Using the theory of reasoned action to explain medication adherence among patients with fracture diagnosed with osteopenia and osteoporosis

Master thesis Health Sciences
Science and Technology Faculty
University of Twente
Enschede

Merle Gijsbers
S1854984

Supervisors:
University of Twente: Dr. J.A. van Til
University of Twente: Dr. R. Wolkorte
Ziekenhuisgroep Twente Almelo: Dhr. Dr. J.H. Hegeman

11-04-2022

Abstract

Osteoporosis a disease which affects the density of the bones. In 2020, approximately 23,900 females and 7,000 males were diagnosed with osteoporosis and it is expected that this will increase by 204,700 diagnoses in the period 2018-2040. Due to the lower bone mineral density, patients have a higher risk of fracture. The use of medication reduces the fracture rate among patients with osteoporosis. However, previous studies report that medication adherence decreases over time after the medication is first prescribed.

The objective of this study is to evaluate the current medication adherence and reasons why patients are not adherent in the population of patients treated at the Ziekenhuis Groep Twente Almelo. The Theory of Reasoned Action (TRA) in combination with the Unified Theory of Acceptance and Use of Technology (UTAUT) is used to evaluate the behavior of the osteopenia and osteoporosis patients in ZGT Almelo.

Interviews with patients were performed to validate the reasons for (non-)adherence, which were identified from literature. Results of interviews and literature are applied to the TRA/UTAUT framework. The constructs of this framework are used to develop an on-paper, postal survey. Part of the survey was the ADherence Evaluation of OSteoporosis treatment (ADEOS) questionnaire to measure the medication adherence via the ADEOS score of patients. Multiple regression analysis is used to measure the effect of the TRA/UTAUT constructs on the ADEOS score.

A 44.6% response rate (n = 162) is reached in this study. Of these 162 respondents, 19.8% were males. Of the respondents, 25.2% had low adherence, 54.1% had neither low, nor high adherence and 20.7% had high adherence. There is a significant difference between the mean medication adherence of the people who are prescribed vitamin D and calcium, and the people who are prescribed bisphosphonates. In future appointments on the Fracture Prevention outpatient clinic, the specialized nurse and the physician needs to be aware of the influence on medication adherence of the following topics: gender, education level, frequency of taking (other) medication, difficulty altering lifestyle, the benefit of the medication, and pain.

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List of abbreviations

ADEOS	ADherence Evaluation of OSteoporosis treatment
BMD	Bone Mineral Density
DEXA	Dual Energy Xray Absorptiometry
FLS	Fracture Liaison Service
MICE	Multivariate Imputation by Chained Equations
OR	Odds Ratio
SD	Standard Deviation
TRA	Theory of Reasoned Action
UTAUT	Unified Theory of Acceptance and Use of Technology
ZGT	Ziekenhuisgroep Twente

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1. Introduction

Osteopenia and osteoporosis affect bone density. Both are characterized by lower bone mineral density (BMD) and disrupted cohesion of the bone tissue. The bone density is measured by a Dual Energy Xray Absorptiometry (DEXA) scan. Osteopenia is the pre-stage of osteoporosis. For osteopenia patients, it is advised to change some aspects of their lifestyle, such as reducing smoking and increase exercising. Besides, it is advised to osteopenia patients to take sufficient calcium and vitamin D by either dietary choices or supplements. This healthy diet is important, since a healthy diet is associated with lower fracture rates (1). Due to the lower BMD associated to osteopenia and osteoporosis, the fracture rate of patients with osteopenia and osteoporosis increases (2). Fractures lead to a major patient burden, namely health loss, decreased quality of life, chronic pain, increased risk of morbidity and mortality, and loss of autonomy (3, 4). Besides the patient burden, fractures also have a social burden; patients are less productive in their work, patients might need to move to residential care facilities or need to use other health care provisions (3-5).

Worldwide, approximately 200 million patients are affected by osteoporosis (6, 7). In the Netherlands, the overall incidence of osteoporosis in 2020 was approximately 507,200. Among other things, menopause and breastfeeding result in higher prevalence and incidence of osteoporosis in females compared to males (2); the prevalence of osteoporosis in females is 48.5 per 1000 females and for males it is 9.4 per 1000 males (8). In 2020, approximately 23,900 females and 7,000 males were diagnosed with osteoporosis (9). Based on changes in demographics (i.e. population age structure), it is expected that the osteoporosis diagnosis will increase by 204,700 diagnosis in the period 2018-2040 (10).

In hospitals, extra attention is paid to patients aged ≥ 50 years old with fractures (after-fracture patients). Their risk of developing a new fracture doubles compared to individuals without fractures with the same characteristics (11). Therefore, it is important that those patients are screened and if necessary treated for osteoporosis, to prevent subsequent fractures. The current care pathway for screening on osteoporosis on after-fracture patients is designed according to the Fracture Liaison Service (FLS) protocol. The FLS protocol consists of six steps: identifying patients, diagnosis of osteoporosis by performing a DEXA scan on after-fracture patients, instruction to patients about osteoporotic care, prescription of calcium and/or vitamin D supplements and prescriptions of anti-osteoporosis medication, and follow-up care (12, 13). To ensure the quality of the steps, one person has been appointed to coordinate the FLS in each department (14). In Ziekenhuis Groep Twente (ZGT) Almelo, the FLS is led by specialized nurses who provide information and is supervised by medical specialists. In ZGT Almelo, the FLS model was implemented in 2005 by trauma surgeons dr. J.H. Hegeman and dr. D. van der Velde as the Fracture Prevention outpatient clinic.

The instruction to osteopenia and osteoporosis patients about osteoporotic care and the prescription of anti-osteoporosis medication is essential to reduce the fracture risk and minimize the patient's burden and social burden. The instruction to patients about osteoporotic care consists of multiple components. First, patients are given lifestyle advice. It is advised to reduce alcohol intake and stop smoking, increase healthy nutrition intake (vitamin D, calcium and protein) and to increase exercising, (11). The FLS provider emphasizes the importance of at least 150 minutes of bone-stressing exercises per week. If all advice is followed, this could reduce the fracture rate and improve the BMD of patients (11). As mentioned before, a healthy diet is associated with lower fracture rates (1). Another part of the osteoporotic care is the prescription of medications. Different types of anti-osteoporosis medications can be prescribed: oral medication (the bisphosphonates alendronate, risedronate, or

ibandronate), intravenous infusion (zoledronic acid) or injections (Denosumab or teriparatide). The most preferable medication type in the Netherlands is bisphosphonate. Bisphosphonates slow down the process of bone breakdown by inactivating the osteoclasts (15).

The instruction to osteoporosis patients about osteoporotic care and the prescription of anti-osteoporosis medication is essential to reduce the fracture risk (Hazard ratio between 0.44 and 0.84 (16)). The consistently use of bisphosphonates reduces the fracture rate among people with osteoporosis, varying from 16% to 33%, compared to people with low adherence (17-19). Low adherence to bisphosphonates is related to an increase in fracture rates of 31% and 46%, compared to high adherence (20, 21).

Furthermore, high adherence to medication is related to the decrease of all-cause hospitalization and is associated with lower monthly and yearly osteoporosis-related costs (22, 23). Despite the clear benefits of the use of bisphosphonates to patients and society, medication adherence generally decreases over the time the medication is prescribed (24-26). Reasons that might impact the adherence are, for example, the side effects of the prescribed medication and the complex instructions for taking the bisphosphonates. Another reason is that patients miss some prove of effectiveness, and think the prescription period of 5 years without any in-between consult is too long. Also, the perception of the disease and the treatment might influence the adherence. For example, patients who underestimate the disease and do not take it seriously. The medication adherence might also be influenced by the type of medication, for example weekly medication or daily medication, or tablet of injection. Lastly, the lack of practical social support and emotional support experienced by patients might influence the medication adherence (25, 27-30).

Currently, patients treated at ZGT Almelo, visit the Fracture Prevention outpatient clinic once after the DXA scan which is the diagnosis consult. After three months, a specialized nurse calls them to evaluate the first three months taking medications. However, it is unknown whether patients remain adherent to their medication after the last follow up contact. As medication adherence is important, the ZGT aims to extent services to this patient group if this is deemed necessary and wants to adapt their services to patient's needs. Therefore, the objective of this study is to evaluate the current medication adherence and reasons why patients are not adherent in the population of patients treated at the ZGT Almelo.

To understand medication adherence as an intended action on the part of the patient, it will be analyzed according to the Theory of Reasoned Action (TRA)). The TRA model is presented in Figure 1. The TRA has six domains, which can potentially influence behavior (31). The degree of medication adherence depends on the intention to be adherent on the part of the patient. The intention to be adherent is influenced by the attitude of the person towards taking bisphosphonates (attitude toward behavior) and how much the person feels social pressure to take bisphosphonates (subjective norm) (32). The attitude is based on the beliefs of the person regarding the possible positive and negative outcomes of taking medications for osteopenia/osteoporosis (behavioral beliefs) and the values related to outcomes or characteristics of this behavior (32). The subjective norm is based on whether relevant individuals of the social environment of the patient accept or disapprove taking the medications (normative beliefs) and the motivation to do what the patient's relevant individuals think you should do (motivation to comply) (32). Besides the six TRA domains, the Unified Theory of Acceptance and Use of Technology (UTAUT) additionally describes the domain facilitating conditions, in which way the content of facilitations (e.g., information) can support medication adherence. This potentially affects medication adherence as well (33).

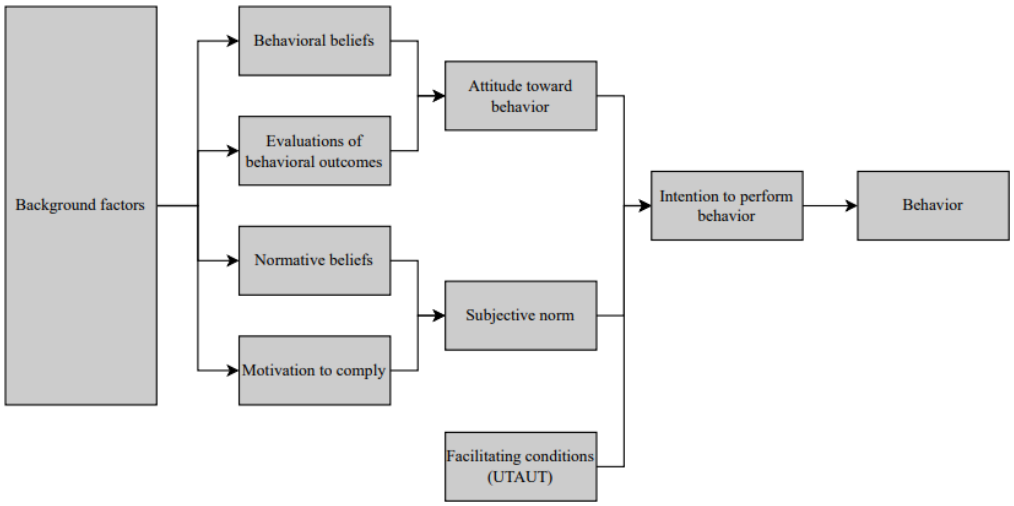

Figure 1 The Theory of Reasoned Action (TRA) and the Facilitating Conditions from the Unified Theory of Acceptance and Use of Technology (UTAUT)ave

Previously, determinants affecting medication adherence have been studied in different studies (25, 27-30). The results indicate that medication behavior is influenced by the side effects, complex instructions, lack of effectiveness experienced by patients, a five year prescription period, disease and treatment perception of patients, type of medication, lack of practical social support, and emotional support. However, the behavior of being adherent to the medication for osteopenia or osteoporosis is not yet evaluated according to the TRA/UTAUT framework. To add new insights to the available literature and the daily clinical practice, the research questions for this study are:

I. What is the medication adherence of after-fracture patients with osteoporosis or osteopenia?
    a. What is the medication adherence of after-fracture patients with osteoporosis treated with bisphosphonates?
    b. What is the medication adherence of after-fracture patients with osteopenia treated with calcium and/or vitamin D?
II. What are the barriers and facilitators for medication adherence according to after-fracture patients with osteoporosis or osteopenia?
III. What are determinants of low adherence in patients in the ZGT Almelo?
IV. How do after-fracture patients with osteoporosis or osteopenia consider different interventions aimed at increasing their medication adherence?

2. Methods

This study was conducted with patients who sustained a fracture and were seen on the Fracture Prevention outpatient clinic in ZGT Almelo, the Netherlands. The data collection was done from the 10th of December 2021 to the 28th of February 2022 and consisted of interviews and a survey.

2.1 Procedure

In literature, reasons for medication adherence were found. To validate those reasons to the ZGT population, interviews were performed. The literature together with the interviews were the basis of the survey.

2.1.1 Interview inclusion

The inclusion criteria for the semi-structured interviews were: patients ≥18 years old, diagnosis of osteoporosis[1], and the prescription of bisphosphonates. Participants were recruited using random sampling by the hospital administration. The interviewer visited five participants at home and one interview was online.

2.1.2 Structure of the interviews

A semi-structured interview guide was used. In total, four topics were discussed during the interview: osteoporosis, treatment, medication, and healthcare improvement. The sub-themes were the description of osteoporosis, consequences of osteoporosis, information about the treatment, current treatment, experience with the treatment, intake of the medication and motivational factors. At the end of the interview, two Dutch questionnaires were administered: general questions (e.g. age and educational level) and the ADherence Evaluation of OSteoporosis treatment (ADEOS-12), 12 questions to measure the medication adherence of the participants (34). Written informed consent was received from all the face-to-face participants and a recorded informed consent was taken from the online participant. The audio recordings were transcribed using Amber script and the data was coded using the ATLAS.ti software (version 22.0.5.0).

2.1.3 Analysis of the interviews

The data was coded deductively along the constructs of the TRA/UTAUT framework (Figure 1). The list of codes can be found in Appendix A. The codes were mapped in networks, which can be found in Appendix B. The networks gave insights in the relations between the different interviews. The interview results were categorized according to the constructs of the TRA/UTAUT framework.

2.2 Survey

The relevant literature and the interviews were the basis for the conduction of the new survey. The survey consisted of twenty questions and is added in Appendix C. The first five questions of the survey were about general information of the patient. Question six to fourteen consisted of the ADEOS-12 questions, to be able to calculate the medication adherence of the respondents. In the survey, 5-points Likert scale questions were asked to the patients, ranging from totally agree to totally disagree. Except for 'pain caused by osteoporosis', which had an extra answer possibility 'I don't experience any pain'. The Likert questions were divided into the four overarching themes of the TRA/UTAUT framework which were drawn from the interviews: 1) beliefs about the medication for osteoporosis; 2) evaluations of the consequences of osteoporosis; 3) the impact of the social environment; 4) the impact of information and contact with professionals was missing: lifestyle advice for osteopenia and osteoporosis patients. Based on the interview results, the constructs of the TRA/UTAUT framework

[1] Diagnosis Treatment Combination 151

provided the basis of the survey questions. In table 1, the constructs are shown with one example question. The complete overview of the TRA/UTAUT model can be found in Appendix D.

Table 1 From constructs of the TRA/UTAUT framework to questions for the survey

Constructs TRA/UTAUT framework	**Quote**	**Survey question example**	**Question numbers**
Behavior beliefs	"De botdichtheid die kan beter worden"	My osteoporosis medications are important to my health.	15a, 15c, 15e, 15g, 15h, 17a, 17b, 17c
Evaluations of behavioral outcomes	"Ik durf niet naar een sportschool te gaan, want dan ben ik bang dat ik nog verder in elkaar zak" "Je bent nu een stuk voorzichtiger"	I take the osteoporosis medication to feel less pain.	15d, 15f, 16a, 16b,
Normative beliefs about the importance of taking medication	"Daarvoor ben je ook met z'n tweeën eigenlijk" "Als zij dat kan, dan kan ik het ook"	The people around me encourage me to take the osteoporosis medication.	18a, 18b, 18c,
Motivation to comply to medication	"Ik hem dat zelf kunnen vertellen en niet via de ander"	I think it is important that I can explain to others what osteoporosis is.	18d, 18e,
Facilitating conditions to take medications	"In het begin wel veel opgezocht, maar ik weet niet meer precies wat waar"	If I am missing information, I will look it up myself.	19a, 19b, 19c, 19d, 19e, 20b, 20c, 20d
Attitude toward behavior (taking medication)	"Het is elke zondagmorgen dus dat is een vaste prik en ik vind het alleen maar goed" "Ja, maar het is zo eenvoudig"	I am used to taking my osteoporosis medication.	20a

2.2.1 Survey inclusion

The inclusion criteria for the survey participants were: patients diagnosed with osteopenia or osteoporosis (by Diagnosis Treatment Combination 151) between 01-01-2017 and 20-06-2021 and age ≥18 years old. In total, 4874 patients fulfilled these criteria. Patients who passed away were excluded. Through random sampling, 365 patients were selected for the survey. The sample size of 365 is based on a sample size calculation (with a confidence level of 95%, a margin of error of 5%, population proportion 50%, and population size of 4874 (= 357)) and taking into account a few errors, such as wrong addresses. The random sample is recruited via letters sent by post, with the option to complete the survey online using the Qualtrics platform.

2.2.2 Statistical analysis

The survey data is coded and entered in Microsoft Excel, taking into account the privacy of the respondents. For example, gender is coded as follows: male = 0, female = 1, other = 2. The Excel file is uploaded in RStudio (version 1.4) and is prepared to be used for statistical analysis. All the steps of data preparing are written down in the roadmap (Appendix E).

A data quality table presented an overview of further data which is not filled in by the respondent (missing data) (Appendix F). The multivariate imputation by chained equations (mice) function from the *mice* package (version 3.14.0) was used to generate values for the missing data. Despite the largest missing percentage, which was 19.8%, multiple imputations reduce bias (35). For numerical data, the predictive mean matching (pmm) method was used. For ordinal data, the proportional odds model (polr) was used. The number of iterations was set on five, which is the default setting (36).

To overcome misleading interpretation, all statements are coded in the same way, so an 'agree' answer is related to a medication adherent behavior. The results of the questions consisting a Likert scale (Likert data) are visualized by Likert plots, which show answer patterns. Similar response patterns can potentially have an identical underlying idea. This can be analyzed using Cronbach's alpha. The higher the Cronbach's alpha, the more the variables have shared covariance and likely overcome the identical underlying idea. According to Cronbach's alpha coefficient, the variables that do have shared covariance are taken together using sum score (Appendix G). This is done for the variables about concerns about the relevance of the medication and concerns about the medication because of different stories of other people or internet. It is also done for the variables about taking the medication to have less pain and because of the pain the patient fears for more pain. Another statistical analysis is the comparison of different groups of respondents based on different characteristics, which is tested by either a one-sample t-test, for mean values, or the Chi-squared test, for group amounts.

For the regression analysis, the five-point Likert scale is recoded to a three-point Likert scale to overcome problems with a low number of observations in each cell (<10 observations (37)). The coding 1 and 2 were merged to 1 (disagree), 3 to 2 (neutral), and 4 and 5 to 3 (agree). If categories still had <10 observations, these categories were removed from the dataset for the regression analysis. An overview of the removed categories can be found in Appendix H. The categorical variables were dummy coded. The dependent variable in the regression was the ADEOS score and the independent variables were the dummy variables of the variables with ≥10 observations. The *fastDummies* package (version 1.6.3) was used. For the multiple regression analysis, the *lm* function from the *stats* package (version 3.6.2) was used. After performing the multiple regression, the regression estimates could be used to calculate the odds ratios of the significant variables ($Odds\ ratio = e^{Estimate}$). Also, interactions are tested between different variables.

Initially, the significance level was set on $\alpha = 0.05$, however, due to the small sample size, it is decided that the significance level was set on $\alpha = 0.1$. A P-value ≤ α means the tested variables have a statistically significant association. A P-value > α means it is not possible to conclude that the variables are associated.

2.3 Ethics

The University Ethics committee approved the proposal on the 9th of November 2021. A local advisory committee of the hospital approved the study on the 22nd of November 2021.

3. Results

3.1 Interview results

3.1.1 Characteristics interview participants

The six interview participants (five females, one male) had a mean age of 67 years old. The characteristics per participant are shown in table 2. The ADEOS score of the participants differed between 20 and 22. According to the ADEOS threshold of ≥20, there is a high probability of treatment adherence among our interview participants (34).

Table 2 Interview participant characteristics

Respondent number	Gender	Age	Higher education	Work status	Intake as prescribed	Other medication
1	Female	58	Yes	1 – 39 hours a week	Yes	No
2	Female	72	No	Retired	Yes	Multiple times a day
3	Female	66	No	Volunteer work	Yes	No
4	Female	69	No	Retired	Yes	Multiple times a day
5	Female	72	No	1 – 39 hours a week	Yes	Daily
6	Male	66	No	1 – 39 hours a week	Yes	Daily

3.1.2 Interview results and the TRA/UTAUT framework

Three participants indicate that it was difficult to adhere to the medication. They had to get used to the medication, had trouble with the instructions, or felt better with alternative medicines.

Behavioral beliefs

There were different beliefs regarding the effects of medications. On one hand, participants believe that medication improves bone density. On the other hand, the risk of side effects of the medication is a topic mentioned by the participants. Two participants knew the risk of side effects, but also knew the possibility to contact their general practitioner if they experienced side effects. However, participants mentioned that information could be a resource to overcome concerns.

Evaluations of behavioral outcomes

Some participants (n = 3) experience daily pain as a result of osteoporosis. This pain motivates them to take the medication as described. Other participants mentioned that they only had pain after the fracture, but not in daily life.

Normative beliefs

The interviews showed that confidence in the doctor's recommendation to take osteoporosis medication varied. For five participants, the participants did not question the doctor's decision to prescribe medication. Participant four mentioned that according to her doctor, it was very important to stop taking the medication directly after five years. So, after five years of taking bisphosphonates, the patient wanted to stop. The other participants did not mention the strict five years of prescription.

During the interviews, it was found that the social environment also influenced the participants medication use. For example, the participants' social environment might have concerns about medication or support the medication use. However, this does not mean that social environment

concerns directly lead to non-adherence or vice versa. For participants, information is a resource to refute other stories of other patients or internet.

Motivation to comply

In addition, support from the participants' social environment, contact with the physician was also mentioned in the interviews as a source of support. Two participants indicated that they would discuss any concerns about medication with their doctor.

Participants also mentioned personal responsibility as motivation to adhere to medication. They said that taking the medication is their own responsibility. They do not feel influenced by, for them, relevant people when taking the medication.

Attitude toward behavior

Participants (n = 3) who had no difficulty taking the medication as prescribed do not understand why other people might find it difficult. They think that the tablets are small or that the intake regimen and procedure are simple. Other reasons are that it is the only medication participants take and that they have made it a part of their daily lives.

Participants had several reminders for themselves, such as having the medication in the kitchen, having a weekly schedule for taking it, or having it be part of their daily routine. In addition, participants mentioned that taking their medication was their own responsibility.

Subjective norm

The participants' social environment could positively or negatively influence the participant's medication intake. However, all participants who were interviewed, had the intention to take the bisphosphonates weekly. Appendix D contains the fully applied TRA/UTAUT framework.

3.2 Survey results

3.2.1 General respondent information

The survey was sent to 365 patients. In total 162 surveys were received, which resulted in a response rate of 44.6%. Two respondents were excluded after sampling because one patient moved and the other passed away. From the 162 responses, 111 responses were found useful for the analysis, since 51 responses were only filled in for <50%. Of the respondents, 19.8% were males and 80.2% were females. The one-sample T-test between the sample results and the usable respondent results resulted in a P-value of 0.855, which means there is no significant difference between the age of the respondents, compared with the sample. The Chi-square test comparing the male/female ratio of the respondents and the sample size, resulted in a P-value of 0.0004. This means there is a significance difference between the gender of the respondents of the different groups. Background characteristics of the respondents can be found in table 3.

3.2.2 Medication adherence

The mean medication adherence score is 17 (Standard Deviation (SD) = 2.6), which means this patient group is neither medication adherent, nor medication non-adherent (ADEOS score between 16 and 20). Respondents taking only calcium and/or vitamin D supplements (n = 49) had a mean score of 18 (SD = 2.7). The mean medication adherence for respondents taking bisphosphonates (n = 56) is significant lower than for respondents taking only calcium and/or vitamin D, namely 17 (SD = 2.7, p-value = 0.004).

In total, 25.2% had an ADEOS score of ≤ 16, which means a high probability of *discontinuation* of treatment. An ADEOS score of ≥ 20, which means a high probability of treatment *adherence*, is reached by 20.7%. An ADEOS score between 16 and 20, which means those respondents were neither

medication adherent, nor medication non-adherent is reached by 54.1% of the respondents. The respondent characteristics per ADEOS group are presented in table 3.

As can be seen in table 3 ([S]), the group of patients who are very likely to be medication adherent consists of significantly more females than males, compared to the group who are not likely to be medication adherent ($p = 0.0472$) and compared to the group who is in between adherent and non-adherent ($p = 0.0474$). The distribution of the levels of education significantly differed between the group of people who are very likely to be medication adherent and the group of people who are not likely to be adherent ($p = 0.0801$).

Table 3 Respondent characteristics divided per ADEOS group: high probability of discontinuation, neutral and high probability of treatment adherence.

	Characteristic	ADEOS ≤ 16 (n = 28)	ADEOS 16-20 (n = 60)	ADEOS ≥ 20 (n = 23)
Age in years, mean (min-max; SD)		69.9 (54-93; 10.29)	71.6 (52-92; 10.05)	73.7 (56-91; 9.05)
Gender, n (%)				
	Male	7 (25%)	14 (23%)	1 (4%)
	Female	21 (75%)[S]	46 (77%)	22 (96%)[S]
Education level* [S]				
	Low	2 (7%)	11 (18%)	3 (13%)
	Middle	18 (64%)	40 (67%)	18 (78%)
	High	8 (29%)	9 (15%)	2 (9%)
Medication**				
	Yes	24 (86%)	49 (82%)	22 (96%)
	No	4 (14%)	11 (18%)	1 (4%)
Other medication				
	Multiple times a day	5 (18%)	12 (20%)	2 (9%)
	Once a day	15 (54%)	29 (58%)	14 (61%)
	Multiple times a week	1 (4%)	1 (2%)	0
	Weekly	1 (4%)	3 (5%)	0
	Monthly	0	0	0

*Education level is defined low for primary school, middle for senior secondary vocational education and high school, high for higher vocational education and university (based on International Standard Classification of Education).

**A 'yes' for medication means the (in)take of bisphosphonates, calcium, calcichew, calciferol, vitamine D, cholecalciferol and/or teriparatide. A 'no' means none of the before mentioned medication is taken.

[S] Significant differences between the groups or variable mentioned with this 's'.

3.2.3 Likert scale questions per ADEOS group

All the Likert scale questions answers are varying from totally disagree to totally agree. To see whether the answers of different adherences differ, a table of all the answers to the Likert scale questions per ADEOS group is made (table 4). The results with the most differences between the adherent and non-adherent groups will be discussed here.

Of the adherent group, 57% totally agree with the statement that the medication the doctor prescribes is being taken. Of the non-adherent group, 29% of the patients agree. Also, 48% of the adherent group do understand the medication period of five years, while in the non-adherent group 21% do understand the medication period. For 52% of the adherent group, it was not a problem to change

their lifestyle, for 25% of the non-adherent group this was not. Lastly, of the adherent group, 65% do not feel pain, and of the non-adherent group 39% do not feel pain.

Table 4 Answers to the Likert scale questions divided in the three adherence categories

Statement	Disagree	Neutral	Agree
Medication strengthens the bones			
Not adherent to medication	1 (4%)*	13 (46%)*	14 (50%)
Not adherent nor non-adherent to medication	0*	4 (7%)*	56 (93%)
Adherent to medication	0*	1 (4%)*	22 (96%)
The medication of the doctor's prescription is taken			
Not adherent to medication	3 (11%)	5 (18%)	20 (72%)
Not adherent nor non-adherent to medication	1 (2%)	5 (8%)	54 (90%)
Adherent to medication	0	1 (4%)	22 (96%)
Side effects unimportant			
Not adherent to medication	13 (46%)	7 (25%)	8 (28%)
Not adherent nor non-adherent to medication	19 (32%)	14 (23%)	27 (45%)
Adherent to medication	5 (22%)	3 (13%)	15 (65%)
Side effects are reported to a professional			
Not adherent to medication	0	2 (7%)	26 (93%)
Not adherent nor non-adherent to medication	1 (2%)	3 (5%)	56 (93%)
Adherent to medication	2 (9%)	1 (4%)	20 (87%)
Important to be informed about side effects			
Not adherent to medication	0	3 (11%)	25 (89%)
Not adherent nor non-adherent to medication	0	3 (5%)	57 (95%)
Adherent to medication	0	2 (9%)	21 (91%)
Understand the prescription period of 5 years			
Not adherent to medication	2 (7%)	10 (36%)	16 (57%)
Not adherent nor non-adherent to medication	6 (10%)	10 (17%)	44 (74%)
Adherent to medication	1 (4%)	3 (13%)	21 (83%)
Changing lifestyle added value to healthier bones			
Not adherent to medication	3 (11%)	2 (7%)	23 (82%)
Not adherent nor non-adherent to medication	0	4 (7%)	56 (93%)
Adherent to medication	2 (8%)	0	21 (92%)
Changing lifestyle is not a problem			
Not adherent to medication	4 (14%)*	11 (39%)	12 (46%)
Not adherent nor non-adherent to medication	4 (7%)*	9 (15%)	46 (77%)
Adherent to medication	1 (4%)*	2 (9%)	20 (87%)
Medication less pain of osteoporosis			
Not adherent to medication (no pain: n = 11, 39%)	5 (18%)	4 (14%)	8 (29%)
Not adherent nor non-adherent to medication (no pain: n = 21, 35%)	12 (20%)	10 (17%)	17 (28%)
Adherent to medication (no pain: n = 15, 65%)	3 (13%)	4 (17%)	1 (4%)
Fear more pain of osteoporosis			
Not adherent to medication (no pain: n = 10, 36%)	3 (11%)	8 (29%)	7 (25%)
Not adherent nor non-adherent to medication (no pain: n = 20, 33%)	8 (29%)	8 (13%)	16 (27%)
Adherent to medication (no pain: n = 15, 65%)	7 (25%)	1 (4%)	4 (17%)
Belief in the effectiveness of the medication			
Not adherent to medication	2 (8%)	12 (43%)	14 (50%)
Not adherent nor non-adherent to medication	5 (9%)	7 (12%)	48 (80%)
Adherent to medication	1 (4%)	3 (13%)	19 (83%)
Doubt about the relevance of the medication			
Not adherent to medication	14 (50%)	11 (39%)	3 (11%)
Not adherent nor non-adherent to medication	42 (70%)	10 (17%)	8 (14%)
Adherent to medication	15 (65%)	4 (17%)	4 (17%)
Different positive or negative stories about the medication			
Not adherent to medication	14 (50%)	10 (36%)	4 (14%)
Not adherent nor non-adherent to medication	46 (77%)	10 (17%)	4 (7%)
Adherent to medication	19 (82%)	2 (9%)	2 (9%)
Support from social environment			
Not adherent to medication	10 (36%)	10 (36%)	8 (29%)

Not adherent nor non-adherent to medication	21 (35%)	18 (30%)	21 (35%)
Adherent to medication	8 (35%)	6 (26%)	9 (39%)
Social environment doubts about the medication			
Not adherent to medication	15 (53%)	12 (43%)	1 (4%)
Not adherent nor non-adherent to medication	49 (82%)	9 (15%)	2 (3%)
Adherent to medication	15 (65%)	7 (30%)	1 (5%)
Social environment tells positive and negative stories about the medication			
Not adherent to medication	12 (42%)	12 (43%)	4 (14%)
Not adherent nor non-adherent to medication	46 (77%)	9 (15%)	5 (8%)
Adherent to medication	16 (69%)	7 (31%)	
Important to explain osteoporosis to other people			
Not adherent to medication	3 (11%)	9 (32%)	16 (57%)
Not adherent nor non-adherent to medication	10 (17%)	14 (23%)	36 (60%)
Adherent to medication	2 (9%)	4 (17%)	17 (74%)
Clearer to environment what osteoporosis is, helps taking medication (better)			
Not adherent to medication	10 (36%)	10 (36%)	8 (29%)
Not adherent nor non-adherent to medication	17 (45%)	16 (27%)	17 (28%)
Adherent to medication	12 (52%)	2 (9%)	9 (39%)
Missing information will be looked up by patients			
Not adherent to medication	5 (18%)	12 (43%)	11 (39%)
Not adherent nor non-adherent to medication	11 (19%)	10 (17%)	39 (65%)
Adherent to medication	5 (21%)	4 (17%)	14 (61%)
Missing information will be looked up in books and internet			
Not adherent to medication	7 (25%)	11 (39%)	10 (36%)
Not adherent nor non-adherent to medication	16 (27%)	10 (17%)	34 (56%)
Adherent to medication	10 (43%)	3 (13%)	11 (47%)
Missing information asked to doctor			
Not adherent to medication	9 (32%)	10 (36%)	9 (32%)
Not adherent nor non-adherent to medication	18 (31%)	18 (30%)	24 (40%)
Adherent to medication	6 (26%)	8 (35%)	9 (39%)
Missing information asked to social environment			
Not adherent to medication	11 (40%)	11 (39%)	6 (21%)
Not adherent nor non-adherent to medication	31 (52%)	16 (27%)	12 (21%)
Adherent to medication	12 (52%)	7 (30%)	4 (17%)
Taking medication on a fixed day helps taking medication (better)			
Not adherent to medication	1 (4%)	8 (29%)	19 (68%)
Not adherent nor non-adherent to medication	0	6 (10%)	54 (90%)
Adherent to medication	0	3 (13%)	20 (87%)
*variable has a significant p-value according to the multiple regression analysis, $p < \alpha$; $\alpha = 0.1$			

3.2.4 The results of the multiple regression analysis

The detailed multiple regression results are presented in Appendix J. Males are less likely to be adherent than females ($\beta = -1.4297$; $p = 0.0203$). Comparing the middle education level with the high education level gives a significantly higher ADEOS score ($\beta = 1.2789$; $p = 0.0525$). Patients who take (other) medication daily are more likely to be adherent ($\beta = 1.0470$; $p = 0.0573$) compared to patients taking (other) medication weekly.

Patients who experience problems with a lifestyle change (e.g., more dairy products and exercising) have a significantly lower adherence ($\beta = -2.2735$; $p = 0.0561$), compared to patients who do not find the lifestyle change a problem. The belief that the medication does not strengthen the bones (-5.8108; $p = 0.0561$) or a neutral opinion about the medication strengthening the bones (-3.0803; $p = 0.0008$) result in a lower adherence, compared to the belief the medication strengthens the bones.

Patients who do not have concerns about taking the medication ($\beta = 3.5070$; $p = 0.0062$) or feel neutral about the concern statements ($\beta = 2.4414$; $p = 0.0105$), are more likely to be adherent

compared to patients who do concern about the medication. Patients who do experience pain, fear for more pain, and take the medication for osteopenia and osteoporosis for less pain, have a lower adherence (β = -1.1320; p = 0.0720) compared to patients who do not experience any pain.

3.2.5 Odds ratios

The odds ratios (OR) of the significant variables can be calculated using the regression estimates. These are presented in table 5. For example, there is a 0.24 times higher chance of having a higher adherence for males compared to females (OR = 0.24). Also, there is a 3.59 higher chance that patients with a middle education level will have a higher adherence compared to patients with a high education level (OR = 3.59).

Table 5 Odds ratios of the significant variables

Variable	Likelihood to have a higher medication adherence (95%-CI)	Compared to
Males	0.24 (0.09-0.65)	Females
Middle education level	3.59 (1.22-10.58)	High education level
Taking medications once a day	2.85 (1.16-7.03)	Taking medications weekly
Problem to change lifestyle	0.10 (0.01-0.72)	Not a problem to change lifestyle
The medication does not strengthen the bones	0.00 (0.00-0.40)	The medication strengthens the bones
Neutral about the medication and the strengthening of the bones	0.05 (0.01-0.20)	The medication strengthens the bones
No concern about the medication	33.35 (4.22-263.52)	Concerns about the medication based on the 5 years and different stories
Neutral about concerns about the medication based on the 5 years and different stories	11.49 (2.45-53.84)	Concerns about the medication based on the 5 years and different stories
Medication is taken because of (fear for more) pain	0.32 (0.11-0.90)	Patients who do not experience pain

3.2.6 Interaction effects

The three tested interaction effects all are insignificant. The interaction between male gender and no concerns about the medication has a p-value of 0.8641. For male gender interacting with neutral concerns, this is 0.3968. And for male gender interacting with a problem to change lifestyle, it is 0.6799.

3.2.7 The consideration of patients about the alternatives

Table 6 presents the statement about alternatives for osteoporotic care for the different adherent groups. To improve the medication adherence of the patients in ZGT Almelo, it is interesting to have a look at the groups “not adherent” and “not adherent nor adherent”, since the adherent group is already adherent. The combination of those improvement groups is shown in the table as italicized. For the first statement, 10% of the improvement groups thinks it would help them taking the medication (better) if there is more contact with the nurse. For 13% of the improvement groups is would be helpful to have more contact with the GP/practice nurse. For 15%, if would be helpful to have more contact with the pharmacist and 50% thinks more information helps taking the medication (better).

Table 6 Statements about alternatives per adherence group

Statement	Disagree	Neutral	Agree
More contact nurse helps taking medication (better)			
Not adherent to medication	7 (39%)	7 (39%)	4 (22%)
Not adherent nor non-adherent to medication	41 (62%)	21 (32%)	4 (6%)
Adherent to medication	17 (63%)	8 (30%)	2 (7%)
Improvement groups: not adherent to medication and not adherent nor non-adherent to medication	*48 (57%)*	*28 (33%)*	*8 (10%)*
More contact GP/practice nurse helps taking medication (better)			
Not adherent to medication	13 (50%)	7 (27%)	6 (23%)
Not adherent nor non-adherent to medication	34 (52%)	26 (39%)	6 (9%)
Adherent to medication	13 (48%)	11 (41%)	3 (11%)
Improvement groups: not adherent to medication and not adherent nor non-adherent to medication	*47 (51%)*	*33 (36%)*	*12 (13%)*
More contact pharmacist helps taking medication (better)			
Not adherent to medication	14 (52%)	7 (26%)	6 (22%)
Not adherent nor non-adherent to medication	31 (47%)	27 (41%)	8 (12%)
Adherent to medication	14 (52%)	8 (30%)	5 (19%)
Improvement groups: not adherent to medication and not adherent nor non-adherent to medication	*45 (48%)*	*34 (37%)*	*14 (15%)*
More information helps taking medication (better)			
Not adherent to medication	3 (17%)	8 (44%)	7 (39%)
Not adherent nor non-adherent to medication	9 (14%)	22 (33%)	35 (53%)
Adherent to medication	3 (11%)	5 (19%)	19 (70%)
Improvement groups: not adherent to medication and not adherent nor non-adherent to medication	*12 (14%)*	*30 (36%)*	*42 (50%)*

As described above, specific percentages of the improvement groups thinks it would be helpful to have more contact with specific professionals to improve their medication adherence. Of the respondents from the improvement groups who do think more contact with the nurse helps them (n = 8), six respondents (75%) also agreed on the help of more contact with the GP/practice nurse (n = 12), five respondents (63%) also agreed on the help of more contact with the pharmacist (n = 14) and eight respondents (100%) agreed that more information would help them (n = 42).

Of the respondents who think more contact with the GP/practice nurse would help them (n = 12), seven respondents (58%) also agreed with more help of the pharmacist (n = 14) and eleven respondents (92%) also agreed with the help of more information (n = 42).

Of the respondents who think more contact with the pharmacist (n = 14) helps them, ten respondents (71%) also think more information (n = 42) would help in taking their medication (better).

These similarities are presented in table 7.

Table 7 The similarity in answers of the improvement groups between two statements. For example, 36 of the 48 respondents who disagree the usefulness of more contact with the nurse, also disagree the usefulness of more contact with the GP/practice nurse

Statements		Disagree	Neutral	Agree
More contact nurse helps taking medication (better)	More contact GP/practice nurse helps taking medication (better)	36/48	22/28	6/8
	More contact pharmacist helps taking medication (better)	35/48	21/28	5/8
	More information helps taking medication (better)	9/48	16/28	8/8
More contact GP/practice nurse helps taking medication (better)	More contact pharmacist helps taking medication (better)	34/47	29/33	7/12
	More information helps taking medication (better)	8/47	15/33	11/12
More contact pharmacist helps taking medication (better)	More information helps taking medication (better)	8/45	14/34	10/14

In total, seven respondents agrees that more contact with the nurse and the GP/practice nurse and the pharmacist and more information would help them. For 44 respondents, all the extra contact and information is not necessary to help them.

4. Discussion

This study examined osteopenia and osteoporosis patients' medication adherence and the predictors of low medication adherence. The results suggest that osteopenia patients (taking calcium and/or vitamin D supplements) have slightly higher significant (p-value = 0.004) medication adherence (mean ADEOS score 18) compared with osteoporosis patients taking bisphosphonates (mean ADEOS score 17). Both mean ADEOS scores can be categorized in the group "not adherent nor adherent to medication". Most important predictors of low adherence are male gender, problems to lifestyle changes, the believe the medication does not strengthen the bones or neutral about it and the medication is taken because of (fear for more) pain. Most important predictors of high adherence are middle education level, taking (other) medication once a day, no concerns about the medication or neutral about it. For 50% of the improvement groups, it would be helpful to have more information to improve their medication adherence. More contact with the nurse helps 10% of the improvement groups, more contact with the GP/practice nurse helps 13% and more contact with the pharmacist helps 15% of the respondents. All respondents who think more contact with the nurse help them, think more information would help them too. There is 75% overlap between the agreement of the help of the nurse and the help of the GP/practice nurse. For the help of the nurse and the help of the pharmacist, the overlap is 63%. For 58%, more contact with the GP/practice nurse and more contact of the pharmacist would help. This is 92% for more contact with the GP/practice nurse and the help of more information. Lastly, 71% thinks more contact with the pharmacist and more information would help.

The National Health Care Institute explained that one cause of non-adherence is that patient's lifestyles are not adapted to taking medications (26). Difficulty in changing their lifestyle also leads to lower adherence to medication in this study. The National Health Care Institute, along with the KNMP, explained that patients might misunderstand osteoporosis and misunderstand the benefits of the medications (26, 38). The results of this study suggest that belief in the medications influences medication adherence, as patients who do not believe in the efficacy of the medications have lower adherence than patients who believe in the medications.

Lower medication adherence for males is consistent with the paper of Hiligsmann et al. (2019) and Yeam et al. (2018), who found that patient-related factors such as male gender were associated with poorer medication adherence (25, 27). A possible explanation for this is the statement of Jung et al. (2019) that males diagnosed with osteoporosis do not believe they are at risk (39). So, they may not understand the usefulness of the medications. Another study about adherence of antihypertensive treatment, declared males' lower adherence to "daily life management". Males are more likely to disregard lifestyle guidelines, even when they are aware of their disease. Furthermore, males are frequently busier than females and are under more stress at work, which might influence the choices they need to make for their lifestyle (40). A Swedish study referred to different studies where females are more likely to be non-adherent compared to males, however they stated that this depends on the different conditions and study settings (41). The study itself concluded that males and females have different reasons for non-adherence and noted that males are more likely to engage in risky health behaviors (41).

The studies of Hilligsmann et al. (2019) and Yeam et al. (2018) also pointed out lower education level as a factor in poorer medication adherence (25, 27), which contrasts with the findings of this study. According to this study, a middle level of education leads to higher medication adherence compared to a high level of education. This contradiction may arise because the distribution of the educational

levels differs. The middle level of education is (over)represented by 68% of the total responses. The low level of education is represented by 14% and the high level of education by 17%. The distribution in the Netherlands is 8% low level of education, 55% middle level of education and 35% high level of education (42). In Almelo, the distribution in 2021 was respectively 22%, 47% and 28% (low to high) (43).

The paper of Yeam et al. (2018) found that higher frequency of taking medication is related to a poorer medication adherence. A meta-analysis of Iglay, K. et al. (2015) concluded that weekly dosing was related to higher medication adherence, compared to daily dosing. Their explanation is that any possibility to make taking medication easier, could influence the medication adherence (44). A systematic review of Rash, J.A. et al. (2016) discusses the possibility to combine different medication tablets into one tablet, the polypill, to simplify medication intake (45). Other literature studied the effect of daily dosing compared to more frequently dosing of medication for chronic diseases and concludes that the medication adherence with daily dosing is higher compared to the more frequently dosing options (46-48). The results of this study suggests the opposite: higher dosing frequency relates to higher medication adherence. For example, the small sample size of this study may have influenced the conflicting results. The results of this study and additional literature has proven that it is not only dosing frequency that influences medication adherence. With lower frequency, there is still room for improvement in medication adherence (48, 49). For further research, it would be interesting to take into account these conflicting results by identifying the patient's vision on different dosing frequencies.

Previous studies by Barrionuevo et al. (2019) and Lindsay et al. (2016) have focused on reasons for treatment discontinuation or medication non-adherence (28, 30). The results of this study show the impact of those reasons on the medication adherence.

4.1 Limitations

The reliability of the data used in this report is compromised by the 44.6% response rate of the survey. Comparing the response rate with other studies, the response rate is low. Briot K. et al. (2020) had a response rate of 92.8% (n = 13,914), Jarab, A.S. et al. (2020) had a response rate of 74% (n = 296), and Roh, Y.H. (2019) had a response rate of 61% (n = 969) (50-52). However, the respondents of this study were randomly selected rather than using a panel or recruiting in the clinic. According to Cheung et al. (2017), voluntary recruitment could result in a strong nonresponse bias compared with mandatory recruitment, which is also an indicator of a low response rate (53). Although the survey was labeled as an "Osteoporosis survey", osteopenia patients were invited to participate in the survey. Osteopenia and osteoporosis patients are two different groups of patients. Both groups take different types of medication, as osteopenia patients take calcium and vitamin D supplements as medication and osteoporosis patients take, among others, bisphosphonates. In addition, the bone density of osteoporosis patients is worse than that of osteopenia patients. These patient groups could be divided according to the medication question. In future studies, a different name for the survey and a question about patients' diagnosis could be added to address this issue.

Because of the low response rate, this study has insufficient power. In general, the larger the sample size, the more statistically significant associations are found (54). The studies by Hiligsmann et al. (2019), Yeam et al. (2018), and Hall et al. (2017) found other variables to be significant in addition to overlapping significant variables (25, 27, 29). A higher response rate in future research should indicate whether other factors are also significant in ZGT Almelo.

For further research, to ensure the results reflect the overall population, the number of respondents needs to be increased. In this study, questionnaires were sent by post, with the option to complete the questionnaire online. Nine respondents used the online option. Therefore, further research should

continue with a postal survey. It is suggested that the data collection process can be expanded with a reminder by post to complete and return the survey. Ideally, the survey should be shortened and the reminder should include the same content as the initial sending (55).

The reliability of the results is also limited by selection bias in the interview portion of this study. All interview participants were taking bisphosphonates as medications, and all were medication adherent. This interview sample does not reflect the targeted population, which is mixed adherent and not adherent. This may have influenced the constructs for the survey in a more adherent perspective. The perspective of not adherent patients is included based on literature and is not validated by interviews. In addition, the interviews were conducted with five females and one male (5:1), whereas the survey respondents had a ratio of 3:1. This might overrepresent females in the interviews. Afterwards, based on the survey results, males have a higher chance of a lower medication adherence. Therefore, the underrepresentation of the males in the interviews might also underrepresent the lower medication adherent perspective.

There might also be a bias in the interpretation of the interview results applied to the TRA/UTAUT framework. The concepts of the TRA/UTAUT can be interpreted differently. On the one hand, the behavioral belief is that taking the medication improves the bone density. The evaluation of the behavioral beliefs is that taking the medication releases the pain of the patient. On the other hand, the behavioral belief is that taking the medication will lead to side-effects and this does not lead to the outcome: an improved bone density. The evaluation of the behavioral outcome is that it is important to have an improved bone density. The survey used in this study is conducted within the first interpretation perspective. The other interpretation perspective might have led to other survey questions. For further research it is suggested to discuss the interview results and the concepts of the framework with more researchers to overcome interpretation issues.

Another limitation that needs to be mentioned is the translation of the ADEOS-12 survey. The questionnaire was originally written in English and French. For this study, the questionnaire was translated into Dutch. The translation is done by the researcher, which could have resulted in misinterpretations of the questions from the English and French survey. In the future, it would be better if several people translate the survey and combine their results (translation study) (56). In this study, the outcomes of the translated survey are not tested in comparison with the outcomes of the original survey. If there are misinterpretations in the Dutch survey, the calculated ADEOS scores could be unreliable. The mean ADEOS score of the original ADEOS survey study is 18.7 ± 2.8 (34). Based on the one-sample t-test, this is significantly different from the mean ADEOS score in this survey: 17 ± 2.6 ($p < 0.1$).

The ADEOS score must also be taken in a certain context of self-adherence and voluntary respondents. Since self-adherence is always higher than objective adherence, e.g., by blood tests (57). And voluntary respondents report more favorable outcomes (53).

4.2 Recommendation

The results of this study contribute to a better understanding of the reasons for medication non-adherence and medication adherence of patients at ZGT Almelo. The results could be useful during the intake of the fracture patients by the specialized nurse or physician at the Fracture Prevention outpatient clinic. For example, males were 4.2 times more likely than females to be non-adherent to their medications, and thus extra attention needs to be paid to males, in order to prevent non-adherence. In addition, patients who have difficulty changing their lifestyle are 10 times more likely to have lower medication adherence than patients who do not have difficulty changing their lifestyle, and thus patients who do experience difficulty could use some extra help. If the specialized nurse or

physician tries to find out if this applies to the patient, they can help the patient to be adherent to their medication. For the specialized nurse and the physician, it is essential to participate in a conversation with patients to ensure that patients make informed lifestyle adjustments. In this decision-making process, decision aids can be helpful (58). Mobile health applications have the potential to improve chronic illness health outcomes, however the value of those applications is not yet studied in randomized controlled studies (59). Before implementing those applications, the effectiveness and cost-effectiveness for ZGT Almelo patients need to be studied.

It is also important for the specialized nurse or the physician to address concerns about osteopenia/osteoporosis medication, because patients who have no concerns about the medication are more likely to be adherent to their medication than those with concerns. Even patients with a neutral opinion about the concerns are more likely (11.49) to have a higher medication adherence, than those with concerns about the medication. Finally, pain experienced by patients has a negative impact on medication adherence. Therefore, it is important for the physician to ask patients if they are in pain. Possibly, the prescription of pain medication as addition to the treatment, might improve medication adherence (60).

This study provides insight into the determinants of low medication adherence in ZGT Almelo. It is still unknown to what extent these insights will improve medication adherence in ZGT Almelo. Follow-up research should show whether an improvement has actually taken place. The new insights can help the specialized nurse or the physician to design the content of the Fracture Prevention outpatient clinic.

5. Conclusion

On average, respondents from the ZGT are neither medication adherent, nor medication non-adherent). Respondents taking calcium and vitamin D are on average more medication adherent than respondents taking bisphosphonates. Most important predictors of low adherence are male gender, problems to lifestyle changes, the believe the medication does not strengthen the bones or neutral about it and the medication is taken because of (fear for more) pain. Most important predictors of high adherence are middle education level, taking (other) medication once a day, no concern about the medication or neutral about it. More attention to those patient specific characteristics at the Fracture Prevention outpatient clinic may improve the medication adherence of ZGT Almelo patients. Further research can give insights in the effectiveness of mobile health applications.

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Appendix A. Codes ATLAS.ti

BELEMMERINGEN OSTEOPOROSE
Linked codes:

- Belemmeringen: Dagelijks last
- Belemmeringen: Doodsbenauwd verder inzakken
- Belemmeringen: Ingezakte ruggenwervels
- Belemmeringen: Minder risico nemen
- Belemmeringen: Zelf mee leren omgaan

BESTELLEN MEDICATIE
Linked codes:

- Bestellen medicatie: Apotheek komende 5 jaar
- Bestellen medicatie: Doosje bijna leeg bestellen
- Bestellen medicatie: Mailtje medicijnen liggen klaar
- Bestellen medicatie: Medicatie uit de muur halen

BEWEGING
Linked codes:

- Beweging: 150 min soms op een dag
- Beweging: Beweging is altijd belangrijk
- Beweging: Dagelijks wandelen
- Beweging: Filmpjes over beweging hebben iets geleerd
- Beweging: Kleine wandelingetjes
- Beweging: Niet veel botbelastende beweging
- Beweging: Telefonisch consult verpleegkundige, wandelen opvoeren
- Beweging: Wandelen goed voor cadans
- Beweging: Wel normale beweging
- Oplossingen positief/Beweging: Met een groepje sporten

MANIEREN HERINNEREN MEDICATIE
Linked codes:

- Manieren herinneren medicatie: App voor herinneren nemen medicijnen, nog niet gebruikt
- Manieren herinneren medicatie: Appje medicijnen zijn klaar
- Manieren herinneren medicatie: Maandag avond in theeglas voor dinsdagochtend
- Manieren herinneren medicatie: Medicatie staat bewust in de keuken
- Manieren herinneren medicatie: Medicijnenbakje
- Manieren herinneren medicatie: Tabletten zitten in ritme

MOEITE?
Linked codes:

- Moeite?: Dat het voor anderen lastig is, is lastig voor te stellen
- Moeite?: Nemen van medicatie is zo eenvoudig
- Moeite?: Slikken medicatie. Geen problemen
- Moeite?: Tablet heel klein

MOTIVATIE SLIKKEN
Linked codes:

- Motivatie slikken: Artsen zullen het wel weten

- Motivatie slikken: Behandeling gaat zoals het gaat
- Motivatie slikken: Beslissen medicatie, waarom niet?
- Motivatie slikken: Doorgaan met medicatie moest
- Motivatie slikken: Gesprek vrienden
- Motivatie slikken: Gevolgen niet nemen gezien
- Motivatie slikken: Helemaal niet getwijfeld
- Motivatie slikken: Iedereen aanraden medicijnen nemen
- Motivatie slikken: Man steunt in nemen medicatie
- Motivatie slikken: Medicatie kan alleen maar helpen
- Motivatie slikken: Medicatie verbetert botdichtheid
- Motivatie slikken: Medicijnen nemen is belangrijk
- Motivatie slikken: Tabletten makkelijk dagelijks leven
- Motivatie slikken: Veel steun vanuit omgeving
- Motivatie slikken: Verder geen medicijnen

OPLOSSINGEN NEGATIEF
Linked codes:

- Oplossingen negatief/positief: Je kan ook een alarm op je telefoon zetten
- Oplossingen negatief: Contact met anderen met osteoporose is niet nodig
- Oplossingen negatief: Contact met ziekenhuis goed zo
- Oplossingen negatief: Informatie over nut niet nodig, anders zelf opzoeken
- Oplossingen negatief: Meer contact HA of apotheek niet nodig, ligt aan jezelf
- Oplossingen negatief: Meer info gebruik medicatie, waarvoor?
- Oplossingen negatief: Niet echt handig een appje
- Oplossingen negatief: Steun omgeving verschillende verhalen
- Oplossingen negatief: Zelf vergeet nooit, man vergeet eerder medicatie

OPLOSSINGEN POSITIEF
Linked codes:

- Oplossingen negatief/positief: Je kan ook een alarm op je telefoon zetten
- Oplossingen positief/Beweging: Met een groepje sporten
- Oplossingen positief: Alarm zou helpen als het misschien lastig zou zijn
- Oplossingen positief: De een zal het meer nodig hebben dan de ander
- Oplossingen positief: Freq. contact prof als vergeetachtiger
- Oplossingen positief: Meer bekendheid geven
- Oplossingen positief: Meer info over gevolgen is goed
- Oplossingen positief: Meer medicatie maakt misschien uit, qua combinaties
- Oplossingen positief: Mekaar informeren, clubje vormen
- Oplossingen positief: Misschien dat meer info over nut helpt
- Oplossingen positief: Uiteindelijk kan iedereen er last van krijgen
- Oplossingen positief: Voor een ander is een herinneringsappje wel handig
- Oplossingen postiief: Herinnering ophalen medicijnen kan handig zijn

OSTEOPOROSE
Linked codes:

- Osteoporose: Beeld bij botbroosheid
- Osteoporose: Bij bijwerkingen contact arts/apotheker
- Osteoporose: Bijsluiter informatie medicijnen
- Osteoporose: Botontkalking
- Osteoporose: Geen last van

- Osteoporose: Geen last van medicijnen
- Osteoporose: Hoe ouder, hoe erger
- Osteoporose: In het begin veel op internet gezocht naar informatie
- Osteoporose: Informatie duidelijk
- Osteoporose: Ingezakte ruggenwervels
- Osteoporose: Je weet dat als je valt dat je sneller wat breekt
- Osteoporose: Snel omzwikken enkel
- Osteoporose: Voorbeelden bothardheid
- Osteoporose: Zwakke botten

OSTEOPOROSE ONBEKEND (VOOR DIAGNOSE)
Linked codes:
- Osteoporose onbekend: Achteraf beseffen dat wel vaker wat gebroken
- Osteoporose onbekend: Andere verwachting osteoporose
- Osteoporose onbekend: Artrose en osteoporose is heel verschillend
- Osteoporose onbekend: Breuk voor diagnose
- Osteoporose onbekend: Goed dat ze naar osteoporose kijken
- Osteoporose onbekend: Wist niet dat ik osteoporse had

REDEN DAGRITME
Linked codes:
- Reden daginname: Advies vaste dag
- Reden daginname: Dinsdag want maandag ophalen en gelijk begonnen
- Reden daginname: Ritme zaterdag 's morgens
- Reden daginname: Zaterdag 's morgens want vrij
- Reden daginname: Zondagmorgen ritme

SUPPLEMENTEN
Linked codes:
- Supplementen: Extra calcium
- Supplementen: Extra supplement vit d en calcium
- Supplementen: Extra supplement vitamine d
- Supplementen: Vitamine d was van nature al hoog
- Supplementen: Zuivel voor calcium

TWIJFEL
Linked codes:
- Twijfel: Als verteld wordt over de medicijnen, vaak troep
- Twijfel: Dokter toen gelijk gezegd niet langer dan 5 jaar
- Twijfel: Gedachte
- Twijfel: Gesprek arts om twijfel uit te spreken
- Twijfel: Inname medicatie wennen
- Twijfel: Medicatie niet klakkeloos genomen
- Twijfel: Meningen van anderen aan het denken gezet
- Twijfel: Moeite instructies. Normaal met medicijnen niet
- Twijfel: Niet zo tablet-achtig, meer met kruiden
- Twijfel: Risico hartklepverkalking bij >5 jaar
- Twijfel: Vit d --> verkalkte hartklep
- Twijfel: Zonder gesprek vrienden misschien gesprek arts ingepland

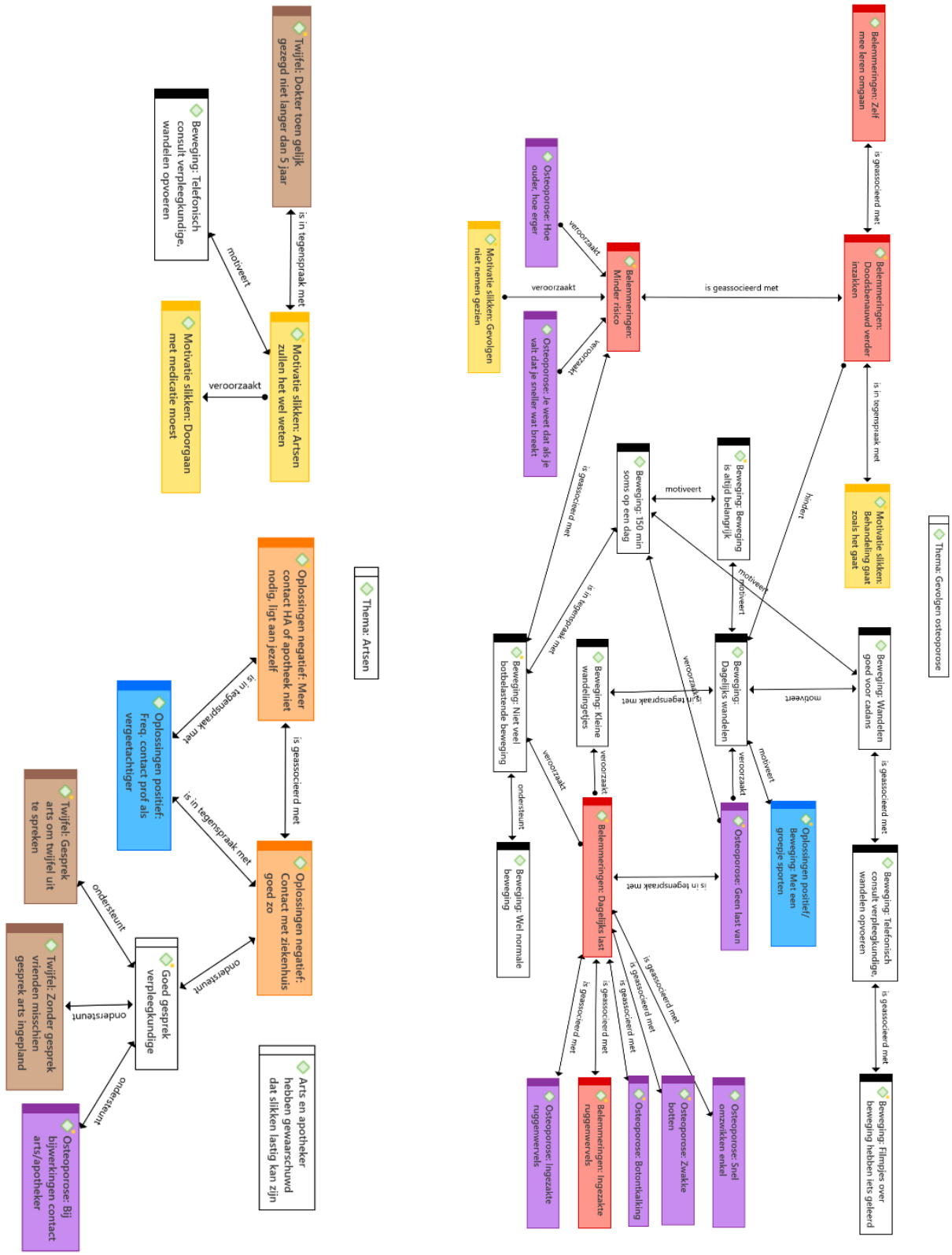
VASTE DAG
Linked codes:

- Vaste dag: Dinsdag
- Vaste dag: Zaterdag 's morgens
- Vaste dag: Zondag

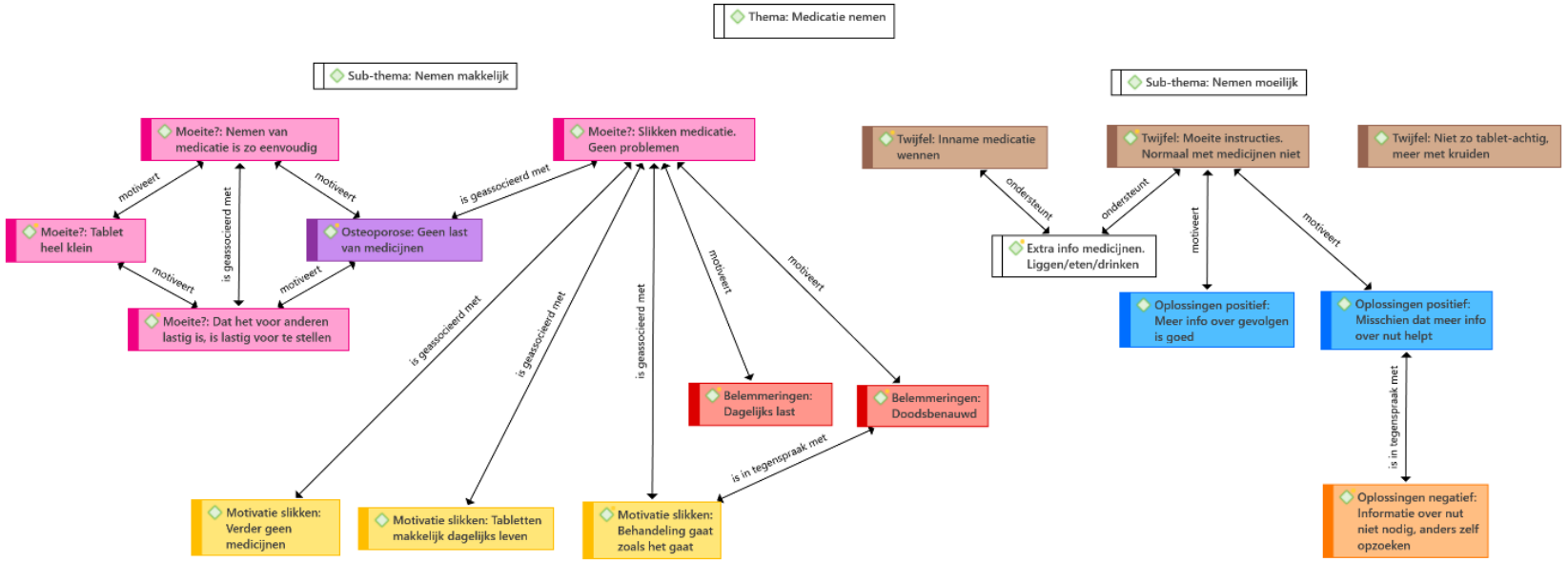
VRAGENLIJST TEKST/TABEL
Linked codes:

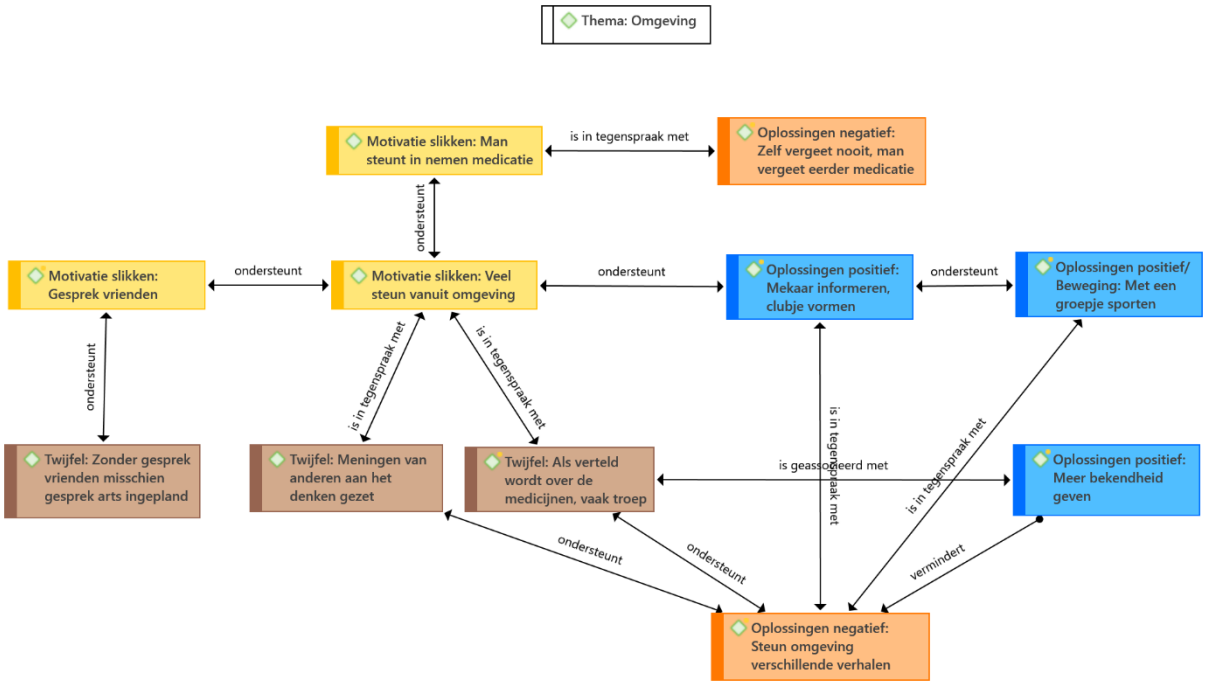
- Vragenlijst: Lastig om af te wegen
- Vragenlijst: Pijnscore geven is moeilijk
- Vragenlijst: Tabel vorm deed denken aan pijnscore geven
- Vragenlijst: Tekstvorm is duidelijker

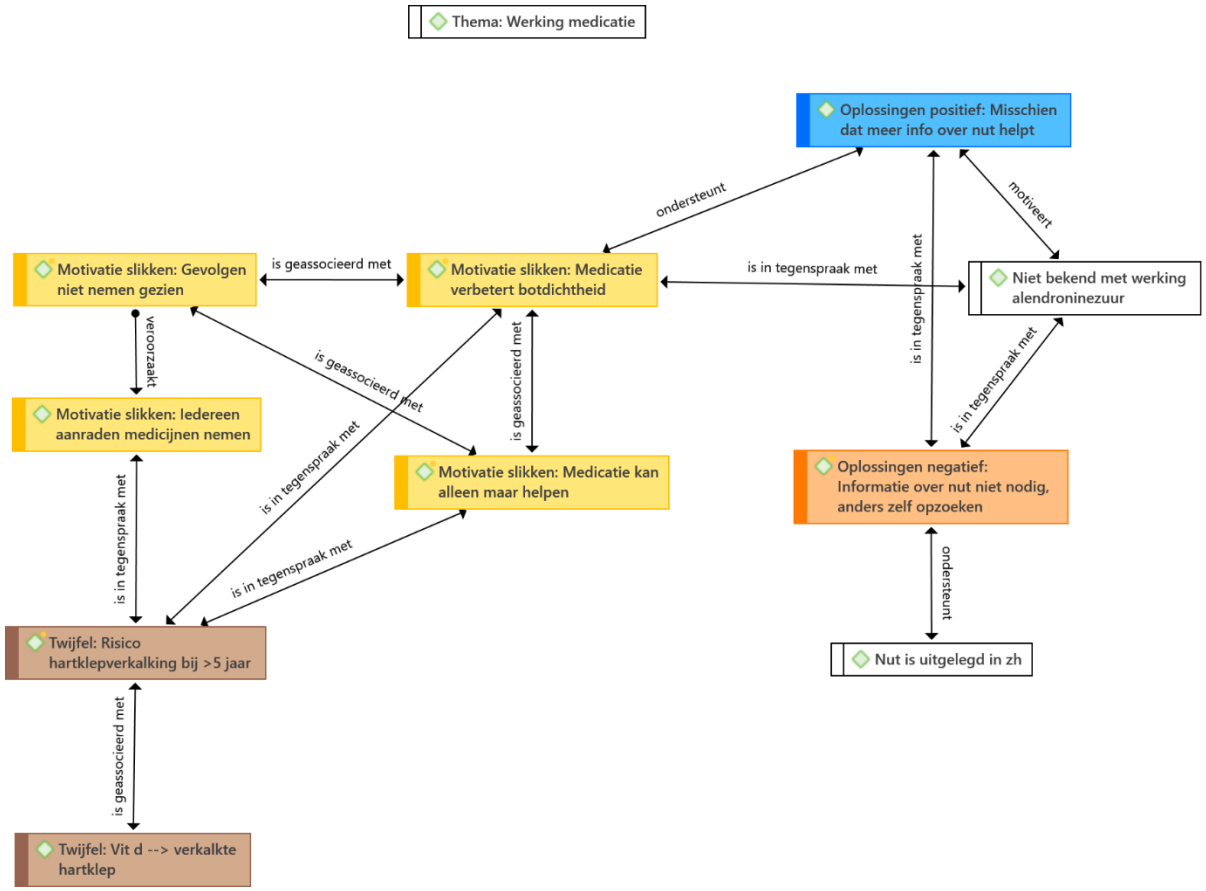
Appendix B. ATLAS.ti Concept Map Themes

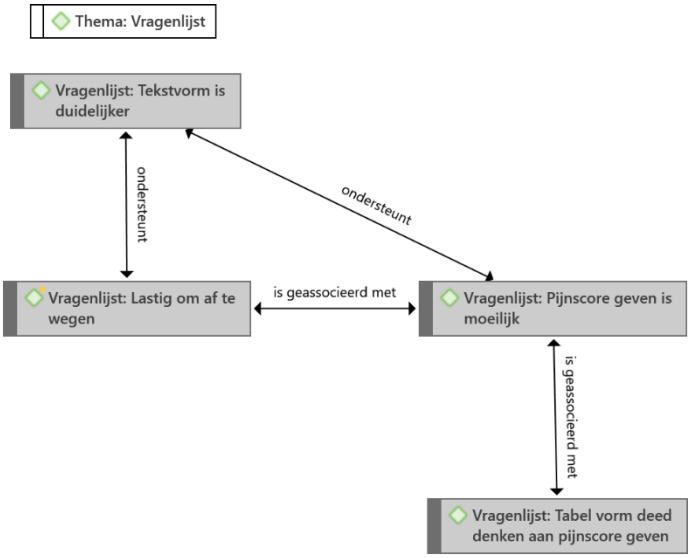



Thema: Ritme medicatie
Manieren herinneren medicatie: Medicijnenbakje
Oplossingen positief: Alarm zou helpen als het misschien lastig zou zijn
Oplossingen negatief/positief: Je kan ook een alarm op je telefoon zetten
Oplossingen positief: De een zal het meer nodig hebben dan de ander
Manieren herinneren medicatie: Maandag avond in theeglas voor dinsdagochtend
Manieren herinneren medicatie: Medicatie staat bewust in de keuken
Manieren herinneren medicatie: Tabletten zitten in ritme
Oplossingen positief: Voor een ander is een herinneringsappje wel handig
Oplossingen postiief: Herinnering ophalen medicijnen kan handig zijn
Bestellen medicatie: Doosje bijna leeg bestellen
Manieren herinneren medicatie: Appje medicijn...
Bestellen medicatie: Mailtje medicijnen liggen klaar
Reden daginname: Advies vaste dag
Manieren herinneren medicatie: App voor herinneren nemen medicijnen, nog niet gebruikt
Oplossingen negatief: Niet echt handig een appje
Vaste dag: Dinsdag
Vaste dag: Zondag
Vaste dag: Zaterdag 's morgens
Reden daginname: Dinsdag want maandag ophalen en gelijk begonnen
Reden daginname: Zondagmorgen ritme
Reden daginname: Zaterdag 's morgens want vrij
Reden daginname: Ritme zaterdag 's morgens
is geassocieerd met
is in tegenspraak met
ondersteunt
veroorzaakt


Thema: Medicatie nemen
Sub-thema: Nemen makkelijk
Sub-thema: Nemen moeilijk
Moeite?: Nemen van medicatie is zo eenvoudig
Moeite?: Slikken medicatie. Geen problemen
Moeite?: Tablet heel klein
Osteoporose: Geen last van medicijnen
Moeite?: Dat het voor anderen lastig is, is lastig voor te stellen
Twijfel: Inname medicatie wennen
Twijfel: Moeite instructies. Normaal met medicijnen niet
Twijfel: Niet zo tablet-achtig, meer met kruiden
Extra info medicijnen. Liggen/eten/drinken
Oplossingen positief: Meer info over gevolgen is goed
Oplossingen positief: Misschien dat meer info over nut helpt
Oplossingen negatief: Informatie over nut niet nodig, anders zelf opzoeken
Belemmeringen: Dagelijks last
Belemmeringen: Doodsbenauwd
Motivatie slikken: Verder geen medicijnen
Motivatie slikken: Tabletten makkelijk dagelijks leven
Motivatie slikken: Behandeling gaat zoals het gaat
is geassocieerd met
is in tegenspraak met
motiveert
ondersteunt


Thema: Omgeving
Motivatie slikken: Man steunt in nemen medicatie
is in tegenspraak met
Oplossingen negatief: Zelf vergeet nooit, man vergeet eerder medicatie
ondersteunt
Motivatie slikken: Gesprek vrienden
ondersteunt
Motivatie slikken: Veel steun vanuit omgeving
ondersteunt
Oplossingen positief: Mekaar informeren, clubje vormen
ondersteunt
Oplossingen positief/ Beweging: Met een groepje sporten
ondersteunt
is in tegenspraak met
is in tegenspraak met
is in tegenspraak met
Twijfel: Zonder gesprek vrienden misschien gesprek arts ingepland
Twijfel: Meningen van anderen aan het denken gezet
Twijfel: Als verteld wordt over de medicijnen, vaak troep
is geassocieerd met
Oplossingen positief: Meer bekendheid geven
ondersteunt
ondersteunt
vermindert
Oplossingen negatief: Steun omgeving verschillende verhalen


Thema: Werking medicatie
Oplossingen positief: Misschien dat meer info over nut helpt
ondersteunt
motiveert
Motivatie slikken: Gevolgen niet nemen gezien
is geassocieerd met
Motivatie slikken: Medicatie verbetert botdichtheid
is in tegenspraak met
Niet bekend met werking alendroninezuur
veroorzaakt
is geassocieerd met
is in tegenspraak met
is in tegenspraak met
Motivatie slikken: Iedereen aanraden medicijnen nemen
Motivatie slikken: Medicatie kan alleen maar helpen
is in tegenspraak met
is in tegenspraak met
Oplossingen negatief: Informatie over nut niet nodig, anders zelf opzoeken
ondersteunt
Twijfel: Risico hartklepverkalking bij >5 jaar
Nut is uitgelegd in zh
is geassocieerd met
Twijfel: Vit d --> verkalkte hartklep


Thema: Vragenlijst
Vragenlijst: Tekstvorm is duidelijker
ondersteunt
ondersteunt
Vragenlijst: Lastig om af te wegen
is geassocieerd met
Vragenlijst: Pijnscore geven is moeilijk
is geassocieerd met
Vragenlijst: Tabel vorm deed denken aan pijnscore geven

Appendix C. Dutch survey osteoporosis

Vragenlijst osteoporose

Om uw privacy te beschermen, worden uw gegevens anoniem verwerkt. De gegevens zijn niet tot u te herleiden. Ook in rapporten en publicaties over het onderzoek zijn de gegevens niet tot u te herleiden. U maakt geen extra kosten voor dit onderzoek. De Adviescommissie Lokale Uitvoerbaarheid van het ZGT Almelo heeft goedkeuring gegeven om dit onderzoek uit te voeren.

Alvast hartelijk bedankt!

- ○ Ik ga akkoord met deelname aan het onderzoek.

1. De volgende 5 vragen zullen algemene vragen zijn. De eerste vraag is: Wat is uw geslacht?

- ○ Man
- ○ Vrouw
- ○ Wil ik niet zeggen
- ○ Anders, namelijk: _____

---

2. Wat is uw leeftijd? _____jaar

---

3. Wat is uw hoogst behaalde opleiding?

- ○ Basisonderwijs
- ○ VMBO-b/k, MBO 1
- ○ VMBO-g/t ((M)ULO), HAVO-, VWO-onderbouw
- ○ MBO 2, MBO 3
- ○ MBO 4 (MTS)
- ○ HAVO, VWO (HBS/MMS)
- ○ HBO-, WO-bachelor (HTS)
- ○ HBO-, WO-master, doctor
- ○ Weet ik niet / onbekend

---

4. Wat zijn de medicijnen die u neemt voor osteoporose? Als u extra calcium en/of vitamine d tabletten neemt, is dit bij deze vraag niet van toepassing.

- ○ Wekelijkse tabletten of drank vorm (Bisfosfonaten: Alendroninezuur, Chodroninezuur, Ibandroninezuur of Risedroninezuur)
- ○ Injectie (Bisfosfonaten: Ibandroninezuur, Pamidroninezuur of Zoledroninezuur)
- ○ Denosumab (injectie)
- ○ Anders, namelijk: _____

---

5. Neemt u naast de osteoporose medicijnen ook nog andere medicijnen of voedingssupplementen?

- ○ Ja, meerdere keren per dag
- ○ Ja, dagelijks
- ○ Ja, meerdere keren per week
- ○ Ja, wekelijks
- ○ Ja, maandelijks
- ○ Nee

De volgende vragen gaan over uw medicijnen voor osteoporose. Er is geen goed of fout antwoord.

---

6. Vindt u dat uw osteoporose medicijnen gemakkelijk in te nemen zijn?

- ○ Heel makkelijk
- ○ Enigszins makkelijk
- ○ Helemaal niet makkelijk

---

7. Heeft u uitleg/instructies gekregen over hoe u de osteoporose medicijnen moet nemen?

- ○ Ja
- ○ Nee
- ○ Weet ik niet

---

8. Is de manier waarop u de osteoporose medicijnen moet nemen lastig voor u?

- ○ Heel lastig
- ○ Enigszins lastig
- ○ Helemaal niet lastig

---

9. Vergeet u weleens uw osteoporose medicijnen te nemen?

- ○ Nooit
- ○ Soms
- ○ Vaak

---

10. Slaat u weleens uw medicijnen over vanwege onverwachte omstandigheden?

- ○ Nooit
- ○ Soms
- ○ Vaak

---

11. Hoe herinnert u uzelf eraan om uw osteoporose medicijnen in te nemen? (u mag meerdere vakjes aanvinken)

- ☐ De mensen om mij heen herinneren mij eraan
- ☐ Ik heb een manier om mijzelf eraan te herinneren
- ☐ Het is voor mij natuurlijk geworden
- ☐ Anders: _____
- ☐ Ik weet niet wat ik moet doen om te onthouden

---

12. Wat motiveert u om uw osteoporose medicijnen in te nemen? (u mag meerdere vakjes aanvinken)

- [ ] Mijn arts
- [ ] De mensen om mij heen
- [ ] Ik ben bang om (weer) een bot te breken
- [ ] Om de gezondheid van mijn botten te verbeteren
- [ ] Het is makkelijk om in te nemen
- [ ] Niets speciaals
- [ ] Anders: _____

---

13. Hoe gemotiveerd bent u om uw osteoporose medicijnen te blijven gebruiken?

- ○ Heel gemotiveerd
- ○ Enigszins gemotiveerd
- ○ Helemaal niet gemotiveerd

---

14. Vink voor elk van de volgende uitspraken het vakje aan dat uw mening het beste weergeeft.

a. "Mijn medicijnen tegen osteoporose zijn belangrijk voor mijn gezondheid."

- ○ Ja, helemaal
- ○ Enigszins
- ○ Nee, helemaal niet

---

b. "Ik ben eraan gewend geraakt om mijn medicijnen tegen osteoporose in te nemen."

- ○ Ja, helemaal
- ○ Enigszins
- ○ Nee, helemaal niet

---

c. "Ik zorg ervoor dat ik de instructies die ik krijg over het nemen van mijn osteoporose medicijnen zorgvuldig opvolg."

- ○ Ja, helemaal
- ○ Enigszins
- ○ Nee, helemaal niet

---

d. "De instructies voor het innemen van mijn osteoporose medicijnen zijn duidelijk genoeg."

- ○ Ja, helemaal
- ○ Enigszins
- ○ Nee, helemaal niet

---

15. De volgende vragen bevatten stellingen over de medicijnen voor osteoporose. Er is geen goed of fout antwoord.

Geef aan in hoeverre u het eens bent met deze stellingen.

	Helemaal mee eens	Eens	Neutraal	Oneens	Helemaal mee oneens
Het nemen van medicijnen voor osteoporose, gaat mijn botten sterker maken.	○	○	○	○	○
De medicijnen die mijn dokter voorschrijft, neem ik.	○	○	○	○	○
Ongeacht wat de bijwerkingen van de medicijnen voor osteoporose zijn, neem ik het medicijn.	○	○	○	○	○
Als ik bijwerkingen ervaar, trek ik aan de bel.	○	○	○	○	○
Ik vind het belangrijk om goed ingelicht te zijn over de bijwerkingen van het osteoporose medicijn.	○	○	○	○	○
Ik begrijp waarom ik de medicijnen voor osteoporose 5 jaar moet innemen.	○	○	○	○	○
Voldoende bewegen en genoeg zuivelproducten eten gaat mijn botten sterker maken.	○	○	○	○	○
Het aanpassen van mijn levensstijl naar genoeg zuivelproducten eten en genoeg bewegen is voor mij geen probleem.	○	○	○	○	○

16. De volgende stellingen gaan over de pijn die u heeft door osteoporose. Geef aan in hoeverre u het eens bent met de volgende stellingen.

	Helemaal mee eens	Eens	Neutraal	Oneens	Helemaal mee oneens	Niet van toepassing (ik heb geen pijn)
Ik neem de osteoporose medicijnen om minder pijn te hebben.	○	○	○	○	○	○
Door mijn pijn door osteoporose, ben ik bang voor meer pijn door osteoporose.	○	○	○	○	○	○

17. De volgende stellingen gaan over de werking van de medicijnen voor osteoporose. Geef aan in hoeverre u het eens bent met de volgende stellingen.

	Helemaal mee eens	Eens	Neutraal	Oneens	Helemaal mee oneens
Ik weet wat de werkzaamheid van de medicijnen is.	○	○	○	○	○
Ik begrijp niet waarom ik medicijnen voor osteoporose moet nemen, ik heb nergens last van.	○	○	○	○	○
Ik heb verschillende verhalen gehoord over bijwerkingen, daardoor twijfel ik aan de medicijnen voor osteoporose.	○	○	○	○	○

18. Het onderwerp van de volgende stellingen is “de mensen om u heen.” Geef aan in hoeverre u het eens bent met de volgende stellingen.

	Helemaal mee eens	Eens	Neutraal	Oneens	Helemaal mee oneens
De mensen om mij heen moedigen mij aan om de medicijnen voor osteoporose in te nemen.	○	○	○	○	○
De mensen om mij heen twijfelen over het nut van de medicijnen voor osteoporose.	○	○	○	○	○
De mensen om mij heen vertellen mij verschillende verhalen over de medicijnen.	○	○	○	○	○
Ik vind het belangrijk dat ik goed kan uitleggen aan anderen wat osteoporose is.	○	○	○	○	○
Als het voor mijn omgeving duidelijker is wat de medicijnen voor osteoporose doen, helpt dit mij om mijn medicijnen goed te nemen.	○	○	○	○	○

19. De volgende stellingen gaan over de informatie over osteoporose en de medicijnen voor osteoporose. Geef aan in hoeverre u het eens bent met de volgende stellingen.

	Helemaal mee eens	Eens	Neutraal	Oneens	Helemaal mee oneens
Meer informatie over het nut van de medicijnen voor osteoporose, helpt mij om deze medicijnen goed in te nemen.	○	○	○	○	○
Als ik informatie mis, zoek ik dat zelf op.	○	○	○	○	○
Ik zoek extra informatie op in boeken of op het internet.	○	○	○	○	○
Ik vraag mijn arts om extra informatie.	○	○	○	○	○
Ik vraag mensen om mij heen om extra informatie.	○	○	○	○	○

20. De volgende stellingen gaan over het contact met de professionals. Geef aan in hoeverre u het eens bent met de volgende stellingen.

	Helemaal mee eens	Eens	Neutraal	Oneens	Helemaal mee oneens
Het helpt mij dat ik de medicijnen voor osteoporose op een vaste dag neem.	○	○	○	○	○
Als de verpleegkundige mij vaker zou bellen, helpt dit om mijn medicijnen voor osteoporose goed in te nemen.	○	○	○	○	○
Als de huisarts/praktijkondersteuner zou voorstellen om meer contact te hebben over de medicijnen voor osteoporose, helpt dit om mijn medicijnen voor osteoporose goed in te nemen.	○	○	○	○	○
Als de apotheker zou voorstellen om meer contact te hebben over de medicijnen voor osteoporose, helpt dit om mijn medicijnen voor osteoporose goed in te nemen.	○	○	○	○	○

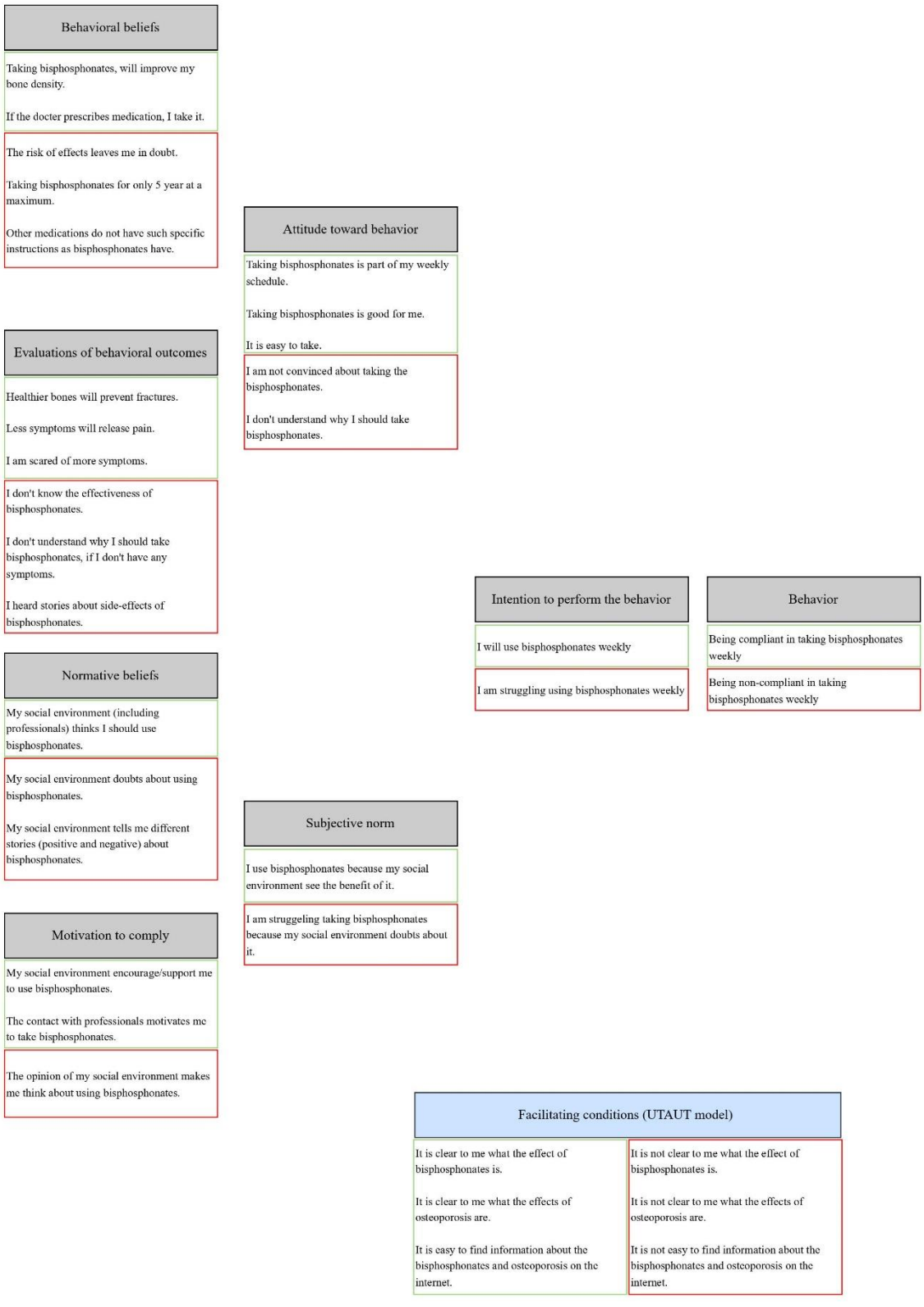
Dit is het einde van de vragenlijst. Hartelijk bedankt voor het invullen van de vragenlijst!

Het kan zijn dat u nog iets kwijt wil. Schrijf dat gerust hieronder op.

Heeft u na het invullen van de vragenlijst nog vragen, aarzel dan niet om contact op te nemen. De contactgegevens daarvoor staan in de bijgeleverde informatiebrief.

Wilt u op de hoogte worden gebracht van de resultaten van het onderzoek, laat dit dan weten door een e-mail te sturen naar m.gijsbers@zgt.nl

Appendix D. Interview results applied to TRA and UTAUT



Appendix E. Roadmap statistical analysis

1. Include the data in R studio
2. Delete rows with more than 50% missing values
3. Delete ADEOS 1-12 questions, since these are used for the ADEOS score
4. Recode the -2 – -1 – 0 – 1 - 2 scale to 1-2-3-4-5 (or the other way around, to overcome misinterpretation by negatively stated statements in the survey)
5. Make factor variables of all the Likert scale questions with the right amount of levels
6. Rename the columns by the English version of the variable names
7. Create data quality table with missing values and missing percentage
8. Impute variables, using mice. For numeric variables use meth = 'pmm', for factor variables use meth= 'polr'.
9. To visualise the Likert data in Likert plots, new data frames need to be created with the same amount of levels (structured by the TRA/UTAUT framework constructs
10. Create Likert plots
11. Check (visually) whether some variables have the same patterns
12. Test the visually observed same pattern variables by Cronbach's alpha
13. If the Cronbach's alpha is significant, merge variables to a new variable, using sum score
14. Test the relation between the general information and the dependent variable ADEOS score by Chi square
15. To get more observations per level of the categorical variables, reduce the 5 point Likert scale to a 3 point Likert scale (agree – neutral – disagree)
16. Create dummy variables
17. Create multiple regression model
18. Check for correlations between variables, delete the variables which are correlated
19. Print summary of the model

Appendix F. Missing data

From the 162 received surveys, 51 surveys where only filled in for < 50%. The other 111 surveys also had missing values, but per respondent this was < 50%. An overview of the missing data is presented in the table below.

Variable	Percentage missing data	Variable	Percentage missing data
Gender	0 %	**Doubt relevance**	5.4%
Age	2.7%	**Doubt stories**	8.1%
Education level	1.8%	**Social support**	1.8%
Medication	19.8%	**Social doubts**	1.8%
ADEOS score	12.6%	**Social stories**	4.5%
Medication stronger bones	2.7%	**Explain osteoporosis**	1.8%
Doctor prescribes	2.7%	**Clearer to environment**	3.6%
Side effects unimportant	4.5%	**More information helps**	3.6%
Report side effects	2.7%	**Look up yourself**	5.4%
Informed side effects	1.8%	**Books and internet**	5.4%
Relevance 5 years	4.5%	**Doctor information**	4.5%
Lifestyle added value	0.9%	**Information environment**	5.4%
Lifestyle change	1.8%	**Fixed day**	1.8%
Medication less pain	2.7%	**Contact nurse**	2.7%
Fear more pain	4.5%	**Contact GP/practice nurse**	2.7%
Effectiveness	4.5%	**Contact pharmacist**	2.7%

Appendix G. Cronbach's alpha

The calculated Cronbach's alpha coefficients statistically represents the overlapping answer patterns, as discussed in the previous paragraph.

Construct (variables)	Cronbach's alpha	95% confidence interval	Cronbach's alpha interpretation (61)
Behavioural beliefs	0.432	0.249 – 0.565	Unacceptable
Behavioural beliefs (Doubt relevance and doubt stories)	0.829	0.701 – 0.906	Good
Behavioural beliefs (Effectiveness and medication stronger bones)	0.679	0.548 – 0.776	Questionable
Evaluations behavioural outcomes	0.601	0.479 – 0.695	Questionable
Evaluations behavioural outcomes (Medication less pain and fear more pain)	0.880	0.793 – 0.942	Good
Normative beliefs	0.111	-0.335 – 0.410	Unacceptable
Normative beliefs (Social doubts and social stories)	0.686	0.509 – 0.825	Questionable
Facilitating conditions	0.448	0.230– 0.590	Unacceptable
Facilitating conditions (Books and internet and doctor information)	0.535	0.297 – 0.706	Poor

Appendix H. Frequencies per category per dummy variable

Variable	Frequencies					
	0	1	2	3	4	5
Education level		0	89	18	4	
Other medications	19	59	4	29	0	0
Books internet as information source		35	24	52		
Doctor as information source		34	37	40		
Environment as information source		53	35	23		
Taking medication on a fixed day (		2	17	92		
Extra contact with nurse		64	47	0		
Extra contact with GP/nurse practitioner		51	60	0		
Extra contact pharmacist		49	62	0		
Different stories from the people around		74	37	0		
Important to be able to explain osteoporosis		15	27	69		
People around patient increase knowledge about medication osteoporosis		34	77	0		
More information helps improving medication adherence		16	95	0		
Missing information, look it up myself		21	26	64		
Familiar with effectiveness of medication		8	22	81		
People around me encourage to take medication		39	34	38		
People around have concerns about usefulness medication		79	32	0		
Understand the medication period 5 years		9	23	79		
Changing lifestyle will strengthen bones		5	6	100		
Lifestyle change is not a problem		10	22	79		
Medication strengthens bones		1	18	92		
Medication the doctor prescribes being taken		4	11	96		
No matter the side effects, medication will be taken		37	24	50		
Report side effects if experienced		3	6	102		
Important to be informed about side effects		0	8	103		
Doubts about relevance of the medication		9	92	10		
Medication is taken because of the pain and fear for more pain		16	27	25	43	

Appendix I. Detailed Likert questions per ADEOS group

	Statement	ADEOS ≤ 16 (n = 28)	ADEOS 16-20 (n = 60)	ADEOS ≥ 20 (n = 23)
Medication stronger bones				
	Totally disagree	1 (4%)	0	0
	Disagree	0	0	0
	Neutral	13 (46%)	4 (7%)	1 (4%)
	Agree	9 (32%)	34 (57%)	14 (61%)
	Totally agree	5 (18%)	22 (37%)	8 (35%)
Doctor prescribes				
	Totally disagree	1 (4%)	1 (2%)	0
	Disagree	2 (7%)	0	0
	Neutral	5 (18%)	5 (8%)	1 (4%)
	Agree	12 (43%)	22 (37%)	9 (39%)
	Totally agree	8 (29%)	32 (53%)	13 (57%)
Side effects unimportant				
	Totally disagree	2 (7%)	3 (5%)	0
	Disagree	11 (39%)	16 (27%)	5 (22%)
	Neutral	7 (25%)	14 (23%)	3 (13%)
	Agree	6 (21%)	15 (25%)	9 (39%)
	Totally agree	2 (7%)	12 (20%)	6 (26%)
Report side effects				
	Totally disagree	0	0	2 (9%)
	Disagree	0	1 (2%)	0
	Neutral	2 (7%)	3 (5%)	1 (4%)
	Agree	15 (54%)	25 (42%)	9 (39%)
	Totally agree	11 (39%)	31 (52%)	11 (48%)
Informed side effects				
	Totally disagree	0	0	0
	Disagree	0	0	0
	Neutral	3 (11%)	3 (5%)	2 (9%)
	Agree	12 (43%)	23 (38%)	7 (30%)
	Totally agree	13 (46%)	34 (57%)	14 (61%)
Relevance 5 years				
	Totally disagree	2 (7%)	2 (3%)	1 (4%)
	Disagree	0	4 (7%)	0
	Neutral	10 (36%)	10 (17%)	3 (13%)
	Agree	10 (36%)	28 (47%)	8 (35%)
	Totally agree	6 (21%)	16 (27%)	11 (48%)
Lifestyle added value				
	Totally disagree	1 (4%)	0	1 (4%)
	Disagree	2 (7%)	0	1 (4%)
	Neutral	2 (7%)	4 (7%)	0
	Agree	11 (39%)	28 (47%)	11 (48%)
	Totally agree	12 (43%)	28 (47%)	10 (43%)
Lifestyle change				

Totally disagree	0	1 (2%)	1 (4%)
Disagree	4 (14%)	3 (5%)	0
Neutral	11 (39%)	9 (15%)	2 (9%)
Agree	6 (21%)	24 (40%)	8 (35%)
Totally agree	7 (25%)	22 (37%)	12 (52%)
Medication less pain			
Totally disagree	1 (4%)	1 (2%)	0
Disagree	4 (14%)	11 (18%)	3 (13%)
Neutral	4 (14%)	10 (17%)	4 (17%)
Agree	7 (25%)	12 (20%)	1 (4%)
Totally agree	1 (4%)	5 (8%)	0
Not applicable, I don't feel pain	11 (39%)	21 (35%)	15 (65%)
Fear more pain			
Totally disagree	1 (4%)	4 (7%)	0
Disagree	2 (7%)	12 (20%)	3 (13%)
Neutral	8 (29%)	8 (13%)	1 (4%)
Agree	5 (18%)	9 (15%)	3 (13%)
Totally agree	2 (7%)	7 (12%)	1 (4%)
Not applicable, I don't feel pain	10 (36%)	20 (33%)	15 (65%)
Effectiveness			
Totally disagree	1 (4%)	1 (2%)	0
Disagree	1 (4%)	4 (7%)	1 (4%)
Neutral	12 (43%)	7 (12%)	3 (13%)
Agree	9 (32%)	36 (60%)	11 (48%)
Totally agree	5 (18%)	12 (20%)	8 (35%)
Doubt relevance			
Totally disagree	14 (50%)	42 (70%)	15 (65%)
Disagree	0	0	0
Neutral	11 (39%)	10 (17%)	4 (17%)
Agree	1 (4%)	4 (7%)	1 (4%)
Totally agree	2 (7%)	4 (7%)	3 (13%)
Doubt stories			
Totally disagree	3 (11%)	22 (37%)	9 (39%)
Disagree	11 (39%)	24 (40%)	10 (43%)
Neutral	10 (36%)	10 (17%)	2 (9%)
Agree	0	0	0
Totally agree	4 (14%)	4 (7%)	2 (9%)
Social support			
Totally disagree	3 (11%)	8 (13%)	3 (13%)
Disagree	7 (25%)	13 (22%)	5 (22%)
Neutral	10 (36%)	18 (30%)	6 (26%)
Agree	5 (18%)	12 (20%)	5 (22%)
Totally agree	3 (11%)	9 (15%)	4 (17%)
Social doubts			
Totally disagree	6 (21%)	21 (35%)	7 (30%)
Disagree	9 (32%)	28 (47%)	8 (35%)
Neutral	12 (43%)	9 (15%)	7 (30%)
Agree	0	0	0
Totally agree	1 (4%)	2 (3%)	1 (4%)
Social stories			

	Totally disagree	6 (21%)	15 (25%)	7 (30%)
	Disagree	6 (21%)	31 (52%)	9 (39%)
	Neutral	12 (43%)	9 (15%)	7 (30%)
	Agree	0	0	0
	Totally agree	4 (14%)	5 (8%)	0
Explain osteoporosis				
	Totally disagree	2 (7%)	2 (3%)	2 (9%)
	Disagree	1 (4%)	8 (13%)	0
	Neutral	9 (32%)	14 (23%)	4 (17%)
	Agree	13 (46%)	25 (42%)	10 (43%)
	Totally agree	3 (11%)	11 (18%)	7 (30%)
Clearer to environment				
	Totally disagree	10 (36%)	27 (45%)	12 (52%)
	Disagree	0	0	0
	Neutral	10 (36%)	16 (27%)	2 (9%)
	Agree	3 (11%)	9 (15%)	6 (26%)
	Totally agree	5 (18%)	8 (13%)	3 (13%)
More information helps				
	Totally disagree	12 (43%)	34 (57%)	17 (74%)
	Disagree	0	0	0
	Neutral	12 (43%)	17 (28%)	3 (13%)
	Agree	1 (4%)	5 (8%)	2 (9%)
	Totally agree	3 (11%)	4 (7%)	1 (4%)
Look up yourself				
	Totally disagree	1 (4%)	1 (2%)	1 (4%)
	Disagree	4 (14%)	10 (17%)	4 (17%)
	Neutral	12 (43%)	10 (17%)	4 (17%)
	Agree	7 (25%)	18 (30%)	8 (35%)
	Totally agree	4 (14%)	21 (35%)	6 (26%)
Books and internet				
	Totally disagree	3 (11%)	4 (7%)	4 (17%)
	Disagree	4 (14%)	12 (20%)	6 (26%)
	Neutral	11 (39%)	10 (17%)	3 (13%)
	Agree	9 (32%)	14 (23%)	4 (17%)
	Totally agree	1 (4%)	20 (33%)	7 (30%)
Doctor information				
	Totally disagree	2 (7%)	5 (9%)	2 (9%)
	Disagree	7 (25%)	13 (22%)	4 (17%)
	Neutral	10 (36%)	18 (30%)	8 (35%)
	Agree	9 (32%)	15 (25%)	5 (22%)
	Totally agree	0	9 (15%)	4 (17%)
Information environment				
	Totally disagree	3 (11%)	9 (15%)	3 (13%)
	Disagree	8 (29%)	22 (37%)	9 (39%)
	Neutral	11 (39%)	16 (27%)	7 (30%)
	Agree	4 (14%)	8 (13%)	3 (13%)
	Totally agree	2 (7%)	5 (8%)	1 (4%)
Fixed day				
	Totally disagree	0	0	0
	Disagree	1 (4%)	0	0

	Neutral	8 (29%)	6 (10%)	3 (13%)
	Agree	7 (25%)	22 (37%)	7 (30%)
	Totally agree	12 (43%)	32 (53%)	13 (57%)
Contact nurse				
	Totally disagree	4 (14%)	6 (10%)	0
	Disagree	0	0	0
	Neutral	11 (39%)	19 (32%)	6 (26%)
	Agree	7 (25%)	23 (38%)	12 (52%)
	Totally agree	6 (21%)	12 (20%)	5 (22%)
Contact GP/practice nurse				
	Totally disagree	6 (21%)	7 (12%)	1 (4%)
	Disagree	0	0	0
	Neutral	12 (43%)	24 (40%)	9 (39%)
	Agree	5 (18%)	20 (33%)	9 (39%)
	Totally agree	5 (18%)	9 (15%)	4 (17%)
Contact pharmacist				
	Totally disagree	8 (29%)	8 (13%)	3 (13%)
	Disagree	0	0	0
	Neutral	12 (40%)	24 (40%)	7 (30%)
	Agree	2 (33%)	16 (27%)	9 (39%)
	Totally agree	6 (15%)	12 (20%)	4 (17%)

Appendix J. Multiple regression results

The intercept of 15 is the mean value of the ADEOS score when all the independent variables are zero.

The reference categories are the category "agree" for all the Likert scale questions. Except for 'different stories from the people around', 'people around patient increase knowledge about medication osteoporosis' and 'people around have concerns about usefulness medication' where it is "neutral", gender where it is "female", medication where it is "other", other medication where it is "weekly", medication yes/no, where it is "yes" and medication less pain and fear where it is "no pain".

Independent variables (level)	Estimate	Standard Error	Statistic	P value
(Intercept)	15.153	1.4868	1.0192	7.12e-15*
Gender (male)	-1.4297	0.6003	-2.3818	0.0203*
Education level (middle)	1.2789	0.6470	1.9766	0.0525*
Frequency of medication (weekly tablets)	-0.8838	0.5436	-1.6259	0.1090
Type of medication (injection)	0.9200	1.6334	0.5632	0.5753
Type of medication (Denosumab)	0.3324	1.4863	0.2236	0.8238
Medication yes or no (No)	-0.5654	0.8277	-0.6831	0.4971
Other medications (multiple times a day)	0.9057	0.6999	1.2940	0.2005
Other medications (once a day)	1.0470	0.5405	1.9370	0.0573*
Other medications (multiple times a week)	-1.0578	1.2886	-0.8209	0.4149
Books internet as information source (disagree)	-0.3226	0.8137	-0.3964	0.6932
Books internet as information source (neutral)	-0.3560	0.8140	-0.4374	0.6634
Doctor as information source (disagree)	-0.0548	0.6265	-0.0875	0.9306
Doctor as information source (neutral)	-0.0373	0.7054	-0.0529	0.9579
Environment as information source (disagree)	0.3482	0.6340	0.5492	0.5848
Environment as information source (neutral)	0.6228	0.6715	0.9274	0.3573
Taking medication on a fixed day (disagree)	-3.2360	2.4777	-1.3061	0.1964
Taking medication on a fixed day (neutral)	-0.1275	0.7294	-0.1748	0.8618
Different stories from the people around (disagree)	0.4392	0.6079	0.7225	0.4727
Important to be able to explain osteoporosis (disagree)	0.1895	1.0863	0.1745	0.8621
Important to be able to explain osteoporosis (neutral)	1.0729	0.6623	1.6201	0.1103
People around patient increase knowledge about medication osteoporosis (disagree)	0.8890	0.6908	1.2869	0.2029
Missing information, look it up myself (disagree)	-0.9116	0.8450	-1.0788	0.2848
Missing information, look it up myself (neutral)	-0.8270	0.7716	-1.0718	0.2880
Familiar with effectiveness of medication (disagree)	1.4127	1.1734	1.2040	0.2332
Familiar with effectiveness of medication (neutral)	-0.1591	0.6561	-0.2425	0.8092
People around me encourage to take medication (disagree)	-0.5443	0.6118	-0.8898	0.3770
People around me encourage to take medication (neutral)	-0.1628	0.6041	-0.2696	0.7884
People around have concerns about usefulness medication (disagree)	-0.5289	0.6629	-0.7979	0.4279
Understand the medication period 5 years (disagree)	0.6652	1.0422	0.6383	0.5257

Understand the medication period 5 years (neutral)	0.5446	0.6951	0.7834	0.4364
Changing lifestyle will strengthen bones (disagree)	0.5921	1.6156	0.3665	0.7153
Changing lifestyle will strengthen bones (neutral)	1.0906	1.4181	0.7691	0.4448
Lifestyle change is not a problem (disagree)	-2.2735	1.1678	-1.9468	0.0561*
Lifestyle change is not a problem (neutral)	-0.9599	0.6700	-1.4328	0.1569
Medication strengthens bones (disagree)	-5.8108	2.9275	-1.9849	0.0516*
Medication strengthens bones (neutral)	-3.0803	0.8686	-3.5463	0.0008*
Medication the doctor prescribes being taken (disagree)	-2.2519	1.5569	-1.4464	0.1531
Medication the doctor prescribes being taken (neutral)	-1.2331	0.8539	-1.4441	0.1537
No matter the side effects, medication will be taken (disagree)	0.1950	0.6492	0.3004	0.7649
No matter the side effects, medication will be taken (neutral)	-0.0573	0.7579	-0.0756	0.9400
Report side effects if experienced (disagree)	1.0041	1.4837	0.6767	0.5011
Report side effects if experienced (neutral)	-0.7012	1.2531	-0.5596	0.5778
Important to be informed about side effects (neutral)	0.7215	1.1460	0.6296	0.5313
Concerns about the medication based on the 5 years and different stories (disagree)	3.5070	1.2380	2.8328	0.0062*
Concerns about the medication based on the 5 years and different stories (neutral)	2.4414	0.9251	2.6391	0.0105*
Medication is taken because of (fear for more) pain (disagree)	0.3938	0.6995	0.5630	0.5755
Medication is taken because of (fear for more) pain (neutral)	0.0172	0.6910	0.0249	0.9802
Medication is taken because of (fear for more) pain (agree)	-1.1320	0.6185	-1.8303	0.0720*
*Significant P-values, $p< \alpha$; $\alpha = 0.1$				