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Review

Quality of life in obstructive sleep apnea: a systematic review of the literature

Cheryl A. Moyer[a,*], Seema S. Sonnad[a,b], Susan L. Garetz[c], Joseph I. Helman[d], Ronald D. Chervin[e]

[a]*Consortium for Health Outcomes, Innovation, and Cost-Effectiveness Studies (CHOICES), Department of Internal Medicine, University of Michigan School of Medicine, 300 North Ingalls Street, 3A00 NIB, Box 0409, Ann Arbor, MI 48109-0409, USA*
[b]*Department of General Surgery, University of Michigan Health System, Ann Arbor, MI, USA*
[c]*Department of Otolaryngology — Head and Neck Surgery, University of Michigan Health System, Ann Arbor, MI, USA*
[d]*Department of Dentistry-Surgery, Division of Oral Surgery, University of Michigan Health System, Ann Arbor, MI, USA*
[e]*Department of Neurology, University of Michigan Health System, Ann Arbor, MI, USA*

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Abstract

Objective: To review the literature on obstructive sleep apnea (OSA) and health-related quality of life (HRQOL).

Background: OSA affects nearly one in four men and one in ten women aged 30–60 years in the United States. Health consequences of OSA can include neuropsychiatric and cardiovascular sequela that disrupt professional, family, and social life and negatively impact HRQOL.

Methods: We conducted a comprehensive review of the literature on HRQOL and OSA, with special attention paid to instruments developed specifically for OSA.

Results: Generic instruments used to study HRQOL and OSA include: Medical Outcomes Study Short Form-36, Nottingham Health Profile, Sickness Impact Profile, Functional Limitations Profile, EuroQol, and Munich Life Quality Dimension List. Specific instruments include: Calgary Sleep Apnea Quality of Life Instrument, Functional Outcomes of Sleep Questionnaire, OSA Patient Oriented Severity Index, the OSA-18, and Cohen's pediatric OSA surgery quality of life questionnaire.

Conclusions: OSA patients have impaired HRQOL when compared with healthy age- and gender-matched controls. Treatment with continuous positive airway pressure appears to improve HRQOL. Other treatment modalities have not been rigorously studied. In addition, more data are needed from preference-based measures that allow conversion to utility scores, which can be used to calculate quality-adjusted life years and cost-effectiveness ratios.

Keywords: Obstructive sleep apnea; Quality of life; Sleep; Review

1. Obstructive sleep apnea: assessment of effects

The breathing pattern that defines obstructive sleep apnea (OSA) affects nearly one in four men and one in ten women between the ages of 30 and 60 years in the United States; 4% of men and 2% of women have OSA with excessive daytime sleepiness, which is only one of several possible symptoms [1]. Other primary health consequences that may result from chronic sleep disruption or recurrent hypoxemia include neuropsychiatric and cardiovascular sequela.

* Corresponding author. Tel.: +1-734-647-8094; fax: +1-734-763-1485.
E-mail address: camoyer@umich.edu (C.A. Moyer).

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Neuropsychiatric effects may include depression and cognitive dysfunction that can disrupt professional, family, and social life and increase risks for automobile and industrial accidents. Cardiovascular sequela can include pulmonary and systemic hypertension, congestive heart failure, arrhythmia, myocardial infarction, and stroke [2].

Given the prevalence of OSA and its detrimental effects on both physical and mental function, it is not surprising that the health-related quality of life (HRQOL) among persons with OSA is receiving increased attention in the research literature [3]. The rapidly growing list of available HRQOL instruments encourages the measurement of HRQOL alongside more traditional, biologic health outcomes.

In obstructive sleep apnea research, HRQOL has been assessed among cross-sectional samples of patients [4–6], diagnosed patients and controls [7,8], patients treated with continuous positive airway pressure (CPAP) [9–15], patients treated with CPAP or uvulopalatoplasty [16], children who underwent sleep apnea surgery or tracheostomy [17], and heavy snorers treated with a nostril dilator [18].

In this article, we examine the role of HRQOL measurement in patients with OSA. We provide information likely to be helpful both in the choice of appropriate HRQOL instruments for research and in the evaluation of published HRQOL studies. We also highlight some of the background, importance, and potential of this rapidly developing aspect of clinical evaluation.

2. Introduction to health-related quality of life

According to Schipper and colleagues, "Quality of life in clinical medicine represents the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient" [19]. They proposed four primary domains for HRQOL measurement: physical and occupational function, psychological function, social interaction, and somatic sensation. Although HRQOL researchers have agreed to include certain specific domains in HRQOL assessment, no consensus has emerged over other domains that may be necessary to accurately and comprehensively measure HRQOL.

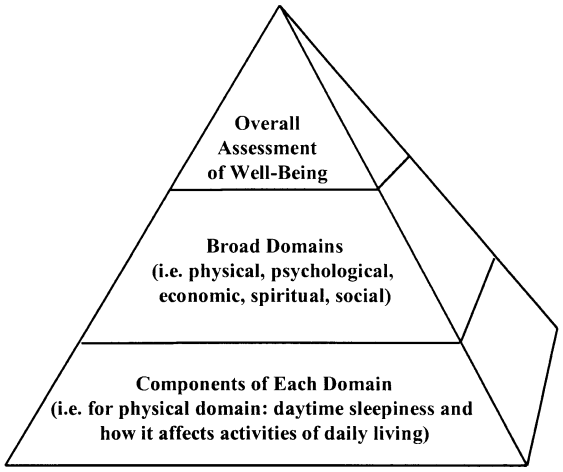
Nonetheless, most researchers agree that the separate 'domains' of HRQOL contribute only partly to a person's overall quality of life. Spilker used a pyramid to illustrate this point, placing the overall assessment of well-being at the top (Fig. 1) [20]. The middle section of the pyramid includes the broad domains of HRQOL that contribute to overall well-being, such as physical functioning. The bottom of the pyramid includes the smaller components that make up each of the specific domains; for example, the ability to get in and out of a chair is classified within the physical functioning realm. Using this model, one may approach HRQOL assessment from a top-down (overall assessment) or a bottom-up (e.g. ability to get out of a chair) direction.

3. The process of measuring HRQOL

Prior to undertaking a study of HRQOL, researchers should answer the following questions. (1) What is the purpose of HRQOL assessment in this study? (2) What level of HRQOL is of interest? (3) Which instrument is most appropriate?

3.1. Purpose

Measurement of HRQOL may be undertaken for the primary purposes of discrimination, prediction, or evaluation [21]. Discrimination divides a large group



(Adapted from Spilker, 1996 [20])

Fig. 1. Levels of HRQL measurement.

into clusters based on quality of life. Prediction allows both classification and comparison to a standard. Predictive indices allow researchers to determine if study subjects are classified appropriately. If change over time is of interest, researchers would want to apply an evaluative index. This is especially important in clinical trials that examine the impact of illness such as OSA or treatment such as CPAP over time.

3.2. General versus specific HRQOL measurement

The next step is to determine the level of assessment desired. If the patient's overall well-being is the interest, the researcher would select an instrument aimed at global assessment. Alternatively, the researcher may select an instrument that targets a specific domain, such as physical functioning or emotional well-being. The researcher may also choose an even more targeted instrument, capable of identifying specified outcomes within an HRQOL domain [22].

4. Instrument selection

The HRQOL instruments are grouped into two basic categories: generic and specific instruments. Generic instruments include single indicators (such as global assessments) and instruments designed for use among a variety of people with different types of illness. They also include health profiles and preference-based (utility) measures [23]. Specific instruments have been developed and validated to measure a narrow topic of interest, such as the effects of treatment on obstructive sleep apnea. Because generic and specific instruments each have both strengths and weaknesses (Table 1), the concurrent use of both types is often optimal in clinical studies.

4.1. Generic instruments

Generic instruments are suitable for use in diverse groups of individuals [24]. They range in sophistication from a single indicator to a detailed health profile assessment. A simple approach using a single indicator asks a general question such as 'How would you judge your quality of life?' Often people are asked to mark a point on a line (sometimes called a Visual Analog Scale) ranging from 0 (worst possible quality of life) to 100 (best possible quality of life). Although a single indicator can provide a clear data point that can be easily compared among patients, this relatively

Table 1
Types of HRQOL instruments: strengths and weaknesses

	Strengths	Weaknesses
Generic instruments	Allow comparison between studies, populations, or disorders	May lack sensitivity to detect differences among patients with a specific disease or condition
	More comprehensive than specific instruments	May lack sensitivity to conditions that affect narrow dimensions of HRQOL
	Some have been widely validated	May not follow framework familiar to clinicians
Single-item global	Easy to administer and interpret	Does not yield information on what goes into global score
		May oversimplify concept of HRQOL
Profile	Generate cross-sectional view of patient's overall well-being	May be confusing to interpret longitudinal changes over multiple dimensions
	Allow for determination of which dimensions of QOL are most affected	Summary scores may lack sensitivity to detect changes, especially if most change occurs in one dimension
Preference-based	Allow generation of a single utility score for a health state	Preferences calculated from other instruments and not assessed directly from patients may not accurately reflect patient preferences
	Allow cost-utility analysis	Single utility score may oversimplify differences in HRQOL
Specific instruments	Well suited to detect changes among patients with specific disorders	May not be available or validated for a particular disease or treatment
	More focused on the area of interest than generic instruments	May not discriminate among similar diseases
	Clinically sensible	Do not allow cross-condition comparisons

crude measure does not explore the many factors that influence the response.

More detailed generic instruments allow measurement of several different aspects of HRQOL, while remaining appropriate for use in almost any population. An example is a profile instrument, which creates a cross-sectional look at a person's quality of life across several dimensions. One commonly used generic health profile instrument is the Medical Outcome Study's SF-36, a 36-item questionnaire that summarizes HRQOL using eight subscales and two summary scores [25]. This type of instrument allows comparison of the effects of different diseases on individual subscale domains, as well as on overall mental health and physical health.

Utility measures, such as Torrance and Feeny's Health Utilities Index [26], are based on economic theory. As a special class of generic instruments, utility scales focus on a broad range of domains. The scales ask a range of questions that help to classify respondents into various health states. The utilities of these health states typically have been assessed previously by a sample of the general public, patients, or a panel of experts. The utilities are expressed on a scale of 0 (death or worst possible outcome) to 1 (complete health or best possible outcome), and refer to the subjective value attached to specific levels of health [24]. Utility scores summarize complex HRQOL influences in a single variable and — in combination with survival data — allow calculation of quality adjusted life years (QALYs) [23], an outcome of intrinsic importance in many different studies and disease states.

4.2. Specific instruments

Although generic instruments do allow for cross-study and cross-population comparisons, they may lack the sensitivity needed to detect differences among patients with the same disease or treatment. Specific HRQOL instruments focus on aspects of health status relevant to more narrowly defined populations. Specific instruments may distinguish by diagnosis (e.g. OSA), treatment (such as surgery or CPAP), population of patients (e.g. patient caregivers or the frail elderly), function (e.g. sexual function), or symptom (e.g. sleepiness) [27]. Specific instruments are more likely to capture subtle differences in outcomes of different treatments for the same disease. They also provide much clearer clinical detail on the effects of a specific disease or treatment on HRQOL.

4.3. What makes a 'good' instrument?

Given the variety of HRQOL instruments available, how can researchers determine which ones are superior or most applicable? Maunder and colleagues [28] published a list of seven criteria they used to evaluate studies that measured HRQOL: reproducibility, reliability, validity, ease of use, responsiveness to change, meaningfulness of results, and sampling of patient's perspective.

Reproducibility is the ability to use an instrument in a setting other than the one in which it was developed. The instrument must be published and available for use by other researchers, and it must be readily applicable to other settings. Instruments that require special circumstances — such as nurses specially trained to administer complicated assessments — are not likely to be easily reproducible.

Reliability is the stability of the data gathered. One common piece of this concept is *test–retest reliability*: If all relevant factors remain unchanged, responses should be the same when the instrument is administered a second time. *Internal consistency* is another form of reliability and suggests that items within a subscale should correlate with each other strongly enough to show that each helps to assess the same concept, though not so strongly that the items are completely redundant [29]. Chronbach's alpha scores of 0.70 or greater generally indicate good *internal consistency* [30]. *Validity* implies that an instrument does in fact measure that which it purports to assess. Evaluation of validity can be challenging in HRQOL research because no 'gold standard' for HRQOL exists. Three main types of validity are content, criterion, and construct validity. *Content validity* is a subjective judgement about whether a measure adequately represents all facets of the concept to be measured [29]. It is often assessed by comparing the instrument's items and domains to what is seen in clinical settings and in the research literature. *Criterion validity* is the extent that a measure corresponds to other observations that accurately measure the phenomenon of interest [31]. For example, one way to test for criterion validity is to assess HRQOL before

and after treatment known to be effective. *Construct validity* suggests that instrument scores (1) relate to other variables in a theoretically expected manner; (2) correlate highly with other measures of the same concept (*convergent validity*); (3) correlate less well with measures of different concepts (*discriminant validity*); or (4) vary among groups known to differ on relevant characteristics [29]. The assessment of construct validity in HRQOL trials frequently involves demonstration that a new measure reflects another that is commonly used and well validated. However, an instrument that correlates too highly with a well-established measure may not contribute new information.

Maunder et al's [28] *ease of use* criteria suggest that instruments should be straightforward, understandable, and fairly simple to fill out. *Responsiveness to change* refers to an instrument's sensitivity to changes in a patient's physical or emotional state. An insufficiently sensitive instrument may require large sample sizes to detect any treatment effects. *Meaningfulness of results* refers to the ability to easily interpret the results of an instrument. For example, response categories that are too broad (good, fair, poor) provide little information, whereas an excessive number of response options may dilute findings. Finally, Maunder et al. [28] recommend instruments that *sample the patient's perspective*, as HRQOL assessed by a health care provider may differ substantially from a patient's assessment.

5. Methods

To review the literature on HRQOL and OSA, we used Ovid MEDLINE (National Library of Medicine, 1966–2000) and performed a systematic search of English-language journals and other electronic databases. We used major MeSH headings and text words 'sleep', 'sleep apnea', 'obstructive sleep apnea', and 'quality of life'. In addition, we evaluated selected references cited in articles for pertinence and applicability, and we scanned recent sleep and otolaryngology journals to avoid omission of applicable articles not yet indexed. Opinion pieces and studies without a HRQOL component were excluded. All articles that appeared to be reviews or original research studies were then reviewed.

6. Measuring HRQOL in patients with obstructive sleep apnea (Tables 2 and 3)

Researchers have used dozens of different instruments to measure HRQOL in patients with OSA. The generic instruments used include, but are not limited to: the Medical Outcome Survey Short Form-36 (SF-36), the Nottingham Health Profile (NHP), the Sickness Impact Profile (SIP), the Functional Limitations Profile (FLP), the EuroQol (EQ-5D), and the Munich Life Quality Dimension List (MLDL). The specific instruments include: the Calgary Sleep Apnea Quality of Life Instrument (SAQLI), The Functional Outcomes of Sleep Questionnaire (FOSQ), the OSA Patient Oriented Severity Index (OSAPOSI), the OSA-18 for pediatric patients, and Cohen's pediatric OSA surgery quality of life questionnaire. Most studies are limited to cross-sectional designs that compare OSA patients to controls or measure HRQOL before and after initiation of CPAP. Despite availability of an array of treatments for OSA, CPAP has received the preponderance of attention in HRQOL studies (Table 3).

7. Generic instruments

7.1. Medical Outcome Study Short Form-36 (SF-36)

One of the most frequently used generic instruments is the Medical Outcome Study's Short Form survey (SF-36, Table 2) [4,7,11,13,15,16,25,32–34]. Ware recommends use of the SF-36 as a 'generic core' of HRQOL assessment to be augmented with specific instruments or specific questions that address the research hypothesis more directly. Researchers can then compare results across studies and measure HRQOL issues specific to the disease or population of interest.

Jenkinson et al. [11] found that the SF-36 showed significant adverse effects of OSA on patients' subjective health assessments and that CPAP treatment produced improvements in SF-36 scores. The effect sizes (differences in scores before and after CPAP divided by the standard deviation at baseline) in the vitality dimension, mental health summary score, and physical health summary score in one study were 0.98, 0.76, and 0.57, respectively: an

Table 2
Instruments used in obstructive sleep apnea HRQOL assessments

Instrument name, Reference	Type of instrument	Domains addressed	Number and type of items	Psychometric data	Settings validated
SF-36 [25,47]	Generic, profile	Physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, mental health	36 items, most scored on a 3–6-point Likert scale	Good internal consistency reliability coefficients (Chronbach's alpha *R*: 0.68–0.93)	Well validated in a variety of research settings and diseases: U.S. normative data derived from 1990 National Survey of Functional Health Status
Nottingham Health Profile (NHP) [35]	Generic, profile	Energy level, pain, emotional reactions, sleep, social isolation, physical abilities	38 items in a yes/no format	Good reliability and validity: moderate correlations with some SF-36 subscales (−0.18 to −0.68) [47]	Well validated in a variety of research settings, including general practice, industry, and several different clinical settings and population groups
Sickness Impact Profile (SIP) [38]	Generic, profile	Physical: ambulation, mobility, body care and movement. Psychosocial: communication, alertness behavior, emotional behavior, social interaction. Independent categories: Sleep and rest, eating, work, home management, recreation and pastimes	136 items in a yes/no format	Chronbach's alphas range from 0.63 (eating) to 0.96 (overall), with most dimensions having an alpha near 0.85; moderate to strong correlations with some SF-36 subscales (−0.42 to −0.78) [47]	Well validated in a variety of research settings, as well as among a variety of patient populations: cancer, head injury, stroke, arthritis, Crohn's disease, insurance enrollees, outpatients, etc.
Functional Limitations Profile (FLP) [48]	Generic, profile	Ambulation, body care and movement, mobility, household management, recreation and pastimes, social interaction, emotion, alertness, sleep and rest, eating, communication, work	136 items in a yes/no format	Physical dimension correlate with expanded disability status scale (EDSS) ($r = 0.77$) and with Illness Severity Score (ISS) ($r = 0.76$). Other subscales correlate with EDSS and ISS (0.59–0.65) [49]	Validated in a variety of settings, including multiple sclerosis patients and disabled outpatients [48,49]
EuroQol EQ-5D [50]	Generic, profile, preference-based	Mobility, self-care, usual activity, pain/discomfort, anxiety/depression	Five items, 3-point Likert response scale	Test–retest reliability = 0.86–0.90 [50]; correlated with Health Assessment Questionnaire (0.46–0.76); ceiling effect found when compared with SF-36 [51]	Validated in a variety of settings, including the general US, UK, and other national populations, patients with arthritis, surgery patients, and outpatients
Munich Life Quality Dimension List (MLDL) [52]	Generic, profile	Physical condition, psyche, social life, everyday life	19 items, Likert scaled	Validated in two separate studies (published in German)	Patients with OSA in Germany

Table 2 (*continued*)

Instrument name, Reference	Type of instrument	Domains addressed	Number and type of items	Psychometric data	Settings validated
Calgary Sleep Apnea Quality of Life Instrument (SAQLI) [43]	Specific	Daily functioning, social interactions, emotional functioning, symptoms, (treatment-related symptoms)	35 questions on a 7-point Likert scale	Validated in two separate studies: overall alpha = 0.92; subscales 0.88–0.92; positively correlated with five domains of SF-36 ($P < 0.05$)	Newly diagnosed OSA patients before and after starting CPAP; snorers referred for polysomnography
Functional Outcomes of Sleep Questionnaire (FOSQ) [44]	Specific	Activity level, vigilance, intimacy and sexual relationships, general productivity, social outcome	30 items with 4–6-point Likert scales	Validated in one study. Global score correlates with overall SIP score, and activity level dimension correlates with PF on SF-36	Patients visiting sleep disorders clinic in academic medical center; patients with documented OSA participating in multi-site research study
OSA Patient Oriented Severity Index (OSAPOSI) [16]	Specific	Sleep, awake, medical, emotional and personal, occupational	32 items on a 5-point Likert scale	Validated in one study: overall alpha = 0.93; correlation with global QOL measure ($P < 0.0001$)	Adults with apnea indices >5 who had not previously undergone uvulopalatoplasty
Franco's Pediatric OSA instrument (OSA-18) [46]	Specific	Sleep disturbance, physical symptoms, emotional distress, daytime functioning, caregiver concerns	18-items rated on a 7-point frequency scale by caregiver	Validated in one study: Good test–retest reliability (0.74–0.93). Correlation with RDI (0.11–0.45), tonsil and adenoid size (0.03–0.45): stronger correlations among least subjective questions	Caregivers of pediatric patients 6 months to 12 years old referred for polysomnography with disrupted sleep and hyperplasia of tonsils and adenoids on physical exam
Cohen's Pediatric OSA Surgery QOL questionnaire [17]	Specific	Health and sleep, medical visits and costs, psychosocial	76 items, most on 5-point Likert scale	Validated in one study: Interrater reliability = 0.86; otherwise minimal validity/reliability information	Caregivers of children (2–7 years old) with airway obstruction who underwent either tracheostomy or other surgery

Table 3
The impact of CPAP on HRQOL

Study authors	Setting/methods	*n*	Instrument used	Changes in HRQOL
Jenkinson et al., 1997 [11]	OSA patients undergoing therapeutic assessment of CPAP at the Oxford Sleep Unit of the U.K. answered three questionnaires before and 5 weeks after therapy	$n = 95$ (SF-36), $n = 98$ (EuroQol, FLP)	SF-36, EuroQol, FLP	CPAP patients returned to QOL levels similar to normal population. Significant improvements (moderate to large effect sizes) in the majority of dimensions on both SF-36 and FLP found post-CPAP. SF-36 Energy/Vitality dimension and FLP rest and sleep dimensions showed the greatest improvements. The EuroQol showed increases in scores, but they were not significant
Jenkinson et al., 1998 [15]	Unselected male patients with OSA referred by clinician for CPAP assessment in the Oxford Sleep Unit of the U.K. were interviewed prior to being placed on CPAP and 3 months after	$n = 89$ for PGI and EuroQol, $n = 86$ for SF-36 (mean age of 49 years)	SF-36, Patient Generated Index (PGI), EuroQol	SF-36 scores were low prior to CPAP, but rose to levels similar to general population at the follow-up. There was very little change in EuroQol scores. The PGI scores indicated substantial improvement after CPAP (very large effect size score of 1.33)
D'Ambrosio et al., 1999 [13]	Polysomnographically documented OSA patients referred to Yale Center for Sleep Disorders, Pulmonary and Critical Care Center for evaluation and CPAP therapy were given SF-36 before and 8 weeks after CPAP	$n = 29$ OSA patients total, 23 males and 6 females	SF-36	All SF-36 dimensions were significantly impaired prior to CPAP, but rose to similar levels of age- and gender-matched population. The diminished QOL scores did not correlate with the severity of OSA. The greatest improvements were in vitality, social functioning, and mental health
Bennett et al., 1999 [34]	OSA patients referred to Oxford Sleep Clinic were given the SF-36 before and 1 month after CPAP	$n = 51$, 46 male and 5 female	SF-36	Compared with the general population, SF-36 subscale scores for role-physical and vitality were abnormal prior to CPAP, but rose to normal levels after CPAP with moderate treatment effect sizes in these dimensions and others related to physical well-being
Piccirillo et al., 1998 [16]	OSA patients from 10 study centers underwent CPAP or surgery and were given the SF-36 and OSAPOSI pre-treatment, at time of treatment, and 4 months post-treatment	$n = 119$ patients, 71 underwent CPAP, and 48 had surgery; 112 were male	SF-36, OSAPOSI	Scores on the role-physical, vitality, and emotional well-being subscales of the SF-36 increased significantly after surgery or CPAP. OSAPOSI scores on the sleep and awake subscales reflect improvements in response to treatment, with the largest change in the total instrument score
Engleman et al., 1999 [33]	New attendees to outpatient sleep clinic in the U.K. with mild sleep apnea/hypopnea syndrome spent 4 weeks on CPAP and 4 weeks on an oral placebo therapy without washout period. The SF-36 and NHP were given before and after the randomized trials to assess changes in HRQOL	$n = 34$ patients, 13 females and 21 males	SF-36, NHP Part 2	Baseline SF-36 scores were impaired on all subscales except general health perceptions. After CPAP treatment, significant improvements were seen in general health, role-physical, bodily pain, social functioning, and vitality. Social functioning and vitality were significantly greater on CPAP than on placebo. In a subanalysis of placebo vs. milder severity patients on CPAP, CPAP patients had significantly higher physical functioning, social functioning, mental health and vitality SF-36 scores than those on placebo. The NHP, however, showed no change after CPAP for health and functional status

Table 3 (*continued*)

Study authors	Setting/methods	*n*	Instrument used	Changes in HRQOL
Jokic et al., 1999 [37]	Patients with positional OSA who were referred to the Sleep Disorders Center in Canada spent 2 weeks in CPAP and 2 weeks in positional treatment. The GHS and NHP were given before and after each treatment limb	$n = 13$ patients, 12 male and 1 female	GHS, NHP	Energy level scores on the NHP were slightly better with CPAP than with positional treatment therapy. There were no differences in GHS scores between the two treatments
Flemons et al., 1998 [43]	Instrument validation study used 113 OSA patients and 50 snorers to generate items for SAQLI. Final group of patients were interviewed before and 4 weeks after CPAP treatment with the SAQLI and SF-36 (for comparison and validity purposes)	$n = 24$ test subjects	SAQLI	SAQLI had a high correlation with SF-36 and showed responsiveness among patients successfully completing CPAP (only 15 of the 24 patients were compliant with the therapy)
Boltischek et al., 1998 [10]	OSA patients that had been treated for at least 3 months with CPAP, patients just diagnosed with OSA, and randomly chosen control (non-OSA) people from the same hospital (the Elizabethinen Hospital in Linz) were given the MLDL questionnaire	$n = 67$ CPAP treatment patients, $n = 16$ OSA diagnosed patients, $n = 187$ control	MLDL	MLDL showed no significant differences between CPAP patients and control group. The OSA diagnosed group showed significantly lower scores than both the control and CPAP group on all domains (physical condition, psyche, social life, and everyday life categories)

effect size over 0.5 is considered moderate; over 0.8 is considered large [11]. In a subsequent study that used the SF-36, the EuroQol, and the Patient Generated Index (PGI), the same authors found that mental and physical health summary scores of OSA patients, in comparison to the general population, were significantly lower at baseline but very similar after 3 months of CPAP therapy [15]. D'Ambrosio et al. [13] also found that all dimensions of HRQOL were significantly impaired in OSA when compared with age- and gender-matched controls, and that CPAP treatment significantly improved vitality, social functioning, and mental health of OSA patients. Engleman et al. [33] found that when compared with placebo, CPAP treatment improved five subscales of the SF-36 ($P \leq 0.03$), including general health, role physical, bodily pain, social functioning, and vitality. Bennett et al. [34] found that compared with general population data, the SF-36 dimensions of vitality and role physical were abnormal before CPAP ($P < 0.05$) and normal with CPAP. Piccirillo et al. [16] showed that treatment with either CPAP or surgery (the authors did not separate patients by treatment modality) improved SF-36 scores significantly in the dimensions of role-physical, vitality, and emotional well-being.

Finn et al. [4] used multiple linear regression to model the relationship between SF-36 scores and the number of apneas and hypopneas per hour of sleep (AHI) during laboratory-based polysomnography. Significant associations were found between AHI and decrements in several SF-36 dimensions — physical functioning ($P = 0.03$), role physical ($P = 0.05$), social functioning ($P < 0.01$), mental health ($P = 0.03$), vitality (energy/fatigue) ($P < 0.01$) and general health ($P < 0.01$) — which suggests that OSA may affect several dimensions of HRQOL.

Gall et al. [7] found that even mild OSA patients scored lower on the social functioning, role physical, role emotional, mental health, and vitality dimensions than non-OSA controls. In contrast, Bes et al. [32] found that the SF-36 did not discriminate between snorers with and without sleep apnea. However, these results could stem from selection bias, as only snorers referred to a sleep laboratory were included. Another possibility is that snorers whose OSA is undiagnosed underestimate the impact on their QOL until a diagnosis is made [32].

7.2. The Nottingham Health Profile (NHP)

The Nottingham Health Profile (NHP) is a generic instrument commonly used to assess the physical, social, and psychological distress associated with medical, social, and emotional problems. The NHP was developed in England and has been tested extensively for reliability and validity (Table 2) [35]. The answers are summarized to produce a maximum score of 100 when all possible problems within the dimension are present and 0 in the absence of any problems. In the same manner, dimensions can be summarized to produce a total quality of life value, in which 100 indicates the worst quality of life and 0 indicates the best [18].

Of the 38 questions on the NHP, fewer than half might be expected to be influenced by sleep apnea [36]. In Sweden, researchers found that total NHP scores among male snorers were significantly worse than among controls ($P < 0.001$); scores in dimensions of emotional reactions ($P = 0.02$) and energy ($P < 0.001$) were particularly depressed. Other dimensions showed differences that were not statistically significant [18]. After 1 month of nostril dilator use, snorers' energy scores and total NHP scores were significantly improved. In a separate study that compared positional treatment to CPAP [37], researchers found that NHP energy level scores were slightly better with CPAP than with positional therapy ($P = 0.04$). Yet Engleman et al. [33] reported that CPAP had no effect on NHP scores among patients with mild sleep apnea.

7.3. The Sickness Impact Profile (SIP)

The Sickness Impact Profile measures health status by the degree of impact that sickness has had on a subject's life [38]. The SIP includes 12 categories and a total of 136 items, each of which has been rated for perceived severity on a 15-point scale by a group of professional and lay judges. The rankings were used to generate weights for each item in each category. These weights reflect the relative impact of specified subjective ill health upon well being. Nine of the 12 categories include items that could be affected by sleep disordered breathing [36].

In one study, researchers found that SIP scores in the areas of alertness, sleep, recreation, and work were

reduced among mild OSA patients in comparison with normal controls [7]. The level of impairment was relatively low, but the sample size was small, with only 20 OSA patients and seven normals.

7.4. The Functional Limitations Profile (FLP)

The Functional Limitations Profile (FLP) is a slightly modified form of the Sickness Impact Profile (SIP) that reflects British rather than American valuations of the impact of certain subjective health states on well being [39]. Patients are asked to affirm items with reference to their perceived health state on the day of completion, and scores then range from 0 (best possible health) to 100 (worst possible health) (Table 2).

Jenkinson et al. [11] found that treating OSA patients with CPAP resulted in significant improvements in nine of the 12 FLP dimensions, even after only 5–7 weeks of treatment. Statistically significant improvements were seen in the dimensions of mobility, alertness bodycare and movement, sleep and rest, recreations and pastimes, social interaction, emotion, ambulation, and work. Not surprisingly, the sleep and rest dimension showed the largest improvement, with an effect size of 0.88. In addition, the overall FLP scores and the physical and psychosocial summary scores showed significant improvements [11].

7.5. The EuroQol EQ-5D

The EQ-5D includes five questions (Table 2), each with three response categories: level 1 = 'no problems', level 2 = 'some problems', and level 3 = 'inability or extreme problems' [40]. The responses combine to give a descriptive health state with five dimensions, such as 1,1,1,1,1 (no problems on any dimension) or 1,2,2,1,1 (some problems with self-care and usual activities, but no problems otherwise). Each of the 243 possible health states can be assigned a utility score using any one of the preference-based assessments (time trade-off, standard gamble, direct assessment), or researchers can use the scores generated from a time-tradeoff study done among 2997 adults in Great Britain [41,42]. In addition, a single overall score can be generated from the EuroQol thermometer, on which respondents mark their overall perceived health from worst to best imaginable health state. This overall score is not a utility score; it is simply a supplemental self-assessment of overall health state [15].

In a group of patients scheduled for treatment with CPAP, Jenkinson et al. [15] found that EQ-5D scores changed little between baseline assessment, follow-up 5–7 weeks later [11], and 3 months on CPAP. The EQ-5D showed that patients with sleep apnea had relatively high scores prior to treatment (indicating good health status), and therefore little change was detected between the survey administrations to untreated and treated subjects. The lack of sensitivity to OSA-related QOL in these settings may have arisen because the EQ-5D is a generic instrument that uses only five questions to cover the major dimensions of HRQOL: no questions specifically address problems such as insomnia, sleepiness, tiredness, and social problems. Lack of change in the EQ-5D with treatment of OSA contrasts with many other data that suggest patients do experience improved HRQOL. The problem may be that single global assessments of QOL are notoriously insensitive to change. People often have difficulty when asked to combine all aspects of their functioning and well-being into a single, global assessment [15].

7.6. The Munich Life Quality Dimension List (MLDL)

The Munich Life Quality Dimension List (MLDL) covers four dimensions (Table 2) within which patients rate, for each item, their degree of satisfaction, importance, desire for change, and belief that changes can be accomplished [10]. In one study using the MLDL, researchers found that the HRQOL of OSA patients treated with CPAP for 3 months or longer was not significantly different from that of people without OSA. Untreated OSA patients showed significantly lower scores than both the treated OSA patients and the healthy controls on all four domains ($P < 0.01$) [10].

8. Specific instruments

8.1. Calgary Sleep Apnea Quality of Life Instrument (SAQLI)

The Calgary Sleep Apnea Quality of Life Instrument (SAQLI) (Table 2) [36,43] is one of the few HRQOL instruments specifically geared toward patients with

OSA. It has shown evidence of good internal consistency, face validity as judged by content experts and patients, and construct validity as shown by its positive correlations with the SF-36 among patients who underwent CPAP. It has also demonstrated responsiveness among patients successfully completing 4-week trials of CPAP [43].

Flemons and Reimer found that all dimensions of the SAQLI were affected by a 4-week trial of CPAP therapy, with the greatest change occurring in the symptom dimension. The least changes were seen in social and emotional functioning. For each of the domains and the total score of the SAQLI rating of change, 33% or more of the patients reported being at least somewhat better. In the symptoms domain, 75% reported being at least somewhat better. The sample size in this validation study was small, however, and replication of the findings in larger studies would be useful: only 24 patients with sleep apnea were studied, 20 underwent the 4-week trial of CPAP, and 15 were compliant in therapy. The authors suggest that the SAQLI is unique among OSA assessment instruments because it includes potential negative consequences of treatment, and therefore may reflect net effects of treatment more realistically [43].

8.2. Functional Outcomes of Sleep Questionnaire (FOSQ)

The Functional Outcomes of Sleep Questionnaire (FOSQ) [44] is a self-report measure that assesses the impact of sleep disorders on activities of daily living (Table 2). Psychometric assessment indicated good reliability and validity, and the FOSQ successfully discriminated between normal subjects and those seeking medical attention for a sleep problem [44]. In addition, the FOSQ global score has been shown to correlate with the SIP overall score, and the activity level dimension correlates with the SF-36 physical functioning subscale. Unlike the SIP and the SF-36, however, the FOSQ includes sleep-specific dimensions likely to be missed by generic instruments, including vigilance (ability to stay awake) and intimacy and sexual relationships.

8.3. OSA Patient Oriented Severity Index (OSAPOSI)

The OSA Patient Oriented Severity Index includes 32 items across five 'problem' subscales (Table 2) [16]. The OSAPOSI asks patients to rate the magnitude of the problem for each item as well as the importance of the problem to the patient. A symptom-impact score is calculated as the product of the magnitude score and the importance score; the higher the score is, the worse the HRQOL [16]. The range of scores on any one item is 0 to 20, and the entire instrument ranges from 0 to 640. Finally, patients are asked to provide a global rating of the overall amount of bother or disturbance they experience as a result of OSA.

Preliminary research indicated that the OSAPOSI is a valid and sensitive patient-based assessment of HRQOL among OSA patients [45]. A subsequent study [16] indicated favorable validity, reliability, and responsiveness to change (correlation between changes in OSAPOSI scores after treatment and patients' overall assessments of their responses, $P < 0.001$). The same study showed that OSA patients' responses to treatment with CPAP or surgery were statistically significant on the sleep and awake subscales, as well as the total instrument score [16]. In this pilot study, the authors did not compare QOL scores among patients who underwent surgery versus CPAP.

8.4. Franco's Pediatric Obstructive Sleep Apnea Questionnaire (OSA-18)

The OSA-18 [46] is a HRQOL assessment for pediatric patients with OSA (Table 2). It is designed for caregivers to complete, and it covers five dimensions of HRQOL: sleep disturbance, physical symptoms, emotional symptoms, daytime functioning, and caregiver concerns. Validated in a study of the caregivers of 61 children referred for polysomnography, the instrument appears to be both reliable and valid among OSA patients between 6 months and 12 years old. Validity was assessed by comparing items on the OSA-18 to objective measures such as the Respiratory Disturbance Index (RDI, or mean number of apneas and hypopneas per hour of sleep) and the size of patients' tonsils and adenoids. Whereas some OSA-18 items — such as frequency of loud snoring, mouth breathing, and breath holding or pauses — did correlate with objective measures, many more subjective questions did not (e.g. caregiver frustration, discipline problems, social problems, and school problems).

This illustrates the challenge of validity assessment in the absence of an overall gold standard; the impact of OSA on HRQOL is likely to be subjective and difficult to capture in single, specific objective measures.

The OSA-18 correlates fairly well with the RDI, and when children are categorized by RDI severity, the relationship still holds [46]. The authors recommend use of the OSA-18 scores as follows: < 60 suggests a small impact, 60–80 suggests a moderate impact, and > 80 suggests a large impact on HRQOL. This classification divided Franco et al.'s sample by severity levels with approximately one-third of subjects in each.

8.5. Cohen's pediatric OSA surgery quality of life questionnaire

Cohen et al. [17] developed a parental questionnaire to assess the HRQOL in pediatric OSA treated with either tracheostomy or sleep apnea surgery (Table 2). They used the instrument in an investigation of physical symptoms, psychosocial functioning, and costs. The survey includes 42 health- and sleep-related questions, four medical visit- and cost-related questions, and 30 psychosocial questions. Participation of both parents in 13 cases allowed evaluation of interrater reliability, which was excellent with a correlation of 0.86. Results from the total of 44 subjects showed that 95% of all questionnaire items were ranked worse for the tracheostomy subjects than for the sleep apnea surgery subjects [17]. These rankings included significant differences in the number of hospital, emergency room, and physician visits, and in time spent on respiratory care ($P < 0.05$). After surgery, children without tracheostomies experienced significant improvement ($P < 0.05$) in all of the symptom variables (e.g. choking, snoring, daytime sleepiness), 75% of the parental care variables, 67% of medical visit items, and 75% of the stress and coping variables. The authors concluded that despite initially higher costs in comparison to tracheostomy, sleep apnea surgery was associated with substantial advantages in HRQOL [17].

9. Discussion

This review illustrates the variety of instruments used to study HRQOL and OSA. The choice of HRQOL instruments should be based on the purpose of the evaluation, the level of assessment to be performed, and instrument attributes and psychometric properties. For clinical purposes, instruments should be used in settings that resemble, as closely as possible, those for which data on validity and reliability have been published. In research, use of at least one OSA-specific instrument and one generic instrument is likely to be advantageous.

Among the generic instruments used to study HRQOL and OSA, the SF-36 has been employed most often. The SF-36 has repeatedly demonstrated that OSA patients have lower quality of life, across several dimensions, than age- and gender-matched controls. In addition, the SF-36 appears to be sensitive to treatment effects, given repeated reports that CPAP therapy for OSA often brings HRQOL scores back in line with population norms. These results suggest that OSA affects many different aspects of a patient's life, including physical, emotional, and social well-being. Yet as a generic measure, the SF-36 does not include questions specific to OSA. The 'vitality' dimension is the closest proxy for sleep-related disturbances. Thus while the SF-36 may successfully discriminate between patients with and without OSA, and while it may be sensitive to treatment-induced changes, it should be accompanied by an OSA-specific instrument if the researcher is interested in more than the eight dimensions and two subscales included in the SF-36.

Some other generic instruments, including the NHP, SIP, FLP, and MLDL, have not been used as extensively in clinical studies of HRQOL in OSA. Preliminary data suggest that these tools may be useful, but more information is needed before definitive conclusions can be drawn. The FLP provides a potential advantage in that it includes sleep and rest dimensions.

The EuroQol (EQ5D) does not appear to be sensitive to the effects of OSA or its treatment. One reason may be the simplicity of the instrument: five global questions may not be enough to discriminate between the presence and absence of untreated OSA.

With regard to specific HRQOL instruments, preliminary evidence suggests that the SAQLI, the FOSQ, and the OSAPOSI are all potentially useful. For children, the OSA-18 and Cohen's pediatric OSA Surgery Questionnaire have demonstrated promising early results. In particular, the OSA-18 may be useful in patient classification according to the amount of

impact OSA has on their lives. Such information may be of clinical use in the selection of pediatric patients who deserve more aggressive therapy.

Overall, although the amount and depth of research on HRQOL in OSA has grown rapidly in recent years, relevant published data remain limited. Many studies cited in this review were cross-sectional and could not assess changes over time. In some studies, small sample sizes produced results that may not apply in other settings. In other studies, short follow-up periods prevented conclusions about long-term impact on HRQOL. No studies used a preference-based HRQOL instrument, necessary for calculation of utility scores and estimation of cost-utility. In addition, the literature is for the most part limited to assessment of CPAP: effects on HRQOL provided by surgical, dental, and behavioral treatments for OSA remain largely unexplored. Without HRQOL assessments of these treatment options, patients and clinicians are left with difficult decisions about treatment options.

The studies of HRQOL improvement with treatment for OSA have rarely addressed compliance. Only one of the studies reviewed above included a definition of patient compliance [43], and few considered whether CPAP was actually used as intended. Lack of adjustment for non-compliance suggests that when used, CPAP may be more beneficial than has been reported.

This review of the published literature suggests that OSA does cause significant impairment in HRQOL, and that treatment with CPAP improves HRQOL. Other treatment modalities may also be effective but require study. Data from preference-based measures will be needed to calculate quality adjusted life years (QALYs) and cost-effectiveness ratios, which are important in the selection of care most likely to be beneficial.

References

[1] Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328(17):1230–1235.

[2] Sher AE. An overview of sleep disordered breathing for the otolaryngologists. Ear Nose Throat J 1999;78(9):694–706.

[3] Flemons WW. Measuring health related quality of life in sleep apnea. Sleep 2000;23(Suppl 4):S109–S114.

[4] Finn L, Young T, Palta M, Evans L, Dempsey J, Fryback D. Association of unrecognized sleep disordered breathing and general health status in the Wisconsin sleep cohort study. Am J Respir Crit Care Med 1996;153:A358.

[5] Chervin RD, Aldrich MS. The Epworth Sleepiness Scale may not reflect objective measures of sleepiness or sleep apnea. Neurology 1999;52:125–131.

[6] Kingshott RN, Vennelle M, Hoy CJ, Engleman HM, Deary IJ, Douglas NJ. Predictors of improvements in daytime function outcomes with CPAP therapy. Am J Resp Crit Care Med 2000;161(3):866–871.

[7] Gall R, Isaac L, Kryger M. Quality of life in mild obstructive sleep apnea. Sleep 1993;16:S59–S61.

[8] Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep 1991;14:540–545.

[9] Sapene M, Nejjari C, Tessier JF, Haran P. Evolution of quality of life and depressive symptomatology of patients with sleep apnea syndrome (SAS) after treatment by continuous positive air pressure (CPAP). Am J Respir Crit Care Med 1996;153:A353.

[10] Bolitschek J, Schmeiser-Rieder A, Schobersberger R, Rosenberger A, Kunze M, Aigner K. Impact of nasal continuous positive airway pressure treatment on quality of life in patients with obstructive sleep apnea. Eur Respir J 1998;11:890–894.

[11] Jenkinson C, Stradling J, Peterson S. Comparison of three measures of quality of life outcome in the evaluation of continuous positive airways pressure therapy for sleep apnoea. Sleep 1997;6:199–204.

[12] Engleman HM, Martin SE, Deary IJ, Douglas NJ. Effect of continuous positive airway pressure treatment on daytime function in sleep apnoea/hypopnoea syndrome. Lancet 1994;343:572–575.

[13] D'Ambrosio C, Bowman T, Mohsenin V. Quality of life in patients with obstructive sleep apnea: effect of nasal continuous positive airway pressure — a prospective study. Chest 1999;115(1):123–129.

[14] Hardinge FM, Pitson DJ, Stradling JR. Use of the Epworth Sleepiness Scale to demonstrate response to treatment with nasal continuous positive airways pressure in patients with obstructive sleep apnoea. Respir Med 1995;89:617–620.

[15] Jenkinson C, Stradling J, Peterson S. How should we evaluate health status? A comparison of three methods in patients presenting with obstructive sleep apnea. Qual Life Res 1998;7:95–100.

[16] Piccirillo JF, Gates GA, White DL, Schectman KB. Obstructive sleep apnea treatment outcomes pilot study. Otolaryngol Head Neck Surg 1998;118:833–844.

[17] Cohen SR, Suzman K, Simms C, Burstein FD, Riski J, Montgomery G. Sleep apnea surgery vs tracheostomy in children: an exploratory study of the comparative effects on quality of life. Plast Reconstr Surg 1998;102:1855–1864.

[18] Löth S, Petruson P, Wirén L, Wilhelmsen L. Better quality of life when nasal breathing of snoring men is improved at night. Arch Otolaryngol Head Neck Surg 1999;125:64–67.

[19] Schipper H, Clinch JJ, Olweny CLM. Quality of life studies: definitions and conceptual issues. In: Spilker B, editor. Quality of life and pharmacoeconomics in clinical trials, 2nd ed. Philadelphia, PA: Lippincott-Raven, 1996. p. 11–23.

[20] Spilker B. Introduction. In: Spilker B, editor. Quality of life

and pharmacoeconomics in clinical trials, 2nd ed. Philadelphia, PA: Lippincott-Raven, 1996. p. 1–10.
[21] Guyatt GH, Jaeschke R, Feeny DH, Patrick DL. Measurement in clinical trials: choosing the right approach. In: Spilker B, editor. Quality of life and pharmacoeconomics in clinical trials, 2nd ed. Philadelphia, PA: Lippincott-Raven, 1996. p. 41–48.
[22] Moyer CA, Fendrick AM. Measuring health-related quality of life in patients with upper gastrointestinal disease. Dig Dis 1998;16:315–324.
[23] Gelfand GAJ, Finley RJ. Quality of life with carcinoma of the esophagus. World J Surg 1994;18:399–405.
[24] De Haan R, Aaronson N, Limburg M, Hewer RL, van Crevel H. Measuring quality of life in stroke. Stroke 1993;24:320–327.
[25] Ware JE. The SF-36 health survey. In: Spilker B, editor. Quality of life and pharmacoeconomic in clinical trials, 2nd ed. Philadelphia, PA: Lippincott-Raven, 1996. p. 337–345.
[26] Feeny DH, Torrance GW, Furlong WJ. Health utilities index. In: Spilker B, editor. Quality of life and pharmacoeconomics in clinical trials, 2nd ed. Philadelphia, PA: Lippincott-Raven, 1996. p. 239–252.
[27] Guyatt GH, Feeny DH, Patrick DL. Measuring health-related quality of life. Ann Intern Med 1993;118:622–629.
[28] Maunder RG, Cohen Z, McLeod RS, Greenberg GR. Effect of intervention in inflammatory bowel disease on health-related quality of life: a critical review. Dis Colon Rectum 1995;38:1147–1161.
[29] Singleton RA, Straits BC, Straits MM. Approaches to social research. 2nd ed. New York: Oxford University Press, 1993.
[30] DeVellis RF. A consumer's guide to finding, evaluating, and reporting on measurement instruments. Arthritis Care Res 1996;9(3):239–245.
[31] Dimenäs E, Glise H, Hallerbäck B, Hernqvist H, Svedlund J, Wiklund I. Quality of Life in patients with upper gastrointestinal symptoms. Scand J Gastroenterol 1993;28:681–687.
[32] Bes A, Aran X, Gea J, Orozco-Levi M, Felez MA, Broquetas JM. Somnolence. Quality of life and quality of sleep in snorers, with and without sleep apnea syndrome. Am J Respir Crit Care Med 1996;153:A353.
[33] Engleman HM, Kingshott RN, Wraith PK, Mackay TW, Deary IJ, Douglas NJ. Randomized placebo-controlled crossover trial of continuous positive airway pressure for mild sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med 1999;159(2):461–467.
[34] Bennett LS, Barbour C, Langford B, Stradling JR, Davies RJ. Health status in obstructive sleep apnea: relationship with sleep fragmentation and daytime sleepiness, and effects of continuous positive airway pressure treatment. Am J Respir Crit Care Med 1999;159(6):1884–1890.
[35] Hunt SM, McKenna SP, McEwen J, Williams J, Papp E. The Nottingham Health Profile: subjective health status and medical consultations. Soc Sci Med A 1981;15(3 part 1):221–229.
[36] Flemons WW, Tsai W. Quality of life consequences of sleep disordered breathing. Allergy Clin Immunol 1997;99(2):S750–S756.
[37] Jokic R, Klimaszewski A, Crossley M, Sridhar G, Fitzpatrick MF. Positional treatment vs continuous positive airway pressure in patients with positional obstructive sleep apnea syndrome. Chest 1999;115(3):771–781.
[38] Bergner M, Bobbitt RA, Carter WB, Gilson BS. The Sickness Impact Profile: development and final revision of a health status measure. Med Care 1981;19:787–805.
[39] Patrick D. Standardization of comparative health status measures: using scales developed in America in an English speaking country. Hyattsville, MD: Department of Health and Human Services, 1981.
[40] EuroQol Group. EuroQol — A new facility for measurement of health-related quality of life. Health Pol 1990;16:199–208.
[41] Dolan P, Gudex C, Kind P, Williams A. A social tariff for EuroQol: results from a UK general population survey. York, UK: University of York, Centre for Health Economics, 1995.
[42] Dolan P, Gudex C, Kind P, Williams A. The time trade-off method: results from a general population study. Health Econ 1996;5:141–154.
[43] Flemons WW, Reimer MA. Development of a disease-specific health-related quality of life questionnaire for sleep apnea. Am J Respir Crit Care Med 1998;158:494–503.
[44] Weaver TW, Laizner AM, Evans LK, Maislin G, Chugh DK, Lyon K, Smith PL, Schwartz AR, Redline S, Pack AI, Dinges DF. An instrument to measure functional status outcomes for disorders of excessive sleepiness. Sleep 1997;20(10):835–843.
[45] Piccirillo JF, Schechtman KB, Edwards D, Sher AE, White DL. Development of the obstructive sleep apnea quality of life measure (abstract). Sleep 1994:A443.
[46] Franco Jr RA, Rosenfeld RM, Rao M. Quality of life for children with obstructive sleep apnea. Otolaryngol Head Neck Surg 2000;123:9–16.
[47] Ware JE, Snow KK, Kosinski M, Gandek B. SF-36 Health Survey, manual and interpretation guide. Boston, MA: The Health Institute, New England Medical Center, 1993.
[48] Patrick DL, Peach H. Disablement in the community. Oxford, UK: Oxford University Press, 1989.
[49] Hutchinson J, Hutchinson M. The Functional Limitations Profile may be a valid, reliable, and sensitive measure of disability in multiple sclerosis. J Neurol 1995;242:650–657.
[50] EuroQol Group. The EuroQol quality of life scale. Revised 1993. In: McDowell I, Newell C, editors. Measuring health: a guide to rating scales and questionnaires, 2nd ed. Oxford, UK: Oxford University Press, 1996.
[51] Hurst NP, Jobanputra P, Hunter M, Lambert M, Lochhead A, Brown H. Validity of EuroQol — a generic health status instrument — in patients with rheumatoid arthritis. Br J Rheum 1994;33:655–662.
[52] Heinisch M, Ludwig M, Bullinger M. Psychometrische testung der munchner lebensqualitatsfragenbogen. In: Bullinger M, Ludwig M, von Steinbuchel N, editors. Lebensqualitat bei cardiovaskularen erkrankungen, grundlagen, messverfahren, ergebnisse, dimensionen liste (MLDL), 1991. pp. 73–90.