

## **Quality of life changes with duration of chronic breathlessness: a random sample of community-dwelling people.**

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## **Abstract**

### **Introduction**

Chronic breathlessness is associated with poorer quality of life. This population study aimed to define dimensions of quality of life (QoL), and duration and dominant causes of breathlessness that most diminished QoL.

### **Methods**

This cross-sectional, population-based, randomised survey of adults (n=2,977) in South Australia collected data on demographics, modified Medical Research Council (mMRC) breathlessness and QoL (EQ-5D-5L; SF-12). Data weighted to the census were analysed for relationships between EQ-5D-5L and its dimensions with mMRC. Regression models controlled for age, sex, education, rurality and body mass index.

### **Results**

2,883 responses were analysed: 49% were male; mean age 48 years (SD 19).

As mMRC worsened, EQ-5D-5L and its dimensions worsened. More severe chronic breathlessness was iteratively associated with lower mobility, daily activities and worse pain/discomfort. For self-care and anxiety/depression, impairment was only with the most severe breathlessness.

Respondents who had chronic breathlessness for two to six years had the worst quality of life scores. People who attributed their breathlessness to cardiac failure had poorer quality of life. Respondents who reported a cardiac cause for their breathlessness had worse mobility, poorer usual activities and more pain than the other causes.

The regression analyses showed that worse chronic breathlessness was associated with worsening QoL in each dimension of EQ-5D-5L, with the exception of the self-care, which only worsened with the most severe breathlessness.

### **Conclusions**

This is the first study to report on chronic breathlessness and impairment across dimensions of QoL and differences by its duration. Mobility, usual activity and pain drive these reductions.

**Key Message**

Quality of life (QoL) decreases with increasing chronic breathlessness. Of five dimensions in EQ-5D-5L, self-care is limited only with the worst chronic breathlessness. Other dimensions worsen progressively with increasing breathlessness. People with cardiac causes report worse QoL, and people in years 2-6 of having chronic breathlessness have most impaired QoL.

**Keywords**

chronic breathlessness, quality of life, population survey, prevalence study

**Running Title**

Chronic breathlessness and quality of life

## **Background**

Chronic breathlessness [1] is prevalent across the community, and is associated with adverse health outcomes including lower activity levels [2], poorer physical and mental components of quality of life [3], depression and co-existing anxiety/depression [4,5], less sexual activity [6] and poorer prognosis [7]. Despite the impact on individuals and society, chronic breathlessness is under-recognised and, even when a clinician does identify its presence, might be under-treated [8].

Chronic breathlessness is an important determinant of people's quality of life (QoL) [3]. A key need in addressing the burden of chronic breathlessness in the community is a clearer understanding of the symptom's impact on each QoL domain. The impact on QoL from the duration of chronic breathlessness has also not been defined. Likewise, whether the attributed causes of breathlessness have differing impacts on people's reported QoL has not been defined at a population level. This knowledge could help focus future interventions to lessen the impact of chronic breathlessness.

The use of population surveys that do not rely on contact with health services is important to explore the impact of chronic breathlessness across the community. This is especially the case for people with very severe chronic breathlessness who are mostly housebound and do almost anything in their power to avoid contact with health services. Through such survey tools, random samples of the population complement findings from disease- or symptom-based cohorts identified through contact with health services.

The primary aim of the current study was to evaluate the relationship between intensity of chronic breathlessness and dimensions of QoL (measured using the EQ-5D-5L) that may be contributing to poorer QoL in community-dwelling adults. Secondary aims were to evaluate duration of chronic breathlessness and, separately, respondent-attributed causes in relation to QoL.

## **Methods**

### *Design and setting*

This was a cross-sectional, population-based survey in South Australia, an Australian state with 7% of the nation's population [9]. South Australia has a slightly older population than the rest of the country and a lower proportion of people born overseas [10].

### *Sample*

Data were collected using the annual 2017 Health Omnibus Survey conducted in South Australia (SAHOS). SAHOS was a clustered area, multi-stage, systematic sample of households with face-to-face interviews conducted in respondents own homes. The interviews were conducted in the southern hemisphere spring (September – December). Australian Bureau of Statistics (ABS) census collector districts (CCDs) were randomly selected according to a pre-defined algorithm and a second randomisation occurred within each of the selected districts. Metropolitan areas and towns with a population of more than

1,000 people were included. Institutions excluded from sampling included: hospitals, residential aged care facilities, hotels/motels and gaols. Prompt cards were utilised for questions relating to breathlessness and quality of life measures.

After an approach letter was sent to the selected households, one person  $\geq 15$  years of age who most recently had a birthday was invited to participate. If the selected person declined to participate, that household was not used. If no one was home, up to six return visits ensued before a non-response was recorded.

In total, 2,977 people engaged with the interviews with an overall participation rate of 65.3%. For the purposes of this study, analyses were restricted to participants 18 years and older who answered questions related to chronic breathlessness, EQ-5D-5L and SF-12 ( $n=2,883$ ). Data were weighted using the 2016 Australian national census data by 5 year age groups, sex, household size and metropolitan / non-metropolitan place of residence.

### *Measures used*

#### *Breathlessness*

The modified Medical Research Council (mMRC) breathlessness scale was developed for population surveys (Web Appendix S1) to evaluate the level of functional impairment from breathlessness [11]. Respondents were asked to choose one of five ordinal statements. Chronic breathlessness was assessed, and to aid comparability to previous use of the mMRC in the Health Omnibus Survey, chronic breathlessness was framed in context of ‘most days for three of the last six months’. If breathlessness was present ( $mMRC \geq 1$ ), respondents were also asked to identify their perceived dominant cause of breathlessness (lung, heart, disorders of nerves or muscles, other) and about how long they had been this breathlessness in years and months as a continuous variable. The duration of their breathlessness was then categorised into five groups: less than 1 year, 1-2 years, 2-6 years, 6-20 years, 20-60 years.

#### *Quality of life (QoL)*

The EuroQol Five Dimension (EQ-5D) is a generic measurement of quality of life across five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) with lower scores indicating more impairment on a 1-5 scale for each dimension [12]. An index value using weights derived in the same population studied varies between 0 and 1, and summarises all Dimensions into a single number, where 0 is equivalent to dead and 1 represents a full health state. Updated to include five levels of severity for each dimension, the EQ-5D-5L is extensively used in the clinical and economic evaluation of health care as well as in population health surveys [12,13,14]. The instrument is quick and easy to use, extensively researched and validated. Most importantly, EQ-5D-5L is not disease-specific and therefore applicable to most disease areas and comparisons between diseases. Further, it has been informative in providing new data on population health characteristics, complementing, for example, morbidity and mortality data.

The primary analysis used the EQ-5D-5L. For some analyses, these five levels were reduced to two (no/slight and moderate/severe/extreme) given the number of responses in each group [12]. The respondent's scoring was analysed descriptively, as well as converted to a single summary index value reflecting societal preference compared to other health profiles. Societal preference weights were derived using national data from the Australian general population [15]. To date, there is no agreed minimum clinically important difference defined, with estimates varying widely. [16]

The Short Form-12 (SF-12) is a validated health status questionnaire that summarises 12 items measuring overall health in eight domains (physical functioning; role-physical; bodily pain; general health; vitality; social functioning; role-emotional; and mental health) into physical component summary (PCS) and mental component summary (MCS) scores [17]. The SF-12 is scored using population norms to transform scores to theoretically range from 0 to 100, with 50 the mean score and a standard deviation (SD) of 10. The current study used norms derived from the Australian Bureau of Statistics (ABS) 1995 Australian National Health Survey dataset [18]. The SF-12 has been validated in general and clinical populations in many countries across the world, including Australia [19].

#### *Other data*

Demographic variables included age, sex, rurality (metropolitan / non-metropolitan), country of birth, highest level of education, marital status, estimated gross annual household income, and current working status. Self-reports included weight and height, from which body mass index (BMI) was calculated ( $\text{kilograms}/\text{metres}^2$ ) and categorised into four World Health Organisation (WHO) levels (underweight (BMI<18.5), normal weight (BMI 18.5-25.0), overweight (BMI >25-30) and obese/morbidly obese (BMI >30) [20].

#### *Statistical analyses*

Data analysis was conducted using Statistical Package for Social Sciences (SPSS) for Windows Version 23.0. All estimates and analyses used population weighted data. No missing data were imputed.

Mean and standard deviations for quality of life scores (EQ-5D-5L index values and SF-12 PCS and MCS scores), and frequencies and percentages for each of the dimensions of EQ-5D-5L were calculated. Duration of respondents' breathlessness by categories and cause of breathlessness were calculated by each category of mMRC. Descriptive statistics were also calculated for socio-demographic and health-related indicators (Tables in Web Appendix S2). The distribution of the mMRC (0-4) and the dominant attributed cause of breathlessness were estimated for the five dimensions of the EQ-5D-5L dichotomised (no/slight problem, moderate to severe problem). SF-12 PCS and SF-12 MCS scores were calculated for comparison to the direction and magnitude of the EQ-5D-5L scores.

For regression analyses, due to small numbers, respondents reporting breathlessness of mMRC 3 and 4 were combined into one group. Associations between mMRC and each QoL measure (EQ-5D-5L, SF-12 PCS and SF-12 MCS) were then analysed using multivariable linear regression. Multivariable logistic regression models were used to examine the associations between the five dimensions for the dichotomised EQ-5D-5L as proposed by the EuroQual team. The covariates included in both the models were age, sex, educational attainment, area of residence, and BMI category. No interaction terms were assessed for the final model.

## Results

After excluding those: under 18 years of age (n= 76); missing chronic breathlessness score (n=1); or quality of life measures (EQ-5D-5L and SF-12; n=17), 2,883 participants were included in the analysis. Socio-demographic factors are shown in Table 1: 49% were male; mean age was 48 years (standard deviation [SD] 19); 23% were aged 65 years and over; and 2,146 (74%) lived in the metropolitan area. These are cross tabulated with level of breathlessness (mMRC; Web Appendix S2).

Not having breathlessness except on strenuous exercise (mMRC 0) was reported by 91%, with the remainder reporting mMRC 1 (6%), mMRC 2 (1%), mMRC 3 (1%) and mMRC 4 (1%; Table 2). The mean EQ-5D-5L Index value was 0.91 (SD=0.15); for SF-12, the PCS score was 49 (SD=11) and the MCS score was 50 (SD=10). QoL (EQ-5D-5L, SF-12 PCS and SF-12 MCS scores) by the severity of chronic breathlessness are presented in Figure 1. As mMRC worsened, so did EQ-5D-5L, each of its dimensions, and the physical and mental components of SF-12. (Figure 1) Web Appendix S3 presents breathlessness by each quality of life tool and their dimensions / component summary scores.

The distribution of moderate-extreme scores on each of the five dimensions of the EQ-5D-5L (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) by the level of mMRC breathlessness is shown (Figure 2 and Web Appendix figure S1). For all five dimensions, respondents who reported moderate-extreme problems on the five dimensions of EQ-5D-5L had higher proportions with mMRC  $\geq 1$  compared to respondents with mMRC 0. More severe chronic breathlessness was associated with lower mobility and activity and worse pain/discomfort (Figure 2). For the dimensions of self-care and anxiety/depression, higher scores reflecting greater impairment were only seen for people with mMRC 4.

QoL measures (EQ-5D-5L Figure 3a and SF-12 Figure 3b; Web Appendix S4) changed from the time that chronic breathlessness was first recognised by the respondent. Respondents who had breathlessness symptoms the longest (more than 20 years) had better QoL than those who have had the condition two to six years.

Respondents who reported a cardiac cause for their breathlessness had worse QoL scores than respondents who reported the cause as respiratory or 'other' (Figure 4a EQ-5D-5L and Figure

4b SF-12; Web Appendix S4). This is also seen in three of the five dimensions of the EQ-5D-5L, although not in the self-care dimension. (Figure 4c) It was not statistically significant for anxiety / depression (Figure 4c).

After adjusting for covariates, the regression analyses showed that chronic breathlessness was associated with poorer QoL in each of the dimensions of EQ-5D-5L, with the exception of the self-care dimension. (Table 3) Self-care was limited with the most severe chronic breathlessness.

## **Discussion**

This is the first study to report on population-level chronic breathlessness and impairment across different dimensions of QoL as well as differences in QoL by duration of chronic breathlessness, collected independently of health service contact. Chronic breathlessness is related to marked reductions in QoL especially impacting on a breathless person's mobility, activities of daily living and pain. Anxiety/depression and self-care were impaired mainly in people with the most severe breathlessness.

The prevalence of chronic breathlessness ( $mMRC \geq 2$ ) was similar to previous studies in the South Australian population and consistent with other population-based studies that are not derived only from people having contact with health services, which supports the validity of the present findings [21].

Relating QoL to duration of chronic breathlessness, impairment was most marked in years 2-6 after chronic breathlessness was recognised by respondents. Although overlapping statistically, QoL gradually improved in the ensuing years. The ability to adapt to the likely changes in lifestyle outlined in each of the dimensions of EQ-5D-5L requires great resilience. The realisation that chronic breathlessness is not going to improve takes adjustment, and at face value it makes sense that early in the trajectory of chronic breathlessness (years 2-6) is a particularly challenging time as people attempt to adapt to marked changes in their life circumstances with little likelihood of improvement in chronic breathlessness in the future. In many ways, this is not dissimilar to the adaptation required after significant and permanent cord injuries where the level of adaptation to new circumstances is remarkable, but takes time [22]. Further, such 'turning points' as the realisation that breathlessness will be chronic and life will be forever different often sees people shift the issues that are important components for them in QoL [23].

The overall impact on quality of life, previously seen with the SF-12 tool in both the physical and mental components of the measure [3], is reflected in a more nuanced way using the EQ-5D-5L. These findings add weight to the assertion that chronic breathlessness affects every part of a person's life and as chronic breathlessness worsens, so do each of these dimensions.



Of note, only the sub-group with the most severe levels of chronic breathlessness reported higher rates of impairment with activities of daily living. It is interesting that mMRC level 4 is also the only item in the breathlessness scale that directly addresses an activity of daily living. With mMRC levels 1-3, people clearly cope with bathing, dressing, and preparing meals. The fact that these things are chronically impaired in people with mMRC 4 is a reflection of just how small their lifespan [24] is – the actual space they occupy – and the difficulties they face with self-care activities that the rest of the community take for granted.

This study also reports novel data on differences in chronic breathlessness in relation to self-reported aetiology. Although people with chronic cardiac failure form a smaller proportion of people with chronic breathlessness, they report worse quality of life (Figure 4a) and much higher proportions of moderate to severe problems with mobility, usual activities pain/discomfort and anxiety/depression (Figure 4c). Problems with mobility may be a particular problem in people with cardiac failure because of the added weight (especially to lower limbs) from chronic oedema.

Anxiety and depression are worse with duration of chronic breathlessness, confirming findings from a different population-based sample that was recently reported. [5] This study can only report associations, and it is likely that there is, for some people, a cycle of worsening breathlessness that may lead to increasing anxiety and depression, and for others it will primarily be anxiety and depression worsening chronic breathlessness especially if the chronic breathlessness is associated with progressive deconditioning. Anxiety and depression are also more marked in people with heart failure as the respondent-identified cause of chronic breathlessness. It is not clear why this should be so, and will be an important question to be answered in future studies.

Despite the relatively small numbers of respondents with more severe breathlessness, the regression analyses confirm the likelihood of significant impairment in each of the EQ-5D-5L dimensions. The magnitude of the effects on people with severe chronic breathlessness cannot be over-stated.

The current study's scores of severity, duration and cause of chronic breathlessness are relevant for future research initiatives. Index values for EQ-5D-5L were generated in this study for an average person in the general population experiencing chronic breathlessness categorised by severity and duration. These baseline population data can be used as input parameters in decision analytic modelling and economic evaluation comparing, for example, a new symptomatic treatment option with the *status quo*.

A strength of the present study is that it used tools validated for population studies in a representative sample of the adult population, normalised to the key parameters of the Australian Census. The mMRC scale was modified to focus specifically on chronic breathlessness (which may have been conflated with acute or short-term breathlessness in many previous studies), and the analysis accounted for a number of important confounders

including BMI [25]. The patterns of change in QoL were seen both with EQ-5D-5L and SF-12, adding validity and weight to these observations.

A potential limitation is that parts of the population were not included in the data collection algorithm such as people from smaller rural towns and people already in hospital or residential aged care facilities who may have a disproportionately higher prevalence of chronic breathlessness. The present study therefore pertains to community-dwelling adults, contributing novel data about the impact of chronic breathlessness, years out from its recognition.

## **Conclusions**

The findings have several implications. In people with chronic breathlessness, clinicians need to systematically evaluate and address factors that may co-exist and impair QoL throughout the disease trajectory, especially as breathlessness worsens. Given the breadth of the impact of chronic breathlessness across QoL dimensions, people with more severe chronic breathlessness require careful history taking, systematic measurement and management of the symptom. Of note, even apparently mild chronic breathlessness (mMRC=1) is associated with impaired quality of life. Given the progressive worsening of QoL for people living with chronic breathlessness from 2 to 20 years, specific thought needs to be given to how best to support patients during this time. This pattern is important to consider as people are newly diagnosed with conditions that are associated with chronic breathlessness in order to facilitate proactive management.

Research implications include the need to understand better the relationship between chronic breathlessness and pain, and chronic breathlessness and usual activities. Work has already identified key issues in activities foregone in people with chronic breathlessness, and this work needs to be expanded at a whole-of-population level.[unpublished observations Kochovska S, Chang S, Morgan D, Ferreira D, Sidhu M, Johnson M, Ekström M, Currow DC. Breathlessness and activities forgone: a cross-sectional, population prevalence study]

## **Disclosures**

**Ethics approval and consent to participate:** The Health Omnibus Survey and research methodology was approved by the University of Adelaide Human Research Ethics committee. All participants gave verbal informed consent and continuing participation in the face-to-face interview was recognised as continuing consent.

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**Conflict of Interest:** All authors report no conflicts of interest.

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