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Cost analysis of the Wound Expertise Centre at the Isala clinics in Zwolle

F. van der Vegt

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Cost analysis of the Wound Expertise Centre at the Isala clinics in Zwolle

F. (Femke) van der Vegt
Industrial Engineering and Management, University of Twente
Specialization: Healthcare Technology and Management

Supervisory committee

University of Twente
Dr. R.A.M.G. (Reinoud) Joosten
Dr. B. (Berend) Roorda

MST Enschede
R. (Robbert) Meerwaldt

UNIVERSITY OF TWENTE.

MST

Management summary

Introduction

This study focuses on the analysis of costs regarding the treatment of chronic wounds at the Wound Expertise Centre (WEC) at the Isala clinics in Zwolle. A patient's health care pathway consists of regular appointments at this WEC combined with home care visits by nurses of QualityZorg. We divide the analysed expenses into costs of specialized medical home care [Medisch Specialistische Verpleging in Thuissituatie (MSVT)] and into costs of medical aids [Hulpmiddelen (HLP)] used during home care.

Problem description

Treatment of patients with chronic wounds involves enormous costs caused by the time-consuming and complex process of care. The implementation of the WEC in Zwolle is one of the measurements that have been taken to reduce these costs, and to improve efficiency and quality of wound care. We conduct this research to gain insights in the average treatment costs of patients who received wound care at the WEC in the Isala clinics.

Approach

We analyse the costs of treatment of the most common types of chronic wounds. Given the skewed data, we use the non-parametric bootstrap method for the calculations of our statistics of interests. For the determination of the composition and size of the bootstrap samples we define four different scenarios. These four scenarios are performed for each type of wound. We create 1000 resamples drawn by random sampling with replacement for the execution of each scenario. We define the following scenarios:

- **Scenario I:** The size of each bootstrap sample is equal to eleven.
- **Scenario II:** The size of each bootstrap sample is equal to ¼ part of the population size of the corresponding type of wound.
- **Scenario III:** The size of each bootstrap sample is equal to the population size of the corresponding type of wound.
- **Scenario IV:** The size of each bootstrap sample is equal to the population size of the corresponding type of wound. The first resample consists of X observations that are drawn by sampling with replacement from the population. Where X defines the total number of patients in this population. The next samples consists of X observations that are drawn from a group composed of the observations of the population plus the previous resamples.

This scenario is clearly explained below, where S denotes the resample number and X is equal to the population size of the corresponding type of chronic wound.

S_1 - X patients from P_0

S_2 - X patients from $P_0 \cup S_1$

S_3 - X patients from $P_0 \cup S_1 \cup S_2$

S_{1000} - X patients from $P_0 \cup S_1 \cup S_2 ,....., \cup S_{999}$

We estimate the average costs of treatment of each type of wound by calculating the average of all these resample means.

Results

The table below shows the most important results of our cost analysis based on the non-parametric bootstrap method. The total costs that are used for bootstrapping are based on the sum of the MSVT and HLP costs.

Type of wound (n)	Arithmetic mean costs population (SD)	Bootstrapped average costs Scenario I (SD)	Bootstrapped average costs Scenario II (SD)	Bootstrapped average costs Scenario III (SD)	Bootstrapped average costs Scenario IV (SD)
Venous ulcer (22)	€ 2,592.27 (€ 3,091.21)	€ 2,555.19 (€ 905.55)	€ 2,617.41 (€ 1,271.78)	€ 2,563.57 (€ 698.02)	€ 2,015.51 (€ 430.91)
Arterial ulcer (33)	€ 2,531.07 (€ 2,466.05)	€ 2,540.68 (€ 716.74)	€ 2,561.84 (€ 893.78)	€ 2,535.78 (€ 427.38)	€ 2,417.43 (€ 416.36)
Pressure ulcer (29)	€ 2,009.05 (€ 1,760.67)	€ 1,993.18 (€ 537.61)	€ 2,027.10 (€ 670.47)	€ 2,010.83 (€ 325.86)	€ 1,998.67 (€ 318.11)
Traumatic ulcer (53)	€ 1,961.35 (€ 2,108.46)	€ 1,955.36 (€ 615.38)	€ 1,943.17 (€ 576.97)	€ 1,961.32 (€ 285.86)	€ 1,771.09 (€ 247.87)
Diabetic mellitus ulcer (65)	€ 1,650.53 (€ 1,546.60)	€ 1,676.22 (€ 453.90)	€ 1,638.48 (€ 384.00)	€ 1,658.51 (€ 195.56)	€ 1,702.06 (€ 176.18)
POWI ulcer (47)	€ 1,507.40 (€ 997.66)	€ 1,505.20 (€ 292.34)	€ 1,495.30 (€ 291.37)	€ 1,511.17 (€ 138.75)	€ 1,625.54 (€ 145.87)
Surgical wound (55)	€ 1,476.52 (€ 1,451.68)	€ 1,494.59 (€ 456.21)	€ 1,459.52 (€ 377.62)	€ 1,477.26 (€ 186.39)	€ 1,350.96 (€ 191.92)

Conclusion

The most expensive treatment in terms of MSVT and HLP costs is the venous ulcer (average total costs range between € 2,015.51 (Scenario IV) to € 2,617.41 (Scenario II)). Followed by the arterial ulcer and the pressure ulcer.

However, our results are based on very small populations, which range between 22 and 65 patients. Therefore, caution is necessary when interpreting our results. In future research more data of MSVT and HLP costs should be used. Then, estimating the average costs can be done more precisely. Our results are based on the created 1000 bootstrap samples within each scenario. We also recommend performing significant more runs of each bootstrap scenario.

Management samenvatting

Introductie

Dit onderzoek richt zich op het analyseren van de kosten van de behandeling van een chronische wond. De patiënten van wie wij de kosten analyseren zijn allemaal behandeld in het Wond Expertise Centrum (WEC) van de Isala kliniek in Zwolle. Deze patiënten hebben reguliere behandelingen in het WEC, daarnaast ontvangen zij medisch specialistische verpleging in de thuissituatie (MSVT) verzorgd door de verpleegkundigen van QualityZorg. De kosten die wij analyseren zijn onder te verdelen in kosten van de MSVT en kosten met betrekking tot de medische hulpmiddelen (HLP) die tijdens de thuiszorg zijn gebruikt.

Probleembeschrijving

De behandeling van patiënten met chronische wonden gaat gepaard met enorme kosten die veroorzaakt worden door het tijdrovende en complexe genezingsproces. Dit onderzoek voeren wij uit om beter inzicht te krijgen in de gemiddelde kosten van de behandeling van patiënten in het WEC in Zwolle.

Aanpak

We analyseren de behandelingskosten van de meest voorkomende type chronische wonden. Gezien de scheve verdelingen van deze data, gebruiken wij de niet-parametrische bootstrap methode. Voor deze methode hebben wij vier verschillende scenario's opgesteld die de grootte en de samenstelling van de bootstrap steekproeven bepalen. Deze verschillende scenario's worden voor elk type wond uitgevoerd. Voor elk scenario creëren wij 1000 bootstrap steekproeven die door middel van trekken met teruglegging zijn gegenereerd. Wij definiëren de volgende vier scenario's:

- **Scenario I:** De grootte van elke bootstrap steekproef is gelijk aan elf.
- **Scenario II:** De grootte van elke bootstrap steekproef is gelijk aan ¼ deel van de populatie van de desbetreffende wond.
- **Scenario III:** De grootte van elke bootstrap steekproef is gelijk aan de gehele populatie van de desbetreffende wond.
- **Scenario IV:** De grootte van elke bootstrap steekproef is gelijk aan de gehele populatie van de desbetreffende wond. De populatie van de eerste bootstrap steekproef bestaat uit een X aantal observaties die getrokken zijn door middel van trekken met teruglegging uit de populatie, waar X het aantal patiënten in de populatie definieert. De volgende bootstrap steekproeven bestaan uit X observaties getrokken uit een groep van observaties die bestaat uit de populatie plus de voorgaande bootstrap steekproef populaties.

Dit scenario wordt hieronder duidelijk weergegeven, waar S het bootstrap steekproefnummer weergeeft en X gelijk is aan het aantal patiënten in de populatie van de desbetreffende wond.

S_1 - X patients from P_0

S_2 - X patients from $P_0 \cup S_1$

S_3 - X patients from $P_0 \cup S_1 \cup S_2$

S_{1000} - X patients from $P_0 \cup S_1 \cup S_2 ,....., \cup S_{999}$

De gemiddelde kosten van de behandelingen worden gewogen aan de hand van de gemiddelde waarden van iedere bootstrap steekproef.

Resultaten

De tabel hieronder presenteert de belangrijkste resultaten van ons onderzoek. Deze tabel geeft de totale kosten weer, dit is de som van de kosten die gerelateerd zijn aan MSVT en medische HLP die gebruikt zijn tijdens de thuiszorg.

Type wond (n)	Rekenkundig gemiddelde kosten populatie (SD)	Bootstrapped gemiddelde kosten scenario I (SD)	Bootstrapped gemiddelde kosten scenario II (SD)	Bootstrapped gemiddelde kosten scenario III (SD)	Bootstrapped gemiddelde kosten scenario IV (SD)
Veneus ulcus (22)	€ 2,592.27 (€ 3,091.21)	€ 2,555.19 (€ 905.55)	€ 2,617.41 (€ 1,271.78)	€ 2,563.57 (€ 698.02)	€ 2,015.51 (€ 430.91)
Arterieel ulcus (33)	€ 2,531.07 (€ 2,466.05)	€ 2,540.68 (€ 716.74)	€ 2,561.84 (€ 893.78)	€ 2,535.78 (€ 427.38)	€ 2,417.43 (€ 416.36)
Decubitus ulcus (29)	€ 2,009.05 (€ 1,760.67)	€ 1,993.18 (€ 537.61)	€ 2,027.10 (€ 670.47)	€ 2,010.83 (€ 325.86)	€ 1,998.67 (€ 318.11)
Trauma ulcus (53)	€ 1,961.35 (€ 2,108.46)	€ 1,955.36 (€ 615.38)	€ 1,943.17 (€ 576.97)	€ 1,961.32 (€ 285.86)	€ 1,771.09 (€ 247.87)
Diabetes mellitus ulcus (65)	€ 1,650.53 (€ 1,54.60)	€ 1,676.22 (€ 453.90)	€ 1,638.48 (€ 384.00)	€ 1,658.51 (€ 195.56)	€ 1,702.06 (€ 176.18)
POWI ulcus (47)	€ 1,507.40 (€ 997.66)	€ 1,505.20 (€ 292.34)	€ 1,495.30 (€ 291.37)	€ 1,511.17 (€ 138.75)	€ 1,625.54 (€ 145.87)
Operatiewond (55)	€ 1,476.52 (€ 1,451.68)	€ 1,494.59 (€ 456.21)	€ 1,459.52 (€ 377.62)	€ 1,477.26 (€ 186.39)	€ 1,350.96 (€ 191.92)

Conclusie

De behandeling met de hoogste kosten is die van de veneus ulcus (de gemiddelde totale kosten variëren van € 2.015,51 (Scenario IV) tot € 2,617.41 (Scenario II)). Gevolgd door de behandeling van de arterieel ulcus en de decubitus ulcus.

Onze resultaten zijn echter gebaseerd op een kleine populatie, variërend van 22 tot 65 patiënten. Daarom moet men voorzichtig zijn met de interpretatie van onze resultaten. Wij raden aan om meer data van de kosten van deze behandelingen te verzamelen, zodat de gemiddelde kosten gebaseerd zijn op een grotere populatie. Onze resultaten zijn gebaseerd op de gemiddelden van één run van 1000 bootstrap steekproeven. Daarnaast raden wij aan om bij volgende kostenanalyses meer runs uit te voeren.

Preface

Dear reader,

This report is the result of my graduation project of the master program Industrial Engineering and Management at the University of Twente (specialization Health Care Technology and Management).

I could not have conducted this research without the help of many people. So, I want to thank all those who helped me carrying out this research. First, I want to thank my Medisch Spectrum Twente supervisor Robbert Meerwaldt for his feedback and insights in the world of (chronic) wounds. Our meetings helped me to understand the organization of wound care in the Netherlands, and the challenges it faces. My grateful thanks also to Abhishta for answering my questions and providing tips for modelling in Excel and Matlab.

Furthermore, I would like to thank my first supervisor Reinoud Joosten from the University of Twente. When I struggled with my research, your advice and feedback has been very helpful. Your feedback and tips encouraged me to continue working on my report. I would like to thank my second supervisor Berend Roorda for your willingness to participate as second supervisor at the last moment.

Finally, I would like to thank my family for their support, encouragement and motivation during my study years and graduating.

I hope you enjoy reading this report. If there are any further questions, please feel free to contact me.

Kind regards,

Femke van der Vegt

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List of abbreviations

CI	-	Confidence interval
HLP		Hulpmiddelen
KCWC	-	Knowledge Centre in Wound Care
LPZ	-	Landelijke Prevalentiemeting Zorgproblemen
MSVT	-	Medisch Specialistische Verpleging in de Thuissituatie
SD	-	Standard deviation
WEC	-	Wound Expertise Centre
Wlz	-	Wet langdurige zorg
ZIN	-	Zorginstituut Nederland
Zvw	-	Zorgverzerkeringswet

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Research introduction

1. Research introduction

This research focuses on the Wound Expertise Centre (WEC) integrated in the Isala clinics at Zwolle. The objective of this master thesis is to estimate the average costs associated to specialized medical home care [Medisch Specialistische Verpleging in de Thuissituatie (MSVT)] and medical aids [Hulpmiddelen (HLP)] used during home care.

This chapter is structured as follows: Section 1.1 describes the background to this research and Section 1.2 is an introduction to the Medisch Spectrum Twente. In Section 1.3 we define the methodology, including the research questions and Section 1.4 describes the outline of this report.

1.1 Background to the research

Chronic wound care involves enormous costs caused by the time-consuming and complex process of care, delay in hospital discharge, complications, long-term commitment of health care professionals, and high costs of medical devices and medical aids (Capgemini Consulting, 2014). Several measures have been taken in the organization of wound care in the Netherlands to improve quality of care, and to reduce the wound expenditures. One of the measures is for example the implementation of WECs in the Netherlands (Capgemini Consulting, 2014; Heyer *et al.*, 2016; Rondas *et al.*, 2015a).

1.2 Introduction to the MST

The Medisch Spectrum Twente (MST) has been created by a merger between the hospitals at Enschede and Oldenzaal. Nowadays, the hospital at Enschede is the main location and the MST has outpatient clinics at Oldenzaal, Losser and Haaksbergen. In January 2016 the MST opened a new hospital located in the city centre of Enschede. One of the main differences in the organization of care is the difference in bed capacity between the two old departments and the new location. The capacity in the current hospital is 620 beds, which is a reduction of 43.6% (MST, 2016).

The MST stated that it wants to achieve the title of the 'Best improvement hospital of the Netherlands' (MST, 2016). Therefore, quality and safety are important parts of the vision of the MST. In addition, one of the improvements which the MST recently established is the opening of a WEC led by surgeons, reconstructive surgeons and dermatologists.

1.3 Methodology

The problem that we are going to solve is a knowledge problem. A knowledge problem can be described as a situation in which you want to know something. Heerkens (1999) stated that a problem statement contains a description of the variable and of the research population. The knowledge problem of this research is a descriptive problem because we want to obtain one or more values. The descriptive problem of this master assignment is 'What are the average total costs of treatment for patients who had been treated at the Wound Expertise Centre at the Isala clinics in Zwolle?'. The total costs consist of costs associated with MSVT and medical aids used during home care.

One well-known method to solve a knowledge problem is the research cycle. This cycle consists of the following phases (Heerkens, 1999):

- Investigating the research goal.
- Defining the problem statement.
- Defining the research questions.
- Defining the research design.
- Operationalize.
- Gathering of data.
- Processing the data.
- Drawing of conclusions (answering of the problem statement).

Due to time constraints we set different priorities for solving the sub questions. Our biggest challenge is to accurately determine the average costs of MSVT and medical HLP used during home care. We determine these two cost items together as the total costs of treatment. On the other hand, answering the other sub questions is important to review the current problem of the enormous costs critically.

The **main research question** is the problem statement of the knowledge problem and it is defined as:

What are the average total costs of treatment for patients who had been treated at the Wound Expertise Centre at the Isala clinics in Zwolle?

A few sub questions are defined below in order to answer the main research question. To understand the importance of efficient wound care it is important to gain more knowledge about chronic wounds in general. Thus the first research questions focus on the healing process, the definition of a chronic wound and how it affects the patient's quality of life. We answer these questions by conducting a literature research.

Research Question 1: *What are the different phases of a normal wound healing process?*
Research Question 2: *What is the definition of a chronic wound?*

In order that we ensure a full understanding of the impact of cost-effective wound care it is important to gain knowledge about the prevalence, organization of care, and the costs involved with treatment of chronic wounds. In addition, we conduct a literature research about previously conducted costs analyses of WECs in the Netherlands. This provides us information how to perform a cost analysis and which costs to include. In addition, it gives an overview of previously estimated costs and (potential) savings of wound care in the Netherlands.

Research Question 3: *What is the total prevalence of chronic wounds in the Netherlands?*
Research Question 4: *What is the current situation of the organization of wound care in the Netherlands?*
Research Question 5: *What are the average costs of (chronic) wound care at this moment in the Netherlands?*
Research Question 6: *How have previous cost analyses of chronic wound care in the Netherlands been conducted?*

Answering these general research questions is important because it gives full understanding about the importance of a good and cost-effective wound care organization. So, Research Questions 1-6 form the background for our research.

Now that all general research questions have been defined, the next step is to focus on the WEC at the Isala clinics in Zwolle. Therefore, it is important to obtain information about the organization of care at this WEC. Excen is an organization that facilitates more than forty WECs in the Netherlands, including the WEC at the Isala clinics. In addition, the company provides advice how to obtain specialized and organized wound care (Excen, 2017).

Research Question 7: *What is the current organization of wound care at the Isala clinics in Zwolle*?
Research Question 8: *What are the average costs of specialized medical home care [Medisch Specialistische Verpleging in de Thuissituatie (MSVT)] provided by QualityZorg for patients of the Wound Expertise Centre at the Isala clinics in Zwolle?*
Research Question 9: *What are the average costs of medical aids [Hulpmiddelen (HLP)] used during home care for patients of the Wound Expertise Centre at the Isala clinics in Zwolle?*

1.4 Remainder of the report

Chapter 2 outlines the literature research and the background to the research problem. In addition, this chapter critically assess the existing literature on previous conducted cost analyses. We discuss the data gathered and we outline the results of our cost analysis in Chapter 3. In Chapter 4 we provide the overall conclusion as the interpretation of the results, the discussion and we provide recommendations for further cost analyses of chronic wounds.

Literature research

2. Literature research

In this chapter we give an overview of the wound healing process, the definition of a (chronic) wound, and their prevalence rate in the Netherlands. Sections 2.1 and 2.2 provide general information about (chronic) wounds and the healing processes. Their prevalence rates are summarized in Section 2.3. Furthermore, in Section 2.4 we present the organizational structure of wound care in the Netherlands, and Section 2.5 presents the current costs related to wound care. In Section 2.6 we describe the two previous cost analyses that have been conducted the Netherlands. Finally, in Section 2.8 we introduce the bootstrap method that is used to analyse our data gathered.

2.1 Wound healing process

The skin is the largest organ of the human body and functions as a protective barrier against harmful external environmental factors. Therefore, damaged tissue must be restored properly and efficiently (Na *et al*., 2017). A wound is a breakdown of this protective barrier with or without loss of underlying connective tissue. Injuries can be caused by traumas, burns, animal bites or stings, connective tissues disorders, metabolic disease, psychosocial disorders, and nutritional deficiencies (Shankar *et al.*, 2014).

The wound healing process consists of three different and overlapping phases: inflammatory reaction, proliferation and remodelling (Flanagan, 2000; Van Mierlo- van den Broek & De Laat, 2012). The inflammatory reaction is subdivided into haemostasis and inflammation. Haemostasis is the first step of the healing process and it is the body's natural response to an injury (Li *et al.*, 2007). Blood vessels in the wound contract and this result in a decreased or restricted flow of blood, and blood loss will be minimized. Once haemostasis is achieved, blood vessels in the wound bed dilate to allow essential cells to reach the damaged tissue (Shankar *et al*., 2014). The function of the inflammation phase is to break down and remove the blood clot, cellular debris and microorganisms. In addition, it prepares the growth of new tissue (Flanagan, 2000). Subsequently, the proliferation starts. It's main function is to create a permeability barrier and to establish an appropriate blood supply (Flanagan, 2000; Li *et al*., 2007; Van Mierlo- van den Broek & De Laat, 2012).

Remodelling is the last part of this complex process and starts when new tissue within the wound bed is formed. The focus of remodelling is to restore tissue structural integrity and functional competence (Li *et al.*, 2007). The tissue function and its shape is restored and new tissue slowly gains flexibility and strength (Van Mierlo- van den Broek & De Laat, 2012).

The healing process is called uncomplicated if all phases are completed without problems, recovery is within a certain duration, and if the anatomical and functional structure is restored (Van Mierlo- van den Broek & De Laat, 2012). However, healing can be affected by different factors. The European Wound Management Association composed an overview of four different categories of indicators that affect this process (European Wound Management Association, 2008):

- Patient-related factors.
- Wound-related factors.
- Professional-related factors.
- Resources and treatment-related factors.

The patient-related factors composed by the European Wound Management association are subdivided into physical, psychological and social factors (European Wound Management Association, 2008). Examples of physical factors are obesity, general health, malnutrition, and ageing (European Wound Management Association, 2008; Flanagan, 2000). Psychological and social factors are for example social isolation, economic status, depression, psychosis, profession, and pain experience (European Wound Management Association, 2008; Van Mierlo- van den Broek & De Laat, 2012). The European Wound Management Associated (2008) defines under the wound-related factors specific characteristics that affect the complexity of the healing process. For example the wound diagnosis, size and depth, wound bed condition, presence of an infection or inflammation, and ischemia. In addition, professional-related factors are related to the knowledge and skills of disciplines who are involved with the patient's treatment. At last, the organization of care and the provision of training are covered by the resources and treatment-related factors.

2.2 Definition chronic wound

The Dutch National Health Care Institute [Zorginstituut Nederland (ZIN)] defines a chronic wound as follows 'A chronic wound is a wound with an impaired healing tendency as a result of pathophysiological factors' (Dutch National Health Care Institute, 2013, p9). The healing process is delayed and incomplete, resulting in a poor functional and anatomical outcome of the injured skin (Graves & Zheng, 2014).

The required healing duration has been estimated between four weeks and up to more than three months (Järbrink *et al.*, 2016). Based on their aetiologies, chronic wounds are classified into different categories with their own characteristics, for example (Järbrink *et al*., 2016; Rondas *et al.*, 2015a):

- Arterial ulcer.
- Burns.
- Diabetic ulcer.
- Oncologic ulcer.
- Post-operative wound infection ulcer.
- Post-surgical ulcer.
- Post-traumatic ulcer.
- Pressure ulcer.
- Venous ulcer.

A reduced quality of life is often perceived by patients caused by pain, poor sleep, mobility restriction, hospitalization, recurring wounds, social isolation, and restrictions in daily functioning (Capgemini Consulting, 2014; Menke *et al.*, 2007; Posnett & Franks, 2008).

2.3 Prevalence of chronic wounds

Information on quality of care, (reimbursement) costs and prevalence rates contribute to the awareness of health problems among caregivers, managers, policymakers and politicians (Rondas *et al.*, 2015b). In addition, statistics on prevalence and incidence provide information for health care planning and resource allocation in relation to characteristics of the population (Järbrink *et al*., 2016). Prevalence is a statistic definition that defines the proportion of a population who have a specific characteristic in a given time period. This is usually reported as a percentage or as the number of cases in a given population (Rümke, 1983).

The Dutch National Prevalence Measurement of care problems [Landelijke Prevalentiemeting Zorgkwaliteit (LPZ)] is a yearly, independent measurement of prevalence and quality indicators of different health care problems in the Netherlands (Halfens *et al*., 2016). The objects of these measurements are for example malnutrition, incontinence and mobility restriction. Since 2012, chronic wounds are included in the LPZ measurements (Rondas *et al*., 2015b). For answering Research Question 3 (*What is the total prevalence of chronic wounds in the Netherlands?)*, we use the results of the LPZ 2015 measurements.

Table 1 shows the characteristics of patients assessed by the LPZ measurements of 2015 (Halfens *et al.*, 2016). Eighteen different organizations, of which fifteen nursing homes and three home care organizations, agreed to participate. In total 1219 patients were assessed for these measurements.

Halfens *et al.* (2016) assume that the results of their research are representative for the prevalence rates of chronic wounds in the Netherlands in 2015. A limitation of this research is the low organization participation rate, and in particular the number of home care institutions. As mentioned above, these wound measurements have been conducted since 2012. So, less information can be given about prevalence rates over previous years. In addition, comparison of prevalence rates of home care organizations over various years is not possible. Namely, 2015 is the first year of assessment of chronic wounds of patients who received treatment in these organizations. So, the results of this study are not significant due to a limited research population.

Halfens *et al.* (2016) also examined the prevalence rates of chronic wounds among various diseases. One of the inclusion criteria was that assessed specific diseases had to occur in more than hundred patients. In general, no major differences were found between the prevalence of chronic wounds in various diseases.

Table 1 Overview characteristics of the LPZ 2015 measurements (Halfens *et al.*, 2016).

	Nursing home	Home care organization
Number of organizations	15	3
Number of assessed patients	1028	191
Number of chronic wounds	71	11
Mean prevalence chronic wounds (%)	5.4	3.7
Diagnosis chronic wounds (%)		
• Pressure ulcer	53.3	58.3
• Venous ulcer	15.5	16.6
• Diabetic ulcer	2.8	8.3
• Arterial ulcer	7	0
• Post-surgical ulcer	1.4	0
• Oncologic ulcer	1.4	0
• Unknown origin	18.3	16.6

Heyer *et al*. (2016) showed that of all assessed patients in 2015, 65 had one or more chronic wounds. This represents a total number of 82 wounds (71 in nursing homes and 11 in home care organizations). In addition, the mean wound prevalence of patients in nursing homes is higher compared to the home care organizations, respectively 5.4% and 3.7%. Furthermore, the prevalence rate in nursing homes slightly increased compared to previous years (4.2% to 5.4% from 2012 to 2015).

Posnett & Franks (2008) stated that rising of prevalence is explained by ageing of the population, demographic changes, and an increased risk of diseases such as diabetes mellitus, obesity and cardiovascular diseases.

Figure 1 shows an overview of the prevalence of different types of wounds compared to the total number of wounds of the LPZ measurements in 2015 (Halfens *et al*., 2016). As shown in Figure 1, the most common types of wounds were pressure ulcers followed by venous ulcers. Only four out of seven types of wounds were discovered in patients who received home care. The arterial ulcer, the post-surgical ulcer and the oncologic ulcer occurred only in patients who received treatment in nursing homes. However, the diagnosis is unknown in one out of six wounds. The researchers stated that the most chronic wounds occurred on the tailbone, heels and ankles. This is logical because the pressure ulcer is the most frequently diagnosed wound of the LPZ 2015 measurements.

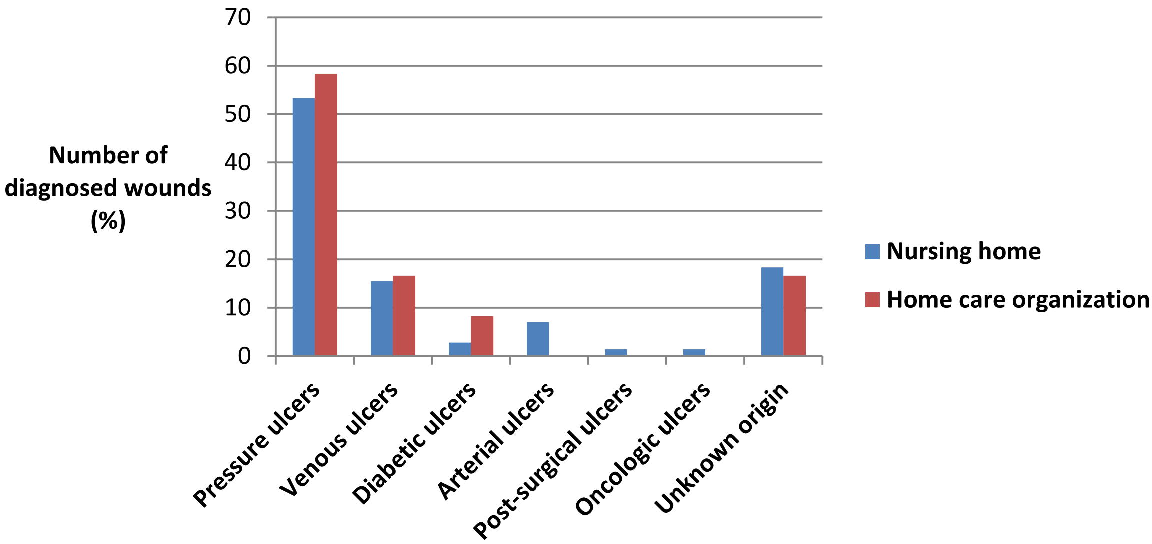

Figure 1 Prevalence of different chronic type of wounds in the Netherlands in 2015 (Halfens *et al*., 2016).

Wound care expenditures are related to the time-consuming healing process. It is important to obtain information about the average healing duration of the different type of wounds. Therefore, the LPZ 2015 measurements also assessed the wound duration. These results are shown in Table 2 (Halfens *et al*., 2016). To illustrate, more than 20% of all wounds were healed in more than six months, while more than 50% had a healing process between three to six weeks.

Table 2 Wound duration of the LPZ 2015 measurements (Halfens *et al*., 2016).

	Nursing home	Home care organization
Number of wounds	71 (100%)	11 (100%)
Wound duration		
• 3-6 Weeks	27 (38%)	2 (18,2%)
• 6-12 Weeks	23 (23,4%)	7 (63,7%)
• 3-6 Months	6 (8,5%)	0
• > 6 Months	15 (21,2%)	2 (18,2%)

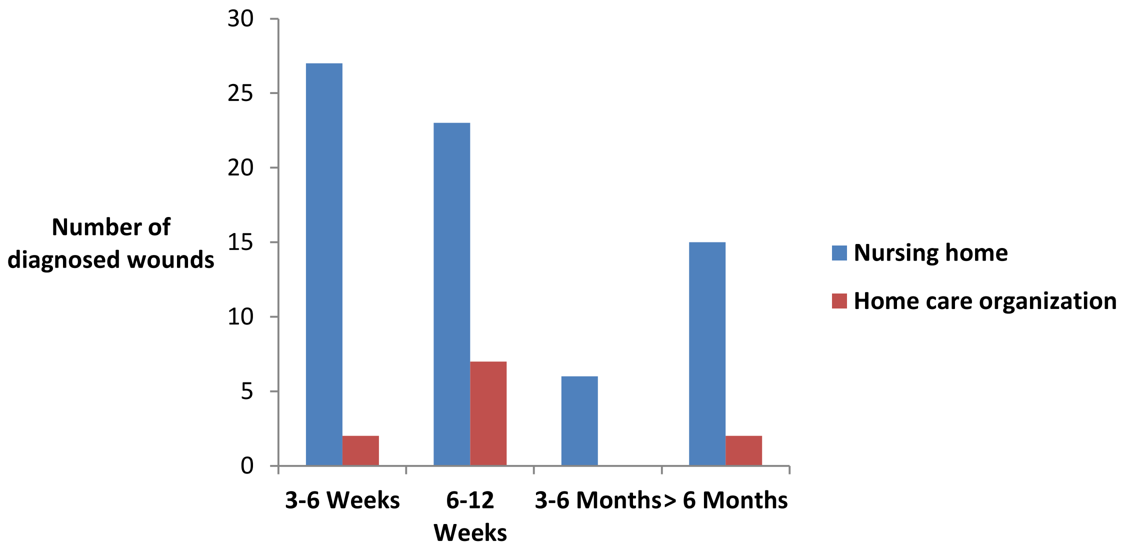

Figure 2 Wound duration of the LPZ 2015 measurements (Halfens *et al*., 2016).

2.4 Wound care in the Netherlands

Section 2.4 provides information about the organization of wound care in the Netherlands. At first, Section 2.4.1 defines the organization related to these treatments in general. Disadvantages and deficiencies are also prescribed. Subsequently, in Section 2.4.2 we describe the idea of a wound expertise centre (WEC).

2.4.1 Organization of wound care

Rondas *et al*. (2015a) mentioned that wound care is given in (long-term) health institutions, secondary care and in the community. In addition, treatment of these patients involves different health care disciplines, for example the general practitioner, (vascular/reconstructive) surgeons, dermatologists, nurse practitioner, wound consultant, paramedic, elderly care specialist, pharmacist, or caregiver. However, the composition of this multidisciplinary team depends on the diagnosis and severity of the wound.

Usually, a patient with a (chronic) wound visits the general practitioner and is treated by home care nurses. An important downside of this approach is that many patients receive this type of treatment for more than thirty weeks before they are referred to a medical specialist at the hospital. So, the organization of wound care is multi-professional, multi-disciplinary and transmural. Therefore, coordination and communication are very important aspects to enhance quality and efficiency of care (Kenniscentrum Wondzorg, 2017).

Often insufficient and inefficient communication occurs across the health care pathway of a patient (Van Mierlo- van den Broek & De Laat, 2012). A delay in the healing process often occurs, with even hospitalization as a result. This results in more burdens for a patient and reduces quality of life (Quataert, 2012). However, a delayed healing process does not only affect the physical and psychological condition of a patient. It involves enormous costs as well (Van Mierlo- van den Broek & De Laat, 2012). Graves & Zheng (2014) have investigated possibilities in the organization of care that will lead to an improvement of quality of care, and to a reduction of costs. This research stated that the implementation of multidisciplinary teams, specialized nurses, control and guidance of patients result in an improved quality of care, shorter healing process, and a reduction of costs.

2.4.2 Wound expertise centre

In the 1990s, the United Kingdom founded specialized leg ulcer clinics within their community (Moffatt *et al*., 1992). Different studies investigated the impact of these clinics on healing duration, cost-effectiveness and quality of care (Gottrup *et al*., 2001; Moffatt *et al.*, 1992). Conclusions drawn from these studies are that treatment of patients at these clinics increase healing rates, improve efficiency of care, and reduce costs regarding wound care (Harrison *et al*., 2005; Moffatt *et al*., 1992).

Mierlo-van den Broek & De Laat (2012) analysed the Dutch wound care organization. One of their conclusions is that the organization in the Netherlands is ineffective, fragmented and has a lack of standardization. They recommend the implementation of an innovative organization structure of chronic wound care in the Netherlands, which focus on the possibility of a quick patient's referral to a WEC, or to a wound care specialist team. In addition, quick referral leads to a faster healing process, fewer burdens for patients and a higher patient satisfaction. Consequently, the researchers expect a reduction of costs regarding wound care in the Netherlands.

The positive research results of the cost-effectiveness of leg ulcer clinics in the United Kingdom, and the exploration of the Dutch wound care organization by Mierlo-van den Broek & De Laat, have led to the establishment of WECs in the Netherlands in the past years (Quataert, 2012). Capgemini consulting (2014) mentioned that differences in the organization's structure and the anchoring of care are seen between various WECs in the Netherlands. A number of WECs is connected to institutions for medical specialized care and others are positioned outside these institutions. However, each WEC has to fulfil specific and important agreements registered in quality indicators for chronic wound care, for example:

- The WEC should consist of a multidisciplinary collaboration between various disciplines.
- Specialized wound care nurses should be involved in the treatment of (chronic) wounds.
- The WEC should provide a plan for triage and case management, which are practical means of sorting patients according to severity.
- The stimulation of expertise enhancing and the work with protocols by health care providers in the region.

2.5 Costs of chronic wound care

This section provides more information about the costs of chronic wound care. Section 2.5.1 defines the organization of the Dutch health insurance system. So, the four different basic laws regarding health care are explained. Section 2.5.2 provides information about the expenses related to wound treatment nationally and internationally.

2.5.1 Dutch health insurance system

The Dutch health insurance system consists of public and private insurances and is regulated by four different basic laws (Ministerie of VWS, 2016):

- Health Insurance Act [Zorgverzerkeringswet (Zvw)].
- Long-Term Act [Wet langdurige zorg (Wlz)].
- Social Support Act [Wet maatschappelijke ondersteuning (Wmo)].
- Youth Act [Jeugdwet] (Ministerie of VWS, 2016).

Wound care is funded by the Zvw and the Wlz (Van Mierlo- van den Broek & De Laat, 2012). The Zvw consists of the basic health insurance, which is obligatory for the Dutch population. This insurance covers costs associated by essential curative care provided by the general practitioner or the medical specialist, hospitalization of patients, used medications and medical aids, or ambulance support. In 2015, the WLZ replaced the Exceptional Medical Expenses Act [Algemene Wet Bijzondere Ziektekosten]. The Wlz provides financing for long-term expensive home care, and institutional care (Ministerie of VWS, 2016; Rondas *et al.*, 2015a). Local authorities are primarily responsible of the Wmo. The Wmo provides support to people who are struggling to be a part of the Dutch society, for example people with learning, physical, mental, or psychological disabilities. The Youth Act provides support for families with children, up to 18 years old, who cope with development and psychological disorders (Ministerie of VWS, 2016).

2.5.2 Costs of chronic wound care

No large-scale, population based studies have been conducted to examine the health care expenditures related to the treatment of chronic wounds in the Netherlands. It is hard to accurately examine expenditures of these treatments, because they are divided across different cost categories. For example, costs of medical consultations with health professionals, hospitalization, home care, and the use of medication, medical devices and wound dressings etc.

However, it is known that the treatment of chronic wounds is an enormous drain on health care resources. The expenditures consist mainly of costs regarding hospitalization, delay in hospital admission, or delay in hospital discharge (Gruen *et al*., 1996). This cost burden does not only affect the Netherlands, it is a public health issue across the world (Harding & Queen, 2010). Gottrup *et al.* (2001) estimated the worldwide prevalence of these wounds at 1%. In addition, costs associated with these treatments are estimated between 2% to 4% of the total health care expenditures in 2001. Sen *et al*. (2009) expect that expenditures in wound care will rapidly grow, because of the ageing of the population and the increasing incidence rate of for example diabetic mellitus.

Since 2011, it has been possible to determine out of health insurance declarations whether a patient used dressings for the treatment of a chronic or a regular wound. Costs of dressings used for the treatment of chronic wounds are reimbursed by the Zvw. On the other hand, dressings used for the treatment of regular wounds have to be paid by the patient (Capgemini Consulting, 2014). The costs for used wound dressings were estimated at € 83 million in the Netherlands for the year 2015 (Zorginstituut Nederland, 2015).

2.6 Previous conducted cost analyses of wound care centres in the Netherlands

Two different cost analyses have been conducted to determine the differences in (wound) care expenditures after the implementation of the WECs in the Netherlands. Section 2.6 outlines these two different cost analyses and describes their methods, results and conclusions. Section 2.6.1 focuses on the analysis conducted by Rondas in 2015. Section 2.6.2 focuses on the analysis conducted by Capgemini Consulting between 2013 and 2014.

2.6.1 Cost analysis of the Knowledge Centre in Wound care at Venray

The Knowledge Centre in Wound Care (KCWC) is one of the first specialized community-based outpatient wound care clinics in the Netherlands. This KCWC is located at Venray and was founded in 2009. A patient's health care pathway consists of regular appointments at the KCWC and home care visits by specialized nurses. The aim of this study is to determine the differences in costs between the year before a patient's initial visit to the KCWC and the year following this consultation (Rondas *et al.*, 2015a).

Rondas *et al.* (2015a) assessed the costs of 172 patients, who all had their initial consultation at the KCWC between 15 September 2009 and 15 September 2010. These patients were all insured at the Dutch health insurance company VGZ.

This study only included reimbursement costs that were qualified under the Zvw. They subdivided those expenditures into four different categories (Rondas *et al.*, 2015a):

- Costs related to contact with health care professionals, such as the general practitioner, the medical specialist and the paramedic.
- Costs associated with medications used.
- Costs associated with the use of medical devices (costs for wound dressings were taken separately).
- Costs associated with hospitalization of patients.

Rondas *et al.* (2015a) mentioned that cost data usually have a skewed distribution and it might be difficult to provide accurate comparisons and inferences. Therefore, the researchers used the non-parametric bootstrap method to estimate the mean and median reimbursed costs. All diagnosed wounds have been included in this cost analysis, even when the research population was very small (for example a population that only consist of two patients). The researchers replicated 1000 bootstrap samples. The 95%-CI was calculated using the percentile method and was based on the 2.5th and 97.5th percentile. Section 2.8 of our report describes the bootstrap method more in detail.

Rondas *et al.* (2015a) also estimated costs of wound care treatment for the most probable estimation of the case, which was called the base case analysis. The base case analysis consisted of five home care nurse visits per week per patient, and one outpatient visit to the KCWC per week per patient. However, the frequency of home care visits had to be estimated because costs reimbursed under the Exceptional Medical Expenses Act were not available for this research. Besides this base case analysis, several sensitivity analyses were conducted to determine the likely impact of different values of variables.

The sensitivity analyses are as follows (Rondas *et al*., 2015a):

- The first sensitivity analysis: The researchers determined the influence of different frequencies of home care visits on the total wound care expenditures. So, they calculated the total costs for one and for thirteen home care visits per week per patient.
- The second sensitivity analysis: The researchers were interested in the impact of different wound durations on the difference in costs between the two years. Therefore, the research population was subdivided into two groups. The first group of patients had a healing duration of less than 75 days, and the second group had a duration that lasted longer.
- The third sensitivity analysis: The researchers determined the effect of expensive wound dressings on the outcome of expenditures between the two years. This particular analysis consisted of two different parts. Firstly, the researchers pinpoint all patients whose dressings cost more than €5,000.00 (n=10). The dressing costs of these ten patients were replaced by the calculated median dressing costs of all patients, which was €1,689.00. Secondly, patients whose dressings cost more than €5,000.00 (n=10) were excluded for the calculations.

Subsequently, the researchers performed a subgroup analysis to determine the difference in reimbursement costs of different types of wounds between the two years. The most common types of wounds were selected for this analysis, namely the leg ulcers, the pressure ulcers and the diabetic ulcers.

Rondas *et al.* (2015a) calculated the arithmetic and bootstrapped costs for the base case analysis for the year before admission to the KCWC, and the year after this initial visit. The results of these calculations are given in terms of mean, median and standard deviation (SD). Table 3 shows the calculated arithmetic and bootstrapped costs per patient for the year before admission. Next, Table 4 shows the results per patient for the year after admission to the KCWC. The mean and median arithmetic reimbursement costs are calculated based on the population. Thus, the SD of the arithmetic mean reimbursement costs is also based on the wound treatment costs of the population. The mean and median bootstrapped reimbursement costs are calculated based on the outcomes of the created 1000 bootstrap samples using the non-parametric bootstrap method, as well the bootstrapped SD. As shown in these tables, the calculated mean bootstrapped costs per patient were respectively € 23,226.00 and € 20,693.00. These costs are calculated based on the means of 1000 bootstrap samples. The researchers showed a decrease in total bootstrapped mean costs of 9% if patients received treatment at the KCWC. In reality, this decrease in costs might by greater. The researchers assumed that the expenditures for home care visits in the year before a patient's initial visit were zero. However, these patients might receive home care visits by specialized nurses for wound dressing changes.

This assumption has been made because of the inability of the inclusion of cost related data other than those qualified under the Zvw. As mentioned above, reimbursement costs qualified under the Wlz were not included in this cost analysis.

Table 3 Arithmetic and bootstrapped costs per patient of the year before admission to the KCWC (Rondas *et al.*, 2015a).

Arithmetic reimbursement costs		Bootstrapped reimbursement costs	
Mean(SD)	**Median**	**Mean (SD)**	**Median**
€ 23,283.00	€ 10,940.00	€ 23,226.00	€ 23,238.00
(€ 32,441.00)		(€ 2,469.00)	

Table 4 Arithmetic and bootstrapped costs per patient of the year after admission to the KCWC (Rondas *et al.*, 2015a).

Arithmetic reimbursement costs		Bootstrapped reimbursement costs	
Mean (SD)	**Median**	**Mean (SD)**	**Median**
€ 18,712.00	€ 8,777.00	€ 20,693.00	€ 20,612.00
(€ 25,911.00)		(€ 1,973.00)	

Rondas *et al*. (2015a) performed different sensitivity and subgroup analyses, there results are shown in Table 5. For these analyses, the researchers also used the non-parametric bootstrap approach to calculate the differences in reimbursement costs between the two years. The results given in Table 5 are the differences in costs per patient per year if a patients received treatment at the KCWC. As shown in Table 5, even if home care visits were estimated at thirteen visits per week per patient, the reimbursement costs were still lower if patient received wound treatment at the KCWC. In addition, another conclusion is that the cost reduction in reimbursement costs is higher for patients whose wound treatment lasted longer than 75 days, compared to a shorter healing duration. The subgroup analysis showed a reduction in reimbursement costs if patients with pressure ulcers or diabetic ulcers received wound treatment at the KCWC. However, an increase in expenses associated with the treatment of patients with leg ulcers is noticed in the year after admission to the KCWC.

However, the research of Rondas *et al.* (2015a) shows remarkable results. Shown in Table 5, the bootstrapped means of two different analyses lie outside the ranges of the CI. This occurs with the 95%-CI of the first sensitivity analysis if a patient receives thirteen home care visits per week, and with the pressure ulcer subgroup analysis. Another remarkable result is that the calculated bootstrapped mean is often not located in the middle of the CI range For example, the range of the CI of chronic wounds that last longer than 75 days is between the € - 11,410.00 and € 5,945.00. However, the mean is calculated at € 2,805.00. Similarly, this can also be seen in the results of wounds that are cured within 75 days, in the results of the first part of the third sensitivity analysis, and in the subgroup analyses of the pressure and diabetic ulcer. Because of these remarkable findings we cannot interpret the results of this cost analysis.

Table 5 Results sensitivity analyses of Rondas' cost analysis (Rondas *et al.*, 2015a).

	Bootstrapped mean reimbursement cost differences	95%-Bootstrapped CI of cost differences in reimbursement mean costs
First sensitivity analysis		
• 1 Home care visit per week	€ 4,134.00	(€ 1,764.00, € 10,198.00)
• 13 Home care visits per week	€ 1,025.00	(€ 5,172.00, € 7,692.00)
Second sensitivity analysis		
• Wound duration > 75 days	€ 2,805.00	(€ - 11,410.00, € 5,945.00)
• Wound duration < 75 days	€ 1,816.00	(€ -10,973.00,€ 6,661.00)
Third sensitivity analysis		
• Replacement by median dressing costs	€ 134.00	(€- 737.00,€ 250.00)
• Exclusion of 10 patients	€ -18.00	(€- 215.00,€ 240.00)
Subgroup analysis		
• Pressure ulcer	€ 8,789.00	(€- 19,333.00,€ 2,212.00)
• Diabetic ulcer	€ 2,152.00	(€- 10,683.00,€ 7,228.00)
• Leg ulcer	€ -1,458.00	(€- 7,645.00,€ 9,533.00)

2.6.2 Cost analysis conducted by Capgemini Consulting

On behalf of the Dutch Healthcare Authority, Capgemini Consulting investigated the possible (potential) savings related to innovative wound care. This study has been conducted from November 2013 till March 2014 and consisted of two different parts, namely (Capgemini Consulting, 2014):

- Cost-benefit analysis: The researchers determined the difference in costs and benefits between patients who are treated regularly or innovatively.
- The prospective analysis: This part estimated the potential savings related to innovative wound care that can be expected between 2015 and 2025.

Capgemini Consulting (2014) mentioned that this innovative approach contains wound care that is delivered in WECs, in which they fulfilled the quality indicators set up by the Dutch Health Care Inspectorate. In the regular situation, a part of home care is being provided by home care nurses and the other part is the patient's or caregiver's responsibility. To determine the average costs regarding to innovative wound care the researchers obtained data from two different experiments. The first experiment was performed by Mitralis Expertise Centre in Wound care and the second one by the Knowledge Centre in Wound Care of Zorggroep. The data obtained for this research gained insight in the patient's gender and age, the type of wound, the healing duration, the number of clinic visits, the total costs of all clinic visits, the costs of used wound dressings, and the total wound care expenditures. In addition, the researchers obtained data provided by Dutch health care insurances of patients who received regularly wound care.

The available data for the research conducted by Capgemini Consulting (2014) provided the ability to conduct a cost-benefit analysis, where expected costs were weighted against the expected benefits of innovative wound care. The wound expenses per patient were calculated based on the amount of weeks which the patients received treatment, multiplied by the average number of weekly medical consultations, multiplied by the rate per consultation. The expected net savings per patient were estimated at a minimum of €1,280.00 if the patient received wound care at a WEC. These savings are mainly due to a reduction in treatment duration of an average of four weeks.

Capgemini Consulting (2014) also calculated potential savings for the years 2015 to 2025. The first step of this prospective analysis was the estimation of the total number of patients who will receive innovative wound care in the future.

Therefore, a state transition diagram has been used. In this diagram, the system is defined as the Dutch population and three different states were distinguished:

- State 1: An individual does not receive chronic wound care.
- State 2: An individual receives regular wound care.
- State 3: An individual receives innovative wound care.

Subsequently, the transition probabilities and the population size of the different states were calculated based on national wound statistics, such as the incidence rate. The researchers calculated the potential savings for five different scenarios, with a differentiation to the implementation rate of innovative care in the Netherlands. The five different scenarios are as follows (Capgemini Consulting, 2014):

- Scenario 1: A minimum yearly growth of approximately 3000 patients with chronic wounds.
- Scenario 2: Twenty per cent of all patients receive innovative wound care within ten years since 2015.
- Scenario 3: Twenty per cent of all patients receive the innovative wound care within five years since 2015.
- Scenario 4: Twenty per cent of all patients receive the innovative wound care in 2015.
- Scenario 5: Maximum of 40% of all patients receive the innovative wound care in 2015.

Table 6 shows the results of the Capgemini Consulting cost analysis (Capgemini Consulting, 2014). We take Scenario 3 as an example to better understand the results of the Capgemini analysis. This scenario assumes that twenty per cent of all patients should receive innovative wound care within five years. This provides a saving of € 29,434,571.00 in 2015, € 64,654,711.00 in 2020, and € 69,131,890.00 in 2025. Assuming scenario 3, the total costs that can be saved are estimated at € 653,291,665.00 in the time period between 2015 and 2025. However, the implementation of WECs in the Netherlands requires investments. Such as the foundation of new WECs, the refurbishment of WECs, training of employees, or hiring new staff. The costs of these investments are not included in these calculations.

Table 6 Results of the cost analysis conducted by Capgemini Consulting (Capgemini Consulting, 2014).

Year	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
2015	€ 5,248,715.00	€ 7,087,690.00	€ 29,434,571.00	€ 57,375,251.00	€ 102,912,264.00
2020	€ 14,795,905.00	€ 49,489,514.00	€ 64,654,711.00	€ 63,273,292.00	€ 113,494,495.00
2025	€ 24,439,035.00	€ 68,786,982.00	€ 69,131,890.00	€ 70,465,774.00	€ 126,400,010.00
Total 2015-2025	**€ 162,790,265.00**	**€ 469,379,431.00**	**€ 653,291,665.00**	**€ 700,062,441.00**	**€ 1,255,718,877.00**

2.7 Wound expertise centre at the Isala clinics

Our cost analysis focuses on the WEC at the Isala clinics in Zwolle. The main aim of the involved therapists is to ensure a fast diagnose, a clear treatment structure and an unambiguous treatment of patients with chronic wounds. Cost-effectiveness is an important part of the vision of this WEC. That is, patients with chronic wounds should receive the most efficient treatment at the lowest possible price (Isala, 2016). Referral of patients to the WEC is done by a general practitioner or medical specialist. A patient's health care pathway consists of regular appointments at the WEC combined with home care visits by nurses of QualityZorg. QualityZorg is a specialized home care organization with wound treatment as expertise (QualityZorg, 2017). They collaborate closely with Excen. Excen is an organization that facilitates more than forty wound expertise centres in the Netherlands, including the WEC at the Isala clinics. Excen provides advice how to obtain the specialized and organized wound care (Excen, 2017).

The home care nurses of QualityZorg consult intensively with the general practitioner, and the specialized nurses and specialists from the WEC, about the patient's treatment, progress or deterioration. Furthermore, there is a high involvement of therapists in the patient's health care pathway due to the multidisciplinary character and their joint responsibility (Isala, 2016). Communication between disciplines of the multidisciplinary team is possible by the use of the online integral patient record called 'PatDoc'. Information regarding the diagnosis, the treatment, the use of materials, the wound images, and the appointments are contained in this record (QualityZorg, 2017). So, by using PatDoc, all involved therapists are informed of the patient's executed diagnostics and treatments. In addition, the amounts of medical aids used during home care are accurately recorded in PatDoc. This ensures a clear overview of the exact use and costs of dressings per patient (Excen, 2017).

2.8 Bootstrap method

Economic health evaluation is important to obtain information about the allocation of health care resources. Estimates of the cost of treatments, and the quantities of resources used by each patient guide health policy decisions. Especially the arithmetic mean cost for a particular treatment is an important measure in the economic health analysis (Barber & Thompson, 2000). The definition of the arithmetic mean is the sum of values of every observation divided by the total number of observations. This equation is shown in Equation 2.8.1, where N is the total number of observations and whose values are represented by $a_1, a_2, \ldots, a_N$.

$$A = \frac{\sum_{i=1}^{N} a_i}{N} \quad \textbf{(2.8.1)}$$

The distribution of cost data is usually positively skewed. Positive skewness is often caused by a minority of patients who utilize large quantities of resources. Another cause of skewness might be the presence of a specific group of patients with zero or small cost values (Barber & Thompson, 2000). It is often difficult to provide an accurate estimation of the arithmetic mean due to a skewed data distribution (Rondas *et al.*, 2015a).

The bootstrap method has been by developed by Efron in 1979. This method can be used if the sampling distribution of a statistical estimator cannot be defined mathematically and is therefore unknown (Barber & Thompson, 2000). The bootstrap resampling method is often used to estimate the CI, but it can also be used to estimate the standard errors, the variance, and to calibrate hypothesis tests (Dixon, 2001). The basic idea of this method is to find the bootstrap distribution that approximates the sampling distribution. This sample should represent the population from which it was originally drawn. It is important to realize that this method is not a substitute for gathering more data to improve accuracy of the results (Hesterberg *et al.*, 2003).

Haukoos & Lewis (2005) stated that for a better understanding of the bootstrap method it is important to gain more knowledge about the different distributions. In statistics there are two different distributions to consider. The first one is the underlying distribution of the given data, which is often described as the probability function. This function shows all values and the probability that each value occurs. The second distribution is the distribution of the statistic of interest. This distribution shows all possible values of the estimated statistic of interest that are calculated from a sample of a given population.

Hesterberg *et al.* (2003) described that the first step of the bootstrap approach is the creation of new samples, also called bootstrap samples or resamples. Suppose x_1, x_2, x_3,…, x_n are the observations of the original sample, which is drawn randomly from a population. Their resamples are represented by x_1*, x_2*, x_3*,…,x_n*. These resamples are originated by sampling with replacement of the observations from the original random sample. Sampling with replacement means that we randomly choose an observation from the original group and replace it before drawing the next one. Therefore, it is possible that any observation can be drawn once, more than once, or not at all.

The statistic of interest (e.g. the mean) is calculated for each bootstrap sample, which results in a set of bootstrap values. The empirical distribution of all these values make up an estimation of the theoretical sampling distribution (Briggs *et al*., 1997; Tong *et al.*, 2016). This distribution provides information about skewness, kurtosis, centre and dispersion of the sampling distribution (Hesterberg *et al.*, 2003).

Barber &Thompson (2000) stated that the number of required resamples depends on the statistic of interest. They recommend at least 1000 resamples to accurately determine the bootstrap confidence interval (CI). To calculate the bootstrap standard error between 25 and 200 resamples are required.

One of the advantages of this approach is the avoidance of distributional assumptions such as normality (Barber & Thompson, 2000). Therefore, this approach does not rely on assumptions concerning the underlying distribution (Briggs *et al.*,1997). However, the only assumption to consider is that the sample distribution is a good approximation of the population distribution. So, this means that the sample is a good representation of the population (Barber & Thompson, 2000).

Method

3. Method

This chapter presents the method of our research. Section 3.1 describes the data obtained from the Dutch company Excen and it provides information regarding the different data, which is available of each patient. In Section 3.2 we describe the different scenarios that we use for the non-parametric bootstrap method. Section 3.3 provides information regarding the implementation of this method in the program Excel.

3.1 Available data

The main aim of our research is the determination of the average costs of specialized medical home care [Medisch Specialistische Verpleging in the Thuissituatie (MSVT)] and the costs of medical aids [Hulpmiddelen (HLP)] used during home care. All assessed patients received wound treatment at the Wound Expertise Centre (WEC) at the Isala clinics in Zwolle. In addition, these patients received home care provided by specialized nurses of QualityZorg.

We obtained data from the company Excen. As mentioned before, Excen facilitates more than forty WECs in the Netherlands, including the WEC at the Isala clinics in Zwolle. Our obtained database includes 487 patients who all received wound care at this WEC in the last couple of years. These patients were insured by different health insurance companies in the Netherlands.

For each patient the following information is available for our research:

- **ID:** The unique patient's identification number.
- **Diagnosis:** The aetiology of the wound.
- **Wnd:** The total number of wounds.
- **Creation:** The date on which the MSVT request for a patient is processed.
- **MSVT Euro:** The costs of received MSVT that is claimed on the health insurances.
- **Unit 5 min:** The total number of five minutes units of received MSVT.
- **Hours:** The total number of received MSVT hours that is claimed on the health insurances.
- **HLP MSVT:** The costs of wound dressing used during home care that is claimed on the health insurances.
- **Start:** The data on which the patient received MSVT for the first time.
- **End:** The data on which the patients received MSVT for the last time.

Table 7 Baseline characteristics of all included patients (n=487).

Diagnosis	n	Rate (%)	Number of wounds
Diabetic mellitus ulcer	81	(16.95%)	106
Surgical wound	70	(14.64%)	92
Traumatic ulcer	66	(13.81%)	87
Arterial ulcer	54	(11.30%)	84
POWI ulcer	54	(11.30%)	61
Pressure ulcer	35	(7.32%)	46
Venous ulcer	33	(6.90%)	53
Amputation wound	20	(4.18%)	26
Pilonidal sinus	17	(3.56%)	18
Mixed arterial-venous ulcer	11	(2.30%)	14
Erysipelas with ulcer	9	(1.88%)	14
Oedema	8	(1.67%)	8
C.V.I. + Oedema	6	(1.26%)	6
Lymphedema leg	3	(0.63%)	3
Vasculitic ulcer	3	(0.63%)	6
Remaining origin	2	(0.42%)	2
Ulcus cruris	2	(0.42%)	2
Artery disease	1	(0.21%)	1
Burn	1	(0.21%)	1
C.A.B.G.	1	(0.21%)	1
Dependent oedema transverse lesion + pressure ulcer	1	(0.21%)	2
Erysipelas without ulcer	1	(0.21%)	1
Fasciotomy	1	(0.21%)	1
Lower leg wound	1	(0.21%)	1
Neuropathic ulcer	1	(0.21%)	1
Oncologic ulcer	1	(0.21%)	1
Psoriasis	1	(0.21%)	1
Pyoderma gangrenosum ulcer	1	(0.21%)	2
Unknown origin	1	(0.21%)	1
Wounds after surgery	1	(0.21%)	2

Table 7 overviews the baseline characteristics of the included patients (n=487). Diabetic mellitus ulcers, surgical wounds, traumatic ulcers, arterial ulcers, POWI ulcers, Pressure ulcers, and venous ulcers were the most common types of wounds. The number of patients with these particular wounds (represented by n) are respectively 81(16.95%), 70 (14.64%), 66 (13.81%), 54 (11.30%), 54 (11.30%), 35 (7.32%), and 33 (6.90%). These percentages are also displayed in Figure 3. Shown in Table 7, the column 'Number of wounds' displays the total number of wounds per category. So, some patients received treatment for more than one wound of a specific type.

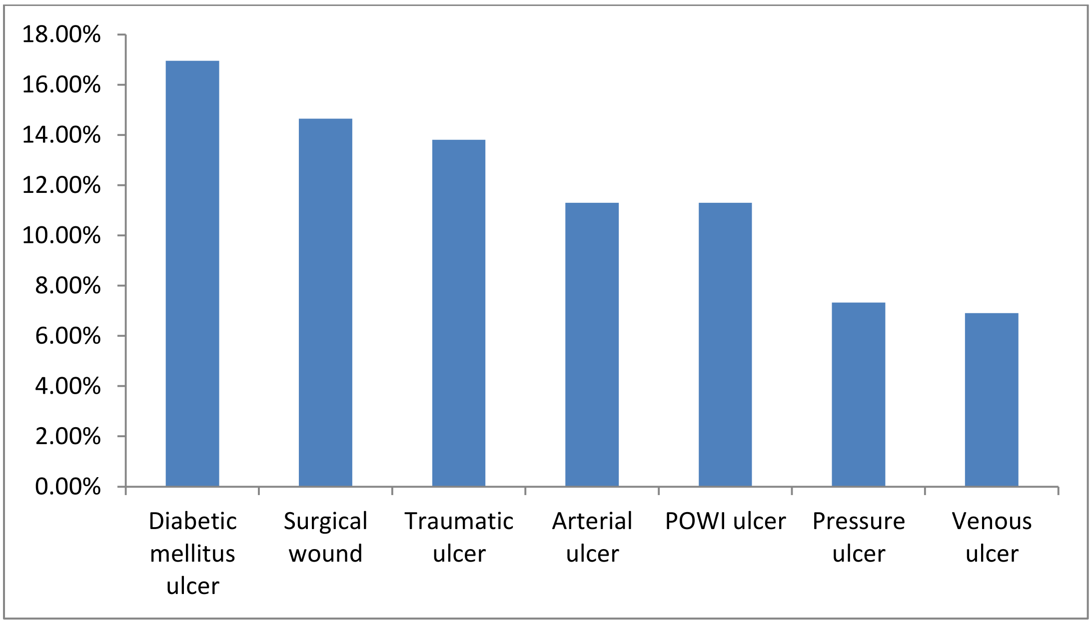

Figure 3 Aetiology of the most common types of wounds of patients included in our research.

For our research it is important to attempt to large population sizes. The calculations of our statistics of interests are more precisely estimated if they are based on large population sizes. Calculations based on small research populations are not an accurate estimation of the expected average costs. Therefore, we decided to only include the most common types of wounds. As mentioned before, some patients within the same type of wound received treatment for more than one wound. In general, these patients received more HLP and MSVT. So, patients with more than one wound generally lead to higher reimbursement costs. Therefore, we decided to only include patients who received treatment for one wound. This arranges similar groups to compare the outcomes of our cost analysis. Table 8 overviews the number of included patients for our cost analysis, which ranges from 22 to 65 patients.

Table 8 Aetiology of the most common types of chronic wounds of our cost analysis.

Diagnosis	**n**
Diabetic mellitus ulcer	65
Surgical wound	55
Traumatic ulcer	53
POWI ulcer	47
Arterial ulcer	33
Pressure ulcer	29
Venous ulcer	22

Each wound type category showed costs outliers, whose treatment of some patients are even significantly expensive. Hospitals and health insurances should not only determine their purchasing policies and their budget overview based on the expected costs of the average patient. They experience problems with the funding of treatment if they do not take the outliers into account. We are as interested in the dispersion of the distribution on the right side of the average. Therefore, we decided to include cost data of all selected patients who received treatment for the most common types of chronic wounds. So, the impact of cost outliers is included in the calculations of the statistics of interest.

3.2 Sample size scenarios

For each type of wound we estimate the mean, the standard deviation (SD) and the 95% confidence interval (CI). For each patient the costs of treatment are subdivided into three categories, namely:

- **Total costs:** The sum of MSVT costs and HLP costs.
- **MSVT costs:** The costs of MSVT. These costs are determined based on the hours received MSVT multiplied by the rate per hour.
- **HLP costs:** The costs for medical aids used during home care. These expenses are calculated by the number of used aids multiplied by their unit prices.

The data obtained is limited because the number of included patients per type of wound ranges from 22 to 65. As mentioned before, cost data is usually skewed and has many outliers. We conduct a literature research to get an idea of possibilities how to carry out a cost analysis if the research population is limited, and if the underlying distribution is unknown. Our literature research showed that the non-parametric bootstrap method offers a possible solution to these problems.

For our cost analysis we use the non-parametric bootstrap method. This contains that we created for every scenario 1000 bootstrap samples, drawn by sampling with replacement from the population of the corresponding type of wound. The different scenarios are as follow:

- **Scenario I:** The sample size of each bootstrap sample is equal to eleven.
- **Scenario II:** The sample size of each bootstrap sample is equal to ¼ part of the population of the corresponding type of wound.
- **Scenario III:** The sample size of each bootstrap sample is equal to the population of the corresponding type of wound.
- **Scenario IV:** For the first bootstrap sample we draw with replacement the same number of observations as the size of the population of the corresponding type of wound. To explain this scenario more clearly we use the diabetic mellitus population (n=65) as example. So, the first bootstrap sample consists of 65 observations that are drawn by sampling with replacement from the diabetic

mellitus ulcer population. The sample population of the second resample consists of 65 observations that are drawn by sampling with replacement from a group that is composed of the 65 patients of the population, plus the 65 observations of the sample population of the first bootstrap sample. So, every time you draw 65 observations from a collection of observations that consists of the observations of the population plus the sample populations of the previous resamples. This scenario is clearly explained in Equation 3.2.1, where X defines the total number of patients in the population group of the particular wound and S defines the bootstrap sample number. Of course, the number of observations drawn by sampling with replacement depends on the population size of the corresponding type of wound.

$$\begin{aligned} S_1 &- \quad X \text{ patients from } P_0 \\ S_2 &- \quad X \text{ patients from } P_0 \cup S_1 \\ S_3 &- \quad X \text{ patients from } P_0 \cup S_1 \cup S_2 \\ S_{1000} &- \quad X \text{ patients from } P_0 \cup S_1 \cup S_2, \ldots, \cup S_{999} \end{aligned} \tag{3.2.1}$$

Table 9 shows the number of observations in a bootstrap sample for each type of wound. However, as mentioned above the size of the sample population is different for the various scenarios and wound categories.

Table 9 Overview of the number of observations in a bootstrap sample.

Type of wound	Population size	Scenario I	Scenario II	Scenario III	Scenario IV
Arterial ulcer	33	11	8	33	33
Diabetic mellitus ulcer	65	11	16	65	65
POWI ulcer	47	11	12	47	47
Pressure ulcer	29	11	7	29	29
Surgical wound	55	11	14	55	55
Traumatic ulcer	53	11	13	53	53
Venous ulcer	22	11	6	22	22

3.3 Excel

For our research we are interested in the outcome of the following statistics:

- The average total costs per type of chronic wound, as well as SD and 95%-CI of the average total costs.
- The average MSVT costs per type of chronic wound, as well as SD and 95%-CI of the average MSVT costs.
- The average costs of medical HLP used during home care per type of chronic wound, as well as SD and 95%-CI of the average HLP costs.

Our statistics of interest are calculated using the program Excel. The first step of our calculations is the classification of patients by their type of wound. This gives us an overview of the costs of treatment per patient. Subsequently, we add per patient the MSVT and the HLP costs. This represents the total costs of wound care per patient. These cost totals are calculated before performing the non-parametric bootstrap method. This is decided because we assume some correlation between the number of received MSVT hours and the amount of medical aids used during home care.

The non-parametric bootstrap method is performed for every cost category of a particular type of wound. Then, we calculate the mean of every bootstrap sample. The average costs of a cost category are calculated by the determination of the average of all 1000 bootstrap samples means. Thereafter, we calculate the SD and give an estimation of the 95%-CI.

The distribution and the frequencies of the resample means are displayed in a histogram. These histograms display a graphical representation of the distribution of our cost data and it shows an estimation of the density of the underlying probability density function. To create a histogram we divide bootstrap sample means into bins. The mean of a resample is included in a specific bin, if this value is greater than the lower bound of the interval, and equal or less than the upper bound.

Normally you would calculate a confidence interval, with an assumption about the underlying distribution. However, the non-parametric bootstrap approach does not rely on any assumption. Therefore, the 95%-CI is calculated using the percentile method, based on the 2.5th and 97.5th percentile. We determine the two-tailed 2.5% cut-off point, so 2.5 per cent of the resample means are cut off at the left and at the right side of the distribution. The smallest and largest value that remain between these two cut-off points estimate the range of the 95%-CI.

Besides the calculation of the average costs and the estimation of the 95%-CI, we calculate the SD. This statistical parameter represents a measure that is used to quantify the amount of variation. A small value indicates a low dispersion around the mean, and the exact opposite applies to high values. Our calculations of the SD are based on the bootstrap sample means.

$$\boldsymbol{X \in \xi(\mu, \sigma^2)} \qquad \textbf{(3.3.1)}$$

In our analysis the parameters are unknown; therefore we estimate the arithmetic mean with Formula 3.3.2.

$$\boldsymbol{\bar{x} = \frac{1}{N} \sum_{i=1}^{N} x_i} \qquad \textbf{(3.3.2)}$$

The estimator of $\bar{x}$ is defined by $\hat{x}$. Suppose N=1000, than the equation of the estimator of the mean is given in Formula 3.3.3.

$$\boldsymbol{\hat{x} = \frac{1}{N} \sum_{i=1}^{N} x_i} \qquad \textbf{(3.3.3)}$$

The estimator of the SD of the estimator of the mean is calculated using Formula 3.3.4.

$$\boldsymbol{s\,(\hat{x}) = \sqrt{\frac{1}{N-1} \sum_{i=1}^{N} (\bar{x}_i - \hat{x})^2}} \qquad \textbf{(3.3.4)}$$

Results

4. Results

This section presents the results of our research. Therefore, the first seven sections represents the results of the corresponding type of wound. Section 4.1 (arterial ulcer), Section 4.2 (diabetic mellitus ulcer), Section 4.3 (POWI ulcer), Section 4.4 (pressure ulcer), Section 4.5 (surgical wound), Section 4.6 (traumatic ulcer) and Section 4.7 (venous ulcer). Finally, Section 4.8 shows the differences in results between the bootstrapped average total costs, and the sum of the bootstrapped average MSVT and HLP costs.

4.1 Arterial ulcer

The arterial ulcer population consist of 33 patients. The arithmetic total costs range from the minimum of € 305.59 to a maximum of € 9,884.06. However, the total expenses of treatment of only three patients cost more than € 5,000.00. The arithmetic mean of the total costs of the arterial ulcer is calculated at € 2,531.07. The MSVT costs range from € 168.00 to € 7,887.21 and the outcome of the estimation of the arithmetic mean is € 1,919.66. The minimum value of the expenses for medical HLPs used during home care is € 25.23 and the maximum is € 3,278.56. The corresponding arithmetic mean is € 611.40.

The distribution of the total costs of the treatment of these patients is shown in Figure 4. Most of the individual total costs are on the left side of the calculated arithmetic mean, € 2,466.05. As can be seen, thirteen observations are located at the right side. So, the minority of patients ensure an increase of the arithmetic mean. The outcome of the calculated standard deviation (SD) based on the total costs of the population is € 2,466.05. So, the dispersion of the different observations is large. Figure 5 displays the dispersion of resample means of the total costs of the arterial ulcer after bootstrapping (using Scenario IV). As you can see, the variance in distribution of data becomes smaller. This histogram resembles the well-known Normal distribution. One outlier of the average costs of treatment of the arterial ulcer is seen in the bin that ranges from € 4,630.00 to € 4,730.00. The other histograms of the average costs using the different scenarios are given in Appendix A (Total costs), B (MSVT costs) and C (HLP costs).

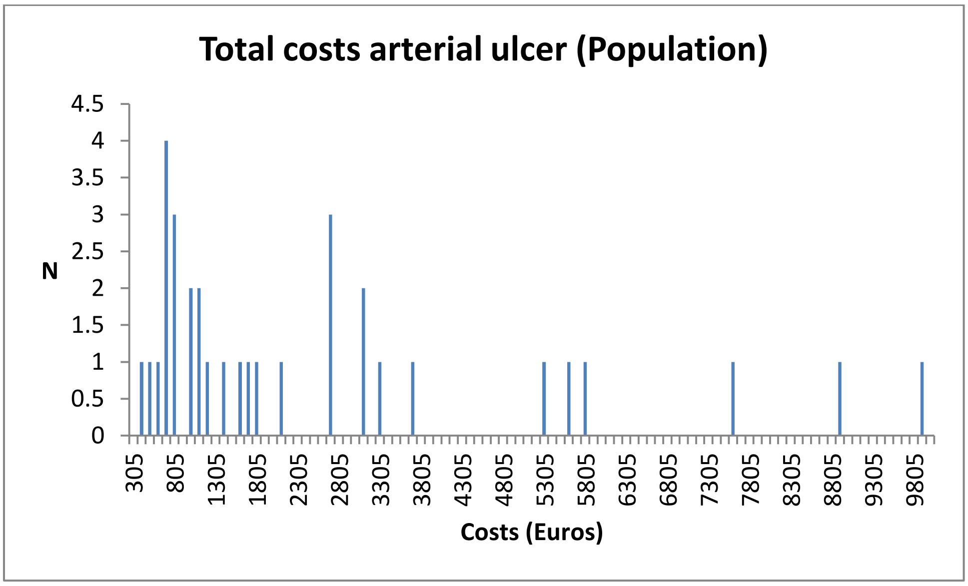

Figure 4 Histogram of the total costs of the treatment of the arterial ulcer (Population).

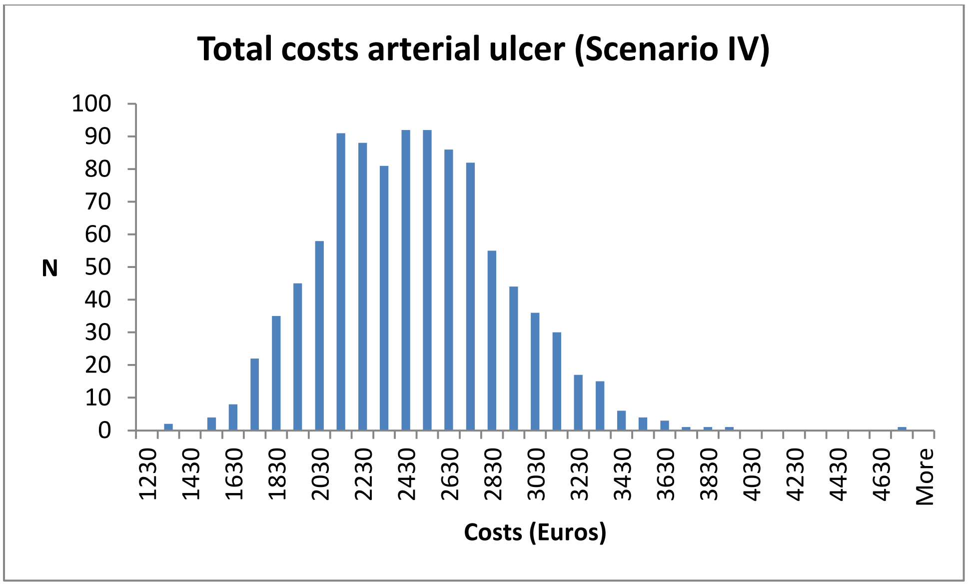

Figure 5 Histogram of the total costs of the treatment of the arterial ulcer (Scenario IV).

Table 10 Standard deviations of the average costs of the treatment of the arterial ulcer.

Arterial ulcer	SD Population	SD Scenario I	SD Scenario II	SD Scenario III	SD Scenario IV
Total costs	€ 2,466.05	€ 716.74	€ 893.78	€ 427.38	€ 416.36
MSVT costs	€ 1,960.90	€ 600.97	€ 705.73	€ 358.05	€ 282.44
HLP costs	€ 686.10	€ 202.58	€ 250.97	€ 121.23	€ 132.51

Table 10 shows the SDs of the average costs based on the bootstrap calculations of the different scenarios. The SD is considerably smaller if you compare the SD of the population with the SDs of Scenarios III and IV. This can partly be explained by the size of the sample population. This change in distribution of the observations of the bootstrapped total costs is clearly visible in Figure 6. This figure shows the differences in histograms of all four scenarios into one figure. The high peak is the histogram belonging to scenario IV, where almost all observations are distributed around the mean of the costs. In Figure 6, data 1 corresponds to the histogram that is drawn from the results of the calculations of Scenario I, data 2 corresponds to Scenario 2 etc.

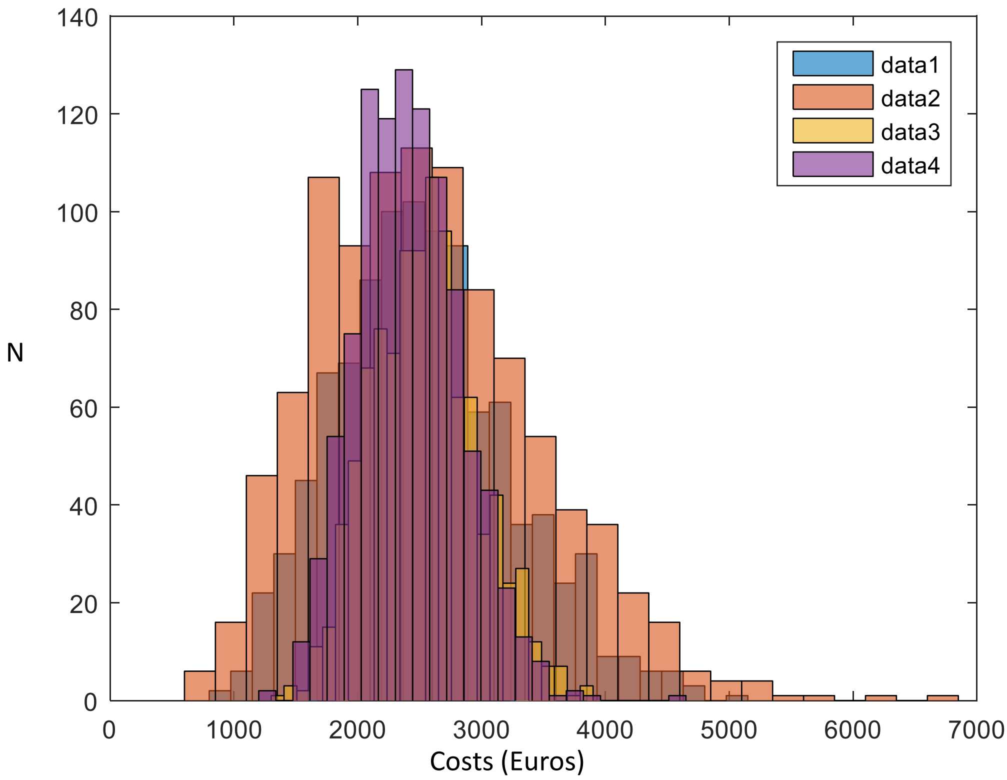

Figure 6 Histogram of the average total costs of treatment of the arterial ulcer (all scenarios).

Table 11 Average costs of the treatment of the arterial ulcer.

Arterial ulcer	Arithmetic mean costs population	Bootstrapped average costs Scenario I	Bootstrapped average costs Scenario II	Bootstrapped average costs Scenario III	Bootstrapped average costs Scenario IV
Total costs	€ 2,531.07	€ 2,540.68	€ 2,561.84	€ 2,535.78	€ 2,417.43
MSVT costs	€ 1,919.66	€ 1,976.65	€ 1,912.22	€ 1,925.74	€ 1,608.54
HLP costs	€ 611.40	€ 607.31	€ 622.07	€ 608.04	€ 696.61

Table 11 shows the average costs that are calculated using the scenarios. These averages are calculated based on all 1000 resample means. The MSVT costs are approximately three higher than the expenses for medical HLP used during home care. The bootstrapped average MSVT and HLP costs calculated using Scenario IV are located relatively far from the calculated averages of the other scenarios. Scenario IV is the only scenario where the population of the bootstrap sample depends on the previous sample populations. In addition, the population of the first bootstrap sample is relatively decisive for the calculated averages. So, the change of higher average costs is somewhat higher if the first resample population consists of patients whose treatments were relatively expensive.

Table 12 95% Confidence intervals of the average costs of the treatment of the arterial ulcer.

Arterial ulcer	95%-CI Scenario I	95%-CI Scenario II	95%-CI Scenario III	95%-CI Scenario IV
Total costs	(1,253.02-4,112.51)	(1,139.03-4,424.70)	(1,778.53-3,414.78)	(1,667.49-3,280.12)
MSVT costs	(948.25-3.307.15)	(790.91-3,403.06)	(1,286.02-2,653.59)	(1,122.73-2,182.42)
HLP costs	(287.52-1,067.36)	(236.14-1,222.77)	(588.74-625.86)	(465.79-980.94)

The ranges of the 95%-CI are estimated using the percentile method, explained in Section 3.3. Table 12 shows the 95%-CIs based on the means of the 1000 resamples. The intervals are bigger for the first two scenarios. This also corresponds to the higher value of the SDs of the average bootstrapped costs calculated. The interval that is calculated using bootstrap Scenario IV is relatively small. This is logical because most of the resample means are located around the average of all resamples. Therefore, you see a reduction in values of the variance and SD and this results in a small 95%-CI range.

4.2 Diabetic mellitus ulcer

We analysed data of 65 patients who received wound treatment for their diabetic mellitus ulcer at the KCWC. The total costs vary between € 123.71 and € 7,629.91, with a calculated arithmetic mean of € 1,650.53. The total costs of treatment of eighteen patients lay at the right sight of the mean. So, this indicates a distribution of the average total costs to the right. The minimum of MSVT cost is € 33.60, and a maximum of € 6,099.90. We calculated the arithmetic mean of the MSVT costs at € 1,195.93. The difference in minimum and maximum costs for medical HLP used during home care is large. The costs of HLP vary between € 11.20 and € 6,060.93 and their average is estimated at € 454.60. A remarkable point is our data is the patient who received five hours of MSVT, which corresponds to € 302.40. However, this patient received significant expensive medical HLP, respectively € 6,060.93. So, there is not always a correlation between the MSVT and the HLP costs. Again, these cost outliers ensure a significant increase in the average costs of treatment.

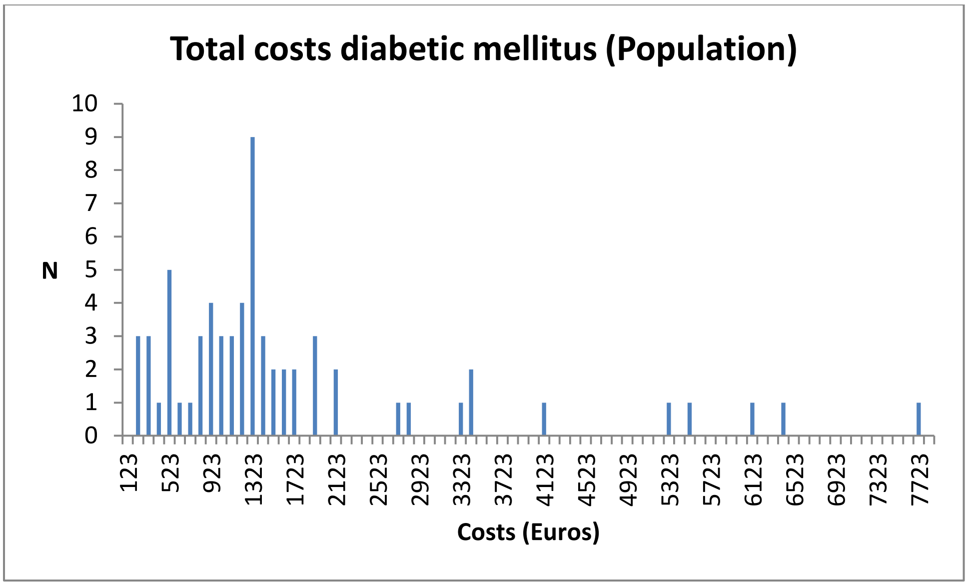

Figure 7 Histogram total costs of the treatment of the diabetic mellitus ulcer (Population)

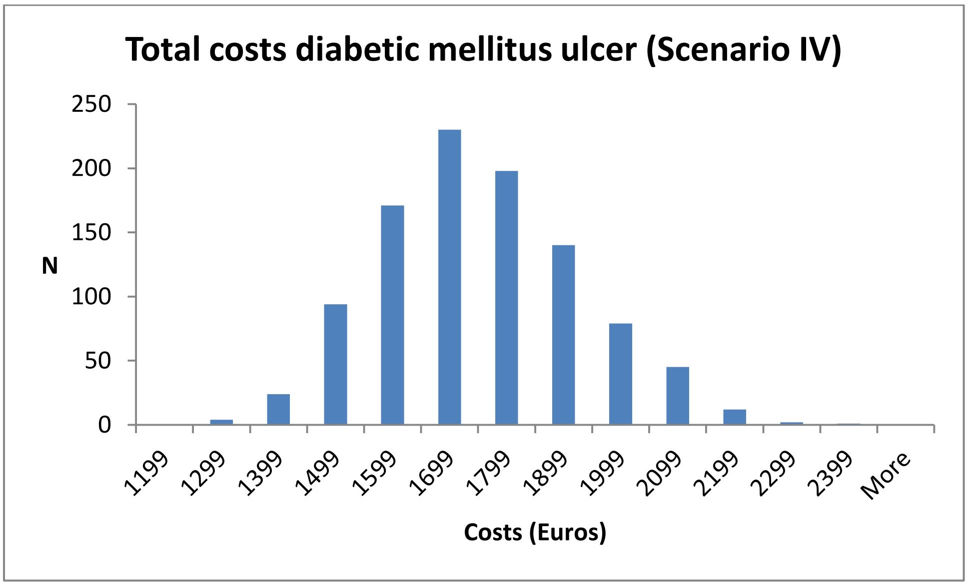

Figure 8 Histogram average total costs of treatment of the diabetic mellitus ulcer (Scenario IV)

Figure 7 shows the distribution of the total cost of the diabetic mellitus population. Most of the observations are situated on the left side of the arithmetic mean (€ 1,650.53). However, the total costs of six different patients were higher than € 4,000. The costs of treatment of these patients are outliers and they are responsible for the high arithmetic mean. In Figure 8 we display the dispersion of resample means of the average total costs of treatment of the diabetic mellitus ulcer using the non-parametric bootstrap method Scenario IV. The difference in distribution of the observations compared to Figure 7 is large. The distribution obtained using Scenario IV has far less cost outliers and most of the resample means are distributed around the average total costs. The other histograms of the average costs using the different scenarios are given in Appendix D (total costs), E (MSVT costs) and F (HLP costs).

Table 13 Standard deviations of the average costs of treatment of the diabetic mellitus ulcer.

Diabetic mellitus ulcer	SD Population	SD Scenario I	SD Scenario II	SD Scenario III	SD Scenario IV
Total costs	€ 1,546.60	€ 453.90	€ 384.00	€ 195.56	€ 176.18
MSVT costs	€ 1,154.13	€ 343.62	€ 279.00	€ 141.51	€ 159.63
HLP costs	€ 815.21	€ 262.84	€ 205.34	€ 102.83	€ 83.39

Table 13 shows the SDs of the average costs based on the means of the bootstrap samples. A large difference between the SD of Scenario I and Scenario IV is noticed. The bootstrap sample means, which are calculated using scenario IV, are more distributed around the average costs compared to the distribution of means of the other four scenarios. The sample size using Scenario I was set at eleven observations per bootstrap sample. So, the mean of a particular resample is quite high if the corresponding sample population contains several observations of patients whose costs were higher than the average. Therefore using Scenario I, the possibility of large variances between the means of each bootstrap sample is higher compared to Scenario IV. Figure 9 shows the different histograms of the average total costs of all four scenarios into one figure. The change in the distribution of resample means is clearly visible. Shown in Figure 9, data 1 corresponds to the histogram that is drawn from the results of the calculations of Scenario I, data 2 corresponds to Scenario 2 etc. We refer to detailed histograms of the average total costs to the respective Appendix D.

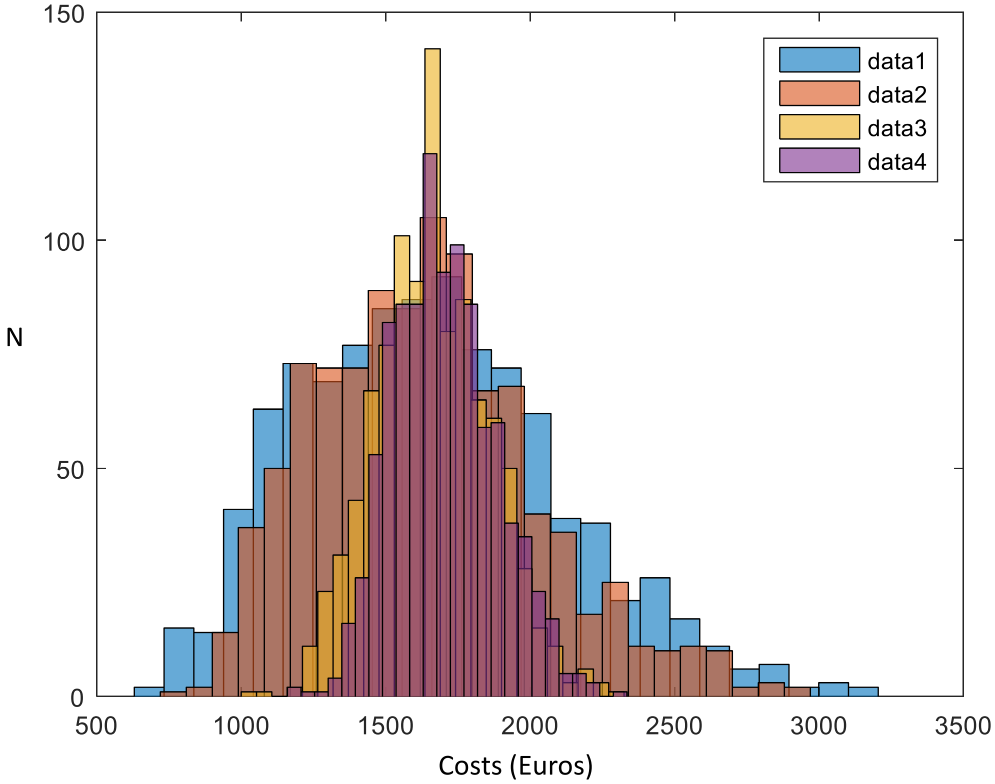

Figure 9 Histogram average total costs of treatment of the diabetic mellitus ulcer (all scenarios).

Table 14 Average costs of the treatment of the diabetic mellitus ulcer.

Diabetic mellitus ulcer	Arithmetic mean costs population	Bootstrapped average costs Scenario I	Bootstrapped average costs Scenario II	Bootstrapped average costs Scenario III	Bootstrapped average costs Scenario IV
Total costs	€ 1,650.53	€ 1,676.22	€ 1,638.48	€ 1,658.51	€ 1.702,06
MSVT costs	€ 1,195.93	€ 1,194.80	€ 1,204.37	€ 1,196.09	€ 1.275,78
HLP costs	€ 454.60	€ 468.74	€ 450.53	€ 454.34	€ 377,57

Table 14 shows the average costs that are calculated ulcer using the non-parametric bootstrap scenarios. These averages are calculated based on all 1000 resample means. Table 15 shows for each bootstrap scenario the 95%-CIs based on the means of all 1000 resamples. These intervals are calculated using the percentile method. The interval that is calculation using bootstrap Scenario IV is relatively small. This is logical because less dispersion between resample means is noticed using this scenario.

Table 15 95% Confidence intervals of the average costs of treatment of diabetic mellitus ulcer.

Diabetic mellitus ulcer	95%-CI Scenario I	95%-CI Scenario II	95%-CI Scenario III	95%-CI Scenario IV
Total costs	(921.05-2,748.98)	(1,021.31-2,541.88)	(1,286.21-2,047.77)	(1,395.30-2,068.82)
MSVT costs	(662.30-1,970.17)	(742.64-1,808.31)	(938.43-1,485.71)	(970.31-1,616.58)
HLP costs	(167.01-1,096.32)	(209.49-954.13)	(298.57-701.51)	(248.96-566.07)

4.3 POWI ulcer

We obtained data of 47 patients who all received wound care for the treatment of POWI ulcers at the KCWC in Zwolle. The minimum and maximum total costs are respectively € 140.54 and € 3,823.60. We estimated the arithmetic mean of the total costs at € 1,507.40. The MSVT costs vary between € 134.40 and € 3,109.50, and the arithmetic mean is calculated at € 1,142.56. The HLP costs vary between € 6.14 and € 1,713.75 and we determined an arithmetic mean of € 364.84. In general, most patients whose total costs are higher than average received many hours MSVT and medical HLP. However, this does not apply to one patient. This patient received few hours of MSVT (eight hours which corresponds to € 537.60), but the costs for medical HLP were relatively quite expensive (€ 1,713.75).

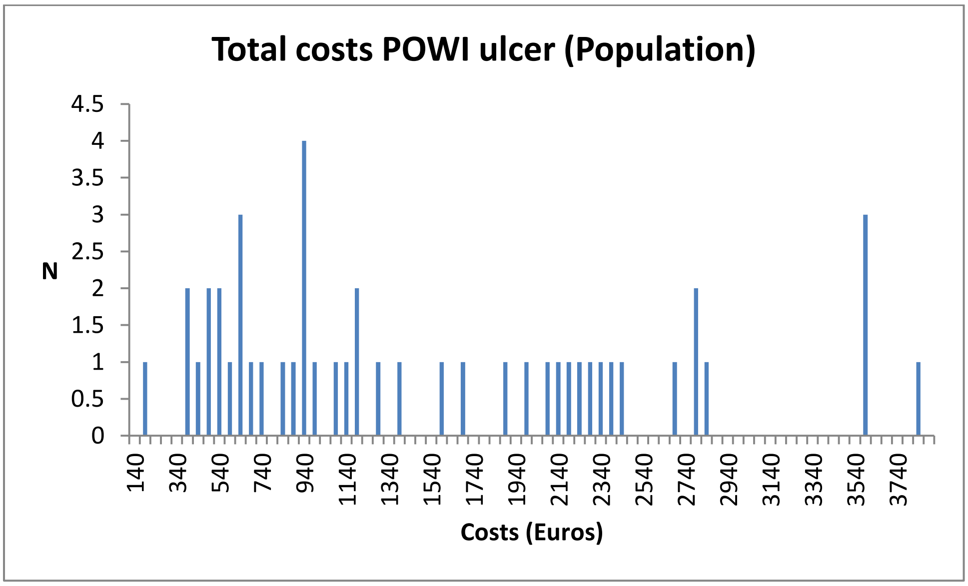

Figure 10 Histogram of the total costs of the treatment of the POWI ulcer (Population).

Figure 10 shows the distribution of the total costs of the POWI ulcer population. This dispersion of data does not show a known distribution. One remarkable point is the presence of some expensive outliers. For example, the three observations located in the bin that ranges from €3,540.00 to €3,590.00.

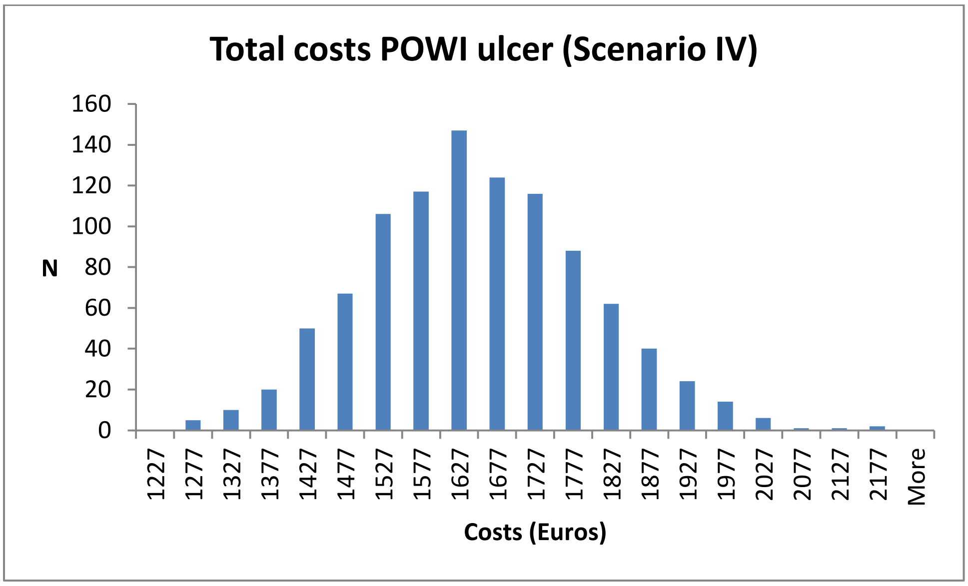

Figure 11 Histogram of the average total costs of the treatment of the POWI ulcer (Scenario IV).

Figure 11 shows the dispersion of resample means of the total costs of the treatment of the POWI ulcer using Scenario IV. The range between the minimum and maximum total costs is smaller compared to the range in Figure 10. Figure 11 shows a distribution of means that looks similar to the Normal distribution. The other histograms of the average costs using the different scenarios are given in Appendix G (total costs), H (MSVT costs) and I (HLP costs).

Table 16 Standard deviations of the average costs of the treatment of the POWI ulcer.

POWI ulcer	SD Population	SD Scenario I	SD Scenario II	SD Scenario III	SD Scenario IV
Total costs	€ 997.66	€ 292.34	€ 291.37	€ 138.75	€ 145.87
MSVT costs	€ 765.59	€ 22.34	€ 222.15	€ 111.23	€ 110.52
HLP costs	€ 409.50	€ 127.53	€ 118.68	€ 58.54	€ 60.00

Table 16 shows the SDs of the average costs based on the calculated resample means of the POWI ulcer. There is a large difference in the SD between the different scenarios. The resample means of the different scenarios are more distributed around the mean than the observations of the population group. Therefore, the variance in the distribution becomes less, and as well the SD. Figure 12 shows the different histograms of the average total costs of all four scenarios into one figure. The change in the dispersion of the observations is clearly visible, but we refer to detailed histograms of the average total costs to the respective Appendixes G, H and I. In Figure 12, data 1 corresponds to the histogram that is drawn based on the results of the calculations of Scenario I, data 2 corresponds to Scenario 2 etc.

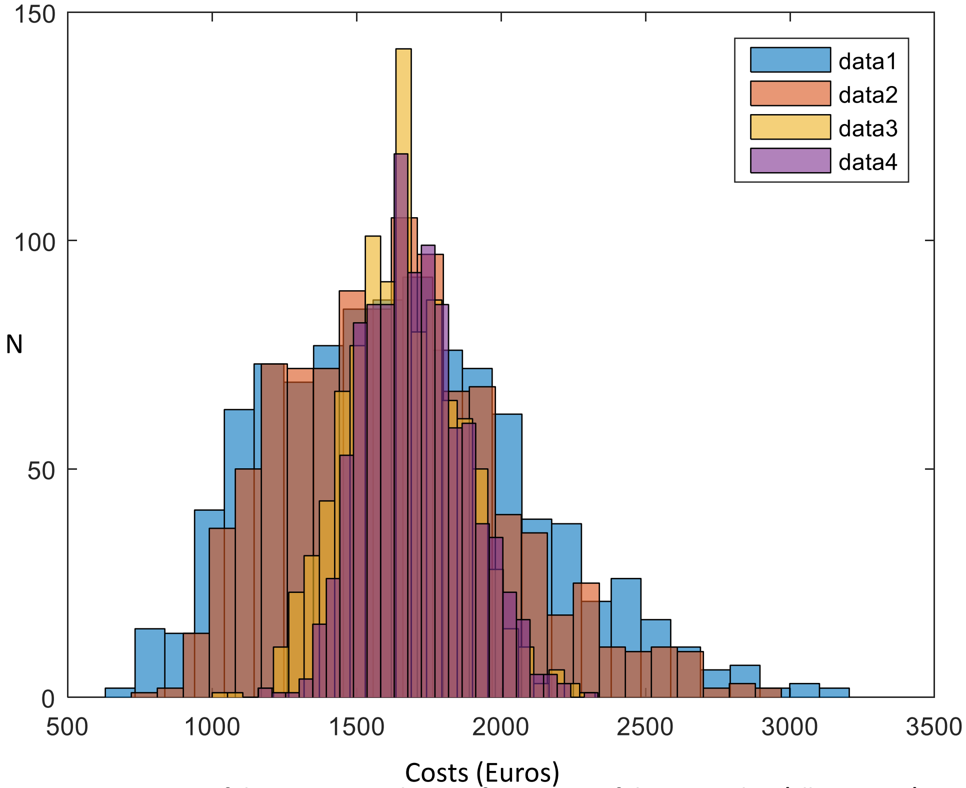

Figure 12 Histogram of the average total costs of treatment of the POWI ulcer (all scenarios).

Table 17 Average costs of the treatment of the POWI ulcer.

	Arithmetic mean costs population	Bootstrapped average costs Scenario I	Bootstrapped average costs Scenario II	Bootstrapped average costs Scenario III	Bootstrapped average costs Scenario IV
Total costs	€ 1,507.40	€ 1,505.20	€ 1,495.30	€ 1,511.17	€ 1.625,54
MSVT costs	€ 1,142.56	€ 1,145.05	€ 1,133.59	€ 1,144.31	€ 1.190,41
HLP costs	€ 364.84	€ 363.54	€ 362.91	€ 363.87	€ 376,86

An overview of the average costs that are calculated using the non-parametric bootstrap scenarios is given in Table 17. The MSVT costs are approximately three times more expensive than the costs for medical HLP used during home care. The bootstrapped average total and MSVT costs calculated using Scenario IV are located relatively far from the calculated averages of the other scenarios. Scenario IV is the only scenario where the population of the bootstrap sample depends on the previous sample populations. So, the change of higher average costs is somewhat higher if the first resample population consists of patients whose treatments were relatively expensive. Probably the first resample of these calculations consisted of the observations of patients whose treatments were relatively more expensive that those of the other patients. The 95%-CIs estimated using the percentile method are given in Table 18. These CIs are based on the resample means. The intervals are significantly bigger for the Scenarios I, II and V.

Table 18 95% Confidence intervals of the average costs of the treatment of the POWI ulcer.

POWI ulcer	95%-CI Scenario I	95%-CI Scenario II	95%-CI Scenario III	95%-CI Scenario IV
Total costs	(957.04-2,094.02)	(948.40-2,093.84)	(1,243.18-1,775.88)	(1,348.90-1,924.17)
MSVT costs	(705.41-1,622.48)	(738.10-1,599.91)	(932.79-1,371.21)	(980.61-1,412.41)
HLP costs	(144.53-655.17)	(160.62-629.09)	(257.07-483.99)	(266.06-506.38)

4.4 Pressure ulcer

Twenty-nine patients received MSVT and wound treatment at the KCWC. The minimum and maximum total costs were respectively € 185.31 and € 6,816.40. We determined the arithmetic mean of pressure ulcers at € 2009.05. The MSVT costs range from € 50.40 to € 4,877.6, with an arithmetic mean of € 1,574.33. The HLP costs vary between € 12.10 and € 1,938.80, with an arithmetic mean of € 434.72.

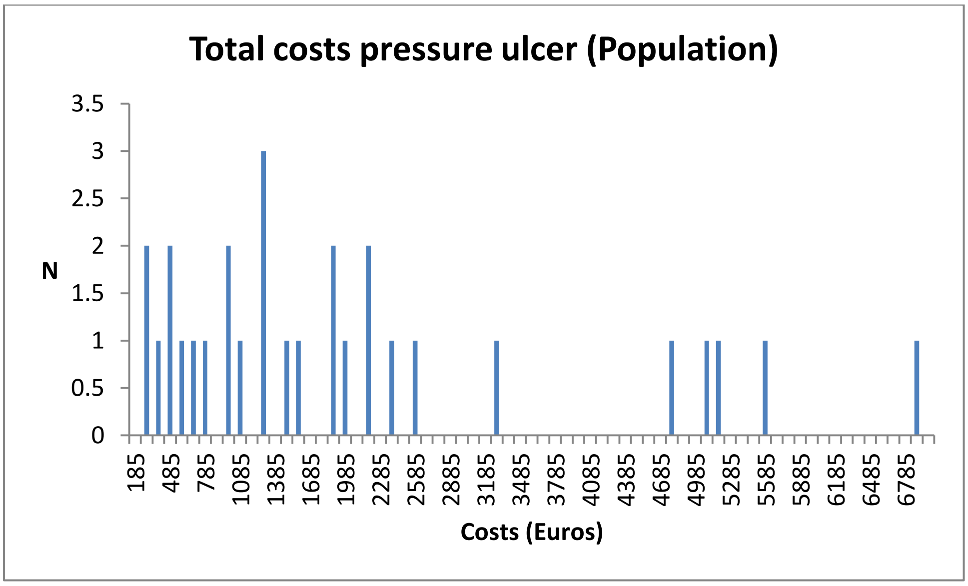

Figure 13 Histogram of the total costs of the treatment of the pressure ulcer (Population).

The dispersion of the total costs for the pressure ulcer population is given in Figure 13. This histogram shows a very distributed graphical view of the total costs. One patient received really expensive wound care and is a significant expensive outlier.

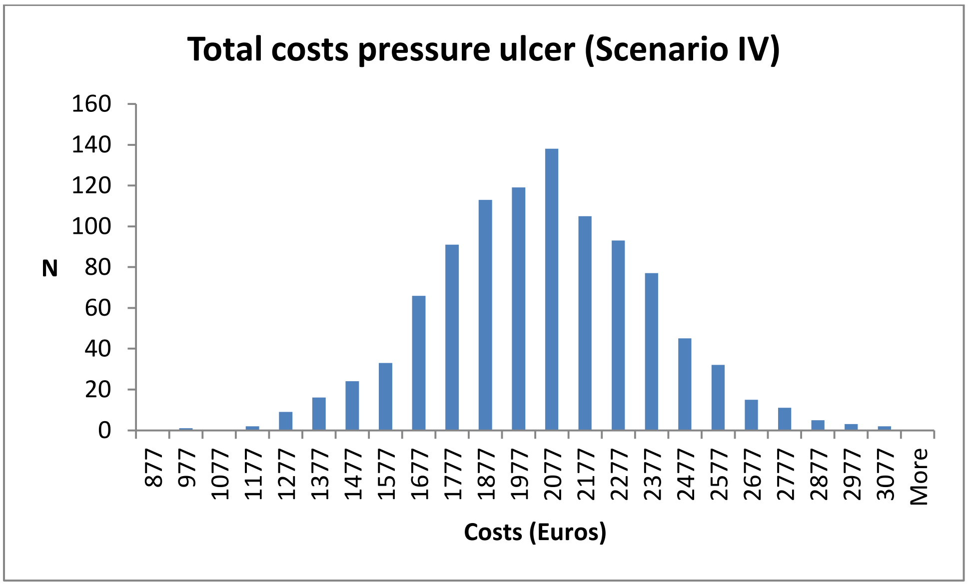

Figure 14 Histogram of the average total costs of treatment of the pressure ulcer (Scenario IV).

Figure 14 shows the dispersion of resample means of the total costs using the non-parametric bootstrap method Scenario IV. The dispersion of these resample means tends to well-known Normality distribution. Most observations are centred on the mean and this distribution also shows less expensive costs outliers. The other histograms of the average costs using the different non-parametric bootstrap scenarios are given in Appendix J (total costs), K (MSVT costs) and L (HLP costs).

Table 19 Standard deviations of the average costs of the treatment of the pressure ulcer.

Pressure ulcer	SD Population	SD Scenario I	SD Scenario II	SD Scenario III	SD Scenario IV
Total costs	€ 1,760.67	€ 537.61	€ 670.47	€ 325.86	€ 318.11
MSVT costs	€ 1,351.44	€ 429.73	€ 510.52	€ 250.64	€ 211.68
HLP costs	€ 478.46	€ 140.30	€ 180.00	€ 87.46	€ 104.70

Table 19 shows the SDs of the average costs based on the means of the bootstrap samples of the pressure ulcer. Also for this type of wound applies that the value of the SD becomes smaller for Scenario III, IV. The reduction of the SD can be explained by the resample means that are more centred on the cost average of the corresponding scenario. Figure 15 shows the different histograms of the total costs of all four scenarios into one figure. Scenario I, data 2 corresponds to Scenario II etc. We refer to detailed histograms of the distribution of the resample means of the average total costs to the respective Appendix J.

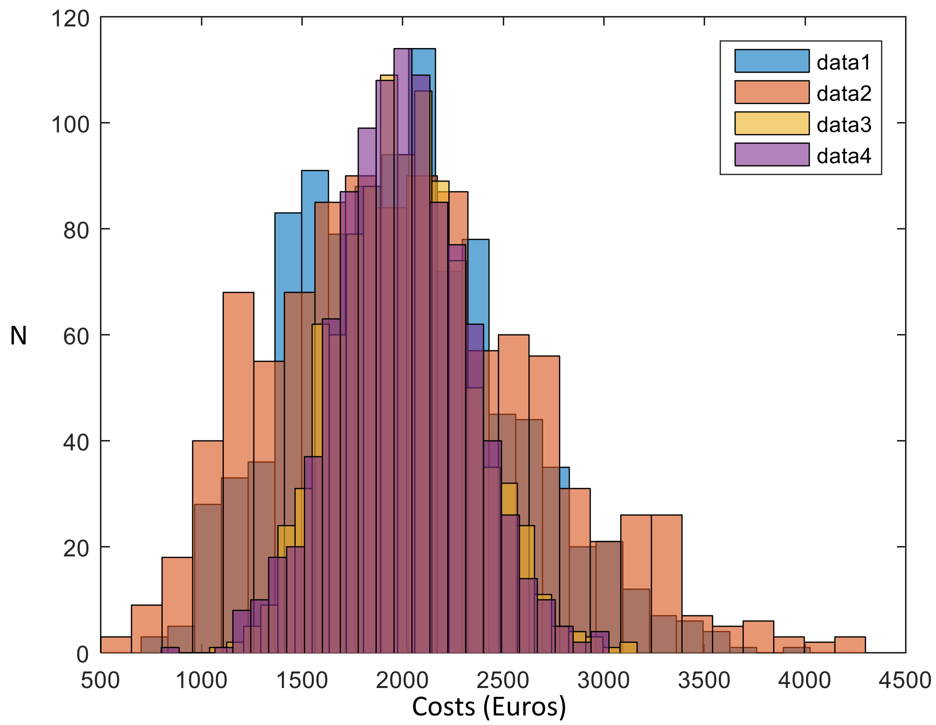

Figure 15 Histogram of the average total costs of treatment of the pressure ulcer (all scenarios).

Table 20 Average costs of the treatment of the pressure ulcer.

Pressure ulcer	Arithmetic mean costs population	Bootstrapped average costs Scenario I	Bootstrapped average costs Scenario II	Bootstrapped average costs Scenario III	Bootstrapped average costs Scenario IV
Total costs	€ 2,009.05	€ 1,993.18	€ 2,027.10	€ 2,010.83	€ 1.998,67
MSVT costs	€ 1,574.33	€ 1,570.96	€ 1,588.41	€ 1,569.02	€ 1.455,29
HLP costs	€ 434.72	€ 436.07	€ 442.76	€ 433.67	€ 532,09

An overview of the average costs based on the resample means is given in Table 20. Some fluctuations between the averages costs using different scenarios are seen. The bootstrapped average MSVT and HLP costs calculated using Scenario IV are located relatively far from the calculated averages of the other scenarios. Probably the first resample of these calculations consisted of the observations of patients whose treatments were relatively more expensive that those of the other patients. Table 21 shows for each bootstrap scenario the 95%-CI based on the 1000 bootstrap sample means.

Table 21 95% Confidence intervals of the average costs of the treatment of the pressure ulcer.

Pressure ulcer	95%-CI Scenario I	95%-CI Scenario II	95%-CI Scenario III	95%-CI Scenario IV
Total costs	(1,059.95-3,125.99)	(948.40-2,093.84)	(1,243.18-1,775.88)	(1,355.04-2,640.23)
MSVT costs	(792.22-2,474.71)	(738.10-1,599.91)	(932.79-1,371.21)	(1.048.66-1,873.34)
HLP costs	(175.20-726.80)	(160.62-629.09)	(257.07-483.99)	(338.72-744.64)

4.5 Surgical wound

We obtained cost data of 55 patients who all received wound care for their surgical wound at the KCWC. The total costs vary between € 86.39 and € 7,707.38, with an arithmetic mean of € 1,476.52. The variation in minimum and maximum MSVT costs is respectively between € 33.60 and € 6,195.48, with an arithmetic mean of € 1,150.90. The costs for medical HLP used during home care range from € 6.20 to € 1,809.02, with an arithmetic mean of € 325.62. The total costs of the most expensive patient are € 7,707.38, and the maximum MSVT costs also belong to this patient. The highest expenses on medical HLP belong to another patient, who also received many hours of MSVT.

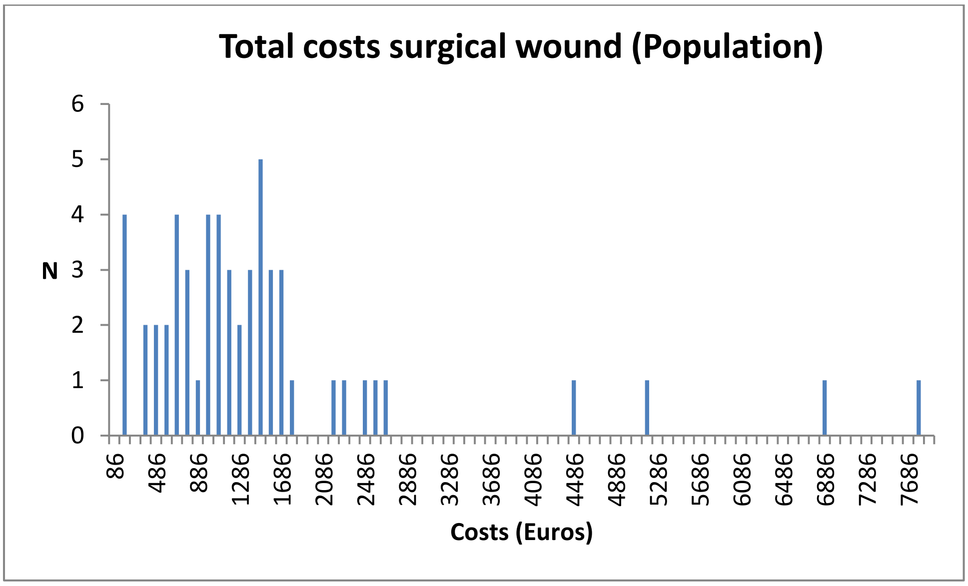

Figure 16 Histogram of the total costs of the treatment of the surgical wound (Population).

Figure 17 Histogram of the average total costs of treatment of the surgical wound (Scenario IV).

Figure 16 shows the dispersion of total costs of the surgical wound population. This histogram shows significant expensive wound treatments for four different patients. These total costs have a big impact on the outcome of the calculated arithmetic mean. Figure 17 displays the dispersion of the 1000 resample means of the average total costs of treatment using Scenario IV. Less variation is seen between the bootstrap sample means. Again, the dispersion of these means tends to the Normal distribution. We refer for detailed histograms to the respective Appendixes M (total costs), N (MSVT costs) and O (HLP costs).

Table 22 Standard deviations of the average costs of the treatment of the surgical wound.

Surgical wound	SD Population	SD Scenario I	SD Scenario II	SD Scenario III	SD Scenario IV
Total costs	€ 1,451.68	€ 456.21	€ 377.62	€ 186.39	€ 191.92
MSVT costs	€ 1,183.43	€ 363.18	€ 319.90	€ 158.55	€ 174.90
HLP costs	€ 367.04	€ 110.01	€ 97.89	€ 49.98	€ 44.60

Table 22 shows the SDs of the average costs based on the bootstrap sample means using the different scenarios. The value of this statistical parameter becomes smaller as the number of observations in a bootstrap sample increases. So in that case, the more expensive observations have less influence on the calculated average costs. Figure 18 combines the four histograms of the average total costs into one figure. This creates a clear overview of the differences in dispersion of the average resample means

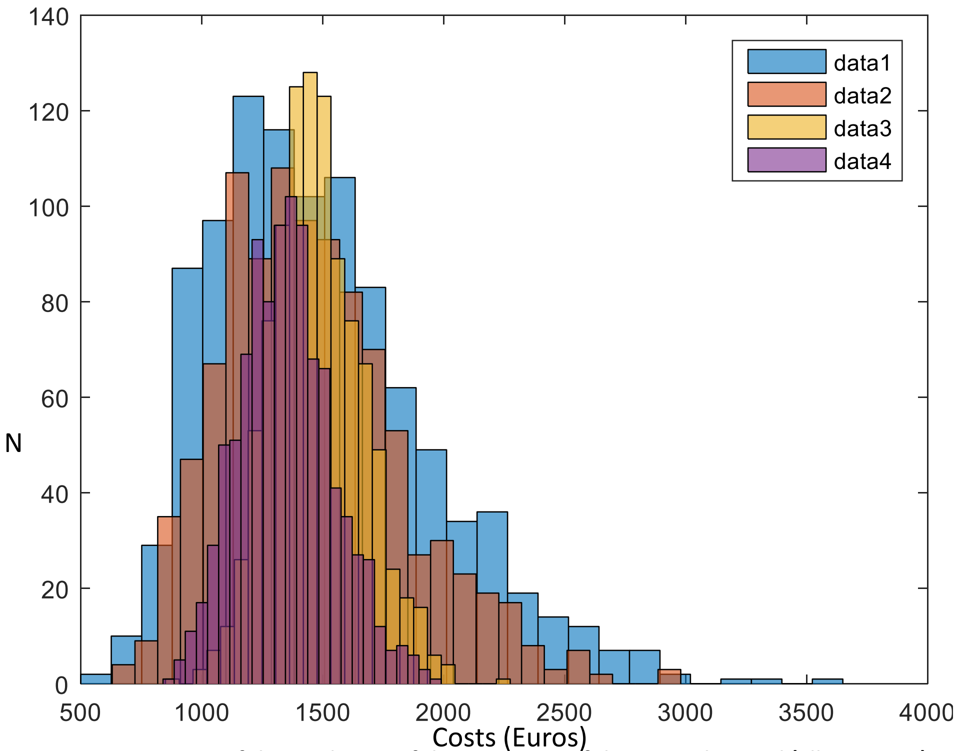

Figure 18 Histogram of the total costs of the treatment of the surgical wound (all scenarios).

Table 23 Average costs of the treatment of the surgical wound.

Surgical wound	Arithmetic mean costs population	Bootstrapped average costs Scenario I	Bootstrapped average costs Scenario II	Bootstrapped average costs Scenario III	Bootstrapped average costs Scenario IV
Total costs	€ 1,476.52	€ 1,494.59	€ 1,459.52	€ 1,477.26	€ 1.350,96
MSVT costs	€ 1,150.90	€ 1,138.06	€ 1,162.21	€ 1,145.05	€ 1.091,32
HLP costs	€ 325.62	€ 324.55	€ 328.85	€ 324.01	€ 298,52

An overview of the average costs of the surgical ulcer for the three different cost categories is given in Table 23. We see that the MSVT costs are approximately three times more expensive than the costs for medical HLP used during home care. This was also visible in the previous type of wounds. The 95%-CIs estimated using the percentile method are given in Table 24. These CI are based on the means of all 1000 resamples within a scenario. This table shows that these intervals are larger Scenario I and II. This also corresponds to the corresponding higher values of the variance and the SDs.

Table 24 95% Confidence intervals of the average costs of the treatment of the surgical wound.

Surgical wound	95%-CI Scenario I	95%-CI Scenario II	95%-CI Scenario III	95%-CI Scenario IV
Total costs	(812.93-2,576.37)	(859.58-2,301.65)	(1,136.41-1,883.15)	(1,004.04-1.763.54)
MSVT costs	(611.06-1,942.61)	(667.66-1,931.12)	(868.99-1,480.39)	(786.49-1,466.41)
HLP costs	(155.33-571.87)	(175.12-540.32)	(230.58-430.50)	(223.68-394.59)

4.6 Traumatic ulcer

The population of the traumatic ulcer consists of 53 patients who all received wound treatment at the KCWC at the Isala clinics. The minimum and maximum total costs are respectively € 228.99 and € 9,982.95, with an arithmetic mean of € 1,961.35. The MSVT costs vary between € 33.60 and € 7,308.84, and their arithmetic mean is estimated at € 1,385.18. The range of the HLP costs lies between the € 60.31 and € 3,983.43, and the arithmetic mean is respectively € 576.17.

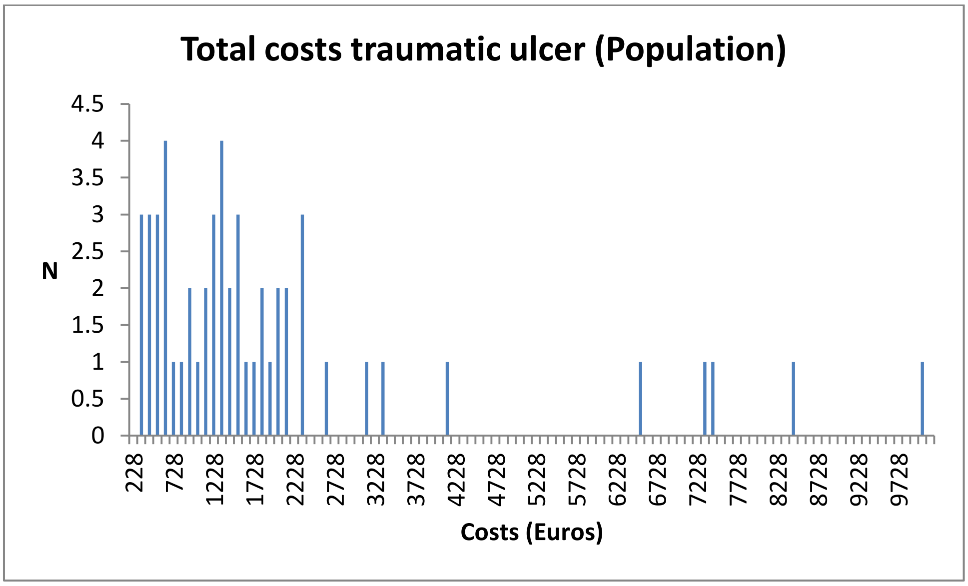

Figure 19 Histogram of the total costs of the treatment of the traumatic ulcer (Population).

Figure 19 shows the histogram based on the total costs of the population. These observations are distributed between a big interval of the minimum and maximum total costs. In Figure 20 we display the dispersion of the resample means of the total costs of treatment using non-parametric bootstrap Scenario IV. These resample means are more centred on the average total costs of this scenario, and less high expensive cost outliers are observed. The other histograms of the average total costs obtained by using the non-parametric bootstrap scenarios are given in Appendix P (total costs), Q (MSVT costs) and R (HLP costs).

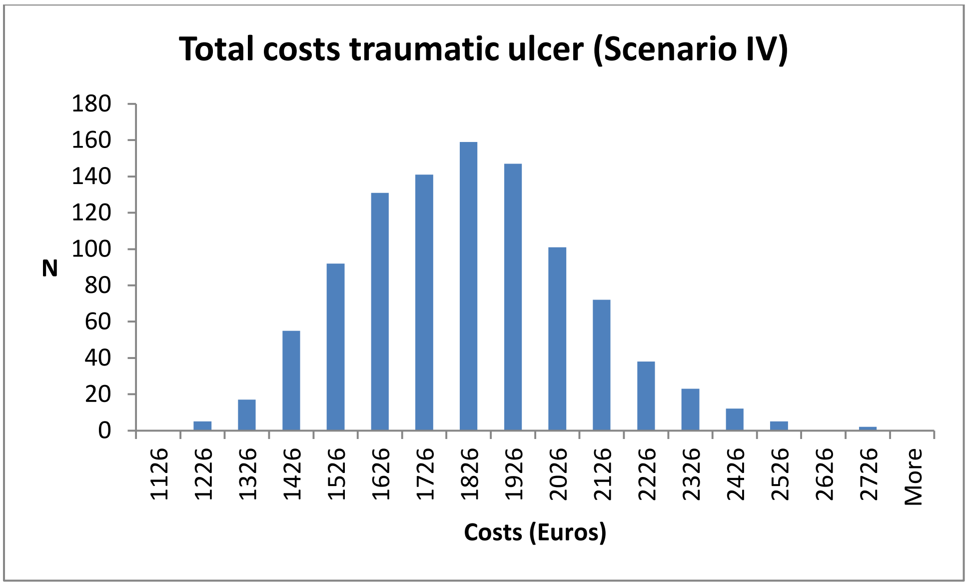

Figure 20 Histogram of the average total costs of treatment of the traumatic ulcer (Scenario IV).

Table 25 Standard deviations of the average costs of the treatment of the traumatic ulcer.

Traumatic ulcer	SD Population	SD Scenario I	SD Scenario II	SD Scenario III	SD Scenario IV
Total costs	€ 2,108.46	€ 615.38	€ 576.97	€ 285.86	€ 247.87
MSVT costs	€ 1,638.50	€ 513.01	€ 448.50	€ 225.67	€ 249.31
HLP costs	€ 693.74	€ 215.64	€ 203.23	€ 96.47	€ 98.39

Table 25 shows the SDs of the average costs based on the bootstrap means. A large difference is observed between the SD of the population, and the SD of the different scenarios. The change in dispersion of the resample means between the different non-parametric bootstrap scenarios is well shown in Figure 21. Shown in this figure, data 1 corresponds to the histogram that is based on the results of the calculations of Scenario I etc.

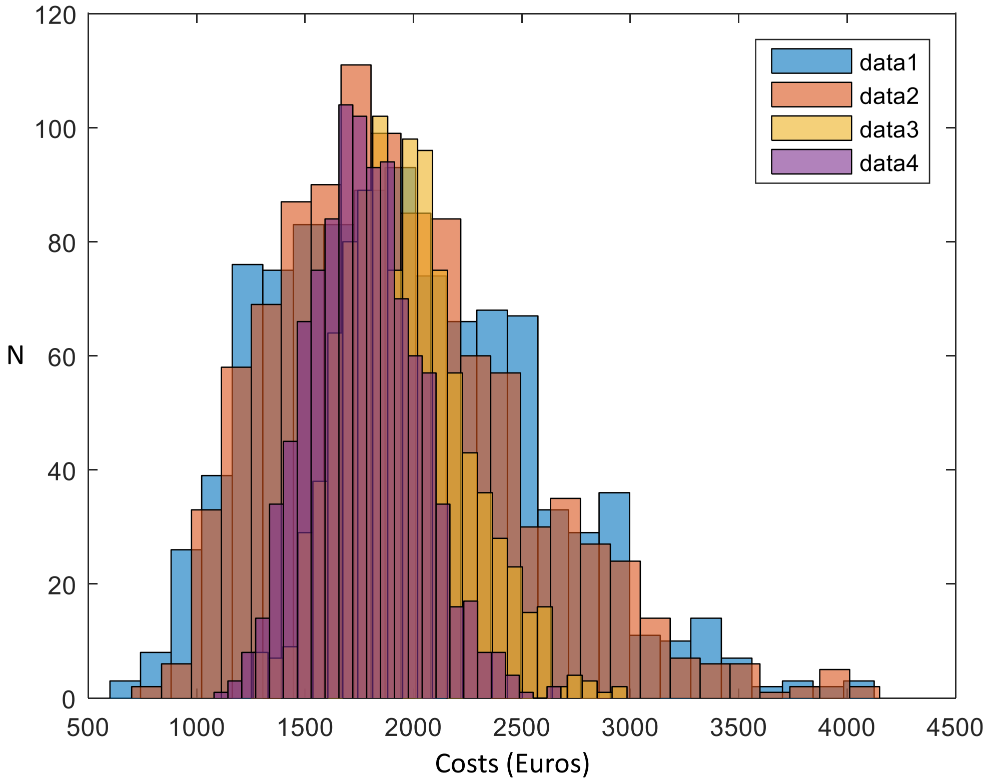

Figure 21 Histogram of the average total costs of treatment of traumatic ulcer (all scenarios).

Table 26 Average costs of the treatment of the traumatic ulcer.

Traumatic ulcer	Arithmetic mean costs population	Bootstrapped average costs Scenario I	Bootstrapped average costs Scenario II	Bootstrapped average costs Scenario III	Bootstrapped average costs Scenario IV
Total costs	€ 1,961.35	€ 1,955.36	€ 1,943.17	€ 1,961.32	€ 1.771,09
MSVT costs	€ 1,385.18	€ 1,398.89	€ 1,391.49	€ 1,374.29	€ 1.390,96
HLP costs	€ 576.17	€ 582.33	€ 573.35	€ 579.15	€ 535,86

Table 26 shows the average costs of the treatment of the traumatic ulcer based on the resample means. The bootstrapped average total and HLP costs calculated using Scenario IV are located relatively far from the calculated averages of the other scenarios. Scenario IV is the only scenario where the population of the bootstrap sample depends on the previous sample populations. So, the change of higher average costs is somewhat higher if the first resample population consists of patients whose treatments were relatively expensive. Probably the first resample of these calculations consisted of the observations of patients whose treatments were relatively more expensive that those of the other patients. Table 27 shows for each bootstrap scenario the 95%- CIs, based on the means of all 1000 replications. The intervals of the CIs are bigger for the first two scenarios compared to Scenario III and IV. This also corresponds to the higher values of the SD.

Table 27 95% Confidence intervals of the average costs of the treatment of the traumatic ulcer.

Traumatic ulcer	95%-CI Scenario I	95%-CI Scenario II	95%-CI Scenario III	95%-CI Scenario IV
Total costs	(953.05-2,346.99)	(1,041.65-3,285.65)	(1,474.56-2,583.31)	(1.332-70-2,283.96)
MSVT costs	(625.59-2,565.39)	(652.13-2,367.53)	(951.48-1,839.46)	(954.07-1,927.93)
HLP costs	(269.47-1,069.42)	(295.79-1,053.48)	(411.55-782.92)	(364.92-749.95)

4.7 Venous ulcer

We analysed cost data of 22 patients who received wound care for their venous ulcer at the KCWC in Zwolle. The total costs vary between € 435.63 and € 13,839.13, and the arithmetic mean is calculated at € 2,592.27. The interval of the minimum and maximum MSVT costs lies between the € 268.80 and € 8,938.80, with € 1,539.59 as the arithmetic mean. The costs of medical HLP used during home care vary between the € 66.04 and € 5,054.42, and the arithmetic mean is estimated at € 1,052.68. Noteworthy, one patient received 133 hours MSVT, which is approximately three times more than the subsequent patient who received many MSVT.

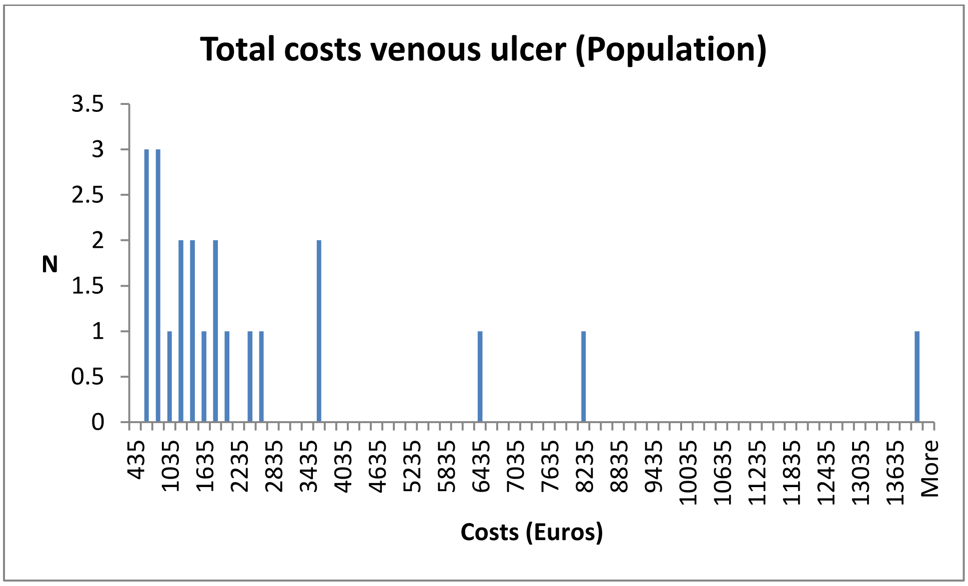

Figure 22 Histogram of the total costs of the treatment of the venous ulcer (Population).

Figure 22 shows the dispersion of the total costs of the venous ulcer population. Noticeable, there are three outliers whose treatment cost more € 5,000. Figure 23 displays the dispersion of resample means of the total costs using the non-parametric bootstrap method Scenario IV. The variance in dispersion of the calculated bootstrap sample means is smaller compared to Figure 22. Besides, this distribution obtained a clear frequency peak and tends towards the Normal distribution. We refer for detailed histograms of the others scenarios to the respective Appendixes S (total costs), T (MSVT costs) and U (HLP costs).

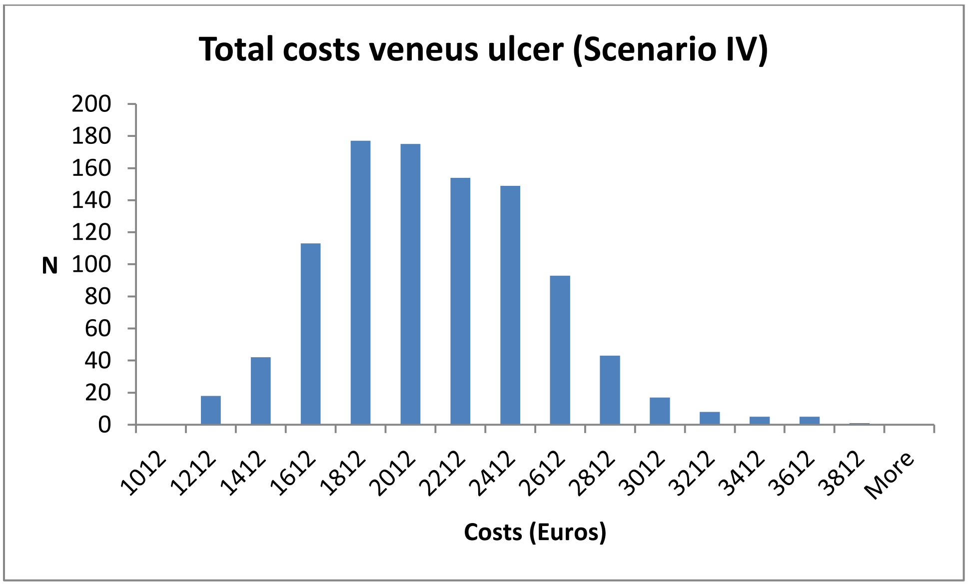

Figure 23 Histogram of the average total costs of treatment of the venous ulcer (Scenario IV).

Table 28 Standard deviations of the average costs of the treatment of the venous ulcer.

Venous ulcer	SD Population	SD Scenario I	SD Scenario II	SD Scenario III	SD Scenario IV
Total costs	€ 3,091.21	€ 905.55	€ 1,271.78	€ 698.02	€ 430.91
MSVT costs	€ 1,902.65	€ 555.24	€ 779.22	€ 392.11	€ 488.07
HLP costs	€ 1,393.71	€ 414.29	€ 533.70	€ 290.19	€ 290.18

Table 28 shows the SDs of the average costs based on the resample means. For this type of wound also applies that the value of the SD becomes smaller for the different bootstrap scenarios compared to the SD of the population. Figure 24 displays an overview of the histograms of the average total costs calculated using the different scenarios. The change in dispersion of these values is clearly visible.

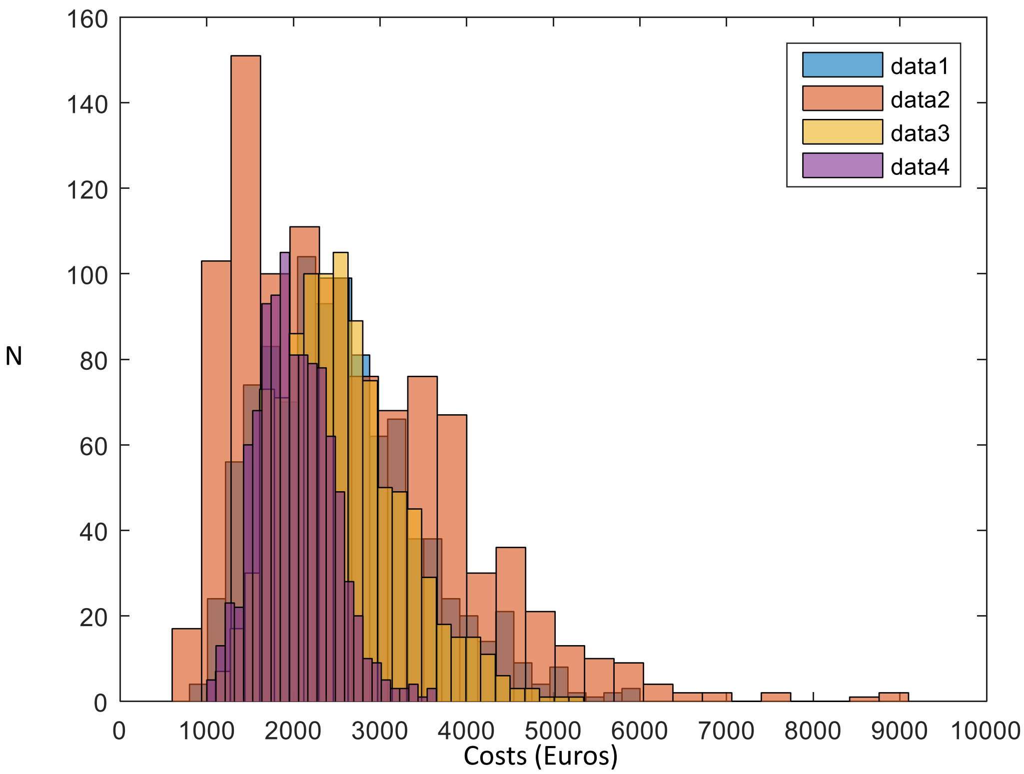

Figure 24 Histogram of the average total costs of treatment of the venous ulcer (all scenarios).

Table 29 Average costs of the treatment of the venous ulcer.

Venous ulcer	Arithmetic mean costs population	Bootstrapped average costs Scenario I	Bootstrapped average costs Scenario II	Bootstrapped average costs Scenario III	Bootstrapped average costs Scenario IV
Total costs	€ 2,592.27	€ 2,555.19	€ 2,617.41	€ 2,563.57	€ 2.015,51
MSVT costs	€ 1,539.59	€ 1,551.59	€ 1,543.36	€ 1,552.77	€ 1.598,83
HLP costs	€ 1,052.68	€ 1,054.07	€ 1,011.86	€ 1,056.65	€ 1.112,51

An overview of the average costs of treatment of the venous ulcer is given in Table 29. We see that the MSVT costs are approximately three times more expensive than the costs of medical HLP used during home care. This was also noticed in the estimated average costs of previous discussed different types of chronic wounds. Besides, we also noticed that the average costs calculated using Scenario IV are less close to the average costs calculated using the other scenarios. This can be explained by the design of this scenario. The population of the first bootstrap sample is relatively decisive for the calculated averages. Table 30 shows for each bootstrap scenario the 95%-CIs based on the means of all 1000 resamples.

Table 30 95% Confidence interval of the average costs of the treatment of venous ulcer.

Venous ulcer	95%-CI Scenario I	95%-CI Scenario II	95%-CI Scenario III	95%-CI Scenario IV
Total costs	(1,173.59-4,704.66)	(982.69-5,641.21)	(1,456.60-4,165.59)	(1,261-10-2,960.30)
MSVT costs	(705.77-2,856.42)	(527.78-3,559.36)	(880.57-2,384.99)	(908.16-2,721.67)
HLP costs	(414.21-1,981.30)	(289.27-2,259.64)	(502.16-1,694.37)	(589.98-1,741.19)

4.8 Comparison of the average total costs

We calculated the total costs (the sum of the MSVT and HLP costs) of each patient of the population of the corresponding type of wound, before performing the non-parametric bootstrap method. Small differences between the bootstrapped total costs, and the sum of the bootstrapped MSVT and HLP costs are noticed. Table 31 shows the bootstrapped average total costs, and the sum of the bootstrapped average MSVT and HLP costs of the diabetic mellitus ulcer. Similarly, Table 32 shows these results of the venous ulcer. We choose these two type of wounds since the venous ulcer has the smallest population, and the diabetic mellitus ulcer the largest. Between the first three scenarios the differences in average costs are very small. However, this difference becomes larger using the results obtained by the non-parametric bootstrap method Scenario IV. As explained in Section 3.3, you draw with replacement observations from a group that consists of the population of the corresponding type of wound plus the sample populations from the previous bootstrap samples. Therefore, the formation of the sample population of the first resample has a large impact on the composition of the sample populations of the following bootstrap samples. So using this scenario, it is logical that larger differences occur between the sum of the bootstrapped average MSVT and HLP costs, and the bootstrapped average total costs. In particular, this becomes larger if the population of the corresponding type of wound consists of more patients. This presumption corresponds to our results, shown in Table 31 and Table 32.

Table 31 Comparison of the bootstrapped average total costs of treatment of diabetic mellitus ulcers.

Diabetic mellitus ulcer	**Scenario I**	**Scenario II**	**Scenario III**	**Scenario IV**
Bootstrapped MSVT costs	€ 1,194.80	€ 1,204.37	€ 1,196.09	€ 1,275.78
Bootstrapped HLP costs	€ 468.74	€ 450.53	€ 454.34	€ 377.57
Sum Bootstrapped MSVT and HLP costs	€ 1,663.54	€ 1,654.90	€ 1,650.43	€ 1,653.35
Bootstrapped average total costs	€ 1,676.22	€ 1,638.48	€ 1,658.51	€ 1,702.06

Table 32 Comparison of the bootstrapped average total costs of treatment of venous ulcers.

Venous ulcer	**Scenario I**	**Scenario II**	**Scenario III**	**Scenario IV**
Bootstrapped MSVT costs	€ 1,551.59	€ 1,543.36	€ 1,552.77	€ 1,598.83
Bootstrapped HLP costs	€ 1,054.07	€ 1,011.86	€ 1,056.65	€ 1,112.51
Sum Bootstrapped MSVT and HLP costs	€ 2,605.66	€ 2,555.22	€ 2,609.42	€ 2,711.34
Bootstrapped average total costs	€ 2,555.19	€ 2,617.41	€ 2,563.57	€ 2,015.51

Conclusions and recommendations

5. Conclusion and recommendations

The aim of this research is to estimate the average costs of medical aids [Hulpmiddelen (HLP)] used during home care, the average costs associated to specialized medical home care [Medisch Specialistische Verpleging in de Thuissituatie (MSVT)], and the total costs of treatment for the most common types of chronic wounds. In Section 1 we introduced our research and defined nine research questions. Each question has been answered in one of our sections. Combining the answers to our research questions would fulfil our research aim. The answers on research questions that we obtained by conducting a literature research are given in Section 2. Section 3 described the method that is used for our research. Section 4 shows our results of the non-parametric bootstrap method. In Section 5 we provide conclusions, limitations and recommendations. Section 5.1 provides the answer of the main research question. In Section 5.2 we discuss the study limitations and in Section 5.3 we define recommendations based on the conclusion and discussion. In Section 5.4 we give directions for further research.

5.1 Conclusion

Chronic wound care involves enormous costs caused by the time-consuming and complex process of care, delay in hospital discharge, complications, long-term commitment of health care professionals, and high costs of medical devices and aids. Therefore, the implementation of cost-efficient wound care is of great significance in the Netherlands. The Dutch government, health insurances, and the management of wound expertise centres (WECs) and hospitals are aware of the importance of this implementation. However, when we started this research the average costs of the treatment of chronic wounds were not known of patients who received wound care at the WEC at the Isala clinics in Zwolle. The objective of our research is as follows:

'To determine the average total costs of treatment for patients who received wound treatment at the Wound Expertise Centre at the Isala clinics in Zwolle'.

Nine research questions give direction to our research. We review the literature to gain more knowledge about the wound healing process (1), the definition of a chronic wound (2), the prevalence (3) and the current organization of wound care in the Netherlands (4), the estimated average costs regarding these treatments (5), results and conclusions of previously conducted cost analyses (6), and about the organization of care at the WEC in the Isala clinics in Zwolle (7). We designed four different scenarios the implementation of the non-parametric bootstrap method. The results obtained using this method gave the estimations of the MSVT (8) and HLP costs (9). The conclusion in this section provides the answer on the main research question.

We succeed in the estimation of the average MSVT and HLP costs of treatment of chronic wounds. Table 33 shows the average MSVT costs, ranked from the most to the least expensive treatment. However, the results depends on the bootstrap scenario that is used. The most costly wound in terms of MSVT costs is the arterial ulcer (averages range from € 1.608,54 (Scenario IV) to € 1,976.65 (Scenario I). Followed by the pressure ulcer (averages range from € 1.455,29 (Scenario IV) to € 1,588.41 (Scenario II) and the venous ulcer (averages range from € 1,543.36 (Scenario II) to € 1.598,83 (Scenario IV).

Table 33 Overview of the average MSVT costs of the treatment of chronic wounds.

Type of wound (n)	Arithmetic mean costs population	Bootstrapped average costs Scenario I	Bootstrapped average costs Scenario II	Bootstrapped average costs Scenario III	Bootstrapped average costs Scenario IV
Arterial ulcer (33)	€ 1,919.66	€ 1,976.65	€ 1,912.22	€ 1,925.74	€ 1,608.54
Pressure ulcer (29)	€ 1,574.33	€ 1,570.96	€ 1,588.41	€ 1,569.02	€ 1,455.29
Venous ulcer (22)	€ 1,539.59	€ 1,551.59	€ 1,543.36	€ 1,552.77	€ 1,598.83
Traumatic ulcer (53)	€ 1,385.18	€ 1,398.89	€ 1,391.49	€ 1,374.29	€ 1,390.96
Diabetic mellitus ulcer (65)	€ 1,195.93	€ 1,194.80	€ 1,204.37	€ 1,196.09	€ 1,275.78
Surgical wound (55)	€ 1,150.90	€ 1,138.06	€ 1,162.21	€ 1,145.05	€ 1,091.32
POWI ulcer (47)	€ 1,142.56	€ 1,145.05	€ 1,133.59	€ 1,144.31	€ 1,190.41

Table 34 Overview of the average HLP costs of the treatment of complex wounds.

Type of wound (n)	Arithmetic mean costs population	Bootstrapped average costs Scenario I	Bootstrapped average costs Scenario II	Bootstrapped average costs Scenario III	Bootstrapped average costs Scenario IV
Venous ulcer (22)	€ 1,052.68	€ 1,054.07	€ 1,011.86	€ 1,056.65	€ 1,112.51
Arterial ulcer (33)	€ 611.40	€ 607.31	€ 622.07	€ 608.04	€ 696.61
Traumatic ulcer (53)	€ 576.17	€ 582.33	€ 573.35	€ 579.15	€ 535.86
Pressure ulcer (29)	€ 434.72	€ 436.07	€ 442.76	€ 433.67	€ 532.09
Diabetic mellitus ulcer (65)	€ 454.60	€ 468.74	€ 450.53	€ 454.34	€ 377.57
POWI ulcer (47)	€ 364.84	€ 363.54	€ 362.91	€ 363.87	€ 376.86
Surgical wound (55)	€ 325.62	€ 324.55	€ 328.85	€ 324.01	€ 298.52

Table 34 shows the results of the calculations of the average HLP costs based on the different scenarios used for the non-parametric bootstrap method, ranked from the most to the least expensive treatment. The highest average costs are expected with the treatment of the venous ulcer (averages vary between € 1,011.86 (Scenario I) and € 1,112.51 (Scenario IV)). The arterial ulcer is the subsequent wound that is the most expensive in terms of medical aids used during home care (averages vary between € 607.31 (Scenario I) to € 696.61 (Scenario IV)). Followed by the traumatic ulcer, whose averages vary between € 535.86 (Scenario IV) to € 582.33 (Scenario I).

Table 35 shows the average total costs for the most common types of chronic wounds, ranked from the most to the least expensive treatment. The most costly treatments in terms of the average total costs is that of venous ulcers, followed by the arterial and the pressure ulcers. The average costs of the venous ulcer range between € 2,015.51 (Scenario IV) to € 2,617.41 (Scenario II). The estimates vary between € 2,417.43 (Scenario IV) to € 2,561.84 (Scenario II) concerning the treatment of the arterial ulcer, and between € 1,993.18 (Scenario I) to € 2,027.10 (Scenario II) regarding wound care of the pressure ulcer. So in general, the treatment of the venous ulcer is the most expensive. This is in line with our expectations, because the healing duration is generally quite long for this type of wound. We expected less high average total costs of the treatment of the arterial ulcer. In general, the wound healing process is relatively fast. However, the research population consist of 33 patients with a considerable number of expensive costs outliers. So, these costs outliers had large impact on the calculations of the expected average costs. The diabetic mellitus population consisted of a mix between the diabetic neuropathic and the diabetic arterial ulcer. We expected the average costs regarding these treatment higher. However, this reduction in average costs might be caused by a referral of patients whose wound were not healed to a podiatrist in Zwolle. The costs of these referrals are not included in our research.

Table 35 Overview of the average total costs of the treatment of chronic wounds.

Type of wound (n)	Arithmetic mean costs population	Bootstrapped average costs Scenario I	Bootstrapped average costs Scenario II	Bootstrapped average costs Scenario III	Bootstrapped average costs Scenario IV
Venous ulcer (22)	€ 2,592.27	€ 2,555.19	€ 2,617.41	€ 2,563.57	€ 2,015.51
Arterial ulcer (33)	€ 2,531.07	€ 2,540.68	€ 2,561.84	€ 2,535.78	€ 2,417.43
Pressure ulcer (29)	€ 2,009.05	€ 1,993.18	€ 2,027.10	€ 2,010.83	€ 1,998.67
Traumatic ulcer (53)	€ 1,961.35	€ 1,955.36	€ 1,943.17	€ 1,961.32	€ 1,771.09
Diabetic mellitus ulcer (65)	€ 1,650.53	€ 1,676.22	€ 1,638.48	€ 1,658.51	€ 1,702.06
POWI ulcer (47)	€ 1,507.40	€ 1,505.20	€ 1,495.30	€ 1,511.17	€ 1,625.54
Surgical wound (55)	€ 1,476.52	€ 1,494.59	€ 1,459.52	€ 1,477.26	€ 1,350.96

5.2 Discussion

This study is a cost analysis of the costs of treatment of patients who received complex wound care at the WEC at the Isala clinics in Zwolle. In our analyses, we focus on the most common types of wounds (given in Table 8 in Section 3.1), thereby leaving out all remaining types. Although we have included costs data of all patients with one wound of these specific chronic wounds. We have not assessed whether this proportion is representative.

The main limitation of our research is the lack of enough empirical data to accurately estimate the costs of treatment of chronic wounds. We were not able to obtain more information of the costs of care of patients who received treatment at this WEC in Zwolle, or at other WECs in the Netherlands. The other WECs that also deliver MSVT did not want to cooperate in the exchange of costs data at this moment. Therefore, our calculated averages are based on small population sizes of the corresponding types of wound, which vary between the 22 and 65 patients. One of the assumptions of the non-parametric bootstrap method is that the sample distribution is an accurate reflection of the population distribution. Our research population is considerably small, but we assumed that the costs of wound care of these patients reflects the variety of all values. This assumption could be validated if more data were available. This lead us to the next discussion point. We set up four different scenarios for the implementation of the non-parametric bootstrap method. However, these scenarios are created by us and they are not based on the outcomes of the conducted literature search. Shown in Table 9 in Section 3.2, the sizes of the sample populations vary from small to large. The estimated outcomes of the statistics of interests are invalid if the distribution of these sample populations does not reflect the population distribution. This risk is increasing for the scenarios that use a small group of observations for each bootstrap sample.

Another limitation of our study is the use of the percentile method for the estimation of the confidence interval (CI). The 2.5^{th} and 97.5^{th} percentile values of the bootstrap distribution are used as the lower and upper bounds of the 95%-CIs. This method of calculation is known for its simplicity. As mentioned above, the calculation of valid CIs becomes more difficult for small sample populations. However, this percentile method does not take into account the bias and skewness of the distribution. So this might jeopardize the validity of our estimated CIs.

The random sampling method with replacement is used for the composition of the bootstrap samples. So in every resample population, it is possible that any observation of the population can be drawn once, more than once, or not at all. We did not perform a statistical test to consider whether the distributions of the samples reflect the population distributions. If a sample consists of many low or high costs outliers, then this affects the calculated average costs. So, this must be taken into account when interpreting our results.

A last remark is intended to the reproducibility of our results. We only executed one run of 1000 bootstrap samples of each scenario. The results of the calculated resample means of Scenario IV are to some extent depending on the composition of the sample population of the first bootstrap sample. So, the creation of 1000 new resamples generates other outcomes of our statistics of interests. When performing multiple runs, differences in average costs between runs will be larger for Scenario IV, compared to other bootstrap scenarios. For the first three scenarios applies that the sample population of each individual bootstrap sample does not depend on the composition of the first resample.

5.3 Recommendations

Perhaps the most important conclusion is, that large-scale measurements of the exact calculations of the total, MSVT and HLP costs are currently not possible due to lack of enough data. To allow the determination of the exact costs, gathering of more data should have the highest priority. The first step for the WEC at the Isala clinics in Zwolle is to collect more costs data of patient over the next years. The second step would be the collaboration between the various WECs, which also deliver MSVT, concerning the exchange of cost data. The availability of more information leads to a more accurate estimation regarding the costs of treatment. However, even with more available data we still recommend the use of the non-parametric bootstrap method. Even then it is useful to compare the bootstrap distributions to the empirical distribution of the data gathered.

We recommend performing significantly more runs of 1000 bootstrap samples of each non-parametric bootstrap scenario. In our research we run each scenario only once. As mentioned above, the reproducibility of the results of some of the scenarios is small. When performing more runs, the average costs of treatment can be determined based on the averages of each individual run.

Another recommendation is the implementation of the chi-squared test. This test checks whether the population distribution of the corresponding type of wound and the sample distribution of a created bootstrap sample fits. If the two distributions fit, then the composition of the sample population of the resample is approved. If not, then remove this sample and again draw by sampling with replacement a certain number of observations of the population. Using the chi-squared test avoids the inclusion of bootstrap sample populations that do not reflect the population. If you include the chi-squared test, the determination of the average costs of wound care will be more accurate.

A last recommendation is intended for the estimation of the 95%-CIs. We recommend the use of the bias-corrected and accelerated method. Haukoos & Lewis (2005) stated that this method calculates two different coefficients, namely the ‘bias correction’ and the ‘acceleration’ coefficient. The first coefficient adapts for the skewness in the bootstrap sampling distribution and the second one adjusts for the non-constant variances within the data of the bootstrap samples. So, this method involves adjustments to the two selected percentiles that serves as the lower and upper bound of the CIs. The ranges of the CIs would probably be more accurate by using this method instead of the percentile method.

5.4 Future research

For further research we recommend more research of the use of the non-parametric bootstrap method for costs calculations of treatments in health care settings. Especially, focus on the validity and accurately of results if bootstrapping is based on small population sizes. And we recommend literature research on the use of other statistical methods that are used for cost analyses of data with small population sizes.

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Appendix A: Total costs arterial ulcer

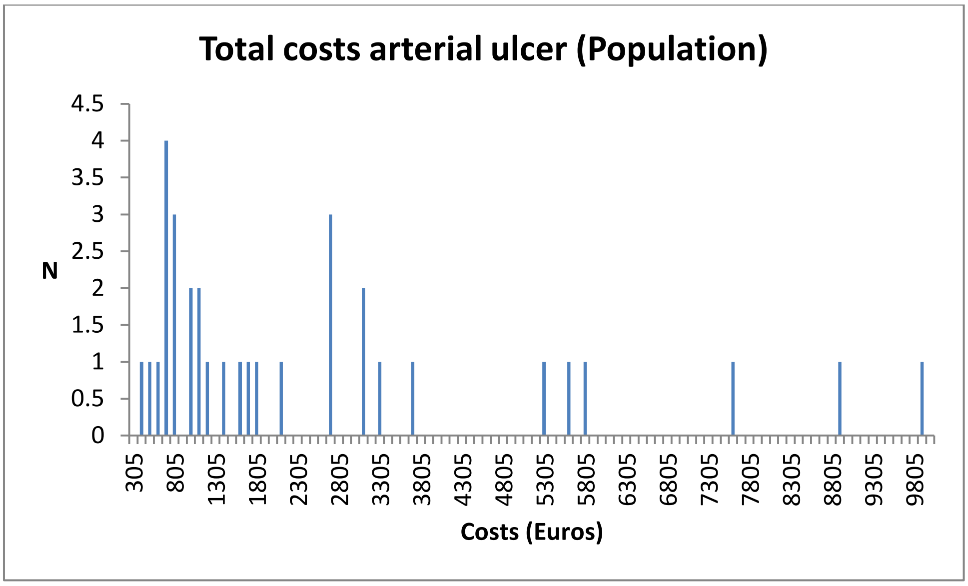

Figure 25 Histogram of total costs of the arterial ulcer (Population, n=33).

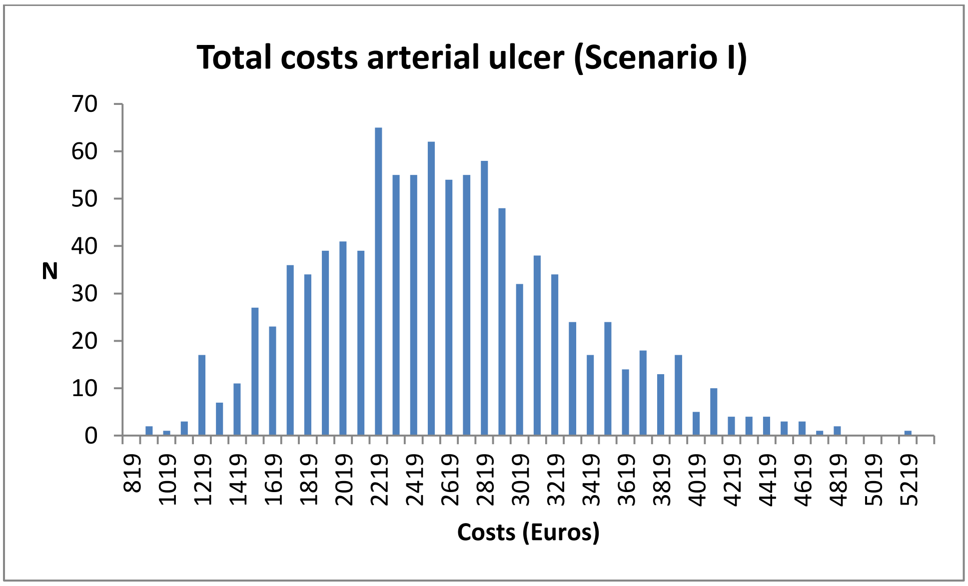

Figure 26 Histogram of the average total costs of the arterial ulcer (Scenario I, n=33).

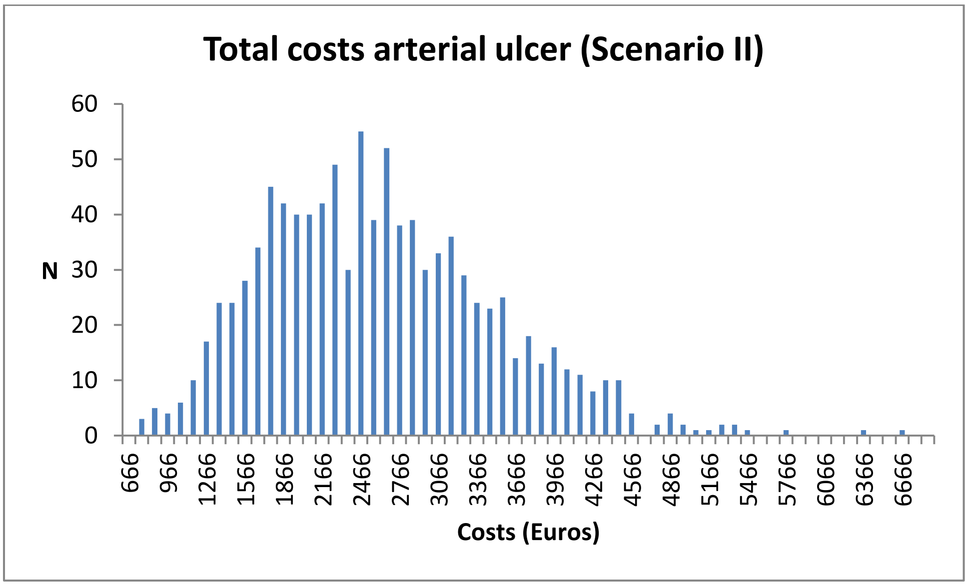

Figure 27 Histogram of the average total costs of the arterial ulcer (Scenario II, n=33).

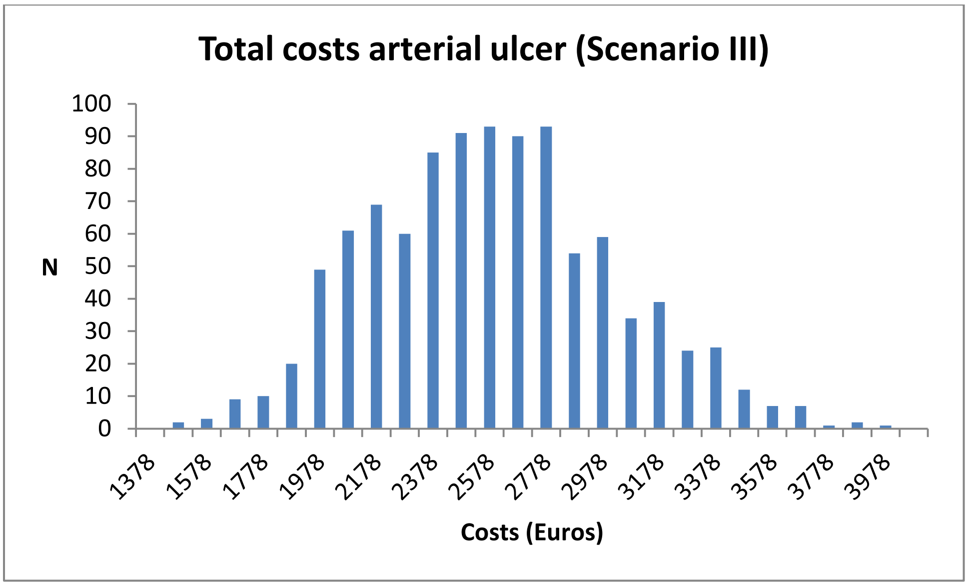

Figure 28 Histogram of the average total costs of the arterial ulcer (Scenario III, n=33).

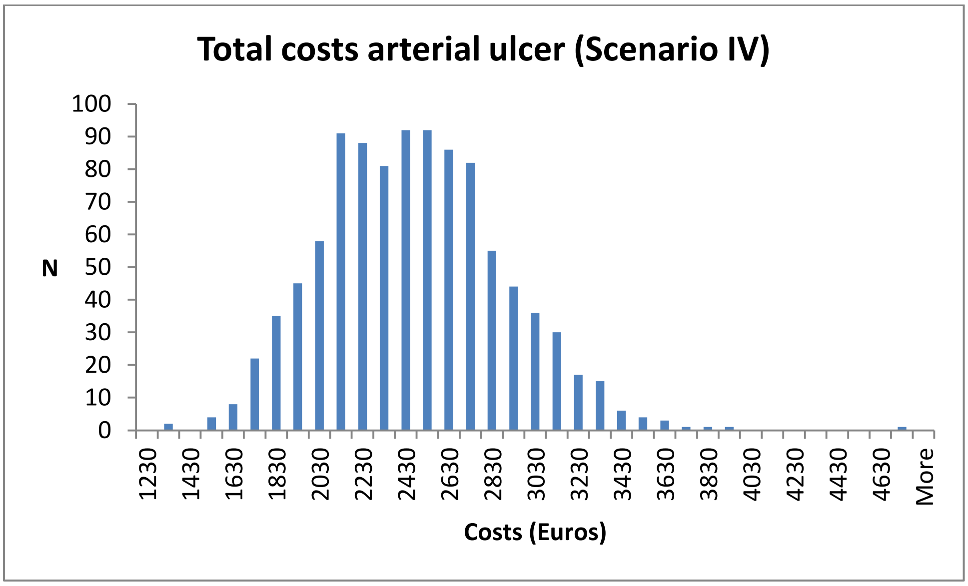

Figure 29 Histogram of the average total costs of the arterial ulcer (Scenario IV, n=33).

Appendix B: MSVT costs arterial ulcer

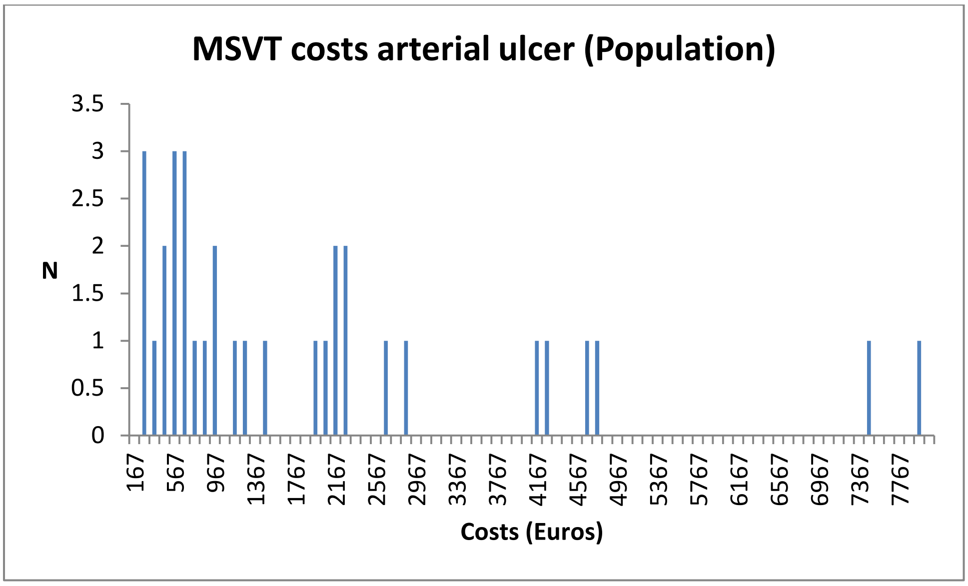

Figure 30 Histogram of the MSVT costs of the arterial ulcer (Population, n=33).

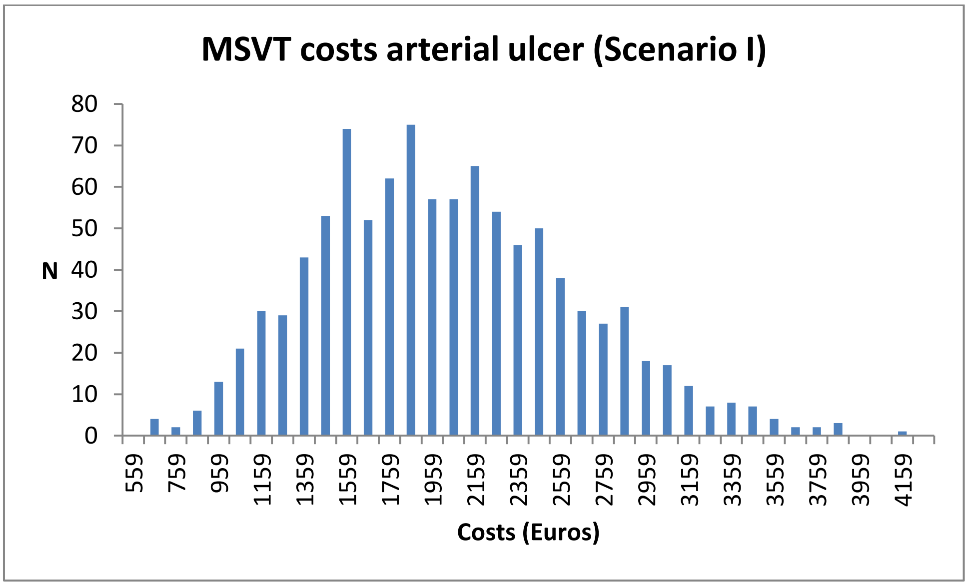

Figure 31 Histogram of the average MSVT costs of the arterial ulcer (Scenario I, n=33).

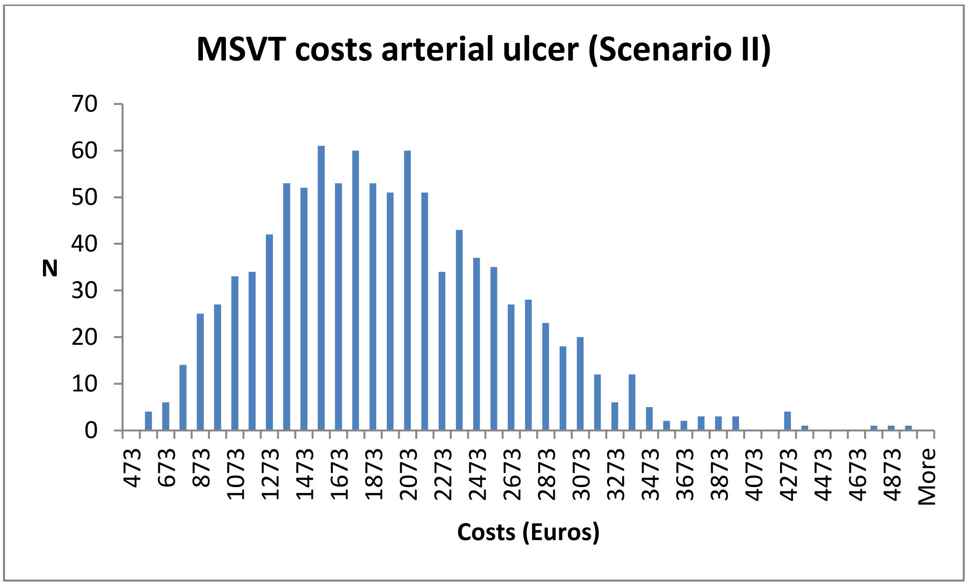

Figure 32 Histogram of the average MSVT costs of the arterial ulcer (Scenario II, n=33).

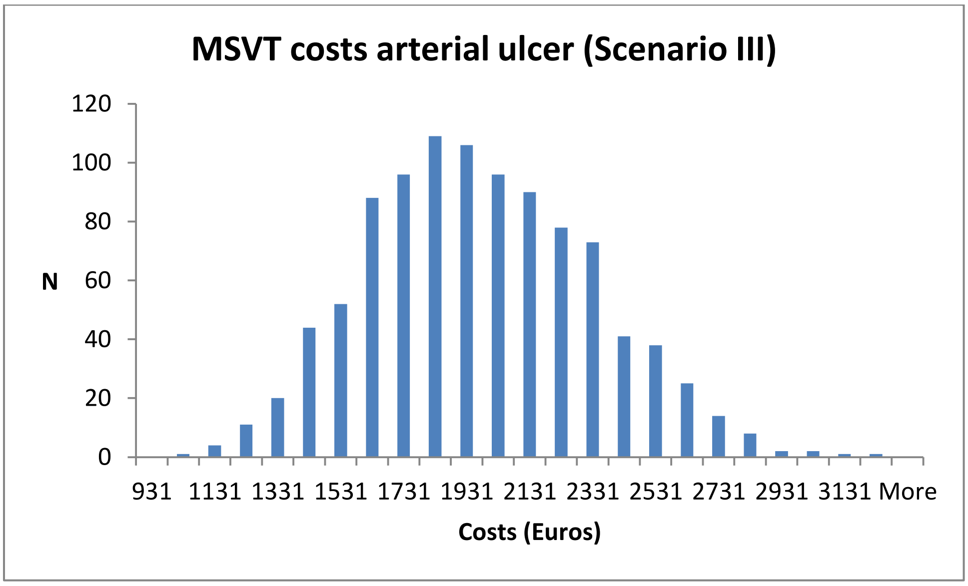

Figure 33 Histogram of the average MSVT costs of the arterial ulcer (Scenario III, n=33).

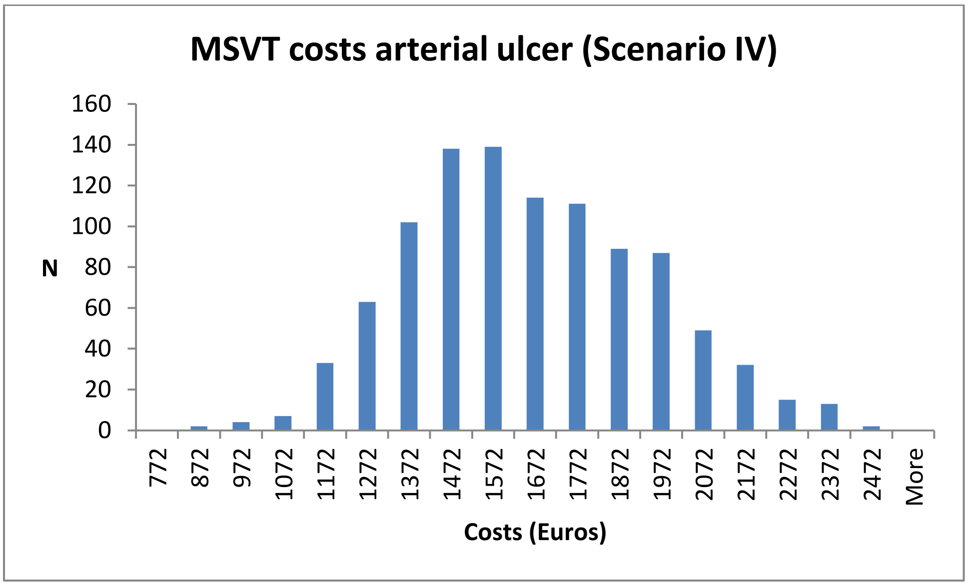

Figure 34 Histogram of the MSVT costs of the arterial ulcer (Scenario IV, n=33).

Appendix C: HLP costs arterial ulcer

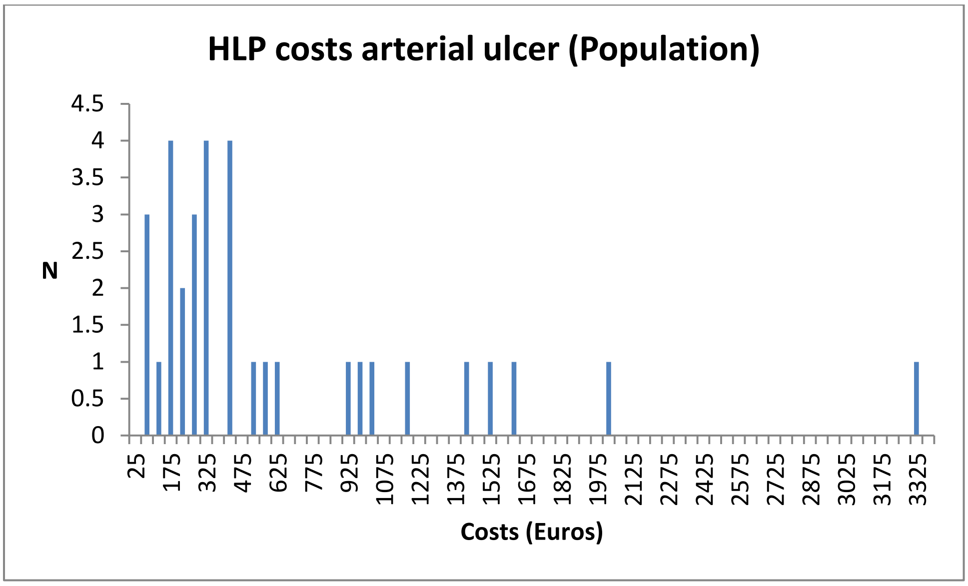

Figure 35 Histogram of the HLP costs of the arterial ulcer (Population, n=33).

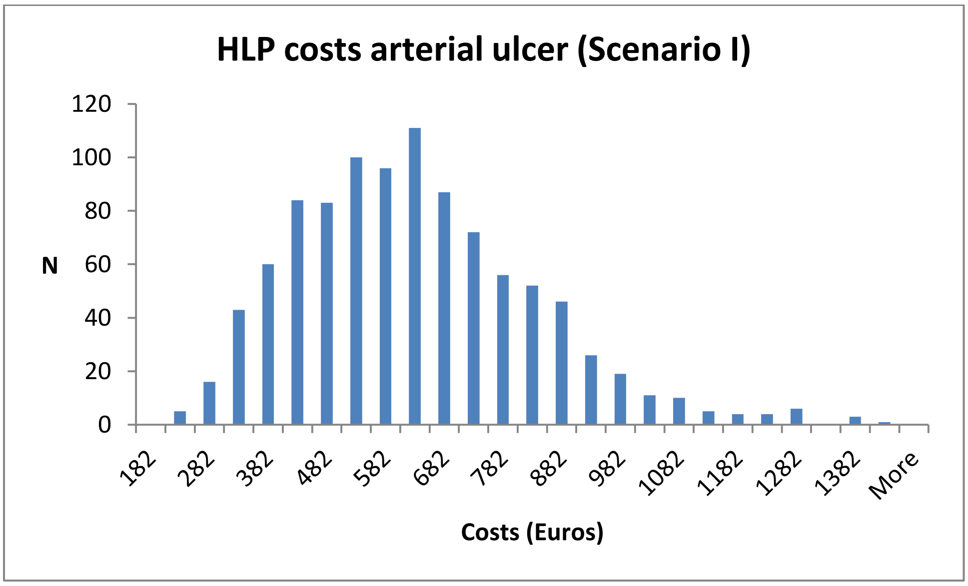

Figure 36 Histogram of the average HLP costs of the arterial ulcer (Scenario I, n=33).

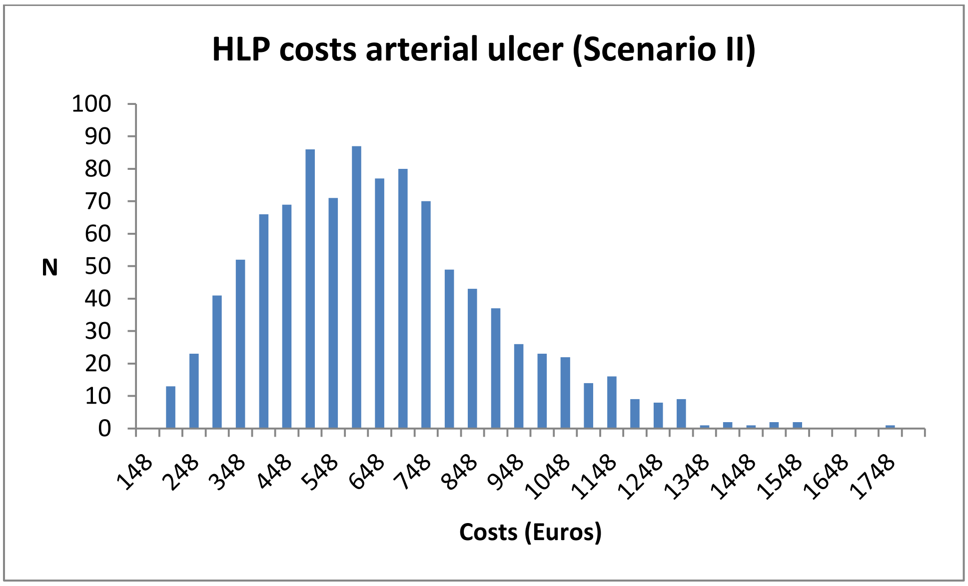

Figure 37 Histogram of the average HLP costs of the arterial ulcer (Scenario II, n=33).

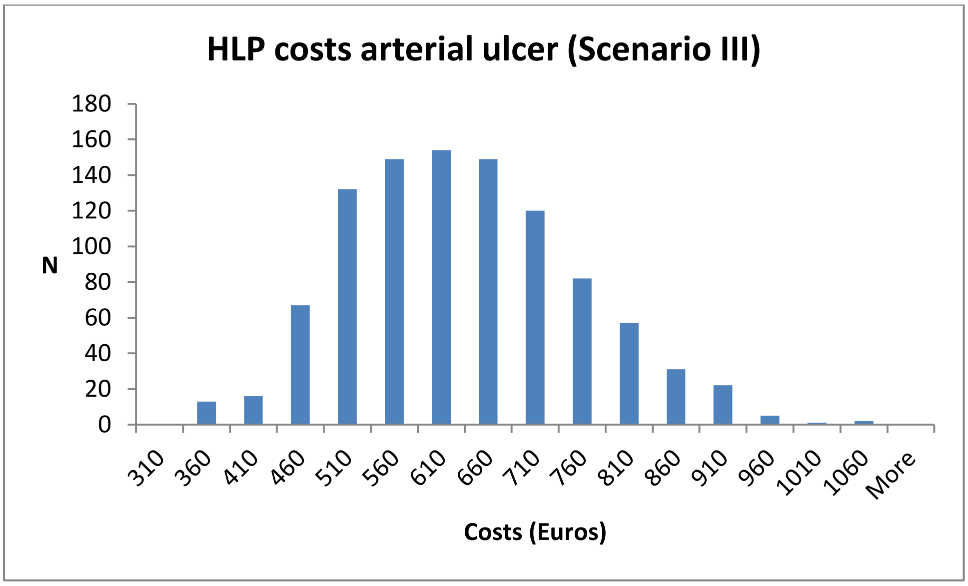

Figure 38 Histogram of the average HLP costs of the arterial ulcer (Scenario III, n=33).

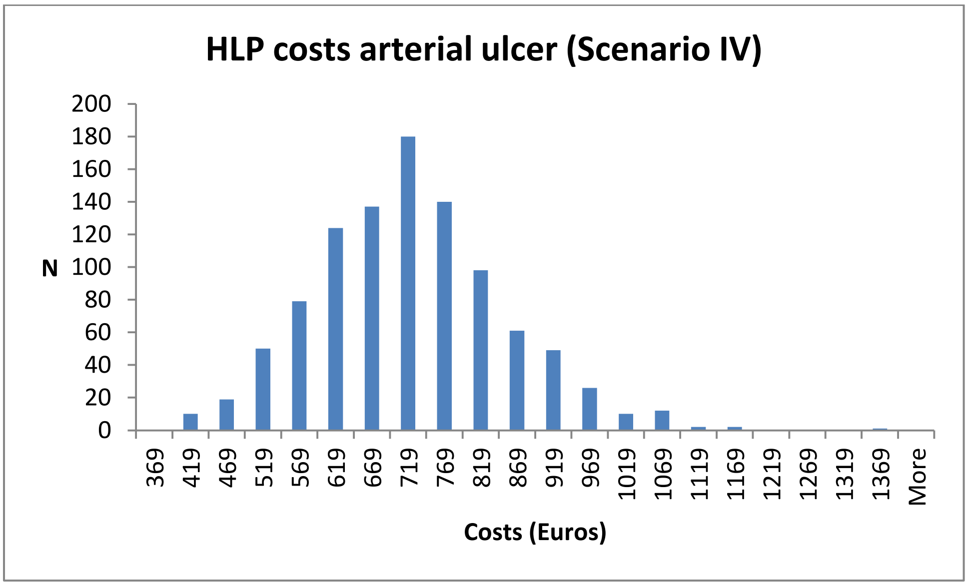

Figure 39 Histogram of the average HLP costs of the arterial ulcer (Scenario IV, n=33).

Appendix D: Total costs diabetic mellitus ulcer

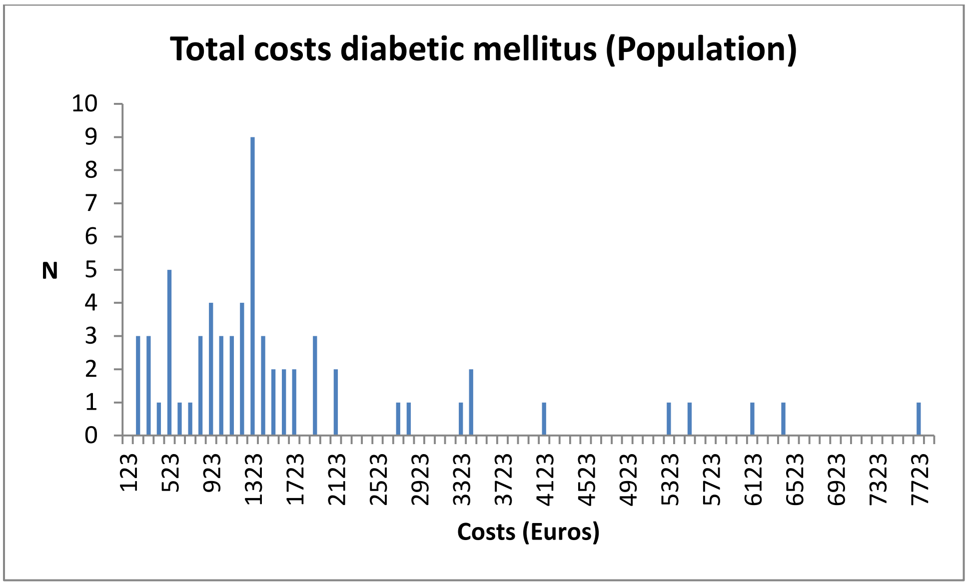

Figure 40 Histogram of the total costs of the diabetic mellitus ulcer (Population, n=65).

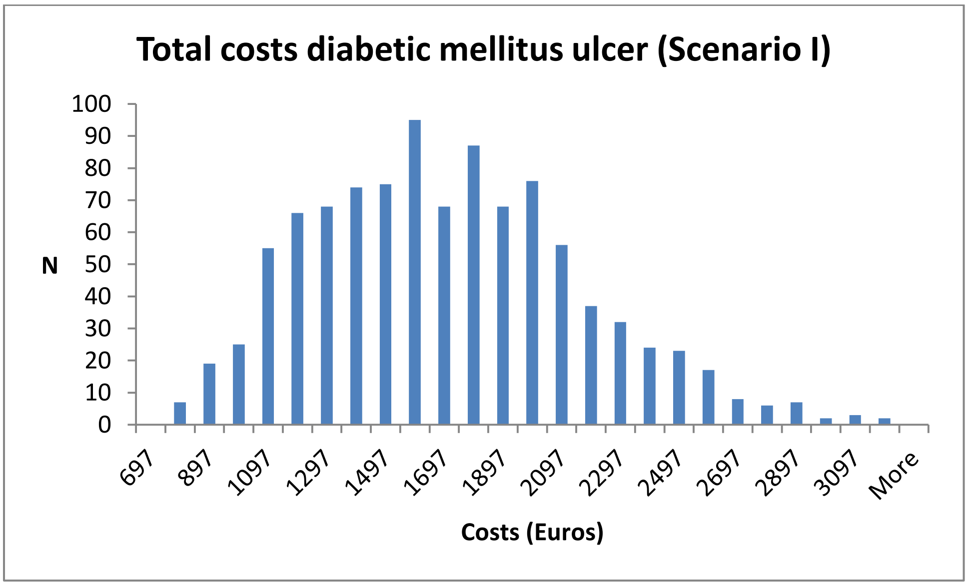

Figure 41 Histogram of the average total costs of the diabetic mellitus ulcer (Scenario I, n= 65).

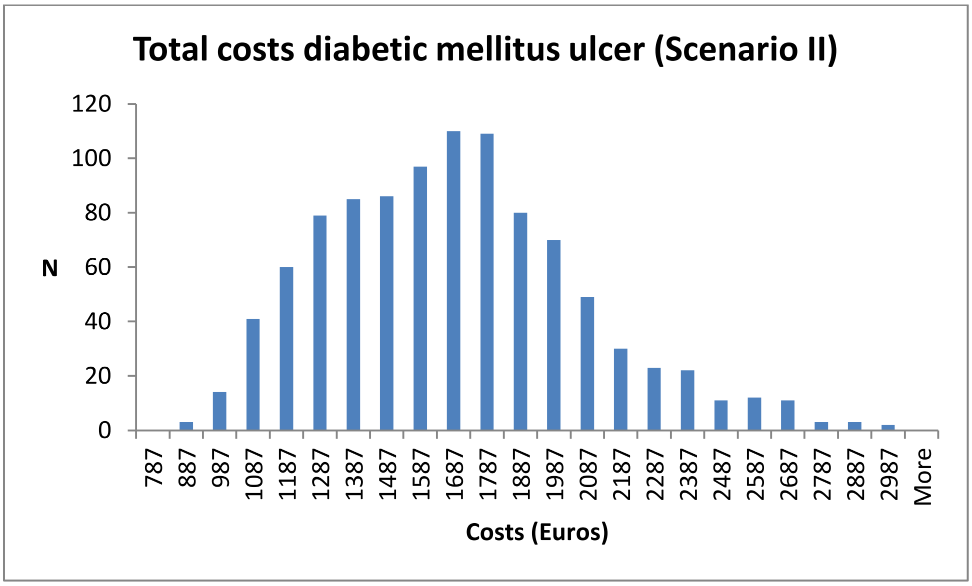

Figure 42 Histogram of the average total costs of the diabetic mellitus ulcer (Scenario II, n=65).

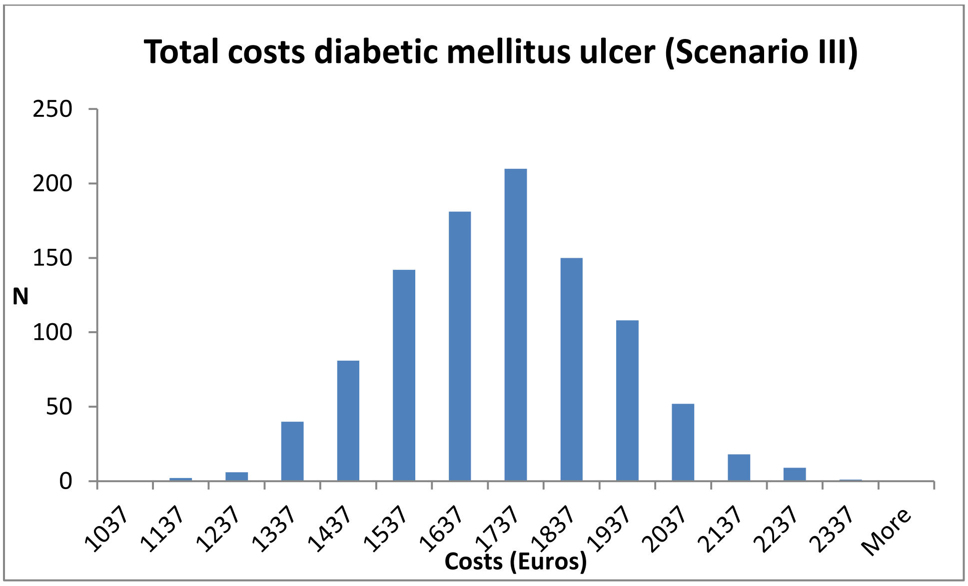

Figure 43 Histogram of the average total costs of the diabetic mellitus ulcer (Scenario III, n=65).

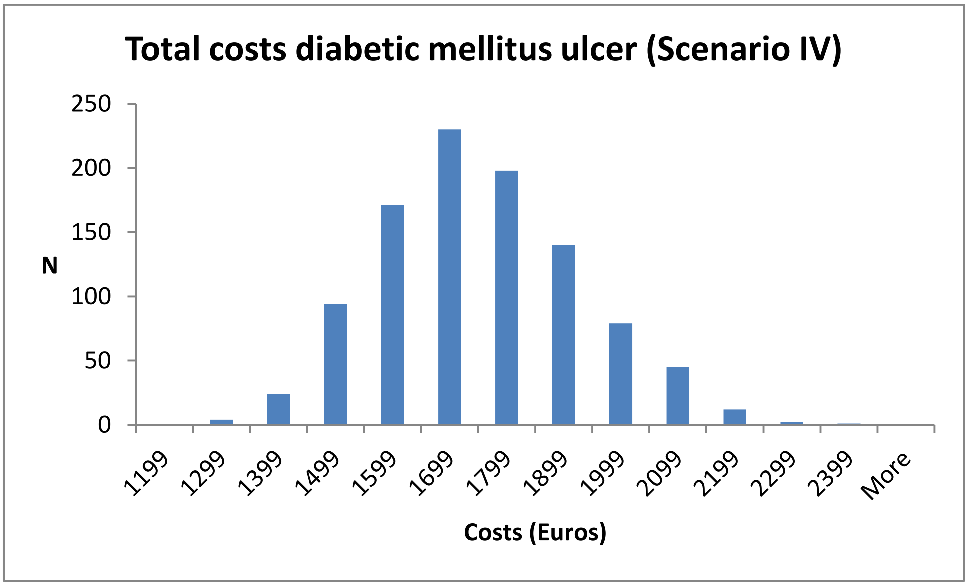

Figure 44 Histogram of the average total costs of the diabetic mellitus ulcer (Scenario IV, n=65).

Appendix E: MSVT costs diabetic mellitus ulcer

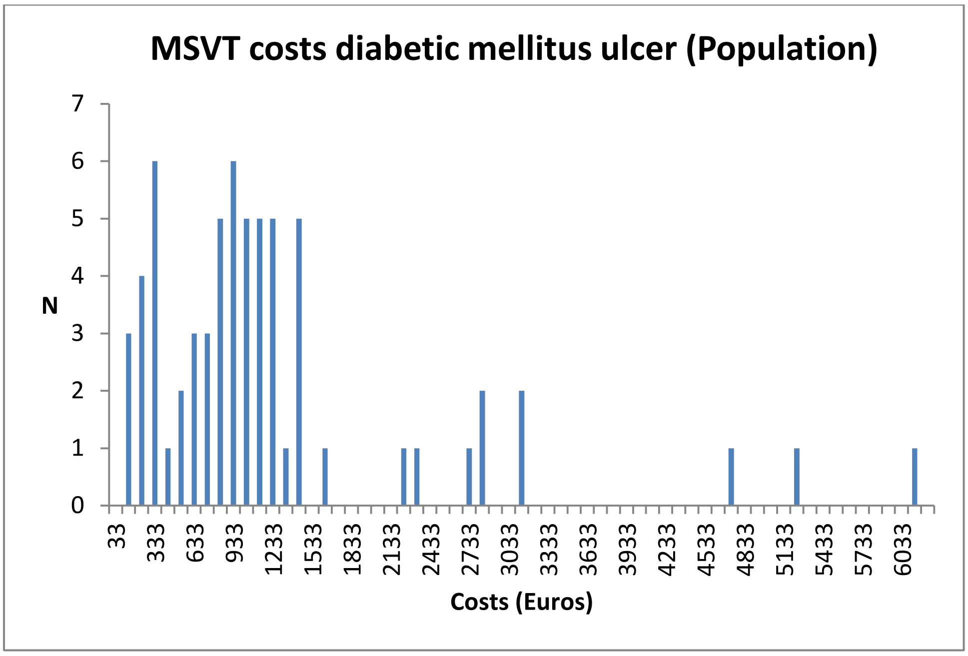

Figure 45 Histogram of the MSVT costs of the diabetic mellitus ulcer (Population, n=65).

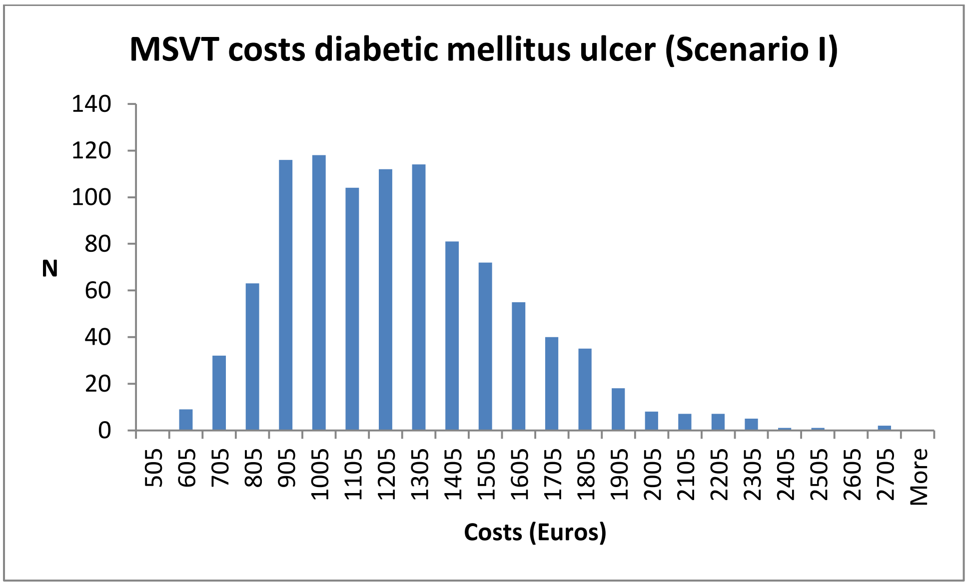

Figure 46 Histogram of the average MSVT costs of the diabetic mellitus ulcer (Scenario I, n=65).

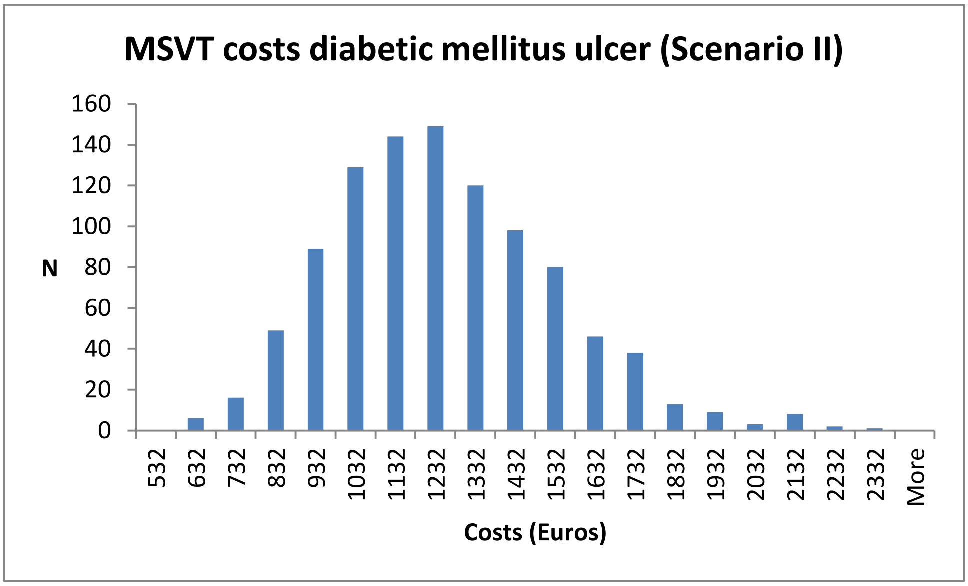

Figure 47 Histogram of the average MSVT costs of the diabetic mellitus ulcer (Scenario II, n=65).

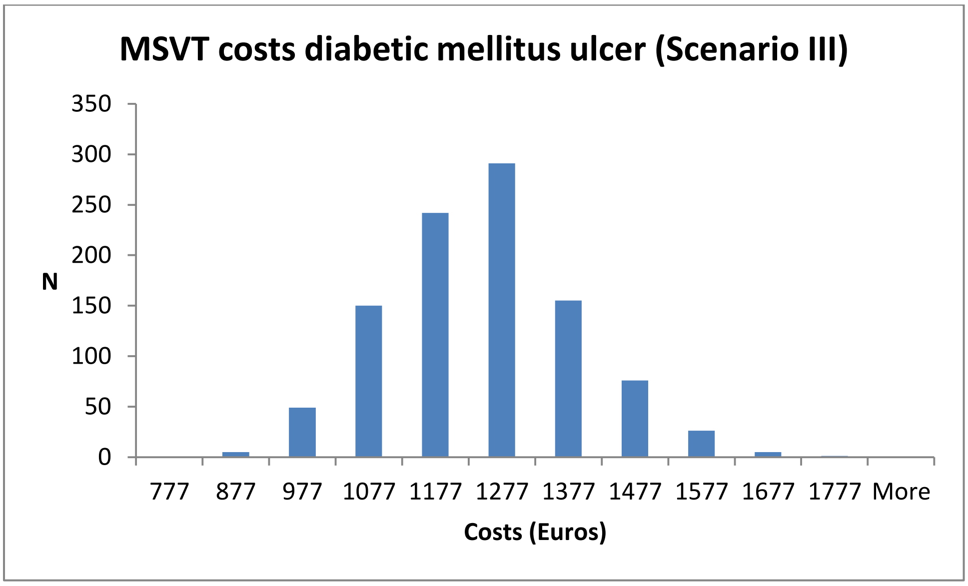

Figure 48 Histogram of the average MSVT costs of the diabetic mellitus ulcer (Scenario III, n=65)

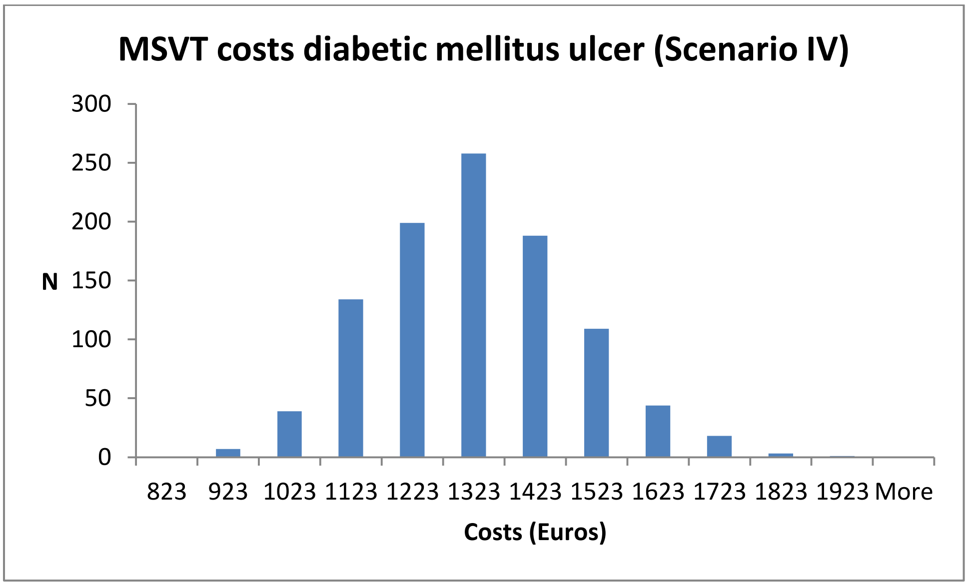

Figure 49 Histogram of the average MSVT costs of the diabetic mellitus ulcer (Scenario IV, n=65)

Appendix F: HLP costs diabetic mellitus ulcer

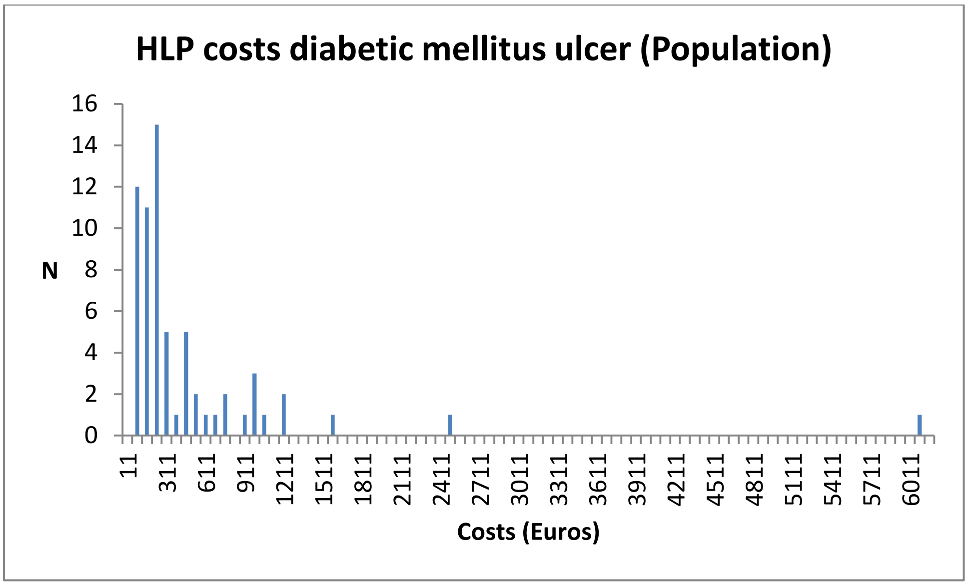

Figure 50 Histogram of the HLP costs of the diabetic mellitus ulcer (Population, n=65).

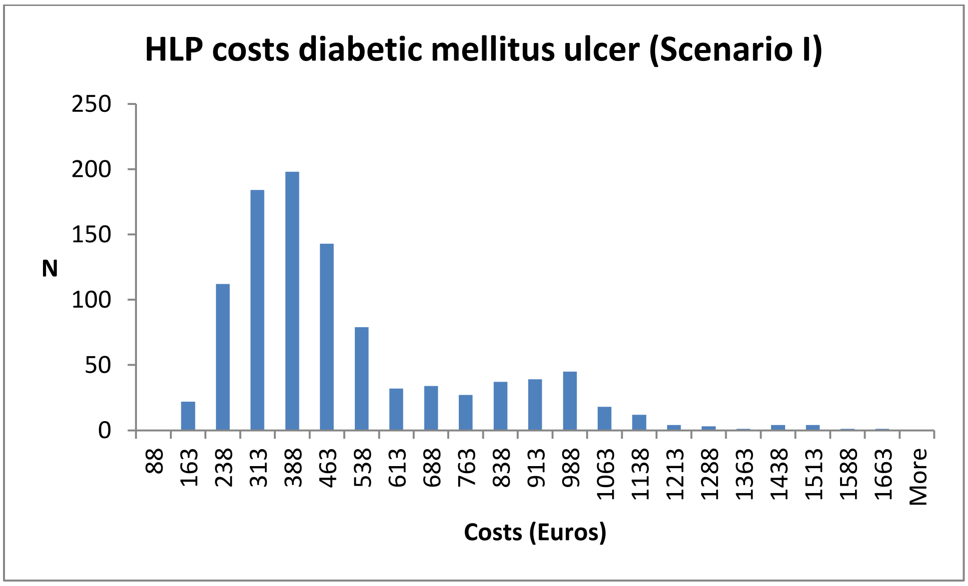

Figure 51 Histogram of the average HLP costs of the diabetic mellitus ulcer (Scenario I, n=65).

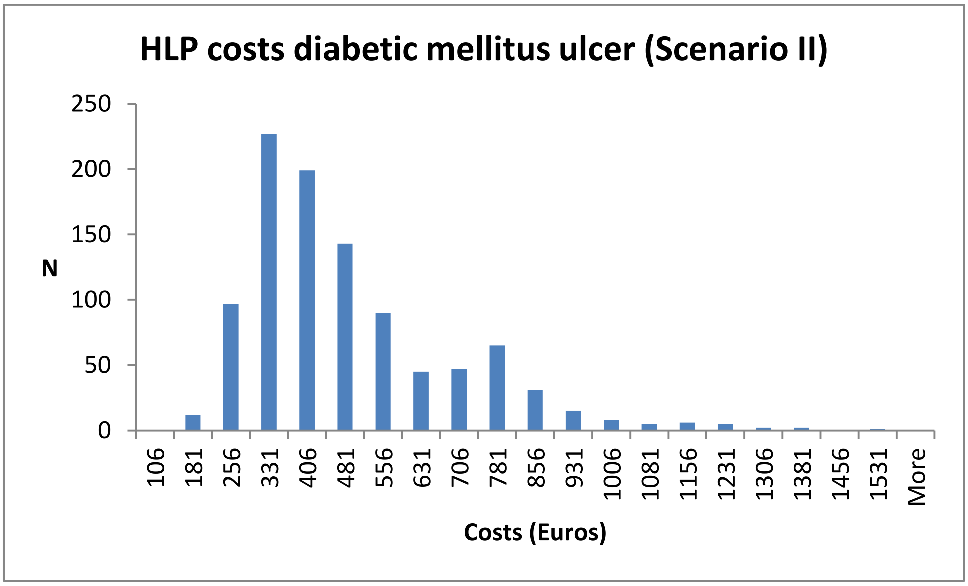

Figure 52 Histogram of the average HLP costs of the diabetic mellitus ulcer (Scenario II, n=65).

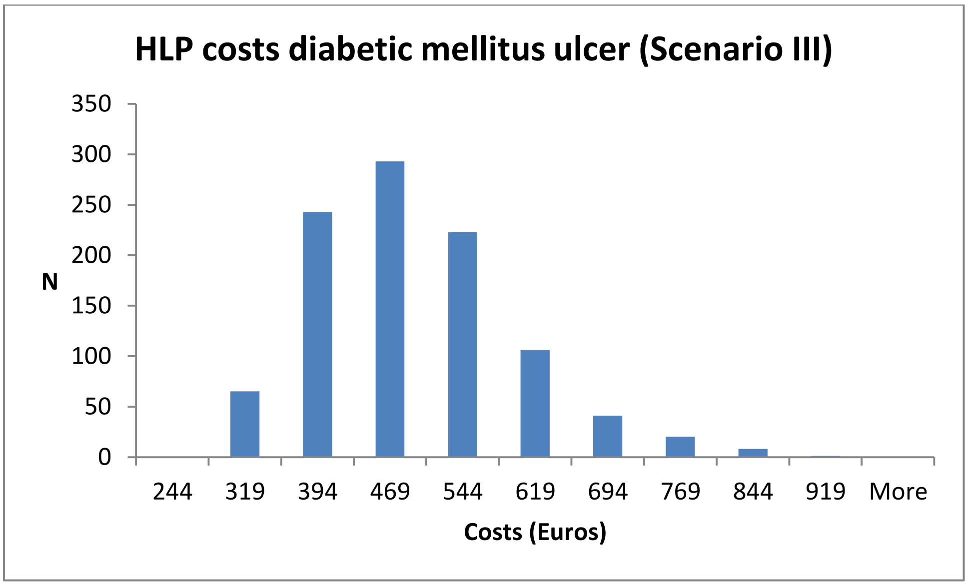

Figure 53 Histogram of the average HLP costs of the diabetic mellitus ulcer (Scenario III, n=65).

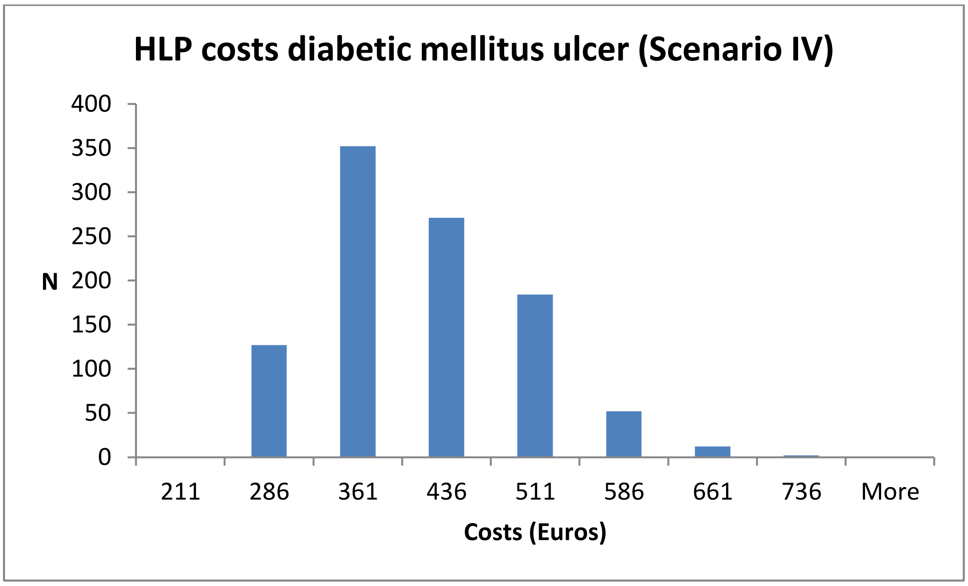

Figure 54 Histogram of the average HLP costs of the diabetic mellitus ulcer (Scenario IV, n=65).

Appendix G: Total costs POWI ulcer

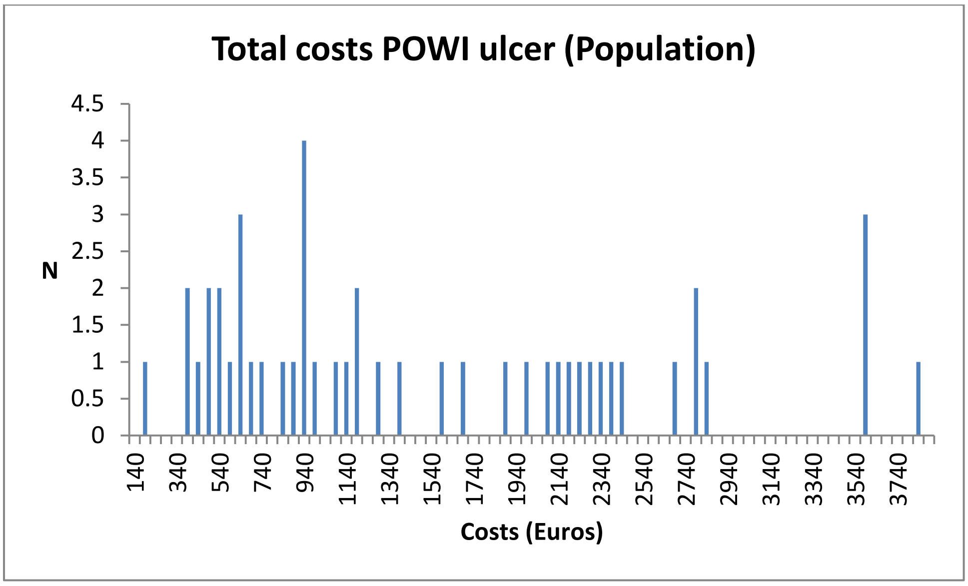

Figure 55 Histogram of the total costs of the POWI ulcer (Population, n=47).

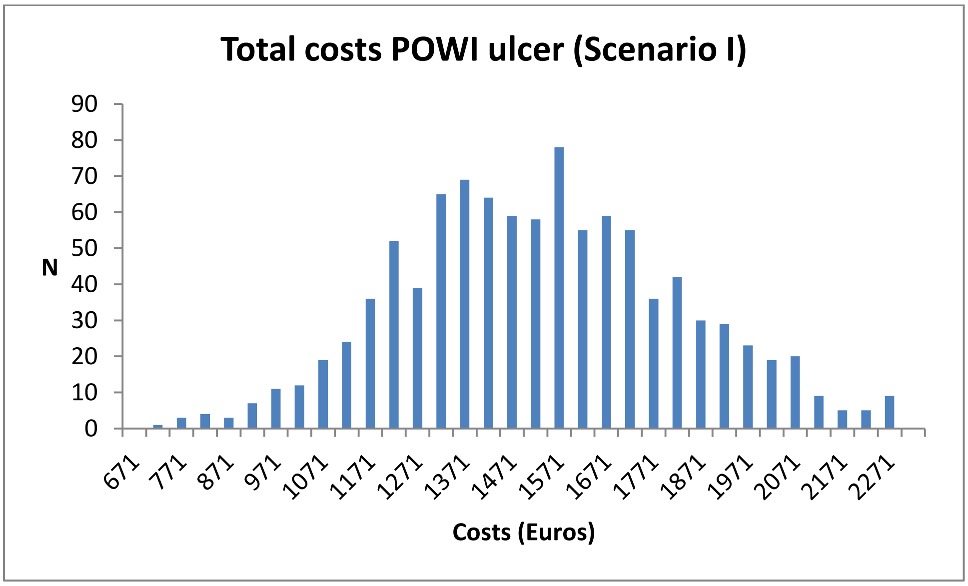

Figure 56 Histogram of the average total costs of the POWI ulcer (Scenario I, n=47).

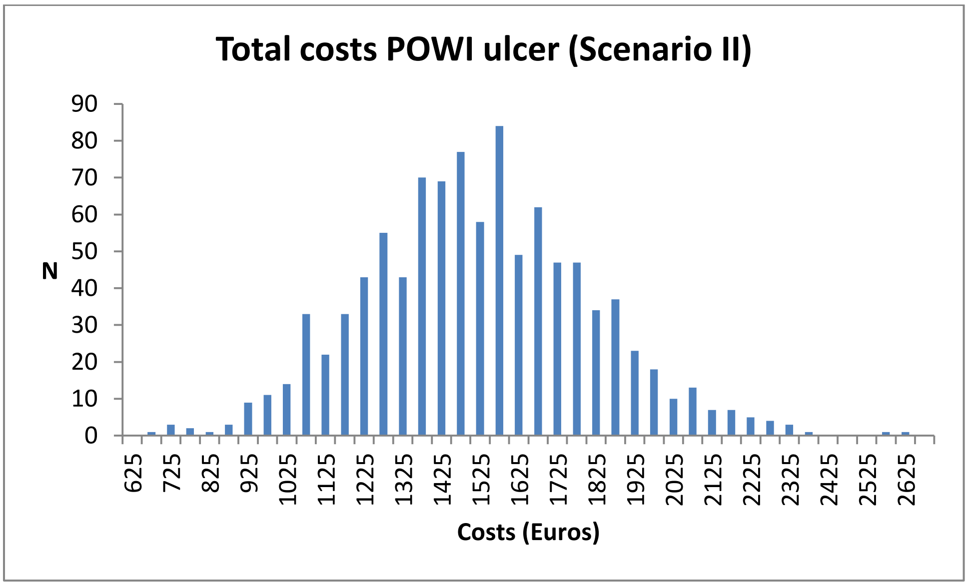

Figure 57 Histogram of the average total costs of the POWI ulcer (Scenario II, n=47).

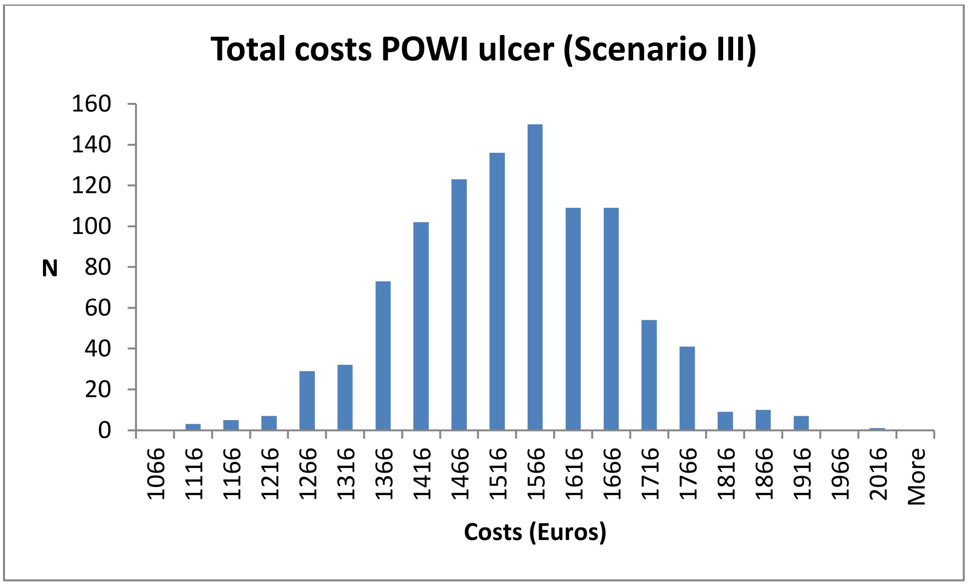

Figure 58 Histogram of the average total costs of the POWI ulcer (Scenario III, n=47).

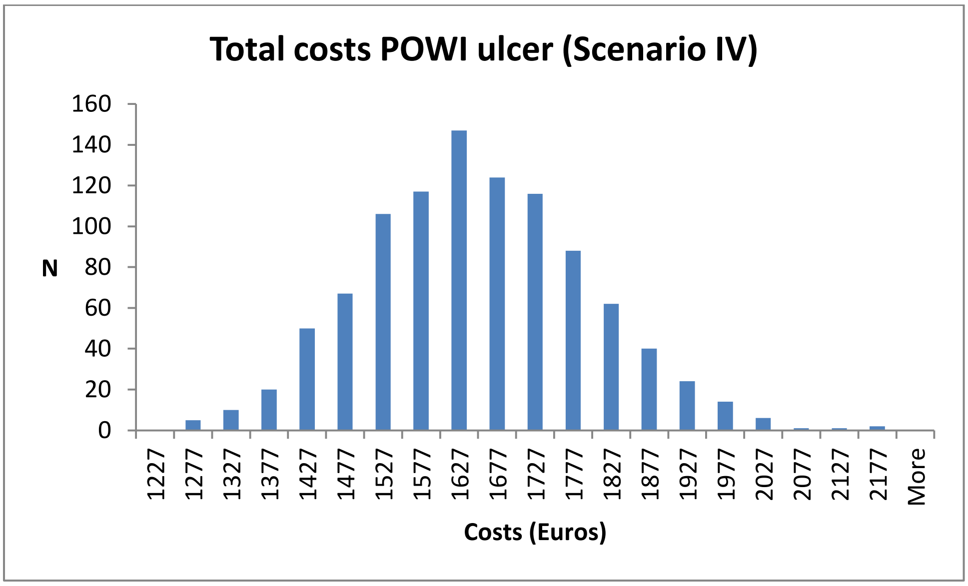

Figure 59 Histogram of the average total costs of the POWI ulcer (Scenario IV, n=47).

Appendix H: MSVT costs POWI ulcer

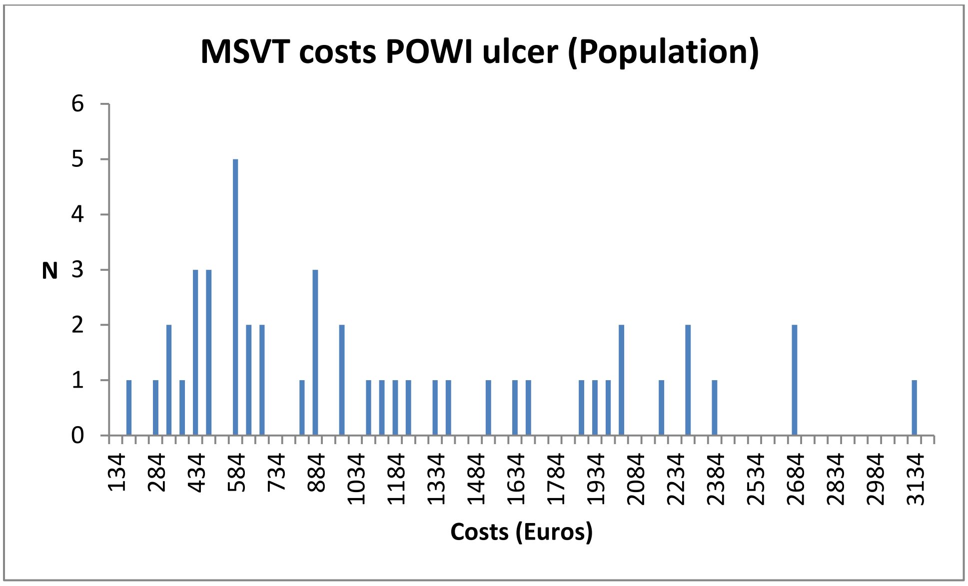

Figure 60 Histogram of the average MSVT costs of the POWI ulcer (Population, n=47).

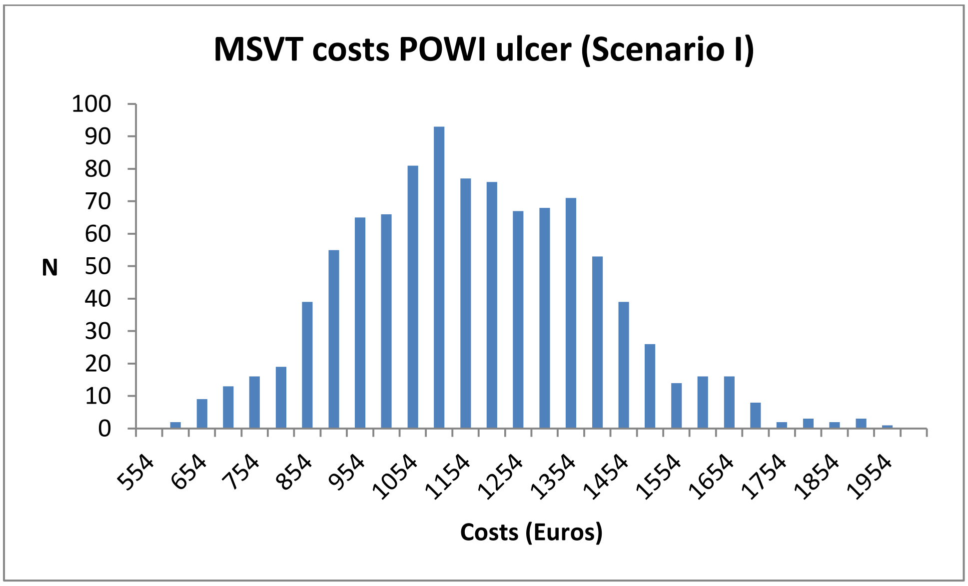

Figure 61 Histogram of the average MSVT costs of the POWI ulcer (Scenario I, n=47).

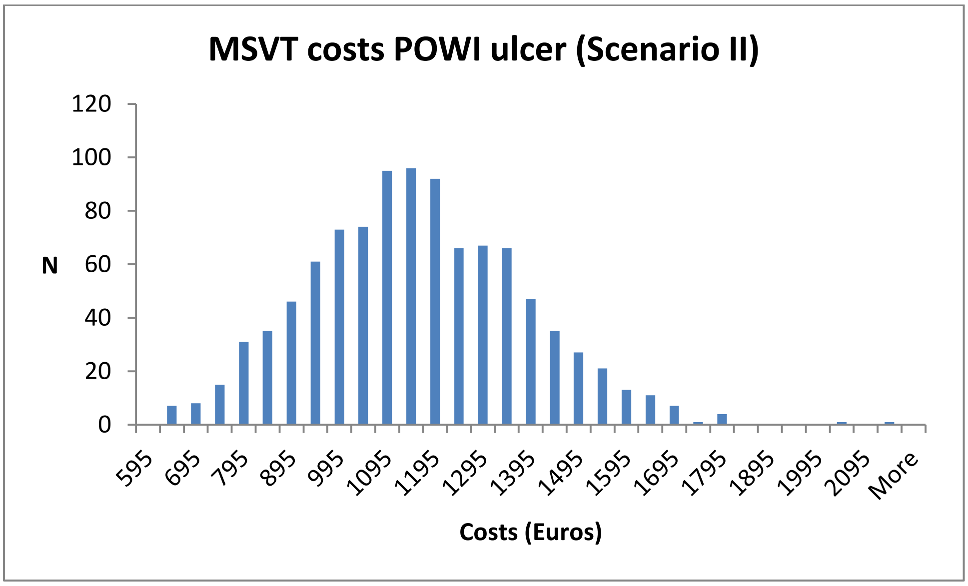

Figure 62 Histogram of the average MSVT costs of the POWI ulcer (Scenario II, n=47).

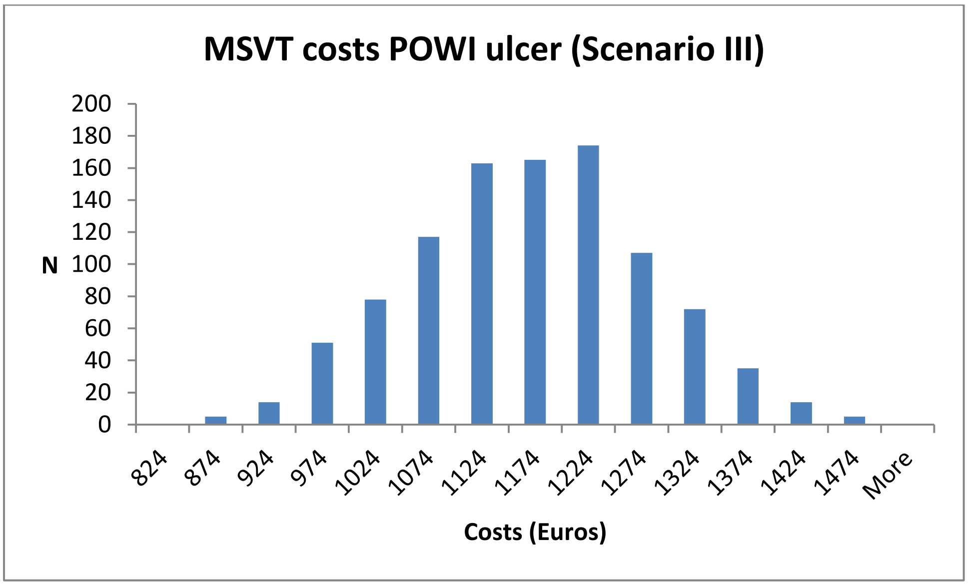

Figure 63 Histogram of the average MSVT costs of the POWI ulcer (Scenario III, n=47).

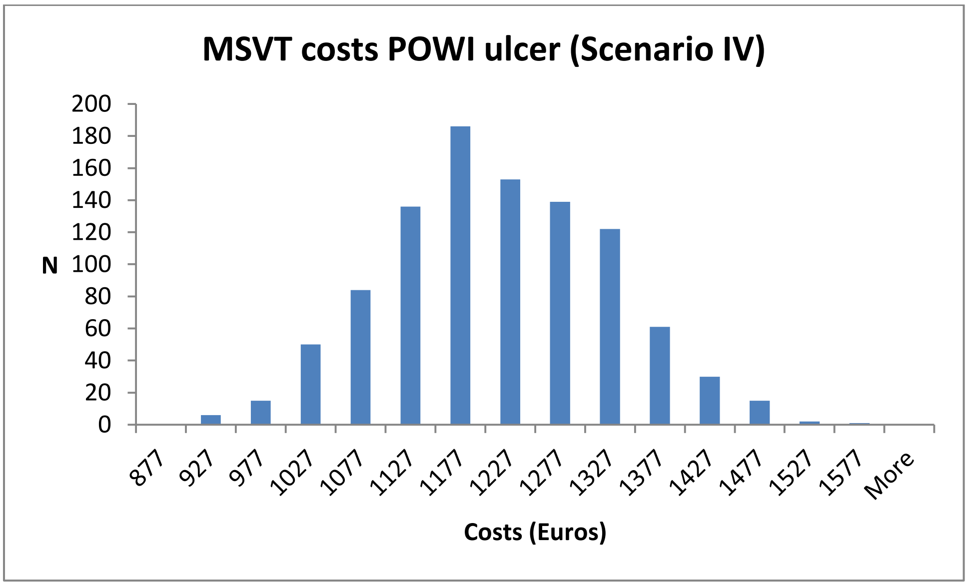

Figure 64 Histogram of the average MSVT costs of the POWI ulcer (Scenario IV, n=47).

Appendix I: HLP costs POWI ulcer

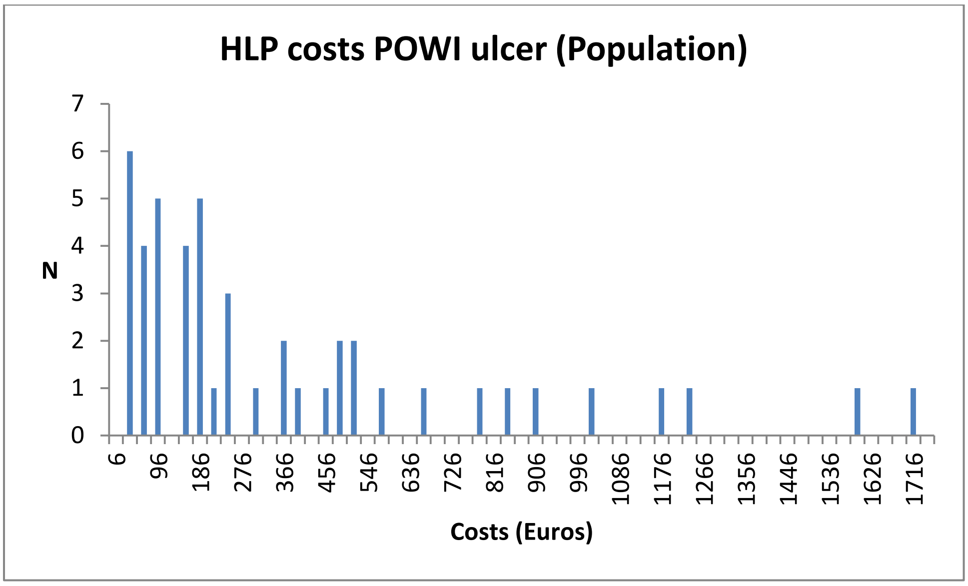

Figure 65 Histogram of the HLP costs of the POWI ulcer (Population, n=47).

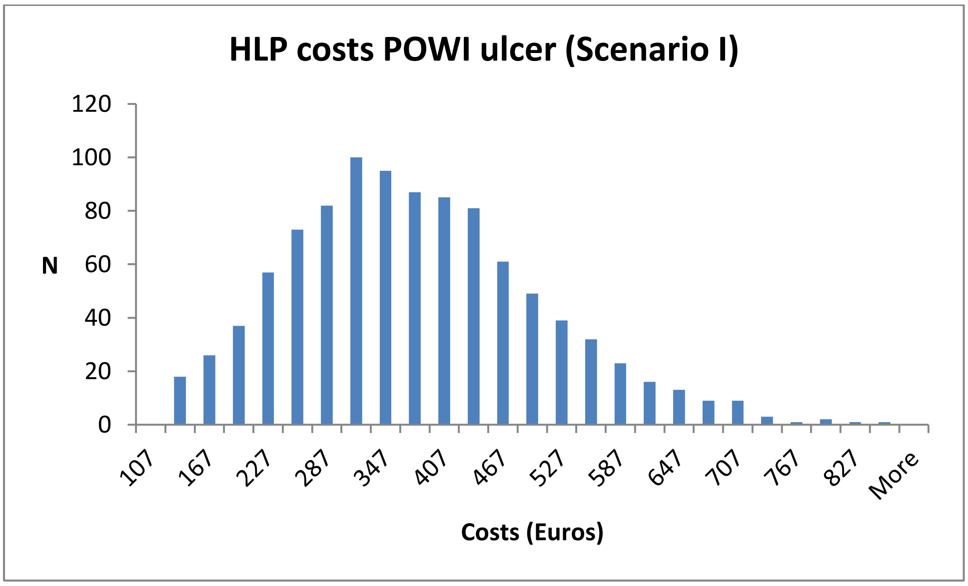

Figure 66 Histogram of the average HLP costs of the POWI ulcer (Scenario I, n=47).

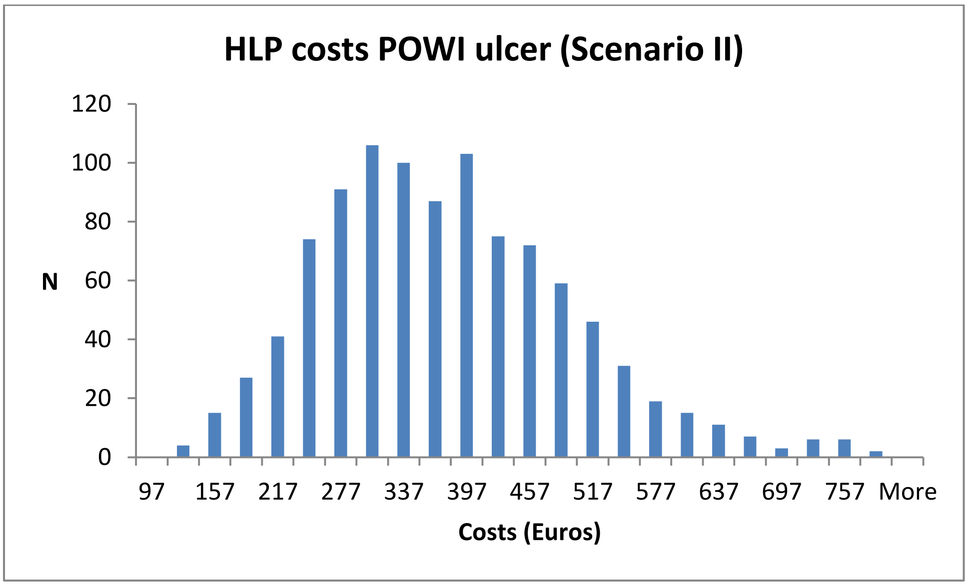

Figure 67 Histogram of the average HLP costs of the POWI ulcer (Scenario II, n=47).

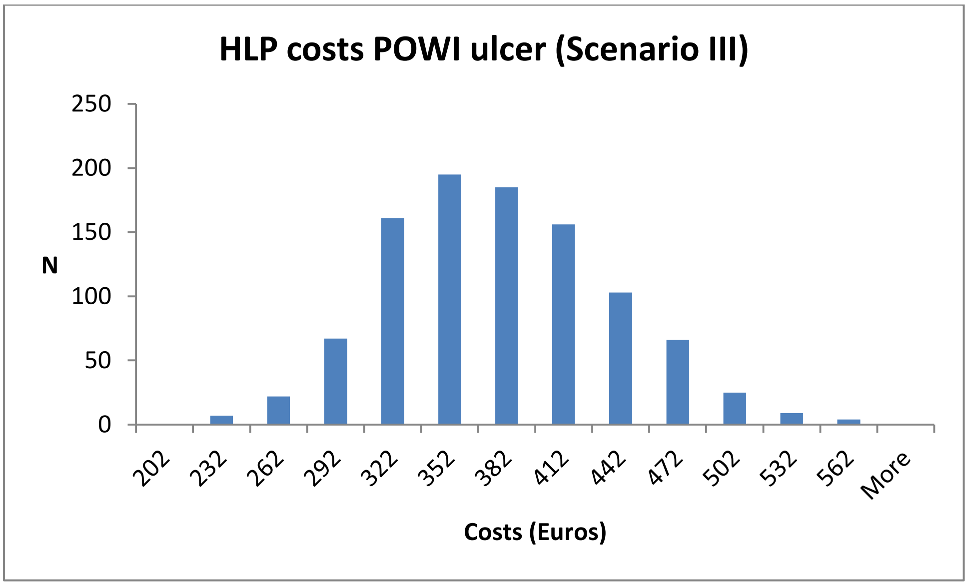

Figure 68 Histogram of the average HLP costs of the POWI ulcer (Scenario III, n=47).

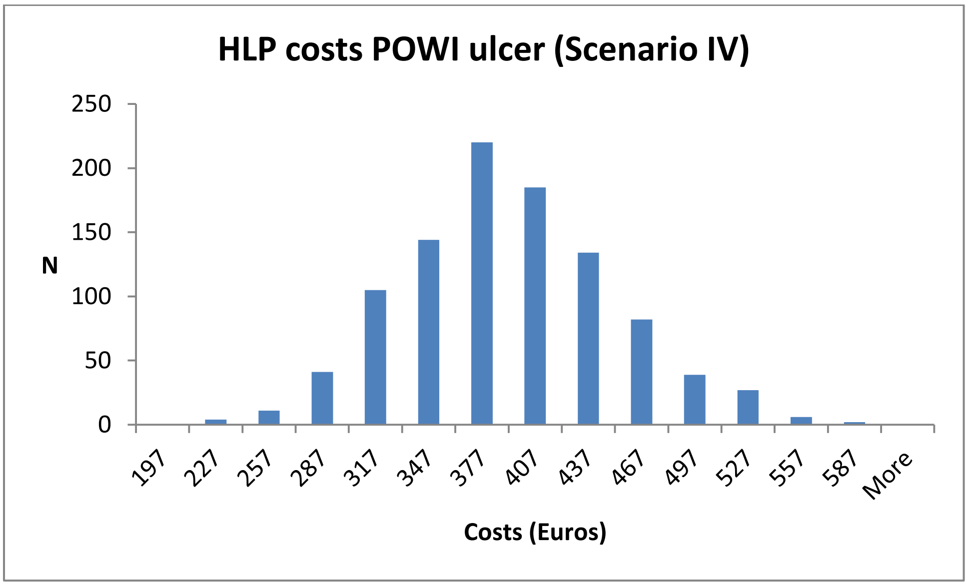

Figure 69 Histogram of the average HLP costs of the POWI ulcer (Scenario IV, n=47).

Appendix J: Total costs pressure ulcer

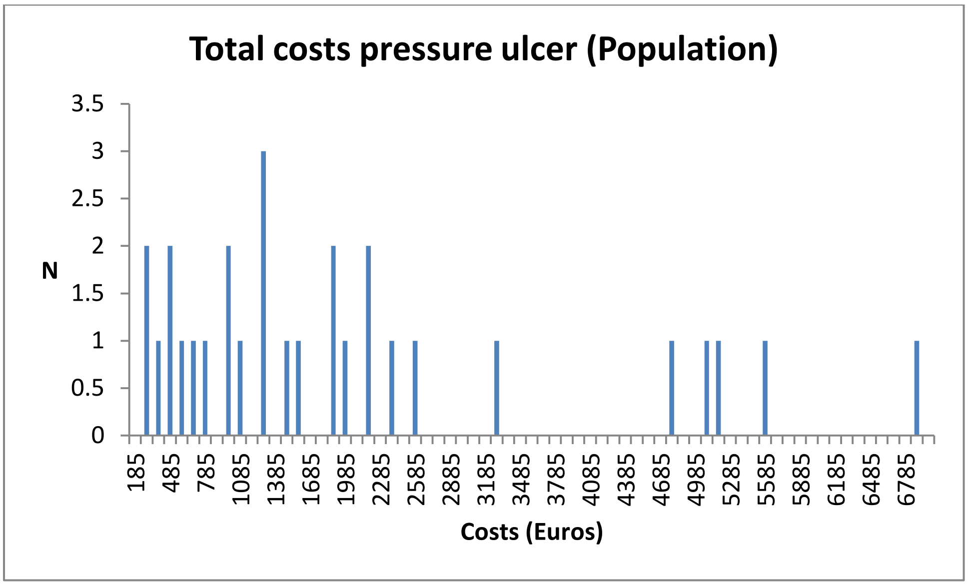

Figure 70 Histogram of the total costs of the pressure ulcer (Population, n=29).

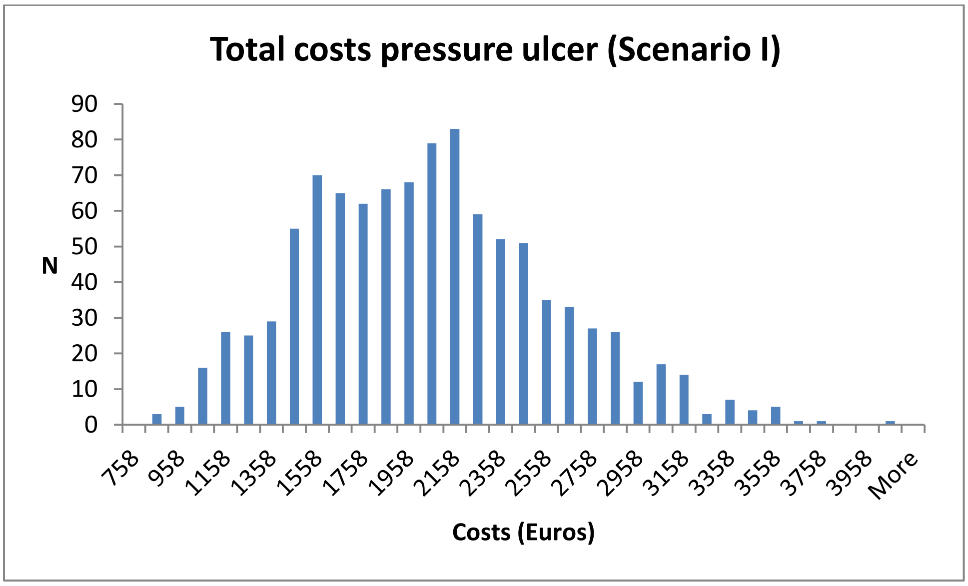

Figure 71 Histogram of the average total costs of the pressure ulcer (Scenario I, n=29).

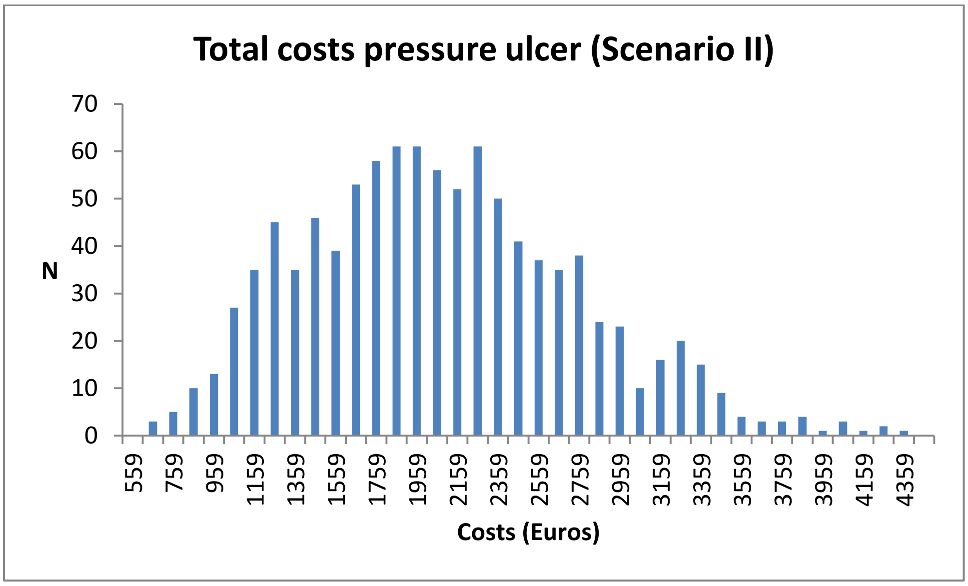

Figure 72 Histogram of the average total costs of the pressure ulcer (Scenario II, n=29).

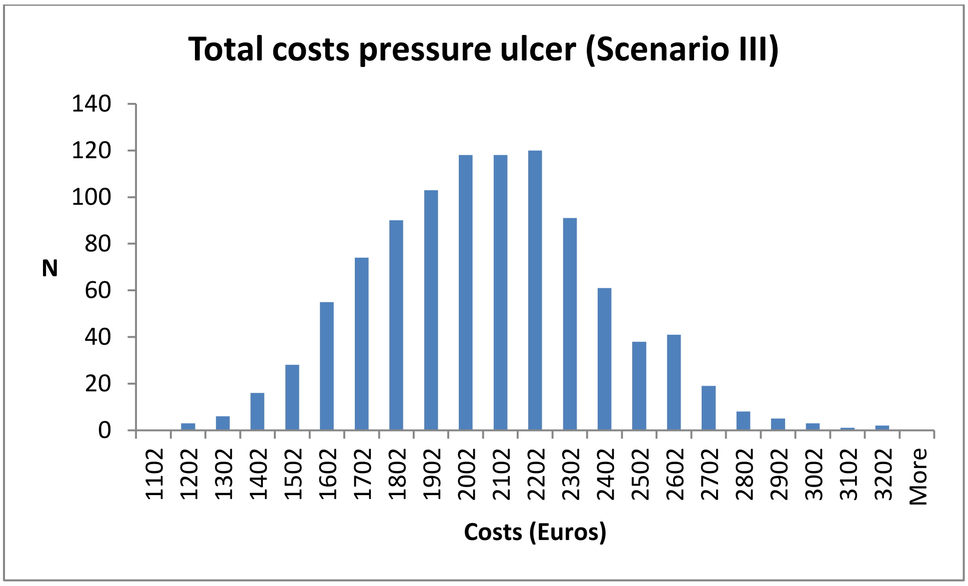

Figure 73 Histogram of the average total costs of the pressure ulcer (Scenario III, n=29).

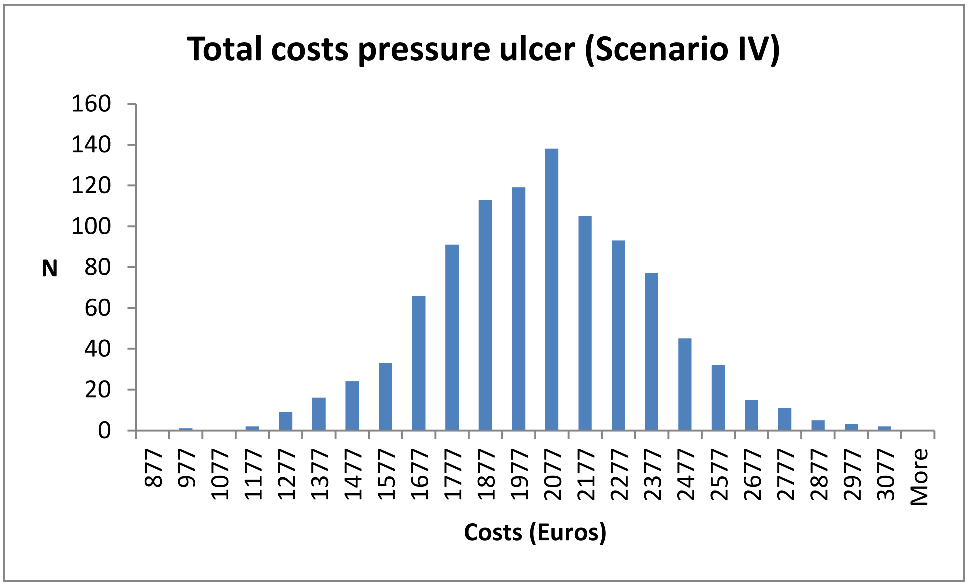

Figure 74 Histogram of the average total costs of the pressure ulcer (Scenario IV, n=29).

Appendix K: MSVT costs pressure ulcer

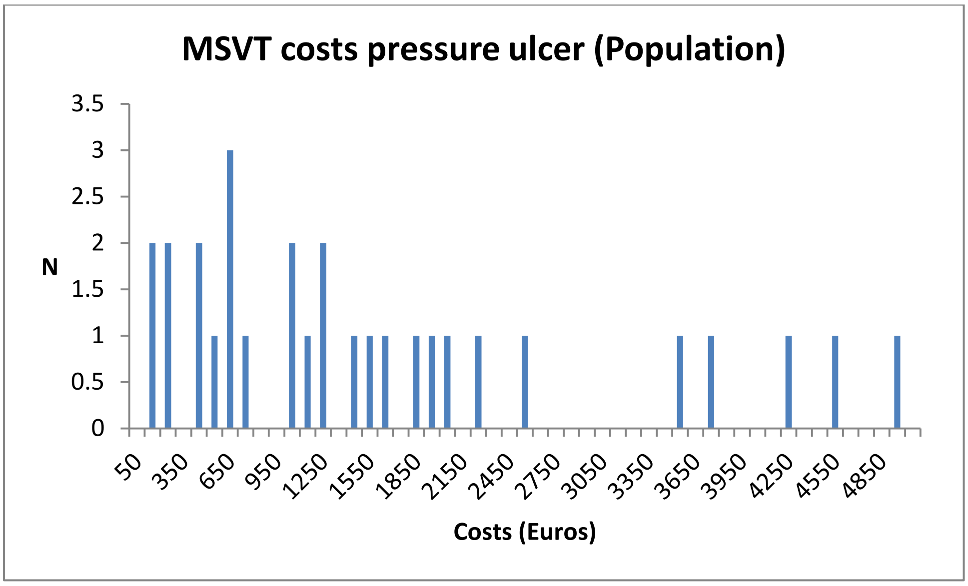

Figure 75 Histogram of the MSVT costs of the pressure ulcer (Population, n=29).

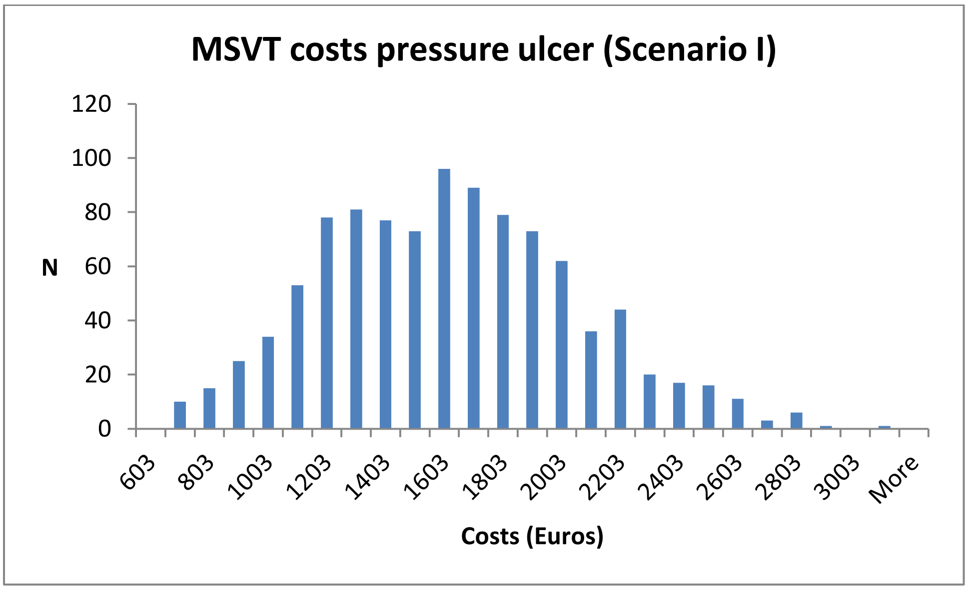

Figure 76 Histogram of the average MSVT costs of the pressure ulcer (Scenario I, n=29).

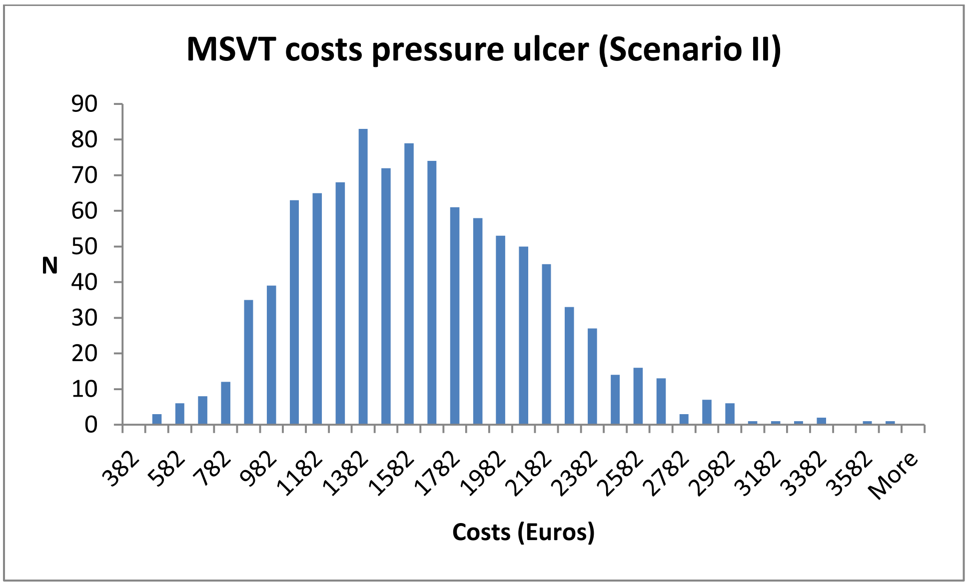

Figure 77 Histogram of the average MSVT costs of the pressure ulcer (Scenario I, n=29).

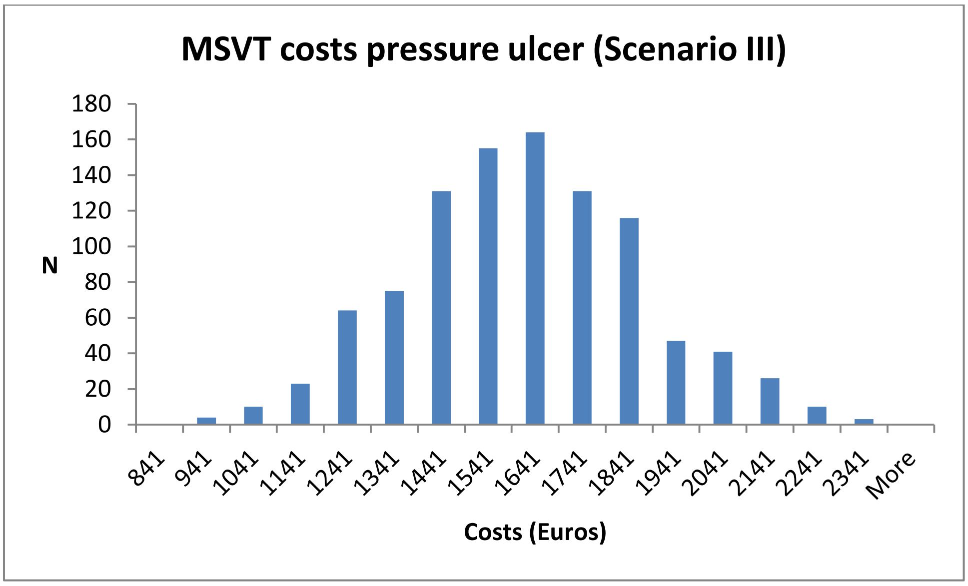

Figure 78 Histogram of the average MSVT costs of the pressure ulcer (Scenario III, n=29).

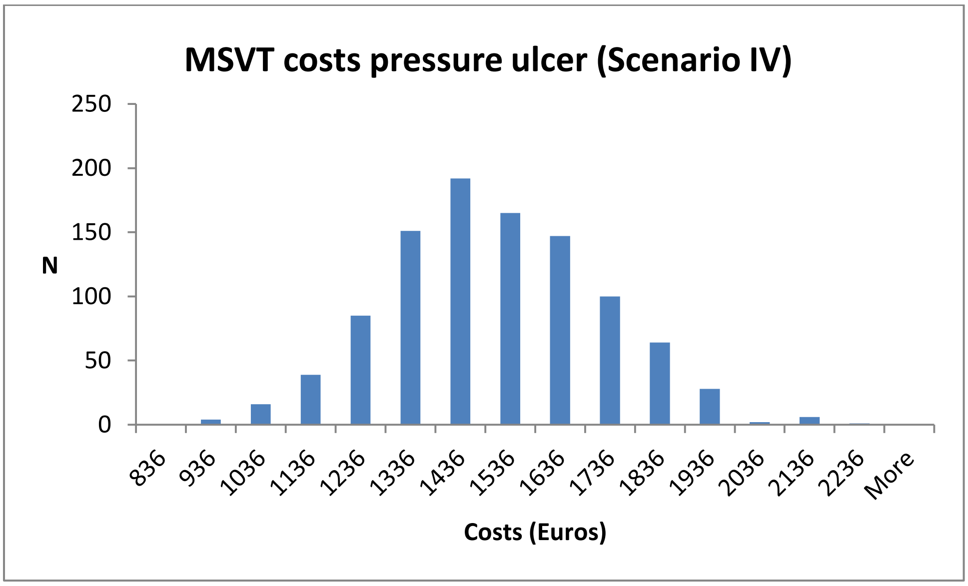

Figure 79 Histogram of the average MSVT costs of the pressure ulcer (Scenario IV, n=29).

Appendix L: HLP costs pressure ulcer

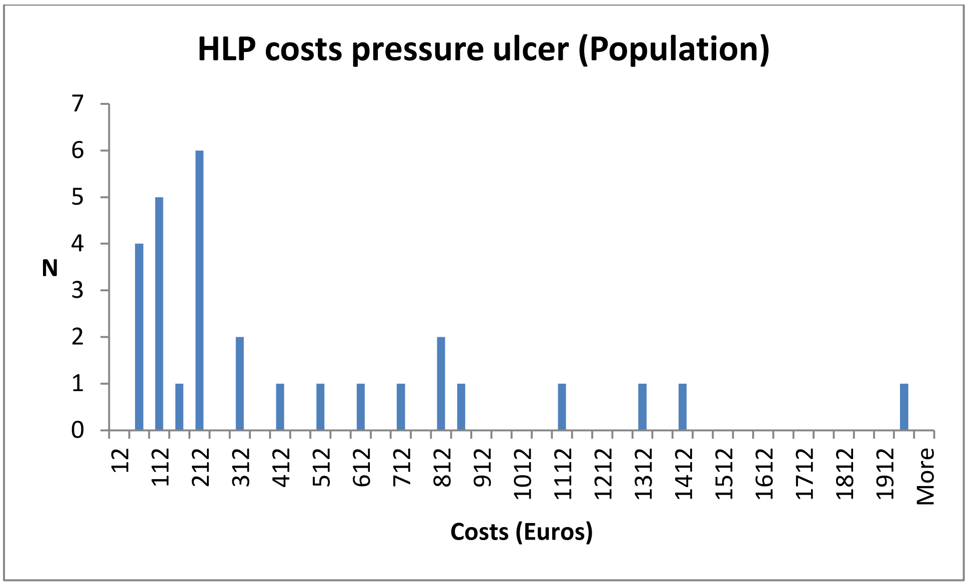

Figure 80 Histogram of the HLP costs of the pressure ulcer (Population, n=29).

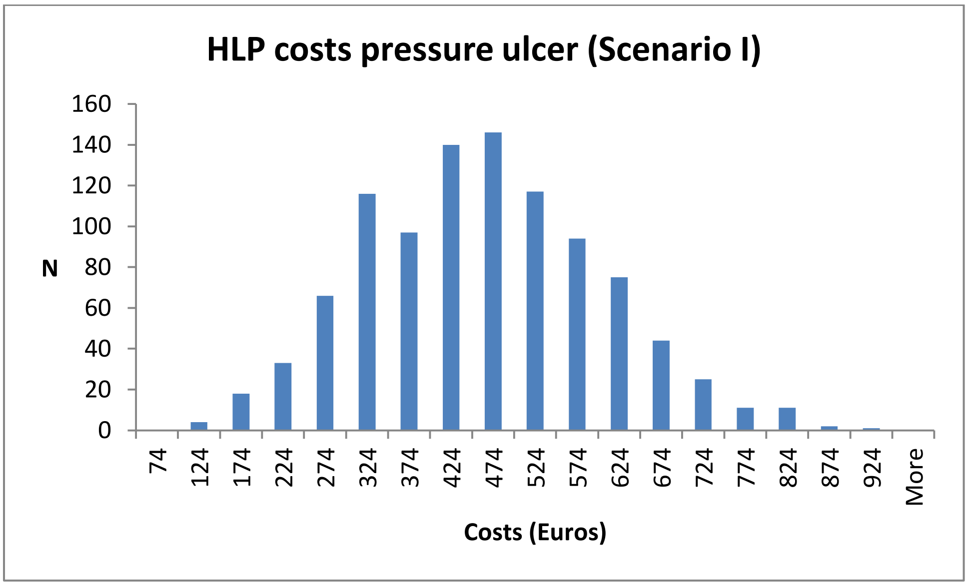

Figure 81 Histogram of the average HLP costs of the pressure ulcer (Scenario I, n=29).

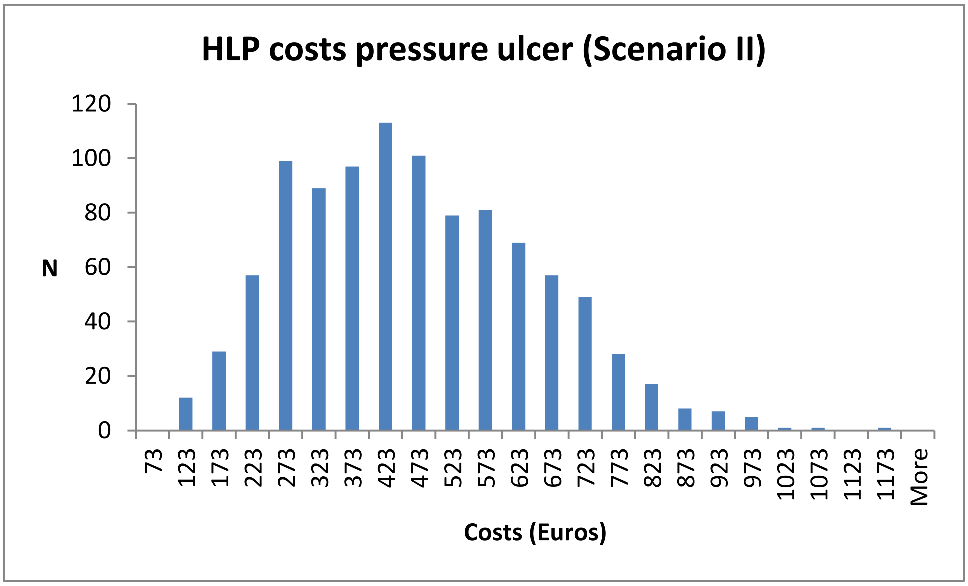

Figure 82 Histogram of the average HLP costs of the pressure ulcer (Scenario II, n=29).

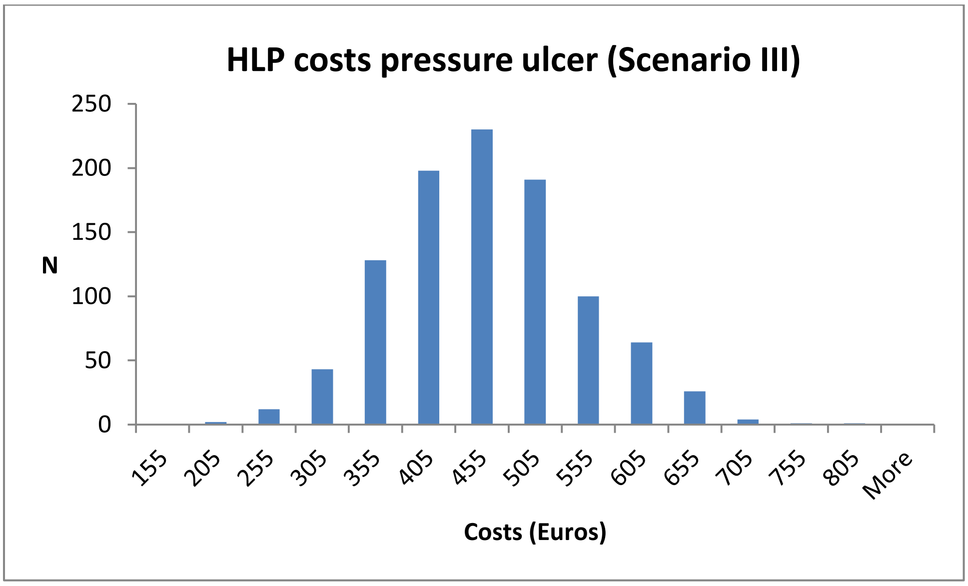

Figure 83 Histogram of the average HLP costs of the pressure ulcer (Scenario III, n=29).

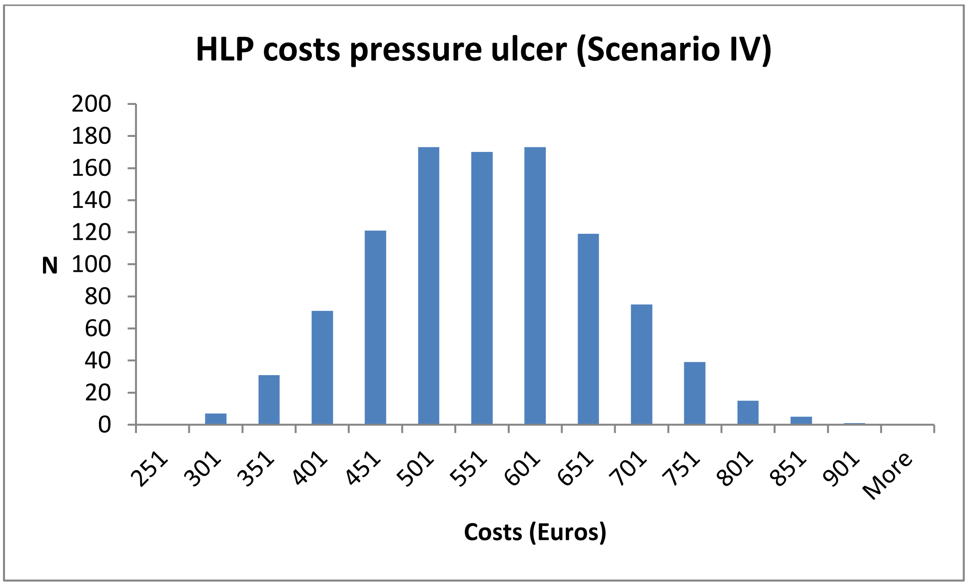

Figure 84 Histogram of the average HLP costs of the pressure ulcer (Scenario IV, n=29).

Appendix M: Total costs surgical wound

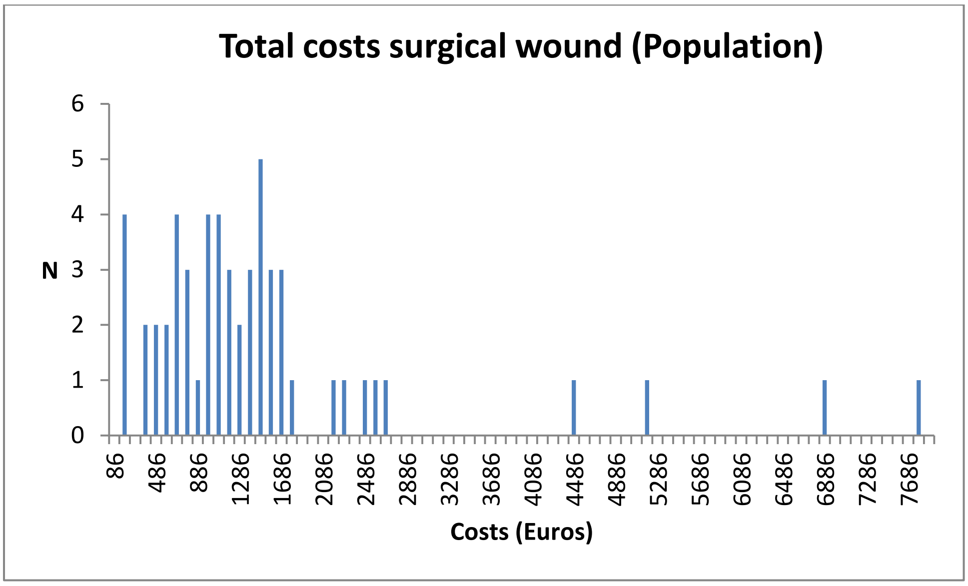

Figure 85 Histogram of the total costs of the surgical wound (Population, n=55).

Figure 86 Histogram of the average total costs of the surgical wound (Scenario I, n=55).

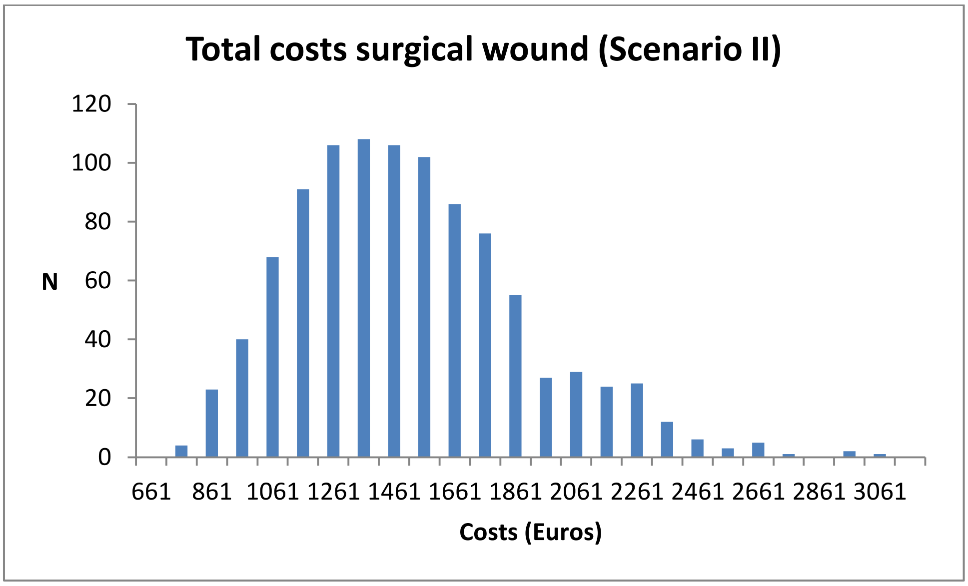

Figure 87 Histogram of the average total costs of the surgical wound (Scenario II, n=55).

Figure 88 Histogram of the average total costs of the surgical wound (Scenario III, n=55).

Figure 89 Histogram of the average total costs of the surgical wound (Scenario IV, n=55).

Appendix N: MSVT costs surgical wound

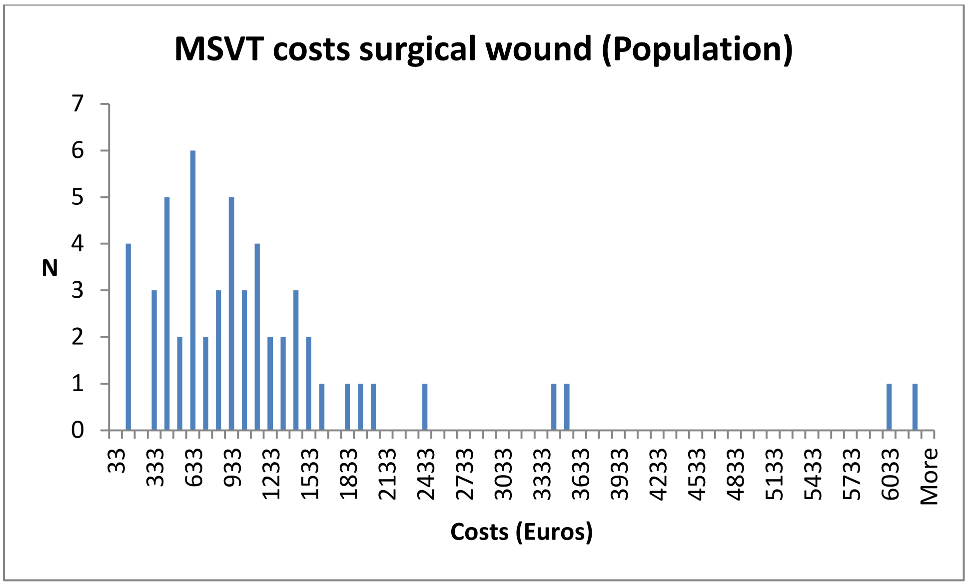

Figure 90 Histogram of the MSVT costs of the surgical wound (Population, n=55).

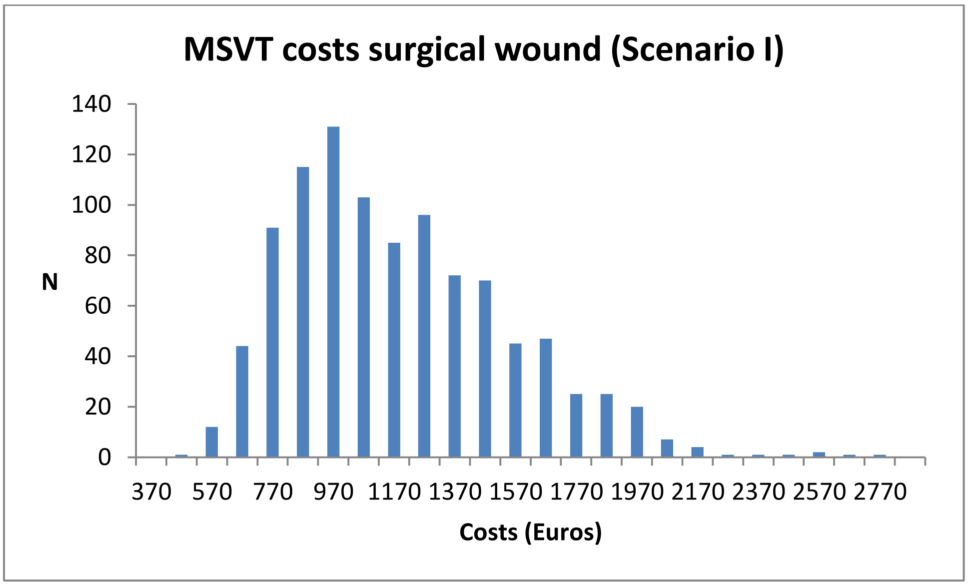

Figure 91 Histogram of the average MSVT costs of the surgical wound (Scenario I, n=55).

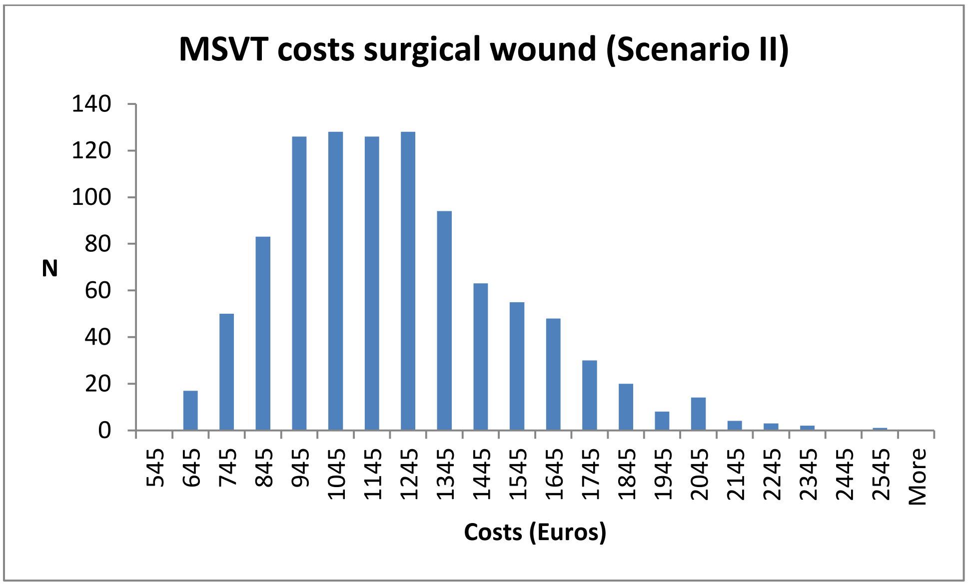

Figure 92 Histogram of the average MSVT costs of the surgical wound (Scenario II, n=55).

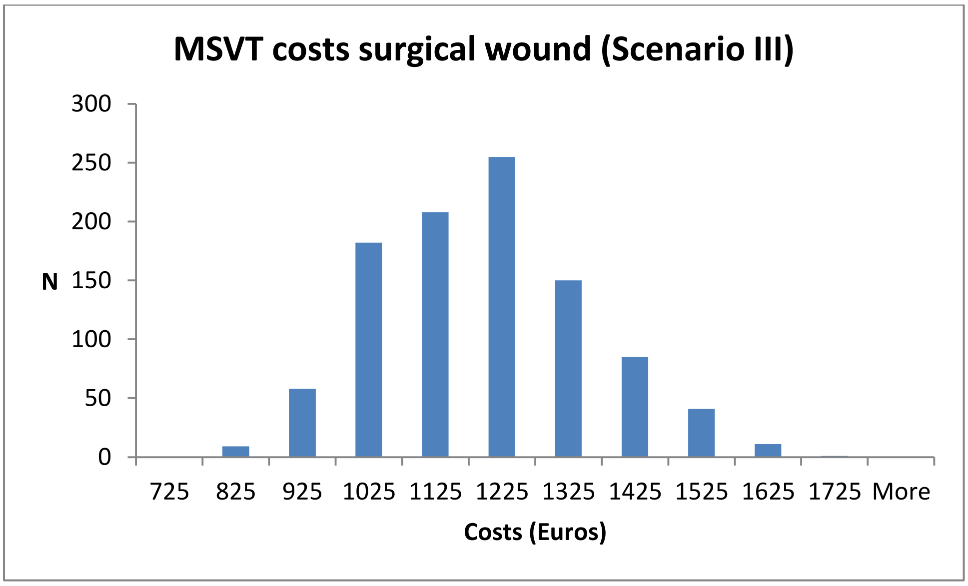

Figure 93 Histogram of the average MSVT costs of the surgical wound (Scenario III, n=55).

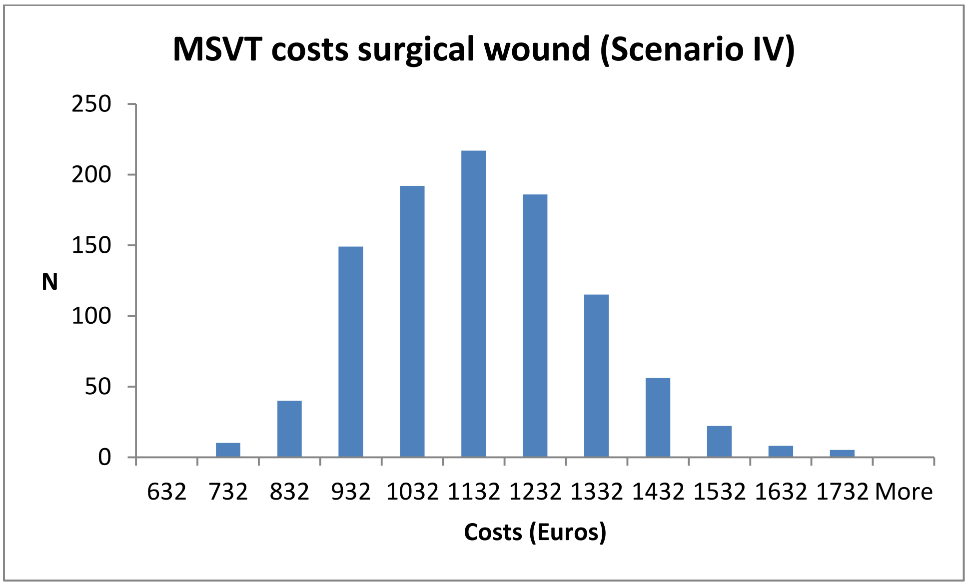

Figure 94 Histogram of the average MSVT costs of the surgical wound (Scenario IV, n=55).

Appendix O: HLP costs surgical wound

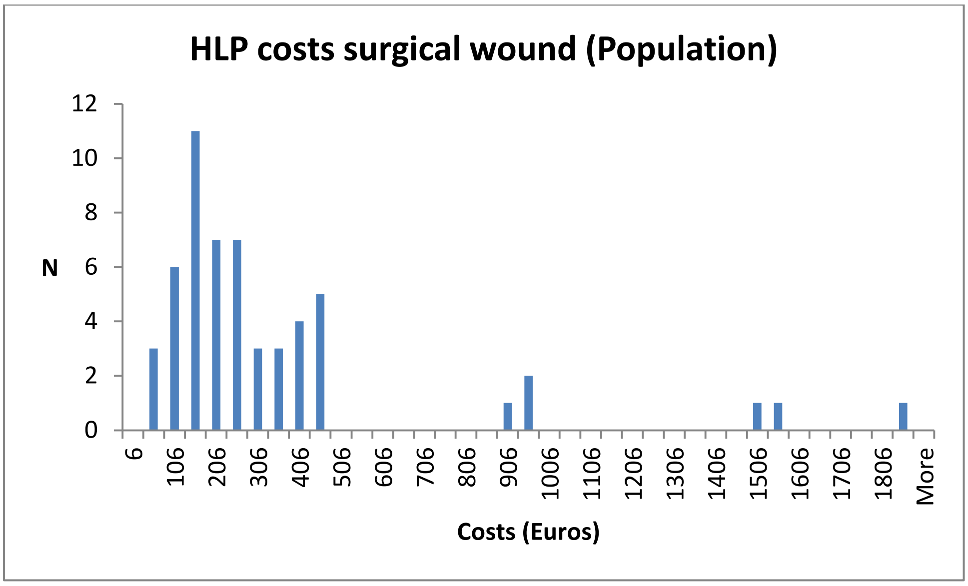

Figure 95 Histogram of the HLP costs of the surgical wound (Population, n=55).

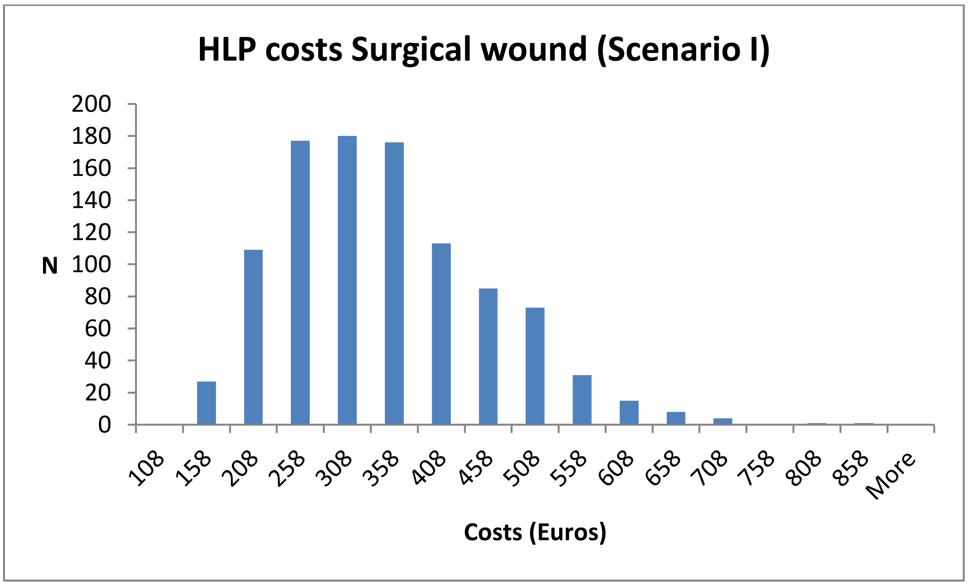

Figure 96 Histogram of the average HLP costs of the surgical wound (Scenario I, n=55).

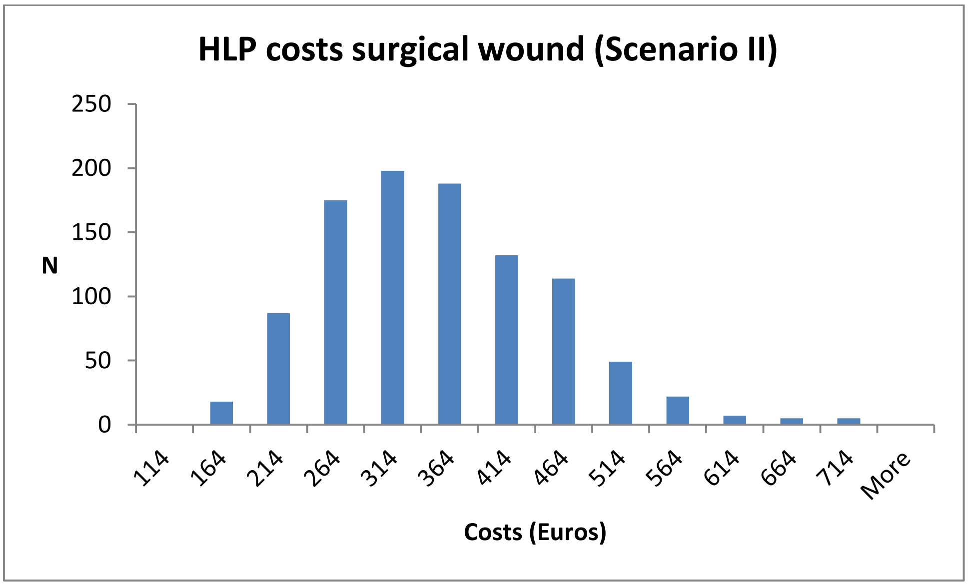

Figure 97 Histogram of the average HLP costs of the surgical wound (Scenario II, n=55).

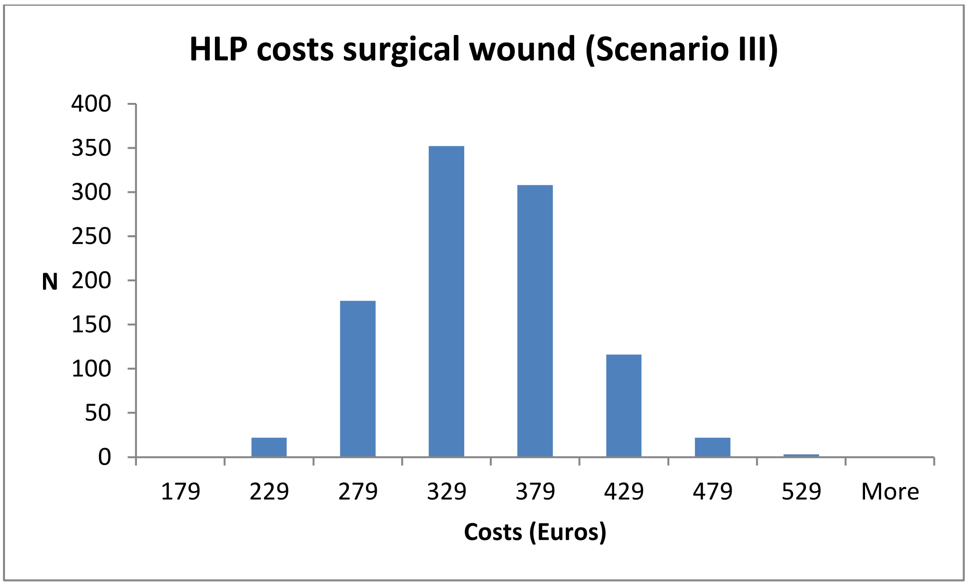

Figure 98 Histogram of the average HLP costs of the surgical wound (Scenario III, n=55).

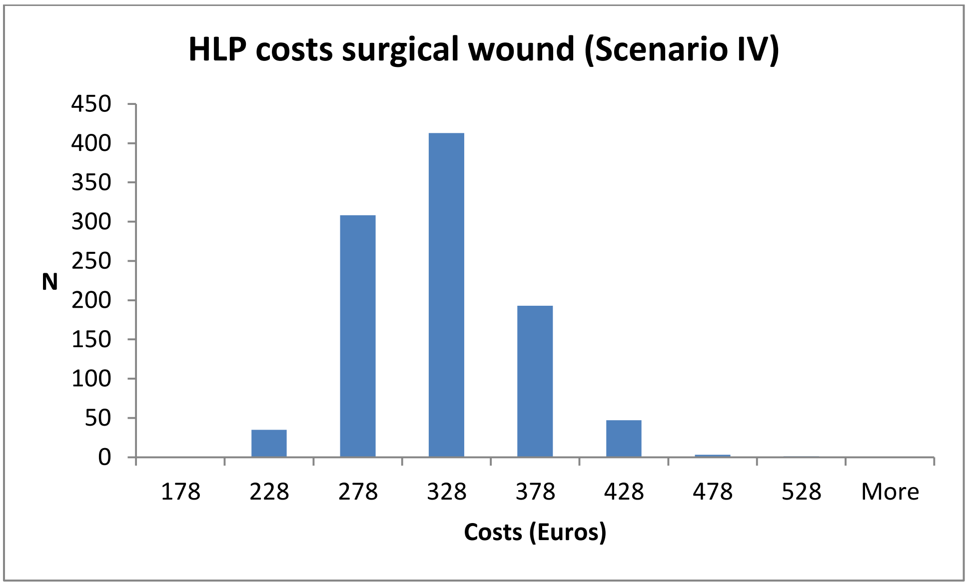

Figure 99 Histogram of the average HLP costs of the surgical wound (Scenario IV, n=55).

Appendix P: Total costs traumatic ulcer

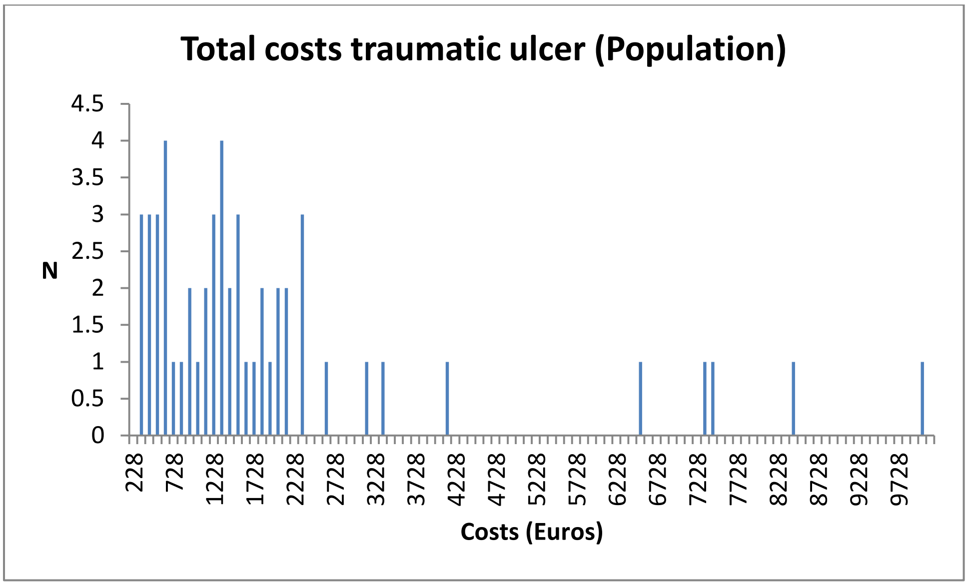

Figure 100 Histogram of the total costs of the traumatic ulcer (Population, n=53).

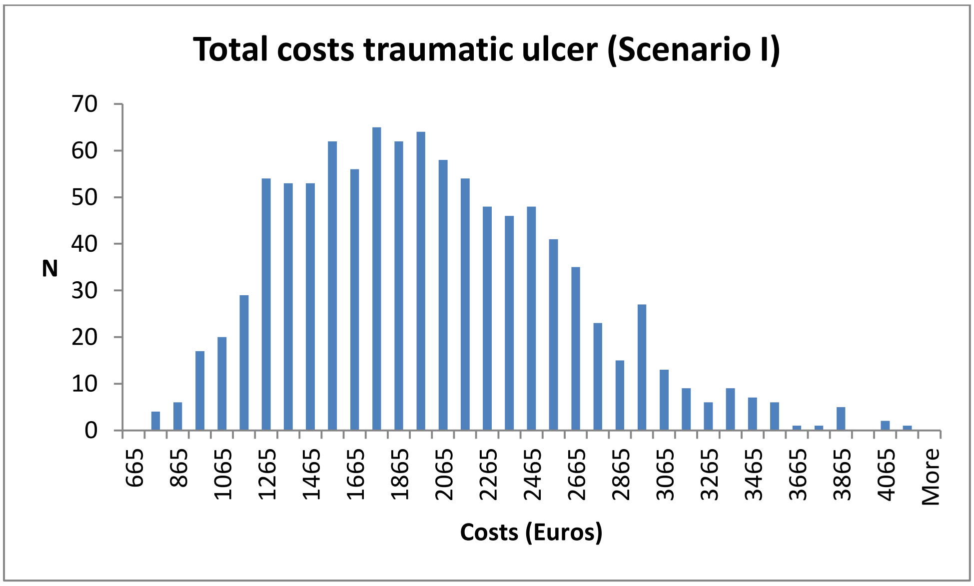

Figure 101 Histogram of average total costs of the traumatic ulcer (Scenario I, n=53).

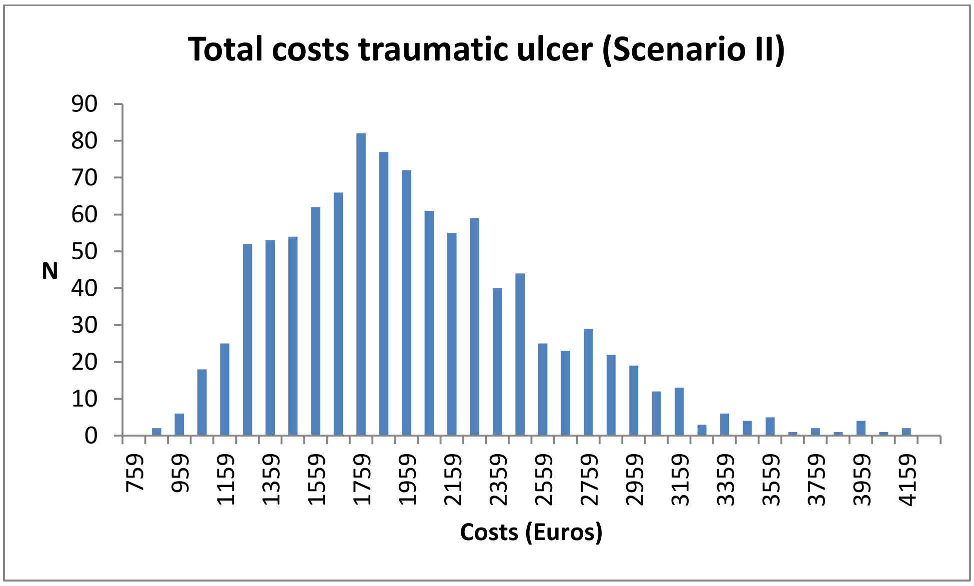

Figure 102 Histogram of the average total costs of the traumatic ulcer (Scenario II, n=53).

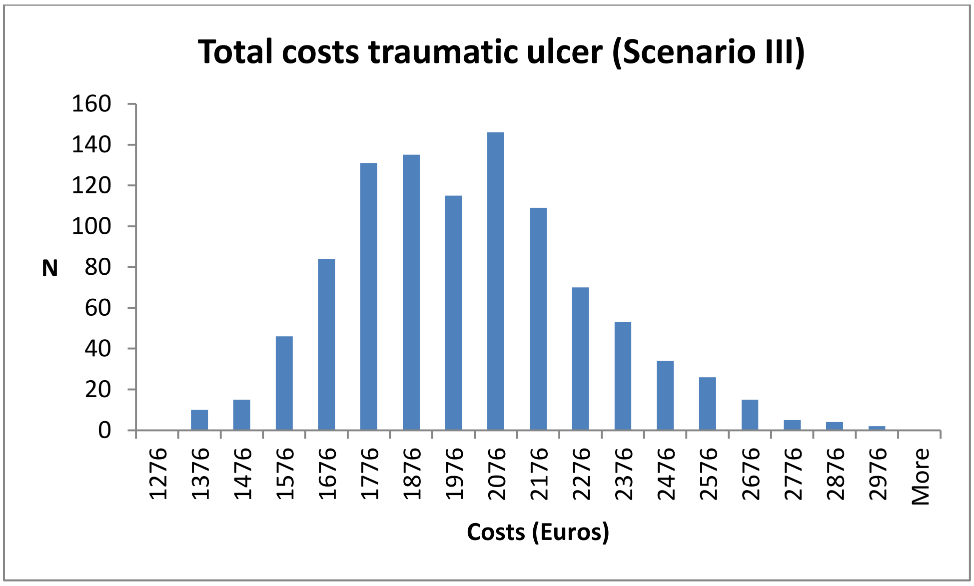

Figure 103 Histogram of the average total costs of the traumatic ulcer (Scenario III, n=53).

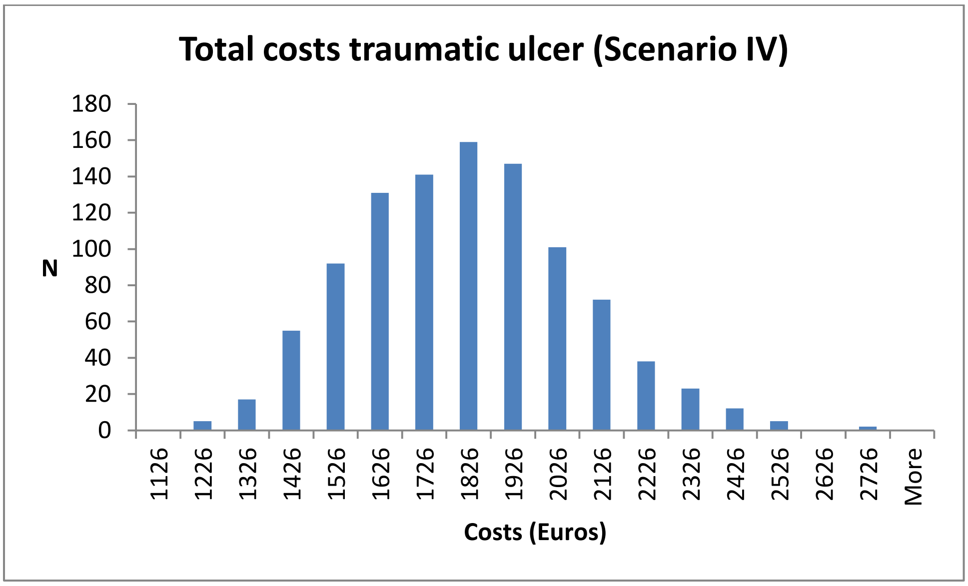

Figure 104 Histogram of the average total costs of the traumatic ulcer (Scenario IV, n=53).

Appendix Q: MSVT costs traumatic ulcer

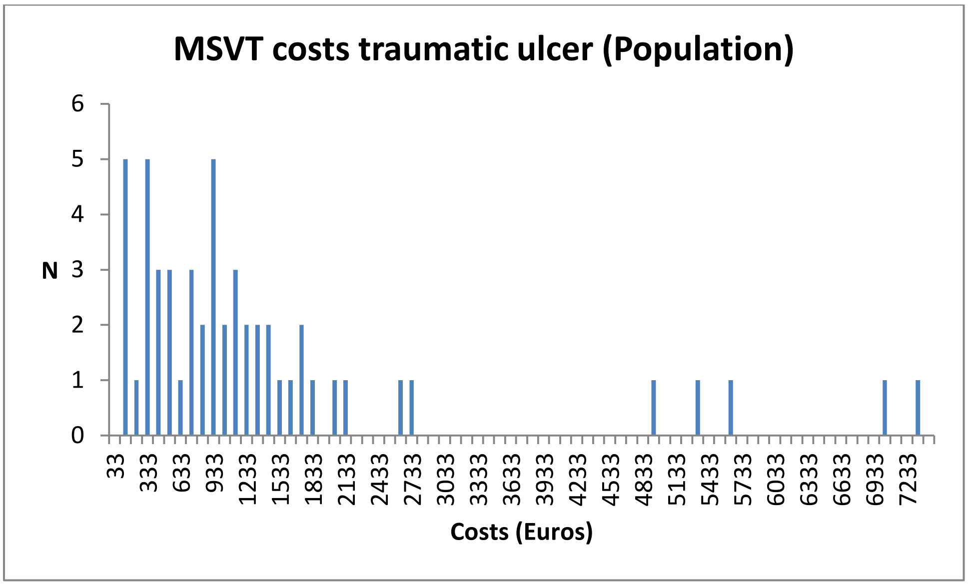

Figure 105 Histogram of the MSVT costs of the traumatic ulcer (Population, n=53).

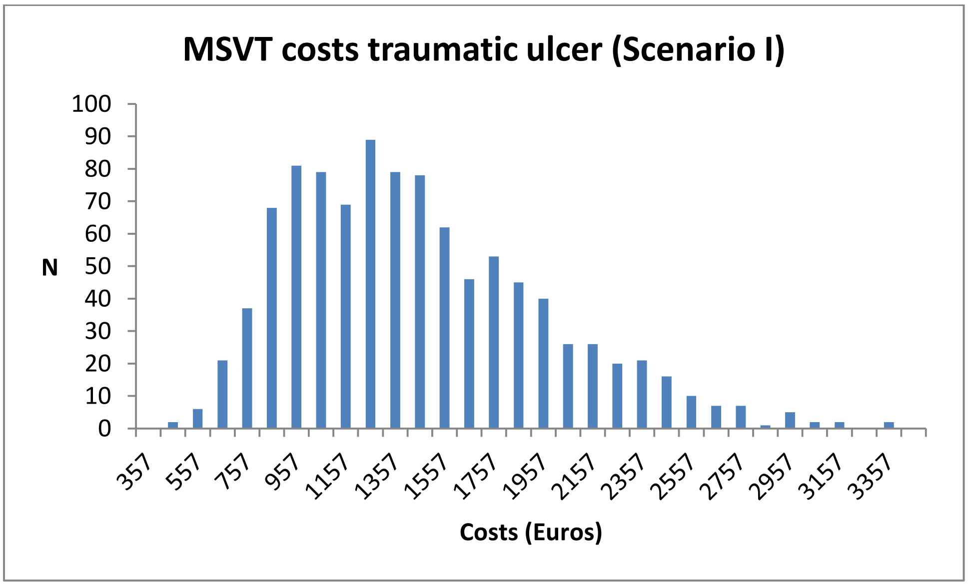

Figure 106 Histogram of the average MSVT costs of the traumatic ulcer (Scenario I, n=53).

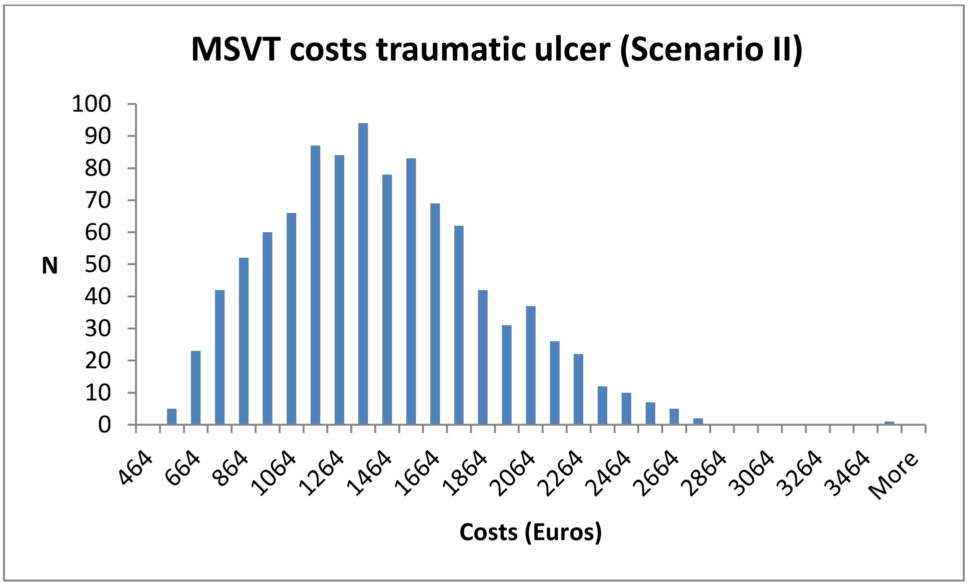

Figure 107 Histogram of the average MSVT costs of the traumatic ulcer (Scenario II, n=53).

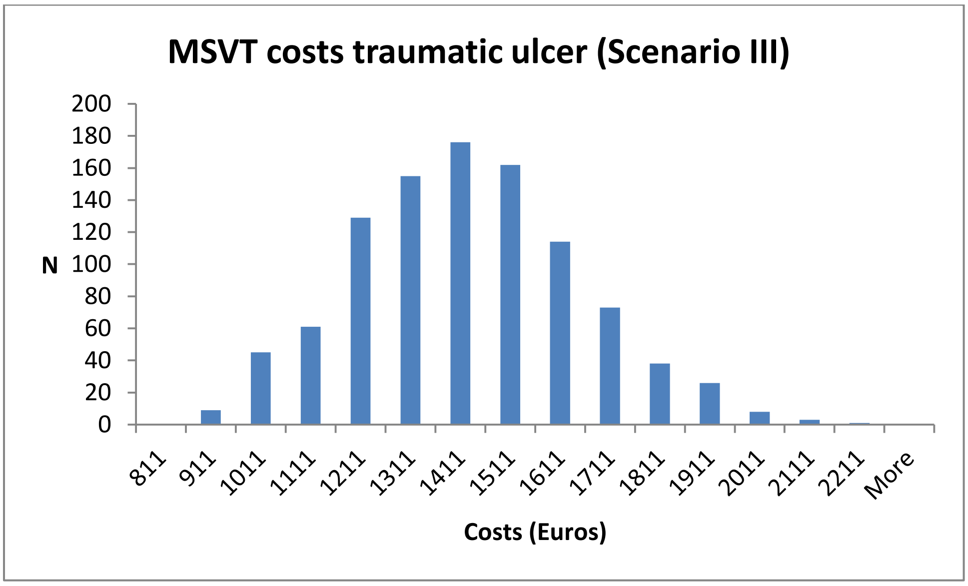

Figure 108 Histogram of the average MSVT costs of the traumatic ulcer (Scenario III, n=53).

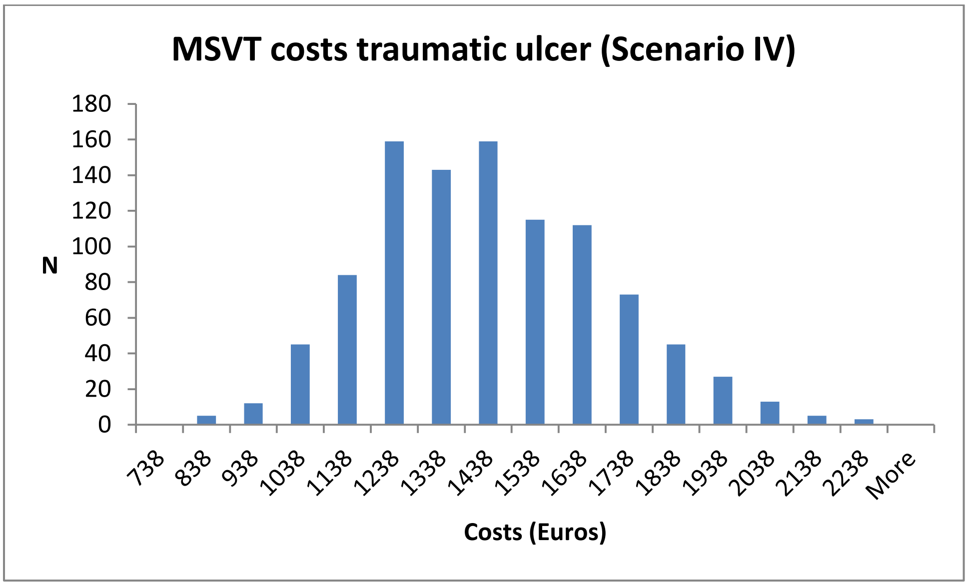

Figure 109 Histogram of the average MSVT costs of the traumatic ulcer (Scenario IV, n=53).

Appendix R: HLP costs traumatic ulcer

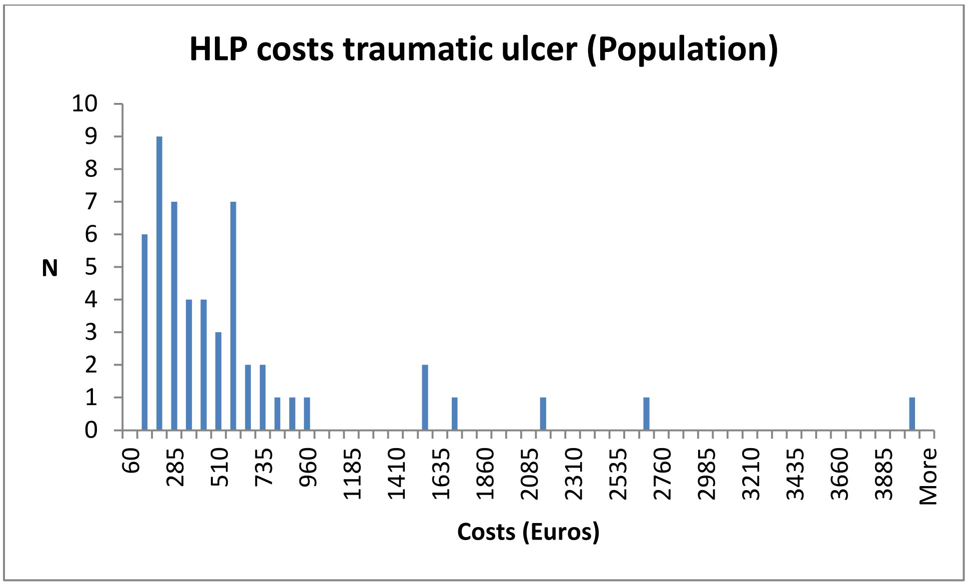

Figure 110 Histogram of the HLP costs of the traumatic ulcer (Population, n=53).

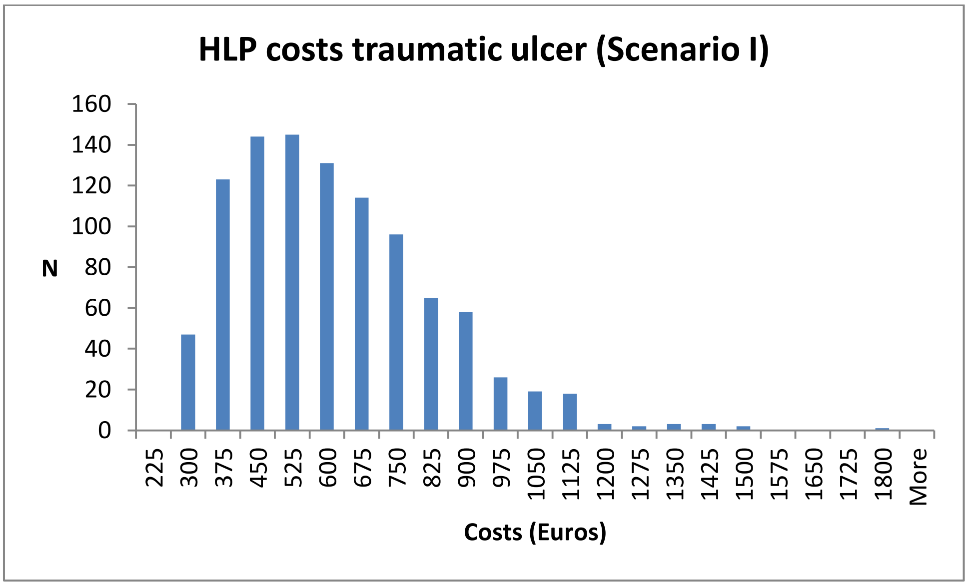

Figure 111 Histogram of the average HLP costs of the traumatic ulcer (Scenario I, n=53).

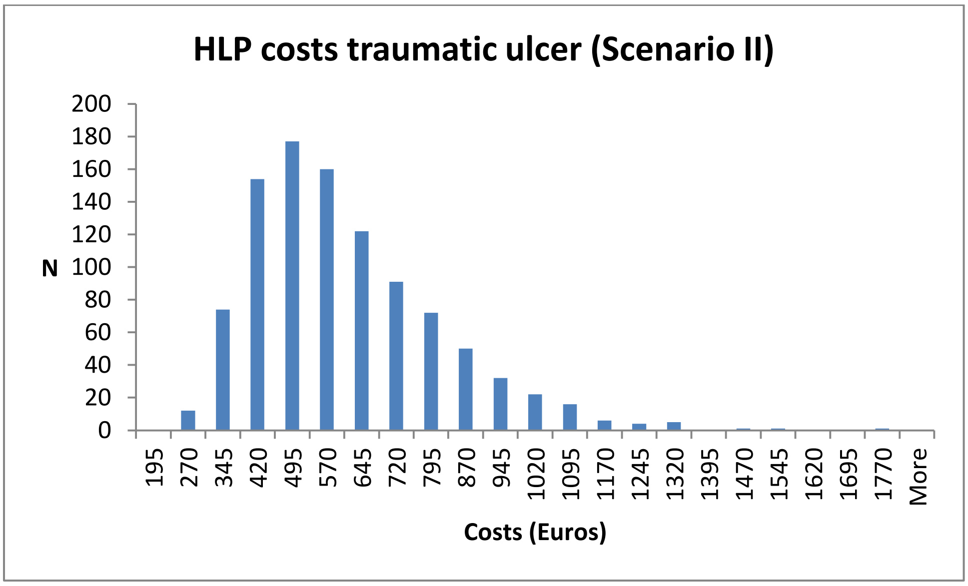

Figure 112 Histogram of the average HLP costs of the traumatic ulcer (Scenario II, n=53).

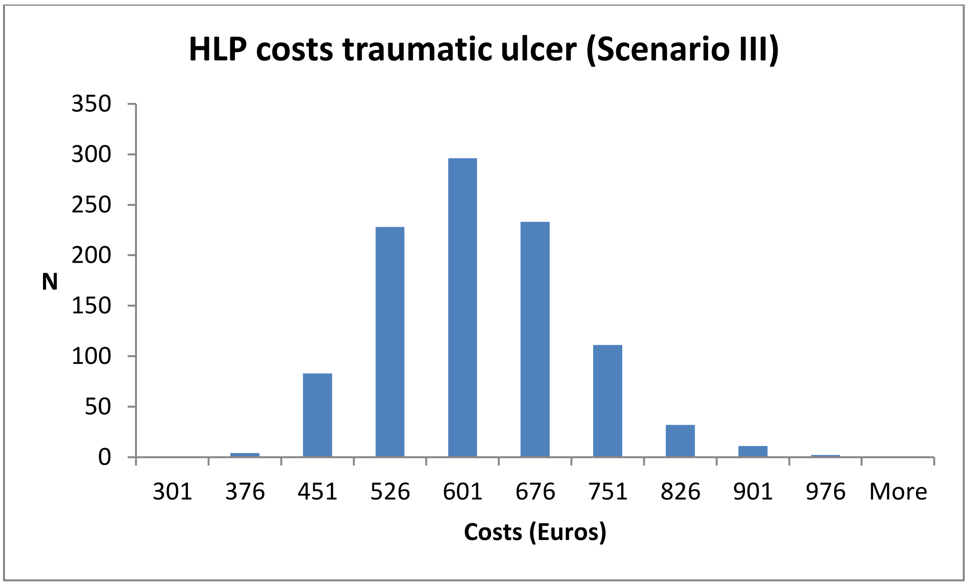

Figure 113 Histogram of the average HLP costs of the traumatic ulcer (Scenario III, n=53).

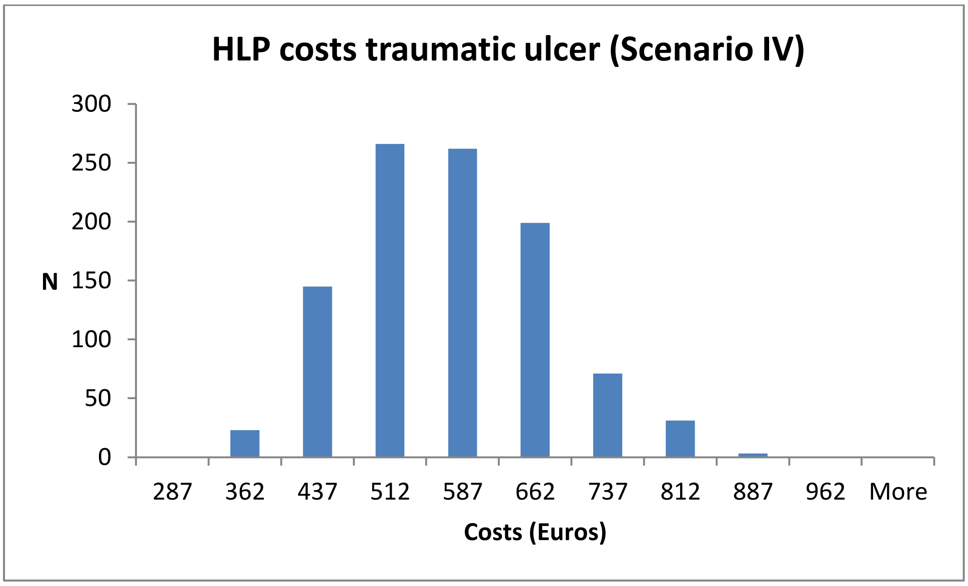

Figure 114 Histogram of the average HLP costs of the traumatic ulcer (Scenario IV, n=53).

Appendix S: Total costs venous ulcer

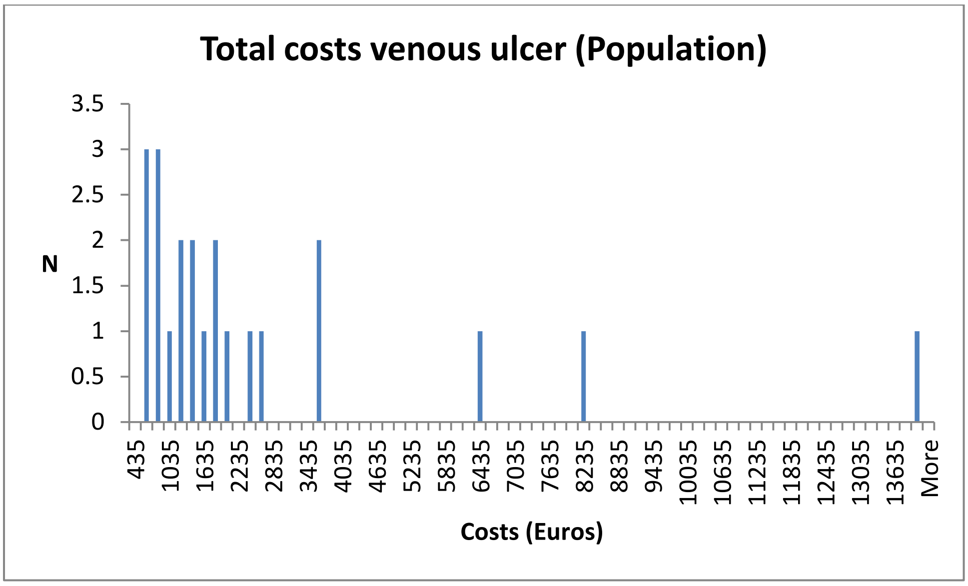

Figure 115 Histogram of the total costs of the venous ulcer (Population, n=22).

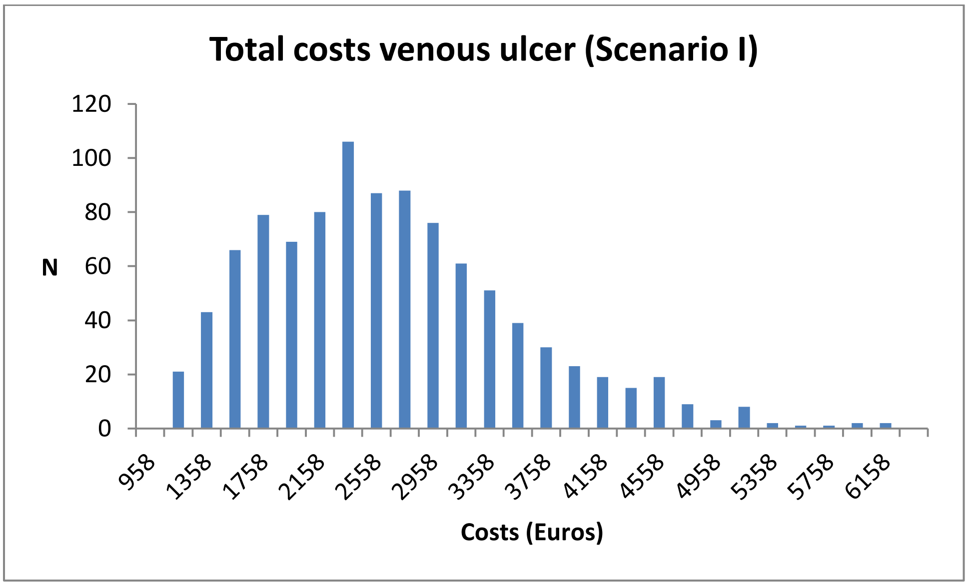

Figure 116 Histogram of the average total costs of the venous ulcer (Scenario I, n=22).

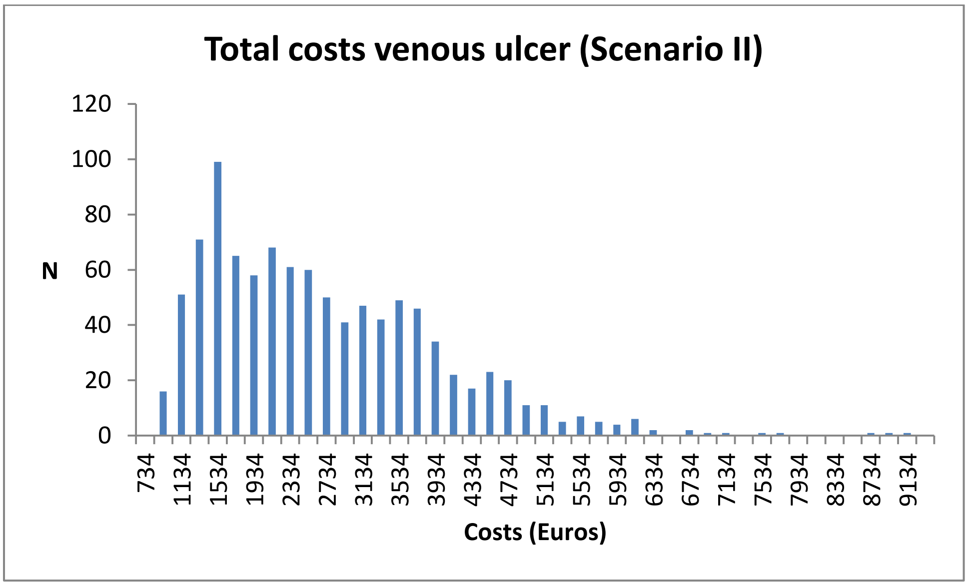

Figure 117 Histogram of the average total costs of the venous ulcer (Scenario II, n=22).

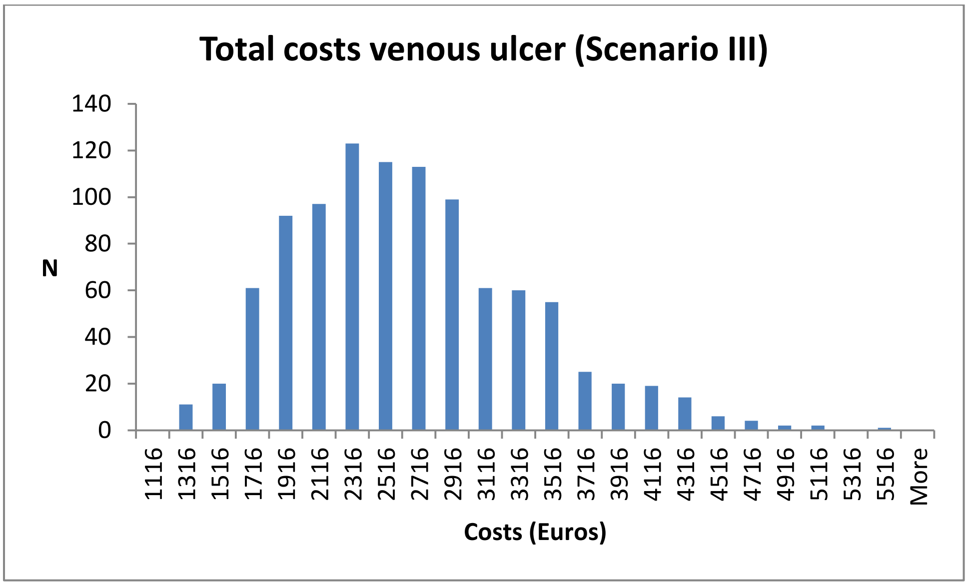

Figure 118 Histogram of the average total costs of the venous ulcer (Scenario III, n=22).

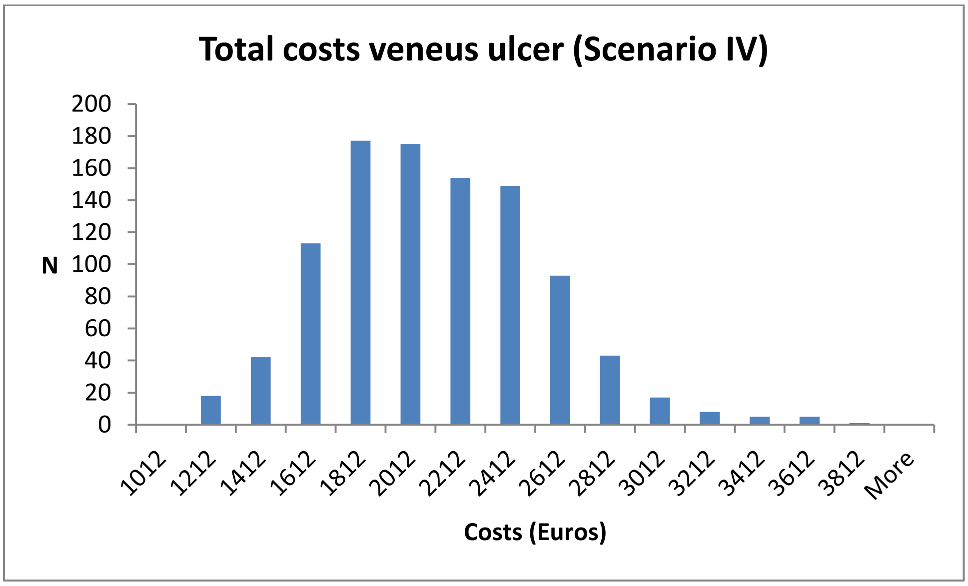

Figure 119 Histogram of the average total costs of the venous ulcer (Scenario IV, n=22).

Appendix T: MSVT costs venous ulcer

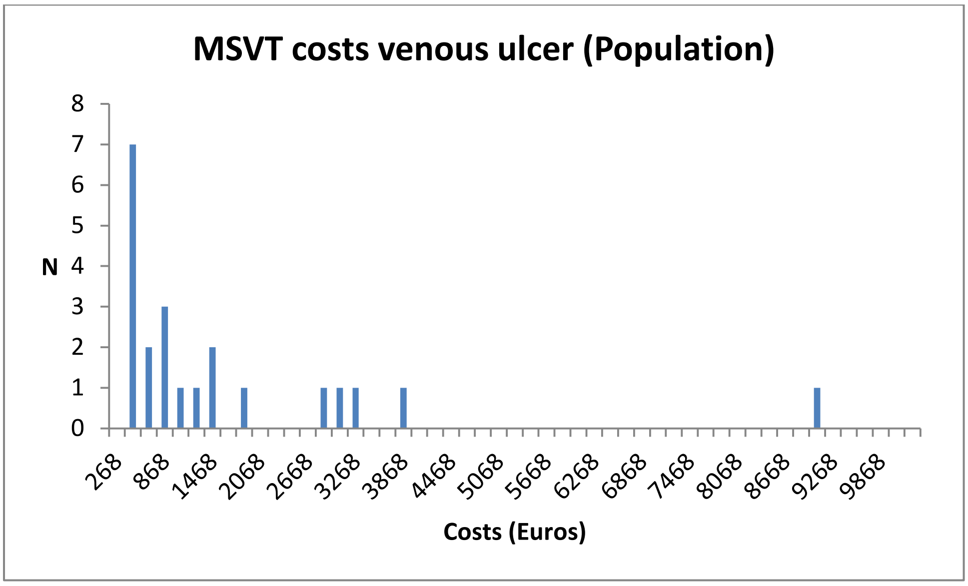

Figure 120 Histogram of the MSVT costs of the venous ulcer (Population, n=22).

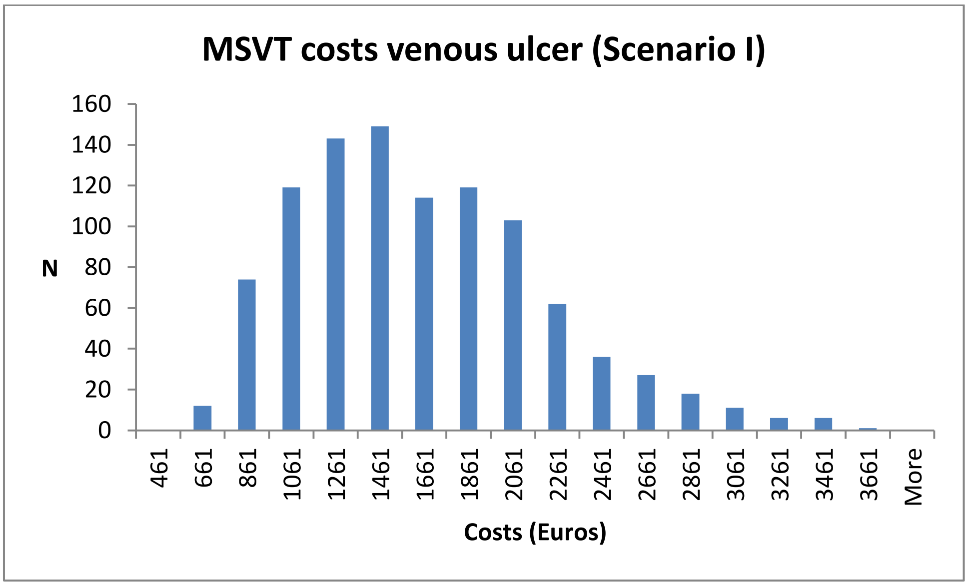

Figure 121 Histogram of the average MSVT costs of the venous ulcer (Scenario I, n=22).

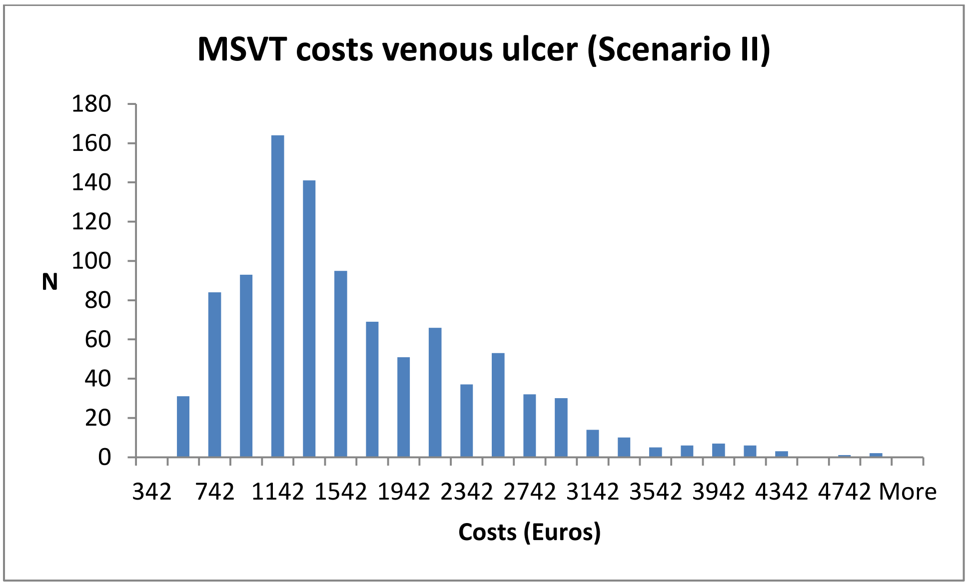

Figure 122 Histogram of the average MSVT costs of the venous ulcer (Scenario II, n=22).

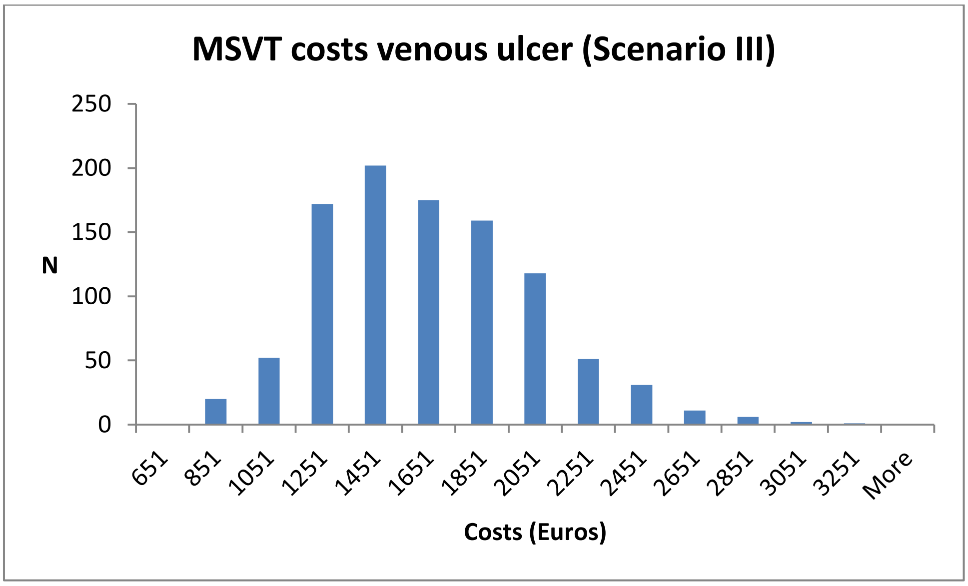

Figure 123 Histogram of the average MSVT costs of the venous ulcer (Scenario III, n=22).

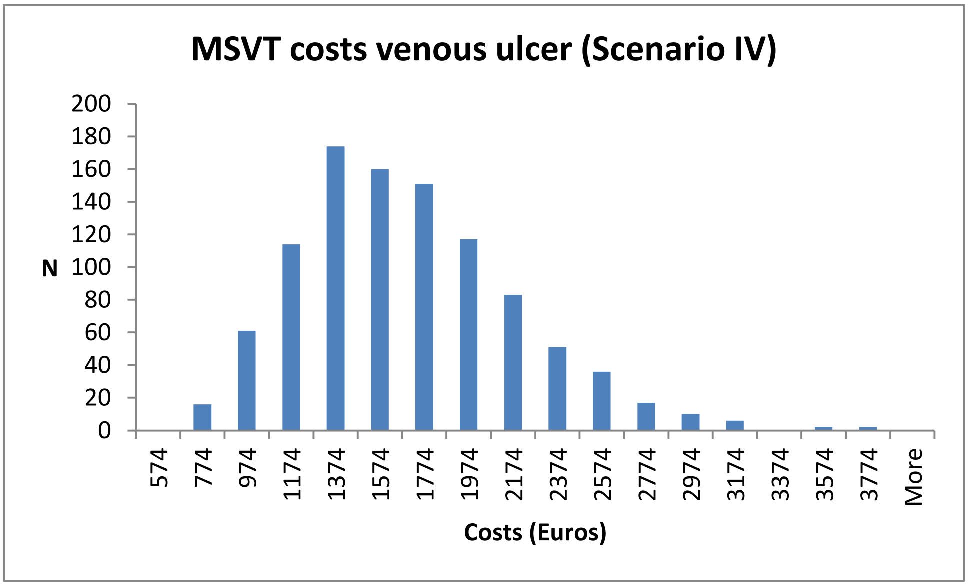

Figure 124 Histogram of the average MSVT costs of the venous ulcer (Scenario IV, n=22).

Appendix U: HLP costs venous ulcer

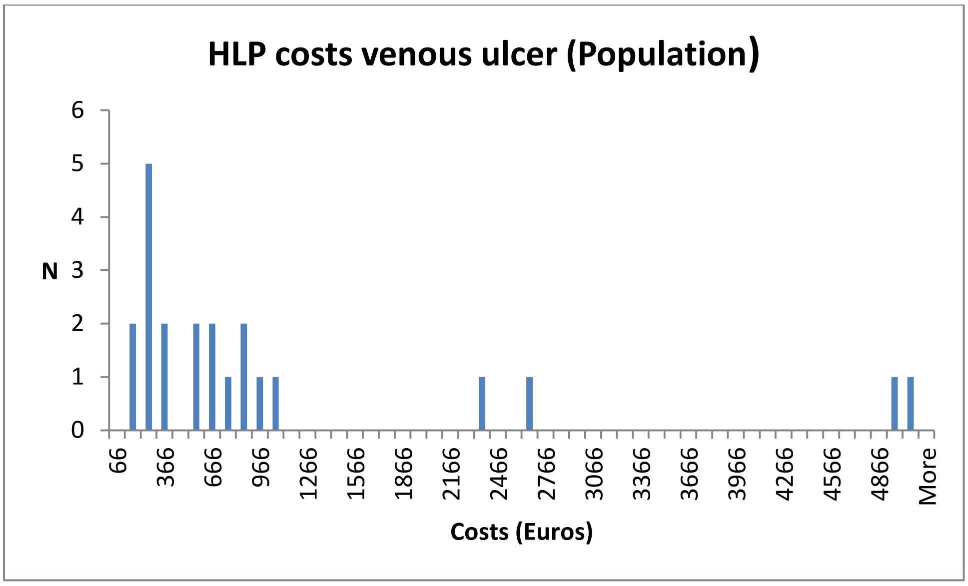

Figure 125 Histogram of the HLP costs of the venous ulcer (Population, n=22).

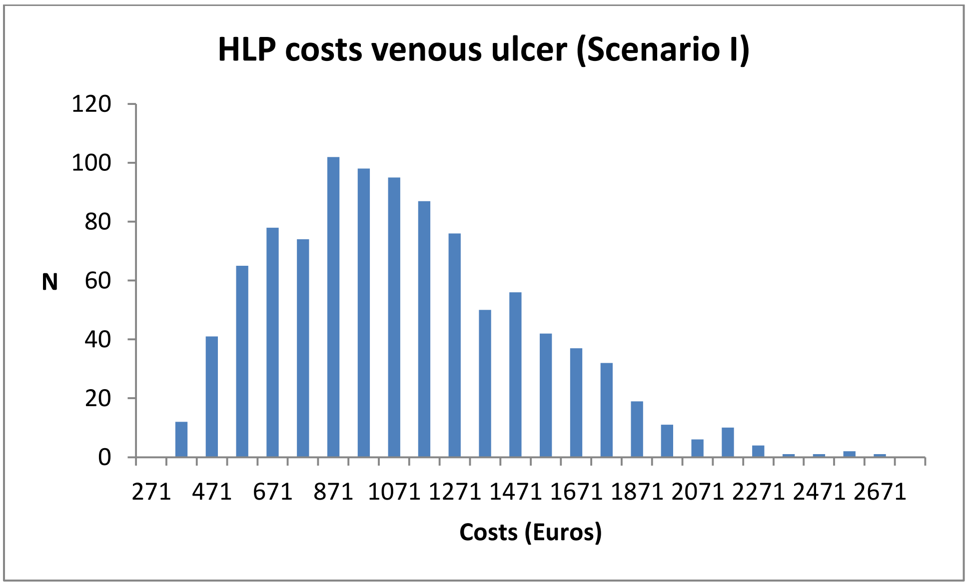

Figure 126 Histogram of the average HLP costs of the venous ulcer (Scenario I, n22).

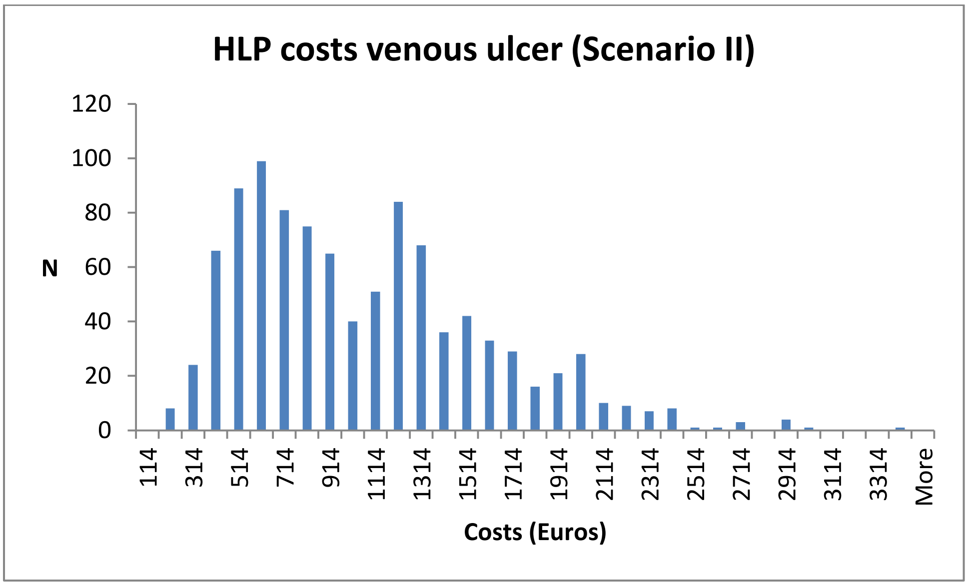

Figure 127 Histogram of the average HLP costs of the venous ulcer (Scenario II, n=22).

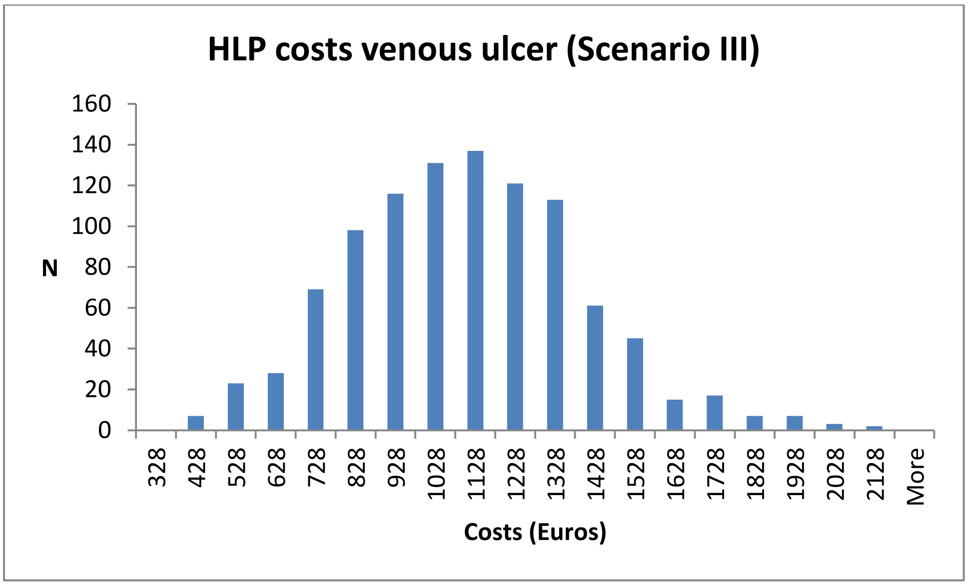

Figure 128 Histogram of the average HLP costs of the venous ulcer (Scenario III, n=22).

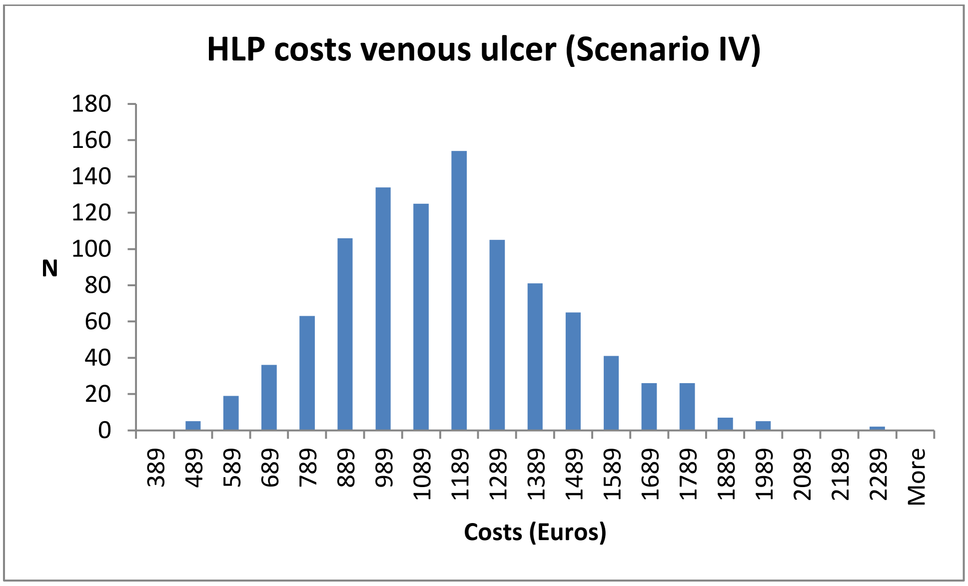

Figure 129 Histogram of the HLP costs of the venous ulcer (Scenario IV, n=22).