Depression Assessment Based on Technology using Smartphone Data

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PREFACE

The work presented in this thesis was performed at the Institute for Systems and Robotics of Instituto Superior Técnico (Lisbon, Portugal), during the period March-September 2019, under the supervision of Prof. João Miguel Raposo Sanches. The thesis was co-supervised at Hospital Beatriz Ângelo by Dr. Miguel Constante.

DECLARATION

I declare that this document is an original work of my own authorship and that it fulfills all the requirements of the Code of Conduct and Good Practices of the Universidade de Lisboa.

ACKNOWLEDGMENTS

First, I would like to thank my supervisor Prof. João Sanches for all the support that he gave to me. The period of the realization of this thesis was probable the most difficult that I have ever had in my personal life and he always understood me and never made me stop believing that I could finish it. It was very important to me and I will never forget that. He consistently allowed this thesis to be my own work but steered me in the right the direction whenever he thought I needed it.

There are 5 people who are essential in my life. My parents, my brother and my girlfriend. Without them I could not achieve anything that I have achieved till today. My father and brother are always by my side and whatever I need I know I can count on them. I'll never be able to thank both enough for that. My mother is the person who helps me the most, that better understands me and is the one I trust the most in the world. I can only thank her for all she has done to help me achieve all my dreams. My girlfriend is my emotional pillar that allows me to have the strength to always overcome everything, without her I wouldn’t have been able to complete this thesis for sure. Thank you all for everything.

Finally, I would like to dedicate this thesis to my uncle and dear friend José that passed away during the period of realization of this thesis.

ABSTRACT

The general definition of psychiatric disorders is based on subjective symptoms, reported by the patient, which normally forms diagnostic patterns. Those symptoms are generally difficult to detect, characterize or quantify mostly because mental health doesn´t have biomarkers to analyse. Smartphones offer the promise of collecting behavioural data unobtrusively, *in situ*, as it unfolds in the course of daily life. Data can be collected from the onboard sensors and other phone logs embedded in today's off the shelf smartphone devices. These data permit fine grained, continuous collection of people's social interactions, daily activities and mobility patterns, which means that we can collect valuable information about psychological states. It was collected objective behavioural data (acceleration, ambient light level, battery level, GPS coordinates and phone logs) with Ethica Health app. Not only objective, but also subjective data (PHQ-9 scores, stress barometer and sleep diary) were collected from all participants with that app to represent the traditional methods of depression diagnosis. Having the two types of data, it was possible to correlate them, and the results were very optimistic, where people more depressed showed more stress (r=0.87), less activity (r=0.89) and less location variability (r=0.85). A desktop application to treat and visualize data as well as provide useful metrics from the data in depression diagnosis was also designed and fulfilled its purpose. This proof of concept study showed that smartphones can be used as instruments for unobtrusive collection of behavioural data that are associated with depression, something that can be revolutionary in this area.

Keywords: Mental Health, Depression, Diagnosis, Objective Data, Smartphone, Passive sensing

RESUMO

A definição de transtornos psiquiátricos é baseada em padrões de diagnóstico relatados pelo paciente, ou seja, é baseada em sintomas subjetivos. Estes sintomas geralmente são difíceis de detetar, caracterizar e quantificar principalmente porque a saúde mental ainda não possui nenhum biomarcador para os analisar. Os smartphones têm a capacidade de fazer uma colheita não invasiva de dados comportamentais, à medida que as pessoas se desenrolam no curso da vida quotidiana. Os dados podem ter proveniência de sensores que estão embebidos no smartphone e de outros registos telefónicos. Esses dados permitem uma recolha refinada e contínua das interações sociais, atividades diárias e padrões de mobilidade das pessoas. Neste estudo, obtiveram-se dados comportamentais objetivos (aceleração, nível de luz ambiente, nível de bateria, coordenadas GPS e registos telefónicos) com a aplicação da Ethica Health. Foram recolhidos não apenas dados objetivos, mas também subjetivos (pontuações do PHQ-9, barómetro de stress e diário do sono) de todos os participantes a partir dessa aplicação para ter dados relativos a métodos tradicionais de diagnóstico de depressão. Foi possível correlacionar os dois tipos de dados e os resultados foram muito otimistas, onde as pessoas com mais tendência para a depressão apresentaram maior stress (r=0.87), menor atividade (r=0.89) e menor variabilidade de localização (r=0.85). Foi construída uma aplicação de computador para tratar e visualizar dados, além de fornecer métricas úteis a partir dos mesmos no contexto do diagnóstico de depressão e a mesma cumpriu a sua função. Esta prova de conceito mostrou que os smartphones podem ser usados como instrumentos para a recolha não invasiva de dados comportamentais associados à depressão, algo que pode ser revolucionador nesta área.

Palavras Chave: Saúde Mental, Depressão, Diagnóstico, Dados Objetivos, Smartphone, Deteção passiva

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1. INTRODUCTION

Nowadays when we think about Health Care, we immediately start to imagine the manifold support of medical devices, technological applications and telehealth systems that leads to a diagnose or helps the physician to get a more detailed state of the patient. All of that is very good but when we talk about Mental Health that scenario is completely different. The psychiatric care is scarcely supported by any technology mainly because the mental illness only manifest itself mainly in the way patients behave in their daily life, and this is the problem, monitoring in every day real life is very difficult [1].

The general definition of psychiatric disorders is based on subjective symptoms, reported by the patient, which normally forms diagnostic patterns. Those symptoms are generally difficult to detect, characterize or quantify mostly because the mental health doesn´t have biomarkers to analyse. In summary, the diagnosis of psychiatric disorders consists of a description by the patient and his family and/or friends, which is most of the times unreliable due to the disruptive conditions that this kind of pathology has, which can lead to an incorrect assessment of the patient situation. This type of diagnosis can be also unreliable because sometimes the symptoms are so subtle and invisible that nobody notices them. So, is very important to get detection, quantification and monitorization methods in order to increase the efficiency of the diagnosis.

What can be measured in order to help the physicians getting the correct diagnosis? This mental illness is related to behaviour changes in people daily lives, as sociability, physical activity or sleeping patterns [2]. Having that in mind, investigators start to think in many devices that could measure those changes without interfere with people normal way of living, the wearable devices.

We can think in a lot of wearable devices, but all of them have one problem: people are not used to wear them, which can affect the reliability of the data, but there is one device that almost all of the people wear it all the time, the smartphone. This sensor rich, computationally powerful and ubiquitous device offer the promise of collecting behavioural data unobtrusively, in situ. Their onboard sensors and other phone logs embedded in today's off the shelf smartphone devices have an amazing capability to collect all the data that we need to detect behavioural changes. With that we can collect in a continuous way people social interactions, daily activities and mobility patterns, which means that we can collect valuable information about their emotional and cognitive states.

In this work, we pretend to design objective methods to increase the efficiency of the therapeutic strategy that is adopted in each situation using the smartphone as a behavioural data collection tool. More specifically our focus is to build an objective tool that could help not only in the moment of the diagnosis, but also to see if the treatment that was adopted was good or bad in a personalized way. This last part is also very important in nowadays Portugal because, with that, the physicians are able to 'control' their patients without the need to have them in the hospital or health care centre, which is very good because most of the times psychiatric consultations in public health are separated by several months and the

physician doesn´t know what happened during that time. Having this king of tool, they will be able to see the evolution of the patient with the treatment adopted, if that is the case, after the consultation.

1.1 MENTAL ILLNESS – DEPRESSION

1.1.1 Epidemiology

Unfortunately, depression is a common disorder in our days and for that reason all of us in some moment of our life have contact with it by knowing someone that suffers from it or even as a patient.

Depression affects people from all ages, all backgrounds, in every country. It causes anguish and has a lot of impact on people's capacity of doing their daily tasks, having terrible consequences to family and friend's relationship.

According to World Health Organization (WHO) [3], around the world exists more than 300 million persons with depression, which is equivalent to 4.4% of global population. Approximately half of these people live in the South East Asia Region and Western Pacific Region, which makes sense due to the larger populations of those two regions (Figure 1).

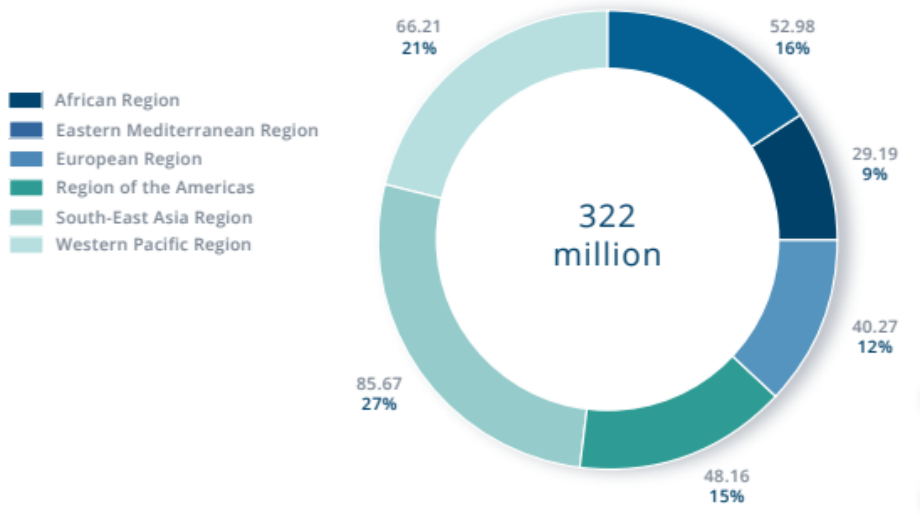

Figure 1 - Cases of depressive disorders (millions), by WHO regions

The age is a critical factor in this mental disorder, having higher prevalence rates in older adulthood, but depression also occurs in children and adolescents, of course in a lower prevalence rate comparing to older age groups. Regarding the genre, depression affects more female than male persons (Figure 2).

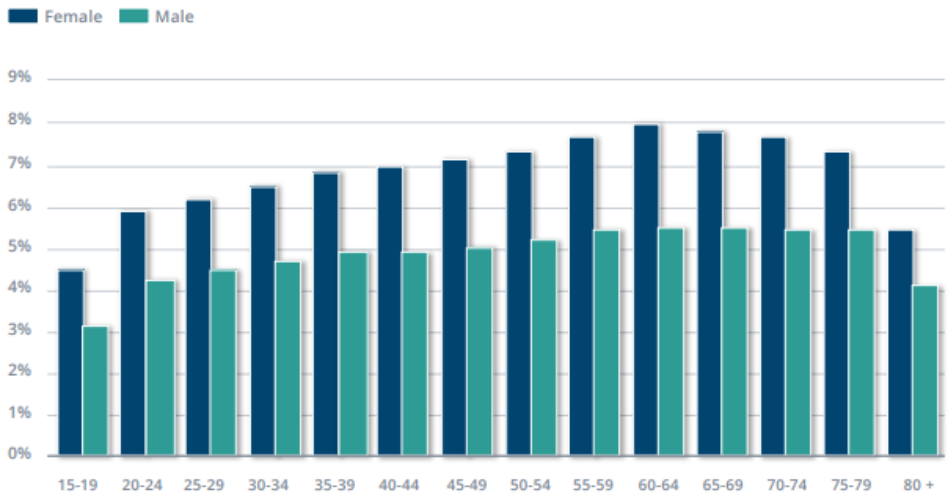

Figure 2 - Global prevalence of depressive disorders

Between 2005 and 2015, the number of people living with depression increased in 18.4% [3] which is due to the growth of the global population allied with a proportionate increase in the age groups that depression is more prevalent that happened in this period.

In Portugal, the numbers are even more worrying. According to official numbers [4]:

- More than one fifth of Portuguese people suffers from some mental disorder;
- At least 8% of the population has depression;
- It is estimated that there are 400 thousand Portuguese people between the ages of 18 and 65 who suffer from depression each year;
- In 70% of suicide cases the cause is depression and every 8 hours a Portuguese die of suicide.

Having all these numbers in mind, it is evident that depression is one of the biggest illnesses of our time and for that reason it is very important that its prevention and treatment is done as efficiently as possible.

In order to help increase efficiency, it is necessary to understand what depression is and the physiology that is behind it.

1.1.2 Definition and Physiology

Depressive perturbations are characterized by sadness, lack of interest or pleasure, guilty and low self-esteem feelings, change of sleeping and eating patterns, tiredness and low concentration levels. It can be lasting or recurrent and can lead to a severe negative impact on people's capacity of doing their daily activities [3]. In the last instance, depression can lead to suicide.

Depression falls into two main categories:

1. Major depressive perturbation: This category is related to depressive episodes and can be defined as mild, moderate or severe depending on the quantity as well as the severity of the symptoms, on which includes depressed mood, loss of interest and decreased energy.
2. Dysthymia: The principal difference is the fact that this category is persistent or chronic contrary to major depressive episode which tend to be last longer and less intense. Regarding the symptoms they are very similar.

As already mentioned before, depression affects persons from all the ages and from all the social extracts, but the probability to develop this disorder increases with poverty, unemployment, stressful life events like the death of a close person, physical disorders and problems caused by drugs and alcohol.

The most important thing to have in mind is that depression is not a sign of weakness or a negative personality. It is a major public health problem and a treatable medical condition.

What is the physiology behind depression?

Most of the people believes that depression is caused by chemical imbalances, but that figure of speech doesn´t capture how complex this disease is. As a matter of fact, chemicals are surely involved in this process, but it isn´t a simple chemical being too low and another too high that explains all. Instead, there are many chemicals involved that act both inside and outside nerve cells. Besides its complexity, it's believed that several causes interact to develop depression, one of them is of course faulty mood regulation by the brain, but also genetic vulnerability, stressful life events, medications and medical problems. Having that in mind, it is common that two persons with the same symptoms can have different inside problems and therefore the treatments that work best are also entirely different.

Investigators believe that nerve cell connections and growth and the functioning of nerve circuits have a great impact in this disorder. Despite that, a completely understanding of the neurological fundamentals that regulates mood is still far away.

The development of neuroimaging techniques has opened the potential to investigate structural and functional abnormalities in living depressed patients. Sophisticated forms of brain imaging such as positron emission tomography (PET) or functional magnetic resonance imaging (fMRI) has led to a better understanding of which brain regions regulate mood and how other functions can be affected by depression. Areas that are most affected by depression are the amygdala, hippocampus and thalamus (Figure 3).

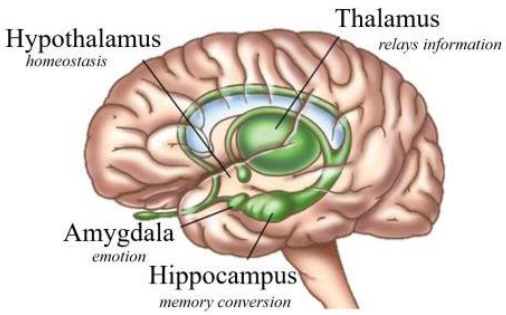

Figure 3 - Areas of the brain affected by depression: Amygdala, Hippocampus and Thalamus.

The amygdala is a group of structures of the limbic system located at deep brain that perform a primary role in the processing of emotional responses such as anger or pleasure. This area is activated when a person recalls emotionally charged memories and for that reason, the activity is higher when a person is sad or depressed.

The human brain has two hippocampi, one in each side of the brain. Is part of the limbic system as well and has a central role in processing of information from short term memory to long term memory and recollection. Several studies showed that in some depressed people the hippocampus is smaller, and the cause is probably related to stress, since experts believe stress can suppress the production of new neurons in this area [5].

The thalamus has several functions including relaying of sensory signals from other parts of the brain to the appropriate part of the cerebral cortex, which controls key functions in our life like speech, behavioural reactions, movement, sleeping, thinking, seeing and memory. Most everything that goes into the cortex must go through the thalamus first [6]. A few studies have reported an increased activation of the thalamus in depression but surprisingly most studies have noted no difference [7].

If depression provokes a decreasing in neurons in the hippocampus, there are some exploratory relations between the low production of new neurons on that area and low moods. The antidepressants support this idea because they increase the concentration of neurotransmitters (chemical messengers in the brain). Yet, normally people don't feel better as soon as levels of neurotransmitters increase and the reason could be that mood only improves with growing of the nerves and formation of new connections, something that can takes weeks. If that's the case, the responsible for mood improvement is neurogenesis (generation of new neurons) and the depressive medications development must take that into account.

As we saw, neurotransmitters play a big role in this process since we can often influence them to good ends. They are chemicals that relay messages from neuron to neuron and the antidepressant medication tends to increase the concentration of them in the spaces between neurons, called synapse. So, the neurotransmitters are essential to nerve cell communication. When a neuron becomes activated it passes an electrical signal from the cell body down the axon to its terminal, where neurotransmitters (chemical messengers) are stored. This signal releases certain neurotransmitters from synaptic vesicles

into the synaptic cleft. As the concentration of a neurotransmitter rises in this space, they begin to bind with receptor sites embedded in the dendrite of receiving neuron (figure 4).

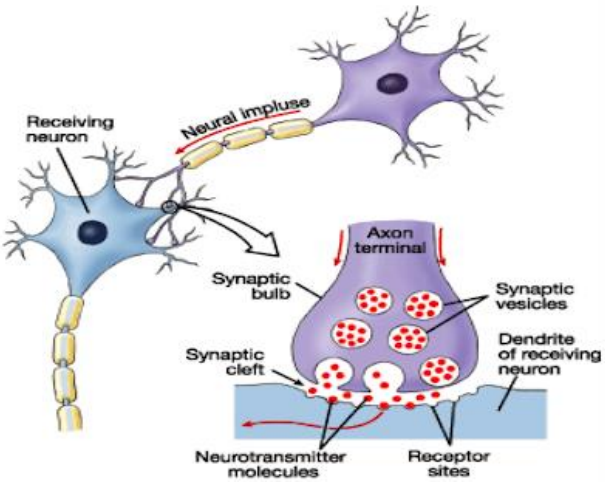

Figure 4 - Neuron and synapse in biological neural network.

Usually, brain cells produce levels of neurotransmitters that keep senses, learning, movements and moods in stable state, but in people with depression the process that is responsible for that is compromised. A fault in some part of these complex system could significantly affect mood, for example receptors may be oversensitive or insensitive to a specific neurotransmitter, causing their response to its release to be excessive or inadequate, which means that the normal release is compromised and that could lead to an significantly alteration of mood.

There are many types of neurotransmitters, but the ones that is believed to be important in depression are:

- Acetylcholine, that has an important role in sustaining attention, in learning and memory. Parts of the body that use or are affected by this neurotransmitter are referred to as cholinergic and has been shown that damages on that cholinergic system are associated with memory deficits;
- Serotonin, also known as the ‘feel good’ chemical. Serotonin is very related to depression because helps regulate sleep, appetite and mood and inhibits anger and aggressiveness, all of them linked to depression symptoms. In depressed people the serotonin transmission is reduced, and the extreme low levels of this neurotransmitter have been associated to a higher risk for suicide. In the past two decades this neurotransmitter has taken a big role regarding depression due to antidepressant medications like Prozac and other selective serotonin reuptake inhibitors (SSRIs), drugs that specifically act on serotonin molecules;
- Norepinephrine or noradrenaline is a neurotransmitter but also a hormone. Along with adrenaline is crucial in the ‘fight or flight response’, which means stress or danger situations. It may trigger anxiety and be involved in some types of depression, but changes in norepinephrine levels do not affect mood in every person. Having this is mind, medications that targets this neurotransmitter may alleviate depression in some people and not in others;

- Dopamine is essential to movement and creates positive feelings associated with reward or reinforcement that motivate us to continue with a task or activity. There is evidence that low dopamine levels can contribute to depression in some people [5]. Medications that have a behaviour like dopamine or that stimulate the release of it in the brain have worked in several people that suffer from depression, but there are also some problems associated with them. Drugs as cocaine or alcohol also stimulate dopamine production and eventually some depressed people tend to self-medicate with these other substances. So, substance use activates dopamine reward cycle and potentially addiction can develop, which means that it's possible that drugs that targets dopamine receptors could carry a high risk for abuse.

There are other neurotransmitters that can be important in depression, including glutamate and GABA, but researchers are still learning about the role these brain chemicals play in this disorder.

We can conclude that low levels of neurotransmitters can contribute to depression, but what is the cause for that? Research founds several potential causes for these chemical imbalances in the brain [5]. Those causes include low production of a specific neurotransmitter; low number of receptor sites; neurotransmitter doesn't reach the receptor cell because presynaptic cells take it back up too soon; not enough chemical precursors (molecules that build neurotransmitters) and/or enzymes (molecules that help build neurotransmitters. When there is a failure anywhere in the process, a problem in neurotransmitters levels can occur.

The biggest challenge that is remaining regarding the connection between neurotransmitters levels and depression is the fact that doesn't exist a way to consistently and accurately measure these levels.

Role of Genetics and Stress

The human body is completely controlled by genes and the brain isn't an exception. With the course of life, different genes turn on and off to make the right proteins at the right time that are involved in biological processes essentials to our body. If there is any problem associated with this process an alteration in our biology probably can happen. That alteration can happen in a way that results in mood instability. If a person is genetic vulnerable to depression, any stress, however small, can take on large proportions.

The literature has shown that someone with a first-degree relative diagnosed with depression (parent, brother) has more probability to get depression in their lifetime compared to those who hasn't [8]. Despite that, is important to note that these links don't account for the many people that suffers from depression and don't have any family history with this disorder.

Hereditary isn't just about individual genes, instead it is a complex interaction between many factors. To study health conditions, investigators analyse possible changes in genes called variants. These variants are classified according to the effect that they have on the gene, if there is any effect at all. If a person has a genetic variant it is more probable that this person will develop a condition associated with that

variant, if that variant has some significance [8]. Besides all of that, there are no studies that have definitively defined a single gene as the cause of depression, instead of that, researchers believe that all genes and genetic variants each contribute to the main person's risk.

Obviously, another factor that is fundamental in depression is stress. Everybody at some moment of life must deal with stressful events that can be many things. These events can be single like a natural disaster, divorce or the death of a loved one or an ongoing problem such as chronic illness or marital strife. If the stress associated with some event exceeds the person capacity to cope, it can lead to depression.

When a person deal with stress events the body immediately starts to react to it. A chain of chemical reactions and responses is triggered when depending on the stress duration, the consequences can be none (the body returns to normal) or can be long lasting. Stress is an automatic physical response to a stimulus that requires an adjust to some change. That physical response can be higher heart rate, muscles more tense, increased breathing rate and sweating.

That stress response starts with a signal from the hypothalamus that joined with pituitary gland (located at the base of the brain) and the adrenal glands (located above the kidneys) form the hypothalamic-pituitary-adrenal (HPA) axis, a trio responsible of a multitude of hormonal activities in the body that is very important in depression. Hormones are signalling molecules that are transported by the circulatory system to target distant organs in order to regulate physiology and behaviour. Initially, after the stimulus, the hypothalamus secrets corticotropin-releasing hormone (CRH) that will follow a pathway to the pituitary gland. There, CRH stimulates the secretion of adrenocorticotropic hormone (ACTH), which is then pulsed into bloodstream to get adrenal glands. Once ACTH reaches adrenal glands, it stimulates them to synthetize and release their hormones, specially cortisol. All steps of stress response system described before are represented at figure 5. This increase in cortisol levels are responsible to prepare the response to stress by raising the heart rate and blood pressure; accelerating the breath as the body takes in extra oxygen and sharpening of senses, such as sight and hearing, in order to increase alertness.

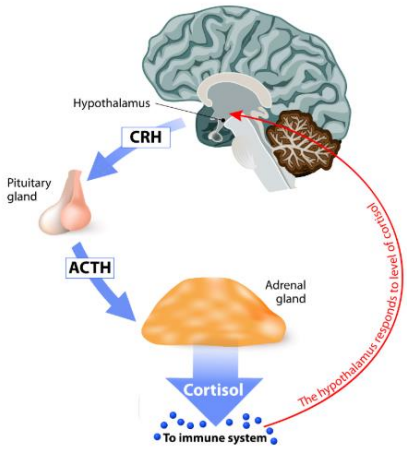

Figure 5 - Stress Response System. (CRH - Corticotropin-releasing hormone; ACTH (Adrenocorticotropic hormone)

Research believes that CRH is an important part on thoughts, behaviours, emotional reactions and involuntary responses coordination [5]. Working with multiple neural pathways, CRH influences neurotransmitters concentration throughout the brain, so perturbations in hormonal systems may affect neurotransmitters and vice versa. Several studies showed that people with depression typically have increased levels of CRH and for that reason multiple antidepressants act to reduce these higher CRH levels. When CRH levels return to normal, depressive symptoms tend to recede [8].

With this sub chapter we can conclude that there are multiple factors and risks that can explain depression development. In fact, the responsible is not only one factor, instead there are several factors that interact with each other (genetic, psychological, environmental and biological factors) to bring on depression (figure 6). So, for that reason, every person that suffers from depression is different and that is the main difficulty when physicians are dealing with this disorder.

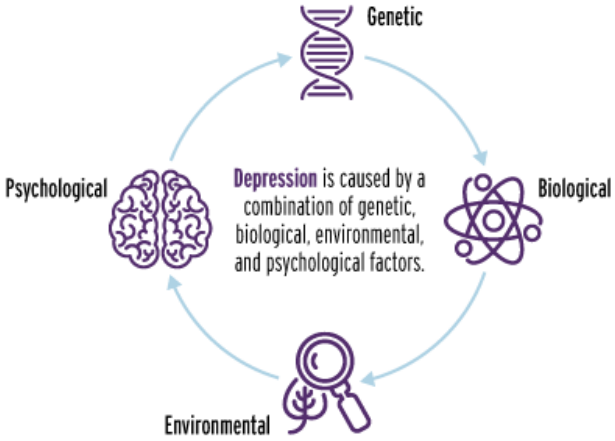

Figure 6 - Common causes for depression. Source: Psychological Health Center of Excellence.

1.1.3 Diagnosis

As mentioned before, depression is a very complex disorder and for that reason it is still difficult to treat. Current common practice for treatment selection is an educated guess approach, in which physicians prescribe their approved therapies in a stepwise manner [9]. There is already a lot of evidence based clinical guidelines to manage depression that can be already a support to specific treatment recommendations, but the symptom heterogeneity present in the diagnosis of depression creates a significant barrier to it. And now we are beginning to get into the main problem that exists nowadays associated with mental disorders, the way that the diagnosis is made and the tools that exist to make it in the best way possible.

Regarding depression, how does a doctor make the diagnosis? Most laboratory specialized test such as blood tests, are not very helpful when it comes to diagnosing depression. The most important tool that the physician has in order to get the correct depression diagnosis is talk with the patient [9]. To do that, there are several recognized series of standard questions to screen for depression symptoms. With

this talk, the physician can learn other things about the patient that can be relevant than just the overall state of health. The patient can report about his mood, behaviours and habits that are very important in this disorder. As we already know, depression can manifest in very different ways and that turns the diagnosis often difficult to make. Depression people can sleep or eat to excess or almost eliminate those activities.

In the consultation, the physician conducts a complete diagnostic evaluation based on depression family history or other mental illness, evaluate the symptoms and duration of them based on patient's report such as [9]:

- Sadness almost every day;
- Loss of enjoyment on things that were once pleasurable;
- Increased or decreased appetite and if were any major weight change;
- Excessive sleep or insomnia almost every day;
- Fatigue or loss energy almost every day;
- Concentration problems;
- Guilty or hopeless feelings;
- Movement retardation that is noticeable by others;
- Thoughts of death or suicide.

A person needs to have at least five of these symptoms with at least one nearly daily for two weeks to be diagnosed with depression [9]. The symptoms duration can last for weeks, months and even years and the episodes may occur only once in a lifetime or may be recurrent or chronic. In severe cases, it could be last forever.

After seeing all of patient and family history, the physician may ask for some physical exams to see if that is any physical condition that may be causing the depression symptoms. One common example is hypothyroidism that can cause some of them [9]. The physician normally also asks for all medications that the patient is taking as well as alcohol and other drugs that he might be using.

Having all the above in mind, we can conclude that the diagnosis of this disease is clearly subject to a lot of subjectivity. If the diagnosis is only based on reports by patients and family, most of the times it can be very unreliable, mostly because sometimes the symptoms are so subtle and invisible that nobody notices them. It is very important in every disease that exists biomarkers that helps the physician to detect, monitor and quantify the symptoms. In order to increase the efficiency of the depression diagnosis, it is now essential to design objective methods that complements the subjective ones that are already recognised.

As we saw, what the physicians wants to know is always related to how the patients behave in their daily live. Mostly they want to know about patient's sociability, physical activity and sleeping patterns. So, now the problem is how it is possible to measure patient's behaviour in their daily lives.

1.2 TECHNOLOGY BASED DIAGNOSTIC SUPPORT TOOLS IN PSYCHIATRY

1.2.1 Wearable Devices

In the past three decades, computational power has increased a lot, the storage space prices have dropped and electronic components are miniaturised in a way that a few years ago it was impossible to even imagine that [10]. With that, researchers started to think about a device that can monitor people in their daily lives, which is the key behind psychiatry diagnosis. If there is something that can measure their habits, the diagnosis efficiency will increase a lot because the physician will have objective data that would describe very well their patient's behaviours and that allied with current diagnostic procedures probably will reduce a lot of possible mistakes. It is important to notice that our job as biomedical engineers is always trying to help the physician to get the most accurate diagnosis possible by developing tools that might be useful and never replace the role of the physician that is always fundamental to make the best diagnosis possible, especially when we are talking about mental health.

The only possible way to monitor behaviour is asking people to wear a device that collects useful data to this purpose and here enters the big importance of wearable devices in psychiatry. Researchers started to think in many possible wearable devices equipped with multiple sensors and this has been an area of great interest from the researcher point of view [10].

Having a wearable device should not restrict the patient's motility and daily activities, which allows monitoring in everywhere. The placement of these devices has been a concern because it must provide flexibility and comfort for patients to behave like they do in normal life, and of course the acceptance of them is also depending on that comfort. There are already many wearable devices in the market for fitness and wellness that can easily be incorporated into clinical practice. Some of them can be placed on the almost any part of the body: wrist, ankle, chest, arm, legs, and many more (figure 7). The location depends on what we want to measure, since we want the data as reliable as possible.

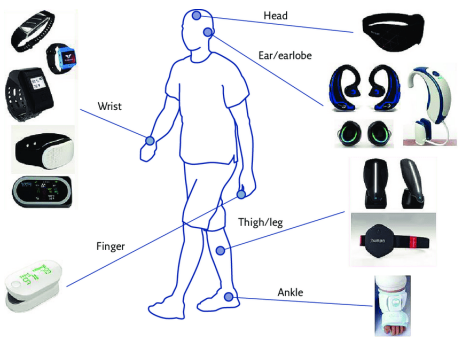

Figure 7 - Location on the body of several commercially available wearable devices. (Image source [11])

Nowadays there is a lot of sensors available at the market. In mental health, we must consider the sensors that can contribute to behaver's description and one that is always present to get that description is the accelerometer because is essential the presence of at least one motion sensor to obtain a good approach of it. Due to that, in the past few decades, actigraphy has been recognized as a useful method to study peoples behave since it provides a good estimate of sleeping patterns and periods of activity/restlessness in people's daily life [12]. Activity levels have been measured using wrist and chest worn actigraphy in younger depressed subjects [13] and the results were very promising. Despite its potential, there are important limitations to the interpretability of the data that actigraphy gives due to its lack of agreement as what constitutes light, moderate or intense activity because it depends on the person obviously, so these arbitrary categorizations reduce data fidelity. Instead, devices should give raw output directly from the accelerometers, like McGinnis R. et al [14] where they incorporated a three-axis accelerometer and three-axis angular rate gyroscope on a belt-worn device to track child motion during some mood induction tasks with a high level of accuracy, sensitivity, and specificity. Is important to notice that in this last study they used more sensors than just the accelerometer and that correlation was obviously very important to get better results. As the author Elle McGinnis said, "the results suggest that wearable sensors can be a great screening tool and with this we maximize the chances of scaling this technology to screen children for internalizing problems".

As we saw, there are a lot of published studies involving mental illnesses and wearable devices, specially using motion sensors to identify activity patterns, but can they represent accurately person's daily life?

As mentioned in the last subchapter, the traditional methods of collecting behavioural data that physicians use in their consultations are associated with a lot of biases due to lack of attention to some critical behaviour, memory limitations and socially desirable responding [15]. With wearable sensors there is also some aspects that have biases associated. Studies with wearable sensors are divided in two sections, the first one is related to those who make the collection in a laboratory environment, where people have to complete a serious of tasks and then researchers do their analysis based on the data they have collected from the behavioural response to those tasks. The bias in this first section is obvious, people aren't acting normally as they do in their normal lives. It is important to collect objective behaviour as people play out in the context of their natural lives. The second one is related to those who do their study with people using the wearable device in their daily lives, but they also have issues. These methods have been difficult and time consuming to use and very intrusive for the participants, and if the person is not feeling as if he has nothing clinging to his body, he is not behaving naturally, which is a very important bias to consider. The best alternative to being as unobtrusive as possible would be to deal with a wearable device that people already wears almost every time. A great candidate to eliminate all those biases referred before is the smartphone, a wearable device that is very powerful and most of the people who use it are unaware of it.

1.2.2 Smartphone as a Behavioural Collection Tool

According to Marktest Telecommunications Barometer [16] in 2018 there was nearly 6.8 million smartphone owners in Portugal, representing close to three quarters of all mobile phone owners. Over the last few years, the possession of this type of mobile phone has been on an upward trend, rising from 32.5% in 2012 to 73.9% in December 2017 (figure 8).

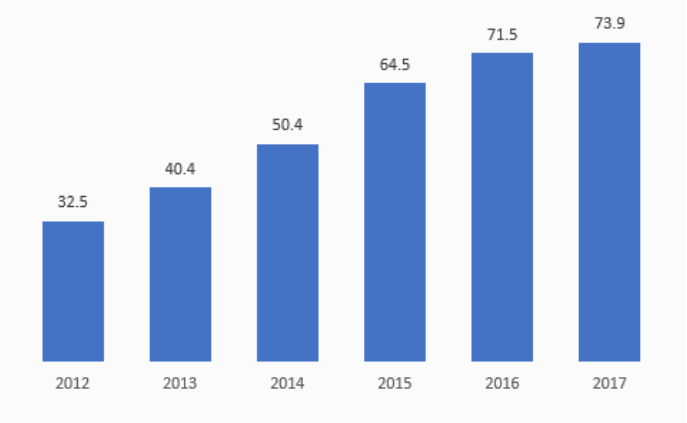

Figure 8 - % of Smartphone Users from all mobile phone owners in Portugal [16].

From this study the authors also concluded that the percentage of smartphone users is higher in the youngest and in the higher social classes. Portugal follows the worldwide trend, since the total number of smartphone user today surpasses three billion and is forecast to further grow by several hundred million in the next few years [16], mostly because the technological advancements in smartphones have led to the support of several everyday tasks. The countries with the highest number of smartphone users are the most developed country and China, India and the United States leads this ranking having each country more than 100 million user mark.

Since this market is already so huge and the trend is to increase in the next years, working with this wearable device seems to be perfect. Adding to that, these phones are very sensor rich, increasingly computationally powerful and, as we saw, their **ubiquity** can be very helpful to us since it provides unparalleled access to people daily lives in an **unobtrusive**, **dense** and **continuously** way. Another factor that contributes to this is the capacity that smartphones have to query people about their subjective psychological states with notifications, which is perfect because with that we have not only objective data but also subjective data that is already validated by years of medical clinic. So, using the smartphone as a diagnostic support tool seems to be an idea with lots of potential.

Smartphones already come equipped with all the sensors that are needed to obtain the best behaviour description possible. The information that they give are divided into three categories: Social interactions, Daily activities and Mobility patterns. The combination of all the sensors data can capture all those behaviours, which are very useful to identify possible depression symptoms. The most common sensors in all smartphones are:

- Accelerometer, a small inertial sensor that records the movement of the body where the device is placed and measures the acceleration force applied to the device, including the force of gravity, with three coordinates (unit m/s^2);
- GPS, that obtains the phone location from satellites in latitude and longitude coordinates;
- Light sensor, that measures the ambient light level, by monitoring the brightness of the environment (lux);
- Microphone sensor, that records audio from the acoustic environment.

There are more kinds of data that we can collect from the smartphone and that they are useful for us, as Phone Logs that are essential to know about patient's social interactions. Call and SMS logs records incoming and outgoing calls and messages. Other phone data includes Battery status log that records the battery recharge times.

Working with some of those data it is possible to describe **social interactions** as Monsivais D. et al [17] did. In that study, the authors explored mobile phone calling activity and concluded that the onset and termination of the resting pattern of urban humans follow sun progression and they also showed that calling activity period follows the same dynamics as solar midnight. Monitoring call and SMS messages logs for frequency, duration and unique persons contacted in incoming and outgoing interactions it is possible to know easily people's social interactions. Adding to that microphone and Bluetooth sensors it is also possible to have an approach of face to face interactions.

Daily activities can also be described with data from smartphone sensors, as physical activity (using the accelerometer as we saw in previous chapter with actigraphy in wearable devices) or sleeping patterns (with exterior light, accelerometer and phone usage logs).

Mobility patterns are also very important to monitor people's routines, which is very important to get the best possible behaviour description. These patterns included people's duration of time spent in various places (home or work), the distance travelled in each time period and of course their routines. All of this can be captured with GPS, accelerometer, exterior light or Wi-Fi sensors.

With all those embedded sensors, smartphone now offers an easy data acquisition offering a lot of opportunities to continuously monitor patients in their natural environments due to its ubiquity. Because of that, smartphone-based tracking studies have started to emerge and today is one of the most relevant subjects in this area and for that reason there are already multiple apps designed to collect data from the smartphone sensors. One of them is MoodRhythm [18] that was built to detect sleep and disturbance of rhythms in affective disorders. The authors worked with patients with bipolar disorder, where they give to them smartphones with MoodRhythm preinstalled for four weeks. This app uses machine learning to estimate scores of rhythm stability of daily life and the results were very reasonable since they were able to distinguish between stable and unstable rhythm days with good accuracy.

There are still very few studies that uses smartphone as a data collection tool in diagnosed depressed people. The only exception is a very important study that is currently being done by Marcham et al. [19] and the results of this study will totally change the way that the community see the smartphone as a

diagnostic tool in depression, positively or negatively speaking. I say this because this study has a lot of advantages comparing to all the other that have ever been done. The length of the study is long (2 years) and the sample is also very large (600 participants from three countries with a recent history of depression). During all that time, participants will be asked to wear a wrist-worn activity tracker as well as to download several apps on their smartphones. Dealing with their own smartphones is also an advantage because in that way the bias of dealing with another smartphone rather than their own is not present. The apps will collect passively data from the sensors but will also send questionnaires (traditional methods), deliver cognitive tasks and speech assessments to analyse also anxiety and quality of life. The smartphone and wearable sensors will collect data in a continuously way and the other tasks will be asked monthly, quarterly or semi-annually depending on what task or questionnaire we are talking about. With all the devices, sensors, questionnaires, tasks, sample and duration this study seems to have the potential to be revolutionary in this field. The authors expect to determine the usability, feasibility and acceptability of their technique to provide "real-time objective multidimensional indications of clinical state in individuals with depression".

Having all of that in mind, our proposal is to get a proof of concept of smartphone sensors utility in depressed people and to build an app that will help the physician with objective measurements about his patients behaviours, never forgetting that our goal is to help the physician to obtain the best diagnosis possible and never to replace his important role. Without a physician sensitivity the efficiency of a mental health diagnosis will greatly decrease, so our goal is to add one more diagnostic aid tool to the panoply that the physician already has to, along with all traditional methods, increase his diagnostic accuracy.

2. METHODS

2.1. DATA COLLECTION

2.1.1. Sensors

First, it was essential to define what sensors we could use in order to capture social interactions, daily activities and mobility patterns of the subject. To decide that, it is necessary to consider that not all smartphones have all the sensors and that it isn't efficient to use many sensors, since the collection must be done continuously and for that reason, typically, the amounts of data produced are huge (several gigabytes) something that can be costly to store on the phone in terms of battery life and also costly to transfer and store on a server. Another consequence of using too much resources that must be considered is the possible termination of the app that is collecting data. If the sensors that are monitoring generate lots of data, the chances of app termination increase, because this kind of apps are supposed to work behind the scenes and without any participant involvement. The app will be continuously running on the phone, capturing data. The problem is that both Android and iOS operating systems are designed such that when an app is not used directly by the user very often, they stop and

terminate it. Battery low levels and the demand of various resources are causes of that termination. The best is to use only fundamental sensors and combine different types of sensor data to obtain the best subject behaviour description possible. The sensors used in this study are presented in table 1 as well as the behaviours that each one capture.

Table 1 - Sensors used and behaviours that each one capture.

Sensor	Behaviours Captured		
	Social Interactions	Daily Activities	Mobility Patterns
Accelerometer		✓	✓
GPS		✓	✓
Battery		✓	
Exterior Light		✓	✓
Call and SMS logs	✓		

The accelerometer, who measures acceleration on three axes, is a motion sensor that is present in almost every smartphone and with the power of it is possible to capture subject's movement along the day due to the ubiquity of the smartphone in people's life. Subsequently it can provide a good estimation of subject's participant's physical activity and it is very important to describe daily activities and mobility patterns. GPS is also very important since it measures the precise location of the smartphone in latitude and longitude coordinates. With that, it is possible to have objective data about people's routines and if it is very variable or not as well as their travelled distance variability. Battery level sensor presence is essential because unlike other data sources which can be unavailable, all smartphones are shipped with batteries and that guarantees that regardless of device type, this data will be surely available. Adding to that, battery level data can be combined to other data and help a lot in behavioural analysis. For instance, if the phone was plugged in all day, we know that data from that day must be treated with caution. Light sensor is also crucial due to its environment description. Whit this data it is possible to know the intensity of light in the phone's context, which combined with other data can be very helpful to capture daily activities and mobility patterns. The last one is to use subject's call and SMS logs. Of course, the goal of using this data isn't to get the content of the calls and messages, instead is to get number and length of incoming and outgoing calls and messages as well as number of unique calls and messages. Having that, it is plausible to describe very well subject's social interactions.

All the sensors give very important data about people's behaviour that might be affected by depression symptoms. If physicians had this data, probably they would probably change the way they make their diagnosis of depression. Obviously, each person is a different person and for that reason this method

should not have the purpose to be general but instead to be one more tool to achieve personalized medicine.

In order to obtain the smallest possible bias, participants must use their own smartphone to behave completely normal when they are dealing with it. If it is with a different smartphone, people will not act naturally. Almost all data collection will be done on a continuous basis, without the need for subject intervention, but during it will be necessary to answer some surveys in a method called experience sampling method (ESM).

2.1.2. Experience Sampling Method

Experience Sampling Method (ESM) is very often used in studies related with mental health disorders and specifically with depression [20]. Since the traditional methods for assessment in clinical psychology typically relies on self-reports collected at clinic visits as we saw before, it is important to have also that kind of subjective methods to be a baseline or to correlate with the objective one using smartphone sensors. For that reason, while the sensor data is being collected, an ESM is also happening. The participants were asked to fill out some surveys with different periodicities, weekly or daily. This can also be done by the smartphone through notifications, the participants receive them at a specific time and then fill out the surveys, which is another big advantage of the smartphone.

In this study there was three different surveys, a stress barometer, a sleep diary and the Patient Health Questionnaire-9 (PHQ-9) that is a recognized test for people with depression [21].

In susceptible people, stress events (chronic or acute) can lead to major depression as we saw previously. So, it is important to consider that in this study. To get that, a survey with a stress barometer was included to be filled daily at the end of the day. It was only one multiple choice question and it had also the function of maintain the collection app active every day to avoid operation system terminates the collection due to user inactivity. Daily Stress scores were calculated as the stress ratings for everyone, daily. The survey was the following:

Today I feel:

a) Very well!
b) Feel ok.
c) A little bit stressed.
d) I am stressed.
e) I am really stressed!

Regarding the sleep diary, it consisted in two surveys, one in the morning when the subject wakes up and the other at night before going to bed. This diary, as the name shows, had the purpose of knowing

people's sleeping patterns and other aspects about daily actions that could influence behaviour. For instance, number of alcoholic and caffeinated drinks, number and duration of afternoon naps, intensity of physical exercise, at what time they have lunch and dinner and of course at what time they go to bed and wake up and how much time did they sleep are some of the questions that this sleep diary has. In attachments A and B there are the exact questions that were asked to the participants. This sleep diary was fill out by the participant in an independent way, i.e. they filled out at the time that was more convenient to them.

The last survey is the PHQ-9 questionnaire. This survey is the major depressive disorder module of the full Patient Health Questionnaire (PHQ). The PHQ is a recognized diagnostic tool for mental health disorders used by health care professionals that is quick and easy for patients to complete [21]. The PHQ-9 is specific for depression and has a score from each of the nine DSM-IV criteria as 0 represents not at all and 3 represents almost every day, providing a 0-27 severity scores. The DSM-IV criteria it's a coding system that mental health care professionals use to make diagnosis of a given mental disorder. As PHQ-9 is a very reliable and valid measure of depressive severity, this questionnaire was used to collect the depression severity of the participants. Higher PHQ-9 scores are associated with decreased function status and increased symptom-related difficulties [21]. This score was very important to aggregate participants in depressed and not depressed ones. This survey was completed weekly as more spacing is required for hypothetical mood changes. The questions that are part of this questionnaire are represented in attachment C.

With all those surveys, it was possible to accurately collect behaviours with traditional methods, the subjective ones. One of the biggest advantages of using smartphone as a behaviour collection tool is that objective (sensors) and subjective (surveys) behaviour data can be collected at the same time.

2.1.3. Ethica Data Systems and Privacy Considerations

There are already available several platforms that collects data from smartphone sensors. In this study data was collected using Ethica Health, an automatic data collection software application from Ethica Data Systems that runs both on the Android and iOS smartphone operating systems [22] which is very good because with that anyone could participate independently of his/her operating system. Ethica Health collects data from all the smartphone sensors available, including the ones that we needed. Data from the accelerometer, GPS coordinates, battery level, exterior light level and call and SMS logs were collected continuously from the participants with Ethica Health. This platform was created for investigative purposes, only investigators that work for some institute or university can create a study in. Before creating any study, the researcher needs to register and to say for who does he work for. Only after that is possible to create a study with the sensors and surveys that are needed. With Ethica Health we can define every setting of the app that is then installed on participant's phone, for instance the duration of the study, how the data should be uploaded, the periodicity of data upload reminders and

each subject participation period. Regarding the surveys, it is possible to define the best triggering logic for us, if it has to notify the participant to fill out or not and it also has all the possible designs for questions, from single choice, multiple choice, free, image, audio, number, calendar and a lot more.

Before choosing sensors and creating surveys, is fundamental to participants know what they are doing. Leading to this kind of personal data is very dangerous due to privacy reasons. With smartphone sensors data it is possible to enable serious privacy intrusions by allowing inferences about a device holder's location, identity, demographics, personality, health status, emotions and activities. Having behaviour data, the privacy is compromised. For that reason, participants had to accept an informed consent that is represented in attachment D. Adding to that, participants can disable data collection by pressing a snooze button within the app and each one's identity was maintained anonyme by randomizing attached a user id. Finally, data didn't include any content of calls and SMS, only the number and duration/length of them.

The app was set to collect data for one minute every 5 minutes from the sensors that were needed, including data from the accelerometer, GPS, exterior light, battery level and phone logs. Ethica Data Systems uses opportunistic sensing method for the data collection and uploads the data to the server based on user settings for preferred network usage to data upload [22]. Battery level records are fundamental to see if the phone is functional, because if it is these records are guaranteed to be recorded. Data quality can therefore be estimated by counting the number of duty cycles for which battery data is available.

Before data collection started and after accepted the informed consent, participants had to complete a short demographic survey including age, gender, qualifications and employment situation. Adding to that survey were the stress barometer and the sleep diary that they had to fill out every day and the PHQ-9 that they had to complete initially and then repeated weekly. The triggering logic of these surveys were daily for stress barometer and sleep diary, but the first one was daily launched with a notification and in the second one the participants could start it by tapping a button that it was created for sleeping diaries. At the end, the app home page that the participants saw was the one in the figure 9:

Figure 9 - Ethica app home page with two buttons, one for morning and the other for the evening sleep diary.

2.2. STUDY DESIGN

The initial idea was to make this study with people that doesn't have any mental disorder diagnosed and with actual patients that suffer from depression. Everything was headed for that even because the study along with informed consent was delivered to the ethics committee of the Beatriz Ângelo Hospital (in Loures, Portugal) to be performed with the depression patients of this hospital. The committee's response was positive, but it was too late because the deadline for submission of the thesis was already very close. Not all is bad because although data from patients with depression could not be obtained, the study has already been approved by the ethics committee of this hospital, so in the future the door is already open for another study, which is very positive.

So, this study had the purpose of a proof of concept. The total number of participants was 10, on which 4 were male, 5 were female and 1 didn't want to say. 5 participants were aged between 21-30 years, 3 between 31-40, 1 between 41-50 and 1 between 51-60. 6 had a degree and the other 4 had compulsory education. Regarding the employment situation, 2 of them were students and the other 8 were employees.

The methodology of this study is represented in table 2, where it is the chronology that each participant followed.

Table 2 - Study Chronology.

Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Procedure Explanation	X																															
Informed Consent	X																															
Demographic survey		X																														
PHQ-9		X							X							X								X								X
Sleep Diary		X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X	X X
Stress Barometer		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Smartphone sensor data and phone logs			Continuous collection of accelerometer data; GPS; intensity of ambient light; battery level; duration and frequency of outgoing and incoming calls and SMS.																													

Detailing, each participant had the application 'Ethica' installed on his smartphone and was associated with our study in the app, a process that was accompanied by the creators of the study. After all the installation process of the required software, the participant was asked to answer a demographic questionnaire and then answered other three questionnaires that had two different time intervals, two of them daily and the other weekly.

They completed two short questionnaires a day (one in the morning and one before bed) called sleep diaries and filled out the stress barometer once a day at night for the entire 31-day study period. At the beginning of the study, each participant answered the PHQ-9 questionnaire and then they repeat it weekly until the last day of the study.

After completing the first questionnaires, the data extraction from the smartphone sensors started. This data collection was continuous throughout the study. Data from accelerometer, GPS, ambient light intensity, battery level and duration and frequency of calls and SMS was extracted (no information was recorded about the content of SMS or calls). Concluding, apart from questionnaires responses, no

further procedure was required except to behave as usual in their normal life. Participants were instructed to enable the GPS sensor at all time during the study. Due to privacy reasons, Ethica Health also provides an option to turn off data collection for a period of one hour at a time and if the sensors are accidentally or not turn off, the app automatically notifies the participants that collection is paused.

The study duration was decided having in account that to notice mood changes in people's life requires some time. After talking with experienced psychiatrists and seeing the length of the studies already done, it was possible to conclude that due to depression subtleness the studies must have some substantial length. The longer the study, the greater the likelihood of happening changes in people's behaviour and due to that more significant will be the results. Keeping this in mind, the experienced psychiatrists said that within a month it is possible to notice mood swings and behavioural changes, so it was decided that considering all the issues, a 31-day period was the best study duration.

2.3. DIAGNOSTIC SUPPORT TOOL

After collecting the data, it is very important to have some program that can handle data processing and visualization and that returns some useful metrics in the depression diagnosis context from the data. If the physicians had a tool like that it would be a major evolution in the way they do their diagnosis. In this work, it was built an app that has the pretension to deal with all those features in order to get an objective tool that can help the physician.

At this stage, we only have raw data in CSV (comma separated values) format. The first thing to do is obviously to download and process the data. The software that was used to build the app was MATLAB [23] because it is a great tool with many professionally developed toolboxes to wear in data analytics. It provides all that is needed for data processing and visualizing. Adding to that, MATLAB has an environment called MATLAB App Designer that allows the creation of standalone desktop and web apps that is perfect because in that way it is possible to build apps with all the processing tools that MATLAB has, which is very good for our purpose. So, the first thing that this app does is the possibility to browse data in archives that are in CSV format. The home page of it is represented in figure 10, where it has buttons to each of the sensor data (accelerometer, GPS, Exterior Light, Phone Logs and battery level) and the path of each one.

Figure 10 - App Home Page

After downloading the data, it is important to pre-process the data. The most problematic data is related to the accelerometer because adding to the noise situation that is common for other sensors, this data combines acceleration due to sensor motion but also due to gravity. To solve this problem, it was used a low pass and high pass filter. The goal is to filter out the portion of accelerometer data caused by gravity from the portion of the data that is caused only by the sensor motion which is the important one for us. The low-pass filter, basically speaking, is a smoothing function because it turns the original signal into a signal that doesn't depend on short-changes. So, with low pass filter, it is possible to reduce the influence of sudden changes on the accelerometer data and the resulting filtered values are the ones related to gravity effects. With that, we separated the gravity component from the acceleration data. But what we want is a filter that allows us to eliminate the gravity component but also to take into consideration only the isolated sudden changes in acceleration. To do that, it is important to reduce the low frequency variations and keep the high-frequency ones, which is the definition of a high-pass filter. The effect of low pass and high pass filtering on each time series is to create gravitational and body acceleration data in different directions. To build the low-pass and high-pass filters, it was used the algorithm describe below. Empirically, it was determined that the best low-value filtering factor was 0.8. With that, it was generated a value that uses 20% of the unfiltered acceleration data and 80% of the previously filtered value. The algorithm used was:

$$alpha = 0.8$$

$$for$$

$$Low_{Pass} = alpha \times PreviousValue + (1 - alpha) \times CurrentValue \quad (1)$$

$$High_{Pass} = CurrentValue - Low_{Pass} \quad (2)$$

$$end$$

The algorithm was performed for all three accelerometer axis values, X Y and Z. The acceleration magnitude was calculated by:

$$|a| = \sqrt{a_x^2 + a_y^2 + a_z^2} \quad (3)$$

In figure 11 there is represented plots of the original accelerometer magnitude signal, also of the magnitude of the low-pass filter values which are the ones related to gravity effects and the bottom one is the plot of acceleration magnitude related to the action of both low and high pass filters, i.e. the values that are related only with sensor motion.

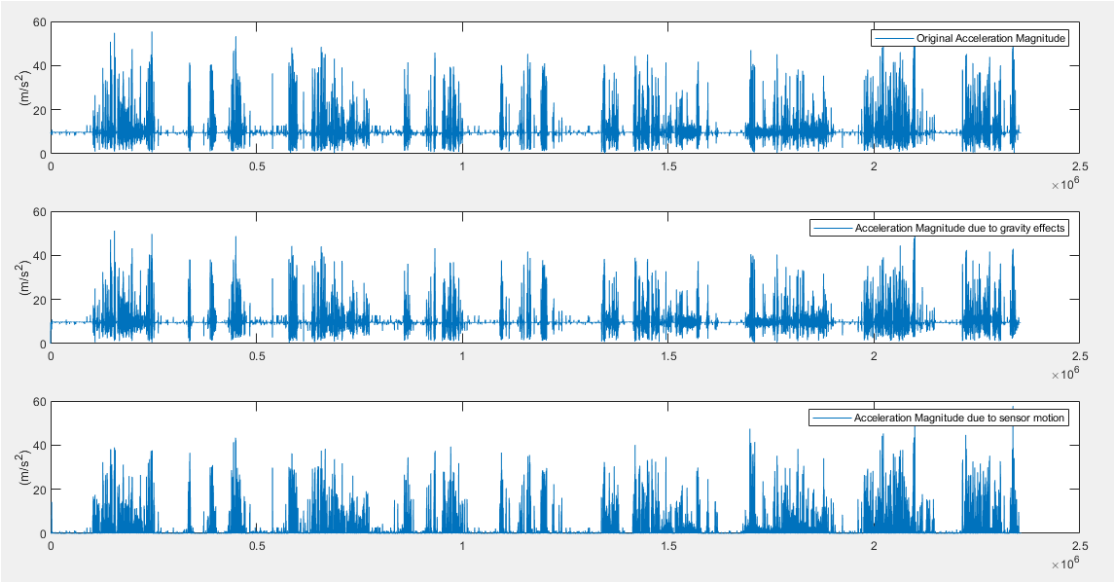

Figure 11 - Acceleration data pre-processing. The first plot is the original acceleration magnitude, the middle one is the acceleration magnitude due to gravity effects and the bottom one is the acceleration magnitude due to sensor motion.

Then, the page that appears in our desktop app is the one represented in figure 12. This page has two buttons that redirects to two different things. The 'Plots' button takes you to a data visualization tool and the 'Metrics' button shows a page of some meaningful metrics in depression context that were developed.

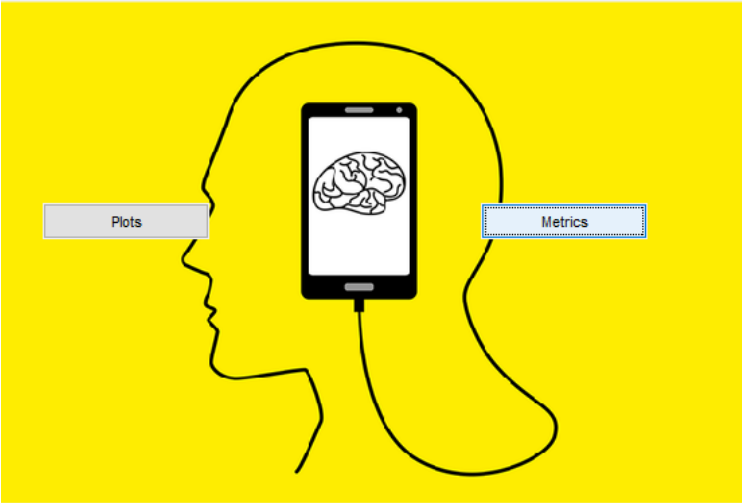

Figure 12 - App page after data download.

If we click on the 'Plots' button, the page that appears is the one represented at figure 13. Visualizing the data is a very important part of this app because it gives to the physician the possibility to see the sensor's data in a timeseries. This can be very helpful for them because in that way they can make their own analyses and get their conclusions analysing it for themselves. For instances if they want to see the mobility patterns of a specific day or week or if the patient makes many social interactions or not at a specific time period this is possible with this tool. This possibility can be a great help in diagnosing depression.

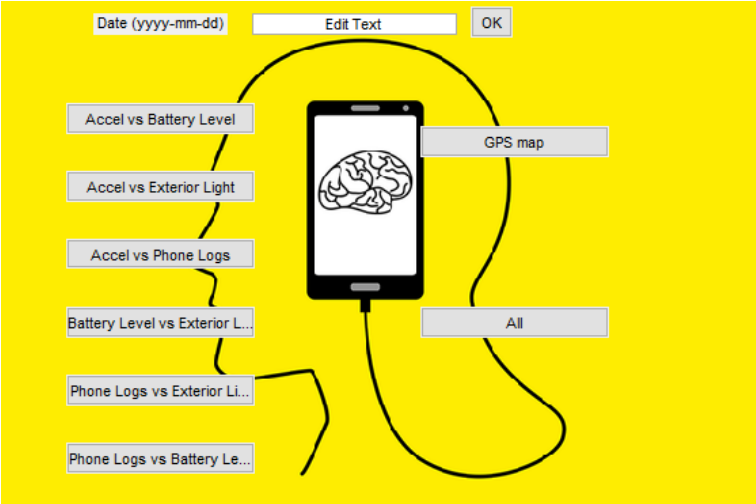

Figure 13 - Data Visualization page.

This page allows to visualize all the sensor's combinations in a specific day. The charts can zoom in and out if it is required. After choosing a date in the format yyyy-mm-dd, the user can see the data from that day of accelerometer and battery level; accelerometer and exterior light; accelerometer and phone logs; battery level and exterior light; phone logs and exterior light; phone logs and battery level. The accelerometer data is on m/s^2, the ambient light is in lux, the battery level is on percentage and the phone logs are isolated events that are characterize by outcoming or incoming call or SMS. It also has the option of plotting all these data together on button with name 'All'. All the charts are in timeseries, which is good to enable a good combination of all the sensors information at a specific time in order to get the best conclusions possible from people's behaviour. The 'GPS map' button shows the trajectory that the subject took on a day on a real map, where it is possible to see the subject's mobility patterns on a specific day.

Instead of clicking on button 'Plots', if you click on 'Metrics' button, the page that appears is the one on figure 14. Here there are three different buttons: 'Social Interactions', 'Mobility Patterns' and 'Daily Activity'.

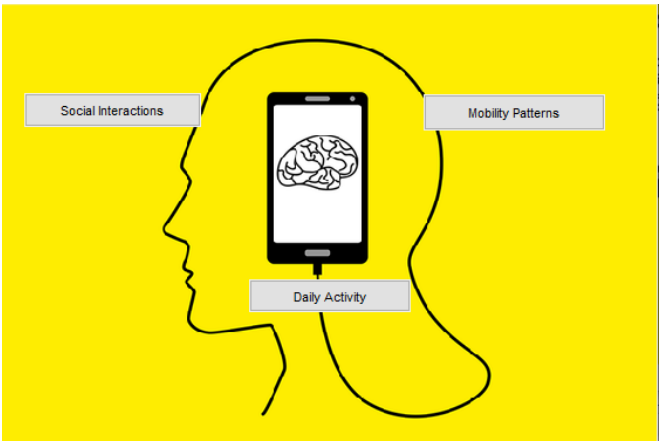

Figure 14 - Page of metrics information.

Of course, letting the physician get their own analyses by data visualization is great, but they also want some meaningful metrics that automatically show up simply by clicking in a button. It is more immediate and requires less time to get meaning from the data. Regarding the possible metrics, an important one is people's sociability. As we saw before, knowing if a person is sociable or not is essential in depression diagnosis. Being sociable or not is essential in depression as we saw before. For that reason, the button 'Social Interactions' shows: the number and duration/length of incoming and outcoming calls and SMS, number of calls missed, number of messages failed and the number of unique calls. This last one is very important because having 20 calls from 1 person has a very different meaning of having 20 calls from 20 persons. The same thing works for SMS obviously. Therefore, with this button it is possible to see the sociability of people during the study time.

Regarding the mobility patterns, this button shows how people mobilized by calculating the travelled distance and location variability with GPS data. With longitude and latitude coordinates, it is possible to know person's travelled distance by using the Haversine formula. This formula allows us to calculate the distance between two points in a sphere, as it is the case with the Earth. This formula was implemented to obtain the daily distance travelled by people based on GPS data. The equations that were used are:

$$a = sin^2(\varphi B - \varphi A/2) + \cos \varphi A \times \cos \varphi B \times sin^2(\lambda B - \lambda A/20) \quad (4)$$

$$c = 2 \times atan2(\sqrt{a}, \sqrt{(1-a)}) \quad (5)$$

$$d = R \times c \quad (6)$$

Where φ and λ are latitude and longitude respectively and R is the Earth's radius. The A and B values are essential trigonometric transformations with the coordinates to pass the angles to radians unit. With that we calculated the travelled distance, which is very good to see if the person follows a sedentary lifestyle or not. In order to see location variability, we computed the sum of the variance in latitude and longitude coordinates and with that the physician can conclude if the travelled distance was made between few places or not. This aspect has also a huge importance in depression due to tendency for sedentarism lifestyle that the patients normally show.

The last button is the one related to daily activity. To show daily activity, we used accelerometer data because it is a motion sensor very common in all smartphones and the subject doesn't have the option to tun off the sensor, which is the case with GPS for example. The accelerometer data was summarized into a high activity variable by calculating the percentage of time at which the summed variance of the device's acceleration on the three axes was above a defined threshold, that was 10 m/s^2. So, when the summed variance exceeded that value, it counted as high activity sample. As the other two metrics, these percentages were aggregated to the day level in order to provide an approximate measure of daily activity.

With this desktop app, it is possible to obtain many crucial things that can support depression diagnosis based on technology. The data is processed, it is possible to visualize and analyse people's behaviour with the plots combination and it also has three metrics that are very important in this context as social

interactions, mobility patterns and daily activity. With this, the physician gets objective data and thus can correlate them with the subjective ones he is already used to deal with. that he already has experience to deal with.

3. RESULTS

First, is important to refer that none of the participants had issues dealing with the Ethica Health application on their smartphones. In fact, all of them report that the interaction with it was simple and didn´t disturb their normal use with the smartphone. The surveys that worked as a baseline were completed by all of them and that is a proof of the simplicity of dealing with the app.

An important factor that distinguished the participants were the PHQ-9 scores. All of them completed that questionnaire weekly till the end of the study. Regarding that, 20% of them showed no depressive symptoms, 20% showed mild depression, 50% reported moderate depression, 10% moderately severe depression and none of them reported severe depression. This separation between the participants were fundamental to all the results that will be show next.

Beginning with the daily stress scores, it was model the relationship between daily stress and PHQ-9 scores. The results showed that people with higher PHQ-9 scores had also higher values of daily stress values (r=0.87). This relationship was established between the mean of the all daily stress scores in a week and the PHQ-9 scores that were obtained weekly. The participants with more stress are also the ones that showed more depression severity. It is also important to refer that in the weeks that the participants showed less score in PHQ-9 questionnaire was also in the weeks that reported less daily stress levels.

Regarding the sensors, is important to refer that all the collected data was stored in a SQL database. With that, it was possible to get only participants that had at least 25 days of participation. At the end all of them completed all the time of the study. The application that was built worked fine with all the data and the plots that will be on the next figures were all of them obtained with the buttons from figure 13.

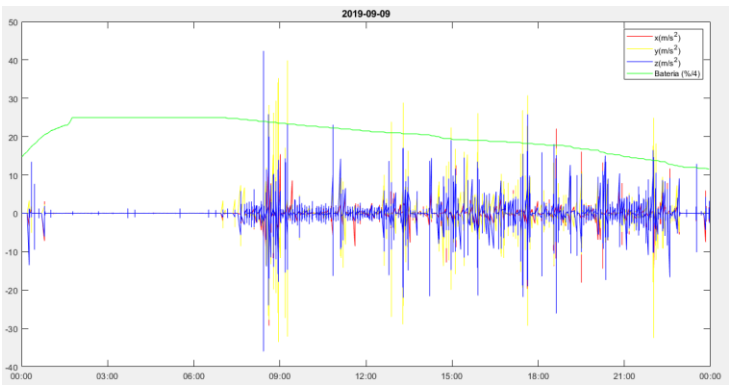

Figure 15 - Chart of acceleration (x, y and z in m/s^2) and battery level over time.

In figure 15, we can see the chart of acceleration over the three axes and battery level over time. With this chart we can see how the subject interacts with his phone throughout the day, knowing when he/she interacts with it the most. For instance, as normally people charge their phone at night, if the battery level increases and the accelerometer values are nearly zero, we have a good representation of person sleep time.

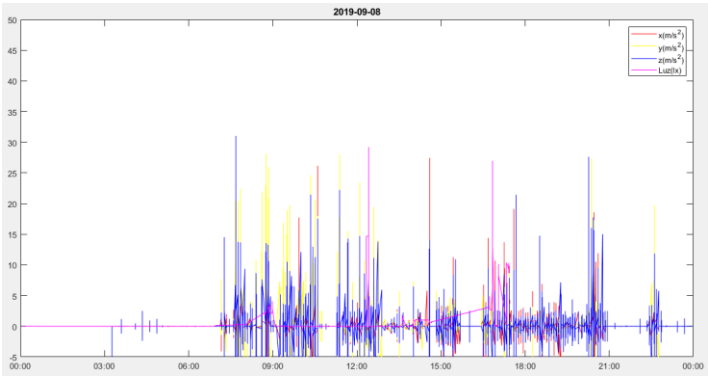

Figure 16 - Chart of acceleration (x, y and z in m/s^2) and ambient light level (lux) over time.

In figure 16, we can see the chart of acceleration over the three axes and ambient light level over time. Even more than the one represented in figure 15, this combination is probable the best one to get people's sleeping patterns because not all persons charge their phones at night but the majority sleeps with darkness.

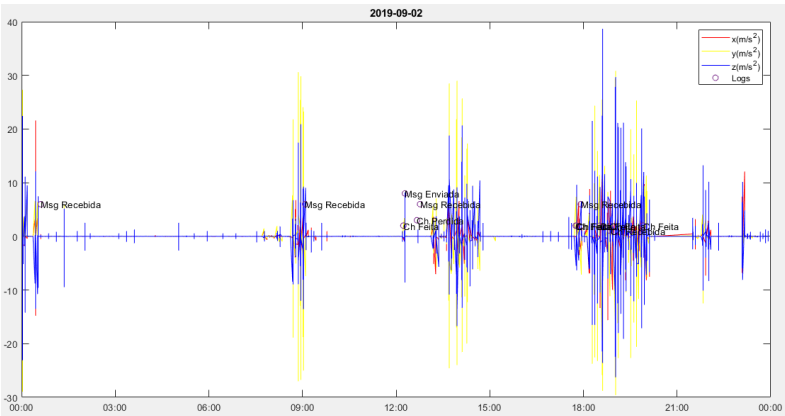

Figure 17 - Chart of acceleration (x, y and z in m/s^2) and phone logs over time.

In figure 17, we can see the chart of acceleration over the three axes and phone logs events over time. Phone logs are represented in the graphs as events with the type being written on top of them. If it is an incoming call, it says, 'Incoming call' and that also works for the other types of phone records. Each type has a specific plot line so that types are not written over each other. Looking at figure 17, it is possible to see that event phone logs happen at the same type that the accelerometer sensor moves with higher acceleration, which makes sense because people needs to be active to receive and make calls.

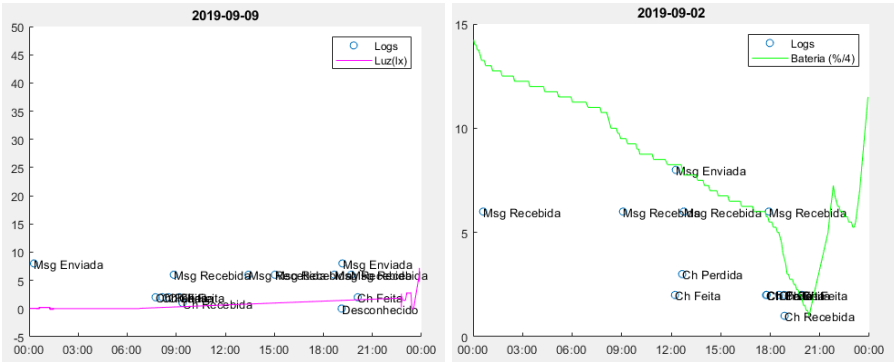

Figure 18 – Chart of phone logs and intensity of ambient light level (lux) over time (left) and chart of phone logs and battery level over time(right).

In figure 18, we can see the other double sensor two charts: the chart of ambient light level and phone logs events and the chart of phone logs and battery level over time.

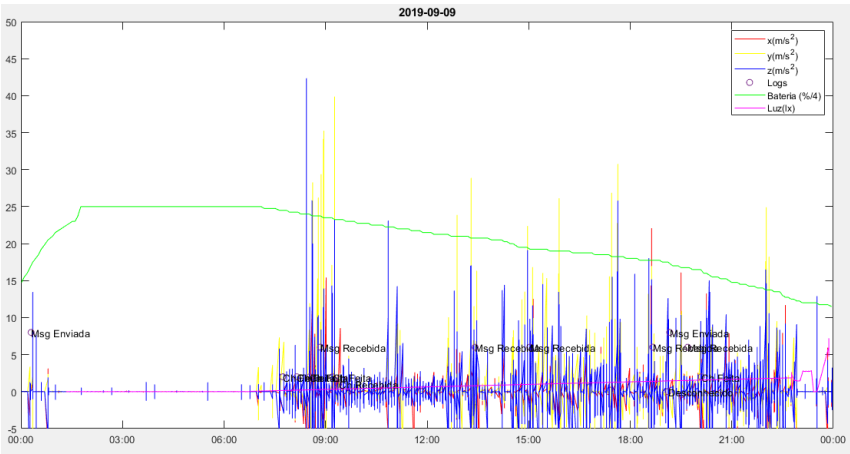

Figure 19 - Chart of all the sensors. Acceleration (x, y and z m/s^2), Phone logs events, battery level and intensity of exterior light (lux) over time.

In figure 19, it is represented the chart of all the sensors over time. This is the most important one, because in this one it is possible to combine all the sensors information to get the most accurate approximation of person behaviour. Looking at figure 19, we can see that at night the ambient light level and the accelerometer values are nearly zero and the phone was on charge. So, the combination of these three sensors values makes a great method to predict sleeping patters. Having that in mind, it was compared the sleep duration of some participants between two methods, the first with these sensors and the second one with the reports that were filled out by the participants in the sleep diaries. The results that were obtained were good, because having the reports as a baseline, the sleeping patterns calculated with the sensors information had only an error by approximately 1 hour, which is actually not bad due to the few participants and few time that this study had. The difference between night and day were clearly notice as we can see in figure 19, during the day people are more active, more exposed to light, have more social interactions and waste more battery due to increased phone usage.

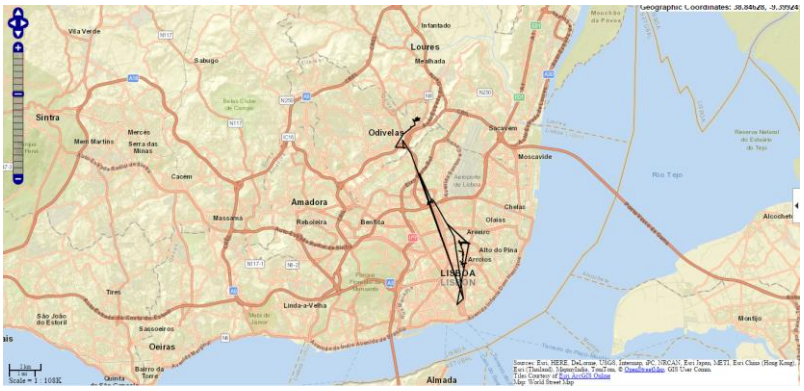

Figure 20 - Participant's trajectory with GPS sensor data in workday.

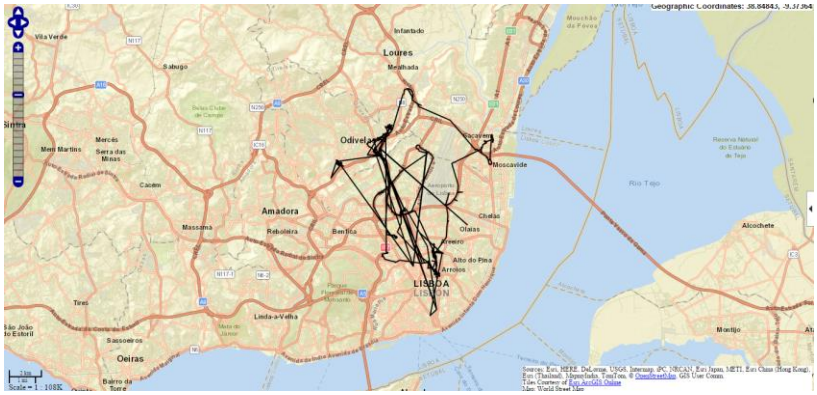

Figure 21 - Participant's trajectory with GPS sensor data in day off.

In figures 20 and 21 is represented the map with participant's trajectory that appears when the button 'GPS map' is pressed (figure 13). With this, is possible to see all the trajectory that the subject did in a day. The difference between figures 20 and 21 is that the first one represents a workday and the second one represents a day off (information obtained by the sleep diary reports). Normally people show more location variability on weekend due to their need to escape routine to rest and that was represented at almost all the participants as it is the case of this figure. So, with this tool we can see people's mobility patterns which is fundamental to our purpose.

Regarding the metrics, it was also correlated with PHQ-9 scores. All the metrics were obtained with the app that was built by clicking on buttons that are presented at figure 14. Starting with mobility patterns, an example is represented at table 3.

Table 3 - Information obtained with GPS coordinates.

	Distance_Travelled	Sum_Variance
2019-08-29	0.5148	0.0000
2019-08-30	37.5890	0.0011
2019-08-31	135.1566	0.0011
2019-09-01	159.2831	0.0014
2019-09-02	123.1133	0.0008
2019-09-03	134.7305	0.0005
2019-09-04	46.2797	0.0002

The distance travelled and location variability correlated very well with PHQ-9 scores, having people with less PHQ-9 scores (people with less tendency to be depressive) higher values in distance travelled and higher location variability (r=0.85). The difference between workday and weekend was also notice in this metric since the values for weekend presented higher values in location variability due to routine behaviours in workdays.

Regarding the phone logs information, this metric report all the social interactions that a subject does during all the study time. Table 4 represents an example of the output of the button 'Social Interactions' that is showed in figure 14.

Table 4 - Phone Logs information.

	Unknown	Incoming_Call	Outgoing_Call	Missed_Call	SMS_DRAFT	SMS_FAILED	SMS_INBOX	SMS_OUTBOX	SMS_SENT	AVG_Duration_IncomingCalls	AVG_Duration_OutgoingCalls	AVG_Length_InboxSMS	AVG_Length_SMS_Sent	Unique_Contacts
2019-08-30	0	1	3	0	0	0	4	0	0	59.0000	67.3333	90.2500	NaN	5
2019-08-31	0	0	4	0	0	0	2	0	0	NaN	20.2500	42.0000	NaN	3
2019-09-01	0	2	4	1	0	0	0	0	0	56.5000	36.5000	NaN	NaN	2
2019-09-02	0	1	6	1	0	0	4	0	1	57.0000	15.3333	111.2500	151.0000	10
2019-09-03	0	1	3	0	0	0	4	0	0	134.0000	35.6667	143.0000	NaN	5
2019-09-04	0	1	3	1	1	0	3	0	1	19.0000	5.0000	112.6667	19.0000	9
2019-09-05	0	0	0	0	0	0	1	0	0	NaN	NaN	145.0000	NaN	1
2019-09-06	0	1	0	0	0	0	2	0	0	106.0000	NaN	101.5000	NaN	3
2019-09-08	0	1	2	1	1	0	1	0	0	58.0000	7.0000	126.0000	NaN	6
2019-09-09	1	1	5	0	0	0	5	0	2	41.0000	35.4000	112.2000	121.5000	6
2019-09-10	0	1	4	0	0	0	5	0	7	55.0000	12.5000	171.2000	31.1429	4
2019-09-11	0	0	5	1	0	0	2	0	0	NaN	35.6000	142.5000	NaN	5

The correlation between social interactions and PHQ-9 scores didn't exist. For that reason, it is not possible to conclude that social isolation is necessarily a depressive signal, it clearly depends on the person. Despite that, people with higher values of PHQ-9 showed fewer social interactions variability, having less unique contacts that other subjects with less scores of PHQ-9 questionnaire. But it is very important to know people background and old habits to be possible to make a robust conclusion with this objective data. As we saw, information can have two distinct meanings, because being antisocial may represent a tendency to depression, but the opposite is also true.

The last metric that was used was daily activity and an example of it is represented in table 5. This metric is also very important in depression diagnosis and a correlation between these values and PHQ-9 scores was obtained. Participants that showed higher values in weekly activity (calculated as a median of all the daily activities of the week) were the ones that reported less scores in PHQ-9 questionnaire (r=0,89). Since activity is an important feature to correctly characterize depression symptoms this is an important conclusion.

Table 5 - Participant's daily activity with accelerometer data.

	Daily_Activity
2019-09-01	4.3169
2019-09-02	5.1965
2019-09-03	5.1526
2019-09-04	5.6866
2019-09-05	6.7249
2019-09-06	3.5541
2019-09-08	4.2400
2019-09-09	3.7112
2019-09-10	4.9506
2019-09-11	6.7703

So, with this app it was possible characterize social interactions, mobility patterns and activity with objective data and compared it with subjective methods (traditional methods) both collected via smartphone, getting significant correlations between them.

4. DISCUSSION AND FUTURE WORK

This proof of concept study showed that smartphones can be used as instruments for unobtrusive collection of behavioural data that are associated with depression. None of the participants had issues dealing with the Ethica Health app, which was very good for the reliability of the results because the goal was to act as more natural as possible. With objective data as acceleration in three axes, GPS coordinates, ambient light level, battery level and phone logs information it was possible to infer some behavioural markers that are very helpful in depression diagnosis. With that and with a collection of traditional methods (as PHQ-9 questionnaire) along with stress and sleep diaries, it was possible to correlate subjective (via surveys) and objective (via smartphone sensors) data. The results were very optimistic since in almost all features that were created the correlation was good.

Beginning with correlation between daily stress and the PHQ-9 scores, this relationship was confirmed in the results. That conclusion makes sense since stress has been an important feature that mental health physicians concerns about whenever they make a diagnosis in the psychological context.

The app that was designed to treat and visualize data as well as provide useful metrics from the data in depression diagnosis fulfilled its purpose. All results associated with smartphone sensor data came from that application, both charts and metrics. With a tool like this, a physician can make an analysis of people's behaviour with higher efficiency because this tool works with objective data (which is an innovation in depression diagnosis) where in the visualization part he can see the sensor combination that he wants, with the possibility of choosing a specific day and zoom in or out at any time of that day. From these graphs and metrics, it was possible to verify the correlation between objective and subjective data.

With data from accelerometer, ambient light sensor and battery level it was possible to calculate people's sleeping patterns, which was then compared to the ones reported by the participants in their sleep diaries. The results were goods, because having the reports as a baseline, the sleeping patterns calculated from the sensors information had only an error by approximately 1 hour. To decrease this error, the ideal for calculate sleeping patterns using only objective data is by combining 6 types of features: light, phone usage, motion and acoustic records. The light sensor will detect if the phone is in a dark environment or not, which is the normal environment where people sleep. When people fall asleep at night, they turn off the light and the light sensor detects that change. The transition from dark to brighter light happens as the morning arrives or because people wake up and turn the lights on in their house. Phone usage information is also an important feature, for example battery levels, because usually when people go to bed, they typically start the recharging process. The motion of the device is also important since normally at night the smartphone is mostly in a static state. Finally, the acoustic records can play an important role in this because generally people sleep in quiet contexts. In future, the combination of all these sensors must be done to decrease the error that was obtained in order to get higher accurate values of sleeping patterns, something that is extremely important in mental health.

Regarding mobility patterns that were calculated with GPS coordinates data and daily activity computed with accelerometer data, the correlations between them and PHQ-9 scores were very significant. People with less location variability and less weekly activity tend to be more depressive. Even in the same participant, the weeks that were more 'depressive' were the ones that had less mobility and activity, which clearly indicates that these sensors are very important in monitoring people's behaviour with smartphone. The difference between workday and day off is also very important because in workdays people tend to follow a routine due to their work responsibilities, so when we are analysing these data it is essential to have that in consideration.

With plots of Phone Logs, it was possible to see if people were very sociable in a specific day and at what time of day, they were more interactive with their phone, something that can be very helpful for physician depression diagnosis. With that it was possible to see participant's social interactions, but a correlation between it and PHQ-9 scores wasn't find. This happened because social interactions are clearly a personalized issue, some people like more to interact than others. For that reason, when we are analysing this metric, is very important to know previously people background to see if the social interactions pattern changed or not, which demands a longer study period. This is an example of the importance of personalized medicine, which is clearly the future of medicine since it will increase its effectiveness.

This study has several limitations. Despite all the relevant findings, the number of participants was very small, but it was representative of the broader population in terms of their demographic characteristics, education, level of functioning, or willingness to engage in smartphone monitoring. All of them worked with the Ethica Health app with no problem. The study duration was also small because for some people one month isn't enough to accurately detect mood changes, but the participants were not monolithic in terms of their behaviours and mental health status. Some were very active while others were not, some reported no mental health difficulties while others endorsed more severe symptoms of depression, which was great for our conclusions. One of the objectives of this study was to have participants with real diagnosed depression and it was unfortunate that the Beatriz Ângelo hospital ethics committee accepted the consent form too late, otherwise patients with depression were present in this study. It is a limitation because PHQ-9 is only a screening tool that tells you if you have an above-average chance of having depression and is not enough to diagnose depression. Future research should use that people with actual depression in order to get more significant conclusions.

As already mentioned, an app like the one created in this study can be an extraordinary tool for mental health physicians. Not only in consultation environment, where they can make their own analyses looking at the data and the metrics while asking the patient questions, but also outside the consultation. When a person goes to a psychiatric appointment, the doctor makes his diagnosis and there will be no further contact between them until the next appointment. In fact, currently in Portugal this is an important issue regarding the waiting time for psychiatric consultation. Most of the time, people wait weeks, months or even a year for a psychiatric appointment [24]. In recent years, the demand for psychiatric consultations has increased a lot, as we can see in figure 22. The evolution of this demand has been so high that the

national health system cannot respond to such demand. Therefore, the waiting time for a consultation in psychiatry is longer than ever.

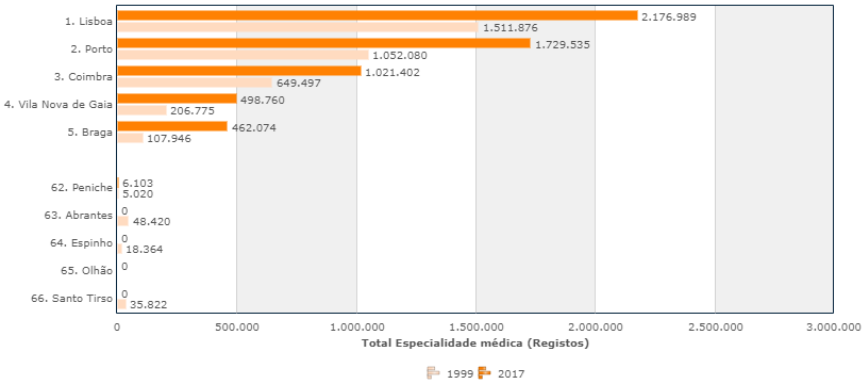

Figure 22 - Psychiatric consultations in 1999 and 2017 in the national health system in some cities of Portugal. Sources: INE | DGS / MS, PORDATA

This tool can be useful for the waiting time problem as the doctor can continue to monitor the patient remotely. For example, when a physician after the diagnosis decides to give a medication to the patient, he/she doesn't see the patient's evolution with the action of the medication, but with this tool it is possible to check remotely for behavioural changes such as sleep patterns. For instance, one of the first actions of some medications in this area is to get people some rest time, known as calming drugs. With this tool, the physician could control the sleeping patterns remotely and analyse if everything is according to planned or not. In conclusion, with this technique, the doctor can verify whether the treatment he has done is having the desired effect or not without the need for consultation, something that would make the need for so many consultations greatly decreased and the follow-up of each person would be better. and more personalized.

In future the ideal is to build an application that receives all the sensors information and within the same application it calculates sleeping patterns with all the combination data sensors that is required as well as mobility patterns, daily activity and social interactions in a personalized way. That means that the app previously knows how each person normally behaves and ideally if a risk behaviour has been taking, the app automatically will send an alert to the physician and notifies the patient that the behaviour he is taken is risky. Obviously, this is very difficult due to many factors, one of them is to handle all the data. Because data is collected continuously, it can generate many gigabytes. The other issue regarding data is the privacy restrictions. To do this, it will be necessary to create a protected database that can handle both problems. Data must always be protected, and people must have control over their own data. To incorporate this into normal psychological consultations at health centres, health organizations need to be interested in this new tool, which is believed to be very soon due to the growing interest in this subject that is nowadays a hot topic when we are talking about fusion between technology and medicine.

When we are building applications like this it is always important to have in mind that this new techniques should never have the pretension to replace the physician, the goal is always to help them in their work

in order to them have the less failure as possible. The physician's sensibility will never be replaced, especially in mental health. Talking with the patients is important, has always been important and it will be always important in depression diagnosis.

5. CONCLUSION

Smartphone technology and telecommunication infrastructure is spreading globally. While the technological sophistication and capabilities of smartphones continue to increase, the costs of devices and data plans continue to drop, which indicates that the tendency is to all people use them. It was demonstrated that these widely available instruments can be successfully harnessed to capture behavioural information that is relevant to changes in mental health.

To see if it is possible to objectively and passively identify if people are depressed, objective behavioural data was collected successfully with Ethica Health application with participants from a differentiated population. Not only objective, but also subjective data were collected with that app to represent the traditional methods of depression diagnosis. Having the two types of data, it was possible to correlate them, and the results were very optimistic, despite the small number of participants.

A desktop application to treat and visualize data as well as provide useful metrics from the data in depression diagnosis was designed and fulfilled its purpose. With a tool like this, it was possible to characterize social interactions, mobility patterns, activity and sleeping patterns with objective data and compared it with subjective methods (traditional methods) both collected via smartphone, getting significant correlations between them.

As technology evolves, it is exciting to imagine a future in which individuals who could benefit from additional support have sensor-enabled data collection systems installed on their smartphones and calibrated to their individual needs. The trend towards personalized medicine is strengthening and discreet monitoring techniques such as this fit perfectly. In the future, the diagnosis of mental health in general and specifically depression will be completely different for sure. All new technology-based approaches will be common to physicians as a tool just like any other tool they use today, and this will make the diagnosis of depression more accurate.

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7. ATTACHMENTS

A) Morning Sleep Diary:

1) Date
2) What time did you wake up?
3) How long did it take to fall asleep?
4) Type of day:
    a) Workday
    b) Day off
5) How long did you sleep?
6) How many times did you wake up?
7) How long were you awake?

B) Evening Sleep Diary:

1) Date
2) Type of day:
    a) Workday
    b) Day off
3) What time did you lie down?
4) How many naps did you take?
5) How long did the naps take?
6) How long did you exercise?
7) What was the exercise intensity?
    a) None
    b) Weak
    c) Medium
    d) High
    e) Very high
8) What time did you have lunch?
9) What time did you have dinner?
10) How many alcoholic drinks did you have?
11) How many caffeinated drinks did you have?
12) Complaints about the day.

C) PHQ-9:

Over the last week, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days	Almost every day
1. Little interest of pleasure in doing things.	0	1	2	3
2. Feeling down, depressed or hopeless.	0	1	2	3
3. Trouble falling or staying asleep or sleeping too much.	0	1	2	3
4. Feeling tired or having little energy.	0	1	2	3
5. Poor appetite or overeating.	0	1	2	3
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down.	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television.	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual.	0	1	2	3
9. Thoughts that you wold be better off dead or of hurting yourself in some way.	0	1	2	3
Total Score =	_____+	_____+	_____+	_____

A) Consent Form:

Student: Rui Barbosa, Biomedical Engineering master student at Instituto Superior Técnico

Supervisores: Professor João Sanches (IST) / Dr. Miguel Constante (Beatriz Ângelo Hospital)

1. **Introduction**: In this study, we are interested in collecting data from your smartphone, a great device to help you understand and track everyone's emotional and cognitive states, particularly in the context of people suffering from depression. This consent describes what will happen to you during the study, as well as the possible benefits and risks. Before deciding whether or not to participate in the study, please read the following information.
2. **What is the purpose of the study?** We intend to collect people's emotional and behavioural data, using the smartphone, capturing information from the sensors embedded in it, to test the viability of this non-invasive monitoring technique in the diagnosis of psychiatric disorders.
3. **What procedures does the study involve?** Each participant will need to have the application 'Ethica' installed on his smartphone and be associated with our study in the app, a process that will be accompanied by the researcher in charge of the study. After all the installation process of the required software, the participant will be asked to answer a demographic questionnaire and then he must answer other three questionnaires that will have two different time intervals, two of them daily and the other weekly.

   You will be asked to complete two short questionnaires per day (one in the morning and one before bedtime) for the duration of the study, which will be 31 days. These surveys will be a kind of sleep diary so that we can correlate with your daily activity. In addition, you will also be daily asked how you feel at a stress level on a scale ranging from 1- 'I feel very good' to 5- 'I am very stressed' (stress barometer).

   At the beginning of the study each participant will have to answer a psychological questionnaire and then will have to repeat it weekly until the last day of the study, which is the PHQ-9, a recognized by mental health care professionals questionnaire that measures depression severity.

   After completing the first questionnaires the data extraction from the smartphone sensors will start. This data collection will be continuous throughout the study. Accelerometer, GPS, ambient light intensity, battery level and duration and frequency of calls and SMS will be extracted (no information will be recorded about the content of SMS or calls). Concluding, apart from questionnaires responses, no further procedure will be required except to behave as usual in your normal life.
4. **Your participation is voluntary**: The decision to participate or not is entirely yours. If you wish to participate, you must sign this consent at the end. Even if you have agreed to participate, you are still free to leave the study at any time without giving any justification. If you don't wish to participate, there is no justification needed for that. The participant is completely free to do what he wants at any time.
5. **What are the possible risks?** We do not anticipate any risk in participating in this study. Still, if any of the questions in the questionnaires make you uncomfortable, keep in mind that you

may not always answer any questions you are not comfortable with and that you are free to leave the study at any time.

6. **What are the benefits of participating in this study?** Being part of this study will not directly benefit you, but it may help in the development of this technique which in turn may help many people in the future.
7. **Your answers / information will be kept strictly confidential**: Your confidentiality will be respected and protected. All your information will only be identified with a code (we will never know the name or other identification in the data). The only people who will have access to the data / responses to the questionnaires will be the people named at the beginning of consent. Once the study is complete, you can request a summary of the results, but it will not provide any identification of you or other study participants. All data will be kept for at least five years. In line with current research best practices, electronic data will be preserved for future use in open science initiatives. Open scientific initiatives allow researchers from different universities to share their data upon completion of studies to stimulate the use and exploitation of existing data sets. Data is sent to a computer software file and these files do not contain any information that can identify you (for instance your name) to ensure maximum confidentiality and anonymity.

Participant

I declare that I have read the consent form. I was able to ask additional questions about the topic. My questions were answered satisfactorily, and I had enough time to decide on my participation.

I declare to know that participation is entirely voluntary. I know that I can quit at any time, including for no reason, simply by informing the researchers of my withdrawal.

I agree that data for this study will remain available to researchers for 5 years after the end of the study.

I freely agree to participate in this study.

☐ Agree / ☐ I don't agree that in future researchers will be able to contact me to participate in new studies

Name: _____

Signature: _____ Date: __ / __ / __

Researcher

I declare that I informed the participant about this study. I confirm that the opportunity to clarify doubts about the study was given for the candidate.

You confirm your consent by signing above.

Name: _____

Signature: _____ Date: __ / __ / __