CONNECARE

WP4 – SELF-MANAGEMENT AND MONITORING

D4.5: QoL Assessment System

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Responsible Author	Carme Zambrana	**Email**	carme.zambrana@eurecat.org
Partner	EURECAT	**Phone**	+34 932 381 400

Abstract	This deliverable presents the research (that has been) performed by EURECAT, in collaboration with ASSUTA and UMCG, to study a solution for automatically assessing quality of life. In this study, quality of life was considered as the patient's overall status (through the EQ-5D-5L questionnaire), her/his perceived level of anxiety/depressions (through the HADS questionnaires), together with the data about sleep from a commercial wristband.

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Executive Summary

This deliverable is related to the task T4.5 “Quality of life assessment system. The task started in the 2nd period of the project (M18) and its main goal was to assess the association of patients’ quality-of-life and their quality of sleep.

It is worth noting that this task started just after the very first release of the overall system and, thus, before the implementation studies. Thus, due to the lack of data from the CONNECARE patients, we decided to use historical data from a healthy volunteer wearing a Fitbit wristband (i.e., the same of the CONNECARE patients). In that direction, EURECAT perform a first experiment (Sleep Quality experiment) to investigated how to assess the sleeping quality by detecting the nights with an abnormal sleeping activity. Subsequently, a second experiment (Workload Assessment experiment) was performed. It was aimed at assessing the quality of life as a continuous variable modelled as the workload due to the historical nature of the volunteer’s data and not having data from quality of life questionnaires. Moreover, in this experiment, we merged the data regarding the sleeping activity together with those related to the performed physical activity (i.e., number of steps and heart rate).

Once the data coming from the pilot studies became available, two new experiments were performed using the patients’ data. In the line of assessing the quality of life as a continuous variable, we performed a third experiment (Quality of Life Assessment as a continuous variable experiment) aimed at applying the models studied in the second experiment to the patient’s data. Encouraged by the reviewers during the 2nd review project meeting in January 2019, we performed a fourth experiment (Quality of Life Assessment focussing on Anxiety and Depression) experiment) devoted to analyse the correlation between the Anxiety and Depression and the sleeping activity, rather than trying to assess the overall quality of life.

This document builds upon the following deliverables, which are encouraged to be read:

Number	Title	Description
D4.4	Assistive Monitoring Tools	This deliverable summarizes the work done regarding the assistive monitoring tools. In particular, due to the requirements from the project during its very beginning, Eurecat took the decision to use a data simulator instead of the sensor-based system decided at the beginning. This deliverable presents a proof of concept related to the fusion of domotic and environmental data with those from the SMS (in particular, the wristband).
D4.6	Recommender System for Self-Management	This deliverable has the twofold goal of (i) reporting on the activities carried out to develop the Recommender System for Self-management, and (ii) describing the resulting software artefact. Accordingly, we first motivate and give context to the work done. Subsequently, we summarise the requirement collection phase and describe the software architecture. Technical details on the implementation are then provided as well as the

		evaluation of the tool. The document end with a look forward to future iterative improvement steps and main conclusions.

1. The Idea

The World Health Organisation (WHO) defines Quality of Life (QoL) as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment[1].

Although methods for measuring QoL have been defined, generally they are based on self-reporting instruments (e.g., WHOQOL-100, EQ-5D). This type of instruments suffers from response shift bias, which refers to the potential of the subject's views changing over the course of a study, thereby adding another factor of change on the end results [1]. In conclusion, self-reported instruments are not suitable for continuous monitoring QoL.

In CONNECARE, the idea is to create a system capable of inferring the overall QoL of the monitored patient. The main goal is to study the behaviour of the patient in terms of performed daily-life and/or fitness activities, both indoors and outdoors, to assess QoL items and sleeping quality. The output of the system will assess the patients' QoL using as input the data coming from the monitoring wristband together with answered questionnaires.

The system output can be used to inform the professionals in charge about any potential change in the QoL of their patients (i.e., worsening or improving). Moreover, recommendations/nudges can be sent to the patient based on the system output to motivate/empower her/him.

[1] https://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/

2. Methodology

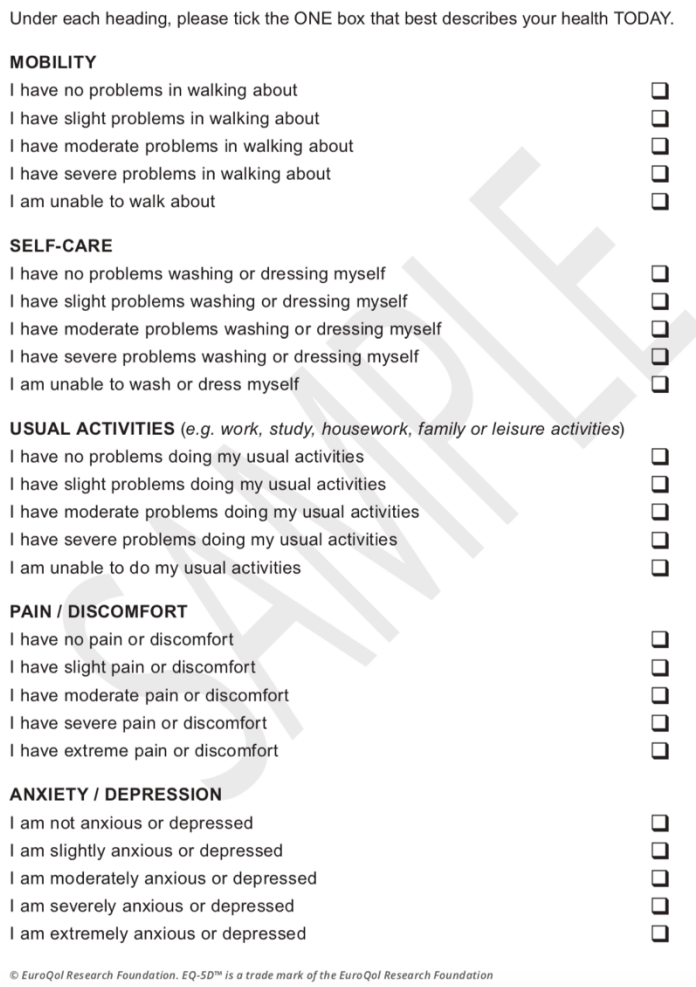
2.1 Data Sources

Different data sources have been used for assessing the patients' QoL. Two self-reported instruments, EQ-5D-5L and Hospital Anxiety and Depression Scale (HADS), have been used as ground truth of the patients' QoL. The patients' daily activity has been monitored through a Fitbit wristband.

2.1.1 EQ-5D-5L

EQ-5D is a standardised measure of health status developed by the EuroQol Group to provide a simple, generic measure of health for clinical and economic appraisal [2]. There are three versions of the instrument: EQ-5D-5L, EQ-5D-3L and EQ-5D-Y. Each EQ-5D instrument comprises a short descriptive system questionnaire and a visual analogue scale (EQ VAS) that are cognitively undemanding, taking only a few minutes to complete. The questionnaire provides a simple descriptive profile of a respondent's health state. The EQ VAS provides an alternative way to elicit an individual's rating of their own overall current health.

The EQ-5D-3L and EQ-5D-5L questionnaires comprise five dimensions: MOBILITY, SELF-CARE, USUAL ACTIVITIES, PAIN / DISCOMFORT and ANXIETY / DEPRESSION. EQ-5D-5L questionnaire improves the previous EQ-5D-3L questionnaire by including five levels of severity in each of the five dimensions compared with the three levels of the EQ-5D-3L. Thus, CONNECARE clinicians choose EQ-5D-5L questionnaire to assess the quality of life of the patients. These five levels of severity are: no problems, slight problems, moderate problems, severe problems, and unable to/extreme problems. The EQ VAS records the respondent's overall current health on a vertical visual analogue scale, where endpoints are labelled 'The best health you can imagine' and 'The worst health you can imagine'. The EQ VAS provides a quantitative measure of the patient's perception of their overall health. Figure 1 and Figure 2 show a sample of the five dimensions' questions of the EQ-5D-5L version and the EQ VAS, respectively.



Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES (*e.g. work, study, housework, family or leisure activities*)

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

Figure 1: The five dimensions of the EQ-5D-5L questionnaire.

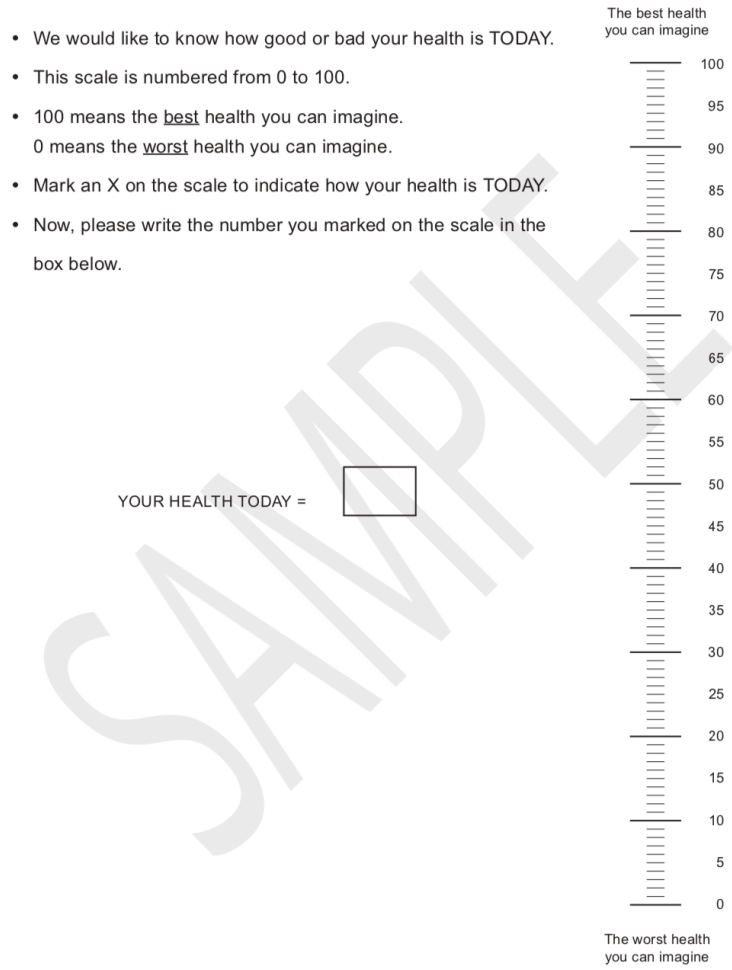


Figure 2: The EQ VAS.

2.1.2 HADS

HADS was originally developed by Zigmond and Snaith [3] and is commonly used by clinicians to determine the levels of anxiety and depression that a person is experiencing. Zigmond and Snaith created this outcome measure specifically to avoid reliance on aspects of these conditions that are also common somatic symptoms of illness, for example fatigue and insomnia or hypersomnia. This, it was hoped, would create a tool for the detection of anxiety and depression in people with physical health problems.

The HADS scale consists of fourteen items, seven of them related to anxiety and seven related to depression. Each item on the questionnaire is scored from 0-3 and this means that a person can score between 0 and 21 for either anxiety or depression (HADS-T). A specific score can also be obtained for anxiety (HADS-A) or depression (HADS-D) by only adding the scores corresponding to the questions related to anxiety or depression, respectively. Figure 3 shows the HADS questionnaire.

Many researchers have explored HADS data to establish the cut-off points, as Singer et al. [4], who published a cut-off for cancer patients in acute care.

Hospital Anxiety and Depression Scale (HADS)

Tick the box beside the reply that is closest to how you have been feeling in the past week.
Don't take too long over you replies: your immediate is best.

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			**I feel restless as I have to be on the move:**
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful:			**I get sudden feelings of panic:**
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			**I can enjoy a good book or radio or TV program:**
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not Often	2		Not often
	3	Not at all	3		Very seldom

Please check you have answered all the questions

Scoring:
Total score: Depression (D) _____ Anxiety (A) _____
0-7 = Normal
8-10 = Borderline abnormal (borderline case)
11-21 = Abnormal (case)

Figure 3: The HADS questionnaire.

2.1.3 Fitbit

Fitbit devices are wristbands capable of monitoring the daily activity of their users, in particular the number of steps, the heart rate, and the sleeping activity [5].

The counting steps module of Fitbit devices is based on the data from a 3-axis accelerometer. The steps are counted by using an algorithm which looks for intensity and motion patterns that are most indicative of people walking and running and includes algorithms to discard other acceleration movements as those produced by other transportations (e.g., cars, bus, train). The algorithm only counts a motion as a step if its duration is long enough.

The heart rate measure is based on blood volume changes produced by the heart beats. These changes are detected by *Pure Pulse* LED lights which are reflected onto the skin. Automatic and continuous algorithms are applied to measure heart rate every minute.

The algorithm that monitors the sleep activity is slightly different depending on the Fitbit model. Old models, such as Charge, base the monitoring on the movement captured by the accelerometer. The algorithm assumes that the user is asleep when s/he has not moved for an hour. Indeed, this assumption arise some false sleep records if the user did not move for an hour, e.g., watching the TV. This model classifies the sleep activity in three levels: *awake, restless*, and *asleep*. Newer models, such as Charge 2 and Alta HR, combine movement and heart-rate patterns for a better tracking of the sleep activity. Instead of the levels of sleep reported by the old models, this model uses the variability of the heart rate to estimate the sleep phases: *light, deep*, and *REM*. The sleeping activity data can be divided into summary variables and time series data. Table 1 shows the complete list of summary variables, differentiating between those exclusive of one model and those common in both models. The time series data sequentially details all the night periods, reporting the start time of the period, the duration and the level or stage, depending on the model.

Common variables	*Old model variables*	*New model variables*
Date of the sleep activity	Minutes in sleep level	Minutes in rem sleep stage
Start time	Periods in sleep level	Periods in rem sleep stage
End time	Minutes in awake level	Minutes in light sleep stage
Duration	Periods in awake level	Periods in light sleep stage
Minutes to fall asleep	Minutes in restless level	Minutes in deep sleep stage
Minutes after wakeup	Periods in restless level	Periods in deep sleep stage
Efficiency		Minutes in awake stage
Minutes asleep		Periods in awake stage
Minutes awake		

Table 1: Sleeping activity variables from Fitbit.

To summarize, the Fitbit data that we used in our experiments are: the number of steps per day, the heart rate per minute, and the sleep activity per night.

2.2 Data Processing

2.2.1 Pre-Processing

The heart rate and sleeping activity data need to be pre-processed before creating the final features used by the models.

Any time the user is not wearing the device the heart rate is not calculated and, thus, there are a lot of missing values. For small periods, a moving median method has been used to input the missing data. For large periods, the missing values are not input and these data are not used to create the models. In fact, inputting large periods may produce errors.

The sleeping activity algorithms of the old models of the wristbands are too sensible to the movements of the users and detect these movements as the user is awake. Thus, any time the wristband registers a sleeping activity shorter than 12 minutes, it recognizes it as a different period of sleeping activity. To address this problem, we joined consecutive sleeping periods shorted than 12 minutes, creating a unique timeslot with the total duration. Moreover, to count the minutes to fall asleep, the wristband considers the minutes from the moment the user manually selects the sleep mode to the moment it detects the user is asleep. It is worth noting that the most of the users did not use this manual functionality and, thus, the minutes to fall asleep were always zero. However, for some sleeping activities the first level or stage is *awake* meaning that the user did not fall sleep immediately. Thus, the minutes to fall asleep have been recomputed using the minutes of the first period if it is *awake* and zero otherwise.

2.2.2 Features Extraction

The design of appropriate data representation is an important task before training the model to analyse the data. Creating the appropriate set of features is extremely important since the corresponding set is the only source of information for any learning algorithm. Moreover, as noted in [6], better performance is often achieved using features derived from the original data rather than using the original data as an input to the model.

Regarding the steps, the number of steps per day reported by the wristband has been used as a feature.

For computing the heart rate features, the heart rate time series has been divided in two periods, day and night, using, for each patient, its usual *go to sleep time* and *weak up time* calculated as the mean time they go to sleep and weak up, respectively. Then, for each period, the heart rate has been aggregated using the following measures: maximum, minimum, median, and mean. Apart from these values, three more features have been computed for each period: counting the number of minutes that the patient has been on the maximum, minimum and median heart rate. Table 2 summarizes the heart rate features.

Day period	*Night period*
Maximum	Maximum
Minimum	Minimum
Median	Median
Mean	Mean
Minutes in Maximum	Minutes in Maximum
Minutes in Minimum	Minutes in Minimum
Minutes in Median	Minutes in Median

Table 2: Heart Rate features.

Fitbit reports as separated sleep activity periods when the awake time in between is higher than a threshold. For example, if one day the user sleeps from 12 a.m. to 8 a.m. and then has a nap between 4 p.m. and 5 p.m., Fitbit reports two different sleep activity periods for that day. 22 features have been created to encapsulate all the sleep activity information of one day. Firstly, for each patient, its usual *go to sleep time* and *weak up time* has been calculated as the mean time they go to sleep and weak up, respectively. Then, each period has been classified depending if the period is entirely at night, i.e., it is between *go to sleep* and *weak up time* (night-period) it is during the day, i.e., it starts after weak up time (day-period) or it is part during the day and part during the night, i.e., it starts before going to sleep time or it ends after weak up time (mixed-period). Three features keep track of the number of periods of each type: *number of night-periods*, *number of day-periods* and *number of mixed-periods*. For the rest of the features, the mixed-periods are reclassified as night-periods if the night part of the period is longer than the day part or as day-periods if the day part of the period is longer than the night part. For day-periods, only one feature is computed, *total time of day-periods* (minutes). These periods are normally short because they correspond to naps. If there are more than one day-period, this feature is computed as the sum of the minutes of all day-periods. For night-periods, several features are computed: *total time of night-periods* (minutes), computed analogously as for the day-periods; *minutes to fall asleep*, the value computed in the pre-processing step; *efficiency*, directly the value provided by Fitbit; *go to sleep time* and *wake up time*; and the *total time* and the *number of periods* of each level or stage, depending of the model. For all these features, if there are more than one night-period, the feature is computed as the sum of the minutes of all the night-periods, except *minutes to fall asleep* which is computed as the average of minutes to fall asleep for all the night-periods; *efficiency***,** which is recomputed using the averaged total time of night-periods and the total time in awake (level or stage); and the *go to sleep time* and *wake up time* which are assigned as the go to sleep time of the first period and the wake-up time of the last period is used. Table 3 shows all the sleep features, differentiating between those exclusively of one model and those common in both models.

Common variables	*Old model variables*	*New model variables*
number of night-periods	total time in sleep level	total time in rem stage
number of day-periods	number of periods in sleep level	number of periods in rem stage
number of mixed-periods	total time in awake level	total time in light stage
total time of day-periods	number of periods in awake level	number of periods in light stage
total time of night-periods	total time in restless level	total time in deep stage
minutes to fall asleep	number of periods in restless level	number of periods in deep stage
efficiency		total time in awake stage
go to sleep time		number of periods in awake stage
wake up time		

Table 3: Sleep activity features.

2.2.3 Features Selection

Depending of each experiment, all of the created features or a subset of them have been used.

In the Sleep Quality (Normal Habits versus Outliers) experiment, all the features related to sleeping activity has been used but the models do not use the steps or the heart rate. On the contrary, the Workload Assessment experiment considers all the features described in the previous sections, steps, heart rate, and those related to sleeping activity.

Regarding the experiments with patients, in the Quality of Life assessment as a continuous variable, the physical activity and the sleeping activity has been considered. The former has been studied using the steps jointly with the steps goal prescribed by the clinician. The latter has been characterised using total time of night-periods and total time awake (level or stage, depending on the model used). In the Quality of Life assessment focussing on Anxiety/Depression experiment, the clinicians have selected just three of the features related to sleeping activity: *total time of night-periods*, *efficiency*, and *minutes to fall asleep*.

3. Preliminary Experiments with Volunteers

Due to the lack of data from the CONNECARE patients, we decided to use historical data from a healthy volunteer (female; period from 41 to 45 years old) to better understand the data from Fitbit and explore possible approaches to assess QoL. Two experiments have been performed Sleep Quality (normal habits vs outliers) and Workload Assessment.

3.1 Sleep Quality (Normal Habits versus Outliers)

The aim of the first preliminary experiment is to assess the sleep quality of the user by detecting the nights with an abnormal sleeping activity. The data used was from a volunteer who wore the Fitbit Charge HR from April 8th, 2015 to November 11th, 2017 (a total of 920 days). As the aim of the experiment is directly related to sleeping activity, the only features used are those related to the sleeping activity.

The used data are historical and unlabelled, i.e., we do not know a priori which nights are abnormal. In machine learning, there exist a several "outlier detection" methods which we can use to try to identify abnormal samples. We defined a model which combines the prediction of three well known outlier detection methods, Elliptic Envelope [7], Isolation Forest [8] and Local Outlier Factor [9] using majority voting. Figure 4 depicts the proposed model.

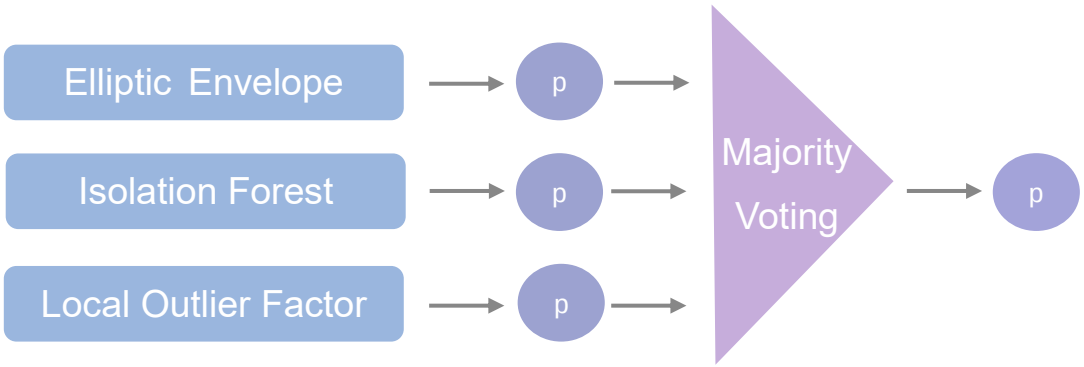


Figure 4: Proposed model for predicting abnormal sleeping activities.

Once the model predicted for each night whether there was an abnormal sleeping activity or not, the volunteer checked the results and indicated when she recalled having an abnormal night or not. To rebuild the activities performed in the past and estimate abnormal nights, she relied on her Google calendar where she saved trips, friends visits, and other relevant events, as well as an app installed in her smartphone that registered all the movements[2].

Figure 5 shows which days the model correctly (green) and incorrectly (red) classified the sleeping activity, either as normal or abnormal. As shown, the model can predict almost all the abnormal sleeping

[2] The Moves app, available until July 2018, was used.

activities (i.e., just a few strong red days), but there quite a few normal sleeping activities predicted as abnormal (i.e., pale red days).

Figure 5: Results of the model for predicting abnormal sleeping activities using a volunteer data.

The main result of this first experiment is that the proposed approach could be used as an intermediate assessment of the patient's QoL, by characterising the quality of sleeping through the objective data gathered through the wristband. Since the sleeping patterns are extremely personal, the model should be trained for each patient with her/his data, which would require a huge amount of data for patient (e.g., we had almost three years for the volunteer).

3.2 Workload Assessment

Since the volunteer is not a final patient and her data are historical, we do not have information directly related with her QoL. In other words, she did not answer the EQ-5D-5L. However, we have an indirect

QoL score which is her workload, in terms of numbers of worked hours [10]. Thus, the main goal of this experiment is to assess the weekly workload based on the variables which are directly related with the QoL: *sleeping activity*, *steps*, and *heart rate*. The workload has been extracted from working hours registered by the volunteer in the ERP (Enterprise Resource Planning) used in her company.

To perform this experiment, we used the data from the volunteer from January 1st to September 30th, 2018 (39 weeks). In that period, the volunteer was wearing a Fitbit Charge 2. In this experiment, all the features explained in section 2.2.2 were computed. Figure 6 shows the relation between the workload and the computed features. As shown, some of the features, such as minutes in the four sleeping phases, have some direct relation with the worked hours.

Starting from this first result and since our target variable is continuous, different types of regression models were then experimented: Linear Regression, Ridge Regression, Lasso, Support Vector Regression, Decision Tree Regression and K-Nearest Neighbour Regression. Table 4 shows the results obtained using these six models for predicting the workload, measured using the Mean Square Error (MSE). As shown most of the models overfit (i.e., they obtain small MSE over the training set), but high MSE over the testing set. Thus, we may conclude that the best model is Support Vector Regression which achieve almost the same MSE over the training and testing set.

Model	*MSE*	
	Train	***Test***
Linear Regression	5.83	4514.11
Ridge Regression	1.05	1132.90
Lasso	11.98	102.62
Support Vector Regression	49.86	53.90
Decision Tree Regression	0.0	110.25
K-Nearest Neighbour Regression	0.0	61.42

Table 4: Results of workload prediction using different regression models.

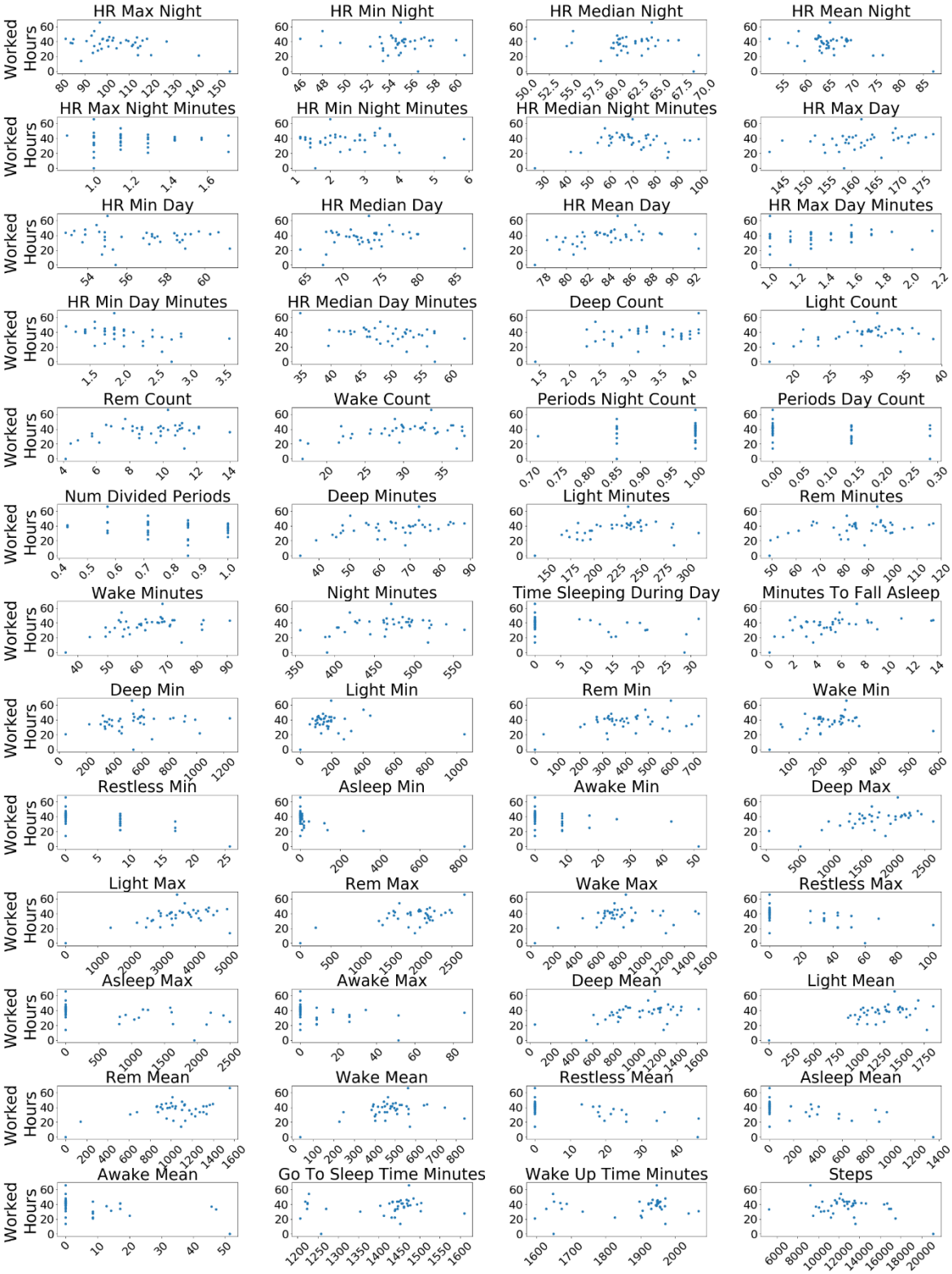


Figure 6: Relation between the worked hours and the features..

Figure 7 shows the predicted values of the Support Vector Regression versus the true values over the testing set. As shown, the error is small for most of the days except for those days (2018-09-10 and 2018-07-30) that the true number of hours was very different from the average. Meaning the trained model is conservative (i.e., its prediction is around the average number of hours).

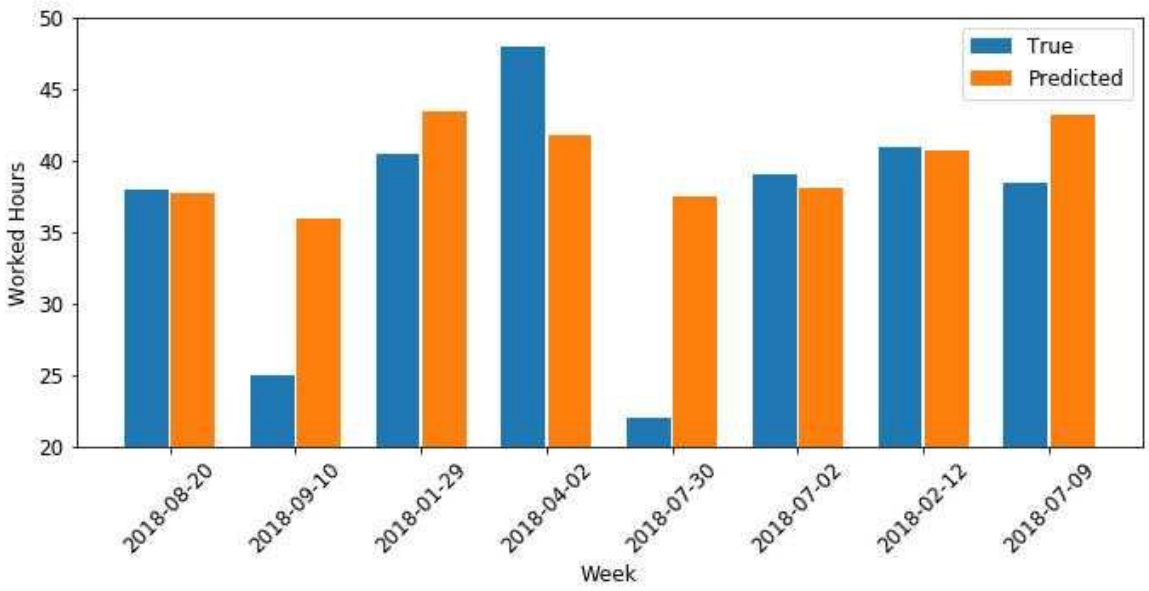


Figure 7: Specific results over the testing set using the Support Vector Regression

To sum up, when trying to predict a continuous variable such as number of worked hours the model tends to predict the average of the worked hours, thus is a good predictor for those days that do not deviate much to the "normal" days. To complement this model, an unsupervised method (e.g., one of those exposed in the first experiment) could be used to split the days between normal and abnormal days and train to different models one on each dataset. The proposed model can be used to assess the QoL by training the model with QoL provided as a continuous variable.

4. Experiments with Patients

Once the data coming from the implementation studies was available (March 2019), we started experiments with the patients' data. This section explains the two experiments performed: quality of life assessment as a continuous variable and quality of life assessment focussing on Anxiety/Depression.

4.1 Quality of Life Assessment as a Continuous Variable

The initial idea was to assess the QoL as a continuous variable (such as the EQ VAS) applying the model explored in the Workload Assessment experiment (Section 3.2). In order to do that, we needed labelled data to train the model. In other words, weekly answers of the EQ-5D-5L were necessary. We discussed it with all clinical partners in CONNECARE and clinicians from ASSUTA agreed to prescribe the EQ-5D-5L weekly through the SACM to be answered by their patients through the SMS.

At the time of performing this analysis (March 2019), there was data for six months, from mid-September 2018 to mid-March 2019. During these months, 22 patients (9 females; 63.14 ± 8.17 years old) were enrolled to the ASSUTA case studies at different times. Patients were asked to wear a Fitbit (Fitbit Alta HR) 24/7 and answer the EQ-5D-5L through the SMS once a week.

Figure 8 shows the available data for each patient. As shown, only 7 patients answer the EQ-5D-5L and only 2 of them answer the questionnaire more than once. Moreover, the figure shows that not all the users worn the Fitbit at night, thus we do not have complete data regarding their sleeping activity. It is worth noting, that due to the very small labelled data we gathered, we had to rethink the approach to be taken because we could not use the model proposed for the Workload Assessment experiment.

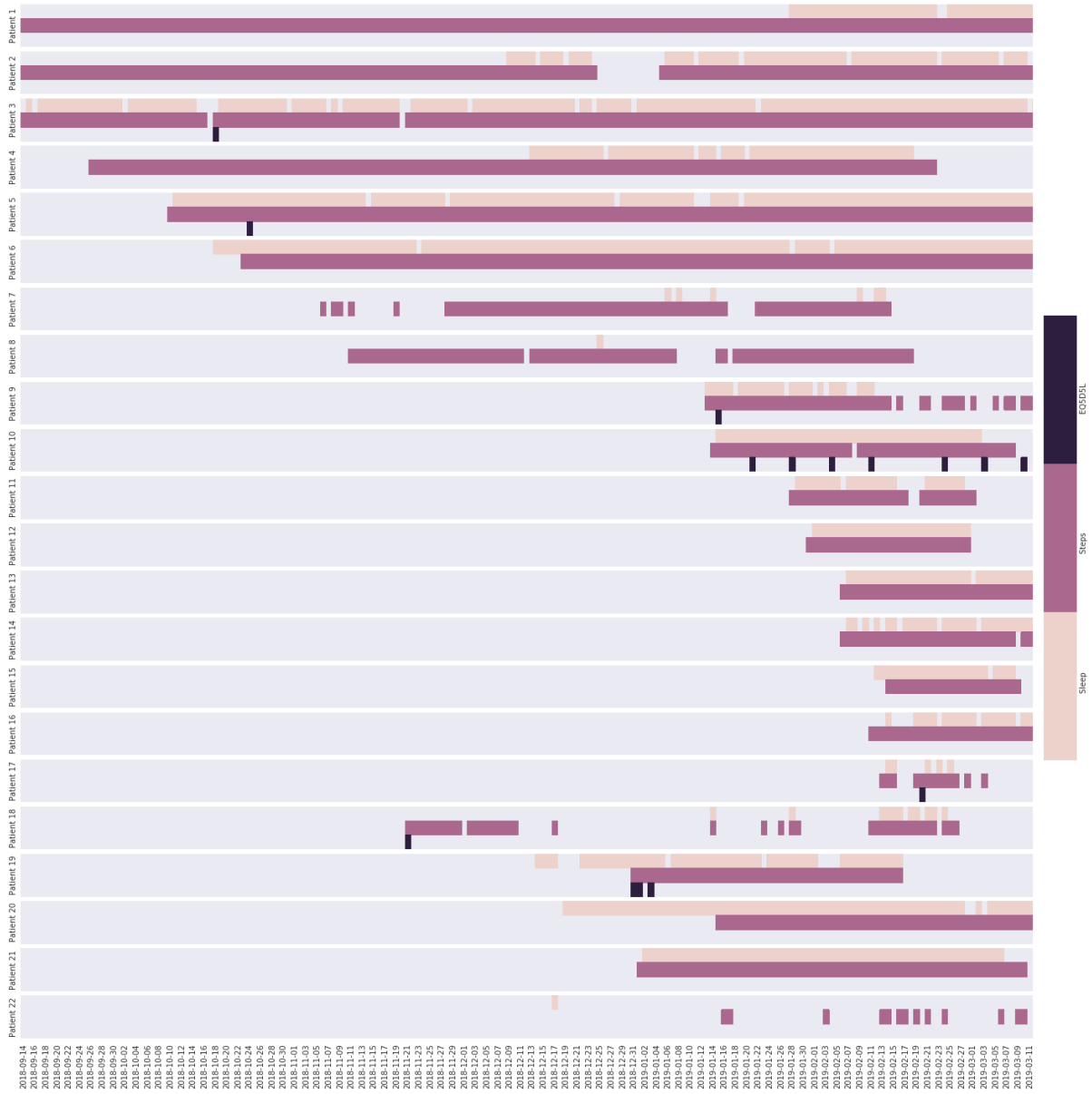


Figure 8: Available data for the 22 patients enrolled in ASSUTA from mid-September 2018 to mid-March 2019. The x-axis is a temporal axis and each horizontal graphic corresponds to a patient. The colours represent the type of data: salmon for sleeping data, fuchsia for physical activity data, and purple for EQ-5D-5L answers. The grey represents no available data.

The data collected from the patients who answered the EQ-5D-5L was further investigated with the objective to find an alternative approach to assess the QoL.

Firstly, we analysed data from those patients who answered only once. Figure 9, Figure 10, Figure 11, Figure 12 and Figure 13 show the data from the Patients 3, 5, 9, 17, and 18, respectively.

As shown, all the patients answered 1 to the questions about Usual Activities and Self Care (i.e., reported no problem in these dimensions). The question about Anxiety and Depression have almost the same answer for all the patients *Not anxious or depressed* (Anxiety/Depression = 1), but for one patient who reported being *Slightly anxious or depressed* (Anxiety/Depression = 2). If we focus on Mobility, we find different answers, 2 patients reported *No problems in walking about* (Mobility = 1), 2 patients reported *Slight problems in walking about* (Mobility = 2) and 1 user reported *Severe problems in walking about* (Mobility = 4). The pain and discomfort question also have different answers depending on the patient: 2 patients reported *No pain or discomfort* (Pain/Discomfort = 1), 1 patient reported *Slight pain or discomfort* (Pain/Discomfort = 2) and 2 patients reported *Moderate pain or discomfort* (Pain/Discomfort = 3). Focusing on the EQ VAS, Patient 17, although answering that he did not have problems with any dimension, he only reported 90 point out of 100 in the EQ VAS. Patient 5 reported 79 out of 100 in the EQ VAS which goes in line with the fact that the patient answered not having problem in any dimension but having slight pain and/or discomfort. Patients 3 and 9 reported 72 out of 100 in the EQ VAS, their answers in the dimensions are the same but for the Mobility dimension were Patient 3 reported having *severe problems in walking* and Patient 9 reported having *slightly problems in walking*. Patient 18 reported 67 out of 100 in the EQ VAS, which is quite low if it is compared to their answer to the dimensions, no problems in Self Care, Usual Activities and no Pain and/or Discomfort and only slightly problems in Mobility and slightly feeling Anxious and/or Depressed.

Almost all the patients achieved their daily steps goals and in some cases, they greatly exceeded it. However, this result varies over time (e.g., Patient 18, who reported *No problems in walking about,* started walking a very few steps a day after about 20 days). Regarding the sleeping data, for those patients with more than a few nights of data (Patients 3 and 5), we see a different behaviour. On the one hand, Patient 3 almost always spent between 6 and 8 hours in bed (sleeping and awake) but slept less than 6 hours. On the other hand, Patient 5 almost always sleep between 6 and 8 hours, but she had a period when she usually spent more than 8h in bed. Thus, to better model the QoL based on the physical and sleeping activity, we would need to know if her EQ-5D-5L answers would have varied accordingly to the changes in physical and sleeping activity.

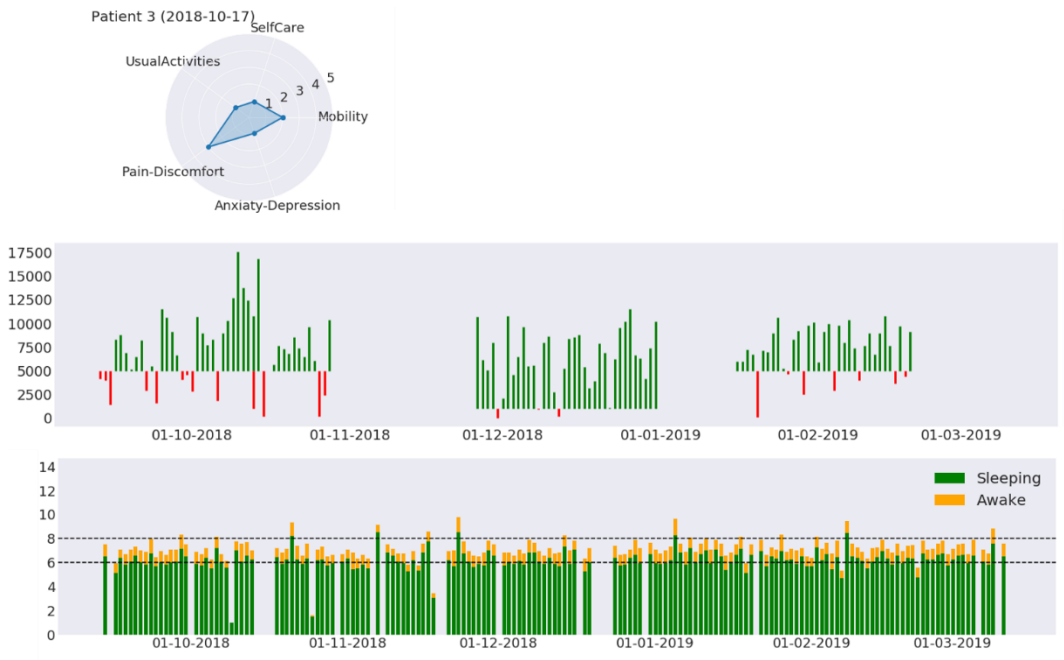


Figure 9: Data from Patient 3 who answered the EQ-5D-5L once. EQ-5D-5L answers, on the left; performed steps with respect to the prescribed steps, in the centre; and sleeping activity (minutes awake and sleeping), on the right.

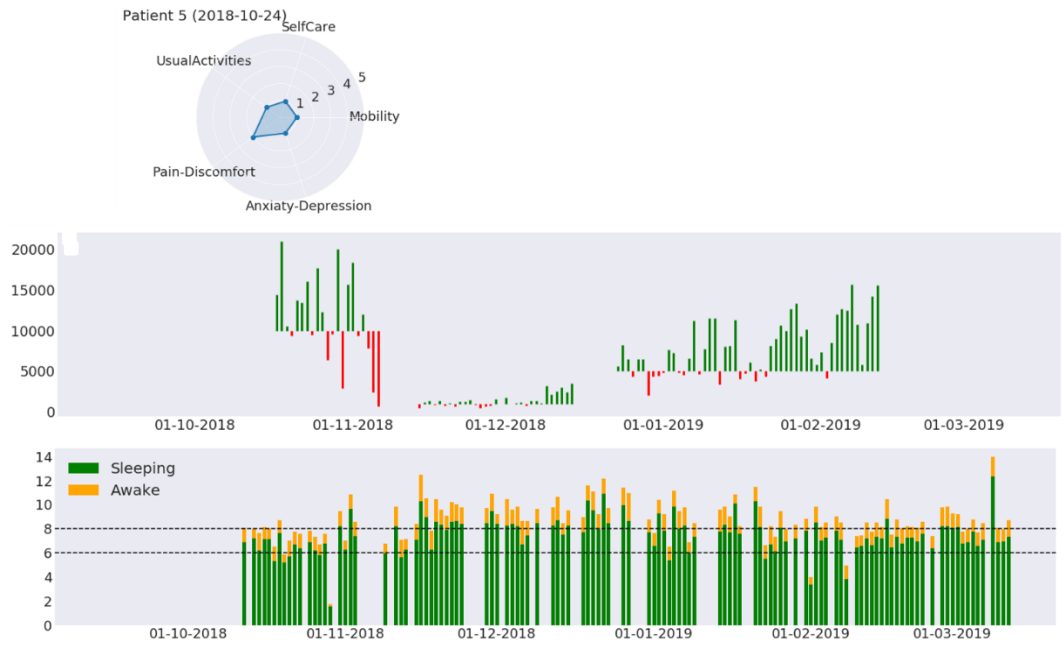


Figure 10: Data from Patient 5 who answered the EQ-5D-5L once. EQ-5D-5L answers, on the left; performed steps with respect to the prescribed steps, in the centre; and sleeping activity (minutes awake and sleeping), on the right.

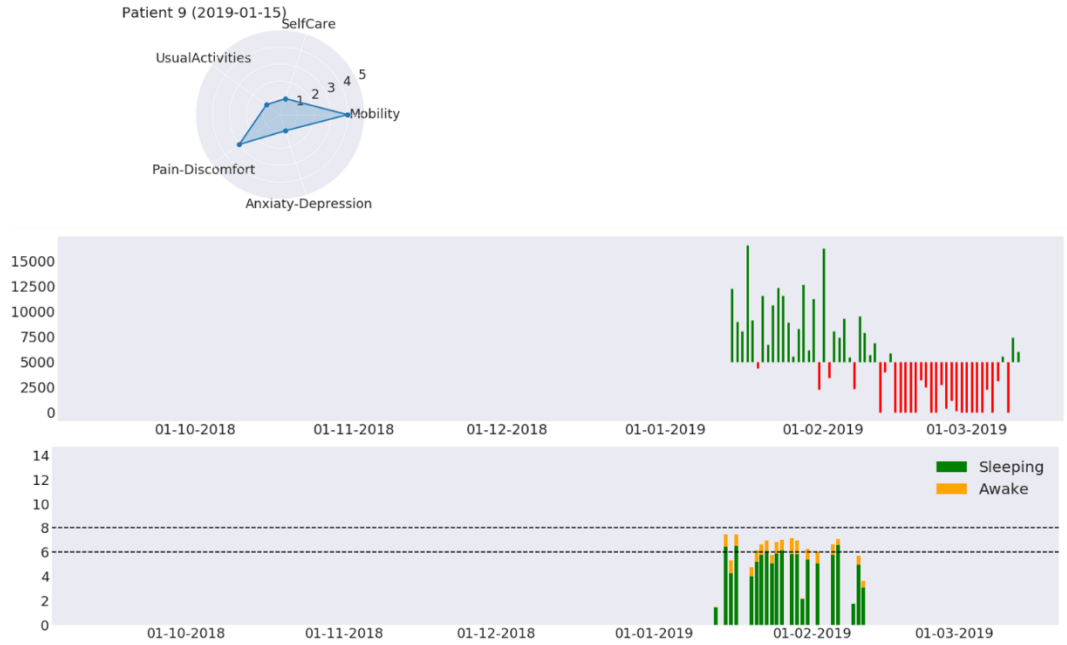


Figure 11: Data from Patient 9 who answered the EQ-5D-5L once. EQ-5D-5L answers, on the left; performed steps with respect to the prescribed steps, in the centre; and sleeping activity (minutes awake and sleeping), on the right.

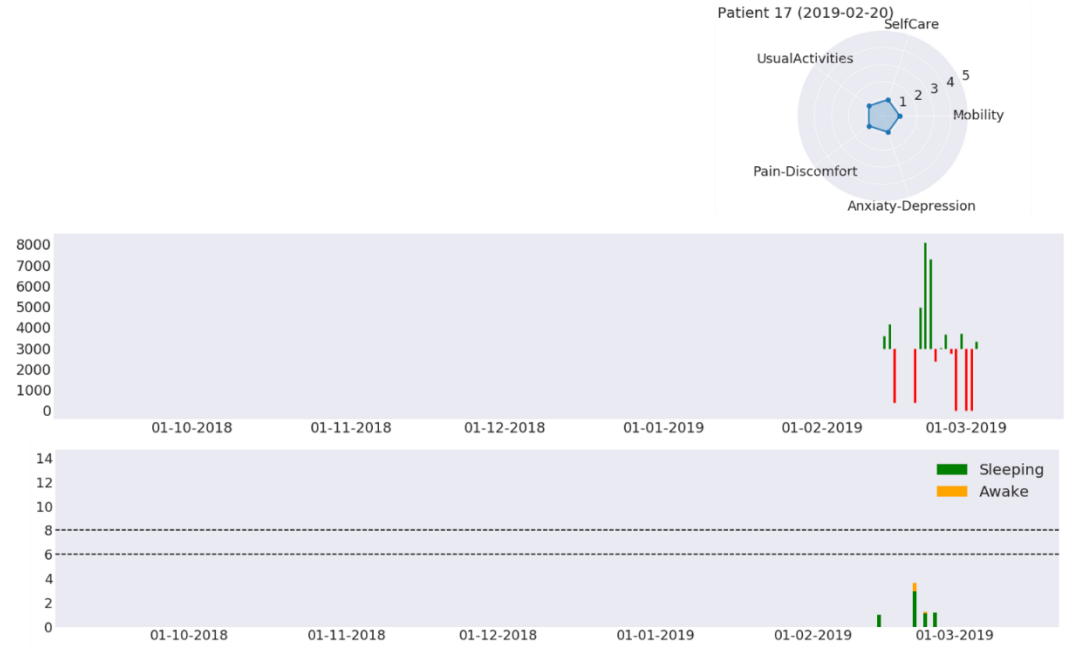


Figure 12: Data from Patient 17 who answered the EQ-5D-5L once. EQ-5D-5L answers, on the left; performed steps with respect to the prescribed steps, in the centre; and sleeping activity (minutes awake and sleeping), on the right.

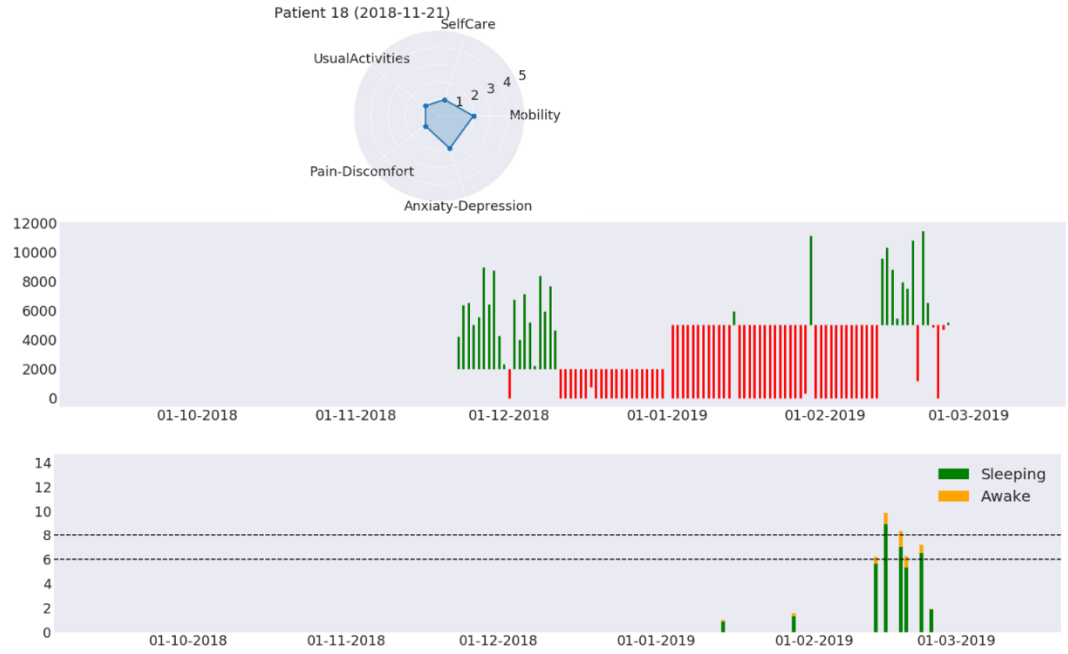


Figure 13: Data from Patient 18 who answered the EQ-5D-5L once. EQ-5D-5L answers, on the left; performed steps with respect to the prescribed steps, in the centre; and sleeping activity (minutes awake and sleeping), on the right.

Subsequently, we analysed the data from Patient 19 who answered the EQ-5D-5L three time: at 31-12-2018, 1-01-2019 and 3-01-2019. Data are shown in Figure 14. On the top, the performed steps with respect to the prescribed steps are visualized; in the centre, the sleeping activity (minutes awake and sleeping) data are visualized; and on the bottom the EQ-5D-5L answers are depicted. The EQ-5D-5L answers were the same in the three days but for the pain and/or discomfort dimension which increased from *moderate* to *severe* in the third day. He reported 40 point out of 100 in the EQ VAS in the first two days and 29 out of 100 in the last one. Focussing on the physical and sleeping activity performed during the dates he answered the EQ-5D-5L, he outperformed his step goal before the date when he reported a worsening in his QoL. Then he did not achieve the goal for several days or achieved it but did less steps than before the worsening, until 18-01-2019. Unfortunately, he did not answer the questionnaire for that dates. Regarding the sleeping hours, we do not have information regarding the first two dates he answered the EQ-5D-5L, but the day he reported a worsening in the pain and/or discomfort dimension he stayed 12 hours in bed, most of the time sleeping.

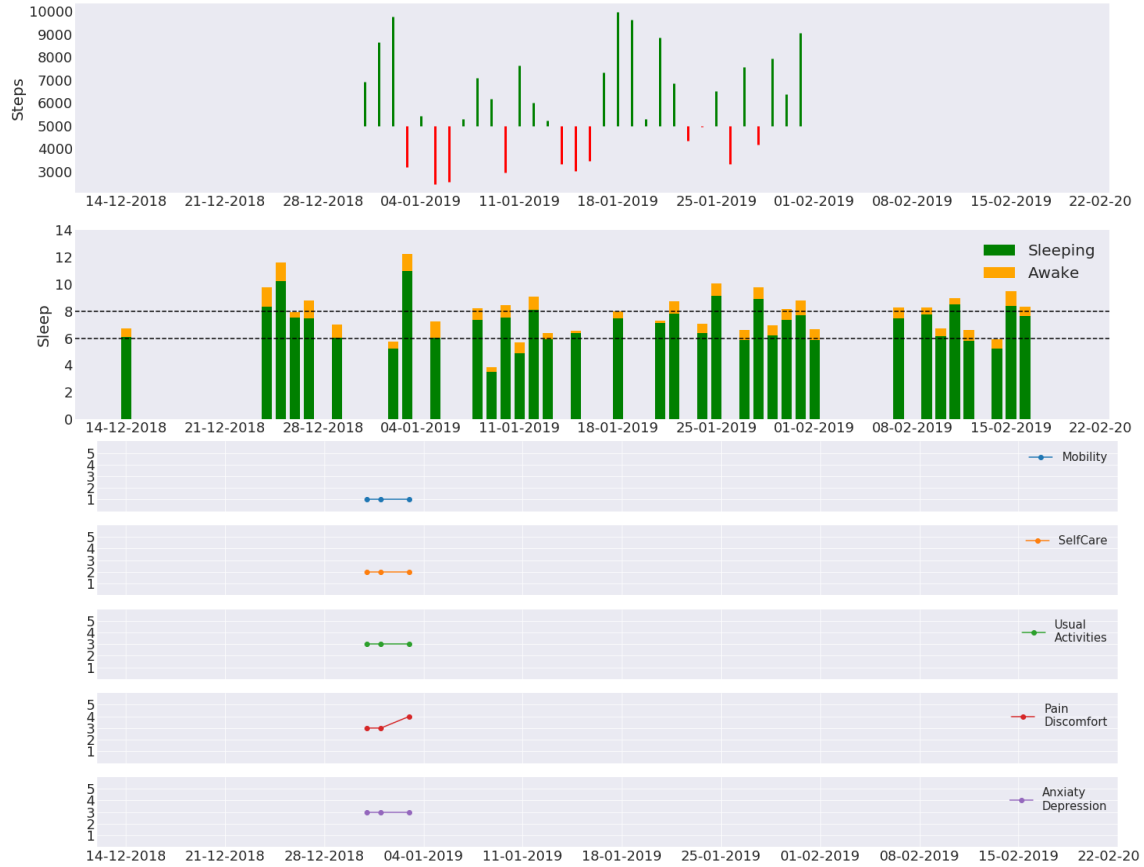


Figure 14: Patient 19's data, who answered the EQ-5D-5L weekly. Performed steps with respect to the prescribed steps, on the top; sleeping activity (minutes awake and sleeping) data, in the centre; and EQ-5D-5L answers on the bottom.

Subsequently, we analyse the behaviour of Patient 10, who answered the EQ-5D-5L weekly as prescribed (see Figure 15). On the top, the performed steps with respect to the prescribed steps are visualized; in the centre, the sleeping activity (minutes awake and sleeping) data are visualized; and on the bottom the EQ-5D-5L answers are depicted. She did not change her answer regarding Mobility (*Slight problems in walking),* Usual Activities *(Slight problems doing my usual activities)*, and Anxiety/Depression *(Not anxious or depressed).* Regarding Self Care, she reported *No problems with washing or dressing myself* on the first day, but change to *Slight problems washing or dressing myself* the rest of the weeks. On the contrary, she started reporting *Slight pain or discomfort* for the first weeks until the last week when she reported *No pain or discomfort.* She reported 0 point out of 100 in the EQ VAS every week, this could mean she forgot to answer this part of the EQ-5D-5L questionnaire. Regarding the physical and sleeping activity, she did not achieve the prescribed steps most of the days and she barely slept 6h per night. As we collected data only from one patient, we cannot investigate if the no change in the EQ-5D-5L answers and the same behaviour in physical and sleeping activity are correlated.

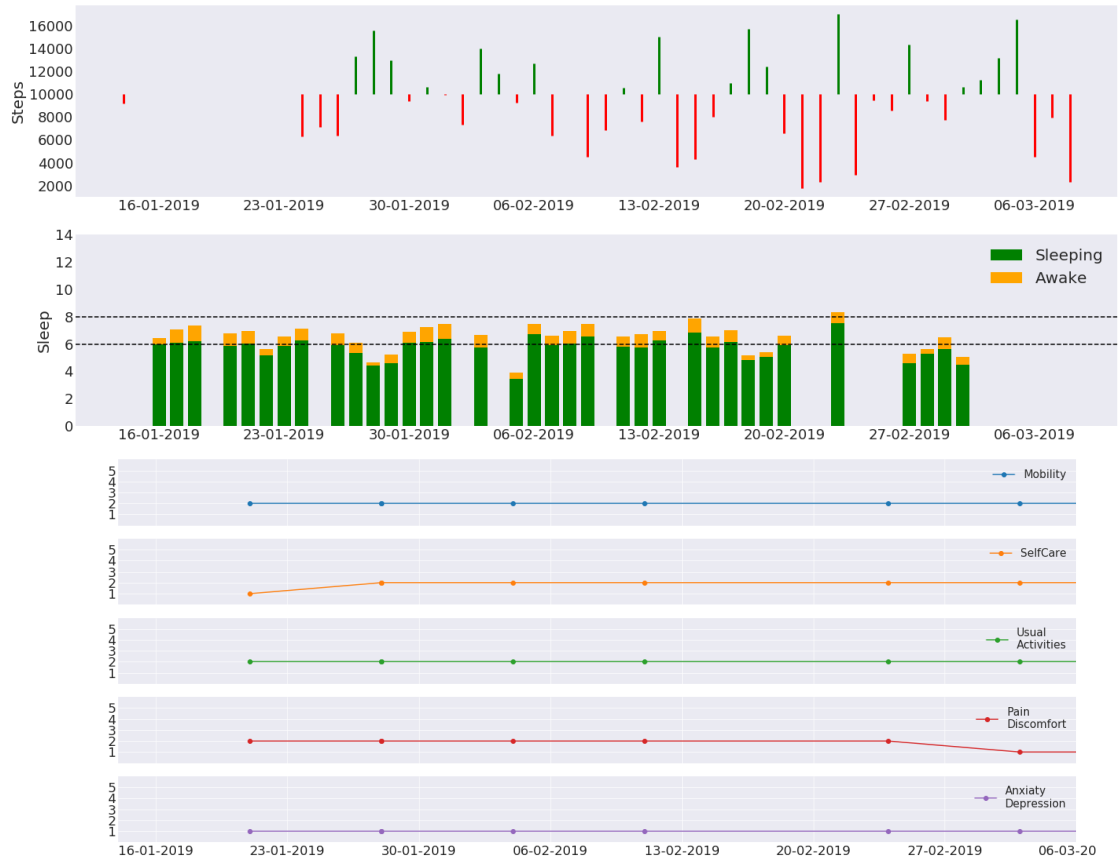


Figure 15: Patient 10's data, who answered the EQ-5D-5L weekly. Performed steps with respect to the prescribed steps, on the top; sleeping activity (minutes awake and sleeping) data, in the centre; and EQ-5D-5L answers on the bottom.

To sum up, the methods explored in the Workload Assessment experiment could not be applied to the patient's data from CONNECARE due to the low patient's compliance to answer the EQ-5D-5L weekly. By analysing the data from the patients who answered the EQ-5D-5L more than one day, we may envisage that that there is some correlation between the QoL and the physical and sleeping activity. More data are needed to confirm this thesis.

4.2 Quality of Life Assessment Focussing on Anxiety/Depression

As already stated, the patient's compliance to answer weekly the questionnaire was very low, meaning that it would be very difficult to obtain the needed labelled data for training a model capable of predicting a continuous variable for assessing the QoL based on the data gathered through the wristband. Following the suggestion by the reviewers during the 2nd review project meeting in January 2019, we focused on Anxiety and Depression rather than trying to assess the overall QoL.

Thus, we decided to analyse the correlation of Anxiety and Depression and sleeping activity, to better understand if the Anxiety and Depression affects the sleeping. We discussed it with all the CONNECARE clinicians and guided by UMCG, we decided to use for the QoL assessment a more specific questionnaire about anxiety and depression, the HADS questionnaire in the CS2. The correlation analysis was done between the anxiety and depression and the sleeping activity. More specifically, the anxiety and depression was obtained through the Anxiety and Depression dimension of the EQ-5D-5L questionnaire and the HADS questionnaire. The sleeping activity was monitored through the Fitbit, as in the other experiments, and we analysed the sleeping hours, the efficiency (as the ratio of the sleeping time and the time in bed) and the time to fall sleep.

The study was performed with the 21 UMCG-CS2 patients. These patients were instructed to wear the Fitbit (Fitbit Charge 2) all day. Researchers in UMCG explained to them that we also want to collect sleep data, but the main purpose was to collect step count. If patients got irritated with the wristband at night, they were asked to just wear it during the day. They were instructed also to answer the EQ-5D-5L and HADS questionnaires at three time points: inclusion time (T1), discharge from hospital (T2), and 3-months follow up (T3). The data was collected from mid-October 2018 to mid-April 2019. At the end, we only analysed 12 of them. The exclusion criteria are the following: 3 patients did not finish the CONNECARE implementation study, 5 did not have available data, and the data from 1 patient data was incomplete (i.e., more than 60% of the days in the study without sleeping data). Figure 166 depicts the flow chart showing how many patients were discarded in each step.

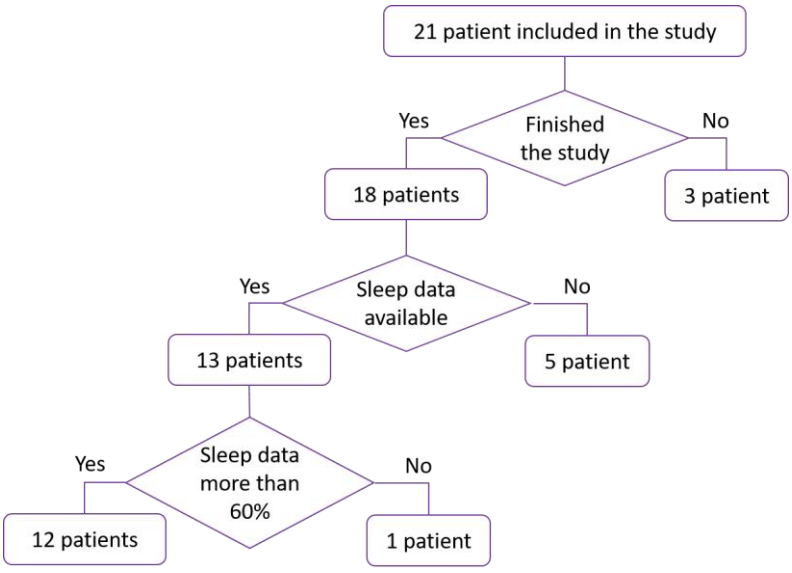


Figure 16: Flow chart showing how many patients were discarded in each step.

The HADS questionnaire answers were acquired at the three time points, whereas the EQ-5D-5L questionnaire answers were only acquired at T1 and T3. Thus, we analyse the correlation between sleep and Anxiety and Depression in three periods: preoperative (at home), hospitalization (including surgery), and postoperative (at home). The sleeping data was continuously monitored from T1 to T3.

Firstly, we analysed the patient distribution of the three datasets: all the 18 patients that finished the study and the 12 patients with more than 60% of sleeping activity data. Figure 17, Figure 18, and Figure 19 show, for each dataset, the distribution of the patients' age grouped by gender. Table 5 summarizes the mean age and standard deviation for each dataset. In the three datasets, the mean age of females is slightly higher than the mean age of males. The three patients who did not finish the study were all males. Although the final dataset only contains about 57% of the patients enrolled in the study (33% of the females and 66% of the males), the mean age of both categories barely varies (0.5 for female and 1.24 for male). Thus, it is a good representation of the original dataset.

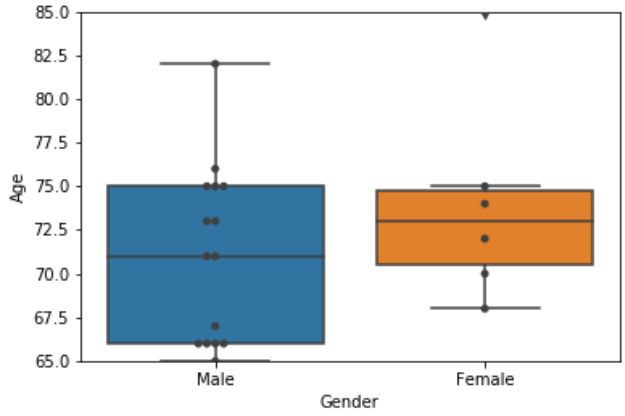


Figure 17 - Distribution of the 21 patients who enrolled in the study.

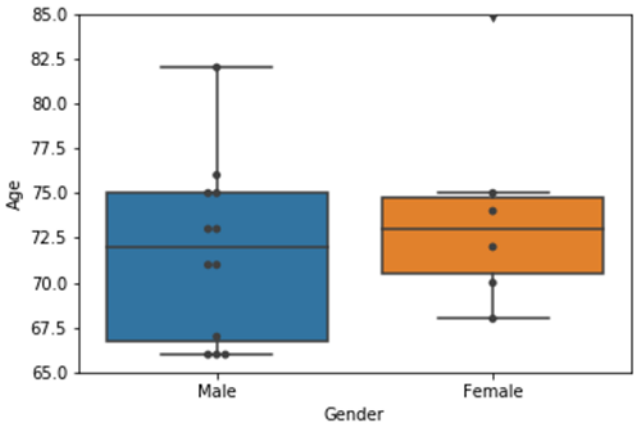


Figure 18 - Distribution of the 18 patients who finished the study.

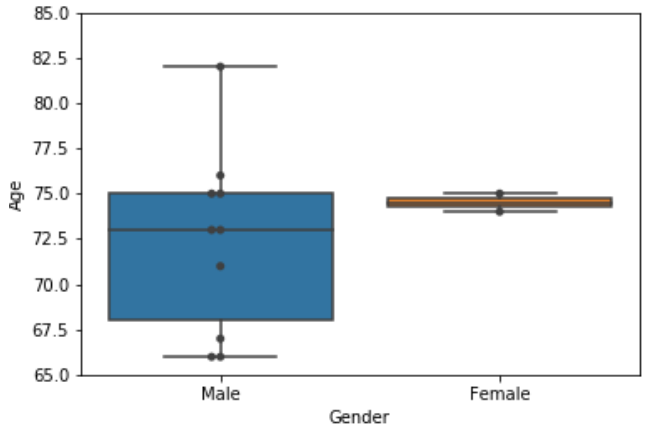


Figure 19: Distribution of the 12 patients with more than 60% of the sleep data.

	All 21 patients		18 patients that finished the study		12 patients with more than 60% of sleep data	
	N	Age (mean + std)	N	Age (mean + std)	N	Age (mean + std)
Female	6	74.00 ± 5.97	6	74.00 ± 5.97	2	74.50 ± 0.71
Male	15	71.16 ± 5.03	12	71.75 ± 4.96	10	72.40 ± 5.08
Total	21	71.95 ± 5.32	18	72.50 ± 5.25	12	72.75 ± 4.67

Table 5: Summary of the patients age for each group.

Then, we analysed in more detail the available sleeping data for each of the 13 patients. More precisely, how many sleeping days from each patient we had and how these days are distributed through the three periods: preoperative at home, hospitalization, and postoperative at home. Figure 20 shows, for each patient, the number of days s/he stayed in each period (right bar) and the number of days with available sleeping data (left column) for period. The number over the two bars shows the percentage of available sleeping data. As stated before, there is one patient with less than 60% of days with sleeping data (this patient is excluded from the following analyses). As shown, the duration of the three periods largely vary within patients (e.g., Patient 12 had just a few days of preoperative but more than 20 days of hospitalization whereas Patient 14 had 40 days of preoperative and just 2 days of hospitalization). These dissimilarities could affect the analysis performed if the analysis is performed grouping the patients. Since the number of patients is reduced to 12, we analysed the patients separately.

Figure 20: Ditribution, for each patients, of the number of days stayed in each period (right bar) and the number of days with available sleeping data (left column) for period.

Since we used two different questionnaires, EQ-5D-5L and HADS, to assess the Anxiety and Depression, before analysing the correlation between the QoL and the sleeping activity, we analysed the correlation of the answers reported by these two questionnaires. As UMCG clinicians suggested, we use the cut-off published by Singer et al. [4] for analysing the HADS dataset, which is based on the best trade between sensitivity and specificity. Thus, we used a score of 5 for the HADS-D, of 7 for HADS-A and of 13 for HADS-T; (i.e., if a patient obtained a score that is over the cut-off, we interpreted that s/he is depressed, anxious or depressed and anxious, respectively).

Figure 21 compares the HADS-T (in purple) score with the EQ-Anxiety/Depression answer (in red). Let us recall that the HADS-T scores was collected at T1, T2 and T3, whereas the EQ-Anxiety/Depression answer was collected only at T1 and T3. The discontinuous line indicates the cut-off score for HADS-T. In this study, all the patients answered that s/he was *not anxious or depressed* (EQ-Anxiety/Depression = 1) in the EQ-5D-5L questionnaire, but two of them (Patient 22 and Patient 2). Patient 22 answered that she was *slightly anxious or depressed* at T1 and T3, whereas Patient 2 answered that he *was slightly anxious or depressed* at T1 but he reported that his anxiety and/or depression increased to *moderate* at T3. All the patients that answered that s/he *was not anxious or depressed* had a higher score than zero for the HADS-T but lower than the cut-off. Regarding the other two patients, they obtained a HADS-T score higher than the threshold at T2.

Figure 22 shows the HADS scores divided in the HADS-D (green) and HADS-A (blue) for each patient. The discontinuous lines indicate the cut-off score for HADS-D (green) and HADS-A (blue). As shown, if we analyse the HADS score divided by depression and anxiety, more patients are classified as depressed

(i.e., their score is over the cut-off), even those who reported to *not be anxious or depressed* through the EQ-Anxiety/Depression questionnaire (i.e., patient 4, 8, 7, 10, 12, 14, 16). Regarding HADS-A, only the patient 22 had a HADS-A over the cut-off.

Thus, we concluded that both questionnaires are correlated even if they do not give exactly the same information. In fact, EQ-5D-Anxiety/Depression question is too abstract making difficult for patient to answer accordingly to the reality s/he is living. On the other hand, HADS questions are more concrete, thus, the patient's answer can be more precise.

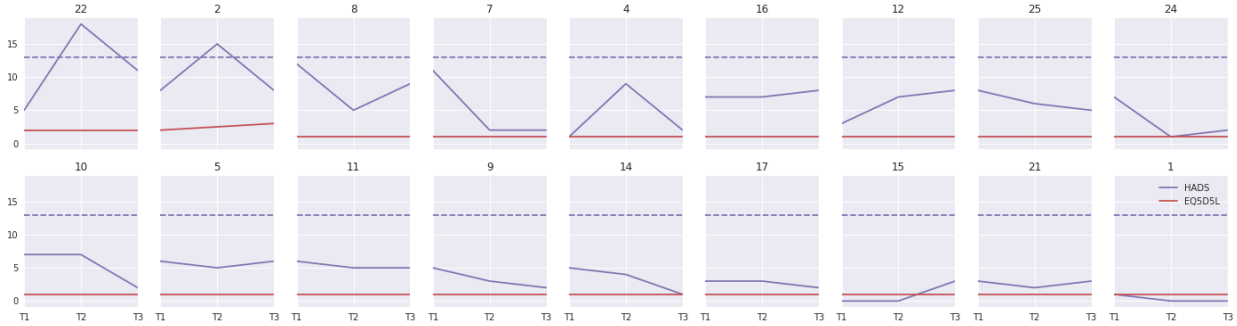


Figure 21: Comparison the HADS-T (in purple) score with the EQ-Anxiety/Depression answer (in red).

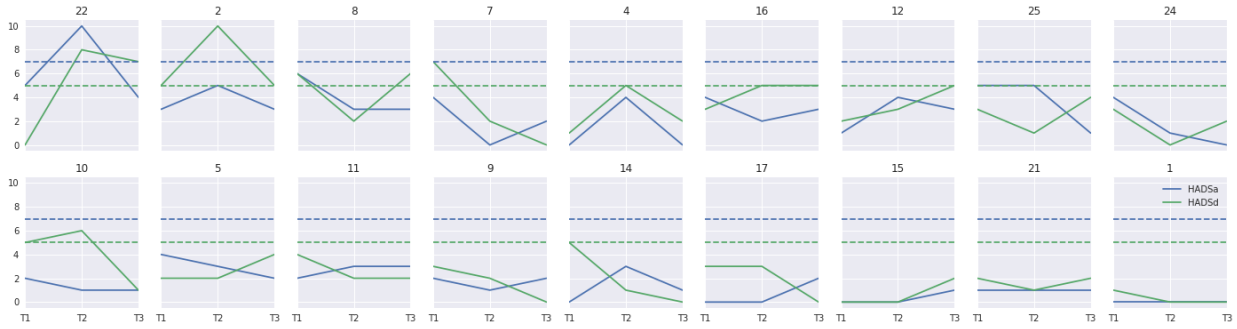


Figure 22: HADS score divided in the HADS-D (in green) and HADS-A (in blue).

The sleeping data were acquired continuously from T1 to T3, whereas the questionnaires were collected in three times points, T1, T2 and T3. Thus, for each patient, the sleeping data variables, total sleeping time of night-periods, efficiency and time to fall sleep, were discretised using the following method. Firstly, its trend was computed with a moving median. Then, for each period, preoperative, hospitalization, and postoperative, the trend was averaged to obtain one value for period.

Figure 23 shows, for each patient, the correlation between the changes of HADS-A and HADS-D and the three sleeping variables. The total time of night-periods is renamed as sleeping time. The grey areas are due to no changes in one of the compared variables. As shown, for HADS-D there is not a clear pattern

since some patients (e.g., Patient 25) have a strong positive correlation for the three variables, others have a negative correlation (e.g., Patient 22), others have a strong correlation positive or negative depending on the sleeping variable (e.g., Patient 15). On the other hand, for HADS-A efficiency and to fall sleep time have negative correlation for all the patients, the strength of the correlation depends on the patient. For the sleeping time variables, the direction (positive or negative) of the correlation depends on the patient but almost all the correlations have a strength over 0.5.

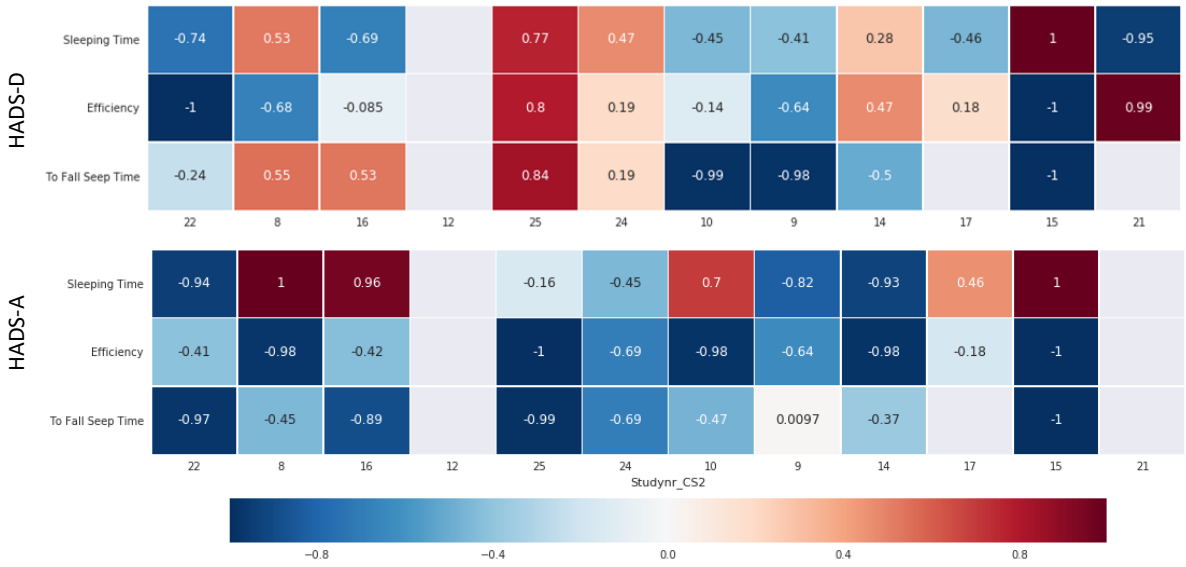


Figure 23: Correlation between the HADS scores (HADS-S and HADS-D) and the sleeping variables (sleeping time, efficiency and to fall sleep time), for patient.

Since the correlation between the sleeping variables, discretized as the average in the three different periods and the HADS scores are not conclusive, we also discretised the sleeping variable as the number of anomalies with respect of the trend for each period. In order to do so, once the trend is computed we count how many days the variable deviate from the trend more than two times the standard deviation.

Figure 24 shows, for each patient, the correlation between the changes of HADS-A and HADS-D and the three sleeping variables discretised as the number of anomalies in each period. These results are also patient depended, though the HADS-D has more positive correlations and the HADS-A more negative correlations. For some patients, these correlations are very strong (e.g., Patient 15).

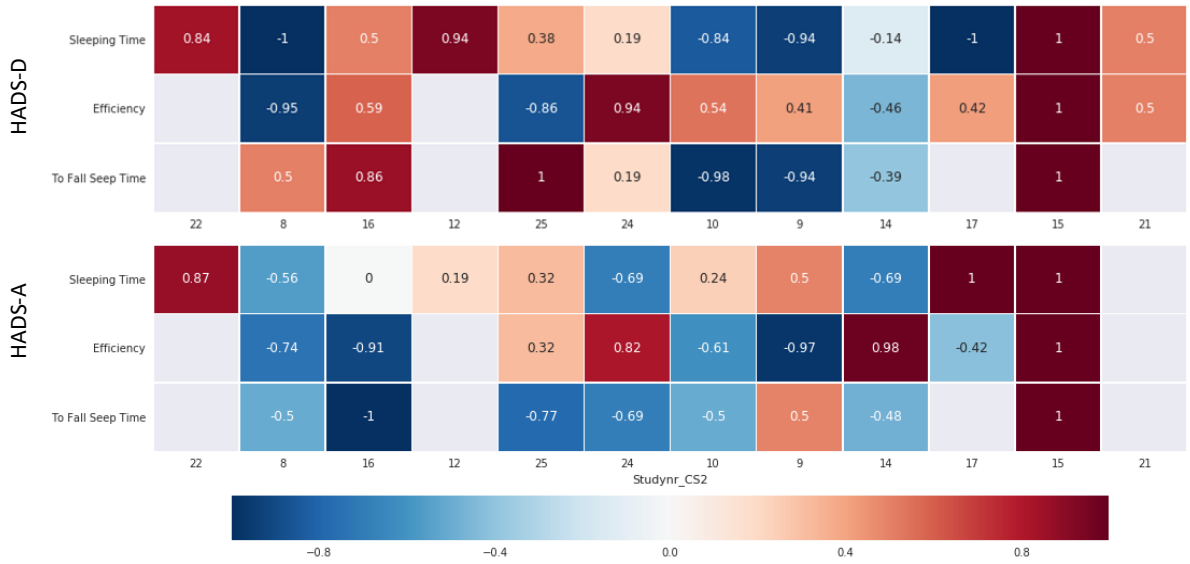


Figure 24: Correlation between the HADS scores (HADS-S and HADS-D) and the number of anomalies in the sleeping variables (sleeping time, efficiency and to fall sleep time), for patient.

To sum up, although EQ-5D-Anxiety/Depression and HADS results show some relation. The EQ-5D is too abstract making difficult for patient to answer accordingly to the reality s/he is living. Whereas the HADS is more precise, since has more concrete questions. No common correlations between the HADS and the sleeping variables have been found among all the patients. The limitations of this study, and possible reason for the results obtained, were the dissimilarities between patients and their number of days in each period, the incomplete sleeping data, and the discretization of just studying three time points. Finally, the lack of other baseline-characteristics of patients (to describe the dissimilarities) and the limited amount of patients (n=12) have to be taken into account.

5. Conclusions and Future Research

In order to create a system capable of inferring the overall QoL of the monitored patient, the patients' behaviour has been studied in terms of performed daily-life activities monitored through a wristband (i.e., Fitbit). Four different experiments have been performed, two with volunteers' data (the Sleep Quality, Normal Habits versus Outliers experiment, and Workload Assessment experiment) and two with patient's data (Quality of Life Assessment as a Continuous Variable experiment and Quality of Life Assessment Focussing on Anxiety/Depression experiment).

The first experiment was aimed at detecting nights with an abnormal sleeping activity, with the final goal of predicting sleep quality. The main result of this experiment is that the proposed approach could be used as an intermediate assessment of the patient's QoL, by characterising the quality of sleeping through the objective data gathered through the wristband. The investigated methods present one relevant limitation: they need a huge amount of data to be successfully trained, since the sleeping patterns are extremely personal and one model should be trained for each patient. This limitation prevents us to apply them to the CONNECARE patients' data, also because the diversity in each site and impossibility to perform the same study in all the site mixing the overall patients' data.

The second experiment was aimed at predicting continuous variables. In fact, our assumption is that characterizing QoL as a continuous variable is useful computing improvements and worsening in the QoL. To complement this model, the unsupervised method explored in the Sleep Quality experiment is proposed to split the days between normal and abnormal days and train to different models to improve the results. Results are promising and, thus, we are recruiting more volunteers in Eurecat that wear a wristband and with historical data to apply the model and to study its replicability. The approach used in this experiment was the base of the following experiment.

In the Quality of Life Assessment as a Continuous Variable experiment, the QoL were meant to be assessed as a continuous variable using the methods explored in the Workload Assessment experiment. In order to have labelled data to train the model, we needed weekly answers of the EQ-5D-5L. The clinicians from ASSUTA agreed to prescribe the EQ-5D-5L weekly through the SMS. By analysing the data from the patients who answered the EQ-5D-5L more than one day, we may envisage that that there is some correlation between the QoL and the physical and sleeping activity. Unfortunately, the patient's compliance to answer the EQ-5D-5L was low and there was not enough labelled data to train the models. The main problem with this experiment is related to the overall CONNECARE scenario. In fact, to perform this experiment continuously measurements are required. In other words, we need that the patients answered to the EQ-5D-5L constantly every week. Being an implementation study and not an experiment in the laboratory, it was quite hard to do that inside the project. In particular, clinicians did not want to stress the patients in answering the questionnaires to not badly influence the overall clinical study, being the quality of life assessment a transversal objective of the project and not a specific goal of the

implementation studies. As a future research, we are planning to perform experiments in a controlled setting with the unique goal of measuring the perceived QoL of the patients. This study is out of the scope of the CONNECARE project and will be performed by researchers in Eurecat in an internal project.

Finally, encouraged by the CONNECARE reviewers and following the recommendations from the 2nd review report, we focused on Anxiety and Depression rather than trying to assess the overall QoL. Thus, in the Quality of Life Assessment Focussing on Anxiety/Depression experiment the correlation of Anxiety and Depression and sleeping activity was analysed to better understand if the Anxiety and Depression affects the sleeping activity. Guided by the clinicians from UMCG, we decided to include HADS questionnaire, which questions are more specific questionnaire than those from EQ-5D-5L. The results of comparing both questionnaires showed that they are correlated even if it is worth noting that patient's perception is not the same when answering them. EQ-5D-Anxiety/Depression question is too abstract making difficult for patient to answer accordingly to the reality s/he is living. HADS questions are more concrete, thus the patient answer can be more precise. The main limitations of this study, and possible reason for the results obtained, were the dissimilarities between patients and their number of days in each period, the incomplete sleeping data and the discretization of just studying three time points. Since UMCG is planning to follow the implementation studies when the CONNECARE project will be finished, we are studying how to repeat the experiment in a more uniform scenario to verify if our thesis is correct and if it is possible to apply it more broadly.

The work presented in this deliverable, even if at a preliminary stage due to the small data from the CONNECARE clinical studies, shows that there is a correlation between anxiety/depression and sleeping activity. The two experiments performed with the volunteer show two interesting approaches to assess quality of life with respect to sleeping activity. The first experiment needs several historical data and, thus, it should be applied by relying on historical data, for example from the Fitbit repository. Its applicability should be in the improvement of the recommender system (currently aimed to monitoring physical activity) to send recommendations also for sleeping activity. The second experiment is very promising and we already applied it to the third experiments in which the CONNECARE patients have been involved. The two experiments performed with the CONNECARE patients, in ASSUTA and in UMGC, have the limitation of the number of patients wearing the wristband during the night and that weekly answering the EQ-5D-5L questionnaire. This limitation is related to the aim of the CONNECARE implementation studies. In fact, it was impossible to have a direct follow-up to ensure questionnaire answering and/or wearing the wristband during the night all the days. It is also worth noting that, even if the QoL assessment was a task of the CONNECARE project, it was not an objective of the CONNECARE implementation studies. Instead it was an exploratory research activity transversal to the overall project. It is worth noting, for example, that in Lleida clinicians did not accept forcing patients to wear the wristband during the night and to answer questionnaires not related to the work-plan concerning the case study. Thus, this research has to be done gathering data in a different context and in a controlled environment (e.g. in a laboratory). In so doing, we will be able to create the models, evaluate their results, and define and implement the QoL assessment

system. In fact, being these preliminary results interesting, in Eurecat we are planning to start experiments with volunteers under the umbrella of an internal project aimed at providing, among other things, recommendations and nudges regarding sleeping activity.

As for the further future directions, from a research perspective, the proposed approach could be adopted in conjunction with the sensor-based system summarised in the deliverable D4.4 “Assistive monitoring tool” to improve the models by including also the environmental data. In so doing, more precise conclusions could be achieved improving the overall performance of the models. The final solution should be adopted to predict worsening in the mental status as well as to send feedback to professionals or patients.

Finally, regarding potential applications of the QoL assessment system, results of the monitoring on sleep and anxiety/depression, could be adopted to provide an intelligent system for clinicians that sends alarms in case of anomalies or worsening of the patient’s status. This intelligent system should be then integrated in the SACM and the alarms showed together with the rest of notifications both in the main dashboard and in the notifications page. Moreover, sleeping and anxiety/depression monitoring could be the input of a recommender system that sends suggestions and nudges to the patient for giving support in improving the mental status. In the context of CONNECARE, the corresponding recommender system should be integrated as a further module in the recommender system described in the deliverable D4.6 “Recommender system for self-management” and available through the SMS.

6. References

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