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A Method of Testing Influences on Tinnitus Symptoms

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BACHELOR'S THESIS

submitted in partial fulfillment of the requirements for the degree of

Bachelor of Science (BSc)

in

Medical Informatics

by

Bernhard Brenner
Registration Number 1025539

to the Faculty of Informatics
at the Vienna University of Technology

Advisor: Univ. Ass. Dipl.-Ing. Dr.techn. Yll Haxhimusa

Vienna, 13. Juni 2014

(Signature of Author) (Signature of Advisor)

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Abstract

Tinnitus aurium, also known as ringing in the ears, is a common issue. Between 10% and 15% of the population is suffering from Tinnitus disease [12]. While there exist treatments that aim to help the patient to habituate to the condition, treatments to reduce or even eliminate the condition are often denoted as not reproducible, not scientifically founded or not significantly changing the patients Tinnitus volume. Additionally, there are many possible causes of Tinnitus and different people may find different treatments helpful. For the patient, it is often frustrating work to find treatments or behavioural changes which influence the loudness of the condition. In this work, we introduce the idea of a smart symptom diary software which aims to find and visualize possible relations between the loudness of a patient's Tinnitus symptom and self chosen life style factors. To test the value of this idea, the software is implemented and also tested by five volunteer Tinnitus patients. The thesis is finalized by showing the use of the results and what further improvements could be made.

Kurzfassung

Tinnitus aurium, umgangssprachlich auch bekannt als „Klingeln in den Ohren“, ist ein sehr verbreitetes Problem. Heutzutage leiden zwischen 10% und 15% der Bevölkerung an dieser chronischen Krankheit. [12]. Zahlreiche Behandlungsmethoden existieren, die vor allem auf Habituation des Tinnitus zielen, nicht aber auf Reduktion oder gar auf Heilung. Oftmals werden Heilungsversuche als nicht reproduzierbar, unwissenschaftlich oder generell als wirkungslos bezeichnet. Die Tatsache, dass Tinnitus sehr viele Ursachen haben kann, hat zur Folge, dass Patienten oft ganz unterschiedliche Behandlungsmethoden als hilfreich ansehen. Gerade ob der Vielzahl der Behandlungsmethoden ist es für einen Betroffenen oft eine mühsame und leidvolle Arbeit, eine Möglichkeit der Linderung zu finden. In dieser Arbeit wird die Idee eines intelligenten Symptomtagebuches für Tinnitus-Patienten vorgestellt, welches zum Ziel hat, mögliche Relationen zwischen frei wählbaren Faktoren des Lebensstils und des Verhaltens des Tinnitus Symptomes zu finden. Um den Effekt der Software zu prüfen, wird sie im Zuge der Arbeit implementiert und von fünf freiwilligen Tinnitus Patienten getestet. Abschließend wird der Nutzen der Idee diskutiert und Verbesserungen werden vorgeschlagen.

Contents

CHAPTER 1

Introduction

1.1 About Tinnitus

Tinnitus is a common issue. Between 10 and 15% percent of the population suffer from this condition [12]. Even more people have already experienced Tinnitus symptoms in their live - after a loud rock concert, for example. There has to be distinguished between the so called objective Tinnitus or somatosound [12] - a sound which is audible by the patient and the doctor as well, and the so called subjective Tinnitus, which is heard only by the patient. In most cases, Tinnitus is of subjective nature, since the causes of a objective Tinnitus appear very rarely. While objective Tinnitus is associated with contraction or twitching of the small muscles in the middle ear [12], there are a lot of possible causes of subjective Tinnitus. In this work, we focus on subjective Tinnitus and from now on, whenever the word Tinnitus is written, we mean subjective Tinnitus. Tinnitus can have a lot of different causes.

1.2 Tinnitus causes

Possible causes of Tinnitus include:

1. Acoustic Traumata
   An acoustic trauma can arise due to long time exposure to high volumes (above 85 dBA), like when being in a disco for hours or when working with loud machines at the building site, but also at very high sound levels (above 120dBA) for very short time (milli- or even microseconds) – like the shot of a gun or a firecracker. [6] [13]

2. Drugs
   Certain pharmaceutical ingredients, such as acetylsalicylic acid [1], which can be found in many painkillers (Aspirine ®, Aspro ®, Axanum ® ....), sertralin, a so called selective serotonin reuptake inhibitor (SSRI), found in some mild anti depressants (Gladem ®,

....) can cause Tinnitus for the short term or even for the long term. Even the intake of caffeine or alcohol causes Tinnitus at some people, but only for the short term.

3. Tumors
   A tumor at nervus vestibularis, which is referred to as vestibular schwannoma can cause Tinnitus symptoms. When people notice Tinnitus for the first time, they often fear they have some serious disease. In fact, one should immediately consult a otorhinolaryngologist to exclude this as a possible cause.[1] [15]

4. Stress/Vascular Problems
   Distress ("negative" stress) can also be referred to as a cause of Tinnitus Symptoms, since the blood flow in the inner ear's blood vessels decreases due to stress. In general, people with vascular problems can develop Tinnitus symptoms. [9] [8] [24].

5. Nerve Damage
   Damages at the nervus acusticus can result in Tinnitus.

6. Brain Traumata
   When a patient experiences a brain trauma, it sometimes has Tinnitus symptom as a consequence. [11]

7. Malpositions at the Neck
   Malpositions at the cervical spine can result in vascular problems at the inner ear. Therefore it can be another reason for Tinnitus.

8. Otosklerosis
   The stiffening of the middle-ear-bones can result in Tinnitus.

9. Otitis Media
   Middle ear infection can result in Tinnitus. However, in most cases, it disappears after the infection.

10. Other Causes
    There is even a huge amount of other possible causes for Tinnitus symptoms, like deficiency of Vitamin B12 (cobalamine), for example. According to Shemesh et. al., many percent of Tinnitus sufferers have a deficiency of cobalamine [22].

1.3 Tinnitus treatment

There are many possible causes for Tinnitus. In most cases, it is a combination of them which is finally the reason for a patient to suffer from Tinnitus. That's why it can be a very hard job to find the reason for a patients Tinnitus symptoms. In many cases, the patient does not even know the causes for his Tinnitus condition. However, the chance of a cure of the Tinnitus condition is often claimed to be very low. Many panel doctors and even many specialized Tinnitus clinic's

[1] `http://flexikon.doccheck.com/de/Akustikusneurinom`

claim that there is no chance for healing the condition, no matter what might be the cause.[2], while other specialized clinics claim to be able to heal or reduce the volume of the Tinnitus sound and say that the main cause of Tinnitus is noise exposure. [3]. Many clinics tend to say that the Tinnitus can be cured, but only in an early phase. These clinics often use infusions of cortisone, B-vitamines, caroverine or a mix of these substances. Patients who still suffer from Tinnitus after this kind of treatment are often left on their own and told to „live with their condition“. However, most patients say that they experience reduction of their Tinnitus volume if they do things like exercise, sleep more, eat healthy food, etc. Many patients assert that their Tinnitus volume increases when they sleep less or after they where exposed to loud noise or after a stressful situation. Some studies exist which suggest the intake or infusion of certain vitamines or minerals [22]. The treatment with magnetic fields is is also told to be helpful in certain cases [32] [17]. Although many treatment suggestions exist for reducing the noise [21], patients often feel left alone, since many doctors do only try to treat Tinnitus in the early period after appearance [4]. After this period, patients often have to look for therapies on their own and are often quite helpless in reflecting the use of a certain treatment method. At this point, we think that it may be very useful for to maintain a symptom diary. With a symptom diary, a patient has a better overview concerning the development of his symptom and maybe can distinguish helpful treatment or behavior from those which do not help. If the patient could do this, it would be much easier for him to help himself on his way to find a good treatment. In addition, as shown by XYZ et. al. A patient who is concerned about his health due to individual medical self-management can improve his health status significantly.

1.4 Aim of this work

The basic idea is to make it easier for a patient to find out what helps him and what not. Therefore, the aim of this work is to test a concept. Hence we create a symptom diary software. The patient records one to three self-chosen possible influence factors together with the loudness of his Tinnitus symptom in a daily frequency. These records will be stored in a database and can be visualized. The system will also try to calculate influences of certain factors on the Tinnitus symptom. For the diary system itself, we defined certain goals: The software itself will be usable by non-technicians. The output of the software should be in a form that is readable by non-technicians as well. The user must be able to delete, modify, and to import and export records. In the scope of this Bachelor Thesis, this concept will also be tested on five patients of different age, gender and different places of residence. The system will treat sensible patient data in a confident way, so that no one except the autor can find out the name of a patient. In addition, our application should motivate a patient to help himself and to be consistent in looking after his health. This is independent from the outcome of the calcualated correlations - it is a

[2] `http://www.tinnituszentrum.at/index.php/therapie-mit-hoergeraeten/erfolgsaussichten/`

[3] `http://www.dasgesundeohr.de/neuer-text-dr-wilden.pdf`

[4] In the first three month, the patient's Tinnitus ist often referred to as “acute”, while after that period, it is often referred to as „chronic“

function, which should be provided by the „diary“ character of the Software. As an addition, the correlation calculation functionality should be a tool for a patient to find an optimal reduction.

1.5 Structure of this work

First, we will create the software, then volunteer Tinnitus patients will test it. We will discuss available technologies like the programming language, database, etc. as well as the possibilities to visualize the data. We will then create a prototype of the system and test it with fictive patient data. When we see that changes have to be made at this point, we will implement them. Then, five volunteer Tinnitus patients will test this prototype and give feedback on how further improvements could be made. After that, they will record data for a period of three to six weeks. When the collection of the data is finished, the results will be shown and we will discuss whether the concept turns out to be useful or not.

CHAPTER 2

Prerequesites

2.1 State of the Art Analysis

The idea of maintaining a diary concerning health or symptom behaviour is not new, and the field of electronic individual health management is growing at the moment. Before starting to think about our own application, we did some research about what is already available today. In fact, there exist some software applications which's goals partly overlap with the goals of Tacet. Here is a list of possible competitors.

Desktop applications

Allmyjournals

Allmyjournals[1] [23] is a general diary software which can also be used to log health related stuff like symptoms or medication. The focus of this app lies in keeping personal written records and there is no grading or graphing. You have the option to print the journal. This feature is intended to submit it to your doctor. A license for this programs costs $29. You can also use this software for free, but then you have limited access to useful functions like printing the journal or maintaining multiple journals at the same time.

Excel Symptom Diary

A powerful symptom diary implemented in MS Excel by Marie Kroun, MD. [2] [14] It is a very powerful symptom diary which is also able to draw detailed graphs of the symptom history. The purpose of this diary is to create a detailed log about the behavior of symptoms so that a pattern in a „normal“ period (i.e. without treatment) can be made by a medical doctor. The same doctor can then apply any treatment for this patient. If the patient records every abnormal

[1] http://www.allmyjournals.com/blog/medical-symptoms-diary-or-journal/
[2] http://lymerick.net/symptomdiary.htm

symptoms and hands over the detailed output of his diary, the doctor can react with changes to the treatment. An interesting point is that this diary uses a more sophisticated grading system, where you can choose between grades ranging from 1 (light symptoms) to 3 (severe symptoms). The grades are all well defined in the excel sheet to reduce bias. In addition, the patient can introduce higher scores later on if it seems necessary for him. The user shall only record his symptoms if they are abnormal, but not in a regular manner.

Mobile Applications

MySymptoms

MySymptoms [3] [5] is a mobile app for Android and iOS, which aims to help a patient who suffers from IBS (irritable bowel syndrome) to find out what he can eat and what not, and to find relations between his food intake and his symptoms, respectively. Stress and other potential influence factors may be recorded as well. This app is very powerful as it gives a lot of output about possible correlations and can even reflect about the confidence of its output. It also benefits from being a mobile application, since it is more convenient for patients to keep recording timely. Records can be made in an irregular manner. You can also see the diary entries as a graph. This app is one of the major competitors of our software, since it has many useful features and it is very powerful. Because this software is very interesting for us, we bought it and spent a more detailed look on it A.5.

Symple

Symple [4] [25] is a free symptom diary app exclusively for iOS which specializes on record tracking. With this app, you can record symptoms and possible triggers. There is a graphing function, but there is no calculation for possible correlations. For grading the intensity of the symptoms, there is a 5-grade scale.

My Pain Diary

My Pain Diary [5] [4] is a mobile app available for Android and iOS. One license costs about $5.

Für Bilder ist der Link gut: https://play.google.com/store/apps/details?id=com.damonlynn.mypaindiary
Vielleicht kommt hier noch das eine oder andere dazu.

Comparison and Summary of existing approaches

Most of the software is not capable of calculating correlations between influental factors and symptoms. In every software we found, the user is able to choose arbitrary factors. Every software we could find uses grade-based record, while the grade scale is varying.

[3] http://skygazerlabs.com/wp/
[4] http://www.sympleapp.com/
[5] http://www.chronicpainapp.com/

Name	Platform	Price
Allmyjournals	Windows	$29
Excel Symptom diary	MS Excel	free
MySymptoms	Android & iOS	$3,5
Symple	iOS	free
My Pain diary	Android & iOS	$5
Tacet	Windows	free

Table 2.1: Comparison of Symptom Diary Applications concerning availability. Prices are rounded.

Name	grading	specialisation	recording freq.	graphs	correlations
Allmyjournals	grades	no	irregular	no	no
Excel Symptom diary	grades	no	irregular	no	no
MySymptoms	grades	yes, IBS[6]	regular	yes	yes
Symple	grades	no	regular	yes	no
My Pain diary	grades	yes, pain	regular	yes	no
Tacet	units	yes, Tinnitus	regular	yes	yes

Table 2.2: Comparison of Symptom Diary Applications concerning functionality.

2.2 Methodology

At the beginning of the project, we were not sure how to implement our idea. Thus we had to look for people who could tell us what requirements have to be met. We needed someone who knew how to treat patients data, how to realise a survey, etc. Therefore, we contacted Mr. Ao. Univ.-Prof. Dr.med. Dr.theol. Mag. Pharm. Matthias Beck, BSc. (Institute for Theological Ethics at University of Vienna[7] [26] to help us from the field of a medical doctor. In fact, Dr. Beck helped us a lot in finding out what a medical practitioner would expect from such a software in order to have great value for a patient. Dr. Beck spent a lot of his time with us and told us the requirements to our product conscientously. He told us the requirements of a symptom diary from the medical and ethical point of view. With his help, we were able to find out what such software should be able to do and how results should be visualised. He also told us that we would have to test the software with real patients and how a good survey should look like. With a plan of **what** we want to do, we went to our supervisor, Mr. Univ. Ass. Dipl.-Ing. Dr.techn. Yll Haxhimusa[8] [31], from Pattern Recognition Department of Vienna UT to talk about which techniques would best fit the requirements. He told us in detail, which techniques we can use to implement the calculation of possible correlations and how good data visualisation would look like. With his help, we found out the requirements given to the software from the technical and mathematical point of view. The results of the correspondence are discussed at 3.1.

[7] http://st-theoethik-ktf.univie.ac.at/fach/team/wissenschaftliche-mitarbeiter/beck-cv/

[8] http://www.prip.tuwien.ac.at/staffpages/yll/index.php

Then it was about finding technologies to implement our ideas. Since we wanted to create a desktop application and wanted to use a high level language with garbage collection and a powerful IDE, we soon landed at some decision between Java (Sun Microsystems/Oracle) and C# (Microsoft). While brainstorming, what tipped the balance in favor of running under Microsoft Windows OSes, GUI, and available libraries was the C# programming language together with the Microsoft .NET Framework. When it came to the implementation of the software, we decided to use the MVVM pattern[9] [16] as our architectural software design. This architectural design pattern is derived from the MVC Pattern and is adapted by Microsoft. Together with the XAML design language, we found a good opportunity to implement Windows Software in a well structured way. The report about our implementation decisions can be seen in **??**. Since measuring the loudness of Tinnitus is a very complicated issue and has to take in account, that people are living in different environments (with different noise level) and having different Hardware (sound card, headphones, ...), we decided not to implement the loudness measurement ourself, but used „HTTS Hörtest Software“[10] [2] by SAX GmbH. This program is quite old (2001), but does also work well on Windows 7 platforms, and, most important: It supports individual calibration of sound hardware - which was essential for our project. We asked one of the CEOs of SAX GmbH if we are allowed to use it in our project (see A.3) and got a positive answer!

We implemented the first version of the Software within two months. Meanwhile, we were looking for volunteer patients to test our software for a period between three weeks and 1.5 months. Therefore, we created some advertisements at Vienna UT and on the internet A.4. It was astonishing, how fast we achieved our goal to find five volunteers. It might be because Tinnitus is really common nowadays. All of the volunteers had to sign an agreement in order to allow us to publish their data anonymously. First, we tested the software with fictive data and made slight improvements. After the first „Roll-Out“, when the first volunteer patients started to use it, we made some further improvements with the help of their feedback. After that, the study was ongoing.

The collected data can be seen in the appendix at A.5 After we finished to collect the data from all five volunteer patients, we contacted Mr. Ao. Univ.-Prof. Dipl.-Ing. Dr.techn. Peter Filzmoser [11] [7], which suggested to use the ARIMA time series model to evaluate the patient's data. With this information, we tried out several future options for the further development of Tacet. Therefore, we first used Matlab 2013b and later IBM SPSS Version 22 in order to find applicable techniques which are capable of giving valuable output for real survey data.

[9] `http://msdn.microsoft.com/en-us/library/hh848246.aspx`
[10] `http://www.sax-gmbh.de/htts/httsmain.htm`
[11] `http://www.statistik.tuwien.ac.at/public/filz/`

CHAPTER 3

Tacet - the software

3.1 Tacet - the software

Requirements

The Software should be able to fulfil the following requirements:

Functional Requirements

The software can collect data of a patient. Data can be displayed, modified or deleted as is. The software will be able to display collected data in a graph. The software is able (or in some cases at least trying) to show possible relations between symptoms and influential factors in a graph. Therefore, regression or a related method should be used. The software is able to transfer the collected data to the authors over the internet. The software runs well on the platforms it will be used on (probably Microsoft Windows)

Non Functional Requirements

Patients do not have to be technically savvy to be able to use the software. The number of collected factors is limited to three to reduce complexity. The software uses reproducible units to measure the symptom (instead of a grading system to rate factors) and the factors to ensure quality of calculation results. The sensitive patient's data is being treated in a confidential way.

Technology Requirements

Our requirements for a technology are: The program has to run perfectly on Microsoft Windows systems It must be a High Level Language A powerful data visualisation library must be available An Open Source cryptographic functions library must be available

Software Implementation

The name of our software will be „Tacet“. Tacet is latin for „he/she/it is silent“ and is also an appeal for musicians to stop playing[1] [27]. It is meant as an appeal for the ears to stop playing, too. The user sould be given a tool to archieve the goal of hearing „silence“ again.

We decided to implement Tacet by using the following technologies:

Field	Selected solution
Language	C# with .NET 4.0 Library
IDE	Microsoft Visual Studio 2012
GUI-Designer	Microsoft Expression Blend 4
Database	Data is stored in XML Files
Targeted Platforms	Windows XP and newer
Data Visualisation	Microsoft Dynamic Data Display (D3) Library Version[2] [19]
Data Transfer	Strong Encrypted Email [3]
Cryptographic Functions	RSA-4096 encryption, PKCS#1v2 padding, BouncyCastle v1.7
Anonymity	Client generates unique ID per patient.

Table 3.1: Summary of used technologies and approaches for Tacet software.

Data Storage

When thinking about collecting the data of the patients, we soon came to the following train of thought: A patient's data is a series of days, whereas every day has two to four parameters stored in, together with some ID and some time stamp. Since the structure of the stored data might be quite trivial and there is no complex sorting/searching/etc. functionality needed, we decided to store the data in an XML file. The used scheme can be seen in Figure 4.4.

Data Collection and Encryption

To implement the data collection, we use the System.Net.Mail library and build in mailing functionality. When the user presses the mail-button, an email with all data objects is generated, sent to the author. The subject of the email is equal to the unique ID of the patient, so that the data can easily be assigned to the right patient. To transfer the data securely over the net, the email is entirely encrypted before it is sent. Therefore, we use RSA 4096 bit encryption based on the BouncyCatle [4] [18]. The public key is stored hard coded in the program. We may think about putting it into the configuration file if necessary. The private key is owned only by the authors their self. But standalone RSA Algorithms is not sufficiently secure in our case: It must be stressed, that in every public key cryptosystem, the attacker has access to the public key and thus is able to encrypt every chosen plain text he wants. Given the assumption that time stamp,

[1] `https://en.wikipedia.org/wiki/Tacet`
[4] `http://www.bouncycastle.org/csharp/`

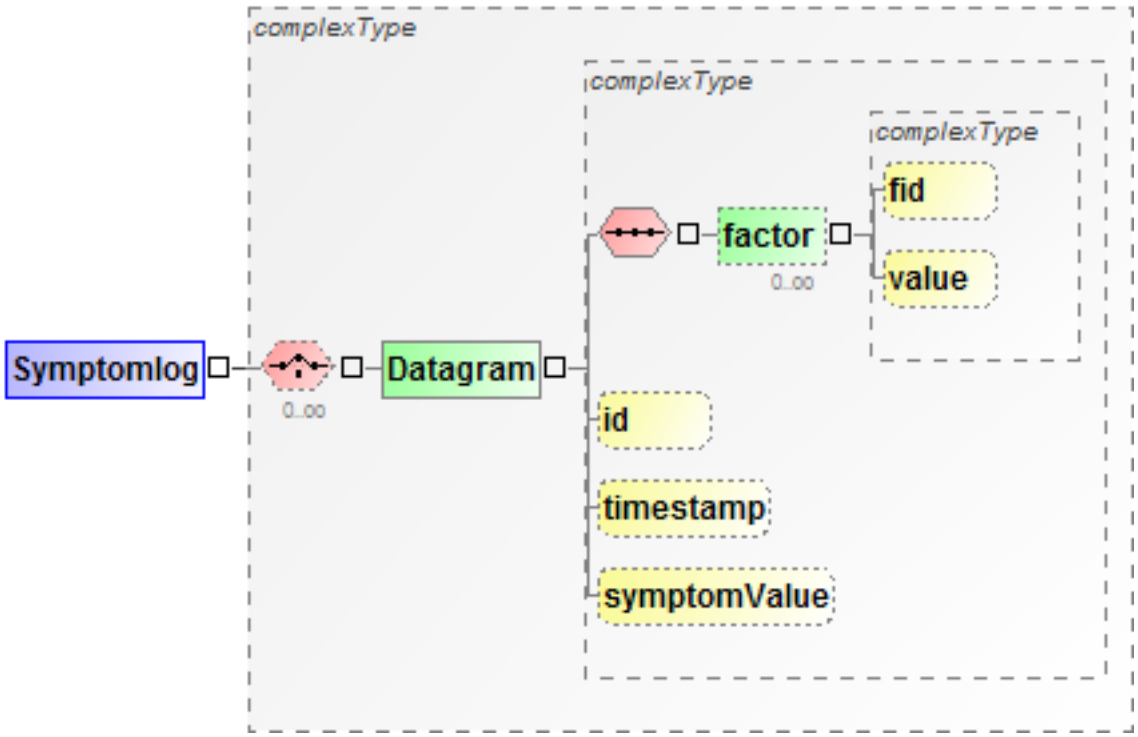

Figure 3.1: XML Scheme of Tacet. Every record is stored in a Datagram object.

symptom value and the values of the factors are in a certain number range, it could be possible in certain cases, to derive every full clair-text data object by brute-forcing the cipher-text with defined chosen plain texts and comparing them to the original cipher-text. E.g.: Data Object sent over the wire looks like:

Some ID	Some Timestamp	Symptom Value	A single factor value

Table 3.2: Structure of a Datagram package sent over the wire.

Cryptanalysis:

Here is an explanation of how some example Data Block can be broken (if PKCS#1v2 is not being used).

- We assume that the ID is a number between one and 1095 (=three years), for example.
- We also assume that the time stamp must be somewhat between now and the past three years, which leads to about $9.5 \cdot 10^8$different possible timestamps.
- We also assume that the symptom value has to be somewhat between zero and 120 decibels, with decimal precision of one decimal, which leads to 1200 different factor values.

- Finally, we assume that the factor, which's name we do not know, might me somewhat between zero and 1000, with decimal precision of one decimal, which leads to 10^4 different factor values.

Then, the entropy of this block is equal to: $1095 \cdot 9.5 \cdot 10^8 \cdot 1200 \cdot 10^4 == 10^{19} =$ **64 bit**, which we claim to be too weak. To improve the security of the encrypted blocks, we implemented PKCS#1v2 Padding [10], also known as OAEP Padding method. A good article explaining why PKCS#1v2 should be used is [3]. With this concept, we state to have a reasonable secure data transfer over the internet. To decrypt the email and automatically convert it to an appropriate XML-File, we created a standalone RSA encryption program, which we call „CryptExpert“ and is part of the outcome of this work. Details can be seen at the section A.2 in the appendix.

Analyses Methods

The analyses of the recorded data is made by several different approaches.

Diary

With the diary, especially with the graphical plotting function, a user has the ability to analyse possible influences himself. Possible events which occured on a certain date which had influences to the loudness of the Tinnitus symptoms may be seen at the graphical plot as an outlier or a tendency.

Statistical Analyses

On the other hand, there will be a built in graphical analysation function, which will calculate a possible correlation and visualise it as a line or curve. Currently, we built in a simple OLS (Ordinary Least Squares) regression. It has to be stressed, that there may occur a lot of false assumptions when using only OLS regression. Therefore, we made a proof of concept for an ARIMA (Adaptive Regression, Integration, Moving Average) time series model. For this PoC, we use IBM SPSS version 22 for Windows x64 with some hypothetical and also with the real data sets.

CHAPTER 4

The survey

4.1 Survey and results

When we finished the first working version of the program, we where looking for volunteer Tinnitus patients. We made some kind of „advertisements“ A.4 at Vienna UT and in the internet.

We tested the application with certain fictive data in order to show what an optimal outcome would look like. Therefore, we created certain personas with certain self chosen influential factors.

Personas

Philomena, 23 years old, Tinnitus since one year (antibiotics), wants to know if certain medication influences her symptom. In figure 4.1, there is the diary of philomena. In figure 4.2, the calculated correlation can be seen.

Harald, 32, Tinnitus since three years (disco), programmer, wants to know if the intake of Vitamin B decreases his symptom. Also, he records his exercises - playing tennis.

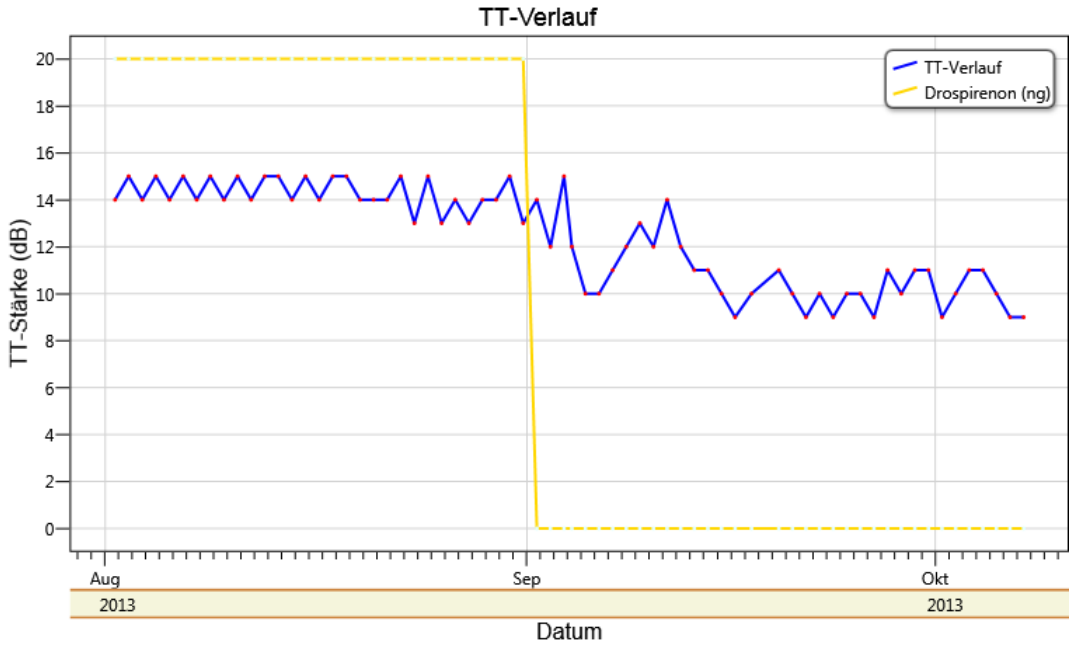

Figure 4.1: Philomena, 23 years old, student, Tinnitus since one year, wants to know if certain medication influences her symptom. In fact, it seems that it does influence.

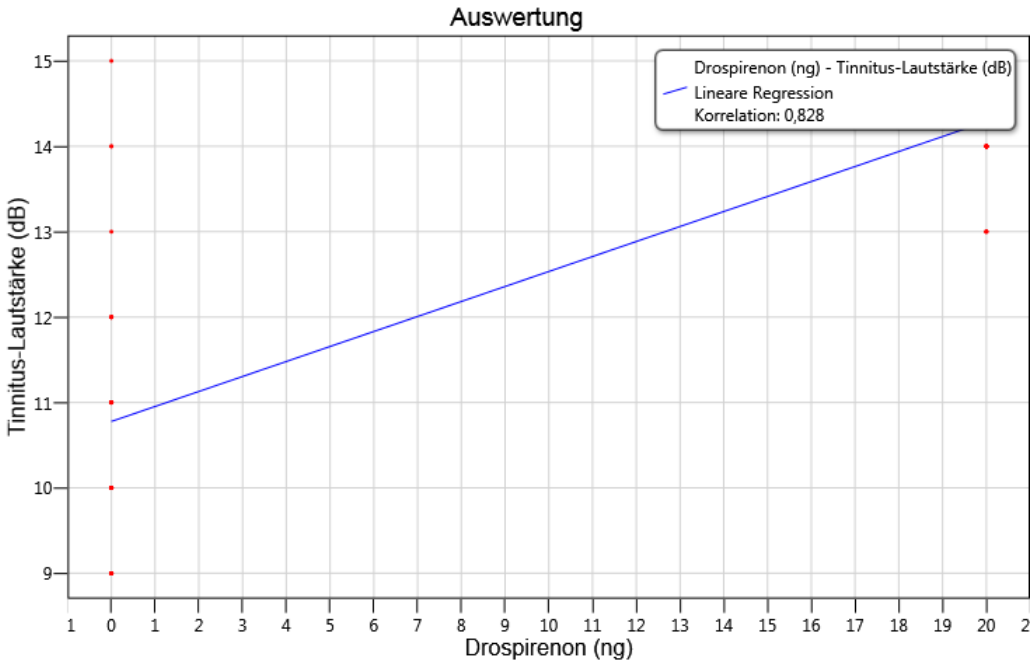

Figure 4.2: Also the correlation diagram shows a quite high positive correlation.

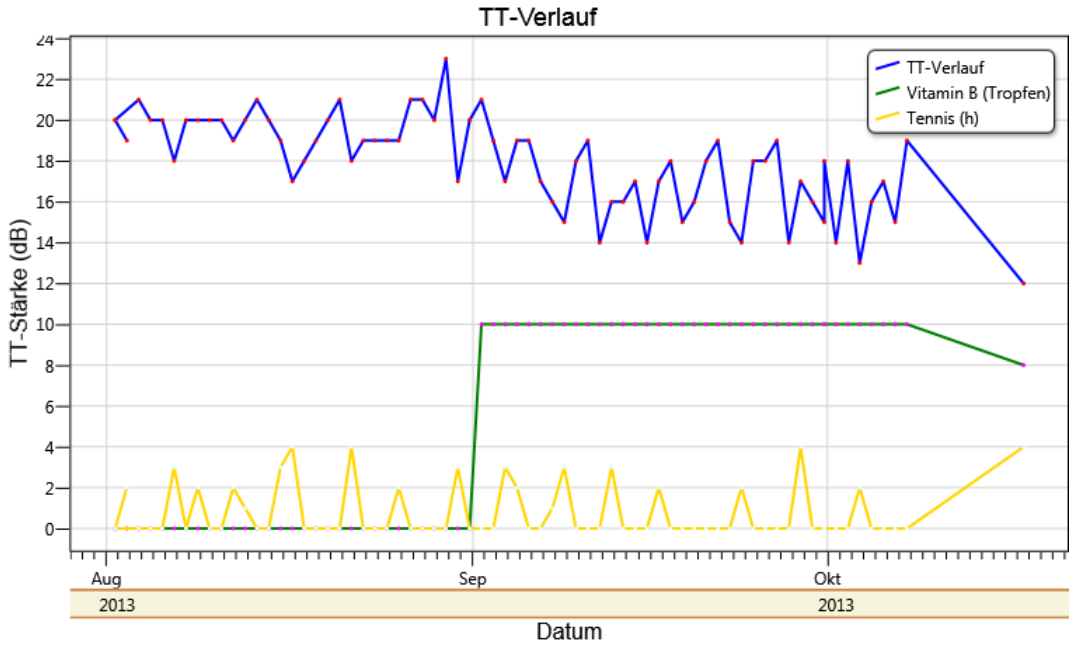

Figure 4.3: Haralds diary.

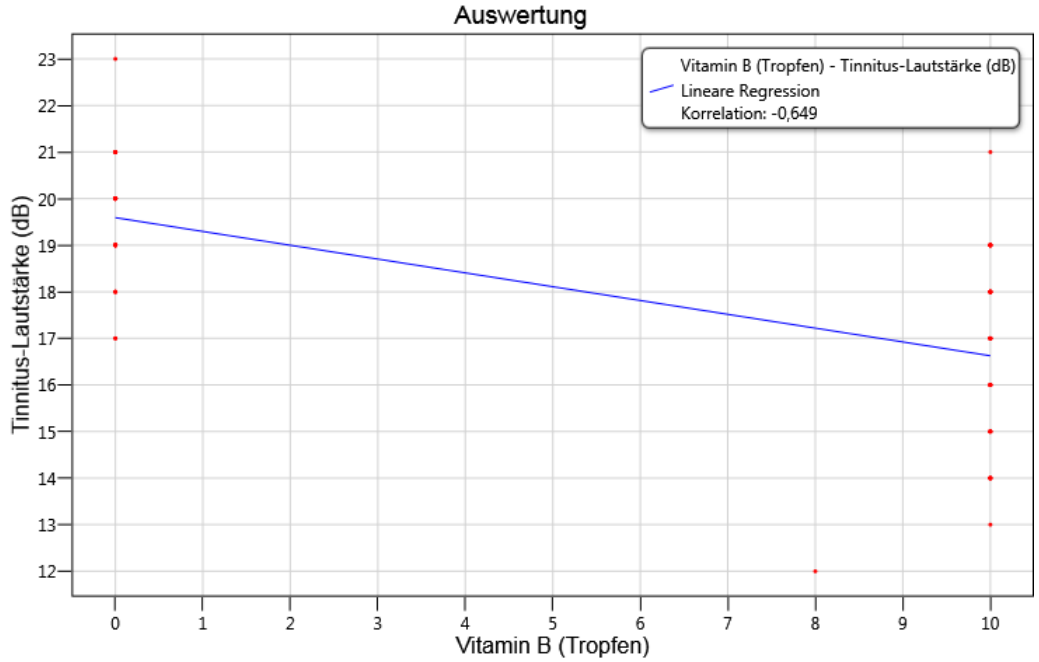

Figure 4.4: Haralds influence of Vitamin B on Tinnitus.

Survey data

At this point of our work, the survey is already finished. We successfully collected a total of 149 recorded days from five volunteer patients with the following symptoms:

- Sleep (85 days)
- Alcohol consumption (21 days)
- Certain Medication (49 days)
- Exercise (79 days)
- Water consumption (58 days)
- Intake of certain healthy food, like Garlic or Ayurveda (43 days)

Our program generated the following IDs, which is used as pseudonym for the name of the patient.

ID	Gender	Age	Job	Residence at	Tinnitus since	Supposed cause
A	Female	50	freelancer	Vienna, Austria	1984	unknown
B	Female	23	student	Darmstadt, Germany	2012	stress
C	Male	30	student	Vienna, Austria	2001	firecracker
D	Female	26	student	Vienna, Austria	2012	unknown or conditional
E	Male	60	retired	Styria, Austria	1999	acute hearing loss

Table 4.1: List of our volunteer patients.

ID	Factor 1	Factor 2	Factor 3
A	Exercise (minutes)	Sleep (hours)	Water (liters)
B	Medication made of herbs (drops)	Medication made of herbs (units)	
C	Sleep (hours)	Alcohol (glasses)	Exercise (minutes)
D	Sleep(hours)	Alcohol (glasses)	Paracetamol (milligrams)
E	Going for a walk (hours)	Medication (yes=1/no=0)	Water (liters)

Table 4.2: The patients's recorded influence factors.

We want to demur that it's a pity we did not find a smoker with Tinnitus. It is a widely known issue that the intake of nicotine has bad influence on the hearing nerve, thus increasing the loudness of someone's Tinnitus noise significantly. Hence, people often stop smoking very soon, when Tinnitus occurs [30]. It would have been interesting to see, if our program could find a correlation! However, in fact: sleep shows a similar correlation.

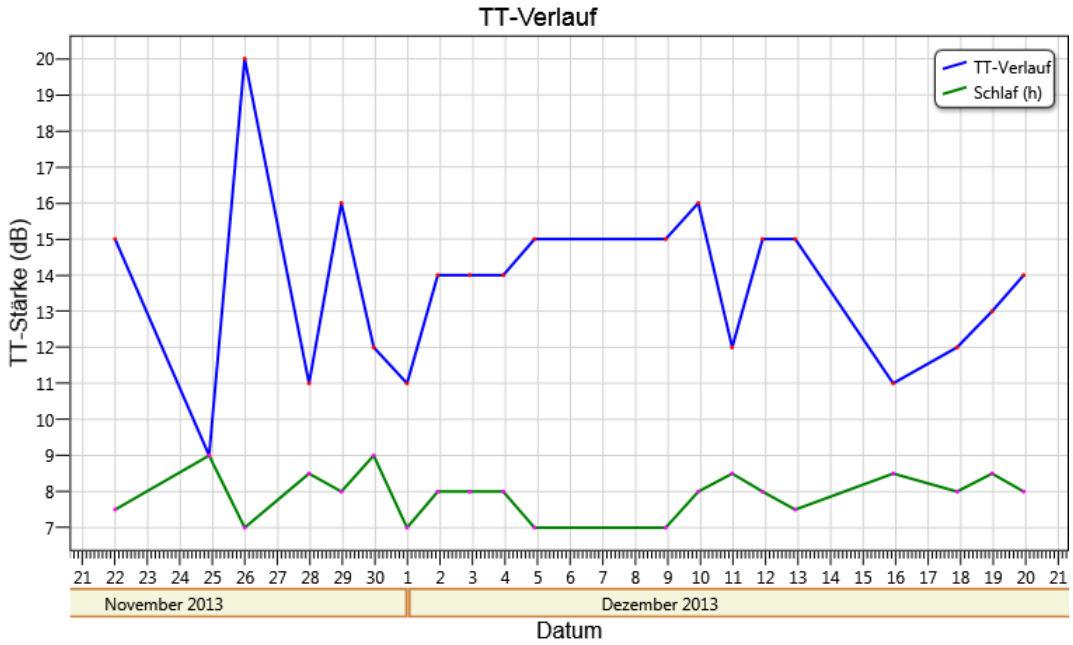

Figure 4.5: Diary of patient C. Sleep (green) together with the development of the symptom (blue) over time.

Selected Graphs from collected Data

Here are some notable examples of the data we could gather. Note that this is real data from real Tinnitus patients!

The ayurveda diary of B is of quite mixed manner. On one hand, it looks a bit like ayurveda with garlic increases Tinnitus noise. But on the other hand, it is also possible that there might be a weakness of Tacet / if you look at it from a different point of view: Everytime B recognized high symtoms, she took some ayurveda with garlic. Thus, the diary looks like there is a positive correlation between the intake of the medication and the Tinnitus noise. The graphs can be seen at **??** and **??**. It has to be noted that B always measured values between 0 and 2 decibels.

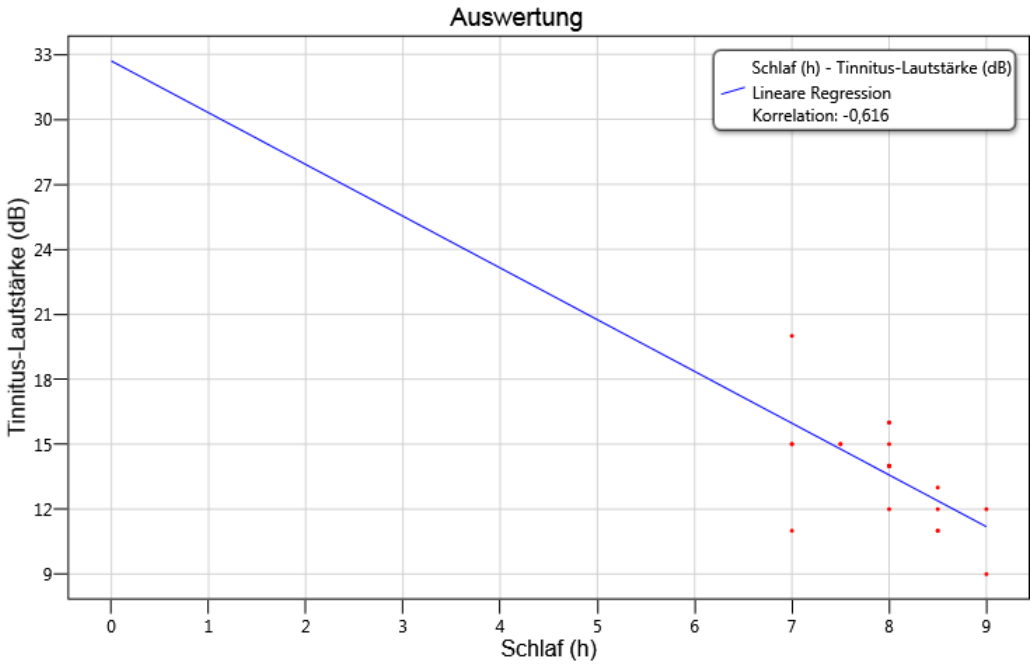

Figure 4.6: Tacet calculated a high negative correlation (-0.616)

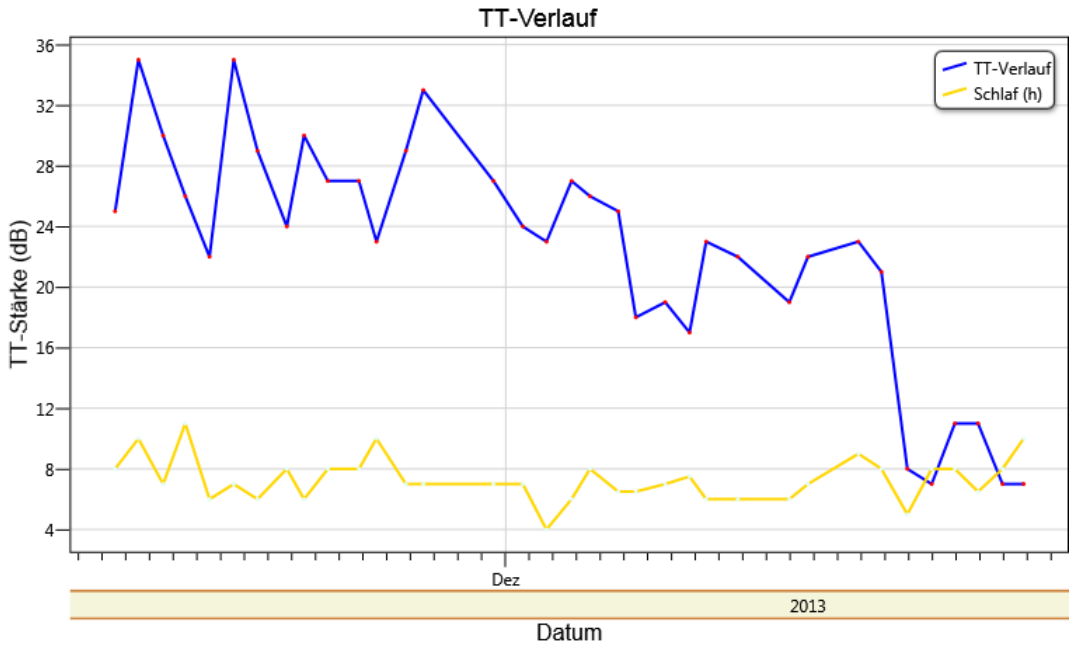

Figure 4.7: Diary of patient A. Sleep (yellow) together with the development of the symptom (blue) over time.

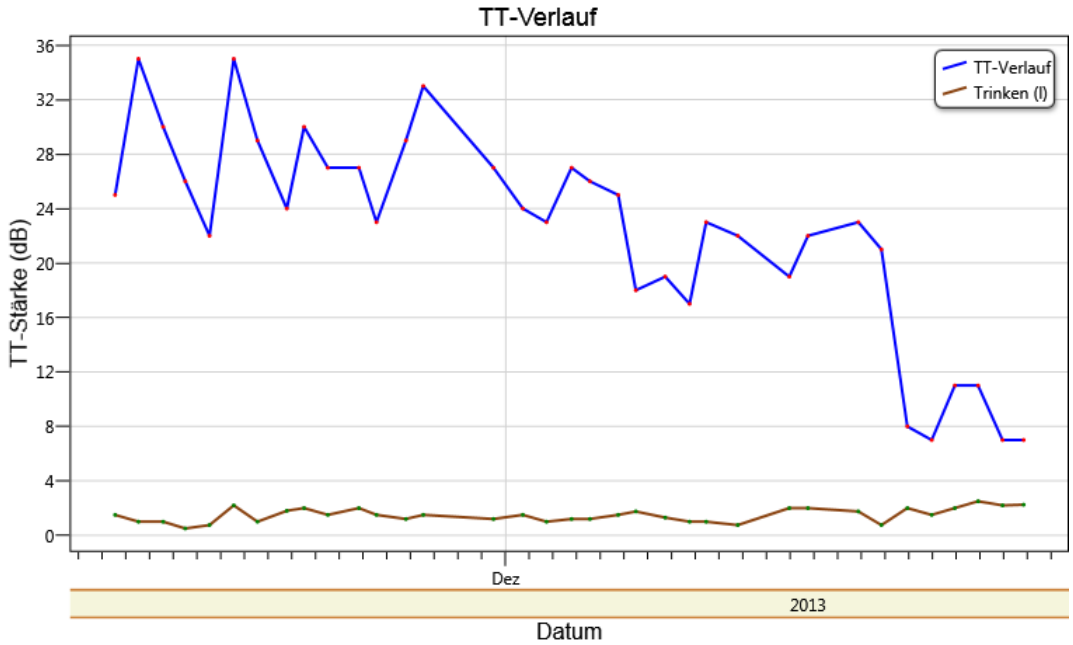

Figure 4.8: Diary of patient A. Intake of Water (brown) together with the development of the symptom (blue) over time.

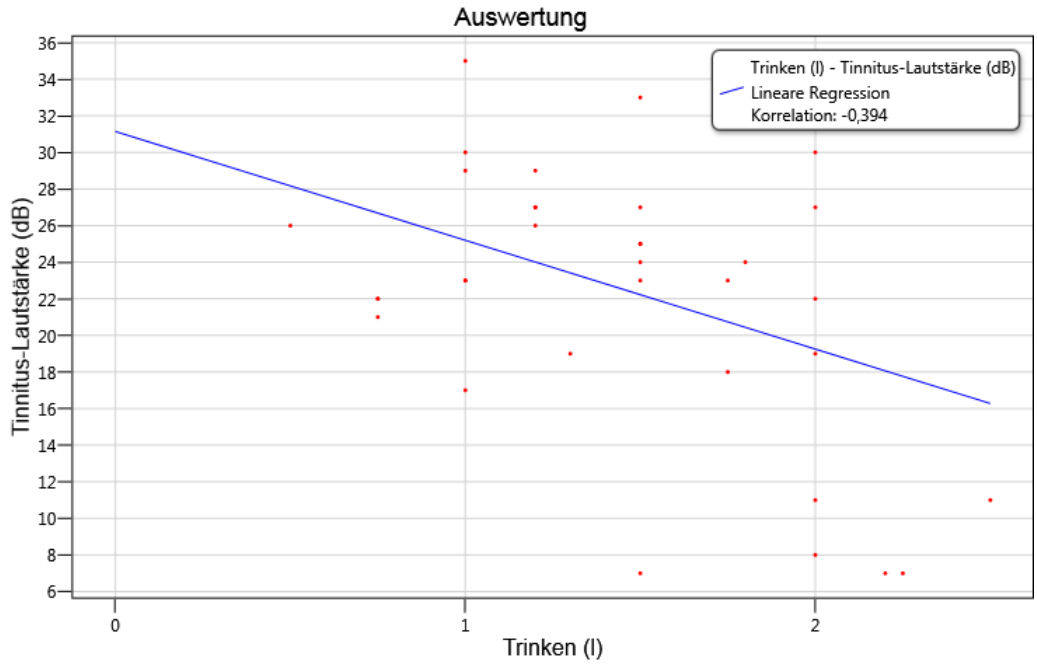

Figure 4.9: A: Tacet calculated a correlation of -0.394 for „drinking“ and the loudness of the symptom.

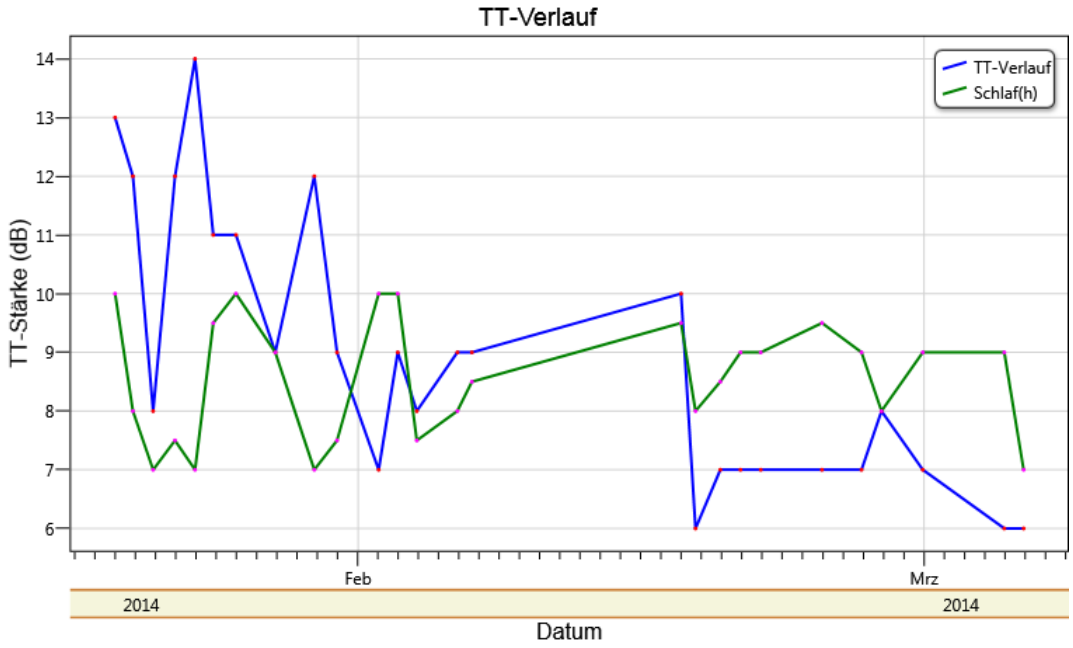

Figure 4.10: Diary of patient D: Sleep (green) together with the development of the symptom (blue) over time.

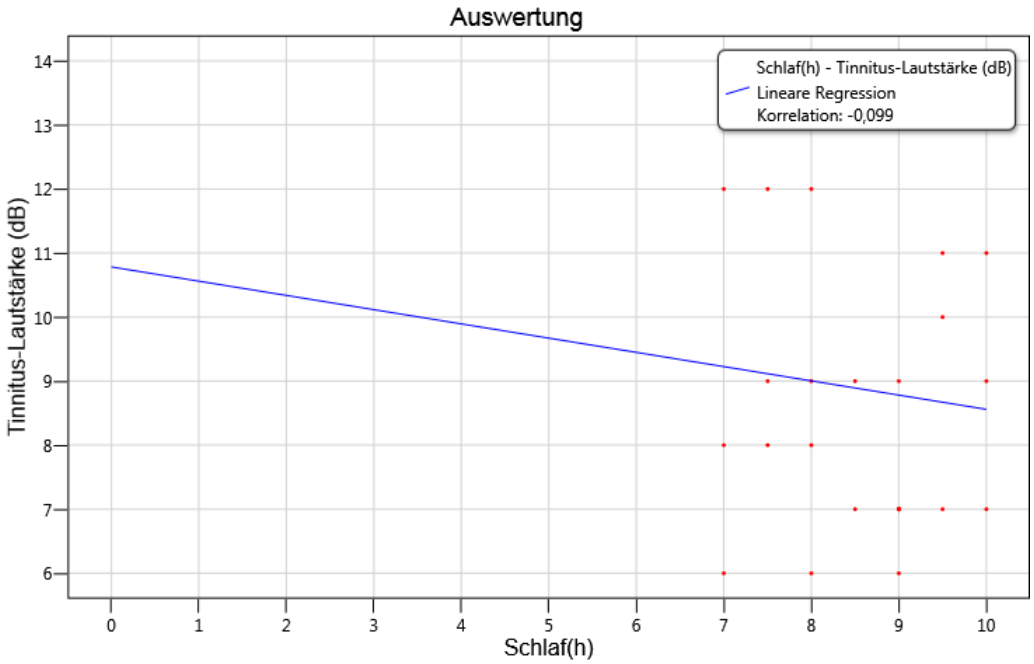

Figure 4.11: D: Tacet calculated a relatively low negative correlation of -0.099 for sleep and the loudness of the symptom. This could possibly be a hint that sleep does not affect her symptoms that much.

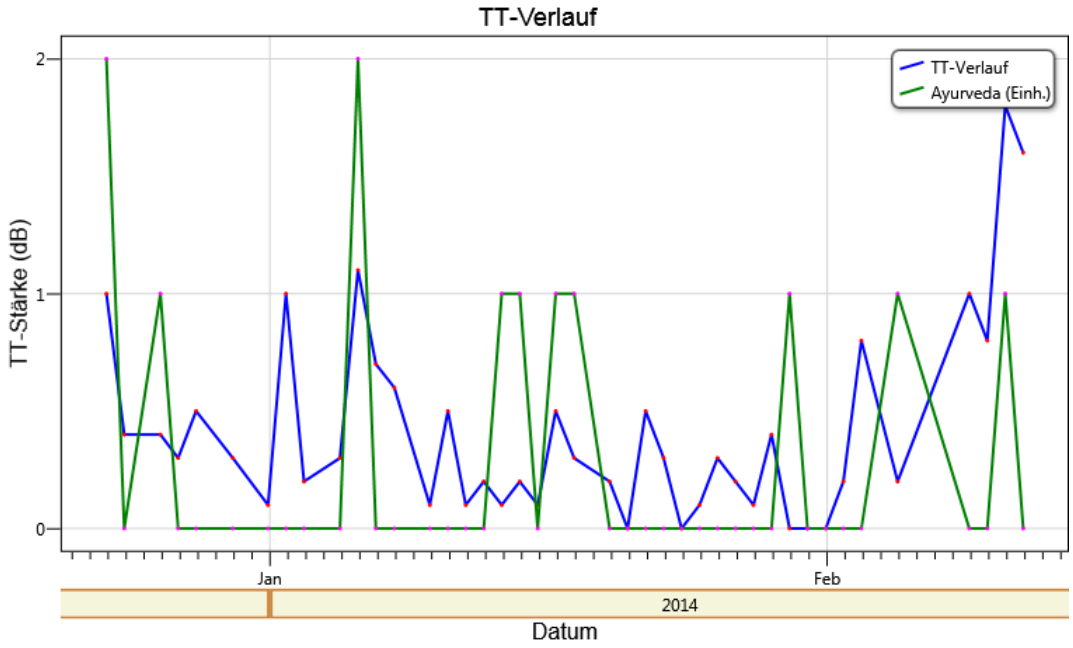

Figure 4.12: The ayurveda diary of B is of quite mixed manner.

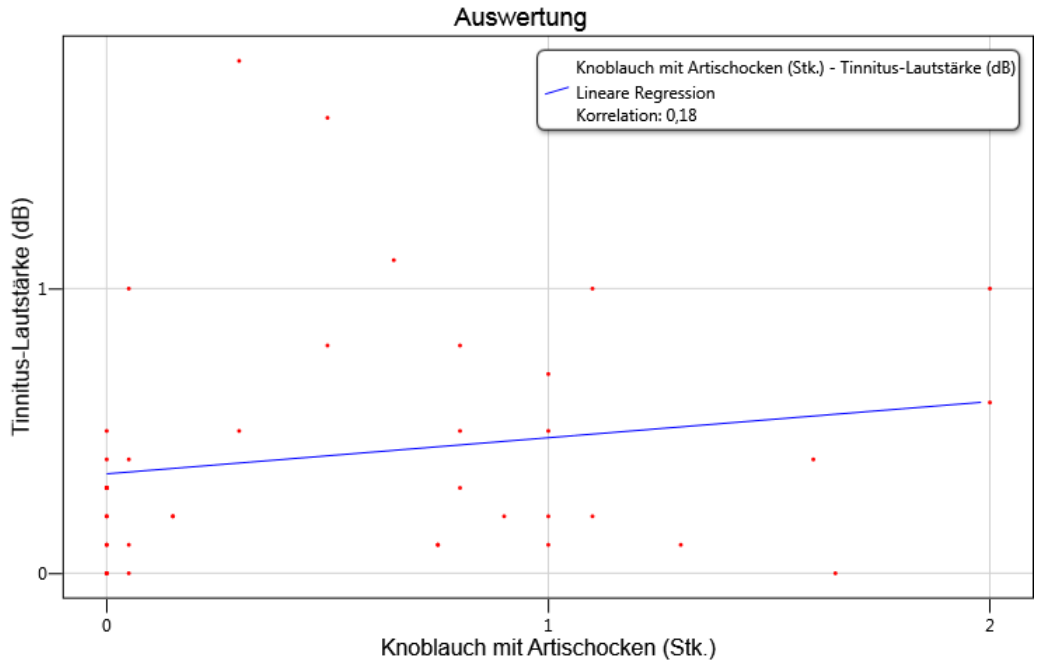

Figure 4.13: Maybe a weakness of Tacet: Positive correlation between healthy food intake and symptom behaviour.

4.2 Proof of Concept: Statistical analysis

We state that OLS regression is not the best tool for analysis of the patients data. In addition to thinking about other models like ARIMA[1] [29], it might be useful to include other statistical analysis techniques into Tacet, too. In this section, we discuss certain statistical experiments in order to find out which of the available methods could be implemented in a later version of Tacet. Therefore, we used IBM SPSS version 22 for Windows x64 for these experiments.

Descriptive statistical analysis

It might be useful to include certain descriptives into the output of Tacet, as there may be the ability to see some unhealthy behavior. As an example, we could take the collected data of A:

Descriptives, Records of 8BFB

	N	Minimum	Maximum	Average	Standard deviation
Loudness of the Tinnitus symptom in decibels	35	7	35	22,34	7,700
Exercise in hours	35	,00	5,00	1,2114	1,12250
Sleep in hours	35	4,0	11,0	7,174	1,4405
Water consumption in liters	35	,50	2,50	1,4800	,50964

Figure 4.14: Descriptives of the recorded data set of patient A

An example: One might conclude here, that patient A is drinking too less water a day, since the average water consumption is quite low (1,48 liters).

Cluster Analysis

Using the k-means cluster analysis algorithm, we thought that it might be possible to find out certain indicators of high or low Tinnitus volume. However, experiments with real and also hypothetical data showed us that outcomes are mostly useless and sometimes even leading to false assumptions!

ARIMA

The ARIMA time series model could be used in order to also consider autocorrellation and partial autocorrelation as well as the time itself for the calculation of certain relations.

[1] ARIMA is an acronym for „AutoRegressive, Integration, Moving Average“.

About ARIMA Models

ARIMA means Auto Regressive / Integrated / Moving Average and is a model for predicting outcomes for unknown inputs based on a given data set. It consists of three parts, building a sum[2]:

$\left(1 - \sum_{i=1}^{p} \phi_i L^i\right) (1 - L)^d X_t = \left(1 + \sum_{i=1}^{q} \theta_i L^i\right) \varepsilon_t$

- AutoRegressive Part

  This is the part consisting of the lags[3] [28] of the differenced series, which are appearing in the forecasting. [20]

- Integration

  If a certain model has to be differenced one or more times in order to get stationary, then it is considered as an „integrated“ model. The variable d equals the order of differencing necessary to stationarize the model.

- Moving Average

  These term describes the lags of the forecast errors. [20]

Thus, according to [20]:

- p is the number of autoregressive terms.
- d is the number of nonseasonal differences.
- q is the number of lagged forecast errors in the prediction equation.

Since these three terms are added to a sum, you can forget them when the related parameter is zero, leading to a special form of an ARIMA model[4]. Furthermore, having one or more parameters to be zero leads to smaller terms: Some examples are listed below:

- **ARIMA(0,1,1)** : $(1 - L)^d X_t a X_t = \left(1 + \sum_{i=1}^{q} \theta_i L^i\right) \varepsilon_t$
- **ARIMA(1,0,1)** : $\left(1 - \sum_{i=1}^{p} \phi_i L^i\right) X_t = \left(1 + \sum_{i=1}^{q} \theta_i L^i\right) \varepsilon_t$
- **ARIMA(1,1,0)** : $\left(1 - \sum_{i=1}^{p} \phi_i L^i\right) (1 - L)^d X_t = 1 + \varepsilon_t$
- **ARIMA(0,1,0)** : $(1 - L)^d X_t = 1 + \varepsilon_t$
- **ARIMA(0,0,1)** : $X_t = \left(1 + \sum_{i=1}^{q} \theta_i L^i\right) \varepsilon_t$
- **ARIMA(0,0,0)** : $X_t = 1 + \varepsilon_t$

[2] Formula from `https://en.wikipedia.org/wiki/Autoregressive_integrated_moving_average`

[3] A Lag or Backshift operator is defined as the operator on a time series to produce the previous element. See: `https://en.wikipedia.org/wiki/Lag_operator` for further detail about backshift operators.

[4] ARIMA(0,1,0) is considered as random walk model, while ARIMA(0,1,1) is referred to as differential smoothing, etc. [20]

Experiments

First, we decided to choose Matlab Release 2013b (with the ARIMA Model in the „Econometrics Package“) for our experiments with the ARIMA time series model. We soon decided to use SPSS instead, as using SPSS for the experiments with ARIMA led to certain benefits compared to using Matlab: With a technique called „Expert Modeler“, SPSS is capable of finding the best parameters for p, d, and q automatically.

Patient	ARIMA Parameters	Predictors
A	P=0,D=1,Q=0	none
C	P=1,D=0,Q=0	none
B	P=1,D=1,Q=0	none
E	P=0,D=0,Q=0	none
D	P=0,D=1,Q=0	none
Hyp: Harald	P=0,D=1,Q=0	1: Tennis
Hyp: Philomena	P=0,D=1,Q=0	1: Drospirenon

Table 4.3: Comparison of Symptom Diary Applications concerning availability. Prices are rounded.

Using SPSS ARIMA with real survey data soon brought disappointing results as the models were often different in parameters, and Expert Modeler did not choose any predictors. In addition, the values which were considered as best for P D and Q were always lower than or equal to one. In comparison, using the hypothetical data with certain strong correlations, which we created prior to the survey, the Expert Modeler chose predictors.

Outcome

We think that the ARIMA model should be implemented in a later Version of Tacet. However, it should be stressed that we will actually not use it for forecasting, but for testing influences of predictor variables. The fact that only hypothetical data led SPSS to choose predictor variables could possibly show how difficult it is in reality to find a factor that really influences the Tinnitus symptom and how complex human beings are in general. And thus, how complex it is to predict or show influences of certain factors. That may be an indicator on how complex it is to create a model that does not provide useless outputs. We do not yet know if it would be better to choose different parameters for the ARIMA Model for real patient data. In addition, it might be difficult to create an algorithm for finding well fitting parameters. Therefore it has to be stressed that finding a good model is a rather complex task. Nevertheless, we state that ARIMA time series methods are the best technique for the calculation of relations we have found yet.

Conclusions of the PoC

We recommend the following additional techniques to be implemented in a future version of Tacet:

- Descriptives
- ARIMA

CHAPTER 5

Summary

5.1 Feedbacks by patients

The overall feedback given by the patients was very good. Patients A and C would have wanted to measure more than the current maximum of three factors. While we were searching for volunteer patients, one patient first agreed to participate in the survey. After a few days, he quit his agreement to participate. He claimed, that to participate in the survey would distress him, since he has to face the fact that he hears his Tinnitus noise everyday. This can be seen as a drawback of such a tool. It hinders one from forgetting the condition. However, it may be stated that every time a patient tries to help himself, no matter which treatment is chosen, he would have to remind himself to have Tinnitus. Patients A and B voluntarily went far beyond the minimal survey time of three weeks, which we interpret as very positive. During his testing, patient C stated that he is not really sure what time span is meant when recording. He recorded his data in the late evening and thus stated that recording the sleep ten or more hours ago might be not very smart. We also noticed in the first days of our survey, that we forgot to tell all people to measure always in the same frequency, the same ear and that, if the appointment to measure can not be met, the actual (real) measurement time has to be taken into account. For example, if the patient had to measure his Tinnitus symptom everyday at 6pm, and once he came home late in the evening at 11pm because of a party, then he should type in all glasses of alcohol he consumed until the actual measurement time, which is 11pm. Consequently, patients with more than one sound asked us how they should proceed with their measurements. We told them to measure their most variable sound. One patient, B, was not really satisfied with this objective, as she wanted to measure and record all of her sounds. The same patient said that she takes her medication everytime her sounds are very loud. Thus the peaks of the medication in the diary often match with them of the symptom itself. She stated that this is kind of inaccurate and that some solution has to be found for that issue, like enabling the user to configure a certain timespan between record and measurement to compare. By ARIMA models, these delays (called „Lags“) are already considered. Regarding the software itself, our very first patient, A gave us really helpful feedback to improve the usability. We were very thankful to her, as it was possible to

improve the software significantly for all other patients right before the other roll outs. Patient C told us once, that he lost the recording data of 3 days. Although our program produces a verbose log file, it was not possible for us to find the reason for that issue.

5.2 Critical reflection

Most feedback we received was either positive or very helpful. Our survey had some problems in the early beginning, as there were some usability issues and it was a quite new challenge for us to do a real survey. The survey has been a great success on one hand, but it would be very useful to gather even far more patient's data. That might be possible, when patient's use the program productively and not in the scope of a survey anymore. But most important, and that is the essence of the whole work, it turned out that such a symptom diary for Tinnitus patients is generally a useful idea and is definitely finding acceptance at patients. With more sophisticated calculation of relations, such as a time series model and with features like some kind of a delay, there is still enough possibility to improve the software.

5.3 Discussion of open issues

Usability has to be improved. The program windows should be variable in size, for example. An appropriate time series model has to be implemented directly into the software.

The following things would have to be improved:

- Building in some delay functionality for certain factors (e.g. taking today's medication intake into account X days later, etc.)
- Improve the usability in general. We admit that the usability can still be improved at the moment. For example, the size of the window should be variable and not fixed.
- Implement an ARIMA or a similar time series model directly into Tacet.

In addition, it would be beneficial, if the software would also run on mobile platforms like iOS, Android and Windows Phone as well as GNU/Linux.

5.4 Summary and future work

In this work, we implemented our idea of a software diary for Tinnitus patients. We asked several professionals to help us creating a software and a survey to test it. Then, we tested the software in the context of a survey with five volunteer tinnitus patients. After the survey, we tried to find out how we can process this data in order to get valuable information about the behaviour of one's Tinnitus symptoms. We got positive feedback on one hand, and some results appear to be useful for a patient to help himself improving his health related condition on the other hand.

APPENDIX A

Appendix

A.1 A closer look to the app „MySymptoms“

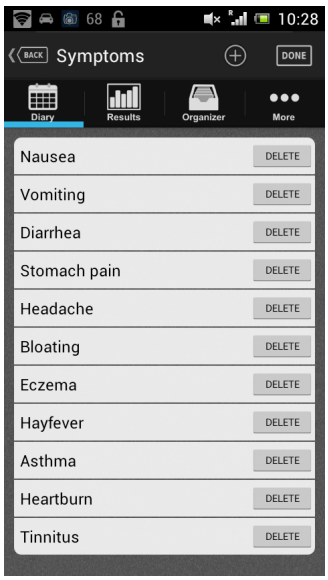

Figure A.1: A List of predefined symptoms, you can define your own if you wish (we defined“Tinnitus“, which is the last one in the list)

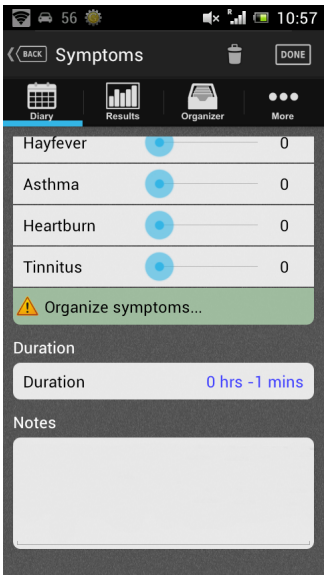

Figure A.2: The User has to measure his symptom after his subjective grading with scale 1 to 10.

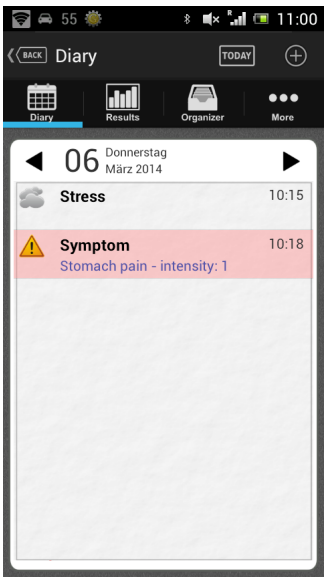

Figure A.3: List of Symptoms noticed on a certain day.

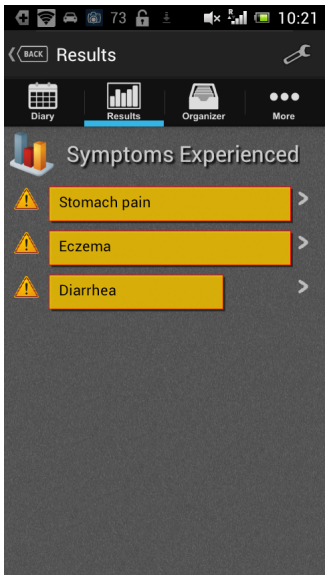

Figure A.4: List of Symptoms which where experienced since the user started recording.

Figure A.5: The app can show certain influental factors which might correlate with a certain symptom.

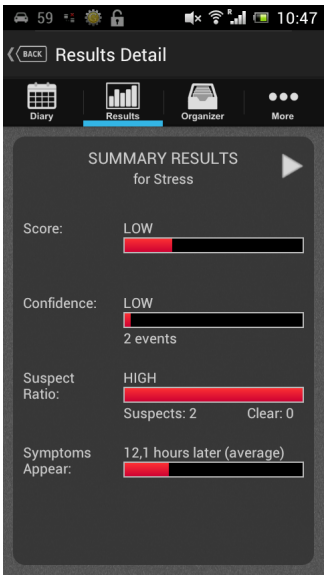

Figure A.6: Results calculated from the app. Remarkable: Confidence is also shown, but only evaluated via the number of recordings.

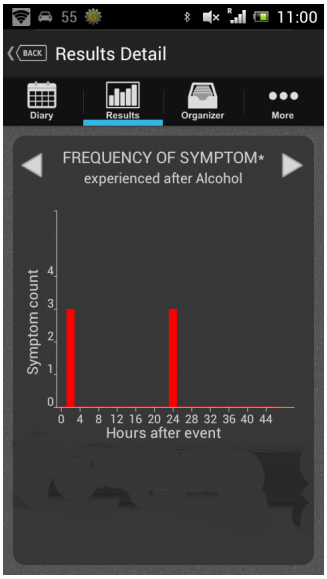

Figure A.7: Delay between influental factor and symptom.

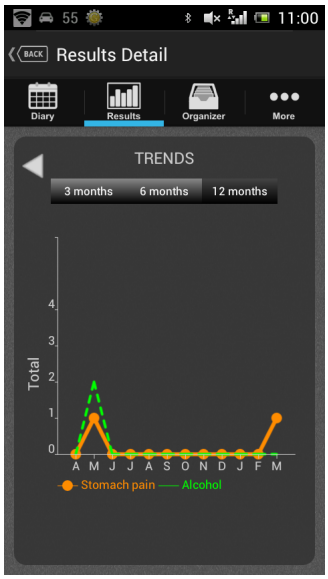

Figure A.8: Graph visualisation of the diary.

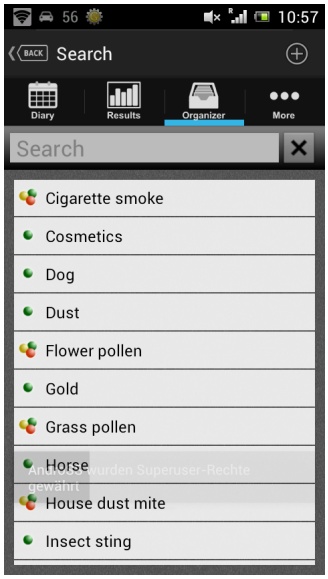

Figure A.9: The user has the ability to create own influental factors as well.

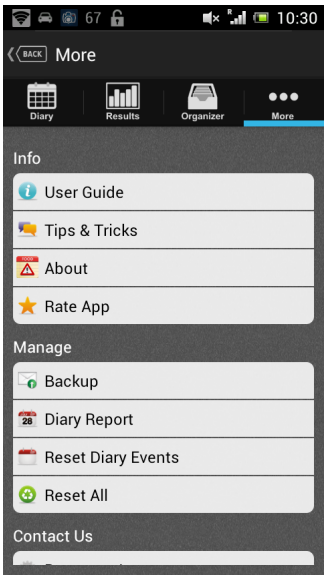

Figure A.10: The user can also export a diary report and has the ability to backup data on a storage outsite of the phone.

A.2 CryptExpert - RSA software

We developed a small additional program to decrypt the emails, we got from our patients. We called our program „CryptExpert“.

It can generate RSA keys of arbitrary length, encrypt and decrypt texts using RSA encryption with PKCS#1v2 padding, and convert decrypted Data sets from emails directly into the Tacet XML diary file format.

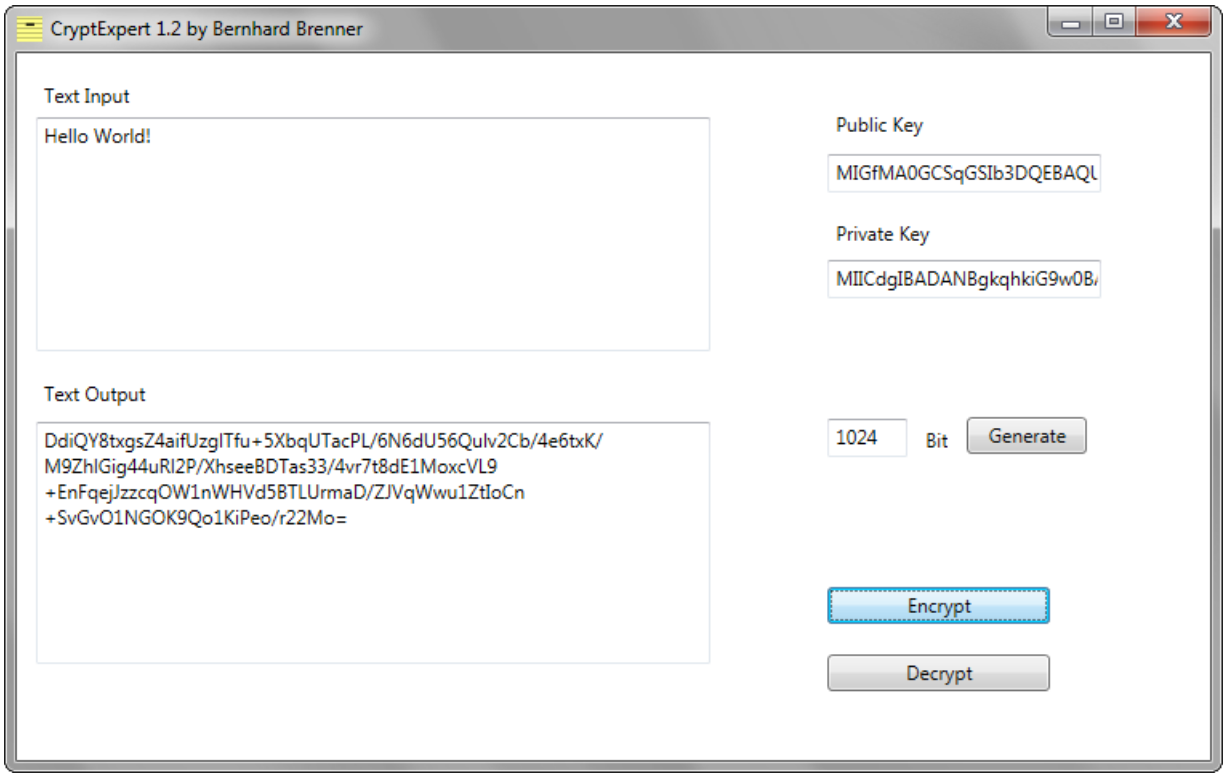

Figure A.11: CryptExpert can generate RSA keys, encrypt and decrypt texts with RSA.

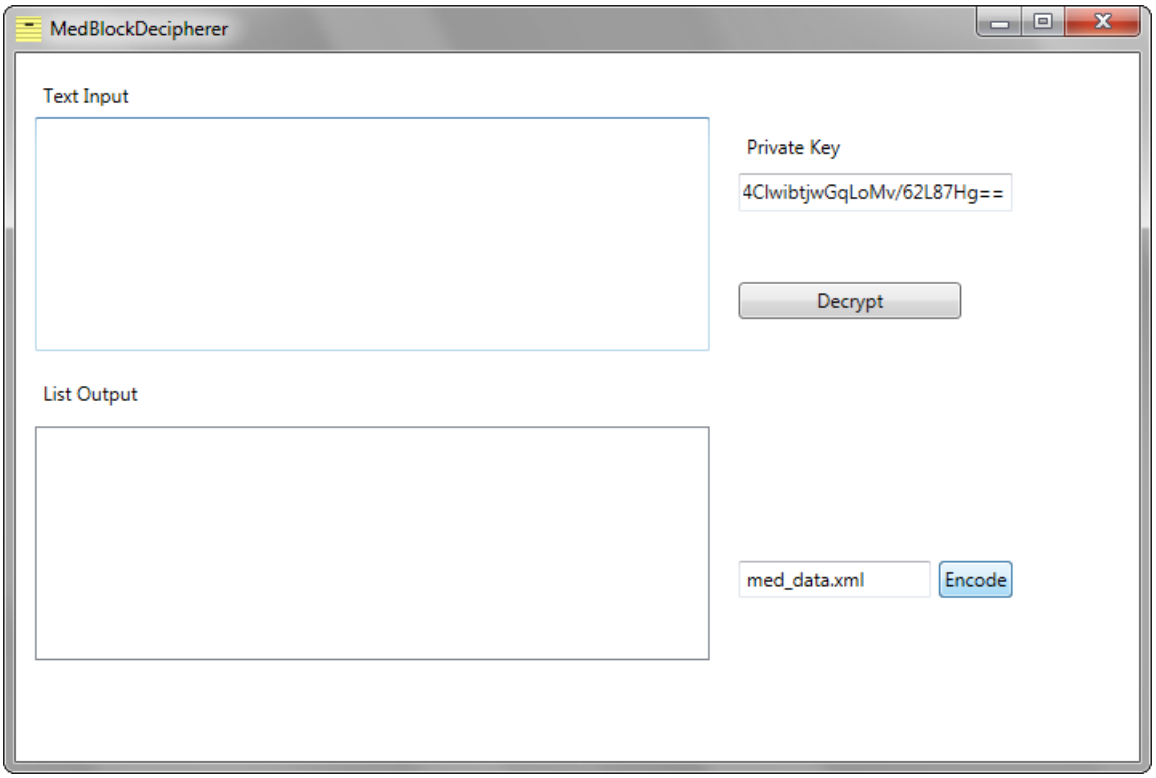

Figure A.12: For our convenience, we built in the functionality to decrypt the data blocks we received via email and to export them directly into a diary file.

A.3 Personal correspondence

Mail answer from Udo Abel, CEO SAX GmbH:

Guten Tag Herr Brenner,

ich freue mich über jeden Erkenntnisgewinn im Umfeld von
Tinnitus-Erkrankungen und wünsche Ihnen viel Erfolg für Ihre Arbeit!

Selbstverständlich können Sie HTTS hierfür einsetzen-
allerdings hatte ich seit langem keine Gelegenheit
zur Weiterentwicklung mehr. Ich bin daher nicht mal
sicher, ob das Programm auf neuen Windows Versionen
überhaupt lauffähig ist.

Sollten Sie Probleme haben, können Sie sich gerne an mich wenden.

Gruß,
Udo Abel.

A.4 Survey engagement

Our flyers:

Figure A.13: This is what our flyers looked like.

A.5 Patient data

Here is the data we have collected.

A

```
ID,Tinnitus-Lautstärke(dB),Bewegung(h),Schlaf(h),Trinken(l)
2,25,1.5,8,1.5
3,35,1,10,1
4,30,1,7,1
5,26,0.25,11,0.5
6,22,0.2,6,0.75
7,35,0.5,7,2.2
8,29,1,6,1
9,24,1,8,1.8
10,30,0.5,6,2
11,27,0.5,8,1.5
12,27,1,8,2
13,23,1,10,1.5
14,29,0.5,7,1.2
15,33,0.2,7,1.5
16,27,0,7,1.2
17,24,3,7,1.5
18,23,2,4,1
19,27,1.5,6,1.2
20,26,0.5,8,1.2
21,25,1.5,6.5,1.5
22,18,3,6.5,1.75
23,19,1,7,1.3
24,17,1,7.5,1
25,23,2,6,1
26,22,0.5,6,0.75
27,19,1,6,2
28,22,0,7,2
29,23,4,9,1.75
30,21,0.75,8,0.75
31,8,5,5,2
32,7,2,8,1.5
33,11,0.5,8,2
34,11,2,6.5,2.5
35,7,1,8,2.2
36,7,0,5.10,2.25
```

B

```
ID,Tinnitus-Lautstärke(dB),Ayurveda-Ohrentropfen(Einh.),Knoblauch
```

```
mit Artischocken,(Stk.)
1,1,2,2
2,0.4,0,1.6
3,0.4,1,0
4,0.3,0,0
5,0.5,0,0
6,0.3,0,0
7,0.1,0,0.75
8,1,0,1.1
9,0.2,0,1.1
10,0.3,0,0.8
11,1.1,2,0.65
12,0.7,0,1
13,0.6,0,2
14,0.1,0,1
15,0.5,0,0.8
16,0.1,0,0.75
17,0.2,0,1
18,0.1,1,1.3
19,0.2,1,0.15
20,0.1,0,0.05
21,0.5,1,1
22,0.3,1,0
23,0.2,0,0.9
24,0,0,0
25,0.5,0,0.3
26,0.3,0,0
27,0,0,0
28,0.1,0,0
29,0.3,0,0
30,0.2,0,0
31,0.1,0,0
32,0.4,0,0.05
33,0,1,0.05
34,0,0,1.65
35,0,0,0
36,0.2,0,0
37,0.8,0,0.8
38,0.2,1,0.15
39,1,0,0.05
40,0.8,0,0.5
41,1.8,1,0.3
42,1.6,0,0.5
```

C

```
ID,Tinnitus-Lautstärke(dB),Schlaf(h),Alkohol(Gläser),Sport(min)
1,15,7.5,0,20
2,9,9,2,0
3,20,7,0,0
4,11,8.5,0,0
5,16,8,0,60
6,12,9,0,0
7,11,7,0,0
8,14,8,0,60
9,14,8,0,0
10,14,8,3,0
11,15,7,0,0
12,15,7,0,0
13,16,8,0,0
14,12,8.5,0,0
15,15,8,0,0
16,15,7.5,0,0
17,11,8.5,0,0
18,12,8,0,0
19,13,8.5,0,0
20,14,8
```

D

```
ID,Tinnitus-Lautstärke(dB),Schlaf(h),Paracetamol(mg)
2,13,10,0
3,12,8,0
4,8,7,0
5,12,7.5,0
6,14,7,0
7,11,9.5,0
8,11,10,0
9,9,9,0
10,12,7,0
11,9,7.5,0
12,7,10,0
13,9,10,0
14,8,7.5,0
15,9,8,0
16,9,8.5,0
17,10,9.5,600
18,6,8,300
```

19,7,8.5,300
20,7,9,0
21,7,9,300
22,7,9.5,0
23,7,9,0
24,8,8,0
25,7,9,0
26,6,9,0
27,6,7,0

E

ID,Tinnitus-Lautstärke(dB),Spazieren gehen(h),Medikament(Einh.),Trinken(l)
1,60,7.5,1,1
2,60,7.5,1,1
3,70,4,1,1
4,60,5,1,1
5,60,5,1,1
6,70,4,1,1
7,60,3,1,1
8,60,3,1,1
9,65,4,1,1
10,70,5,1,1
11,60,7.5,1,1
12,60,4,1,1
13,65,3,1,1
14,60,5,1,1
15,60,3,1,1
16,60,4,1,1
17,65,3,1,1
18,60,4,1,1
20,60,4,1,1
21,70,3,1,1
22,60,5,1,1

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