiting the ED were diagnosed with COPD.\textsuperscript{166} A similar study which found 21\% of emergency

\begin{flushleft}


\textsuperscript{163} Jolly DT. Dyspnea In Primary Care. Can Fam Physician. 1978 October; 24:983-984.

\textsuperscript{164} Pratter MR. Cause and evaluation of chronic dyspnea in a pulmonary disease clinic. Archives of internal medicine. 1989;149(10): 2277.


\end{flushleft}
admissions being related to breathlessness, reported that 17% of them then received a diagnosis of COPD.  

In light of the data collected in the review, we are be able to quantify the burden of COPD and breathlessness at the CCG level and for a GP.

At the CCG level\textsuperscript{168}, a COPD prevalence rate of 13%, as reported by Shahab and colleagues\textsuperscript{169}, would correspond to about 23,000 adults, and about a third of them (about 8,000, 4,400-12,000) would report some level of breathlessness. Assuming that 10% of the CCG population would complain of breathlessness (about 17,300 patients, 15,400-19,000), we can estimate that in 19% of them (about 3,500) their breathlessness may be caused by COPD.

Table 5 – Estimate of the burden of disease of breathlessness associated with COPD at the CCG level

<table>
<thead>
<tr>
<th>Population baseline</th>
<th>No. patients per CCG</th>
<th>Prevalence rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median CCG population (adult only)</td>
<td>172,730</td>
<td></td>
</tr>
<tr>
<td>Prevalence of spirometry-based COPD</td>
<td>2,973</td>
<td>13.3%</td>
</tr>
<tr>
<td>QOF diagnosed prevalence for COPD</td>
<td>2,936</td>
<td>1.7%</td>
</tr>
<tr>
<td>Prevalence of smokers in COPD patients</td>
<td>9,189</td>
<td>40%</td>
</tr>
<tr>
<td>Breathless patients in the general population</td>
<td>15,373</td>
<td>19%</td>
</tr>
<tr>
<td>Breathless patients diagnosed with COPD</td>
<td>3,316</td>
<td>19%</td>
</tr>
<tr>
<td>COPD patients complaining of breathlessness</td>
<td>4,360</td>
<td>19%</td>
</tr>
</tbody>
</table>

Scaling down these data at the level of a single GP, we estimate that s/he would see roughly 150 COPD patients per year, and a third of them (about 52, 29-80) would be breathless. Of the 115 patients (101-126) presenting with breathlessness, in 19 their breathlessness would be explained by COPD.

Table 6 – Estimate of the burden of disease of breathlessness associated with COPD at the GP level

<table>
<thead>
<tr>
<th>Population baseline</th>
<th>No. patients per GP</th>
<th>Prevalence rates</th>
</tr>
</thead>
</table>


<table>
<thead>
<tr>
<th>Population baseline</th>
<th>No. patients per GP</th>
<th>Prevalence rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average patients list per GP in England (adult over 20)</td>
<td>1,140</td>
<td></td>
</tr>
<tr>
<td>Prevalence of spirometry-based COPD</td>
<td>152</td>
<td></td>
</tr>
<tr>
<td>QOF diagnosed prevalence for COPD</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Prevalence of smokers in COPD patients</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>Breathless patients in the general population</td>
<td>101 126 114</td>
<td></td>
</tr>
<tr>
<td>Breathless patients diagnosed with COPD</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>COPD patients complaining of breathlessness</td>
<td>29 80 52</td>
<td></td>
</tr>
</tbody>
</table>

**Obesity**

Obesity has become major public health problem worldwide. The UK in particular has been defined the ‘fat man’ of Europe. Obesity, which is sometimes a lifelong condition which should be preventable, is increasing in prevalence in the UK such that approximately 25% of adults are obese. The rate of increase may be slowing but projections remain valid – namely that by 2050 the population of Britain will be mainly obese.

According to the 2011 Health Survey for England (HSE) data analyzed by the National Obesity of Observatory around 62% of adults were overweight or obese (BMI ≥ 25). Men and women have a similar prevalence of obesity (25%), but men are more likely to be overweight (33% for women and 41 % for men). The adult prevalence of severe obesity (obesity III: BMI ≥ 40) is around 2.5%.

According to the Quality Outcome Framework (QOF) statistical bulletin, in 2011-12 approximately 5 million out of 55 million people in England could be defined obese, for a prevalence of 10.7%. In 2006/2007 there were almost 4 million obese patients, and the prevalence at that time was about 7.4%.

Breathlessness on exertion is common in people with obesity. Nevertheless, there is no reference to breathlessness in the recent report by the Academy of Medical Royal Colleges “Measuring Up”, which aims to be “the medical profession’s prescription for the nation's obesity crisis; 2013. Available from http://www.aomrc.org.uk/publications/statements/doc_view/9673-measuring-up.html


173 i.e. they are aged 16 and over with a BMI greater than or equal to 30 in the previous 15 months


nation’s obesity crisis”. Similarly, the RCP’s Action on obesity report mentions breathlessness only marginally.

Many overweight or obese people suffer from breathlessness that impairs their ability to be physically active, and stay or gain physical fitness. Quite a few patients are unable to exert sufficiently to feel breathless because of other musculoskeletal or mobility problems.

In a large epidemiological study, 80% of obese middle aged subjects reported shortness of breath after climbing two flights of stairs compared with only 16% of similarly aged non-obese controls, and this was despite smoking being significantly less frequent in the obese. The large population study conducted by Bowden et al. in Australia, among the adults who were classified as obese (1,063 out of a study sample of 5,331 participants), 18.1% experienced breathlessness compared to 8.7% of those who were not obese. Among adults aged 50 years and over, breathlessness was experienced by 22.2% of those who were obese, compared to 12.3% who were not obese. In another study of 23 obese but otherwise healthy men (with normal spirometry), two thirds reported breathlessness. According to Ho and colleagues among obese elderly subjects, it occurs in about 40% of them. In another large study of patients with non-insulin dependent diabetes, one third reported troublesome breathlessness and its severity increased with BMI.

A relationship between obesity and asthma has been established in the literature: obesity has been associated with an increased risk of asthma and increased prevalence of physicians diagnosed and self-reported asthma has been observed in obese subjects, mainly in women. Both asthma and obesity cause breathlessness and there is a risk of misdiagnosis of asthma in patients who are obese. Scott and

colleagues studied a group of subjects who were overweight with physician-diagnosed asthma and found that of 91 subjects (mean BMI, 38 kg/m²) 36.3% had a possible misclassification of asthma diagnosis. Similarly, in a study of 16,171 patients, subjects in the highest weight quintile had an odds ratio of 2.66 for breathlessness on exertion compared with the rest of the population, and they were more likely to report a diagnosis of asthma or to be on bronchodilators despite no evidence of obstruction on PFTs, thus raising the possibility that some obese people with breathlessness are misdiagnosed as having asthma.

Obesity has a first diagnosis for breathlessness has been studies in different settings. Obesity is a very common cause of breathlessness, and the study by Johnson and colleagues seems to confirm that obese patients are aware of and accept breathlessness as part of their condition.

Remarking one of the main results of the study by Ho et al., Berner reinforces that obesity is the main contributory factor in breathlessness in the elderly. In fact, about 30% of the study population had been breathless, of whom 33% were obese. In another study of breathlessness in the elderly, 50 patients out of 210 reported breathlessness (Borg score > 0). Of them, 78% were categorized as overweight according to the Quetelet Index (QI=weight/height).

In a study performed in primary care patients in order to document the relationship between obesity and breathlessness found that obesity was not significantly related to the presence of breathlessness in male or female presenting with new or persistent breathlessness. For males with continuing complaints of breathlessness, 46% were obese, and the same proportion of the controls was obese. Likewise, 55.6% of males newly presenting with breathlessness were obese, compared to the same proportion of controls. In women with persistent breathlessness, 55.6% of patients were obese, as were 42.2% of controls. For women with new cases of breathlessness 37.5% were obese compared to 56.3% of the controls.

Prevalence rates of obesity in patient complaining of breathlessness vary between 4% in a group of 284 patients referred with breathlessness from their GPs to a breathlessness diagnostic clinic and 16% among a study group of 148 patients with a chief complaint of breathlessness of unknown cause present for more than 8 weeks. The same prevalence rate (16%) was found in a group of 152 patients aged 60-79, for whom

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obesity appeared to be the only explanation of their breathlessness. A much lower proportion of patients with chronic unexplained breathlessness referred by their GPs to a pulmonary clinic was found in an American study. Out of 77 study participants, only two were found to have breathlessness in association with significant weight gain and lack of physical exercise.

The data available help us understand the burden of breathlessness in obesity. At the CCG level, we would expect about 43,200 patients being obese. 18 to 80% of them (average about 50%) would complain of some level of breathlessness. Obesity would be found as the underlying cause of breathlessness in 1-16% (average 7%) breathless patients in the CCG population.

### Table 7 – Estimate of the burden of disease of breathlessness associated with obesity in a CCG

<table>
<thead>
<tr>
<th>Population baseline</th>
<th>No. patients per CCG</th>
<th>Prevalence rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median CCG population (adult only)</td>
<td>172,730</td>
<td></td>
</tr>
<tr>
<td><strong>Prevalence of obesity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breathless patients in the general population</td>
<td>15,373 19,173 17,273</td>
<td>9% 11% 10%</td>
</tr>
<tr>
<td>Breathless patients diagnosed with obesity</td>
<td>154 2,460 1,076</td>
<td>1% 16% 7%</td>
</tr>
<tr>
<td>Obese patients complaining of breathlessness</td>
<td>7,816 34,546 21,131</td>
<td>18.1% 80% 48.9%</td>
</tr>
</tbody>
</table>

A GP would have 285 obese patients on his list. Of them, 140 [52-228] would report also breathlessness. Among the breathless patients, about 114 [101-126], 7 [1-16] would have obesity as the reason for their breathlessness.

### Table 8 – Estimate of the burden of disease of breathlessness associated with obesity at the GP level

<table>
<thead>
<tr>
<th>Population baseline</th>
<th>No. patients per GP</th>
<th>Prevalence rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average patients list per GP in England (adult only)</td>
<td>1.140</td>
<td></td>
</tr>
<tr>
<td><strong>Prevalence of obesity</strong></td>
<td>285</td>
<td>25%</td>
</tr>
<tr>
<td>Breathless patients in the general population</td>
<td>101 126 114</td>
<td>9% 11% 10%</td>
</tr>
<tr>
<td>Breathless patients diagnosed with obesity</td>
<td>1 16 7</td>
<td>1% 16% 7%</td>
</tr>
</tbody>
</table>

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### Anxiety

Anxiety is a feeling of unease, such as worry or fear, which can be mild or severe. It is considered an adaptive process until its magnitude or persistence renders it a dysfunctional response that can have negative consequences. It exists on a continuum from normal to pathologic and it is considered the generalized symptom of a myriad of abnormal and pathological fear and anxiety states, including generalised anxiety disorder (GAD), panic disorder (PD), agoraphobia, neurocirculatory asthenia, obsessive-compulsive disorder (OCD), and phobic disorders.

The main diagnostic criteria for anxiety are (i) the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders published by the American Psychiatric Association (DSM-5) – also adopted by NICE guidelines on GAD and on anxiety disorders and depression – and (ii) the ICD-10 Classification of Mental and Behavioural Disorder published by the World Health Organization (WHO).

According to the DSM-5, people with generalized anxiety disorder (GAD) experience constant, chronic, and unsubstantiated worry, often about health, family, money, or work. This worrying goes on every day, possibly all day. It disrupts social activities and interferes with work, school, or family. Physical symptoms of GAD include the following:

- muscle tension
- fatigue
- restlessness
- difficulty sleeping
- irritability
- edginess
- gastrointestinal discomfort or diarrhoea

It requires two major symptoms (6 months or more of excessive anxiety and worry, occurring on more days than not, about a number of events and activities and difficulty controlling the worry) and two or additional symptoms.

ICD-10 focuses more on somatic symptoms of anxiety, particularly autonomic reactivity and tension. For a diagnosis of GAD it requires 6 months or more prominent tension, worry and feelings of apprehension, and four from a list of 22 symptoms, of which at least one must be from a list of four autonomic symptoms (palpitations, sweating, trembling, dry mouth).

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198 [http://www.nhs.uk/conditions/Anxiety/Pages/Introduction.aspx](http://www.nhs.uk/conditions/Anxiety/Pages/Introduction.aspx)
201 [http://www.dsm5.org/Pages/RecentUpdates.aspx](http://www.dsm5.org/Pages/RecentUpdates.aspx) accessed on 9th October 2013
A number of measures and instruments have been developed in order to measure the presence of symptoms and to calibrate the severity of general symptoms of anxiety. Some of them, such as the Generalised Anxiety Disorder Assessment, the State-trait Anxiety Inventory (STAI), the Beck Anxiety Inventory (BAI) and the Hospital Anxiety and Depression Inventory (HADS) are self-reported.

The Generalised Anxiety Disorder Assessment (GAD 7) is a self-administered patient questionnaire used as a screening tool and severity measure for anxiety. The GAD-7 score is calculated by assigning scores of 0, 1, 2, and 3, to the response categories of “not at all,” “several days,” “more than half the days,” and “nearly every day,” respectively, and adding together the scores for the seven questions. Scores of 5, 10, and 15 are taken as the cut off points for mild, moderate, and severe anxiety, respectively. When used as a screening tool, further evaluation is recommended when the score is 10 or greater.

The State-Trait Anxiety Inventory (STAI) is used to measure the self-reported presence and severity of current symptoms of anxiety and a generalized propensity to be anxious. There are 2 subscales within this measure. First, the State Anxiety Scale (S-Anxiety) evaluates the current state of anxiety, asking how respondents feel “right now,” using items that measure subjective feelings of apprehension, tension, nervousness, worry, and activation/arousal of the autonomic nervous system. The Trait Anxiety Scale (T-Anxiety) evaluates relatively stable aspects of “anxiety proneness,” including general states of calmness, confidence, and security. Scores range from 20 to 80, with higher scores correlating with greater anxiety. A cut off score of 40 detects patients suspected of suffering from significant anxiety symptoms.

The Beck Anxiety Inventory (BAI) is a brief measure of anxiety with a focus on somatic symptoms of anxiety that was developed as a measure adept at discriminating between anxiety and depression. It includes assessment of symptoms such as nervousness, dizziness, inability to relax, etc. For each of the 21 items patients indicate how much they have been bothered by each symptom over the past week. The BAI has a maximum score of 63: scores between 16 and 25 indicates moderate anxiety, scores above 63 signal severe anxiety.

The Hospital Anxiety and Depression Scale (HADS) is commonly used to identify caseness (possible and probable) of anxiety disorders and depression among patients in medically ill patients in secondary care settings. It is divided into an Anxiety subscale (HADS-A) and a Depression subscale (HADS-D) both containing seven intermingled items. To prevent ‘noise’ from somatic disorders on the scores, all symptoms of anxiety or depression relating also to physical disorder, such as dizziness, headaches, insomnia, anergia and fatigue, were excluded. The HADS-A includes items that assess generalized anxiety such as tension, worry, fear, panic, difficulty in relaxing and restlessness. Each item on the questionnaire is scored from 0-3 and this means that a person can score between 0 and 21 for either anxiety or depression. According to Bjelland’s literature review, anxiety or depression are identified by a cut-off point of 8/21.

Latest estimates of the current global prevalence of anxiety disorders ranged between 0.9% and 28.3% and past-year prevalence between 2.4% and 29.8%. After adjusting for methodological differences across studies, the global current prevalence of anxiety

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204 Julian LJ. Measures of Anxiety. Arthritis Care & Research. 2011 November;63(S11):S467–S472.
disorders was 7.3%, suggesting that one in 14 people around the world at any given time has an anxiety disorder and one in 9 (11.6%) will experience an anxiety disorder in a given year. Regional burden estimates ranged from 5.3% in African countries to 10.4% in Euro/Anglo cultures. The results of the World Mental Health Surveys of the WHO confirm this same pattern.

According to the most recent Adult Psychiatric Morbidity in England the estimated proportion of English people (including adults between 16 and 74 years of age living in private households) with GAD was 4.4%, a figure that has been almost constant across the last three surveys (1993, 2000, 2007). This figure is almost in line with the American rate (4.3%), but higher than rates reported from other European countries.

Anxiety is the most common anxiety disorder seen in primary care, and one of the most neglected. A number of studies have reported its under-detection or under-reporting by GPs. People with anxiety disorders are often frequent users of primary care resources, but if the anxiety component of their problem is not detected they may not receive the correct treatment and may undergo unnecessary and costly investigations, in particular for their physical symptoms.

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207 The Adult Psychiatric Morbidity Survey is run every 7 years, the 2007 report is currently the most recent available. An alternative source of information is the IAPT Quarterly reports which provide information on activity in IAPT services – see http://www.hscic.gov.uk/pubs/iapt1314q1exp. However, the quality of the data available in this report remains low, as only 48.4% of records were valid in the July final data (http://www.hscic.gov.uk/searchcatalogue?productid=12554&q=Improving+Access+to+Psychological+Therapies&sort=Relevance&size=10&page=1#top).


209 Prevalence rates were as follows: 4.4% in 1993, 4.7% in 2000 and 4.7% in 2007. Estimates were based on those aged 16 to 64 and living in England.


A study performed in a large sample of UK general practices found that incidence of GP recorded anxiety diagnosis fell from 7.9 to 4.9/1000 person years at risk from 1998 to 2008, thus conflicting the increasing prevalence rates reported in the Adult Psychiatric Morbidity Survey in England 2007. The reasons for this under-recording seem to be manifold. Patients may have symptoms of anxiety, worry, tension, irritability or tiredness, about which they feel reluctant to complain to their GP because they do not view these symptoms as being ‘medical’. Moreover, anxious patients tend not to report somatic symptoms (such as dizziness and breathlessness) which are seldom attributed to psychological causes, and the focus for clinical examination is kept on somatic conditions. GPs, on their side, may see these as symptoms of a more general malaise and not specifically consider or ask about anxiety as a possible cause. There may be also some issues about coding behaviour of physicians, reluctant to appropriately disclose or document anxiety.

Anxiety has been studied also in particular population groups. Wolitzky-Taylor’s review found that prevalence estimates of anxiety disorders in late age (not strictly defined) range from 3.2% to 14.2%, whereas prevalence estimates for GAD more specifically range from 1.2% to 7.3%. Studies comparing different age groups generally find a decrease in prevalence with age.

Anxiety and smoking are often interrelated problems. Data from the 2007 Adult Psychiatric Morbidity Survey for England showed that among the 23% of the population with any of the mental disorders covered by the survey, the smoking rate was 33%, higher than the rate for the English population (22%). Real rates of smoking rates among people with a mental disorder might be underestimated in the Adult Psychiatric Morbidity Survey, which surveyed people living in private households. Certain groups such as prisoners or homeless people, among whom mental disorders are more prevalent, were not represented.

Patients with anxiety experience a high-degree of comorbidity, with 80-90% presenting at least one additional current psychiatric diagnosis. Moreover, anxiety disorders are strongly and independently associated with chronic medical illness such as cardiovascular disorders, stroke, diabetes, hyperthyroidism, gastrointestinal disorders,

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Such comorbidities are associated with poorer clinical outcomes, with higher morbidity, higher mortality, increased disability, higher healthcare utilization. Furthermore, the comorbidity between medical and psychiatric conditions poses difficulties for differential diagnosis, detection and treatment. In turn, many physical conditions can mimic the symptoms of anxiety, making it difficult to establish the underlying diagnosis.

Costs to the health care system are also significant – by interacting with and exacerbating physical illness, co-morbid mental health problems raise total health care costs by at least 45 per cent for each person with a long-term condition and co-morbid mental health problem. It has been calculated that the presence of poor mental health increases the average cost of NHS service use by each person with a long-term condition from approximately £3,910 to £5,670 a year. This suggests that between 12 per cent and 18 per cent of all NHS expenditure on long-term conditions is linked to poor mental health and wellbeing.

People with respiratory conditions experience increased levels of psychosocial morbidity, when compared with those associated with other chronic physical disease groups.

Rates of anxiety disorders in patients with COPD, particularly generalized anxiety disorder (GAD) and panic disorder, are much higher than in the general public. A meta-analysis of 13 studies (900 patients) found that the prevalence of anxiety was 36%, significantly higher than those observed in the general population (4.4%).

The recent meta-analysis conducted by Willgoss and colleagues found that the rates of clinical anxiety reported in 8 studies ranged from 10-55%. Four studies examined the prevalence of clinical anxiety in inpatient settings, which varied from 10-55%, whereas in the 4 studies that reported the prevalence of clinical anxiety in outpatient samples, prevalence ranged from 13-46%. A recent study comparing psychiatric comorbidity between hospitalized COPD patients and a hospitalized clinical control group without pulmonary dysfunction showed that 55% of patients with COPD received a diagnosis of a mental disorder compared to 30% of the control group.


Similar results have been found in older age patients with COPD: between 18 and 50% of older age patients with COPD report significant symptoms of anxiety.254 255

Anxiety has also been found to be related to the disease characteristics of COPD, including breathlessness. Gift’s pilot study reported that COPD patients had greater anxiety during times of higher breathlessness levels.256 257

In their primary care based study of about 250 COPD patients assessed for their health status and perceived breathlessness, Falker and colleagues found that regardless of the severity of COPD, patients with COPD and comorbid depressive/anxiety disorder have worse perceived breathlessness and physical health-related quality of life than patients with COPD alone.258

Not only is anxiety highly common among COPD patients but the reverse is also true. The lifetime prevalence of respiratory disease is higher in people with panic disorder (47%) than with other psychiatric diagnoses.259

Anxiety appears to be a significant problem also among patients with cardiovascular disease (CVD). Findings from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) in the USA suggest that anxiety disorders, mood disorders, and CVD are highly comorbid in the community, and CVD was associated with increased likelihood of any anxiety disorder (OR=1.43).260

Yohannes and colleagues who reviewed the literature around HF and anxiety found that few studies have examined co-morbid anxiety in HF patients. In the 8 studies available they found that anxiety has been found in 11% to 45% of the HF patients studied.261

It is important also to mention the difficulty of differentiating between anxiety and cardiac disease. A number of studies have reported that 43% to 61% of patients with a negative cardiovascular diagnostic test receive in the end a diagnosis of anxiety.262

Research on the relationship between obesity and mental health has traditionally explored the first as a consequence of an underlying psychopathology. More recently


work has investigated the causal relationship between body weight and psychological distress, which can influence also treatment outcome.

A systematic review pointed to a weak but positive association between obesity and anxiety, (with a pooled odds ratio from published cross-sectional studies of 1.4). The work done by Baumeister and Härter showed that the prevalence rates of anxiety disorders significantly increased in the individuals who are overweight and obese. In their sample of 2,955 individuals the 12-month prevalence rates of anxiety were 17.2% in overweight patients, 20.4% in the obese and 26% in the obese rehabilitation patients groups, contrasting the lower rate (10.2%) among the healthy patients.

In a study group of 253 patients referred to two UK weight management specialist centres preliminarily assessed also for their psychiatric or psychological disorders, Tuthill and colleagues found that 56% exceeded the minimum criteria for an anxiety disorder (HADS >8). The likelihood of exceeding the cut-off points for probable or severe anxiety (HADS > 11 and HADS > 15, respectively) increased as BMI increased.263

A relation between asthma and anxiety appears to be established in the literature, not only for severe asthma patients but also for milder cases. In a cohort of patients with predominantly mild asthma, Gada and colleagues found a 43.5% increased risk of anxiety.264 In other studies, anxiety was found in ranges between 21% and 45% in asthmatic patients.265 266 267 268

Comorbid anaemia was found in 4.4% of men and 22.5% of women from a total of 169 patients diagnosed with anxiety.269

Patients who are anxious report more physical symptoms than do patients who are not.270 271 One hypothesis is that these patients experience specific distress related physical symptoms. This makes sense because mental disorders have specific physiological aspects, which are part of the definition. Anxiety disorders can be accompanied by autonomic arousal, e.g., palpitations and sweating, or breathlessness. The number of physical symptoms rather than the specific type of symptom is found to be predictive for depression or anxiety.272 273 274 275 276

Research has usually focused on clinical predictors of anxiety disorders in patients presenting with physical complaints, thus estimating the ORs of anxiety associated with breathlessness between 2.13 and 18.6.\textsuperscript{277} The study by Leivseth found also that having symptoms of anxiety increased the adjusted ORs for reporting breathlessness within ppFEV1 level or COPD stages.\textsuperscript{278}

Data on the prevalence of breathlessness in patients with anxiety seems to be less available. The study by de Waal and colleagues reported the breakdown of prevalence rates for different symptoms experienced by 1,458 patients in general practice. Breathlessness was found in about 15% of the patients with mental distress, and the same rate was also found in patients with mental distress and a known somatic disease.\textsuperscript{279}

Dales and colleagues studied the association between respiratory symptoms and psychological problems in a sample of 600 healthy subjects. A consistent trend toward higher respiratory symptom reporting by subjects with higher scores for psychopathology was present for all respiratory symptoms. In total, 42% of the patients with anxiety reported some sort of breathlessness that could be associated exclusively with their psychological status, given the sampling method adopted in the study which minimized possible confounding factors.\textsuperscript{280}

Janson et al. found a clear association between psychological disturbances, such as anxiety and depression, and the report of respiratory symptoms in subjects with or without lung diseases, thereby confirming the previous results in healthy subjects.\textsuperscript{281}

The HUNT study realized in Norway in 1995-1997 representing a large sample from the general population aimed at examined the association of lung function, anxiety symptoms and breathlessness in different situations. According to its results, 13.5% of women and 11.5% of men with anxiety (HADS 11-21) reported breathlessness when

\begin{thebibliography}{99}
\end{thebibliography}

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walking on flat ground, 6.5% of women and 4.6% of men with anxiety reported breathlessness when sitting still, and 8.9% of women and 8.5% with anxiety reported to be woken at night by breathlessness.\textsuperscript{284}

In the general population, the number of adults presenting with breathlessness which is caused by anxiety has been estimated in the range of 0 and 16%, depending on the characteristics of the populations studied and the definition of anxiety adopted.

According to the data collected through the BEACH program, a continuous national study of general practice activity in Australia, among the 602,100 encounters recorded from April 1998 to March 2004, there were 5215 at which the patient gave shortness of breath as one of their reasons for encounter (RFE), therefore presenting at a rate of 0.9 per 100 encounters. Of these, 3.4% received a diagnosis of anxiety.\textsuperscript{285}

In his 50 patients newly presenting with breathlessness in his practice, Jolly found a much higher rate. According to his results, 16% of the patients were found with psychological disorders possibly explaining their breathlessness.\textsuperscript{286}

A couple of study realized in specialist clinics reported prevalence rates in the range of 5-10%. In order to test diagnostic approach based on objective confirmation of suspected diagnoses, Pratter et al. prospectively studied 85 patients with a primary complaint of breathlessness seen in a pulmonary subspecialty clinic and found psychogenic breathlessness in 5% of them.\textsuperscript{287}

In Pratter et al. (2011), the study group consisted of 123 patients with a chief complaint of breathlessness of unknown cause present for >8 weeks referred to a university pulmonary practice. Patients underwent an algorithmic approach to breathlessness which was treated at any time that data supported a treatable diagnosis. Whenever possible, accuracy of diagnosis was confirmed with an improvement in breathlessness after therapy. For 10% of the patients enrolled breathlessness did not have a physiologic explanation, being therefore associated with a possible psychogenic cause.\textsuperscript{288}

At the CCG level, a prevalence rate of anxiety of 4.4% for the adult population would correspond to 7,600 patients and of them, 680 to 1,200 patients (average 1,000) would complain of breathlessness. Assuming that 10% [9%-11%] of the CCG population would complain of breathlessness, about 17,200 patients [15,300-19,000], we can estimate that in 8.6% of them, about 1,300 [520-2,500] their breathlessness may be caused by anxiety.


\textsuperscript{287} Pratter MR. Cause and evaluation of chronic dyspnea in a pulmonary disease clinic. Archives of internal medicine. 1989;149(10):2277.

Table 9 – Estimate of the burden of disease of breathlessness associated with anxiety at the CCG level

<table>
<thead>
<tr>
<th>Population baseline</th>
<th>No. patients per CCG</th>
<th>Prevalence rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median CCG population (adult only)</td>
<td>172,730</td>
<td></td>
</tr>
<tr>
<td>Prevalence of anxiety</td>
<td>7,600</td>
<td>4%</td>
</tr>
<tr>
<td>Breathless patients in the general population</td>
<td>15,373</td>
<td>19,000</td>
</tr>
<tr>
<td>Breathless patients diagnosed with anxiety</td>
<td>523</td>
<td>2,460</td>
</tr>
<tr>
<td>Patients with anxiety complaining of breathlessness</td>
<td>678</td>
<td>1,216</td>
</tr>
</tbody>
</table>

Scaling down these data at the level of a single GP, there would be 50 patients diagnosed with anxiety. Of them about 7 [4-8] would complain of breathlessness. Of the 114 patients presenting with breathlessness [range 91-125], in about 10 [3-20] their breathlessness would be caused by anxiety.

Table 10 – Estimate of the burden of disease of breathlessness associated with anxiety at the GP level

<table>
<thead>
<tr>
<th>Population baseline</th>
<th>No. patients per GP</th>
<th>Prevalence rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average patients list per GP in England (adult only)</td>
<td>1,140</td>
<td></td>
</tr>
<tr>
<td>Prevalence of anxiety</td>
<td>50</td>
<td>4.4%</td>
</tr>
<tr>
<td>Breathless patients in the general population</td>
<td>91</td>
<td>125</td>
</tr>
<tr>
<td>Breathless patients diagnosed with anxiety</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>Patients with anxiety complaining of breathlessness</td>
<td>4</td>
<td>8</td>
</tr>
</tbody>
</table>

Anaemia

Anaemia is defined as a state in which the quality and/or quantity of circulating red blood cells are below normal. Blood haemoglobin (Hb) concentration serves as the key indicator for anaemia because it can be measured directly, has an international standard, and is not influenced by differences in technology. According to the WHO, the diagnostic criteria for anaemia are Hb < 12 g/l for women and <130 g/l for men.

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Prevalence of anaemia in the general population (men and women 50 years or older) have been estimated at 2-5%. Higher rates are known for pregnant women (16%, 15.2% in the UK) and the elderly (men and women over 65) with data ranging from 3 to 26%.

Anaemia is often present in persons with a high burden of chronic disease without a clearly defined aetiology. Anaemia of Chronic Disease (ACD) occurs in patients with acute or chronic infection or inflammation, such as COPD, and it represents the systemic inflammatory response often occurring in some chronic conditions.

Anaemia has been reported in 23-40% of HF patients. Lower cormorbidities have been found for COPD (8.8-23% of COPD patients also have anaemia) and asthma (10% of asthmatic have also anaemia). Almost half (45%) of cancer patients are also anaemic. Anaemia can be pretty common in patients with chronic renal insufficiency (with prevalence rates ranging between 27 and 72%).

According to the Third National Health and Nutrition Examination Survey (NHANES III) possible causes of anaemia are distributed as follows: one third of anaemia appeared related to a nutrient deficiency (within this group, half the anaemia is related to iron deficiency), approximately another third of older anaemic persons have anaemia of chronic and the remaining one third have unexplained anaemia. 291

Prevalence rates of anaemia increase with comorbidity in the elderly. The Leiden 85-plus Study showed that anaemia was present in about 35% of patients with one diagnosed condition and in 46% of those with two or more diagnoses. 292

When looking for evidence of the association between anaemia and breathlessness, we found very little. To our knowledge no study has been published on the prevalence of breathlessness in anaemic patients, whereas anaemia barely features in studies assessing the possible underlying causes of breathlessness.

In Pratter et al. (2011), the study group consisted of 123 patients with a chief complaint of breathlessness of unknown cause present for >8 weeks referred to a university pulmonary practice. Patients underwent an algorithmic approach to breathlessness which was treated at any time that data supported a treatable diagnosis. 3% of patients enrolled received a final diagnosis of anaemia (defined as a haemoglobin level below 10gm/dl). 293 Severe anaemia was found in an a marginal proportion of patients (1%) also in a group of 284 patients with breathlessness of at least two-weeks duration referred from the GPs to an hospital-based breathlessness clinic. 294

Running a model using the prevalence rates of anaemia in different population groups allows estimating that the number of anaemic patients in a CCG would range between 7,100 and 17,800 (average 11,600). We are not able to estimate how many of them would be breathless as we could not find the prevalence of breathlessness in anaemia.

According to the data available we can quantify that the number of breathless patients in


whom the underlying cause of their breathlessness is anaemia is between 150 and 200 (average 170).

Table 11 – Estimate of the burden of disease of breathlessness associated with anaemia in a CCG

<table>
<thead>
<tr>
<th>Population baseline</th>
<th>No. patients per CCG</th>
<th>Prevalence rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median CCG population (adult only)</td>
<td>172,730</td>
<td>MIN</td>
</tr>
<tr>
<td>Prevalence of anemia in the general population (men and women 50+)</td>
<td>1,733</td>
<td>4,332</td>
</tr>
<tr>
<td>Prevalence of anaemia in non pregnant women 15-50</td>
<td>4,306</td>
<td>4,306</td>
</tr>
<tr>
<td>Prevalence of anaemia in the elderly (men and women 65+)</td>
<td>1,062</td>
<td>9,207</td>
</tr>
<tr>
<td>Cases of anaemia - total</td>
<td>7,101</td>
<td>17,845</td>
</tr>
<tr>
<td>Breathless patients in the general population</td>
<td>15,373</td>
<td>19,173</td>
</tr>
<tr>
<td>Breathless patients receiving a diagnosis of anaemia</td>
<td>154</td>
<td>192</td>
</tr>
<tr>
<td>Anaemic patients who complain of breathlessness</td>
<td>nk</td>
<td>nk</td>
</tr>
</tbody>
</table>

Table 12 – Estimate of the burden of disease of breathlessness associated with anaemia at the GP level

<table>
<thead>
<tr>
<th>Population baseline</th>
<th>No. patients per GP</th>
<th>Prevalence rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average patients list per GP in England (adult 20+)</td>
<td>1,140</td>
<td>MIN</td>
</tr>
<tr>
<td>Prevalence of anemia in the general population (men 20-65 and women 50-64)</td>
<td>12</td>
<td>29</td>
</tr>
<tr>
<td>Prevalence of anaemia in women 20-49</td>
<td>27</td>
<td>8.8%</td>
</tr>
<tr>
<td>Prevalence of anaemia in the elderly men and women 65+</td>
<td>7</td>
<td>64</td>
</tr>
<tr>
<td>Anaemic patients total</td>
<td>46</td>
<td>121</td>
</tr>
<tr>
<td>Breathless patients in the general population</td>
<td>101</td>
<td>126</td>
</tr>
<tr>
<td>Breathless patients receiving a diagnosis of anaemia</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Anaemic patients breathless</td>
<td>nk</td>
<td>nk</td>
</tr>
</tbody>
</table>

Similarly, we can estimate that a GP with a patient list of about 1,150 adults would have 50 to 120 anaemic patients (average 77): about 30 would be elderly, 27 would be women in their reproductive age and the rest would be men aged 20-65 and women in
their middle age (50-65 year old). Due to the lack of date we cannot estimate how many of them will report also breathlessness.

According to the data available, of the 10% of the breathless patients in the GP list [101-126, average 114], 1% of them would have their breathlessness caused by anaemia [1-3].

**Multimorbidity**

We have performed a review of the studies which investigated the prevalence of multi and comorbidity in breathlessness-related conditions. A synthetic analysis of the data collected is as difficult as ever because of the usual heterogeneity of methodologies.

Starting with studies on cohorts of HF patients, anxiety has been found to be in 3-45% of the study populations, asthma in 5-15.9%, obesity in 14.4% of men and 16.3% of women, COPD in 14.5-32.9%.

Studies investigating the occurrence of comorbidity in patients diagnosed with COPD reported prevalence rates in the following ranges: mental health problems in 8.6-28%, overweight in 6-33% and obesity in 4.3-54%, HF in 7-32% and anaemia in 5-10% of the study samples. In a particular study of the elderly, breathlessness was found in all the patients diagnosed with both COPD and HF. Only one study assessed the severity of breathlessness in COPD patients who were also overweight or obese. Among the overweight, 21.4% had mild, 55.1% moderate and 23.4% severe breathlessness. The obese patients showed greater prevalence of moderate and severe breathlessness: in fact only 9% reported a mild problem, whereas 57 and 34% were found with moderate and severe breathlessness respectively.

Anxiety has been found in ranges between 16.8-56% in obese people. More agreement has been found in studies assessing the concomitant presence of obesity or overweight and asthma. Asthma has been found in 32-36.7% of the patients overweight and in 24-33% of the obese.

Studies looking at physical comorbidity in patients diagnosed with anxiety are more rare. Asthma has been found in 13% of patients with anxiety (but the reverse, namely anxiety in patients who already received a diagnosis of asthma was found in 5-45% of them), anaemia in in 4.4% of men and 22.5% of women, obesity in 17.3%. Great variability have been reported both for COPD (8.3-62%) and HF (2.6-70%) in patients with anxiety.

We conclude with studies assessing multiple causes of breathlessness. Unsurprisingly comparability across these studies is difficult, therefore we do not try to combine the data available but we only present them.

In the community-based study by Jolly on 50 patients over age 14 newly presenting with breathlessness, combined respiratory and cardiovascular disorders were found in 10% of the study sample, 11% of men and 9.4% of women.

Another study testing a diagnostic algorithm for evaluating breathlessness in 152 elderly patients recruited from general practice investigated also the overlap between heart

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disease, lung disease and obesity as possible causes of breathlessness. Seven patients (5%) were found to have both heart and lung disease, 9 of them (7%) had lung disease and were obese, 4 (3%) had obesity and concomitant heart disease. The simultaneous combination of obesity, lung disease and heart disease was not found in any patient included in the study population.\footnote{Pedersen F, Mehlsen J, Raymond I, Atar D, Skjoldborg US, Hildebrandt PR. Evaluation of dyspnoea in a sample of elderly subjects recruited from general practice. International journal of clinical practice. 2007;61(9):1481-91.}

The objective of the study by Pratter and colleagues was to prospectively evaluate an algorithmic approach to the cause(s) of chronic breathlessness in a group of 123 patients with a chief complaint of breathlessness of unknown cause present for >8 weeks. In this sample about 80% of the patients received a single diagnosis for their breathlessness and the rest had two diagnoses. Almost half the diagnoses were non-respiratory (31% non-cardiorespiratory diagnoses and 16% cardiovascular and circulatory diagnoses).\footnote{Pratter MR, Abouzgheib W, Akers S, Kass J, Bartter T. An algorithmic approach to chronic dyspnea. Respir Med. 2011 Jul;105(7):1014-21.}

To conclude

The review we conducted allows trying to describe how the population of breathless patients may look like, both at the CCG and the GP level.

Table 13 – Estimate of the burden of breathlessness in a CCG

<table>
<thead>
<tr>
<th>Condition</th>
<th>MIN</th>
<th>MAX</th>
<th>AVG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients diagnosed with a breathlessness related conditions</td>
<td>84,336</td>
<td>74,878</td>
<td>67,235</td>
</tr>
<tr>
<td>Total patients diagnosed with a breathlessness related conditions and complaining of breathlessness</td>
<td>14,773</td>
<td>52,775</td>
<td>33,230</td>
</tr>
<tr>
<td>Of whom</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety diagnosed</td>
<td>5%</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>HF diagnosed</td>
<td>13%</td>
<td>9%</td>
<td>10%</td>
</tr>
<tr>
<td>Obesity diagnosed</td>
<td>53%</td>
<td>65%</td>
<td>64%</td>
</tr>
<tr>
<td>COPD diagnosed</td>
<td>30%</td>
<td>23%</td>
<td>24%</td>
</tr>
<tr>
<td>Anaemia diagnosed</td>
<td>na</td>
<td>na</td>
<td>na</td>
</tr>
<tr>
<td>Breathless patients in the general population</td>
<td>15,373</td>
<td>19,000</td>
<td>17,273</td>
</tr>
<tr>
<td>Total breathless patients</td>
<td>6,944</td>
<td>11,917</td>
<td>9,039</td>
</tr>
<tr>
<td>Of whom breathlessness caused by</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>8%</td>
<td>21%</td>
<td>15%</td>
</tr>
<tr>
<td>HF</td>
<td>40%</td>
<td>29%</td>
<td>35%</td>
</tr>
<tr>
<td>Obesity</td>
<td>2%</td>
<td>21%</td>
<td>12%</td>
</tr>
<tr>
<td>COPD</td>
<td>48%</td>
<td>28%</td>
<td>37%</td>
</tr>
<tr>
<td>Anaemia</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
</tr>
</tbody>
</table>

According to the data we collected, at the CCG level we would expect in total about 67,000 patients [84,300-74,900] diagnosed with a condition such as COPD; HF, anaemia or anxiety. Of them, about 33,000 [14,800-52,800] would complain of some
level of breathlessness: the obese patients represent the biggest proportion of these patients (64%), followed by COPD patients (24%), HF patients (10%) and patients diagnosed with anxiety (3%).

Given the epidemiological evidence available, at the CCG level we would expect about 17,200 breathless adults [15,400-19,000]. Of them, 9,000 would receive a diagnosis of COPD, HF, obesity or anxiety. Patients whose breathlessness would be caused by either COPD or HF would account for about two thirds. Anxiety would be diagnosed in about 15% of the breathless cases. 12% would be breathless because of their obesity. Anaemia would represent only 2% of the breathless cases.

Similar consideration can be replicated for a GP. We would expect in total about 600 patients [560-650] diagnosed with a condition such as COPD; HF, anaemia or anxiety. Of them, about 220 [100-350] would complain of some level of breathlessness: the obese patients represent the biggest proportion of these patients (64%), followed by COPD patients (24%), HF patients (10%) and patients diagnosed with anxiety (3%).

Given the epidemiological evidence available, a GP would expect about 114 breathless adults [91-125]. Of them, 60 would receive a diagnosis of COPD, HF, obesity or anxiety. Patients whose breathlessness would be caused by either COPD or HF would account for about two thirds. Anxiety would be diagnosed in about 16% of the breathless cases. 12% would be breathless because of their obesity. Anaemia would represent 5% of the breathless cases.

Table 14 – Estimate of the burden of breathlessness for a GP

<table>
<thead>
<tr>
<th>No. patients per GP</th>
<th>MIN</th>
<th>MAX</th>
<th>AVG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total patients diagnosed with a breathlessness related conditions</strong></td>
<td>556</td>
<td>649</td>
<td>596</td>
</tr>
<tr>
<td><strong>Total patients diagnosed with a breathlessness related conditions and complaining of breathlessness</strong></td>
<td>97</td>
<td>348</td>
<td>219</td>
</tr>
<tr>
<td><strong>Of whom</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety diagnosed</td>
<td>5%</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>HF diagnosed</td>
<td>13%</td>
<td>9%</td>
<td>10%</td>
</tr>
<tr>
<td>Obesity diagnosed</td>
<td>53%</td>
<td>66%</td>
<td>64%</td>
</tr>
<tr>
<td>COPD diagnosed</td>
<td>30%</td>
<td>23%</td>
<td>24%</td>
</tr>
<tr>
<td>Anaemia diagnosed</td>
<td>na</td>
<td>na</td>
<td>na</td>
</tr>
<tr>
<td><strong>Breathless patients in the general population</strong></td>
<td>91</td>
<td>125</td>
<td>114</td>
</tr>
<tr>
<td><strong>Total breathless patients</strong></td>
<td>43</td>
<td>82</td>
<td>60</td>
</tr>
<tr>
<td><strong>Of whom breathlessness caused by</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>7%</td>
<td>25%</td>
<td>16%</td>
</tr>
<tr>
<td>HF</td>
<td>43%</td>
<td>28%</td>
<td>34%</td>
</tr>
<tr>
<td>Obesity</td>
<td>2%</td>
<td>20%</td>
<td>12%</td>
</tr>
<tr>
<td>COPD</td>
<td>45%</td>
<td>24%</td>
<td>32%</td>
</tr>
<tr>
<td>Anaemia</td>
<td>2%</td>
<td>4%</td>
<td>5%</td>
</tr>
</tbody>
</table>

IMPRESS Breathlessness Working Party
2 January 2014
For a full list of participants see http://www.impressresp.com
APPENDIX
Relevant NICE Public health guidance as at December 2013

PH1 Brief interventions and referral for smoking cessation (PH1)
PH2 Four commonly used methods to increase physical activity (PH2) (partially updated by PH41 and PH44)
PH5 Workplace interventions to promote smoking cessation (PH5)
PH6 Behaviour change (PH6)
PH8 Physical activity and the environment (PH8)
PH9 Community engagement (PH9)
PH10 Smoking cessation services (PH10)
PH13 Promoting physical activity in the workplace (PH13)
PH14 Preventing the uptake of smoking by children and young people (PH14)
PH15 Identifying and supporting people most at risk of dying prematurely (PH15)
PH16 Mental wellbeing and older people (PH16)
PH17 Promoting physical activity for children and young people (PH17)
PH21 Reducing differences in the uptake of immunisations (PH21)
PH23 School-based interventions to prevent smoking (PH23)
PH26 Quitting smoking in pregnancy and following childbirth (PH26)
PH41 Walking and cycling (PH41)
PH42 Obesity - working with local communities (PH42)
PH44 Physical activity: brief advice for adults in primary care (PH44)
PH45 Tobacco harm reduction (PH45)
PH46 BMI and waist circumference - black, Asian and minority ethnic groups (PH46)
PH48 Smoking cessation - acute, maternity and mental health services
   Obesity: the prevention, identification, assessment and management of overweight
   and obesity in adults and children

1 Our cut off was December 2013 but please note there is the useful NICE Public Health guidance