

# **The impact of gender on access to pulmonary rehabilitation for people with Chronic Obstructive Pulmonary Disease**

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## Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressive lung disease associated with breathlessness, inability to exercise, frequent infections and hospitalisation. COPD is a major cause of morbidity and mortality around the globe [1-3] and in England approximately 1.2 million people were living with diagnosed COPD in 2012.[4] Annual direct healthcare costs of COPD in England have been estimated to increase from £1.50 billion in 2011 to £2.32 billion in 2030.[5]

Pulmonary rehabilitation (PR), providing supervised exercise and education, is an evidence-based non-pharmacological treatment for COPD. PR leads to clinically significant improvements in exercise capacity, symptoms and health-related quality of life,[6] supports self-management skills [7] and results in fewer and shorter hospital admissions [8] and readmissions.[9] It is a recommended [10] and cost-effective treatment [11] with published guidelines [12] for patients who are functionally disabled by COPD. British Thoracic Society guidelines recommend that PR should be offered to patients with COPD with a view to improving exercise capacity, dyspnoea, health status and psychological wellbeing.[12]

However, PR is significantly underutilised and low rates of referral and uptake impede access to this effective therapy. In England and Wales in 2013/14 the estimated prevalence of COPD patients eligible for PR was 446,000 but only 68,000 patients were referred to PR programmes. Of those, 31% did not attend for assessment [13]. There is an urgent need to review and address barriers to patient access.

Referral rates are impacted by difficult referral processes, lack of information about PR and unclear roles and responsibilities regarding referral.[14-27] Uptake is impacted by the quality of the conversation between patient and referring clinician about PR and the patients' beliefs about the benefits, as well as timing, location and transport.[28-30] However, much of the literature exploring barriers to PR referral or uptake does not differentiate between men and women to identify the impact of sex or gender on access to PR.

Sex and gender are recognised as determinants of health and disease.[31] Sex is a classification based on reproductive organs and functions assigned by chromosomes,[32] whereas gender encompasses cultural and social aspects of attitudes, feelings and behaviours as well as biology.[33] Over recent years there has been increasing focus on sex and gender differences in the incidence, prevalence, diagnosis, manifestation and treatment of COPD which may be related to biological and sociocultural factors.[34] Differences in sex account for some differences in COPD while others are related to gender [35-36] although in some cases it may be difficult to discriminate between the two [37] and the terms may be used interchangeably simply to distinguish between male and female. The distribution of treatments across socio-demographic differences such as gender as well as age, social situation and disease severity needs to be explored [38] and differences in the natural history of the condition in men and women may warrant different treatment strategies.[34]

While sex-specific data on COPD are still scarce a pattern of sex-specific characteristics is nevertheless emerging and is summarised in a review by Jenkins et al.[39] These include under-diagnosis and sub-optimal treatment in women and sex differences in disease presentation, socioeconomic status, tobacco use and occupational and non-occupational exposures. Gender related differences have also been identified in susceptibility to cigarette smoke, disease perception, disease phenotype and co-morbidities.[37]

This report is a narrative summary drawing on the literature concerning the influence of sex and gender on COPD and how these factors may impact on access to PR for people living with COPD.

## Methods

A search was conducted in PubMed and CINAHL databases in May 2018. Search terms included combinations of the terms COPD, pulmonary rehabilitation, sex, gender, referral, uptake, attendance. Filters applied were: publication date from January 1998; English language; academic journals; human subjects; adults. The aim was to identify the latest evidence, reviews and key papers.

## Results

More than 1,000 publications were manually screened for articles of interest. There was little direct evidence of the impact of sex or gender on access to PR but there is an emerging literature on the impact of sex and gender on other aspects of COPD and its treatment. This report describes what is known in this area and considers the implications for access to PR.

### Incidence and prevalence of COPD

A recent meta-analysis reported that the global summary prevalence of COPD from more than 150 studies was 9.2% for men and 6.2% for women [40] which is comparable to estimates from previous systematic reviews.[3,41] There was higher prevalence for men across various regions of the world and various settings and the differences between men and women were smaller than previously thought, although the review included studies from 2005 onwards so the authors could not comment on longer term historical trends; however, they concluded that the gap in prevalence between men and women was closing, especially in developed, high income countries and urbanised settings.[40] Other reports show prevalence increasing more rapidly in women than in men globally,[35,41-47] even though females may be under-represented in research populations [48] and despite a possible gender bias in diagnosis.[49-50]

Smoking is the primary risk factor for COPD in both men and women[37] and the more rapid increase in prevalence among women may be due to increasing tobacco consumption by women over several decades [51-52,37] combined with increased susceptibility to tobacco use and to COPD development.[35-36,47,53] Women have similar levels of impaired lung function for

lower levels of smoking suggesting accelerated decline in lung function in women who smoke.[54-56] Greater exposure to indoor air pollution in some countries, anatomical and hormonal differences and behavioural differences in response to therapies may also be influencing factors.[40]

Data are limited but women with COPD are generally younger, more likely to present with COPD before the age of 60 years, to smoke less, have lower BMI and to be more likely to be of lower socioeconomic status than men.[47,53,57-61] Women also differ in their phenotypic response to cigarette smoke, being more predisposed to chronic bronchitis phenotype and men to emphysema.[37]

### ***Implications for access to PR***

The rising incidence and prevalence of COPD in women will mean that more women will be eligible for referral to PR and this is one factor of which referring clinicians need to be aware.

If women are more likely to present with COPD under the age of 60 then there is a greater likelihood that they may still be in employment. This has implications for the timing of classes which are often held during working hours and may result in women being disproportionately unable to access such classes. A greater variety of provision may be needed, e.g. classes outside working hours or home based programmes, to address the needs of working people.

### **Diagnosis of COPD**

Inadequate diagnosis of COPD is a problem for men and women [62] but under-diagnosis is more prevalent among women.[37] A bias against diagnosing COPD in women has been reported since 2001.[50, 57,63-64] Two studies have shown that given similar clinical scenarios physicians are more likely to diagnose COPD in males [49-50] and in a US study women reported a longer diagnostic delay and difficulty reaching a physician.[65] Women with COPD may present differently from men [57] and a better recognition of the different presentation in women would aid earlier diagnosis.[34]

Whereas identical symptoms are more likely to lead to a COPD diagnosis in men this doesn't happen if spirometry data are available to aid diagnosis.[34,49,66] However, an international survey conducted in North America and Europe exploring gender differences in diagnostic procedures found that women had spirometry tests less often than men.[67]

A male dominated bias in physician awareness of COPD can lead to delayed or misdiagnosis in women and potentially sub-optimal treatment [44,49,57,65] and poorer outcomes.[34,57] There is a need to improve timely diagnosis by raising awareness of COPD in women.[39]

## *Implications for access to PR*

Delayed or misdiagnosis of COPD in women will be a barrier to timely access to PR for women. A bias towards spirometry in men compared to women will compound this inequality of access.

## Manifestation of COPD

For the same degree of airflow obstruction there is heterogeneity in the clinical manifestations of COPD and the influence of gender on this heterogeneity is of increasing interest.[37] A difference in presentation of symptoms in men and women may contribute to diagnosis being more difficult in women.[34] While some studies show similar symptoms in men and women [68-69] others report differences in several areas.

Among women dyspnoea appears earlier in life and at an earlier stage of the disease than for men.[58,70-71] Women more likely to report prevalence and higher intensity of dyspnoea [63,67] even for similar airflow limitation [4,37,67] and after accounting for FEV1% predicted, age, pack years smoked and degree of emphysema.[53] Greater dyspnoea may be related to different exposure to risk factors [72-73] and different thresholds of symptoms awareness and reporting for men and women.[39]

Anxiety and depression are the best studied comorbidities in COPD [37] and there is a clear gender difference. Women with COPD experience higher levels of anxiety and depression than men.[44,68,71,74-80] Anxiety and depression are associated with more impaired quality of life and reduced adherence to treatment.[81-82] Older women may experience greater psychosocial impairment.[83]

Women have a higher burden of comorbidities than men [84-87] particularly asthma, osteoporosis, anxiety and depression but they are less likely to have cardiovascular disease [60,63,68,74,85,87-88] and diabetes.[63] Other studies have found osteoporosis, inflammatory bowel disease, chronic heart failure and diabetes are more prevalent in women, while alcoholism and ischemic heart disease are less frequent in women compared to men.[86,89] There is an ongoing need to consider the impact of comorbidities on COPD treatments.[39]

For the same degree of airway obstruction women have worse health-related quality of life than men [37,64,90-92] and this can occur at a younger age and at an earlier stage of the disease.[43] In addition women may develop symptoms that influence health-related quality of life in the presence of relatively small degrees of airway obstruction.[91] The factors that determine health-related quality of life for men and women may differ [91] and women may be more susceptible to the detrimental effects of smoking.[47]

Women have been reported to have a greater risk of COPD-related hospitalisation [93] and to have more exacerbations than men,[38,94] although outcomes following acute exacerbation may be better in women.[95-96]

### *Implications for access to PR*

Depression is a risk factor for poor adherence to PR (see below) and so may be a reason for women being disproportionately unable to gain the full benefit from PR compared to men.

A higher level of dyspnoea in women would suggest that a greater proportion of women with COPD should be referred to PR compared to men but no data could be identified to verify if this is the case.

Improvement in health-related quality of life is an important outcome from PR and so women may have more to benefit from PR in this regard.

Hospitalisation for exacerbation is an opportunity for PR referral and therefore a potential route to PR that would favour women, although not all hospitals have protocols in place to ensure this happens.

### **Coping styles**

Knowledge about gender differences in coping with COPD is more limited than knowledge about symptoms and susceptibility to tobacco exposure.[65] However, one study has reported that women are more likely to use emotion-focused coping strategies (a response characterised by emotions such as anxiety and depression) while men are more likely to use problem focused strategies: this could be linked to women showing more anxiety than men.[97] Women may therefore benefit more from PR programmes that include emotional support and social interaction.[98] More research is needed into how coping strategies differ between men and women in order to determine how best to support women.[39]

### *Implications for access to PR*

Patients' beliefs about the benefits of PR impact on uptake. To encourage uptake by women it may be necessary to emphasise the ways in which PR can provide emotional support.

### **Treatment and healthcare experience**

Given the different presentation of COPD in men and women we would expect to see different COPD treatment strategies in men and women [34] but data are limited on whether men and women receive differential care.[37]

In a study in Sweden Hensch et al.[38] found that although there were differences in disease expression and management, pharmacological and non-pharmacological treatments were mainly prescribed according to severity of disease irrespective of gender. A lack of a consistent gender differential in treatment is also reported in other studies.[99] However, a large international survey of 3,265 participants with COPD found that women were less likely to receive spirometry (perhaps because there is male bias in suspecting COPD) and more likely to receive smoking

cessation advice.[67] In a study of US veterans women were less likely to have received an appropriate outpatient pharmacological regimen prior to admission.[100]

There are reported differences in healthcare utilisation between men and women with COPD. Women may be more aware of symptoms which could prompt them to seek care earlier.[37] Studies also show that women are more likely to have more frequent interactions with HCPs and to use more health care resources than men.[86-87,92,101] Henocho et al.[38] reported that 22% of patients on the Swedish National Airway Register had participated in patient education programs, women to a larger extent, and that women were more likely to have had contact with a physiotherapist or dietician than men.

Emotional health is a determinant of patient experience of the healthcare system [102-103] and is associated with healthcare use.[104] Evidence shows that women with COPD are more likely to experience anxiety and depression [44,68,71,74-80] and so it is possible that any differences between men and women in their experience of healthcare could be due to different levels of anxiety and depression. However, an independent effect of gender has been found. In a survey of COPD patients in the US, more women found their physician difficult to reach and felt that time with their doctor was insufficient after anxiety and depression were adjusted for. In the same survey fewer women believed that their doctor was sympathetic to their condition.[65] Healthcare experience may well differ in differing health economies and healthcare systems around the world and so such findings must be considered in context. Studies in various medical settings have shown physician patient concordance on a number of social characteristics, including gender, is associated with less positive perceptions of care.[105-106]

Current smoking is a predictor of non-attendance at PR [107] and smoking cessation is an important element of managing COPD. Quitting smoking may be more difficult for women than men.[37] US data suggest that smoking cessation may be less common among women [108] and women have more difficulty maintaining long term abstinence from smoking.[109] Depression, anxiety and low self-esteem may contribute to relapse in women.[110] Women seem to have greater behavioural dependence on tobacco and so need a tailored behavioural approach.[101]

The recent review by Jenkins et al.[39] calls for more research into sex-related differences in treatment and utilisation of healthcare resources by women, better consideration of sex-relevant factors such as co-morbidities and highlights an urgent need for improvements in disease management in women.

### ***Implications for access to PR***

If women tend to have a greater number of interactions with healthcare professionals this could in theory provide more opportunities for referral to PR and therefore be an enabler of access for women, depending on the type of interaction and the role of the healthcare professional.

Evidence shows that the quality of the conversation between the referring clinician and the patient is an important influencing factor in take up of PR. More research is needed to

understand whether the quality and nature of the conversation differs for male and female patients and whether it is influenced by the sex of the referring clinician.

Smoking cessation support prior to or in conjunction with PR may be more important for women in order for them to take advantage of the benefits offered by PR.

## Benefits of PR

Some studies have found no differences in outcomes between men and women following PR [111-118] suggesting that they are likely to benefit equally. Other studies report that men and women show different responses to treatments including PR.[44,99,119-120] A greater improvement in dyspnoea [121] and health-related quality of life has been reported for women following PR,[121-122] a greater improvement in health-related quality of life for men [98,123] and an improvement in the 6 Minute Walk Test for men but not women.[123] However, data are still scarce.[39] A systematic review of gender-associated differences in PR outcomes in people with COPD concluded that the conflicting results may be due to heterogeneity among studies and that there is insufficient evidence to support or refute gender differences in PR outcomes.[31]

Robles et al.[31] argue that quantitative and qualitative studies are needed to gain a better understanding of how PR programmes meet the needs of men and women, given the differences in disease presentation, and whether customized treatment would result in better outcomes. They conclude that it is reasonable to assume that men and women will encounter similar benefits in PR but there may be differences in how those benefits are perceived.

## *Implications for access to PR*

Based on current evidence there is no reason to suppose that PR is more important as a treatment for COPD for either men or women and practitioners should assume that benefits are achievable by both. Referral should not be influenced by a patient's gender and referral should be considered equally for men and women.

## Uptake of PR

The national COPD audit captured all consenting patients with a primary respiratory diagnosis of COPD who were assessed for or began PR between 3 January and 31 March 2017 in PR services in England and Wales.[124] The audit sample comprised 53% (3,928) males and 47% (3,548) females, the same percentages reported in a previous audit in 2015. This mirrors the slightly higher prevalence of COPD among men compared to women.

Data unstratified by gender show poor uptake for PR as low as 50%.[28] In a retrospective analysis of a research database in the UK of patients who had been offered PR 31.8% failed to attend a single session.[107] Gender may have a role in uptake. In a UK study patients were less

likely to attend a first PR session if they were female (62.8% v 72.1% for men), current smokers or lived alone.[107] It is unclear why gender would be a predictor of uptake but Hayton et al. suggested that women without social support in their cohort may be less likely to be car drivers and thus less likely to attend.[107]

Gender did not predict adherence to PR in the study by Hayton et al.[107] However, depression, which is more common among women with COPD, has been identified as a predictor of non-adherence to PR.[125-126] Depressed patients were almost twice as likely to drop out compared to non-depressed patients.[125]

### ***Implications for access to PR***

Women may be more likely not to start PR but once they do start they may be no more likely to drop out than men when only gender is taken into account.

Referrers may need to consider whether there are any particular needs among women that might prevent them being able to attend PR.

In particular, the greater likelihood of depression in women patients should be considered and addressed in order to support access.

# Recommendations to support equal access to PR for men and women

## Healthcare systems and processes

- There is an urgent need to raise levels of awareness of COPD in women and implement more successful strategies to improve diagnosis, prevention and treatment that take into account the inherent differences.
- Based on current evidence there is no reason to suppose that PR is more important as a treatment for COPD for either men or women and practitioners should assume that benefits are achievable by both. Referral should not be influenced by a patient's gender and should be considered equally for men and women.
- Delayed or misdiagnosis of COPD in women will be a barrier to timely access to PR. Widespread use of spirometry can help to overcome gender bias in diagnosis and therefore enable consequent access to PR for women.
- Hospitalisation for exacerbation is an opportunity for PR referral and therefore a potential route to PR that would favour women. It is recommended that hospitals have protocols in place to ensure this happens.
- Women may have a greater number of interactions with healthcare professionals and this could in theory provide more opportunities for referral to PR and therefore be an enabler of access for women, depending on the type of interaction and the role of the healthcare professional.

## Communication with patients

- Patients' beliefs about the benefits of PR may impact on uptake. To encourage uptake by women it may be necessary to emphasise the ways in which PR can provide emotional support. Providers also need to consider the possibility that men and women may require differing degrees of emotional support during PR.
- Evidence shows that the quality of the conversation between the referring clinician and the patient is an important influencing factor in the take up of PR. More research is needed to understand whether the quality and nature of the conversation differs for male and female patients and whether it is influenced by the sex of the referring clinician.
- Women may be less likely to start PR but once they do start they may be no more likely to drop out than men. Referrers may need to consider whether there are any particular needs among women that might prevent them being able to attend PR. The greater likelihood of depression in women patients should be considered and addressed in order to support access.

## Provision of support

- Education programmes tailored for women and families would empower patients to manage their disease more effectively.
- Women seem to have greater behavioural dependence on tobacco and so need a tailored behavioural approach to smoking cessation. Smoking cessation support prior to or in conjunction with PR may be more important for women in order for them to take advantage of the benefits offered by PR.
- Providers need to consider the provision of classes outside of working hours in order to increase accessibility for patients who are in employment. As women are more likely to present before the age of 60 years this may be disproportionately important for women compared to men.

## Conclusion

The prevalence of COPD in women is increasing more rapidly than in men. Women with COPD tend to be younger, more likely to present with COPD before the age of 60 years, to smoke less, have lower BMI, to be more likely to be of lower socioeconomic status than men and differ in their phenotypic response to cigarette smoke, being more predisposed to chronic bronchitis phenotype and men to emphysema. There is a male bias in the diagnosis of COPD. While there is an increasing amount of evidence concerning the differing presentation of COPD in men and women, there is little direct evidence of the impact of gender on access to PR, although female sex has been shown to be a predictor of non-attendance. However, what is known about the differing experiences of men and women can be drawn on to highlight factors to consider in facilitating equality of access for both sexes. An awareness by referrers and PR providers of gender differences in the presentation and experience of COPD can maximise the opportunity for PR referral and uptake at a system level and during one to one consultations with patients.

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