

Impairment of Quality of Life and Daytime Performance in Mild Form of Sleep Related Breathing Disorder

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Sleep related breathing disorders (SRBD) refer to various types of clinical entities, from severe obstructive sleep apnea syndrome (OSAS) to partial upper airway obstruction. It is known that OSAS has a clear effect on the quality of life (QOL) and cognitive performance. Usually attention is paid to clear-cut OSAS with notable hypoxia. A large variety of other respiratory events, characterised by partial upper airway obstruction, causing sleep fragmentation are thus ignored. The purpose of the present work was to see, whether milder SRBD with repetitive nocturnal respiratory events and transient arousals, but without marked hypoxia would have a corresponding impact on the QOL and daytime performance as has been reported for OSAS. The QOL and cognitive functions of 15 mild SRBD patients were compared to those of healthy control subjects. The QOL was studied by a questionnaire, and cognitive functions were measured by standardised internationally utilised tests. Six out of 11 QOL items were significantly ($p < 0.05$) lower in the SRBD group. For instance, sense of well being, social satisfaction, and mood were notably reduced. Patients showed also signs of various physical symptoms, such as feeling dizzy or sick. Statistically significant results were found in two out of 22 cognitive tests: visual memory, concentration and auditory reaction time. Although mild SRBD patients seemed to do worse subjectively than objectively, as measured by standardised neuropsychological tests, sleep fragmentation caused by repetitive respiratory disturbances seems to have an impact on daytime performance and well being. SRBD should not be ignored even if the respiratory events do not fulfil the formal criteria usually applied for the recognition of the apneic events. (Sleep and Hypnosis 1999;1:163-172)

Key words: sleep related breathing disorder (SRBD), quality of life (QOL), neuropsychological testing.

INTRODUCTION

There is a growing recognition of sleep disorders with excessive daytime sleepiness (EDS) in patient groups and in the general population (1). Sleep disorders with EDS

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are found in all age groups. They are especially common among middle-aged people (2) causing decreased working ability and exposing subjects to industrial and driving accidents (3-6). Sleep disorders account for a great deal of both social and economical burden for the society.

EDS and reduced daytime efficiency are most likely caused by impaired and fragmented night sleep. One of the most common disorders causing sleep fragmentation and EDS is the obstructive sleep apnea syndrome (OSAS). The prevalence of OSAS in the adult population has generally been estimated to lie between 2 and 4 percent (2), but percentages as high as 10% have been described (7-9). In recent years, increasing attention has been paid to patients with a medical history suggesting OSAS, but without sufficient findings in the whole-night polysomnography in order to fulfil its diagnostic criteria (10). By definition a

total airflow cessation of at least 10 s or at least 50% reduction in measured airflow amplitude for over 10 s is required for the recognition of an apnea or hypopnea, respectively. An additional requirement is often that the event is associated with an at least 4% reduction of blood oxygen saturation (SaO₂) measured by oximetry. There is, however, some evidence that also respiratory events, not fulfilling these criteria, can cause marked daytime symptoms. Some of the respiratory patterns were first described by Alihanka et al. (11) and later by Polo (12) as partial obstruction or increased respiratory resistance (IRR). The patients evidently correspond to those suffering from heavy snorers disease at its early stage described by Lugaresi et al. (13). Later Guilleminault and his co-workers described the upper airway resistance syndrome, which is characterised by repetitive transient arousals from sleep with increases of respiratory effort and intrathoracic negative pressure, but without notable hypoxic events (14-16). Altogether these entities can be called sleep related breathing disorder (SRBD). SRBD would consequently include all sleep related respiratory disturbances caused by total or partial occlusion of the upper airways causing arousals and sleep fragmentation. Snoring would be included only if it is clearly associated with arousals.

Decreased QOL (17), impaired social functioning, limited function due to physical and emotional reasons as well as decreased sense of well-being have been reported (18) in patients with EDS. The neuropsychological deficits in the area of memory, attention, and executive functions associated with OSAS have been notably described (19-23).

So far sufficient data about similar findings in SRBD patients without notable hypoxia, but for whom all apneic events would have been taken into account is not available. Although the patients often have severe sleep fragmentation we decided to call the disease entity mild SRBD because of their relatively high oxygen saturation. If mild SRBD has a major impact on QOL and daytime functional efficiency, that would in turn have a considerable effect on the number and type of patients requiring diagnosis and treatment for upper airway obstructive disease.

The aim of the present work was to study whether the QOL and cognitive performance of the patients with mild SRBD is impaired as compared to those of healthy controls. The study was divided into two parts: subjective evaluation of the QOL through the use of a questionnaire, and administration of neuropsychological tests.

METHODS

Study Population

Fifteen male patients, aged 24 to 60 years (Table 1), had all been referred to the Sleep Disorders Unit at Tampere University Hospital due to EDS and heavy nocturnal

snoring. All subjects participated in the study voluntarily. They did not receive any material benefit for their participation. Only men were selected for this research because they constituted the majority of the patient population.

Selection Criteria

The patients were diagnosed as having mild SRBD according to their results in nocturnal polysomnography (see Table 2 below). The apnea index (no. of apneas per hour) had to be lower than 5 and the minimum SaO₂ level higher than 90%. The arousal index (no. of arousals per hour of sleep) had to exceed 10. The majority of the arousals had to be clearly associated to signs of upper airway obstruction (see below). Patients with other significant medical disorders, medication that could adversely affect their cognitive functioning, known or suspected alcohol abuse, and a reported history of learning disability or head trauma were excluded.

Control Group

The control group consisted of 15 healthy males, mainly technical employees of the hospital. Their age range was from 27 to 58 years. They had daytime work, and reported neither somnolence during the day nor sleep disturbances. Thus, since there was no clinical evidence of any kind of sleep disorder, polysomnographic recordings were not administered. The controls performed the same psychological tests at the same time of day as the patients.

The subjects in the control group matched the patients closely in terms of age, sex, and body mass index (BMI). The control group had 1.5 more years of education than the SRBD group (Table 1). The subjects' general level of daytime sleepiness was measured by the Epworth Sleepiness Scale, a short and simple self-administered questionnaire (24). Its scores differed statistically significantly between the two groups indicating that the

Table 1. Descriptive characteristics of the SRBD and control groups

Variable	SRBD Group		Control Group	
	Mean	SD	Mean	SD
n	15		15	
Sex	M		M	
Age (years)	43.3	10.8	41.1	11.1
Body mass index ^a	27.5	4.3	27.4	4.1
Education (years)	10.3	2.3	11.9	3.3
ESS 21, ^b	8.80	4.3	3.7	1.5

^a weight (kg)/ height x height (m)

^bEpworth Sleepiness Scale, statistically significant difference between the groups (p<0,001).

patients with mild SRBD were substantially sleepier than the controls. All control subjects were volunteers. They did not receive any benefits for their participation either. Permission was granted by the hospital management for their participation to take place during the regular working hours.

Polysomnographic Recordings

All-night polygraphic recordings were performed using a digital polysomnograph (Healthdyne Alice III, program version 1.16). EEG was recorded through four channels (C3, C4, O1 and O2 referred to the contralateral mastoid) by using silver-silver chloride electrodes. Eye movements were recorded by two channels with EOG electrodes placed above the right and below the left eye (25) both referred to the mastoid. Submental muscle tonus (EMG) was measured on one channel by two chin EMG electrodes. Respiratory variables were measured by transducers especially designed for the Healthdyne polysomnograph. Airflow was recorded by three naso-oral thermistors. Respiratory movements were measured by thoracic and abdominal belts with piezo transducers. SaO₂ was recorded by a finger-pulse oximeter (Biox III, Ohmeda). Snoring was recorded by a microphone attached to the anterior neck above the trachea. Body movements, respiratory movements and the ballistocardiogram (BCG) were recorded by using a special whole-body transducer placed under a foam plastic mattress called the static charge sensitive bed, SCSB (11,12,26) In addition, the ECG and anterior tibialis muscle activity were measured.

All recordings were classified into sleep stages according to standard criteria (27) by experienced technicians. An epoch length of 30 s was used. A 21-inch monitor (Nokia Multigraph 445X) with a screen resolution of 1280 by 1024 pixels was used. The arousals were manually scored according to the criteria of the American Sleep Disorders Association (28). The patients were considered to suffer from SRBD if sleep was fragmented as judged by the hypnogram, if the arousal index was clearly above 10 per hour for the whole-night sleep and if the arousals were evidently respiratory related. Besides apneas and hypopneas longer than 10 s and more than 50% diminution of the respiratory signal, also shorter events and those with a lesser diminution of the airflow were included. So-called crescendo snoring where the snoring sound is gradually increasing from breath to breath until an arousal takes place (29) were taken into account as well. In addition, signs of increased respiratory resistance were judged from the signal recorded by SCSB transducer (12, see above). Increased respiratory resistance can be observed as so-called spiking on the high-frequency channel after high-pass filtering with a cut-off point of 10 Hz. The respiratory signal, which is visualized after low-pass

filtering, also changes its form, often showing a diminution with a curved shape and followed by an arousal. A high

Table 2. Polysomnographic Characteristics of the SRBD Group

	Mean	SD
Sleep latency (min)	27.4	30.3
TST; total sleep time (min)	473.6	60.0
Sleep efficiency	84.9	11.0
Wake	9.9	9.0
REM	17.7	5.9
S1 %	15.7	10.3
S2 %	44.5	15.7
S3 %	7.5	4.6
S4%	1.5	2.6
SWS%	9.0	5.6
MVT	3.3	1.2
Apnea index	3.2	5.9
Arousal index	21.5	12.8
Lowest SaO ₂ %	90.8	2.6

Note: Sleep efficiency= TST x 100/ time in bed, Wake= percentage of time awake in bed, REM= percentage of REM sleep, SWS%= percentage of slow wave sleep (S3%+S4%), MVT= percentage of movement time during sleep period time, Apnea index= no. of apneas per hour. Arousal index= no. of EEG alpha arousals per hour of sleep.

increase in resistance with paradoxical breathing is seen by the increase of the second component of respiratory curve and, if long lasting, a gradual increase of the whole signal until an arousal takes place. The sleep data are shown in Table 2.

Measurement of Quality of Life

A nationally used self-assessment questionnaire was utilised to evaluate the subjects QOL. It was based on subjective experiences and symptoms and had previously been validated for similar studies (30). The questionnaire was also practical and easy to fill-in. It was completed by the patients in the evening after arriving at our Sleep Unit for the polysomnography. The control group also filled in the questionnaire in the evening in order to match the timing of the patients.

The questionnaire included two types of questions: visual analogue scales (see appendix) which varied from 0 (minimum) to 100 (maximum) for each variable (see Table 3), and summated ratings also widely known as the Likert scale (30-32).

The Likert scales were rated from one to five or one to ten, one being the minimum and five (ten) the maximum value of the matter in question. The results were analysed by factor analysis and t-tests using the Statistical Package for Social Sciences (SPSS), version 6.0 for Windows. Factor analysis was run with 73 subjects in order to clarify the structure of the variables. This group included e.g. patients with apnea, with other medical disorders and voluntary controls.

Table 3. Description of the Visual Analogue Scales of the quality of life variables

Variable	Minimum Scale Value (0)	Maximum Scale Value (100)
Control of life	I have no influence on my life.	I strongly believe, that I can influence everything that happens to me.
Self-confidence	I fail in everything I do.	I don't doubt my chances. Even if I sometimes fail, it doesn't influence my self-confidence.
Well-being	My condition is so poor that I do not know how I manage.	At this moment I have no symptoms or troubles.
Mood	My mood is very desperate and I can't work or attend to my own affairs.	I'm almost always in a good mood.
Physical competence	I get very easily out of breath, my exercise is limited to short walks.	I am in excellent shape.
Satisfaction with life	I'm very dissatisfied with my in general life. Things couldn't be worse.	I'm very satisfied with my life. Things just couldn't be better.
Anxiety ^a	I only know the word, I am not anxious at all.	I'm continuously strained and in a state of high tension.

^ascale reversed

Satisfaction with Life

This variable was measured by 12 items that described various areas of life e.g. social relationships, career, and economical situation. The patient was asked how satisfied he was with a specific item rated on a 10-point scale (very dissatisfied-very satisfied). After factor analysis (n=73), nine of the 12 items were combined to form the variable Satisfaction with life. The items Social relationships and Satisfaction with life in general had the highest loadings on this factor.

Experienced Difficulties and Problems

This broad field was measured by 17 items. The patient was asked to evaluate on a 5-point scale how often in the past six months he had had specific symptoms, troubles or difficulties (not at all - daily). After factor analysis (n=73), 9 items out of the 17 were combined to constitute the variable Submissiveness. Submission to somebody's will and Feeling of inferiority reached the highest loadings on this variable. Eight items out of 17 were also summed up to form a variable which was named Self-centeredness. Aim to subordinate other people and Jealousy scored the highest loadings on this variable.

Symptoms, Troubles, and Problems

These negatively oriented matters were measured by 24 items rated on a 5-point scale. The patient was asked to evaluate how often in the past 30 days he had had specific problems. After a factor analysis, 15 items out of the 24 were constituted into one variable: Psychosomatic symptoms, Feeling dizzy or feeling sick, and Problems with the heart had the highest loadings on this variable.

In order to make these summated variables easier to comprehend, they were normalised to vary from 0 (for minimum condition of the matter) to 100 (for maximum condition).

Neuropsychological Testing

In a milder form of SRBD in which there is no hypoxia, such cognitive functions as attention, concentration and memory are expected to be impaired due to sleep fragmentation (20). The test battery was composed accordingly.

In the morning after the polysomnography, the neuropsychological test battery was administered to the patients. It consisted of standardised, internationally widely used tests (see Table 4 below). In addition to manually

Table 4. Description of neuropsychological tests

Test	Task measures	Type of score
Benton Visual Retention Test, modified version ^a , (34,35) form C, adm. A	Visual memory, concentration visuospatial perception	Age-corrected scaled score, no. of correct designs and no. of errors
Rey-Osterreiths Complex Figure drawing (34) immediate and 1-hour recall	Visual memory, perceptual organisation	Age-corrected score
Wechsler Memory Scale (WMS) (36,37) logical stories, imm. and 1-hr recall	Verbal memory	Age-corrected score
Wechsler Adult Intelligence Scale Revised (WAIS-R) (34,38)		Age-corrected scaled score in each subtest
Digit Symbol	Psychomotor performance	
Object Assembly	Visual organisation	
Picture Arrangement	Sequential thinking, social response, relationships between events	
Block Design	Visuospatial organisation	
Digit Span: Digits Forward, Digits Backward	Auditory attention and working memory	
Corsi Block Test ^b , (34) Blocks forward and backward	Visual attention, recall of sequences	Comparison to control group
Trail Making Test, Part B (34)	Visuomotoric speed, attention	Age-corrected score
Wisconsin Card Sorting Test (33)	Conceptual flexibility, task shifting aspect	Comparison to control group
Auditory reaction time (33)	Reaction time to sound	Comparison to control group
Visual reaction time (33) group	Reaction time to a square flashing on the PC screen	Comparison to control

^aEach design was reproduced twice (r I, r II). After the immediate reproducing of two consecutive designs (1st and 2nd, 3rd and 4th, etc.) the patient was requested to re-draw from memory the figure(s) of the next to last card followed by the last card.

^bThe numbers of the Digit Span and the setting of the Corsi Block test³³ were used.

administered tasks, the patients auditory and visual reaction times and flexibility of thinking were measured by separate computer-assisted tasks (33). The subjects of the control group were administered the same battery of tests at the same time of the day. The duration of the test battery was 3-3.5 hours. Descriptions of the neuropsychological

tests are given in Table 4.

Statistical Analysis

The results are expressed as means – SD. The comparison of the differences between the groups was

Table 5. Descriptive features of the SRBD and control groups Quality of life^a

Variable	SRBD		CONTROL		t-score	p-value
	Mean	SD	Mean	SD		
Control of life	69.0	17.3	76.7	19.5	-1.14	0.265
Self-confidence	68.0	17.7	79.3	11.0	-2.11	0.044
Well-being ^b	68.3	16.0	86.3	11.7	-3.52	0.002
Mood	67.7	15.9	79.0	11.4	-2.24	0.033
Anxiety	30.0	11.3	27.0	12.2	0.70	0.492
Physical competence	63.0	17.9	68.3	18.0	-0.81	0.423
Satisfaction with life in general (visual analogue scale)	64.0	18.3	77.7	9.2	-2.58	0.016
Satisfaction with life ^b (Likert scale)	69.6	11.0	80.5	8.0	-3.1	0.004
Submissiveness	44.4	11.8	37.6	10.7	1.72	0.112
Self-centeredness	37.7	8.7	32.7	9.1	1.54	0.135
Psychosomatic symptoms	37.0	13.1	28.4	7.1	-2.24	0.033

^aAll the scales varied from 0 to 100. The maximum is described in the variable title.

^bStatistically significant results using Bonferroni correction (p<0.005)

analysed with the independent samples t-test, (SPSS for Windows 6.0), Bonferroni correction and/or T-scores (30).

Somewhat surprisingly, the level of anxiety did not differ significantly between the two groups.

Table 6. Cognitive differences between the SRBD-patients and the control group^a

	SRBD		Control		t-score	p-value
	Mean	SD	Mean	SD		
Benton (r l) corrects	7.40	0.91	8.27	0.96	-2.54	0.017 ^b
Aud. reaction time	294.80	67.42	249.33	50.47	2.09	0.046 ^b

^a Total of 22 neuropsychological tests were performed as described in Table 4 and in methods.

^b No statistically significant differences were found using Bonferroni correction (p<0.002)

The validity of the visual analogue scale items (QOL) were analysed by correlation analysis (data not shown).

RESULTS

Quality of Life Performance

The normalised parameters describing the QOL of the SRBD patients compared to the controls are shown in Table 5. Six out of 11 parameters showed statistical differences (p<0.05). These results describing the SRBD group logically reflected a person who does not sleep well; the feeling of well-being was remarkably reduced due to daytime sleepiness. Similarly, the patients self-confidence was affected by fatigue, i.e. their initiative was reduced. Their social life was also suffering, and their mood and life satisfaction were reduced. In other words, the bases of a persons functioning capacity were seriously hampered.

Neuropsychological Test Performance

The independent samples t-test (SPSS for Windows 6.0) was used to test the differences from the neuropsychological point of view between the SRBD group and the controls.

Statistically significant differences (p<0.05) were found in the modified version of Bentons Visual Retention Test (1st reproduction, no. of correct designs) and in auditory reaction time with the dominant hand.

T-score Profile

Figure 1 shows a T-score profile of the results of the administered test battery of the two groups. The T-scores (31) are modifications based on the z-values of the variables

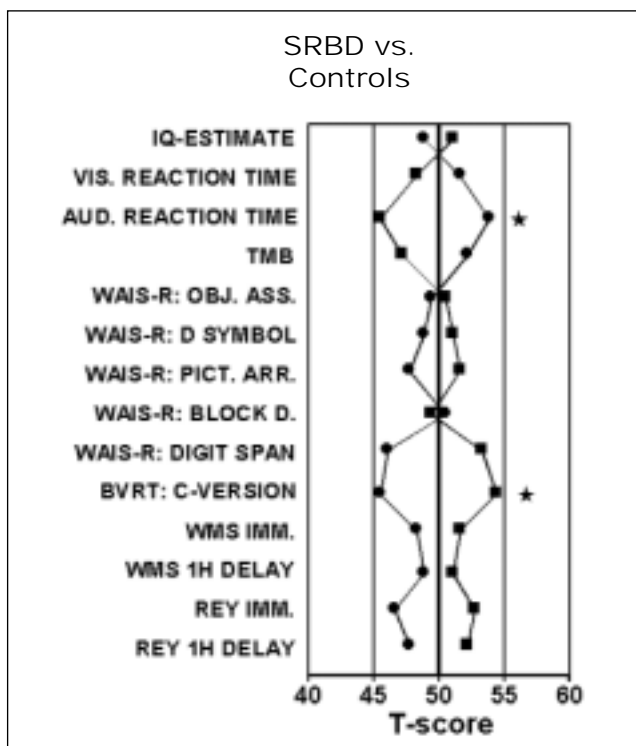


Figure 1. T-score Profile of Neuropsychological Tests. The results of various tests with different scores were converted into T-scores (mean =50, SD=10) in order to make the test results comparable with each other as described in the text.

- SRBD, N=15
- Controls, N=15
- ★ $p < 0.05$

(mean=50, SD=10). This modification was made in order to make the test results commensurable with each other and in that way more readable. The higher the T-score, the better the condition in the specific ability. The results of the Trail B-test and reaction time tests, which measured the time spent with the task, were reversed, that is a higher T-score means a faster performance. The differences between the groups, although not statistically significant, can be seen in almost every variable (see Figure 1).

DISCUSSION

Our study concentrated on the role of cognitive functions and QOL in the patients with mild sleep disorders. In the earlier studies done with apneic and narcoleptic patients it has been found that daytime sleepiness may reflect a persons life in many ways. Marital, social, and vocational problems may arise and exhibit a negative socio-economic impact (18,39-43). According to our results the same applies also to SRBD patients even if polygraphic results do not fulfil the criteria required for the diagnosis of OSAS. The onset of exhaustion, reduced sense of well-being and the signs of depression were observed in patients but not in healthy controls. The SRBD patients QOL was significantly lower as compared to the controls.

The representation of the small control group can be questioned. However, in two large Finnish studies by Ojanen (multi-branch company workers and police school

applicants) the means and standard deviations of the variables of the visual analogue scales were quite similar to those of the present control group.

It can also be argued that the comparison between the patient material and healthy controls is unspecific. However, since the mild SRBD patients were healthy with the exception of the sleep disorder, the only obvious reason for their symptoms and findings is the respiratory problem during sleep.

We used mostly visual analogue scales (see appendix) in measuring the QOL. It is fast and easy for the patient to fill-in and thus serves as a practical screening method. It is especially useful for the evaluation of comprehensive entities, such as satisfaction with life. The very same variable was also measured with a Likert scale. The correlation between the methods in measuring satisfaction with life was 0.81 which is remarkably high and speaks for the validity of the visual analogue scale.

Deficits in measures of attention, memory, motor efficiency, executive tasks, verbal fluency and perceptual-organisational skills (20-22) have been found in the more severe forms of SRBD. The duration of the illness may also be an important factor influencing neuropsychological status (19) suggesting that the disorder is progressive.

If untreated, the disease may finally result in unrecoverable impairments in cognitive functions and consequently lowered intelligence. In the severe forms of SRBD at least part of the symptoms are caused by numerous nocturnal hypoxic events. Due the absence of significant hypoxia in mild SRBD, it seems that the main factor causing the patients cognitive deficits in this study is sleep fragmentation. It brings about deficits especially in attention, concentration and memory functions (5).

According to the results of the neuropsychological tests used, although differences could be seen in almost every variable in favour to the control group, only two statistically significant ($p < 0.05$) differences out of 22 tests were found between the two groups: visual memory and concentration, and auditory reaction time. These differences may be due to chance because of the small size of the groups. Nevertheless, the impairments found in the two tests might reflect a risk factor in tasks where constant alertness and reactivity are required, for example, in traffic and in process control. However, taking into consideration the results obtained by the QOL questionnaire, it seems that the mild SRBD patients do worse subjectively than objectively.

Nasal continuous positive airway pressure (nCPAP) has proved to be an effective treatment especially in the more severe forms of SRBD (44-46). Cognitive functions improve quite rapidly along with the QOL (45). Good results have also been obtained by surgical treatment (47-48). In our unit also mild SRBD patients have been treated by nCPAP with moderate success. Systematic studies are needed in order to evaluate the value of treatment of mild SRBD even when these events are not associated with hypoxia.

CONCLUSION

One major finding in this study was that patients with mild SRBD, which has earlier been considered to be a rather subtle sleeping disorder, have evident impairments in cognitive functions and QOL as compared to healthy controls. The impact of mild SRBD should be foreseen in time. The beginning of treatment also in mild cases without hypoxia could prevent potential accidents in traffic and industry, and improve the working ability and QOL of the patients. This speaks for an active approach towards the early treatment of mild SRBD. Since SRBD is a common finding, systematic and preferably randomised studies with follow-up are required to confirm the justification of treatment in large patient groups.

APPENDIX

WELL-BEING

How is your health today? Estimate your current state of health with the help of using the line below. Draw a line across the vertical line at the point which best indicates your situation at this moment. You can choose any point on the line, even between the descriptions. If, for example, your condition is somewhere between good and quite good" but closer to "good", draw the line closer to "good".

EXTREMELY GOOD 100

At this moment I don't have any symptoms or complaints. I feel very healthy.

VERY GOOD 90

The symptoms and complaints I have are so minor that they're not worth mentioning. I am very well at the moment.

GOOD 80

I have a few mild symptoms or complaints, but they don't noticeably disturb my life.

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QUITE GOOD 70

Although my health is more good than bad, I have some symptoms or complaints which disturb my life to some extent.

RATHER GOOD 60

I have irritating complaints or symptoms which disturb my life and cause difficulties. If I have to choose between "good" and "bad", I would nevertheless say slightly good.

MODERATE 50

I have difficulty stating that my health is either good or bad. The phrases "in between" or a little of both seem most suitable.

RATHER POOR 40

My estimation of my health tends toward "bad" because the symptoms and complaints I have are bad enough that they disturb my every day life.

POOR 30

My health is quite bad. I have quite a lot of symptoms and complaints and they are troublesome.

BAD 20

My health is bad at the moment. I have symptoms and complaints which noticeably disturb my life.

VERY BAD 10

The symptoms and complaints I have are so irritating and difficult that I just manage to cope with them one day at a time.

EXTREMELY BAD 0

My condition is so bad at the moment that I don't know how to cope with it.

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