MS Dissertation
Health Economics

Cost-Benefit Analysis of Iceland's Search and Destroy Policy Against Methicillin-Resistant *Staphylococcus aureus*

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Supervisors: Professor Thorolfur G. Matthiasson and M.D. Olafur Gudlaugsson

Faculty of Economics

June 2013

HÁSKÓLI ÍSLANDS

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Abstract

Methicillin-resistant Staphylococcus aureus (MRSA) is a strain of the bacteria Staphylococcus aureus (SA). Methicillin is an antibiotic that is effective in treating infection caused by SA but is ineffective in treating MRSA infection. The cost of treatment and the mortality rate of MRSA infection is estimated to be higher than another strain of SA, Methicillin-susceptible Staphylococcus aureus (MSSA). In Nordic Countries and the Netherlands, health care authorities employ a Search and Destroy Policy/Program (SDP) to hinder the spread of MRSA within hospitals. However, the actual benefit from the use of SDP is almost unknown. The aim of this study is to estimate the societal cost and benefit of the SDP applied against MRSA in Iceland. The research method involves calculations based on a hypothetical scenario model. The incremental benefit of the program and the cost for each year over 50 years are calculated then these amounts are discounted to estimate the present value of the program. In Iceland, the net social benefit (NSB) of the SDP is worth a total of ISK 833m. The NSB of each healthy and saved life year is worth ISK 0.5m, with the internal rate of return of the program at approximately 11% for the base case. Scenario analysis indicates that in order for the NSB to be positive the ratio of MRSA infections out of all SA infection needs to be higher than at least 17.5% and the mortality rate for MRSA infected patients needs to be at least 15.0% to 20.0% higher than the rate for MSSA infected patients. The results therefore indicate that the NSB of the Icelandic SDP is positive but is subject to differences in the consequences when compared to MSSA at a given level. Recommendations are made regarding the importance and validity of using cost-benefit methods to improve decisions and effective policies within the health care system.

Keywords: Cost-Benefit Analysis, Methicillin-resistant *Staphylococcus aureus*

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This dissertation is dedicated to the memory of my grandmother,

Rósa Guðrún Stefánsdóttir

Author's Declaration

I declare that this dissertation is an original version, except where indicated by special reference in the text, and no part of this dissertation has been submitted towards any other degree.

Any views expressed in this dissertation are those of the author and in no way represent those of the University of Iceland. This dissertation has not been presented to any other university for examination either in Iceland or elsewhere. References to work of other authors are included at the end of this dissertation.

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List of Abbreviations

AE	Accident and Emergency
ALOS	Average Length of Stay
DIC	Department of Infection Control
CAI	Community-Acquired Infection
CBA	Cost-Benefit Analysis
ECDC	European Centre for Disease Prevention and Control
HAI	Healthcare-Associated Infection
IRR	Internal Rate of Return
MRSA	Methicillin-resistant *Staphylococcus aureus*
MSSA	Methicillin-susceptible *Staphylococcus aureus*
NSB	Net-Social Benefit
NSDP	Non Search and Destroy Policy/Program
OR	Odd Ratio
SA	*Staphylococcus Aureus*
SDP	Search and Destroy Policy/Program
SSTI	Skin and Soft Tissue Infection

1 Introduction

From a health-economics perspective, contagions are very interesting phenomena. One reason to consider this phenomenon is that it is possible to mitigate the negative externalities of an infection. Gwartney and Stroup (1992, p. 729) relate negative externalities to external costs and describe these as harmful effects of an individual's or a group's actions on the welfare of non-consenting secondary parties, which are not accounted for in market prices. The methods used to mitigate the spread of contagions and, consequently, the external costs associated with contagion infection, consist of applying aseptic operations, such as the isolation of infected people, and antibiotic treatments to cure infections.

1.1 Background

As described by Marcel et al. (2008, p. 897), Staphylococcus *aureus* (SA) can be found on skin and in the nasal cavities of about 30% of healthy people. In interview Kristjansson M.D. (personal communication, 2005), such colonization is not harmful to individuals as long as the bacteria do not transmit into certain areas, for example, into wounds or the blood. However, certain habitats, such as those found in hospitals, increase the likelihood of infections caused by SA bacteria. This habitat includes greater exposure to open wounds, patients are in close proximities, there is increased tactile contact, sharing of toilets, and the afflicted immune systems of the inpatients.

According to the review in Appendix A, bacteria have a unique biological ability to adapt to their environment. This trait is established throughout studies that have found that many strains of bacteria are immune to antibiotics because they have developed a "self-protection" mechanism wherein they change their genetic structures. The bacteria SA is one example of these adaptive bacteria, evident in the increased use of antibiotics during the 20th Century and the corresponding development of the strain named Methicillin-resistant Staphylococcus *aureus* (MRSA). This development is consistent with the findings of Schito (2006) who stated, "this organism (SA) has a remarkable capacity for adapting to new types of antimicrobial agents" (p. 7). By referring to the conclusions of authors such as Marcel et al. (2008, pp. 895-907), Witte et al. (1997, pp. 414-422), and Schito (2006, pp. 3-8), the definition of Methicillin-resistance is not perfectly

homogenous in terms of its biology. This is because the definition of MRSA includes bacteria with different clones in their genetic structures. The joint characteristic of MRSA is that the strain, as a whole, is immune to primary antibiotics.

According to Dryden et al. (2010, p. 3), MRSA is a common cause of Healthcare-Associated Infection (HAI) and places heavy clinical and financial burdens on hospitals around the world. Notably, health care authorities in different countries respond differently to the situation. According to Holzknecht et al. (2010, p. 4221), Iceland is among the Nordic countries and Netherlands which all apply a search and destroy policy (SDP) against MRSA within their health care institutions on a national level. This method includes a screening policy or screening program, precautions against infections, and eradication of MRSA in carriers in order to reduce the likelihood of transmission between people and further infections caused by that strain within the institutions. However, an economic evaluation of the costs and benefits has not yet been completed in Iceland so the actual cost and the actual benefit of the Icelandic policy is currently unknown by the policymakers.

1.2 Research Focus and Research Objective

As noted above, Iceland is one of the countries that follows the SDP against MRSA. The grand size and influence of Landspitali University Hospital (LUH) compared to other institutions within the Icelandic health care system, supports the assumption that this hospital's actions and policy are illustrative of the "national" fight against MRSA. According to the Ministry of Welfare (Hospitals and Health Care Institutions, 2012), LUH is the main hospital of Iceland and serves both as tertiary hospital for the whole country as well as a university hospital for students in all main health care professions. Data from Statistic Iceland (National accounts and public finance, 2013), (National accounts and public finance, 2013), and LUH (About Landspitali, 2013) reveals that LUH is prominent and is the largest health care institution among all health care institutions in Iceland. It accounts for around 2.5% of the country's gross domestic product and in 2012 it comprised approximately 30% of the total public expenditure in the health care system.

As LUH applies the SDP, the hospital consumes resources to prevent MRSA transmission among its patients and personnel. LUH operates the Department of

Infection Control (DIC), which operates on a premise expressed in Dryden et al. (2010, p. 3) that one of the important tasks of health care institutions is to prevent patients and personnel from picking up any contagions within health care establishments. According to LUH's policy (Infection Control, 2009), the main objectives of the DIC are to follow up with antisepsis, control and register infections, and share knowledge in order to educate LUH's personnel about aseptic operations and infections. Further, another significant objective is to control possible routes of infection. As its overall role, the DIC manages and controls the SDP applied in LUH.

Immunity is not only a biological or medical phenomenon, but also an economic one. As discussed above, negative externalities consist of contagions' harmful, but not priced, effects of transmission. Further, as discussed in Appendix B, the use or misuse of antibiotics might lead to an antibiotic immunity among bacteria, which in turn can be defined as an externality of antibiotic use. Therefore, some of the very actions taken to *prevent* externalities, i.e., to hinder the spread of transmission by bacteria, actually entail *creating* externalities by increasing immunity against antibiotic medicine. This immunity can have a costly result by leading to unsuitable methods being used to treat infections. As Schito (2006, p. 3) and Holzknecht et al. (2010) state: the consequence of SA (and therefore MRSA) can be described in terms of "morbidity", "mortality", "health care cost", and "socioeconomic cost" (p. 4221).

According to data from Statistics Iceland (National accounts and public finance, 2013), the expenditure in the Icelandic health care system is mostly paid by the state. The public expenditure to health care services in the year 2012 totalled 7.2% of the Gross Domestic Product while the household expenditure totalled 1.8% of the Gross Domestic Product. Therefore, the state paid around 80% of the total health care expenditure in Iceland for the year 2012. In accordance with this finding, by using data in LUH's annual financial statement for the year 2012 (Database, 2013), it is estimated that the hospital's clients paid around 10.3% of LUH expenditures.

It is a well-founded principle in economic literature that health care programs should be evaluated in a world of scarce or limited resources. Brent (2003, pp. 3-4) notes that we have to choose between alternatives in health care services due to limited resources. Further, Drummond et al. (2004, pp. 8-9) discusses the importance of

economic evaluation, first, in order to identify relevant alternatives, second, to recognize that different viewpoints can create different results and, third, to determine the magnitude that a single program may have on costs and benefits.

Further to the above discussion, the implementation of the SDP against MRSA in Iceland raises many considerations. First, it is understood that countries and hospitals "choose" between two different strategies regarding MRSA; some countries choose to "search and destroy" MRSA while other countries do little or nothing to fight against it within the walls of their hospitals. From an economic perspective, the fact that some choose not to implement a SDP provokes the question of whether or not LUH *should* fight against MRSA as it currently does. Second, on must consider if the activity of the DIC is beneficial to LUH from a sociological perspective. Third, the external cost of immunity is an interesting economic phenomenon, which can, and should, be estimated at some point. Fourth, the use of taxpayer money within the hospital demands some analysis of the benefit that patients receive from the use of preventive measures. Finally, there is the question of whether the current order of prioritisation in expending funds through measures, such as the SDP, is justifiable compared to possible alternative programs within the hospital. All of these thoughts are directly or indirectly connected to the following research question: **What is the cost-benefit ratio of the SDP against MRSA that is currently implemented at LUH?**

The SDP as a combat method against MRSA within hospitals is analogous to "building a firewall" against this strain of bacteria, but it may not realistically be the best option if the prevalence[1] and incidence[2] of MRSA infections increase. Therefore, this essay includes an exploration into scenario analyses pertaining to the research question. The objective of this thesis is therefore to estimate the cost-benefit ratio of LUH's search and destroy strategy against MRSA. My intention is to estimate the cost of the present policy and to make a cost comparison to one of the alternative options, specifically, the cost of doing "nothing".

[1] See the definition of this concept in the Glossary.

[2] See the definition of this concept in the Glossary.

1.3 Value of the Dissertation

The result of this research is valuable for the managers at LUH as it will inform them of the cost and the benefit of the SDP against MRSA. This dissertation will provide them with information which they can use to improve decisions regarding policy prioritisation and, therefore, ways in which they can make more efficient use of the hospital's scarce resources. In addition, this may provide a benchmark by which foreign hospitals can measure the costs and the benefits of this preventive activity against that of their own policies. The value of this research for the Icelandic health care system and the hospital is significant given that economic research into the cost-benefit ratio of the system and its institutions is currently lacking.

1.4 Reflexivity[3]

Indeed, the reader should be aware of the author's background because it influences the choice of subject for this dissertation and the approach and methods used to answer the research question, including the interpretations of the results and conclusions. I hold a B.Sc. degree in economics and a M.Sc. degree in business administration. Furthermore, I was an assistant director within the division of Finance at LUH between 2000 and 2006 and, at that time, my interest for the subject of this dissertation was incited. Moreover, it is a personal belief that efficient methods in (health) economics should be more widely used within the Icelandic health care sector. Valuable research and knowledge could improve the hospital's decision-making process in this regard.

Due to my background (including education, work experience, and personal opinions), there is the chance of certain biases. For example, the subject of this thesis pertains to the activity of LUH, however, I am not educated as a health care professional, nor do I have extensive experience as an inpatient, which creates a possibility that important factors may be excluded from this approach, the discussions, and/or the conclusions. That stated, the same circumstances creating that possible bias

[3] This section is a revised version of the same section in my first M.S. dissertation in Business Administration.

might also, in turn, reduce “existent bias” as I am an outsider presenting a different viewpoint. This more diverse point of view is implemented to tackle the dissertation subject.

2 Literature Review

In order to answer the research question, further explanation of the subject matter is required as well as a review of the related literature. Specifically, there is a need to identify the possible biological/medical consequences of infection by MRSA, the epidemiology of MRSA, and the past research completed in efforts to evaluate MRSA from an economics perspective. Lastly, emerging issues and developments pertaining to this subject are discussed further.

2.1 Clinical Consequences of SA Infection

As discussed in the Introduction, SA bacteria, referring also to the MRSA strain, are harmless to healthy individuals who carry them because MRSA (like other bacteria) is only harmful to the health of individuals in certain conditions. Wenzel and Perl (The significance of Nasal Carriage of Staphylococcus Aureus and the Incidence of Postoperative Wound Infection, 1995, pp. 13-14) support this conclusion by describing how SA infection can occur when there is a break in the dermal surfaces, for example, by vascular catheterisation. The standard means of SA infection is from nose via hand carriage to sites of body where the dermal surface is contacted. In other words, MRSA infects the human body by interception on skin or mucous membranes.

Marcel et al. (2008, p. 896) notes that invasive procedures are major risk factors for Healthcare-Associated Infections (HAI). Dialysis, surgery, and a generally impaired immune system increase the probability that one will become infected.[4] Furthermore, Laupland et al. (2003, p. 1454), found that the main risk factors for invasive SA acquisition include being of a higher age, being of the male sex, staying in a hospital, undergoing dialysis, having HIV infection, staying in intensive care units, and having multiple traumas.

The risk (or the risk-ratio) of being infected with MRSA within hospitals, depends mainly on three interrelated factors: the prevalence or the distribution of MRSA within the population as a ratio of SA, the clinical procedures or habits within the hospital, and the clinical status of the patients. This statement is supported by Davis et al. (2004, p.

[4] A more detailed description of the progress of SA infection is given in Appendix C.

776) who conclude that MRSA colonization increases the risk for MRSA infection and Humphreys et al. (2009, p. 124) who conclude that the success of controlling MRSA depends, amongst other factors, on attitude, professionalism, and standard preventive measures. Finally, if the patient has no interception on skin or does not receive any service that demands an "invasive" operation then the risk of being infected by MRSA is low.

As discussed in the Introduction, SA is common causes of Healthcare-Associated Infections (HAI) and the means of infection are described previously. Dryden et al. (2010, p. 3) describes the particular *types* of infections such as skin and soft tissue infections (SSTI), pneumonia (in lungs), bacteraemia (in blood), endocarditis (in heart valves), osteomyelitis (in bones), prosthetic joint infections, and catheter related infections. In research conducted by Diekema et al. (2001, p. 114) the amount of SA infection by body site and geographical region was estimated. The result of the study is described in Table 1:

Table 1. Percentage of SA pathogen as a cause of infection by body site and geographical region from the year 1997 to the year 1999.

Region/Site of infection	USA	Canada	Latin America	Europe	Western Pacific	All Regions
Bloodstream	25.3%*	19.2%*	20.6%*	18.6%**	21.6%*	**22%***
Lower respiratory tract	25.5%*	22.8%*	21.6%**	20.4%*	20.3%**	**23.2%***
Skin/soft tissue	41.6%*	43.9%*	31.9%*	37.1%*	46.8%*	**39.2%***

*Rank of prevalence of SA compared to other pathogens; 1
*'Rank of prevalence of SA compared other pathogens; 2

Table 1 shows that SA is the main agent for bloodstream infection, lower respiratory tract infection, and especially for SSTI. This finding is supported by Naber (2009) who states that "staphylococcus aureus is a major cause of bacteraemia, and S. aureus bacteraemia is associated with higher morbidity and mortality, compared with bacteraemia caused by other pathogens" (p. 231).

Klein, Smith and Laxminarayan (2007, pp. 1842-1843) report that in the United States of America in the year 2005 there were 477,927 SA diagnosed infections and, of those, 278,203 were MRSA infections. There were 11,406 deaths caused by SA infections and 6,693 of those deaths were caused by MRSA specifically (these numbers represent cases wherein SA/MRSA was coded as the primary diagnosis). Furthermore, deaths in the year 2005 accompanying any diagnosis code that was SA related were estimated at 29,164

(6.1%)[5] and deaths in which any diagnosis code was MRSA-related were estimated to be 17,260 (6.2%), equalling a total of 46,424 deaths. However, the authors note that the number of deaths related to MRSA does not indicate an increasing trend of SA/MRSA infection. On the contrary, deaths accompanying any diagnosis code that is MRSA-related actually decreased about 30% from the year 1999 to the year 2005. The number of deaths caused by hospital acquired SA and MRSA is not reported in their study.

Asgeirsson et al. (2011, p. 513) estimated the incidence and mortality rate caused by SA in the period of 1995 to 2008 in Iceland. The authors determined that the all-cause, 30-day mortality rate for individuals was 22.2% for the years 1995 to 1999, 18.7% for the years 2000 to 2004, and 11.4% for the years 2005 to 2008. Furthermore, the all-cause, 365-day mortality was 38.9% for the years 1995 to 1999, 32.8% for the years 2000 to 2004, and 28.2% for the years 2005 to 2008. The mortality rate per 100,000 in the population was 5.0 individuals, 4.3 individuals, and 3.3 individuals for these periods, respectively, calculated by using 30-day mortalities. The authors also point out that bacteraemia caused by MRSA constituted none of the death cases over the period of 1995 to 2008.

As revealed, the bacterium SA and its strain MRSA can seriously affect the health of numbers of individuals, particularly if the bacteria have a high rate of prevalence. The overview above indicates that the clinical consequences of MRSA infection are significantly extensive. MRSA infections affect both the individuals and the society to a substantial degree if the pathogen is “allowed” to be part of hospitals’ ecosystems. The main difference between the clinical consequences of infection by SA and MRSA lies in the fact that SA can be treated with primary antibiotics with a relatively low cost whereas MRSA is immune to primary antibiotics. Therefore, it is difficult and costly to cure infections caused by MRSA. However, as noted above, the mortality rate associated with SA and MRSA seems to be decreasing in recent years.

[5] Mortality rates are shown, given that one has SA or MRSA infection, respectively.

2.2 Epidemiology of MRSA

Examining the epidemiology of MRSA demonstrates the scale of the problem and aids in determining possible preventive measures. Gordis (2004, pp. 3-4) explains that epidemiology is used to identify the cause of disease and its risk factors, to find out the extent of disease inside the population, and study the prospect and evolution of disease. Further, epidemiology can be used to evaluate methods of dealing with disease (e.g., preventive measures or medical treatments) as well as to assign a relevant method for policy-making and other decisions.

For the purpose of this thesis, the main epidemiological focus is on review of the extent of the MRSA strain inside a population or health-care institution in order to evaluate the scale of the problem and calculate the cost-benefit of LUH's SDP. However, as noted above, other dimensions of epidemiology will also be examined within the scope of this review. In accordance with the main subject of this dissertation, first, the distribution of MRSA is reviewed, followed by reviews of the incidence of infections caused by MRSA and SA.

2.2.1 Distribution of MRSA – The European Image

As noted in the Background section above, Marcel et al. (2008, p. 897) explained that SA can be found on skin and in the noses of approximately 30% of healthy people, i.e., 30% of healthy people in the population are colonised by SA and/or MRSA. However, the exact prevalence of SA, and therefore MRSA, is unknown amongst the general population because, as Wenzel and Perl (1995) state, "the prevalence of nasal carriage varies widely depending upon the population" (p. 13). The authors further note that the prevalence of SA in nares is from 10% to 15% amongst healthy people, from 20% to 35% in hospital personnel, and even higher in some patient groups. Gorwitz et al. (2008, pp. 1226, 1229) studied the changes in the prevalence of nasal colonization with SA in the U.S.A. from 2001 to 2004. They determined that the prevalence of colonization with SA decreased from 32.4% in 2001–2002 to 28.6% in 2003-2004, but the prevalence of colonization with MRSA increased between these periods. Additionally, colonization with MRSA was associated with certain variables, for example, males exposed to health care institutions have been found to be particularly susceptible. Den Heijer et al.

(Editor's Choice, 2013) determined that the prevalence of SA within nine European countries differs from 12.1% in Hungary to 29.4% in Sweden.

The European Centre for Disease Prevention and Control (ECDC) publish data regarding the number of MRSA isolates samples and the ratio of MRSA isolates out of total SA isolates (from blood and spinal fluid) which are collected yearly throughout European countries (Susceptibility of Staphylococcus aureus isolates to Methicillin in participating countries in 1998 - 2011, 2013). While it might be tempting to use this data set as an indication of the prevalence of MRSA, for many reasons it is not appropriate, mainly because the sampling method varies considerably between the participating countries.[6] Therefore, the ratio of MRSA isolates of all SA isolates and the number of participating countries in 2000 to 2011 is used to describe the estimated distribution of MRSA as the following Figure 1 depicts (European Centre for Disease Prevention and Control, 2013):

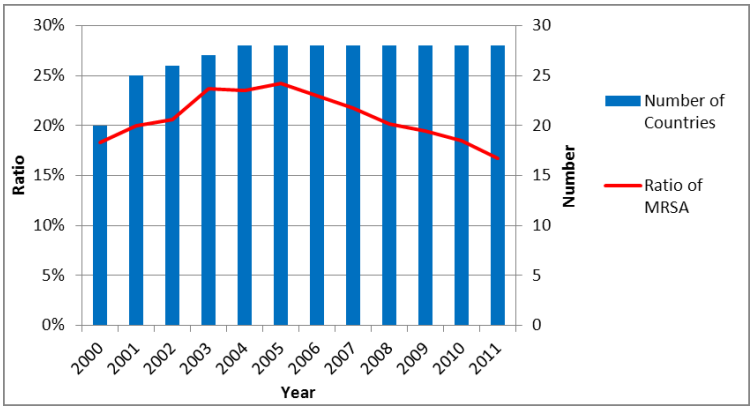

Figure 1. Ratio of MRSA of all SA isolates and number of participating countries in 2000 – 2011.

[6] According to the homepage of the European Centre for Disease Prevention and Control: (2013) *The data have been collected at the national level under the responsibility of each participating country. The laboratories in the countries serve a variety of health-care institutions (e.g. university or specialised hospitals; general and district hospitals; rehabilitation centres; nursing homes). Sample sizes and coverage may vary considerably between countries. The number of isolates reported per country to EARS-Net can vary substantially due to large variations in the number of inhabitants or reporting laboratories. To avoid extreme values, country data are only shown on maps if they are based on at least 10 isolates. When using the map function in the interactive database it is advised to examine the exact numbers listed in the underlying tables* (Susceptibility of Staphylococcus aureus isolates to Methicillin in participating countries in 1998 - 2011).

This figure indicates that the MRSA ratio of SA isolates was increasing from the year 2000 to the year 2005 but declined from the year 2005 to the year 2011 across Europe. By the year 2011, the ratio of MRSA isolates out of all isolates is distributed in the following manner amongst the participation countries (2013, p. 205):

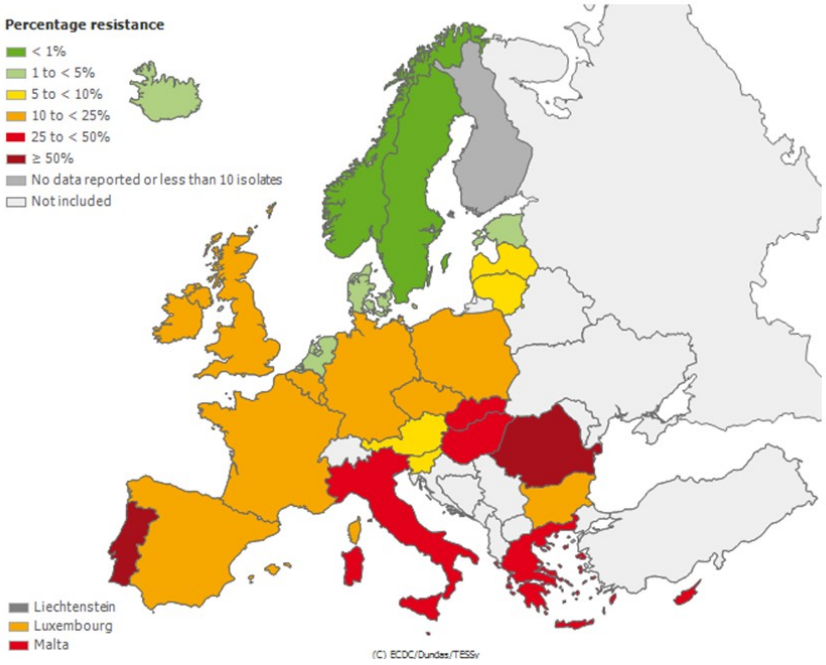

Figure 2. Profile of MRSA isolates out of all SA isolates by participating countries within Europe in the year 2010.

As Figure 2 shows, there is considerable difference in the ratio of MRSA isolates out of SA isolates amongst the participating countries. By clustering countries in four groups according to their rank by order of the ratio of MRSA isolates out of SA isolates, the following demographic percentages are determined:

Table 2. Clusters of countries by MRSA isolates out of all SA isolates of MRSA in 2011.

	0%-6%	7% - 17%	20% - 26%	38% - 55%
Country	Norway	Slovenia	France	Italy
	Sweden	Austria	Luxembourg	Greece
	Denmark	Latvia	Bulgaria	Cyprus
	Netherlands	United Kingdom	Spain	Malta
	Estonia	Czech Republic	Ireland	Romania
	Iceland	Germany	Poland	Portugal
	Lithuania	Belgium	Slovakia	
			Hungary	

Iceland has one of the lowest ratios of MRSA isolates out of all SA isolates but, referring to information provided by Holzknecht et al. (2010, p. 4221) Iceland is among the Nordic countries and Netherlands which are countries that apply the search and destroy method against MRSA within their health care institutions. Therefore, the profile in Table 2 supports Holzknecht et al.'s (2010, p. 4221) conclusion that the SDP contributes to (constant) low MRSA incidence. Furthermore, Tacconelli (2009, p. 32) refers to Bootsma et al. who concluded that screening for MRSA and isolating carriers is effective and could in fact reduce the prevalence of MRSA to below 1% in high endemic settings. However, this conclusion requires further consideration because, as Tacconelli discusses (2009, p. 33), there is a lack of evidence regarding the clinical effectiveness or cost effectiveness of active surveillance cultures. Further, not everyone is screened who is admitted to a hospital because it does not seem to be cost effective, instead it is deemed more effective to use targeted screening.

The discussion above reveals that no general inference can be made about definitive distributions of MRSA because the spread of the bacterium depends on many factors such as prescriptions, surveillance culture, SDP, genetic adaptation, and, possibly, the general infrastructure of the health care system. Furthermore, while there is evidence regarding the effectiveness of the SDP, the evidence is not absolute.

2.2.2 Distribution of MRSA – The Icelandic Image

According to the ECDC, the development of the ratio of MRSA isolates out of SA isolates in Iceland from the year 2000 to the year 2011 is as follows (European Centre for Disease Prevention and Control, 2013):

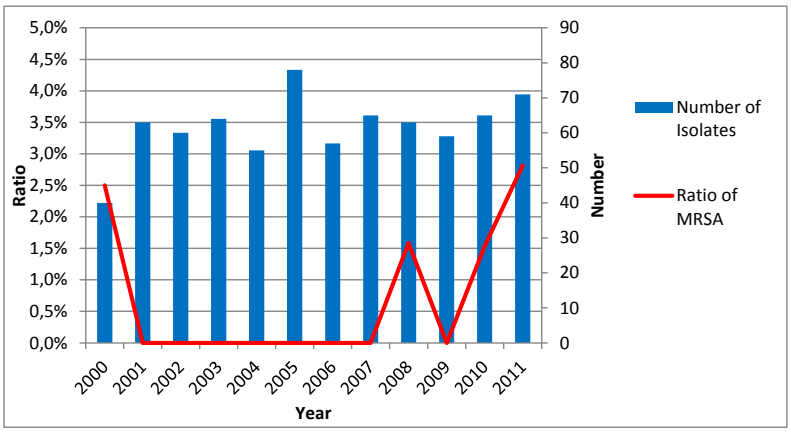

Figure 3. Profile of MRSA isolates out of all SA isolates in Iceland in the years 2000 – 2011.

Holzknecht et al. (2010, pp. 4222-4223), reports that altogether were 226 individuals infected and colonised by MRSA from the year 2000 to the year 2008. Of those, 135 (60%) were infected and 91 (40%) were colonized. By summarizing the authors' results further, the following depicts the statistics for the epidemiology of MRSA in Iceland in the years 2000 to 2008:

Table 3. Descriptive statistics for epidemiology of MRSA in Iceland from the year 2000 to the year 2008.

Variable	Number	Percent	Variable	Number	Percent
Median Age	44		**Outbreaks - Overview**		
Position			Health Care-Associated Outbreaks:		
Health Care Workers	32	14%	Inpatients in Outbreak 1	10	4%
Public	194	86%	Inpatients in Outbreak 2	25	11%
Origin of Isolates			Family Member in Outbreak 2	1	0%
Clinical Diagnosis Isolates	111	49%	Health Care Workers in Outbreak 2	11	5%
Diagnosed by Screening Isolates, thereof:	115	51%	Hospitals/Wards in Outbreak 2	3/4	
Screened due to Risk Factors	40	18%	**Origin of Acquisition**		
Screened Due to Close Contacts of Newly Dected	75	33%	Imported, thereof:	65	29%
Type of Infecion			Transferred Patients from Foreign Hospitals	13	6%
Skin and Soft Tissue Infection	109	81%	Passangers	6	3%
Genitourinary tract infection	15	11%	Tourists	4	2%
Respiratory tract infection	8	6%	Community Acquired	60	27%
Bacteremia	2	1%	Health Care Acquired	46	20%
			Community Acquired with Health Carse Associated		
Osteomyelitis	1	1%	Risk Factors	48	21%
			Not Classifiable	7	3%

In addition to the epidemiology of MRSA, the epidemiology of the SA profile is given. Please note that the strain of SA which is methicillin-susceptible is hereafter abbreviated MSSA. In the next section, a profile of SA (MSSA and MRSA) is given because it is necessary to examine the comprehensive attributes of SA (MSSA and MRSA) to answer the research question.

2.2.3 Distribution of SA – The Icelandic Image

Arna Hardardottir, Project Manager at the Department of Economics, Finance and Information at LUH (Enquiry for MRSA Dissertation, 2012), provided information on the number of SA infections at LUH for the year 2011. The number of hospitalized individuals coded by ICD codes[7] for SSTI caused by SA is 245 and the number of hospitalization coded by ICD codes[8] for endocarditis caused by SA is 38 in the year 2011. This information was collected under instructions by Kristjansson (M.D).

[7] ICD-10 codes given for SSTI are L03.0, L03.1, L03.2, L03.3, L03,8 and L03.9.

[8] ICD-10 codes given for SSTI are I33.0, I33.9, I38 and I39.8.

Asgeirsson et al. (2011, p. 510) provide the following table which presents certain characteristics associated with SA bacteraemia infection from the year 1995 to the year 2008:

Table 4. Characteristics associated with SA bacteraemia from the year 1995 to the year 2008.

	1995–1999 (*n* = 216)	2000–2004 (*n* = 242)	2005–2008 (*n* = 263)	p-Value
Incidence, per 10^5 per year				
Total >18 years	22.4	23.1	28.9	0.012
18–34 years	3.41	6.67	8.49	
35–54 years	12.3	13.9	15.4	
55–74 years	55.7	43.3	51.1	
>75 years	79.8	94.0	122.8	
Mean age (years)	63.0	62.3	62.5	NS
Male (%)	59.3	57.4	60.1	NS
Acquisition (%)				
Nosocomial	54.6	45.9	38.4	<0.001
Healthcare-associated	9.7	11.2	14.1	NS
Community-acquired	35.6	43.0	47.5	<0.001
30-day mortality (%)				
Total >18 years	22.2	18.7	11.4	0.001
18–34 years	0.0	0.0	0.0	
35–54 years	18.2	10.9	3.8	
55–74 years	19.6	22.8	7.1	
>75 years	35.8	25.4	24.7	
365-day mortality (%)				
Total >18 years	38.9	32.8	28.2	0.061
18–34 years	0.0	4.2	3.8	
35–54 years	29.5	25.5	9.4	
55–74 years	35.5	43.5	25.3	
>75 years	62.3	33.8	50.6	
Mortality rate, per 10^5 per year	5.0	4.3	3.3	0.048
Resistance (%)				
Penicillin	84.3	83.0	78.7	NS
Erythromycin	1.9	3.7	6.8	0.032
Clindamycin	0.9	0.0	3.1	0.028
Oxacillin	0.5	0.4	0.8	NS

NS, non-significant.
Mortality rate per 100 000 was calculated by using 30-day case mortality. p-Values were derived from Kendall's correlation for trends in data over years, and by linear trend test (for incidence and mortality rate).

Asgeirsson et al. (2011, p. 515) noted that for the years 2007 and 2008 the mortalities within 365 days was 27.9 per 100.000 individuals and the mortalities within 30 days was 8.1 per 100.000 individuals, but notably the rate of mortality decreased over the study period. However, the authors also note increasing incidence of SA bacteraemia by higher average age of the population: "higher numbers of individuals are being diagnosed with malignancy, and more people are living with chronic diseases such as diabetes and obesity" (p. 515).

2.2.4 The Nature of Transmission

As discussed before, the risk (or the risk-ratio) of being infected with MRSA within the hospital depends mainly on three (interrelated) factors: the prevalence or the distribution of MRSA within the population as a ratio of SA, the clinical procedures or habits within the hospital, and the clinical status of the patients. Rothman and

Greenland (1998, p. 542) provide a mathematical presentation of this relationship by the equation $I(t) = cpP(t)$, where:

$I(t) =$ Incidence rate

$c =$ Contact rate

$p =$ Transmission probability

$P(t) =$ Prevalence

As demonstrated in Appendix A, the genetic structure of MRSA can vary in some ways, which means the infection rate will differ from the ratio of MRSA samples out of SA samples. Miller et al. (2009, p. 1) found that SA colonization was not significantly associated with serious SSTI in any analysis.

Due to all of the above, my conclusion is that the correlation of the prevalence/distribution of MRSA (such as the ratio of MRSA samples out of SA samples) is not absolute. More precisely, if the ratio of MRSA samples out of SA samples is 30% on carriers, the incidence of MRSA infection can be lower or higher, for example, depending on the clinical procedure or preventive measures.

2.3 Economic Evaluation

As discussed in the Introduction, Drummond et al. (2004, pp. 8-9) note the importance of identifying relevant alternatives in an economic evaluation, first, in order to recognize that different viewpoints can result in different results and, second, to realize the magnitude that a single program may have in terms of costs and benefits. Furthermore, the authors define an economic evaluation as a comparative analysis of alternative courses of action in terms of both their costs and consequences; the basic tasks are to identify, measure, value, and compare because “activity” has costs and consequences and we live in a world of scarcity but with some alternatives.

2.3.1 The evaluation methods within health economics

Drummond et al. (2004, pp. 9-11), explains that the definition of costs and consequences, and whether there is a comparison of two or more alternatives, corresponds to the choice of the method used to evaluate health care programs.

Boardman et al. (2001, pp. 437-448) and Brent (2003, pp. 7-10) altogether introduce four main methods by which to evaluate health care programs: cost-minimization analysis, cost-effectiveness analysis, cost-benefit analysis (CBA) and cost-utility analysis. As the aim of this thesis is to answer the question about cost, particularly the cost-benefit of LUH's search and destroy policy against MRSA, the literature review is limited to that method.

2.3.2 Cost-Benefit Analysis

According to Drummond et al. (2004, p. 16) CBA requires measuring the cost and consequences of alternatives in monetary units or, precisely, as stated: "CBA provides an estimate of the value of resources used up by each program compared to the value of resources the programme might save or create" (p. 16). Furthermore, the estimation is based on the incremental net benefit of a program. By using Drummond et al.'s (2004, pp. 19, 21) model of CBA's components in health care economic evaluation analysis, all types of cost and all types of consequences (value created or saved) are included. Notably, Drummond et al. defines the valuation (or estimate) of a program's consequence(s) as the global willingness to pay for a program.

2.3.2.1 Measurement of Resources Consumed by the Health Care Program

The measurement of resources consumed depends on the purpose of the study. Drummond et al. (2004, pp. 18-20) categorizes costs into cost of the health care sector, cost of other sectors, cost of the patient and family, and cost due to productivity losses. An estimation of cost in the health care sector and cost in other sectors is not complicated, but one must keep in mind that the prices for the measured quantity used in these sectors are not clear market prices because the health care sector is dominated by market failures. Additionally, the state is a dominant participant and appears often as a single or the main buyer within the sector, which affects the prices of resources used.

According to Drummond et al. (2004, pp. 20, 57), costs are incurred by patients and their family in terms of out-of-pocket expenses, other costs, and their time resulting from use of health care services. Time can be defined as time dedicated to the treatment (both by the patient and by the family as caregivers), leisure time, or work

time. Leisure time and time dedicated to treatment and care have no known market value. Therefore, the cost of time and possible productivity loss due to informal care is a bit more complicated to estimate than other costs of the resources consumed.

2.3.2.2 Measurement of the Consequences of the Health Care Program

According to Drummond et al. (2004, pp. 20, 215, 223), the valuation of the global willingness to pay for a program includes a measurement of the expected health effect of a program, other values created, and resources saved. In other words, the categories of benefits from health programs are threefold. First, there is increased productivity output because of better health status. Second, there is an intangible benefit of improved health to the receiver of the health care services and, third, there is cost avoided in the future.

A measurement of the health effect of a program can be done by three general approaches which pertain to estimating the effect of a program in monetary value. These approaches are the human capital approach, the revealed preference approach, and the contingent value approach. Drummond et al. (2004, pp. 215-216) describes how in the human capital approach the health care program is defined as an investment in human capital and, presumably, to renew or increase individuals' production capabilities, which is defined as the positive effect of the health care program. Consequently, monetary units weigh the healthy time gained by using market wage rates. The future cash flow of increased earnings is discounted to get the net present value of a program. Further, the method can be used as the only basis for valuing all aspects of health care improvements or as a method of valuing part of the benefits of health care interventions. According to Drummond et al. (2004, p. 216), the main difficulties in using the human capital approach are that the market rates of wages do not always reflect the true wage because of imperfections such as discrimination by race and gender and the estimation of value of healthy time gained that is not in exchange for wages in societal studies.

Drummond et al. (2004) refers to Mishan (1971) to note that the human capital approach is a production based method which is "not consistent with the theoretical foundation of CBA from welfare economics" (p. 217), i.e., the only focus is on the productivity of the labour. Drummond et al. (2004, pp. 218-219) describes that in the

revealed preference approach, the value of health (risk) is estimated according to differences in wage rates for jobs that vary regarding the risk to health. The strength of the method is the revealed preferences about how people value health at given risk but the weaknesses are that there is a difference in the estimated values where the context and the type of job dominate the outcome and the variables are dependent on many others variables. Furthermore, there is not always a clear relationship between wage rates according to the difference in risk, the wage rates do not always reflect the "true" relativity because of imperfections such as intervening, also people sometimes show limitations in perceiving occupational risk.

According to Drummond et al. (2004) the contingent valuation approach is based on survey methods where participants have to "think about contingency of an actual market existing for a programme or health benefit and to reveal the maximum they would be willing to pay for such program or benefit" (p. 219). Another aspect of the contingent approach is that the utility concept can be expressed either from the compensating point of view or from equivalent points and, accordingly, there are questions regarding the willingness-to-pay or willingness-to-accept. Furthermore, it should be noted that the estimation of willingness-to-pay is just for the components of benefits that have no money value on the market. Moreover, according to Drummond et al. (2004, pp. 224-225) there are at least three ways to define goods and services when one uses the willingness-to-pay method to estimate value. First, a certain health outcome can be defined, second, a treatment with uncertain outcomes can be defined and, third, access to a treatment program where future use and treatment outcomes are uncertain can be described. In addition, questions regarding the willingness-to-pay method have two perspectives, specifically, the ex post or user-based perspective and the ex-ante or insurance-based perspective.

To measure intangible benefits created, Drummond et al. (2004, p. 20) discuss how other values created from a health care program can be represented by factors such as information and reassurance about the health status, which demonstrates that these values are not necessarily related to improvement in health. Brent (2003) explains further that the main methods for measuring intangible benefits are to use "similar markets" (substitution), use "adjusted market price" (prices include externalities) and

use “implicit markets” (for example, higher wage for higher risk in the labour market) (pp. 272-273).

Furthermore, resources saved are measured and valued in a similar manner to costs of the health care sector, costs of other sectors, costs of the patient and family, and costs due to productivity losses. The issues are the same regarding these estimations.

2.4 Economic Evaluation of SA/MRSA Programmes – Studies

Studies of cost, cost-effectiveness analysis, and cost-utility analysis are special variations of CBA studies wherein different dimensions of health care programs are explored. Therefore, cost-effectiveness analysis and cost-utility analysis can be said to be included in the following overview. Moreover, inclusion of these studies provides the opportunity for broader, deeper, and more profound discussion where it is appropriate. Additionally, a review of the studies presumptions or epidemical findings is in keeping with the subject of this dissertation.

Murthy et al. (2010, pp. 1747-1749) studied the cost-effectiveness of MRSA screening on admission to surgery (surgery patients) by comparing strategies of not screening for MRSA, of universal rapid polymerase chain reaction screening MRSA, and of risk factor screening combined with preemptive isolation and contact precautions pending chromogenic agar result. The risk factor was defined as prior hospitalization or antibiotic use. The authors determined that the universal rapid polymerase chain reaction screening MRSA and risk factor screening were more costly to the hospital than no screening of MRSA. The authors assumed that the probability of MRSA infection per hour by patient with nasal carriage was 0.051%, efficacy of decolonization treatment was 90%, and probability of MRSA carriage on admission was 5.1%. Furthermore, they assumed that probability of spontaneous loss of MRSA carriage per hour was 0.01125%, probability of cross transmission from colonized individual to un-colonized individual was 0.8%, and reduction in cross transmission due to the infection control procedures was estimated to be 50%. The incremental cost of excess lengths of stay due to MRSA infection was estimated to be CHF 8.292, the cost of decolonization treatment was estimated to be CHF 18.50, and the incremental cost per day of infection control for suspected carriers was estimated to be CHF 182. The author concluded after performing a sensitive analysis that the local epidemiology of MRSA plays an important role in the

strategy, i.e., higher prevalence of MRSA colonization may find universal screening to be cost effective and even cost saving.

Wernitz et al. (2005, pp. 466, 469) analyzed the cost of a hospital-wide selective screening program for a period of 19 months where 539 inpatients were screened and 111 of those were MRSA positive. The authors found that the average cost for screening patients during two days of preventive contact isolation was EUR 39.96 for screened patients found to be MRSA negative and EUR 82.33 for screened patients found to be MRSA positive. The difference in the cost was due to the difference in laboratory costs and costs for room cleaning. Furthermore, the average length of overstay for patients with MRSA infection was identified by tract. The average length of overstay for 21 patients with post-operative wound infection was 28.85 days, the average length of overstay for nine patients with pneumonia was 28.55 days, and the average length of overstay for 15 patients with bloodstream infection was 21.93 days. The average length of overstay for five patients with urinary tract infection was 14.00 days and the average length of overstay for 11 patients with other types of infection was 24.55. The authors also calculated the cost of screening per year for a different ratio of patients screened and the cost saved because of prevented HAI. The main result was that a screening program became cost-effective at a low MRSA and a higher incidence rate justified screening a higher rate of inpatients.

Wernitz et al. (2005, pp. 457-458) studied the effect of hospital-wide screening of defined risk groups in a 700-bed acute care hospital during 19 months. The method used was a cohort study where the frequencies of HAI MRSA were compared with and without screening. The main result was that the screening program prevented 48% of expected HAI MRSA. The screening program was defined to screen all patients with known histories of MRSA (both colonization and infection), to screen all patients that were admitted from foreign hospitals or all patients from hospitals with high prevalence rates of MRSA. Further, patients with at least two of the following characteristics were screened: “residing nursing home; requiring dialysis and with skin or soft tissue infection; receiving treatment involving any invasive device; pressure scores; aged >65 years with acute sialadenitis or diabetic gangrene” (p. 458). The samples were taken at admission “from nares, throat, skin or soft tissue lesion, the surroundings of invasive

devices and any other clinically sites" (p. 458). The authors concluded that the screening program was effective in preventing HAI MRSA.

Rubio-Terrés et al. (2009, pp. 722, 726) studied the difference in the use of resource utilization and the associated cost of bacteraemia between MSSA and MRSA in Spain. The method used was an observational retrospective, cohort multicentre study in the year 2005. The sample was 366 patients from 27 hospitals ad of those 121 were cases of MRSA bacteraemia. The result was that antibiotic treatment was 3.1 days longer for patients with MRSA infection than for patients with SA infection and the average length of stay (ALOS) for MRSA patients was 2.2 days longer than for patients with SA bacteraemia. More diagnosis testing was completed for patients infected by MRSA and the rate of admission to intensive-care units was 7.6% higher for that group compared to patients with SA infection. The authors also found that the average cost per patient with MRSA bacteraemia was EUR 1,205.34 (12%) higher, compared to the average cost per patient with SA bacteraemia. Additionally the authors calculated the mortality rate of the groups after 12 months. The 12-month mortality rate for patients with MRSA bacteraemia was 39.7% whereas the 12-month mortality rate for patients with SA bacteraemia was 25.3%.

Graves et al. (2007, p. 280) estimated both the effects of a single HAI on length of stay and variable cost as well as the bias from omitting variables in such estimates. The data set was from two Australian hospitals where the patients were individuals 18 years and older with a minimum stay of 1 night. The method used was a prospective cohort study with regression model. The main result was that urinary tract infection did not lead to increasing length of stay nor increasing variable cost, lower respiratory tract infection lead to increasing length of stay by 2.58 days, and increasing variable cost by AUD 24. Other types of HAIs lead to increasing length of stay by 2.61 days but the variable costs were unchanged. The authors concluded that the cost attributed to HAIs might be overstated because many other variables, which have been excluded, are related to length of stays and variable cost along with HAI. Notably, the authors discuss the methods of direct attribution and comparative attribution. The direct attribution method (attribution of extra cost from HAI) is criticised to be "subjective and not reproducible" (p. 281) and the comparative method (matching and comparing

treatments of non-HAI cases and HAI-cases) is criticised because matching patients can only be done for several variables.

Cosgrove et al. (2003, p. 53) conducted a meta-analysis to explore the consequences of the methicillin-resistance in terms of mortality caused by SA bacteraemia based on studies from January 1, 1980 through December 31, 2000. The overall odd ratio (OR) for increased mortality associated with MRSA bacteraemia compared with MSSA bacteraemia was estimated to be 1.93. Furthermore, for studies where ≥ 70% of the MRSA cases were defined as HAI, the comparable OR was estimated to be 2.03.

Datta and Huang (2008, pp. 176, 178-179) evaluated the risk of subsequent infection by 282 individuals who had been colonized by MRSA for more than 1 year and the mortality rate for that group. The main results were that 65 individuals (23%) had 96 discrete infections within a year. The types of infections were pneumonia (39%), soft-tissue infection (14%), central venous catheter infection (14%), primary bloodstream infection (11%), bone/joint infection (8%), and other types of infections (15%). Additionally, the percentage of total infections associated with MRSA bacteraemia was 24%. Furthermore, the OR for MRSA infection in individuals who had been colonized by MRSA for more than 1 year but less than 2 years was calculated to be as high as 2.2 and the OR for MRSA infection by individuals who had been found colonized at the time of detection was calculated to be as high as 1.9.

Naber (2009, p. 234) explores several studies. He notes that studies show that mortality rates for SA bacteraemia vary substantial, i.e., within the range of 0.0% to 83.0% but this can be explained in part by differences in patient groups, settings, and the mortality measurements used. For example, in a Belgian study, the MRSA bacteraemia–associated mortality rate was measured as high as 23.4% but MSSA bacteraemia–associated mortality rate was 1.3%. Meta-analyses have demonstrated a significantly higher risk of mortality associated with MRSA bacteraemia compared with MSSA bacteraemia. Nader also explains that an analysis of 1000 US hospitals revealed that inpatients with SA bacteraemia had a three times longer mean duration of hospital stay or 14.3 days versus. 4.5 days. Therefore, three-fold increases in treatment costs and treatment of MRSA bacteraemia can be up to 24% higher compared to treatment of

MSSA bacteraemia. Finally, causes SA higher cost due to complications and mortality of the SA infected individual.

Cosgrove et al. (2005, p. 166) evaluated the impact of methicillin-resistance in SA on mortality, length of stay, and hospital charges for a 630-bed urban, tertiary-care teaching hospital for the period of July 1, 1997 to June 1, 2000. They found that the mortality rate was 22.9% for the patients diagnosed with MRSA bacteraemia compared to 19.8% for the patients diagnosed with MSSA bacteraemia. The lengths of stay were nine days for the MRSA patients and seven days for the MSSA patients and the charges were USD 19,212 and USD 26,424 respectively. A multivariate analysis revealed that MRSA bacteraemia increased the average length of stay by 1.29 (median 2.0 days) and on average increased the hospital charges by 1.36 (median USD 6,916).

Köck et al. (2010, p. 3) outlined the burden of MRSA infections across Europe and the threats according to the recent evolution in MRSA's epidemiology in order to determine what is needed to improve surveillance, prevention, and control of MRSA in the continent. According to the authors, research indicates that MRSA adds to the MSSA burden. First, they describe the burden of MRSA on the mortality rate using two meta-analyses where it was estimated that invasive MRSA infections increase mortality (by 1.93 and 2.03). Additionally, by referring to 15 studies where the OR for MRSA-associated mortality is compared to MSSA-associated mortality, the minimum OR is estimated to be 0.73 but the maximum OR is estimated to be 5.4.[9]

Second, the authors describe the burden of MRSA on cost of care. The general conclusion is that MRSA causes extra cost of care, mainly because of prolonged stays in hospitals. They describe five studies where the MRSA infected patients stayed two days, four days, nine days, ten days and five days longer compared to MSSA patients. In one study infected MSSA patients stayed nine days longer than uninfected patients. The effect on cost was that the cost for patients infected by MRSA compared to patients infected by MSSA was from 38% to 170% higher or from USD 7,212 to USD 71,715. It should be noted that these five studies are not comparable because their subjects were not entirely analogous. Further, the prevalence of HAIs from MRSA have been

[9] It should be noted that the mortality references in the study have different spans (in days).

decreasing over the past five years which is attributed to the success in prevention and control of MRSA in health care institutions. Finally, the authors point out that systematic assessment of current strategies is needed in addition to review of guidelines for MRSA prevention and control. They recommend that emphasis be placed on controlling the spread between units where MRSA can be found.

Cosgrove (2006, p. 82) discussed associations between the antimicrobial resistance and mortality, length of stay in hospital, and health care costs for SA amongst other bacteria. She notes that the host, the organism, and the treatment are factors that may contribute to increased mortality, length of stay in hospital, and cost when one is dealing with a resistant organism. Finally, she concludes that the association between the antimicrobial resistance and mortality, length of stay in hospital and health care cost is "likely result of inadequate or delayed therapy and may be related to the degree of severity of the underlying disease." (p. 87)

Chaix et al. (1999, p. 1745) aimed to research the cost and benefits of MRSA control programs in endemic settings with a case control study applied on data from medical intensive care units of university hospital in France. The assumption of the prevalence of MRSA carriage at admission was 4%. The result was that the mean and the median cost of MRSA infection was USD 9,275 and USD 5,885, respectively, but the total cost of the control program ranged from USD 340 to USD 1,480 per patient. A 14% reduction in MRSA infection made the control program beneficial.

Resch, Wilke and Fink (2009, p. 287) studied the incremental mortality, length of stay and cost of MRSA patients (both infected and colonized) by retrospective matched-pairs analysis. Their result was that the MRSA patients compared to the control group: stayed 11 days longer in hospitals, the OR for the mortality rate was 1.07, the likelihood of undergoing mechanical ventilation was 7% higher, and the cost was EUR 8,198 higher.

Papia et al. (1999, p. 473) studied the cost-effectiveness of screening programs for MRSA colonisation on high-risk patients on admission by a 980-bed university-affiliated tertiary-care hospital. Laboratory and nursing costs were found to be USD 8.34 per specimen and the average cost of the infection control for each patient was found to be approximately USD 5,235 per patient. The authors concluded that if the identification

could hinder transmission of the bacteria to six or more patients, then the screening program seems to be beneficial.

Nulens et al. (2008, p. 301) calculated the Maastricht University Hospital's cost for the SDP and treatment for MRSA bacteraemia for the period 2000 and 2004. The ALOS for 22,412 patients was 8.7 days but the ALOS for all patients with MRSA bloodstream infection was 39.9 days. The annual cost of proactively screening 246 patients for MRSA was EUR 1,383,200 and the annual cost for prevention of MRSA spread through a treatment of SA bloodstream infections was EUR 2,736,762. In the study, the authors attributed only costs spent within the hospital but not opportunity costs such as cost due to loss of production.

Simoens, Ophals and Schuermans (2009, p. 1853) analysed, amongst other factors, the cost and the benefit of a SDP by the prospective method. The cost was defined as the screening and isolation, while the benefit was defined as hospital savings through the avoidance of isolation, decontamination, antimicrobial therapy, and extended hospital stays of affected patients. The result was that the cost benefit ratio was 1:17 in the intensive care unit and 1:16 in the gerontology unit. Based on these results, the authors recommended the SDP for MRSA.

Van Rijen and Kluytmans (2009, p. 1245) researched the costs and benefits of the MRSA SDP in a Dutch hospital during the years 2001 to 2006. The authors defined costs as the costs for the building of isolation rooms and the salary of one full-time infection control practitioner. To estimate the benefit they calculated the transmission rate for the hospital and estimated the number of cases of MRSA bacteraemia prevented, as well as its associated prevented costs and saved patient lives. The estimated prevention cost per admission was EUR 5.54, daily isolation costs for indidviduals suspected to be colonised/infected by MRSA were EUR 95.59, and daily isolation costs for individuals who were MRSA-positive were EUR 436.62. The estimated rate of MRSA transmission was 0.30 and the SDP was estimated to prevent 36 cases of MRSA bacteraemia yearly, which annually was estimated to save EUR 427,356 for the hospital and ten lives per year. The author concluded that application of SDP in a hospital in a country with a low endemic MRSA incidence saves money and lives.

The methods of economic evaluation in the studies reviewed are different, as discussed in the beginning of this section. These studies use data regarding length of stay, cost, benefit, and OR for mortality of MRSA colonised individuals and/or MRSA infected individuals. Presumably, reviewed studies are not uniformly reliable and valid as sources for reference but it should be noted that the referred studies have been peer reviewed for publishing in recognised scholastic and professional journals. by that fact, and in accordance with the purpose of this dissertation, I will not expend effort in determining all of the possible weaknesses in the referred to studies. However, as Drummond et al. (2004, p. 212) submits, studies are mislabelled as CBA, where they are in fact cost analysis. This "mislabelling" can also be recognised in the review above, for example, by Chaix et al. (1999), Simoens, Ophals and Schuermans (2009) and Van Rijen and Kluytmans (2009) where these studies do not fully recognise, report and calculate ***all*** costs and ***all*** benefits of their subjects, respectively.[10]

2.5 Emergent Issues

The results of the studies indicate strongly that the economic burden of MRSA is above the economic burden of SA and it seems to be a challenge to execute a CBA that is fully compatible with the requirement of the theoretical definition of the method. Additionally, there is a great lack of economic evaluation as a basis for decisions in the Icelandic health care system. These issues provide valid reasons to research the cost-benefit of a program that aims to keep seemingly more costly strains of SA, namely MRSA, out of the Icelandic hospital environment.

[10] Even though it has been stated up to here that the Nordic countries and Netherlands are the only countries in Europe that apply the SDP on a national level, some other hospitals within other countries apply this policy as well as.

3 Method

In order to answer the research question regarding the cost-benefit of the SDP against MRSA at LUH, I describe the data collection process, the framework of LUH's SDP, the framework of the economic evaluation, and the following sensitivity analysis. Lastly, the strengths and the weaknesses of the method are discussed.

3.1 Data Collection

The data for this dissertation was preliminary collected in the year 2005. Due to workload in other projects, the work on the dissertation discontinued until the year 2011.

The head physician of the department of contagious diseases, Olafur Gudlaugsson, M.D., and the head physician of the inpatient ward of contagious disease and internal medicine, Mar Kristjansson, M.D., each provided descriptions and further information on the physical consequences of MRSA infection. Olafur Gudlaugsson, M.D. also provided a description of the medical treatments of MRSA infected people and the medical eradication treatment of MRSA carriers, in addition to reviewing information regarding the MRSA prevention processes at LUH.

Asdis Elfarsdottir, a Registered Nurse (RN), who is the head nurse of the department of contagious diseases, gave descriptions and information about the preventive measures and related published guidelines applied at LUH. Stefania Arnardottir (RN), who is the head nurse of the inpatient ward of contagious disease and internal medicine, gave descriptions and information about caring for MRSA infected or MRSA carriers. She also gave descriptions about the processes applied to hinder contamination of the MRSA bacteria within the ward. Ragna Gustafsdottir (RN), who is the head nurse of Accident and Emergency (AE), gave descriptions and information, and reviewed information about the MRSA prevention process within the AE.

Helga H. Bjarnadottir, director of the Department of Economics, assisted in gaining information about hospital cost and activity. Arna Hardardottir, Project Manager, gave information about the number of SA infections. Rannveig Einarsdottir Pharmacologist, who is the head pharmacist at the division of pharmaceutical, gave information about the price of the relevant medicine.

Linda Helgadottir and Holmfridur Jensdottir, who are both biomedical scientists at LUH's Department of Clinical Microbiology, collected the data for the number of individuals in the screening sample and the number of screening tests. Karl G. Kristinsson, who is the head physician at LUH's Department of Clinical Microbiology, assisted in gathering information about the number of samples. Ingunn Thorsteinsdottir M.D, gave information about the application of the laboratories price list for relevant items.

Helga Helgadóttir Project Manager and Kristinn Petursson Foreman, gave information about prices of medical devices and Steinunn Asta, Larusdottir Cleaning Manager, gave information about the cost of cleaning the rooms.

3.2 Framework for MRSA Preventive Program at LUH

Four processes best describe the framework of LUH's MRSA preventive program in which the goal is to hinder the transmission of MRSA from the "outsiders" to the "insiders". These processes are the MRSA preventive process for inpatients, the MRSA preventive process for patients of Accident and Emergency (AE), the MRSA preventive process for employees and individuals other than patients, and the MRSA preventive process that is applied following MRSA outbreaks within a hospital/hospital ward.

The following sections provide an overview of these MRSA preventive processes. In Appendix D, cost items are listed up. Where the MRSA preventive processes are similar or even identical, references are made between or within them to avoid repetition in the text.

3.2.1 MRSA Preventive Process for Inpatients

Prevention of MRSA in hospitalized patients is the first line of defence in which the purpose is to prevent MRSA from entering inside "the walls" of the hospital. The MRSA preventive process for inpatients is described in Figure 4:

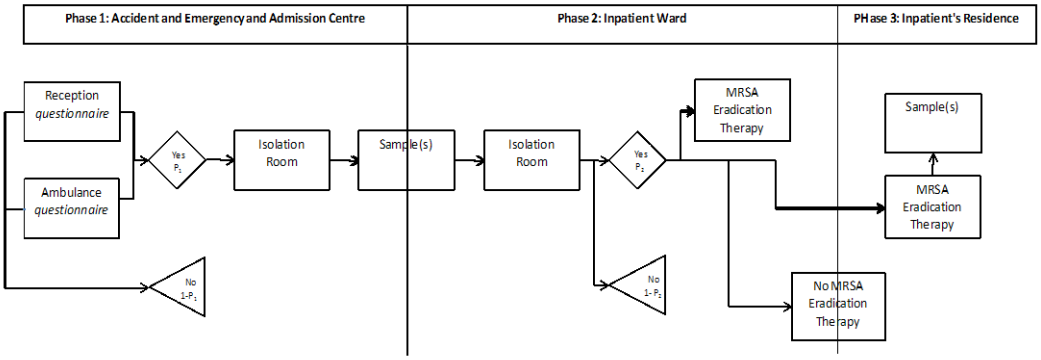

Figure 4. MRSA preventive process for inpatients.

Phase 1: Emergency Room and Admission Centre: According to the procedures *07.01.02 Caution at Arrival or Admission to Hospital* and the *MRSA Checklist-Questionnaire,* it is compulsory to ask each patient on arrival at AE and the Admission Centre[11] three questions in the waiting room before he/she goes to a service unit of the division. The first question is whether the patient has ever been diagnosed with MRSA, the second question is whether the patient has worked, lived or been treated in a foreign hospital in the last six months, and the third question is whether a family member who shares a home with the patient has ever been diagnosed with MRSA.

In an interview with the head nurse of the main AE, it was confirmed that the arriving patient is always simply asked whether he/she has stayed in a foreign hospital in the last six months. This practice is justified by the fact that if the patient has ever been diagnosed to carry MRSA or be infected by MRSA prior to arrival, that information will be visible in the patient's medical record. Furthermore, it is assumed that if someone close to the patient has ever been diagnosed to carry MRSA or be infected by MRSA, the patient will give that information to the health care workers. The head nurse of the main AE advised that if a patient comes to the hospital by ambulance, the paramedics ask the patient whether he/she has stayed in a foreign hospital in the last six months given that the transferred patient is a foreign one. If people come unconsciously into the AE, MRSA preventive measures are applied if the patient is a foreigner, but not if the patient is an Icelander. Ambulances transporting patients are expected to disinfect

[11] LUH operates within several buildings; therefore, there are five ERs at the hospital and at least two Admission Centres. The main ER is at Fossvogur.

the ambulance after transferring a patient that is suspected of carrying or being infected by MRSA.

If a patient answers in the affirmative to the question about foreign hospitalization and/or the patient medical records report a prior diagnosis of MRSA, and/or the patient informs that his or her family member had MRSA then additional aseptic conditions are applied in the service to the patient.[12] Such a patient can now be defined as a suspected MRSA carrier and/or infected by MRSA, i.e., *suspected MRSA patient*. If an individual is known to be an MRSA carrier or be infected by MRSA, all of the same preventive measures are conducted as are conducted for the suspected carrier/infected.

The procedure *07.01.02 Caution at Arrival or Hospitalization*, the procedure *07.01.04 Instruction for Isolation of Suspected or Infected MRSA Patient*, and the instruction card entitled *MRSA Procedure for AE*, include several (and similar) preventive measures regarding the conduct and isolation of suspected MRSA patients.[13] A suspected MRSA patient is supposed to wait in the same spot within the waiting room of AE in order to prevent the possible distribution of MRSA to other areas.

While a suspected MRSA patient is waiting for service, the patient's room is prepared as an isolation room as soon as possible and prior to the patient entering the room. Preparation for isolation includes the removal of loose objects, covering the walls and static interiors, and bringing medical tools into the room before the patient enters. The patient's room is marked as "Isolation Room" to prevent employees from entering the room unnecessarily. When a suspected MRSA patient has arrived in the isolation room, every employee who enters the room is obliged to wear a gown with long sleeves, use gloves, and, if needed, wear a plastic apron and a mask. When the employee has attended to a suspected MRSA patient, the employee must leave the gown in the Isolation Room, throw away disposable protective equipment, and wash his or her hands with soap and rubbing alcohol. Notably, it is forbidden to bring paper into the

[12] Fundamental Aseptic conditions are always applied with hospital patients, these include regular hand washing by the personnel.

[13] The MRSA Procedure for AE is an instruction card that the employees of the ER carry with themselves. These cards instruct how to act if a patient is a suspected or confirmed MRSA patient.

isolation room but a suspected MRSA patient may use multiple forms of tableware (e.g., meal trays) which are sealed up and sent to the washing room after use.

Immediately after a suspected MRSA patient enters the isolation room, patient sample(s) is/are obtained. According to the procedure *07.01.05.01 Samples Obtained due to MRSA Search,* samples are obtained from the nasal cavity, throat, perineum, spit, urine, and wound(s) by wetting cotton pins with sterile water/salt water and stroking the area which is under examination. The sample areas depend on a clinical estimation but, at minimum, there are samples obtained from the nasal cavity and throat. The minimum number of samples is one cotton pin. In addition, personal information is filed and sent to LUH's Diagnostic Medicine Services.

If a suspected MRSA patient needs to leave the isolation room, such as to undergo X-Ray examination within the hospital, procedure *07.01.10 Transfer of a Patient between Wards* instructs that the suspected MRSA patient must wear a gown with long sleeves and gloves. Transportation of the patient must be in a wheelchair, which is disinfected by rubbing alcohol after its use. Employees who transport a suspected MRSA patient must wear gowns with long sleeves, use gloves, and, if needed, wear plastic aprons and masks.

If a suspected MRSA patient needs to be transported in an ambulance, the employees must follow the guidance document *07.01.12 Transfer of a patient in an ambulance*. According to the guidance document, a suspected MRSA patient must wear a gown with long sleeves and gloves. The mattress in the ambulance is covered with a plastic cover and the blankets and pillows used can be disinfected. The employees protect themselves by wearing gowns with long sleeves, using gloves, and, if needed, wearing plastic aprons and masks when they put a suspected MRSA patient in the ambulance and take him or her out of it. All linen, blanket, and pillows are placed in a water-soluble bag, disposable products/equipment used during transport are put in a bag for contaminated waste, and all surfaces which the patient is expected to have touched are disinfected with rubbing alcohol.

Employees who give a suspected MRSA patient services such as surgery or X-rays outside of the isolation room (ward) must follow the procedure *07.01.11 Tests and Operations on Patient*. When a suspected or infected MRSA patient is operated on, the

employees must follow special instructions given by the Division of Surgery. When a suspected or infected MRSA patient undergoes a test such as X-Rays, the employees must wear gowns with long sleeves, use gloves, and, if needed, wear plastic aprons and masks. After a test, all surfaces which the patient is expected to have touched are disinfected with rubbing alcohol.

When a patient leaves AE, the isolation room is cleaned according to the procedure *07.01.12.02 Cleaning After Isolation.* First, preparation for cleaning is conducted by a nurse assistant who must put on a gown with long sleeves and gloves before entering the isolation room. Upon entering the room, all linen, blankets, and pillows are put in a water-soluble bag, which is then put in a normal linen carrying bag and all disposable products/equipment used to transport the patient are put in a bag for contaminated waste. Items that are used multiple times are disinfected with rubbing alcohol. After this, nurse assistants must wash their hands with soapy water and dry their hands thoroughly before washing their hands with rubbing alcohol. Then the employees put on new gloves, take all washing items to the washing room, and repeat the above-described hand cleaning procedure.

Second, nurses or nurse assistants ensure that the cleaning employees are familiar with the situation and receive guidance concerning the proper cleaning procedures for the isolation room. Cleaning employees must put on gowns with long sleeves, plastic aprons, and gloves before entering the isolation room. The cleaning of the isolation room includes taking down curtains and putting them into water-soluble bags and then into linen carrying bags. All of the room should then be washed with chlorine solution or “Virkon” mixture. Special emphasises should be on cleaning all surfaces that the patient is expected to have touched, such as taps, handles, remote controls, electrical switches, and other horizontal surfaces, as well as the walls. Furthermore, the cleaning employees should alert a nurse if heavy contamination has come from the patient. After cleaning, dressing gowns must be put in water-soluble bags and all disposable protective clothing is classified as contaminated waste. Cleaning equipment should be disinfected immediately after use with 90-degree hot water and all rubbish should be put in specially marked bags. Before leaving the room, all staff who attended to the cleaning

are required to wash their hands with soap and dry their hands thoroughly before washing their hands with rubbing alcohol.

Another set of samples is taken one to four hours after the patient entered the isolation room. These samples are either taken in the AE or inpatient ward, depending on how long the inpatient needs to stay in the AE.

Phase 2: Inpatient Ward: After the patient's stay in AE, the inpatient is transferred to an isolation room in one of the LUH's speciality wards and additional preventive measures are implemented onward in the service to the patient. That means that the same preventive measures are applied in accordance with the previously described procedures. Notably, there is a difference between a suspected or infected MRSA inpatient who is hospitalized via AE and a suspected or infected MRSA inpatient who is hospitalized via the Admission Centre. Specifically, the cost of a suspected or infected MRSA inpatient who is hospitalized via AE is higher than and an inpatient who becomes an inpatient via the Admission Centre. The reason is that the set-up of preventive measures is doubled for a suspected or infected MRSA inpatient who is hospitalized via AE.

In addition to the previously noted preventive measures, the procedure *07.01.14.01 Daily Cleaning of Isolation Room* gives instruction regarding the daily cleaning of an isolation room. The procedure is similar to the procedure *07.01.12.02 Cleaning after isolation,* i.e., that the cleaning staff should wear the same protective suits as described above. Furthermore, patients' bedsteads, tables, all "contact surfaces", and horizontal surfaces are cleaned with rubbing alcohol and floors are washed with soap-water. After cleaning, dressing gowns must be put in water-soluble bags and disposable protective clothing is classified as contaminated waste. Cleaning equipment should be disinfected immediately after use with 90-degree hot water and all rubbish should be put in specially marked bags. The cleaning staff should call a nurse for further guidance if heavy contamination has come from the patient. After cleaning the room, dressing gowns are put into water-soluble bags and disposable protective clothing is classified as contaminated waste. All staff who clean are required to wash, dry, and apply alcohol to their hands before leaving the room. Immediately after a suspected MRSA patient enters the isolation room, patient samples are obtained as previously described. When

a patient leaves a ward, the isolation room is cleaned according to procedure *07.01.12.02 Cleaning after isolation,* as earlier described.

If an MRSA sample from a patient is positive, an environmental sample is obtained about one hour by an employee of DIC, after cleaning is finished as described in procedure *07.01.15 Environmental Samples after Final Cleaning.* Samples should be obtained from all surfaces that the patient is expected to have touched, such as taps, handles, remote controls, electrical switches, horizontal surfaces, the patient's bedstead, tables, mattress, and multifunctional equipment. The sample results arrive within three days during which time the room is not used.

Generally, a patient who is suspected of carrying or being infected with MRSA is detained in an isolation room with a detached toilet, shower, and entrance room. If there is the danger of infection/transmission of MRSA because of pneumonia or purulence from a wound, the patient is placed in a special isolation room, which is equipped with a vacuum device.

After three days, a response comes from the Diagnostic Medicine Services regarding the MRSA sample(s). The additional preventive measures expire if the result(s) of the sample(s) are negative. If the result(s) of the sample(s) is positive and the patient is infected with MRSA, he/she undergoes MRSA medication therapy to cure the infection. If the result(s) is positive and the patient "just" carries MRSA, a physician evaluates whether MRSA eradication therapy will be applied in order to eradicate the bacteria from the patient's body.[14] The main factors that affect whether MRSA eradication therapy will be applied or not are the clinical condition of a patient and how long he/she is supposed to stay in the hospital. For example, if a patient has a catheter, MRSA eradication therapy could possibly increase the risk of infection. After the physician's evaluation, three situations are possible going forward. First, the patient finishes his/her medical treatment within the hospital and is discharged without MRSA eradication therapy. Second, the patient finishes his/her medical treatment and MRSA eradication therapy within the hospital and is then discharged. Third, a patient finishes his/her

[14] If an MRSA carrier shares a household with a health care employee(s), samples are obtained from the employee(s) as well.

medical treatment within the hospital and is discharged but then undergoes MRSA eradication therapy at home.

According to procedure *07.01.01.02 Information for Individual about MRSA Eradication Therapy*, MRSA eradication therapy from a patient's body is primarily a threefold process: the patient is bathed with Chlorhexidine soap, Mupirocin cream is delivered into the patient's nose, and Chlorhexidine powder is applied in the skin folds. Normally MRSA eradication therapy takes five days. It should be noted that MRSA eradication therapy depends on where MRSA was found on the body. If MRSA is found in the intestine, MRSA medication therapy is added to the MRSA eradication therapy.

According to the procedure *07.01.09 Searching MRSA after Treatment*, samples are taken from hospitalized patients, three, five, and seven days after the MRSA eradication therapy is completed. Two sets of samples are obtained at 1 to 4 hour intervals and if all samples are negative then the patient is transferred into a standard room. The room that the patient stayed in is then disinfected as previously described. If a patient is discharged before it is known whether he/she carries or is infected by MRSA, a clinical evaluation is completed regarding whether or not the isolation room will be disinfected.

Phase 3: Patient's Residence: If it is decided that a patient carry out or keep on MRSA eradication therapy at home he/she is given the appropriate information and medicine and asked about the medical status of people in his/her residence in accordance with procedure *07.01.16 Discharge of MRSA Patient*. The information that the MRSA carrier is given is contained in the procedure *07.01.01.02 Information for Individual about MRSA Eradication Therapy*. According to that procedure, the patient bathes with Chlorhexidine soap on a daily basis, delivers Mupirocin cream into the nose with a cotton pin three times per day, and applies Chlorhexidine powder to skin folds (backs and groin) once per day. In addition, the patient should wash, dry, and clean his/her hands with rubbing alcohol regularly.

The patient needs to have a towel and a washcloth for their own private use, replace underwear and clothing on a daily basis, and replace linen and vacuum the bed after the first two days of the MRSA eradication therapy. While the MRSA eradication therapy is executed, the patient's bed has to be covered with plastic foil and all loose carpets, pillows, and covers that cannot been washed have to been removed. Notably, linen,

towels, facecloths, underwear and socks must been washed in hot water that is a minimum of 60 degrees Celsius.

After the first two days and at the end of the MRSA eradication therapy it is necessary to clean all "contact surfaces" and horizontal surfaces with wet rags in addition to vacuuming all interiors that are made of cloth upholstery.

Samples must be obtained from a patient four and 14 days after MRSA eradication therapy. The samples are obtained as previously described. If MRSA eradication therapy fails, the doctor evaluates the continuing treatment.

3.2.2 MRSA Preventive Process for Accident and Emergency Patients

A process for MRSA prevention that is conducted when the patients go home after the service at AE is described in Figure 5:

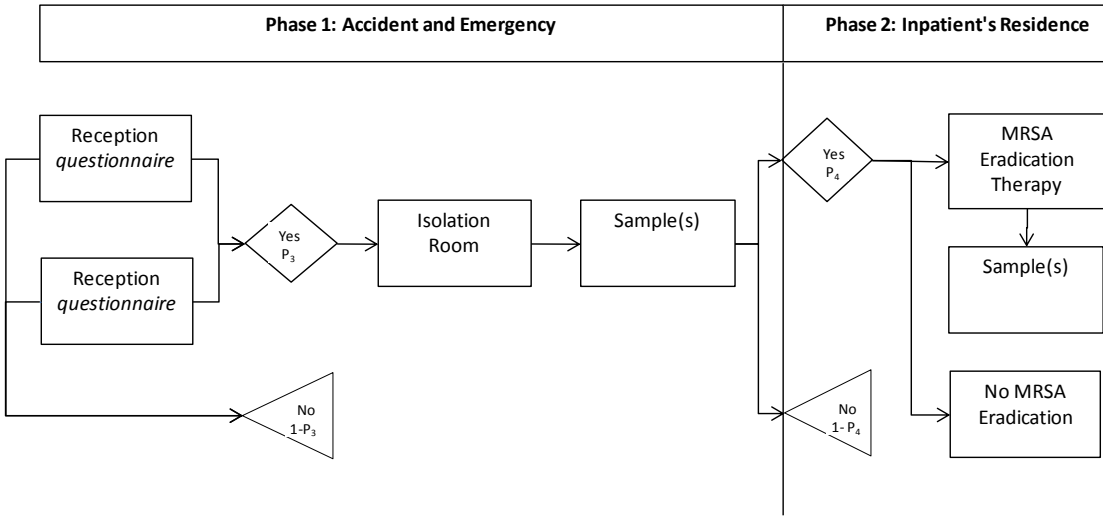

Figure 5. MRSA preventive process for emergency reception's patients.

Phase 1: Accident and Emergency: The preventive process in this phase is almost identical with the process described in the section MRSA Preventive Process for Inpatients – Phase 1: Emergency Room and Admission Centre. The patient goes home when he/she has received AE's service and the finding of the sample is presented to the patient after three days. Subsequently, a physician decides, with the patient's consultation, whether the patient undergoes MRSA eradication therapy or not. The reason why a patient participates in the decision about undergoing MRSA eradication

therapy is based on the fact that more and more people seem to carry MRSA and the MRSA eradication therapy is not simple or without cost, as previously described.

Phase 2: Patient's Residence: If it is decided that a patient carry out MRSA eradication therapy at home, he/she follows the preventive process, which is almost identical with the procedures described in the section MRSA Preventive Process for Inpatients – Phase 3: Patient's Residence. If MRSA eradication therapy fails, a physician evaluates the continuing treatment for the patient. In an interview with Gudlaugsson (2012) it was noted that MRSA eradication therapy is usually not continued if it was not effective the first time. The reason is that such a treatment is difficult, especially if the clinical condition of a patient is complicated.

3.2.3 MRSA Preventive Process for Groups Other than Patients

As a matter of course and in accordance with the aim of keeping LUH free of MRSA, preventive processes are also necessary for some individuals other than the patients. Considering that the involvements of these groups are ideologically at every ward in LUH, Figure 6 describes the MRSA preventive process for groups other than patients:

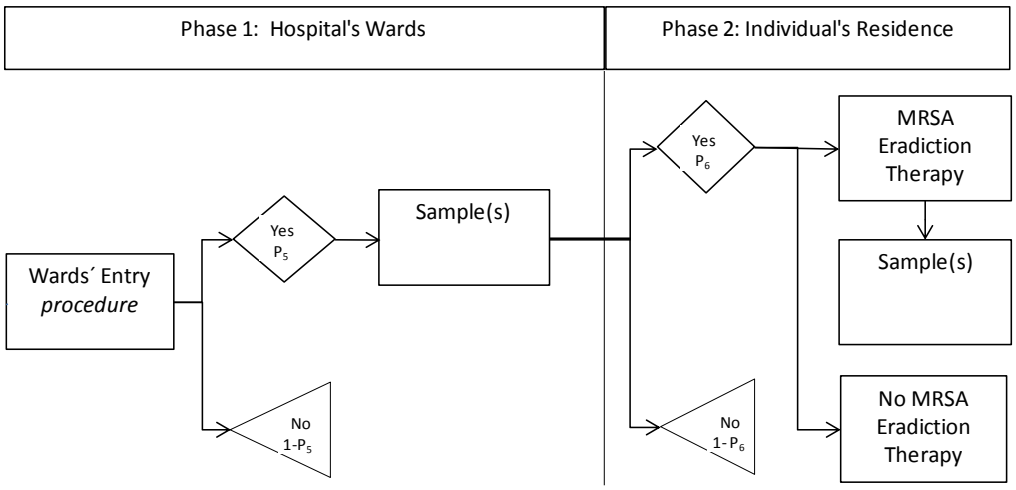

Figure 6. MRSA preventive process for groups other than patients.

Phase 1: Definition of Risk Group:

According to procedure 07.01.05.01 *Samples Obtained due to MRSA Search* and to procedure *07.01.04.01 Searching MRSA by New Employees and Students*, wards' head nurses and head physicians are responsible for obtaining MRSA samples from the

following groups of people: (1) individuals who accompanied patients in LUH's ward and individuals who have been with a patient in a hospital abroad, (2) employees and students who have worked in foreign medical institutions over the past six months, (3) employees who are working occasionally in foreign medical institutions parallel with their work at LUH, (4) employees and students who have been diagnosed with MRSA (in order to assess the distribution of MRSA on their bodies). As previously described, obtaining samples should be done in accordance with procedure *07.01.05.01 Samples Obtained due to MRSA Search*.

Phase 2: Individual's Residence:

If it is decided that a patient will carry out MRSA eradication therapy at home he/she follows the preventive process, which is almost identical to the process described in the section MRSA Preventive Process for Inpatients – Phase 3: Patient's Residence. However, MRSA eradication therapy is usually not continued if it was not effective the first time.

3.2.4 MRSA Preventive Process for Unexpected Detection of MRSA and Outbreaks within LUH

If MRSA is detected and/or spreads within a department of LUH, this indicates that the first line of defence has not been effective in keeping the bacteria outside of the hospital's walls. If such an event occurs, a process is activated where the aim is to eradicate the existence of MRSA within the department. Such action can be defined as a second line of defence.

If MRSA is detected on an employee's body, the reactive measures are in accordance with procedure *07.01.06.02 Unexpected Diagnosis of MRSA by Employee*. The first step is to call in specialists from DIC who obtain more samples from the employee. The employee cannot work while the result of the first MRSA test is being confirmed and while treatment is being executed. Samples are also obtained from colleagues and patients, and possibly from others at the employee's residence(s). Consequently, if MRSA eradication therapy is applied, the previously mentioned procedure, *07.01.01.02 Information for Individual about MRSA Eradication Therapy,* is applied.

According to the procedure *07.01.06.01 Unexpected Diagnosis of MRSA by Inpatient*, the first reaction to an unexpected diagnosis of MRSA for an inpatient is to transfer the diagnosed MRSA patient into an isolation room (or isolate him/her in his/her current room). Following, an evaluation is completed to determine the extent of action that should be taken but, at the very least, samples are obtain from various people, which is defined as the minimum circle of screening. The minimum circle of screening entails screening employees who have administered services to the diagnosed MRSA individual, screening patients who are at risk (patients with implants and/or psoriasis) as well as patients who shared a room with the diagnosed MRSA individual, and obtaining samples from the diagnosed MRSA individual's environment. If additional individuals are diagnosed with MRSA, the circle of screening is repeated (and expanded) and hospitalization in that ward is stopped.

As a matter of course, the previously described procedures, such as those for cleaning, are applied in managing any unexpected detection of MRSA. If an outbreak does occur, an "Outbreak Committee" controls the reactionary measures. According to the procedure *07.01.07 MRSA Outbreak*, the individuals appointed to the Outbreak Committee are the head physician and head nurse of the ward in which the outbreak is occurring, DIC's head physician and head nurse, and the chairman of the Committee for Infection Control.

The consequences of closing the entire ward are considerable. The first step is to stop admission into that ward. The hospital's employees must discharge every patient that can go home and must find room in other ward(s) for the patients who must remain in the hospital. Unfortunately, some patients must be sequestered in isolation rooms, i.e., if the are suspected MRSA patients following the outbreak. In addition, some employees must remain in their homes while they await the results of MRSA sample testing. Furthermore, the whole ward must be disinfected, which includes replacing operational goods and mattresses, in addition to paying overtime for the cleaning and transferring of the patients, and obtaining numerous MRSA samples from employees, inpatients, and the ward's environment.

An overview has now been given regarding MRSA preventive processes. In the next chapter, a framework of a hypothetical MRSA medical process is developed for the

purpose of economic evaluation or, more specifically, for comparison of the economic cost and benefit of these two processes.

3.3 Framework of SA Medical Processes

MRSA preventive processes, such as the SDP, constitute one out of two (or more) possible alternative strategies for dealing with MRSA. The other strategy is to allow MRSA to be part of the LUH environment in the form of bacteria flora. The clinical consequences of that strategy are that the number of MRSA infection will very likely increases. Therefore, to be able to compare cost of these two alternatives, the frameworks of MSSA and MRSA Medical Processes needs to be considered.

3.3.1 Definition of the Medication Processes and Clinical Consequences

Demonstrating or providing a full description of all possible MSSA and MRSA medical processes is not an easy task, nor is it even a realistic one. This is apparent based on the following considerations.

First, the clinical consequences of SA and MRSA infection vary significantly, which leads to the requirement for multiple medical processes. According to the overview provided in the Literature Review and the noted study by Dryden et al. (2010, p. 3), the clinical consequences of SA infection are widespread. For example, they can include skin and soft tissue infections, pneumonia (in the lungs), bacteraemia (in blood), endocarditis (in heart valves), osteomyelitis (in bones), prosthetic joint infections, and catheter related infections.

Second, the attribute status and the clinical status of individuals affect which medical procedure will be applied. As Laupland et al (2003, p. 1454) concluded if the likelihood of acquiring invasive SA is increased by individual risk factors, such as age, sex, being HIV positive, and being a patient with multiple traumas, then individual attributes and the individual's clinical status both affect the result of the medical process applied. In short, the exact same medical process for the same medical diagnosis may not give the same medical result between two individuals.

Third, there are no written clinical guidelines at LUH defining how to deal with MRSA infection, which is likely attributed to the fact that the number of MRSA infections at LUH was relatively low during the last decade(s). As noted in the section

entitled Distribution of MRSA – The Icelandic Image, and referring to the work of Holzknecht et al. (2010, pp. 4222-4223), from the year 2000 to the year 2008 only two individuals were infected by MRSA. These two individuals were infected abroad and were the only two diagnosed cases of MRSA infection in Iceland.

Fourth, as mentioned in the section Clinical Consequences of MRSA, according to Gudlaugsson (personal communication, 2011), the process and escalation of infection varies between clinical episodes, e.g., abscess does not necessarily entail blood infection, in addition, there are clinical episodes where abscess is not diagnosed before blood infection. Fifth, there is no one correct way to deal with MRSA infections, and therefore SA infections. As Liu (2012) explains, she and her co-authors "*aimed to create a framework to help clinicians evaluate and treat uncomplicated and invasive MRSA infections*." They continue, stating that *"[a]s with all IDSA guidelines, they are voluntary and are not meant to replace clinical judgment, but rather synthesize the available evidence and support the decision-making process, which must be individualized for each patient."* (Preventing Infections in Healthcare Settings Safe Healthcare).

Furthermore, these clinical guidelines which Liu et al. (2011) expressed in the article, Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant Staphylococcus aureus Infections in Adults and Children: Executive Summary address following as Liu describes it:

> *Eleven topics commonly encountered by adult and pediatric clinicians. They provide guidance in the management of: skin and soft tissue infections including recurrent infections; use of intravenous vancomycin; and invasive infections, such as pneumonia, and infections in the bones, joints, blood or heart. In the midst of our battle against medicine resistance, IDSA hopes the guidelines highlight the importance of the judicious use of antibiotics* (Preventing Infections in Healthcare Settings Safe Healthcare).

It is clear that, even though written clinical processes exist, the medical procedure seems ultimately based on the clinical judgment of physicians and their judicious use of antibiotics in treating their patients.

As discussed above, there are many clinical consequences of SA. The studies discussed in the Literature Review demonstrate that the prevalence of the various

clinical consequences is uneven. Diekema et al. (2001, p. 114) classified the clinical consequences of SA roughly in three categories, from the year 1997 to the year 1999 and on a global scale. By calculating the ratios as a percentage of all SA infections, bloodstream infection (bacteraemia) counted for 26%, lower respiratory tract infection counted for 27%, and skin/soft tissue infection counted for 46%. In the USA, Klein, Smith and Laxminarayan (2007, p. 1843) revealed that in the year 2005, cellulitis and abscess were the major reasons for hospitalization whereas SA is one of the main pathogen. For Iceland, Holzknecht et al. (2010, p. 4223) revealed that from the year 2000 to 2008, 135 individuals were diagnosed with clinical infections. Out of this 135 there were 109 patients (81%) diagnosed with skin and soft tissue infections, 15 patients (11%) were diagnosed with genitourinary tract infections, eight patients (6%) were diagnosed with respiratory tract infections, one patient was diagnosed with osteomyelitis, and two patients were diagnosed with bacteraemia.

As SSTI is a prevalent consequence of SA, it is logical to establish a medical procedure for SSTI as a "standard" procedure. This conclusion was supported by Gudlaugsson M.D. (personal communication, 2012) in an interview when he recommended that two types of infections should be used as platform (or standard) for the analysis of Non Search and Destroy Policy (NSDP) situations; those two being the medical procedure for SSTI and the medical procedure for endocarditis.

While only two medical diagnoses were initially noted, SSTI and endocarditis infection, in further discussions with Gudlaugsson (2012) it was determined that genitourinary tract infection, respiratory tract infection, and osteomyelitis should be classified, or grouped in, with SSTI. It was subjectively estimated that these infections have more similar profiles to SSTI in terms of cost attributes rather than to the cost attributes of bacteraemia. Therefore, the definition of SSTI hereafter includes these listed diagnoses.

As described in the Literature Review, the early phase of the evolution of SA infection manifests in the form of ruptures on skin followed by the development of an abscess. The second phase is cellulitis and the third phase is blood infection, which has three main serious consequences: (1) infection in the cardiac valve, (2) abscess in inner organs such as the brain, joints, liver, bones, spleen, and lungs, etc., and (3) abscess in implants

such as artificial hip joints. In order to reduce the number of medical procedures required and make rational decisions about which clinical consequences should be chosen as the averages. For a standard medical process for the serious clinical consequences of SA infection, I follow Guðlaugsson's (2012) recommendation which is, in fact, the clinical judgment of a physician.

3.3.2 Medication Processes for SA Infections

As previously described, the medication process for SSTI and medication process for endocarditis[15] have been chosen as two typical medication processes for curing SA infections. Medication processes for SA infections are distinguished as to whether the infection is caused by MSSA or MRSA. There are four medication processes altogether. In the following descriptions of the processes, it is assumed that the SA patients receive the same level of services during their stay in LUH, but in the economic evaluation, I will elaborate on the more specific differences between the consequences of MSSA infection and MRSA infection. All of the following descriptions of the medication processes are based on one interview with Gudlaugsson (personal communication, 2012).

The medication process for SSTI infection for MSSA infected patients consists of intravenous Ekvacillin 2 g, four times per 24-hour period for 10 to 14 days or intravenous Kefzol 2 g, three times per 24-hour period for 10 to 14 days. If the veins of the patient are not suitable for intravenous injection, the medication process for treatment is four tablets of Staklos 1 g, four times per 24-hour period for the same duration.

The medication process for endocarditis infection for MSSA infected patients consists of intravenous Ekvacillin 2 g, six times per 24-hour period for four to six weeks. The efficiency of this medication process is estimated at approximately 95%. If the medication process is unsuccessful, then the subsequent medication process applied is the same as that applied for endocarditis infection by MRSA.

[15] The prescription of medication for endocarditis is the same as that given for bacteraemia

The medication process for SSTI infection for MRSA infected patients consists of several steps. The number of steps depends on the bacteria's medicinal immunity. The first step is to give the patient, intravenously, Vancomycin 1 g, two times per 24-hour period for 10 to 14 days. During the time this medication process is applied, blood samples have to be obtained once every week in order to measure the medicine's concentration in the blood. If the bacterium is immune to Vancomycin then two alternatives are available. The first alternative is to administer intravenously Bactrim 8 mg, three times per 24-hour period up to two weeks, or Bactrim tablets, 8 mg, four times per 24-hour period for one to two weeks. The second alternative is to administer intravenously Dalacin 600 mg, three times per 24-hour period for one to two weeks or Dalacin tablets 150 mg, three to four times per 24-hour period for one to two weeks.

The medication process for endocarditis infection for MRSA infected patients consists of intravenously injected Vancomycin 1 g, two times per 24-hour period for four to six weeks. The efficiency of this medication process is estimated at approximately 85%.

3.3.3 Epidemiology of SA under Current SDP

As explained in the section Medication Process for SA Infections, the clinical consequences of SA are classified into two categories: SSTI and endocarditis. Furthermore, it is assumed that the description of the medication process for endocarditis is equal to the medication process for bacteraemia. Based on this assumption and the information in the Literature Review, the following epidemiology is depicted under the current SDP in Table 5:

Table 5. Epidemiology of SA under SDP by yearly numbers of individuals and internal ratios.

Type of Infection	MRSA Individuals	MRSA Ratio	MSSA Individuals	MSSA Ratio	SA Individuals	SA Ratio
SSTI	14.8	4.9%	284.2	95.1%	299.0	78.9%
Bacteraemia	0.2	0.3%	65.8	99.7%	66.0	17.2%
Mortalitiy	0.0	0.0%	18.4	100.0%	18.4	4.8%
Total	**15.0**	**3.9%**	**368.4**	**96.1%**	**383.4**	**100.0%**

Therefore, it is estimated that there are 383.4 individuals infected by SA per year in Iceland. Where:

$MRSA - SSTI_{SDP}$ is calculated by summation of the number of skin and soft tissue infections, genitourinary tract infections, respiratory tract infections, respiratory tract infections, and osteomyelitis in Table 3 and divides the number by 9 years, i.e., the study period. This classification corresponds with the decisions referred to in the section titled Definition of the Medication Processes and Clinical Consequences, which are aimed at reducing the number of medication processes.

$MRSA - Bacteraemia_{SDP}$ is calculated by dividing the number of bacteraemia in Table 3 by 9 years.

$MRSA - Mortality_{SDP}$ is zero as confirmed by Holzknecht et al. (2010, p. 4223) and Asgeirsson et al. (2011, p. 516).

$MSSA - SSTI_{SDP}$ is calculated by subtracting the number of skin and soft tissue infections caused by MRSA in Table 3 from the given number of SSTI hospitalizations caused by SA (245). Then I have the estimated number of skin and soft tissue infections caused by MSSA, i.e., 233. To find out the number of other types of infections except bacteraemia, it is assumed that the ratio of soft tissue and skin infection to the sum of genitourinary tract infections, respiratory tract infections, respiratory tract infections, and osteomyelitis is similar for MRSA and MSSA. Then the estimated annual number of SSTI is 233 plus 51 or 284.

$MSSA - Bacteraemia_{SDP}$ is determined by using data from Asgeirsson et al. (2011, p. 515) for the years 2005 to 2008. It is, therefore, 263 divided by four years.

$MSSA - Mortality_{SDP}$ is given by using data from Asgeirsson et al. (2011, p. 515) or by estimating the one year, all-cause mortality rate for the years 2005 to 2008 for individuals 18 years and older or 28.2%.

It should be noted in the CBA that it is assumed that no one dies from SA infection after one year of becoming infected.

3.4 Framework of Economic Evaluation

The framework of the CBA is based on incremental analysis and comparison of the existent social cost of existent SDP and the marginal cost of not applying the SDP. By revising Drummond et al.'s (2004, p. 212) expression of NSB, I will use the following equation to calculate the net social benefit (NSB) of LUH's SDP:

$$\mathrm{NSB}_{SDP} = \sum_{t=1}^{T} \frac{B_{SDP}(t) - C_{SDP}(t)}{(1+\mathrm{r})^{t-1}}$$

Where:

NSB_{SDP} = net social benefit of LUH's SDP.

$B_{SDP}(t)$ = benefits derived within a year *t* by applying SDP .

$C_{SDP}(t)$ = accrued cost within a year *t* by applying SDP.

$1/(1+\mathrm{r})^{t-1}$ = discount factor at the annual interest rate.

$t = 1, 2, 3, \dots, T$ = time of the calculated value of the project, 50 years.[16]

3.4.1 Benefit Function of the Search and Destroy Policy

By reviewing Drummond et al. (2004, pp. 20, 215, 223), expression, represented in Chapter *2.3.3 Cost-Benefit Analysis*, the valuation of the global willingness to pay for a program includes a measurement of the effect of a program, other values created, and resources saved. In other words, this means valuation of some intangible benefits of improved health to the receiver of the health care service, such as cost avoided in the future and increased productivity output because of better health status. According to this definition, the following model is used to estimate the benefit derived in one year at time *t* for LUH's MRSA SDP:

$$B_{SDP}(t) = \Delta P(t) + IU(t) + \Delta HC(t) + \Delta HH(t) + \Delta OC(t)$$

Where:

$\Delta P(t)$ = incremental total value of lost production by individuals due to the difference in incidence rate of MRSA infections under the SDP compared to NSDP in year *t*.

$IU(t)$ = intangible benefits due to the decision of having active SDP in year *t.*

[16] The reader should keep in mind that in the result all numbers about cost and benefit are based on the definite lifetime of the project to the next 50 years.

$\Delta HC(t)$ = saved cost within the health care system[17] due to the difference in incidence of MRSA infections under SDP compared to NSDP in year *t*. The incremental cost equals to the incremental value of saved cost due to SDP being applied, compared to if NSDP were applied at LUH.

$\Delta HH(t)$ = saved cost of households due to the difference in incidence of MRSA infection and consequent mortality under SDP compared to NSDP in year *t*.

$\Delta OC(t)$ = incremental cost or benefit of sectors other than household and health care system sectors due to the difference of infection and mortality under SDP compared to NSDP in year *t*.

3.4.1.1 Estimation of Incremental total Value of Lost Production

The variable $\Delta P(t)$ is an incremental total value of lost production.

The model for estimation of $\Delta P(t)$ is:

$$\Delta P(t) = E[PR(t)_{NSDP} - PR(t)_{SDP}]$$

$$= \left(E\left[IR(t)_{NSDP}^{E[PO(t)]}\right] - IR(t)_{SDP}^{E[PO(t)]}\right) x\, E\left[\frac{PR(t)^{E[G(t)]} / N_{WL}}{360}\right] x\, E[ALOS_{MRSA} - ALOS_{MSSA}]$$

$$+ \left(E\left[MR(t)_{NSDP}^{E[PO(t)]}\right] - MR(t)_{SDP}^{E[PO(t)]}\right) x\, E\left[\frac{P(t)^{E[G(t)]} / NN_{WL}}{360}\right] x\, LEAW$$

Where:

$E[PR(t)_{NSDP} - PR(t)_{SDP}]$ = expected difference in average value of society's production by individuals under NSDP compared to current SDP.

$E\left[MR(t)_{NSDP}^{E[PO(t)]}\right]$ = number of individuals infected by MRSA in year *t* under NSDP. To estimate this number, I use data from Table 2, Clusters of Countries by MRSA Isolates out of all SA Isolates of MRSA in 2011, collected by the European Centre for Disease Prevention and Control (Susceptibility of Staphylococcus aureus isolates to Methicillin in

[17] As discussed in *Chapter 1.2 Research Focus and Research Objectives*, LUH is the largest hospital in Iceland and therefore can be said to represent the Icelandic health care system.

participating countries in 1998 - 2011, 2013) as follows. The ratio from countries that apply SDP or have a low rate (<6%) of MRSA positive isolations are not included in the estimation to avoid underestimation of the expected rate of MRSA isolates. Furthermore, data from Portugal, Romania, and Malta which have infection rates of 54.6%, 50.5%, and 49.2%, respectively, are also not included in the sample as they are deemed to be outliers in the data.[18] Additionally, according to Figure 2, there is an indication of a difference in incidence of MRSA between Northern Europe and Southern/East Europe and Portugal, Romania, and Malta belong to South Europe and former Eastern Europe. Therefore, to estimate a hypothetical ratio of MRSA infections out of all SA infections within Iceland without current SDP, the following calculation is completed:

$$E\left[IR(t)_{NSDP}^{E[P(t)]}\right] = {\sum_{c=1}^{u} IR_c(2011)}/{u}$$

Where:

${\sum_{c=1}^{u} IR_c(2011)}/{u}$ = average rate (calculated to a number in the model) by MRSA isolates out of SA isolates in 18 European countries (u=18) in the year 2011 or 21.7%. Furthermore, the median is 21.5%, the maximum is 41.6%, and the minimum is 7.1%. Therefore, the hypothetical ratio of MRSA infections out of all SA infections within Iceland without the current SDP used in the base case will be 22.0%.

Notably, $IR(t)_{SDP}$ and $E[IR(t)_{NSDP}]$ are assumed to increase yearly by the number of individuals in accordance with the expected increase of 65 years and older people within the population, i.e., $E[PO(t)]$. The variable, $E[PO(t)]$, is estimated on a yearly basis according to Statistic Iceland's (2012) estimated population projection at a medium rate, for the years 2013 to 2061, rather than the average estimated growth of the population.

$IR(t)_{SDP}^{E[PO(t)]}$ = expected average number of individuals infected by MRSA at time *t*.

[18] Descriptive statistics reveal that the average ratio of MRSA isolates out of SA isolates for 28 countries is 20% and the standard deviation is 16%.

$E\left[\frac{PR(t)^{E[EG(t)]/N_{WL}}}{360}\right]$ = expected value of average compensation of employees per day estimated by following the function for the first year by using data from Statistic Iceland on compensation (2013) and population, 18 to 69 years old (2013):

$$E\left[\frac{PR(t)^{E[EG(t)]/NN_{WL}}}{360}\right] = \frac{Compensation\ of\ Employees\ 2012}{(Population\ 18-69\ years\ \ 1st\ of\ January\ 2012 + Population\ 18-69\ years\ 1st\ of\ January\ 2013)/2}/360$$

$$= 12{,}075\ \text{IKR}$$

$E[PR(t)]$ is assumed to growth in accordance with economic growth over the time per capita or $E[EG(t)]$ because of increased productivity over time. This change in productivity over time is estimated by the following formula using data from Statistic Iceland (2013):

$$E[EG(t)] = Average\ Growth\ rate\ of\ National\ Income\ per\ Capita$$

$$= \left(Gross\ Domestic\ Product\ per\ Capita, Index_{2012}/Gross\ Domestic\ Product\ per\ Capita, Index_{1945}\right)^{\frac{1}{68}} - 1$$

$$= 2.2\%$$

$E[ALOS_{MRSA} - ALOS_{MSSA}]$ = expected difference between average lengths of stay of MRSA inpatients and average lengths of stay of MSSA inpatients.

The difference in the ALOS between MRSA inpatients and MSSA inpatients is estimated within the Literature Review.

Also in the Literature Review, an overview is provided regarding estimations from several studies of the difference in the ALOS between MSSA inpatients and MRSA inpatients:

- Wernitz et al. (2005, p. 466) found that the average length of overstay for 21 patients with post-operative wound MRSA infection was 28.9 days, the average length of overstay for nine patients with pneumonia caused by MRSA was 28.6 days, and the average length of overstay for 15 patients with bloodstream infection was 21.9 days. The average length of overstay for five patients with MRSA urinary tract infection was 14.0 days and the average length of overstay for 11 patients with other types of infection was 24.6 days.
- Rubio-Terrés et al. (2009, p. 722) found that the ALOS for the administering of antibiotic treatment was 3.1 days longer for patients with MRSA infection than

for patients with SA and the ALOS for MRSA patients was 2.2 days longer than for patients with SA bacteraemia.

- Graves et al. (2007, p. 280) estimated the effects of a single HAI on length of stay. The main result was that urinary tract infection did not lead to increased length of stay nor increased variable cost, whereas lower respiratory tract infection led to increasing length of stay by 2.6 days. Other types of HAIs led to increasing length of stay by 2.6 days.
- Naber (2009, p. 234) explains that inpatients with SA bacteraemia had a three-times longer mean duration of hospital stay or 14.3 days versus 4.5 days.
- Cosgrove et al. (2005, p. 166) estimated that lengths of stay were nine days for the MRSA patients and seven days for the MSSA patients.
- Köck et al. (2010, p. 3) describe five studies where the MRSA infected patients stayed 2.0 days, 4.0 days, 9.0 days, 10.0 days, and 5.0 days longer compared to MSSA patients and in one study infected MSSA patients stayed nine days longer than uninfected patients.
- Resch, Wilke and Fink (2009, p. 287) found that the MRSA patients compared to the control group stayed 11 days longer in hospitals.
- Nulens et al. (2008, p. 301) calculated that the ALOS for 22.412 patients was 8.7 days but the ALOS for all patients with MRSA bloodstream infection was 39.9 days.

The results of these studies are evidently not uniform. Although, there is sufficient evidence to conclude that one should evaluate the consequence of the difference in ALOS between MSSA infected inpatients and MRSA infected patients when the ratio of MRSA infections is raised in absence of SDP because the cost of each lay in hospital does matter in CBA whereas it is considerable.

As revealed above Wernitz et al. (2005) and Nulens et al. (2008) estimate the overstay of MRSA infected patients by comparing them to a non-SA infected group, therefore, their result will not been used in the estimation of differences of ALOS between MRSA infected inpatients and MSSA inpatients. Data from Rubio-Terrés et al. (2009), Graves et al. (2007), Nader (2009), Cosgrove et al. (2005), Köck et al. (2010), and Resch, Wilke and Fink (2009) are used to estimate the difference in ALOS between

MSSA infected inpatients and MRSA infected inpatients or the numbers of days; 2.0, 2.2, 2.6, 2,6, 3.1, 4.0, 5.0, 9.0, 10.0, 11.0, and 14.3. The mean of these numbers is 6.0 and the median is 4.0. With reference to the above data, it is concluded that for a base case in the CBA estimation, the difference in ALOS between MRSA and MSSA infected inpatients is 4.0 days for the base case.

$\left[MR(t)_{NSDP}^{E[PO(t)]}\right]$ = expected mortality rate due to MRSA infection in year t under NSDP, based on reference to epidemiological data in the Literature Review.

In the Literature Review, an overview is provided of the estimates on mortality rates from several studies. The studies where the mortality rate presented as a ratio of deceased persons out of infected individuals were as follows:

- Klein, Smith and Laxminarayan (2007, pp. 1842-1843) measures only a slight difference in mortality rates between MSSA and MRSA infected patient groups or 6.1% and 6.2%, respectively.
- Asgeirsson et al. (2011, p. 513) estimated mortality rates caused by SA in the period between 1995 to 2008 in Iceland. The authors found out that the all-cause, 365-day mortality rate was 38.9% for the years 1995 to 1999, 32.8% for the years 2000 to 2004, and 28.2% for the years 2005 to 2008.
- Rubio-Terrés et al. (2009, p. 726) found that the 12-month mortality rate for patients with MRSA bacteraemia was 39.7%, but the 12-month mortality rate for patients with SA bacteraemia was 25.3%.
- Cosgrove et al. (2005, p. 168) determined that the mortality rate was 22.9% for the patients diagnosed with MRSA bacteraemia and it was 19.8% for the patients diagnosed with MSSA bacteraemia.
- Naber (2009, p. 234) explains that studies show that mortality rates for SA bacteraemia vary substantially, i.e., within the range of 0% to 83% but this can partly be explained by differences in patient groups, settings, and the mortality measurements used. For example, in a Belgian study, the MRSA bacteraemia–associated mortality rate has been measured as high as 23.4%, but the MSSA bacteraemia–associated mortality rate was 1.3%.

In the following studies, the overall OR for increased mortality associated with MRSA bacteraemia compared with MSSA bacteraemia was estimated:

- Cosgrove et al. (2003, p. 53) found that the OR for increased mortality associated with MRSA bacteraemia compared to MSSA bacteraemia was estimated to be 1.93. Furthermore, for studies where ≥ 70% of the MRSA cases were defined as HAI, the comparable OR was estimated to be 2.03.
- Köck et al. (2010, p. 3) outlined how in two meta-analyses it was estimated that invasive MRSA infections increased mortality by 1.93 and 2.03. In addition, by referring to 15 studies where the OR for MRSA-associated mortality was compared to MSSA-associated mortality, the minimum OR was estimated to be 0.73 but the maximum OR was estimated to be 5.4.

The results of the above studies are not uniform. Although, there is sufficient evidence to conclude that one should evaluate the consequence of difference in mortality rate between MSSA infection and MRSA infection when the ratio of MRSA infections increases in absence of SDP. The reasons is that the cost of premature death due to MRSA infection can be considerable in term of opportunity cost i.e. an individual that is alive produces goods and services which is not supplied if the person is dead.

As revealed is the difference in mortality rate caused by MRSA bacteraemia compared to mortality rate caused by MSSA bacteraemia confounding. Therefore, a baseline is developed by "intuition" (considering that there is high mortality in some studies, low in others, and no one has died in Iceland from MRSA bacteraemia). Assume that for the base case the mortality rate of patients with MRSA bacteraemia is 25% higher than for patients with MSSA bacteraemia. Further, the age of the MRSA infected individual at the time of death is set at 65 years old for the base case. This is premised on the fact that the average age of individuals *infected* by SA bacteraemia is 62.5 years, as seen in Table 4, Characteristics associated with SA bacteraemia from the year 1995 to the year 2008, so it logically follows that the average age at the time of death must be higher than 62.5 years. Several researchers also support this conclusion. For example, Pastagia et al. (2012, p. 1076) determined that older age increases the risk of death of patients with concomitant MRSA bacteraemia; Engemann et al. (2003, p. 594) found out that the mean age of patients with SSTI caused by MSSA was 55.1 years old compared to the mean age of patients with SSTI caused by MRSA which was 63.1 years old; finally, as discussed in the Literature Review, Laupland et al. (2003, p. 1454) found that one of the main risk factors for the acquisition of invasive SA is older age.

$MR(t)_{SDP}^{E[PO(t)]}$ = estimated mortality rate due to MRSA infection in year *t* under current policy.

$LEAW$ = days, calculated by estimating the duration between 65 years old (the estimated average age of death by MRSA infection) to the time that the elderly person receives social benefits (given that the average life expectancy age is higher than 65). According to Icelandic law (Statute book, 2000) it is assumed that individuals begin to receive social benefits at age 70 and according to Statistics Iceland (2011) the life expectancy of males was 79.2 years and the life expectancy of females was 83.7 years in the year 2010. Therefore, $LEAW$ is equal to 1.800 days.

Further, the following constraints are in effect:

$$E[PR(t)_{NSDP} - PR(t)_{SDP}] \geq 0$$

$$IR(t)_{SDP}^{E[PO(t)]} - \left[IR(t)_{NSDP}^{E[PO(t)]}\right] \geq 0$$

$$E[ALOS_{MRSA}] - E[ALOS_{MSSA}] \geq 0$$

$$MR(t)_{SDP}^{E[PO(t)]} - E\left[MR(t)_{NSDP}^{E[PO(t)]}\right] \geq 0$$

$$P(t)/_{N} = P(t)_{SDP}/_{N_{SDP}} = P(t)_{NSDP}/_{N_{NSDP}}$$ [19]

3.4.1.2 Estimation of Intangible Benefits

Measuring intangible benefits, i.e., $IU(t)$ of the MRSA program, is difficult to execute even though this is an important component when estimating global willingness to pay from an economics perspective. The reason being that, in many ways, individuals in society are very likely to experience a positive utility of the MRSA program, the patients directly and other members of society indirectly. The human capital approach measures only the value of individuals (carriers and infected) on the labour market, not the value of the opportunity for health. Furthermore, is it very likely that individuals in society positively value both the assurance of an MRSA free hospitals and the goals of

[19] This is based on the assumption that production per healthy capita is equal under both SDP and NSDP

diminishing the negative effects of contagion diseases. While it is beyond the scope of this study to estimate the intangible benefit of LUH's MRSA program in a precise way (indeed, it may not even be possible to do so) a rough estimation of this component of the CBA is used. To reflect the value that society places on medical care as well as the hindrance of disease transmission, half of an average medical doctor salary and half of a registered nurse's salary are added to equal a numerical value

3.4.1.3 Estimation of Health Care's Incremental Cost

The equation for estimating the health care's incremental cost is following:

$$\Delta HC(t) = E[HC(t)_{NSDP} - HC(t)_{SDP}] = \left(E\left[IR(t)_{NSDP}^{E[PO(t)]}\right] - IR(t)_{SDP}^{E[PO(t)]}\right) x\,(HCMC)] + E[ALOS_{MRSA} - ALOS_{MSSA}] * A/2) + \left(E\left[MR(t)_{NSDP}^{E[PO(t)]}\right] - MR(t)_{SDP}^{E[PO(t)]}\right) x\, E[MCD]$$

Where:

$E[HC(t)_{NSDP} - HC(t)_{SDP}]$ = expected difference in average value of health care services' cost under NSDP compared to current SDP.

$HCMC$ = marginal cost due to the difference in medication cost between MRSA infected patient and MSSA infected patient. This cost is determined by the following equation:

$$\text{HCMC} = \alpha SSTI_{MRSA}\left(\sum_{r=1}^{R}\sum_{s=1}^{S_{MRSA}}(p_{rs}\,x\,\Delta q_{rs})_{MRSA} - \sum_{r=1}^{R}\sum_{s=1}^{S_{MSSA}}(p_{rs}\,x\,\Delta q_{rs})_{MSSA}\right) + (1-\alpha)\text{Endocarditis}_{MRSA}\left(\sum_{r=1}^{R}\sum_{s=1}^{S_{MRSA}}(p_{rs}\,x\,\Delta q_{rs})_{MRSA} - \sum_{r=1}^{R}\sum_{s=1}^{S_{MSSA}}(p_{rs}\,x\,\Delta q_{rs})_{MSSA}\right)$$

Where:

$\alpha SSTI_{MRSA}$ = the ratio of MRSA to SSTI in the changing infection rate due to the change from SDP to NSDP.

$(1-\alpha)\text{Endocarditis}_{MRSA}$ = the ratio of MRSA to endocarditis infections in the changing infection rate due to the change from SDP to NSDP.

p_{rs} = price of resource *s*, which is utilized in medication process *r* per lay day.

q_{rs} = quantity of resource *s*, which is utilized in medication process *r* per lay day.

A/2 = average cost per lay day within the division of medicine and measures the predetermined marginal fraction of the lay day cost.

$E[MCD]$ = expected excess cost per deceased inpatient. According to Cheryl (2009) the estimated cost of dying in hospital was about 26,000 USD compared to the estimated cost of being discharged alive of 9,447 USD. The ALOSs were 8.8 days and 4.5 days,

respectively. According to these estimations, the cost of dying in hospital is nearly double the cost of patients who are discharged alive. Notably, no other reports were found regarding the higher cost per lay day of dying patients and, according to RN Bjarnadottir (Hospital cost of dying inpatients, 2013), there is no obvious indication of higher cost per lay day of dying patients, rather, the cost of terminal patients is reflected in the longer ALOS. Therefore, the cost for the hospital of inpatients dying (because of MRSA bacteraemia) is already (partly) reflected in the difference of ALOS between MRSA and MSSA infected patients. By using this information, it is estimated that the expected excess cost per deceased inpatient essentially equals to a fixed hotel cost per one lay day.

Furthermore, the following constraint is in effect:

$E[HC(t)_{NSDP} - HC(t)_{SDP}] \geq 0.$

The interpretations and constraints for other variables used in equation five above are in effect.

3.4.1.4 Estimation of Households' Incremental Cost

Incremental household cost is estimated by the following formula:

$$\Delta HH(t) = E[HH(t)_{NSDP} - HH(t)_{SDP}]$$

$$= \left(E\left[IR(t)_{NSDP}^{E[PO(t)]}\right] - IR(t)_{SDP}^{E[PO(t)]}\right) \; x \; E[CV_{HH}] \; x \; E[ALOS_{MRSA} - ALOS_{MSSA}]$$

Wherea:

$E[HH(t)_{NSDP} - HH(t)_{SDP}]$ = expected difference in average value of household cost under NSDP compared to current SDP.

$E[CV_{HH}]$ = expected household cost per visit of each relative households, which is estimated at 25% of daily production (one working hour or one visit per day + travel costs) of healthy individual or:

$$\frac{E\left[\frac{PR(t)^{E[EG(t)]}/_{N_{WL}}}{360}\right]}{8} = \frac{12{,}075 \text{ IKR}}{8} = 1{,}509 \text{ IKR}$$

Furthermore, the following constraint is in effect:

$E[HH(t)_{NSDP} - HH(t)_{SDP}] \geq 0$

The interpretations and constraints for other variables used in equation six above are in effect.

3.4.1.5 Estimation of Other Values Created

Other values of the SDP program reflect the fact that every individual faces definite uncertainty regarding his or her own health outcome under both policies, i.e., the SDP lowers the risk of being infected and, therefore, of dying from MRSA infection but does not eliminate it. The value (or utility) for the individual or society of lowered risk of MRSA infection is not known.[20]

A way to approach the problem of estimating other values created by the SDP is to look at two interrelated facts. First, people are willing to save money in private pension funds, in addition to compulsory payments into pension funds ordered by Icelandic law. According to the Icelandic Financial Supervisory Authority (Statistical information, 2013) the number of people who owned private property rights to pensions in private pension funds was 68% of the number that paid the compulsory payment in the year 2011. Further, 27.7% of the individuals who paid the compulsory payment in the year 2011 added payments into private pension funds, even though the economic situation was poor in that year. Hence, the Icelandic system of pension funds reveals the preference of individuals to "buy" or pay for what amounts to the equivalent of insurance. In other words, paying into pension funds is theoretically equal to paying into insurance that covers the cost of living if one lives longer than 70 years (as they expect to do) because he/she will lose the opportunity to utilize the pension (or use the insurance) if one dies to early. In this relation, it is implicitly assumed that the individual has no ability to pass on the pension to his/her relatives. Furthermore, some individuals earn wages, but almost all of them also receive social benefits as described in more detail in the following text. A model based on this discussion is depicted as follows:

$$\Delta OC(t) \;= E[OC(t)_{NSDP} - \; OC(t)_{SDP}]$$

$$= -\left(E\left[MR(t)_{NSDP}^{E[PO(t)]}\right] - \; MR(t)_{SDP}^{E[PO(t)]}\right) x\, E\left[\left(\frac{WB(t)^{E[G(t)]}/_{N_E}}{360}\right) + \left(\frac{PB(t)^{E[R(t)]}/_{N_E}}{360}\right) - \left(\frac{GB(t)^{E[G(t)]}/_{N_E}}{360}\right)\right] x\, LEAP$$

[20] This is one of the reasons that the revealed preference method or the contingent valuation method is not viable to estimate the individual value of the program.

Where:

$E[OC(t)_{NSDP} - OC(t)_{SDP}]$ = expected difference in average value of other values created under NSDP compared to SDP.

$E\left[\frac{WB(t)^{E[G(t)]}/_{N_E}}{360}\right]$ = expected value of paid wages (wage benefit) to individuals 70 years and older per day, measured as the average wage for people based on data from Statistics of Iceland (2012) and estimated by the following equation:

$$E\left[\frac{WB(t)^{E[G(t)]}/_{N_E}}{360}\right] =$$

$$\left(\frac{Wages\ Paid\ to\ Individuals\ 70\ Years\ and\ Older\ in\ the\ Year\ 2011\ x\ PI_{2011-2012}}{(Number\ of\ Individuals\ 70\ Years\ and\ Older\ 1st\ of\ January\ 2012 + Number\ of\ Individuals\ 70\ Years\ and\ Older\ 1st\ of\ January\ 2013)/2}\right)/360$$

= 3,674 IKR

N_E = number of people 70 years and older in the population.

$E\left[\frac{PB(t)^{E[R(t)]}/_{N_E}}{360}\right]$ = expected value of individuals' benefits for those 70 years and older per day, measured as the average pension paid by pension funds per day per individual 70 years and older. This variable is estimated by the following function:[21]

$$E\left[\frac{PB(t)^{E[R(t)]}/_{N_E}}{360}\right] =$$

$$\left(\frac{Old\ Age\ Pension\ 2011\ paid\ by\ Compulsory\ Pension\ Funds\ x\ PI_{2011-2012}}{(Number\ of\ Individuals\ 70\ Years\ and\ Older\ 1st\ of\ January\ 2012 + Number\ of\ Individuals\ 70\ Years\ and\ Older\ 1st\ of\ January\ 2013)/2}\right)/360$$

= 4,835 IKR

Where:

$E[R(t)]$ = expected growth of compulsory pension funds estimated by the National Association of Pension Funds in Iceland (2013) real interest rate for the last 15 years equals to 3.1%.

PI = price level index calculated by Statistics Iceland (Statistics Iceland, 2013) equals to 5.3%, which is lower than the rise in the wage index which is 7.8%.

$E\left[\frac{SB(t)^{E[G(t)]}/_{N_E}}{360}\right]$ = expected value of payments by the government to individuals 70 years and older per day. This variable is estimated by the following function for the first year by using data from Statistic Iceland (2012) regarding social benefits of elderly

[21] Payments by private pension funds are not included because, according to Icelandic law, individuals could withdraw money out of the private pension funds by exemption due to the economic situation.

people in the year 2011 indexed to the price level of 2012 and data on the population by age from Statistics Iceland (2012):

$$E\left[\frac{SB(t)^{E[G(t)]}/N_E}{360}\right] = \frac{Old\ Age\ Pension\ and\ Supplements\ 2011\ paid\ by\ the\ State\ x\ PI_{2011-2012}}{(Number\ of\ Individuals\ 70\ years\ and\ Older\ 1st\ of\ January\ 2012 + Number\ of\ Individuals\ 70\ years\ and\ Older\ 1st\ of\ January\ 2013)/2} /$$

$$360$$

$$= 3.439\ \text{IKR}$$

Because of strong private pension funds for elderly people in Iceland and regulations on the diminishing social benefits for elderly who can afford to live on their own savings (pension funds), the social benefits paid by the government are regarded as comprising net outflow to elderly people and, therefore, is subtracted in the CBA.

$LEAP$ = life expectancy at pensions measured in days. This variable is calculated from the estimated average age of receiving social benefits for elderly, in consideration of that life expectancy. According to Icelandic law (2000) it is assumed that individuals begin to receive social benefits at age 70 and, according to Statistics Iceland (2011), the life expectancy of males was 79.2 years and females 83.7 years in the year 2010 or approximately 81.5 years averaged the life expectancy of the individual. Therefore, $LEAP$ is equal to 4,140 days.

Furthermore, the following constraint is in effect:

$$E[OC(t)_{NSDP} - \ OC(t)_{SDP}] \geq 0$$

The interpretations and constraints for other variables used in equation five above are in effect.

3.4.2 Cost Function of Preventive Processes

The cost of LUH's SDP is estimated in accordance with the preventive processes described in the section Framework of the MRSA Preventive Processes at LUH. Consequently, the cost function for the SDP is represented in the following:

$$C_{SDP}(t) = \sum_{i=1}^{k} E[r_i] \sum_{j=1}^{m(i)} E[P_{in}](p_{ij}\ x\ q_{ij}) \quad (12)$$

Where:

$E[r_i]$ = expected number of individuals who met the criteria to be admitted to preventive process *i*.

p_{ij} = price of resource *j* that is utilized in preventive process *i*.

q_{ij} = quantity of resource j that is utilized in preventive process *i*.

k = number of preventive processes applied within LUH's SDP, as described in section 3.2., marked as i = I, II, III and IV.

$m(i)$ = number of preventive measures applied in preventive process *i*, on a yearly basis. This number is determined by probability of applying preventive measurement in preventive process *i*, on a yearly basis.

$E[P_{in}]$ = expected number of individuals for phase *n* in process *i*. $E[P_{in}]$ is P_1 or P_1*P_2 in preventive process *i* = 1, P_3 or P_3*P_4 in preventive process *i* = 2, P_5 or P_5*P_6 in preventive process *i* = 3 and P_7 in preventive process *i* = 4, depending on which preventive stage is applied. This is in accordance with the definition set previously in the section Framework of MRSA Preventive Program at LUH.

Information given by Helgadottir (MRSA Screening Samples, 2013) about screening samples is used to estimate $E[P_n]$. In the following table, averages are shown for the type of preventive process over the years 2008 to 2011:

Table 6. Numbers of screened individuals by preventive process in the years 2008-2011.

Preventive Process	2008	2009	2010	2011	Average Number 2008-2011
Wards' Inpatients via Accident and Emergency's	90	64	58	50	**66**
Wards' Inpatients via Admission Centre	113	115	133	152	**128**
Accident and Emergency's Patients	699	461	456	604	**555**
LUH's Outpatients' Wards and Employees and Other Units Outside LUH	892	927	487	994	**825**
Total Number of Screened Individuals due to SDP	**1.794**	**1.567**	**1.134**	**1.800**	**1.574**

The numbers of obtained samples per location are also based on the information of Helgadottir (MRSA Screening Samples, 2013), as depicted in the following Table 7:

Table 7. Numbers of samples obtained by locations.

Location of Obtained MRSA Samples	2008	2009	2010	2011	Average Number 2008-2011
Accident and Emergency's Patients	1.422	937	937	1.062	**1.090**
Wards' Inpatients	601	713	690	683	**672**
LUH's Outpatients' Wards and Employees and Other Units Outside LUH	1.794	1.987	1.082	1.947	**1.703**
Total Number of Samples Obtained	**3.817**	**3.637**	**2.709**	**3.692**	**3.464**

Furthermore, by using information provided by Helgadottir (MRSA Screening Samples, 2013), the result of the screening program has been as follows:

Table 8. Result of MRSA screening.

Preventive Process	2008	2009	2010	2011	Average Number 2008-2011
Wards' Inpatients via Accident and Emergency's	2	7	2	2	**3**
Wards' Inpatients via Admission Centre	7	11	3	15	**9**
Accident and Emergency's Patients	5	-	5	8	**5**
LUH's Outpatients' Wards and Employees and Other Units Outside LUH	8	9	7	15	**10**
Total Number of Individuals Detected by LUH's MRSA Screening Program	**20**	**20**	**15**	**38**	**23**

Consequently the estimation of P_n is depicted in the following table:

Table 9. Estimation of number of individuals within each preventive process.

Variable	Expected Value
$E[P_{11}] = P_1$	182
$E[P_{12}] = P_1 * P_2$	12
$E[P_{21}] = P_3$	550
$E[P_{22}] = P_3 * P_4$	5
$E[P_{31}] = P_5$	815
$E[P_{32}] = P_5 * P_6$	10
$E[P_{41}] = P_7$	-
Total Number of Individuals	**1574**

As shown, P_7 is not estimated. In Table 3, Descriptive Statistic for Epidemiology of MRSA in Iceland 2000 to 2008, it was revealed that two outbreaks occurred in the period of the reference study. These two outbreaks included 10 patients and 25 health care workers and family members. To include the outbreak scenario, I assume that an outbreak will occur every 5 years. This "estimation" is based on the fact, according to Holzknecht et al. (2010, p. 4222), that over a 9 year period, two outbreaks occurred. The cost estimation is approached by calculating how much it will cost to run a 12-bed ward for one month.

Estimations of the quantity of resources utilized in each preventive process is based on descriptions in the section Framework or MRSA Preventive Program at LUH. Therefore, the main categories of cost are material and work related to preventive measures such as obtaining samples, cleaning, and eradicating the MRSA bacteria.

Appendix D contains a list of resources used in preventive processes and therefore in the calculation of its cost.

All prices are based on average price level of the year 2012 in and without value-added-tax. Unfortunately, all prices given by LUH are confidential according to clauses in LUH's suppliers' contracts so no information can be provided regarding the exact quantity and prices estimated in each preventive process.

3.4.3 Estimation of the Discount Rate

To determine the discount rate, the following information is retrieved from the website of Government Debt Management (Government Debt Management - Market Overview, 2013):[22]

Table 10. Yield of indexed treasury bonds.

Indexed	Duration (Bp 01)	Bid Yield	Ask Yield	Bid Price	Ask Price	Last Yield	Last Trade	Yield (price) Change	Value Traded *	Trade Count
RIKS 21 0414	6.94 (0.08%)	1.86%	1.78%	114.40	115.03	1.82%	114.72	0.07 (-0.52%)	0	0
HFF150224	5.41 (0.06%)	2.26%	2.12%	108.25	109.05	2.16%	108.80	-0.01 (0.05%)	0	0
HFF150434	9.59 (0.10%)	2.56%	2.43%	112.00	113.29	2.49%	112.64	0.04 (-0.36%)	0	0
HFF150644	13.51 (0.15%)	2.74%	2.65%	114.30	115.71	2.69%	115.03	-0.01 (0.09%)	0	0

The yield curve of indexed treasury bonds is upwards over a longer time, as can be seen in Table 10. Where the MRSA preventive program of LUH gives a benefit to the lifetime of the individual and that time exceeds 13.51 years, the discount rate for the CBA of LUH SDP is set at 2.7%.

3.4.4 Epidemiology of SA under NSDP

In the base case of the estimated distribution of clinical consequences under NSDP it is assumed that the total number of infections will be unchanged. Specifically, the total number of SA infections is unchanged, the hypothetical ratio of MRSA infections out of all SA infections within Iceland without current SDP used in the base case will be 22.0%, and the mortality rate will be 25% higher for MRSA.

[22] Government Debt Management is a unit within the Central Bank of Iceland and is responsible for debt management of the state treasury on behalf of the Icelandic government.

Therefore, the following formulas are used to set up the epidemiology of SA under NSDP for the base case:

$$\text{MRSA} - \text{SSTI}_{\text{NSDP}} = 22.0\% * \text{Total SA} - \text{SSTI}_{\text{SDP}}$$

$$\text{MRSA} - \text{Bacteraemia}_{\text{NSDP}} = 22.0\% * \text{MSSA} - \text{Bacteraemia}_{\text{SDP}}$$

$$\text{MRSA} - \text{Mortality}_{\text{NSDP}} = 28\% * 1{,}25 * \text{MRSA} - \text{Bacteraemia}_{\text{NSDP}}$$

$$\text{MSSA} - \text{SSTI}_{\text{NSDP}} = 299 - \text{MRSA} - \text{SSTI}_{\text{NSDP}}$$

$$\text{MRSA} - \text{Bacteraemia}_{\text{NSDP}} = 66 - \text{MRSA} - \text{Bacteraemia}_{\text{NSDP}}$$

$$\text{MSSA} - \text{Mortality}_{\text{NSDP}} = 28.0\% * \text{MRSA} - \text{Bacteraemia}_{\text{NSDP}}$$

Consequently, the following table of epidemiology of SA under NSDP is depicted as a base case for the CBA:[23]

Table 11. Epidemiology of SA under NSDP by yearly numbers of individuals and internal ratios.

Type of Infection	MRSA Individuals	MRSA Ratio	MSSA Individuals	MSSA Ratio	SA Individuals	SA Ratio
SSTI	65.8	22.0%	233.2	78.0%	299.0	77.7%
Bacteraemia	13.5	22.0%	47.4	78.0%	66.0	17.2%
Mortalitiy	5.1	35.0%	18.4	65.0%	19.6	5.1%
Total	**84.3**	**28.2%**	**280.6**	**77.8%**	**384.6**	**100.0%**

3.4.5 Expression of the Result

All calculations above aim to give an estimation of the total net benefit of the SDP. To supplement the result, I also calculate the estimated total net present value of the benefit and cost, and consequently the NSB per healthy life year gained by the program for individuals who are hindered by infection from MRSA but survive. I also execute the

[23] Higher mortality rate leads to "fine tuning" of the number $\text{MRSA} - \text{Bacteraemia}_{\text{NSDP}}$ and, therefore, the ratio of mortality seems to be inaccurate.

same calculations for the saved life years of people who would die by MRSA infection in the absence of SDP. Consequently, the following equations are used in the calculation:

$$Number\ of\ Healthy\ Life\ Years = \sum_{t=1}^{50}\left(E\left[IR(t)_{NSDP}^{E[PO(t)]}\right] - IR(t)_{SDP}^{E[PO(t)]} * ALOS\right)\Big/_{360}$$

$$Number\ of\ Saved\ Life\ Years = \sum_{t=1}^{50}\left(E\left[MR(t)_{NSDP}^{E[PO(t)]}\right] - MR(t)_{SDP}^{E[PO(t)]} * (LEAW + LEAP)\right)\Big/_{360}$$

$$Benifit\ of\ Healthy\ Life\ Year = {Total\ Benefit\ of\ Lower\ Infection\ Rate}/{Number\ of\ Healthy\ Life\ Years}$$

$$Benefit\ of\ Saved\ Life\ Year = {Total\ Benefit\ of\ Lower\ Mortality\ Rate}/{Number\ of\ Saved\ Life\ Years}$$

$$Cost\ of\ Healthy\ Life\ Year = Cost\ of\ Saved\ Life\ Year$$
$$= Total\ Cost\ of\ SDP * Ratio\ of\ Healhty\ Life\ Years/Number\ of\ Healthy\ Life\ Years$$
$$= Total\ Cost\ of\ SDP * Ratio\ of\ Saved\ Life\ Years/Number\ of\ Saved\ Life\ Years$$

Where the ratio of healthy life years is calculated as follows:

$$Ratio\ of\ Healthy\ Life\ Years\ =$$
$${Number\ of\ Healthy\ Life\ Years}\Big/{(Number\ of\ Healthy\ Life\ Years + Number\ of\ Saved\ Life\ Years)}$$

And ratio of saved life years is calculated as follows:

$${Number\ of\ Saved\ Life\ Years}\Big/{(Number\ of\ Healthy\ Life\ Years + Number\ of\ Saved\ Life\ Years)}$$

Consequently, the following is calculated:

$$NSB\ of\ Healthy\ Life\ Year$$
$$= {(Benifit\ of\ Healthy\ Life\ Year - Cost\ of\ Healthy\ Life\ Year)}\Big/{Number\ of\ Healthy\ Life\ Years}$$

$$NSB\ of\ Saved\ Life\ Year = (Benifit\ of\ Saved\ Life\ Year - Cost\ of\ Saved\ Life\ Year) / Number\ of\ Saved\ Life\ Years$$

$$Total\ NSB\ of\ Each\ Healthy\ and\ Saved\ Life\ Year = (Total\ Benefit - Total\ Cost) / (Number\ of\ Healthy\ Life\ Years + Number\ of\ Saved\ Life\ Years)$$

Note that all numbers are *estimates* as stated previously.

In addition, the "approximated" internal rate of return (IRR) of each scenario is calculated by Excel-function. This is done by dropping out the benefit in the first year and allowing the estimated total cost of the SDP in year one denote the outflow of the benefit. Then the net benefit is calculated for year two to year 50 (benefit inflow – benefit outflow) in each year, regarded as the net inflow of benefit. This series is then calculated to give insight into IRR of the preventive program at macro-economic level.

3.5 Framework of Scenario Analysis

The prevalence of SA, incidence of SA infections (infection rate), and the relative distribution between its sub-strains MSSA and MRSA affects the CB of the MRSA preventive program as well as differences in ALOS between MRSA and MSSA infected inpatients and differences in mortality rates between the patients groups. The framework of the scenario analysis is based on changing these variables and examines the effect of such changes on the CB of the MRSA preventive program. In the scenario analysis, I assume that the data regarding prices and quantity of resources used per unit are fixed, but the discount rate can vary.

3.5.1 Varying the SA Infection Rate

As discussed in the Literature Review, the prevalence of SA (including MSSA and MRSA) is not homogenous and depends on many factors such as hygiene, group of population/groups situations, and more. Further, the transmission rate and incidence of SA infections depends on the prevalence and hygiene habits, amongst other factors, i.e., the variables that affect transmission rates and incidences of SA infections are

interdependent. While it is beyond the scope of this dissertation to model the research interrelations between prevalence, transmission rates, and incidence of SA infections, I calculate incidences of SA infections by using data from the ECDC (Susceptibility of Staphylococcus aureus isolates to Methicillin in participating countries in 1998 - 2011, 2013) and population data from Eurostat (2013). The focus is on the year 2001 to the year 2011 and the incidence per 100.000 in the population is calculated. Estimation of incidence of SA per 100.000 in the population is done by calculating the following:

$$\frac{SA\ incidence\ in\ country\ i}{100{,}000} = \frac{Number\ of\ SA\ Bacteraemia\ in\ country\ i}{Number\ in\ population\ in\ country\ i}\ x\ 100.000$$

$$SA\ Incidence\ per\ year\ k = \frac{\sum_1^{24} \frac{Incidence\ of\ SA\ bacteraemia\ \ in\ country\ i}{100{,}000}}{24}$$

The result is depicted below in Figure 7:

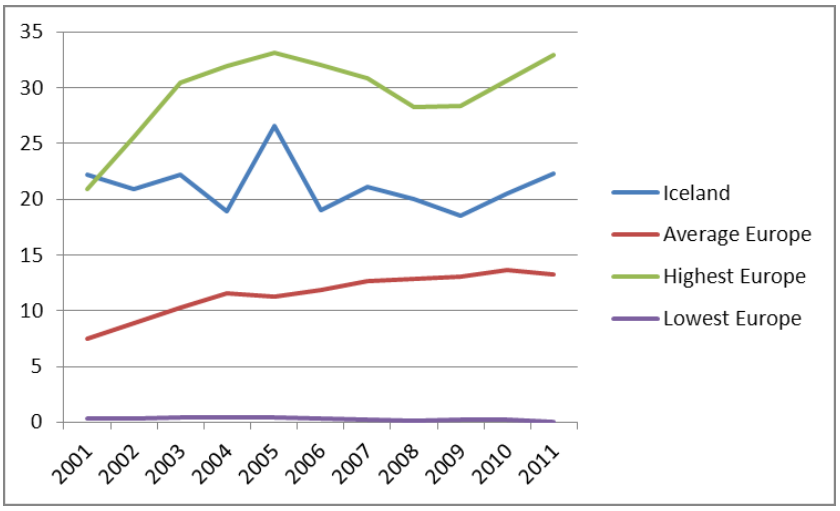

Figure 7. Incidence of SA bacteraemia per 100.000 in the population in Iceland and 24 european countries for the period of 2001 to 2011.

While the highest rate of prevalence of SA per 100.000 in the population is on average 46% higher in Europe than in Iceland, the total number of SA infections will vary from 383.4 individuals to 559.8 individuals and by 8 intervals in the variance analysis. The main reason for completing this variance analysis is that it is likely that the total number of SA infections can go up when the in absence of SDP.

3.5.2 Varying the MRSA Infection Rate

As concluded in the section Benefit Function of the Search and Destroy Policy, the number in the base case is 22.0% but the ratios of MRSA isolates out of all SA isolates in 18 European countries at the year 2011 were 41.6% at maximum and 7.1% at minimum. Therefore, in the scenario analysis the ratio of MRSA infections out of all SA infections will vary from 7.0% up to 42% by 3.5% interval in the scenario analysis.

3.5.3 Varying the Difference in Average Length of Stay

As concluded in the section Benefit Function of the Search and Destroy Policy, the base case difference in ALOS between MRSA and MSSA infected inpatients is four days but in the "data set" the maximum difference was estimated at 14.3 days and the minimum was estimated at two days. Therefore, the range of difference in ALOS between MRSA and MSSA infected inpatients in the scenario analysis is two days, three days, and so forth, up to 15 days.

3.5.4 Varying the MRSA Mortality Rate

According to the discussion in the section Benefit Function of the Search and Destroy Policy, I assume that the mortality rate for MRSA bacteraemia is in excess of the mortality rate for MSSA bacteraemia and will vary from 0% to 100% by 10% intervals.

3.5.5 Varying the Discount Rate

According to the Central Bank of Iceland (2013), the average of general real interest rates on indexed loans from July 2001 to April 2013 was 5.3%. Furthermore, according to Statistics Iceland (2012), the weighted average real interest rate of commercial banks from 1980 to 2011 for indexed loans (and mortgage loans from 2004) was 7.5%. While this information indicates that consumptions and, therefore, health seems to be relatively "highly" evaluated at present as opposed to future times, the discount rate varies from 1.00% + 0.5% intervals up to 6.5% in the scenario analysis. It is noticed that the real interest rates of government projects are generally lower than for the private market.

3.5.6 Varying the Average Age of Infected and Death Individuals by MRSA

It is noteworthy to examine how the average age of infected individuals, and therefore the average age of individuals at death, affects the CBA. The scenario analysis is calculated as though the average age of people dying by MRSA bacteraemia varies from 45 to 70 years old with 5-year intervals.

3.6 Limitations

There are several limitations of the executed CBA analysis. Mainly, these limitations are in the data collection process, in model specification, and in the estimation of procedures and variables.

3.6.1 Limitation of Estimated Procedures

The mapping of LUH's preventive program/processes according to its SDP was executed by interviewing individuals separately within the hospital, meaning over two years. While the hospital is comprised of high expertise staff members, it was not plausible to request that anyone confirm the adequacy of the description of overall preventive program/processes. As such, there is the possibility that the descriptions of LUH's preventive program/processes are not fully adequate and/or comprehensive.

As discussed, the "measurement" of procedure variables was executed by interviewing physicians and other experts. This "measurement" was used to standardize descriptions/estimations of preventive program/processes and medication processes. Through the data collection process I was aware that these descriptions (or experiences) of LUH's preventive program/processes could be slightly different between individuals interviewed. Furthermore, if the use of time and resources were measured by reading medical records or simply by follow up interviews with a few patients, it is very likely that the standard descriptions of preventive program/processes and medication processes would be at least slightly different from the ones described and used here.

3.6.2 Limitations in the Data Collection Process and Variables

The data on cost of resources (labour, operational goods, and medicine) are regarded as reliable. The data on wages are based on paid wages by each professional and data on

operational goods and medicine was retrieved from LUH's e-purchase systems. Further, there was follow up research to confirm that the data on prices per item were correctly determined.

The data on hospital's activity "within" each preventive program/process and medication process has its weaknesses as discussed in the section Limitation of Estimated Procedures. In addition, the validity of several data used is questionable. First, the estimated data on the number of $MSSA - SSTI_{SDP}$ patients were collected by provided ICD-codes, but the result was not reviewed. Second, the data from the ECDC used to modify variance analysis has flaws, i.e., as presented. Third, the data about the number of screened individuals and samples obtained in Iceland regarding MRSA is somewhat doubtful because the collection of that data was not without a significant "effort" and explanations from the experts of the Department of Clinical Microbiology.

3.6.3 Limitations by the Model Specification

The aim of the expression of the CB model, and consequent elaborations, is to correctly measure the CB of current SDP. Therefore, there must be a direct and true relationship between the cost and benefit of LUH's preventive program and lower infection rate and mortality rate caused by MRSA. If this requirement is fulfilled, all relevant cost and benefit of the MRSA SDP must also rightly be identified measured and quantified.

In a "perfect" world, the model would include some estimation of the infection rate as explained in the section The Nature of Transmission. Furthermore, it is noted that the screening tests are not 100% effective in detecting MRSA, which affects the effectiveness of the SDP. Even though these "attributes" are not included, which can be considered a limitation, this critique is somewhat countered in the scenario analysis.

For the sake of simplification, the censoring between the working age and retirement age is set at 70 years old. Some individuals begin to take retirement at 60 years old, some at 65, but in general, the retirement age is 67 years old even though people have the right to work until 70 years old. Furthermore, some people are disabled and prevented from working. By using average numbers, the distortions due to these simplifications are corrected at some point.

The method to calculate the value of (social) programs and therefore of decreasing negative externalities, i.e., diminishing contagious diseases, is rather “unformed” in the term intangible benefits. Primarily because there does not seems to be any obvious method to estimate the value of such programs for the participants. Therefore, this element is assessed to be weak in the model.

The model specification of incremental health cost regarding the incremental medication cost due to MRSA compared to MSSA is standardised in order to simplify it and, arguably, it may be too simple whereas the cost of capital is for example not directly included. Moreover, the health care cost of terminal people, shown by the incremental mortality rate caused by MRSA compared to MSSA, is based on a rather imperfect examination and is, in fact, mainly based on primitive estimation. Furthermore, it is assumed that the medication processes are 100% effective, but it is actually known that the effectiveness is lower than 100%, as discussed above.

The cost of capital (housing, etc.) was intentionally not specified in the analysis of cost nor was there some estimation of the effect created by a non-market situation in the health care sector. This was partially because the cost of lay days already include some cost of capital but likely not sufficiently even though it is assumed that the hospital capital is fixed and unattached to the decision of applying SDP. Further the estimation of non-market effect on prices is difficult to adequately estimate. Undeniably, if SDP is applied then isolation rooms are required and that for example count as a cost of capital.

Finally, the estimation of other values created is likely to be set up rather properly, even though more precise estimations could have been completed regarding the cost and benefit attributed to the elderly, especially in the scenario analysis.

Even though there is a limitation of specification of the model regarding the estimation of the cost and the benefit of the SDP, the model is estimated to be sufficiently appropriate for the estimation.

4 Result, Analysis and Discussion

In this section, the result of the calculations described in the Method section are presented and analysed. Furthermore, I discuss the result and examine the assumptions which were derived from a combination of the literature, the appropriateness of the model applied, and estimates of the validity of the results.

4.1 Result and Analysis

To summarize the assumptions described in the Method section, the base case variables and numbers of the calculations and its variations are expressed in the following table:

Table 12. Values of the model's variables in the base case and its variations.

Variables	Base Case	Minimum Value	Interval	Max Value
Variables in the Variance Analysis				
SA Infection Rate	383.4	383.4	22.1	559.8
MRSA Infection Rate	22.0%	7.0%	3.5%	42.0%
MRSA Mortality Rate	35.0%	28.2%	2.8%	56.4%
MRSA Average Dying Age	65	45	5	65
Difference in ALOS between MRSA and MSSA	4	2	1	15
Discount Rate	2.7%	1.0%	0.5%	6.5%
Fixed Variables				
MSSA Mortality Rate	28.2%	Fixed	Fixed	Fixed
Economic Growth	2.2%	Fixed	Fixed	Fixed
Real Interest Rate of Private Pension Funds	3.1%	Fixed	Fixed	Fixed
Growth of Population	2%*	Fixed	Fixed	Fixed

*Average Growth of 65 Years and Older next 50 Years

The model estimated is in equation 3 depicted in the Method section, that is:

$$B_{SDP}(t) = \Delta P(t) + IU(t) + \Delta HC(t) + \Delta HH(t) + \Delta OC(t)$$

In this section, each part of the model will be further deconstructed as needed to give the reader deeper insight and information about the attributes of the results. Furthermore, the results on benefit and cost per life year is presented.

4.1.1 Cost and Benefit of Iceland's SDP against MRSA

According to equations in the Method section, the total NSB of Iceland's SDP in the base case is as follows:

Table 13. Cost and benefit of the preventive program.

SA Infection Rate (Number of Individuals)	Benefit of Individuals' Production (ISK in millions)	Intangible Benefit (ISK in millions)	Benefit of Health Care System (ISK in millions)	Benefit of Households (ISK in millions)	Other Benefit Created (ISK in millions)	Cost of SDP (ISK in millions)	Net Social Benefit (ISK in millions)	IRR
383.4	2,208	676	967	70	666	-3,754	**833**	**11%**

The benefit of individuals' production has two origins as modelled in the Method section. The benefit of more production because of fewer lay days of inpatients due to lower number of infected individuals (lower infection ratio) is estimated to be ISK 281m.[24] The benefit of more production because of longer life is estimated to be ISK 1,927m, so the estimated NSB of additional production due to SDP is ISK 2,208m.

As demonstrated, the benefit of the health care system is threefold. First, the estimated savings according to the cost difference in treating MRSA and MSSA is ISK 55m, second, the saving due to a difference in ALOS of four days was estimated to be ISK 909m, and, third, the estimated saving of fewer dying inpatients is ISK 3m. The benefit to household cost is estimated to be mainly due to fewer visits to the hospital because of fewer lay days, which accords with the lower number of MRSA infected inpatients.

The cost of the SDP is attributed to the four types of preventive processes described above. The cost of preventive processes for inpatients is estimated to be ISK 2,097m, the cost of preventive processes for Accident and Emergency's patients is estimated to be ISK 1,024m, and the cost of preventive processes for LUH's Outpatients' Wards and Employees and Other Units Outside LUH is estimated to be ISK 388m. Finally, it is estimated that the cost of dealing with outbreaks is ISK 244m.

Estimated NSB of the preventive program is ISK 794m and estimated IRR is 10.4%. Therefore, the program is economical at a macro level.

[24] The *m* stands for million(s).

A meaningful measurement of the result of a health care program is the benefit and the cost per life year. According to the Method section, the following table depicts the result of life year(s) related to CB:

Table 14. Cost and benefit of each healthy and saved life year by the preventive program.

SA Infection Rate (Number of Individuals)	Benefit of each Healthy Life Year (ISK in millions)	Benefit of each Saved Life Year (ISK in millions)	Cost of each Healthy/Saved Life Year (ISK in millions)	NSB of each Healthy Life Year (ISK in millions)	NSB of each Saved Life Year (ISK in millions)	NSB of each Healthy and Saved Life Year (ISK in millions)
383.4	18.0	2.0	-2.2	15.8	-0.2	**0.5**

Notably, the benefit of each healthy life year is significantly more than the benefit of each saved life year or ISK 16.3m compared to ISK 2.0m, respectively. The main source of benefit of each healthy life year is in the health care system as fewer lay days due to a lower number of MRSA infected inpatients. In contrast, the main sources of benefit of each saved life year is in the form of avoiding lost production and other benefits created by hindering premature death. Finally, the average cost of each individual who goes into the preventive programs is ISK 47,516 per individual and is therefore a marginal cost of finding one person carrying or infected by MRSA, which is ISK 3,251,770.

4.1.1 Scenario Analysis

As shown in table 12, the following variables in the model were varied in the scenario analysis, i.e., the number of SA infected individuals, the infection rate of MRSA (number of individuals infected with MRSA), mortality rate of MRSA (number of deaths of individuals infected with MRSA), average age at time of death, ALOS, and the discount factor. The scenario analysis is created to examine the effect of changes in the variables on NSB in order to be better able to discuss the model and its variables for the ultimate purpose of determining whether the method is overall credible, useful, and what result can be judged as the most realistic.

4.1.1.1 Varying the SA Infection Rate

As explained in the Method section, infection rates are considered to be assessed by number of individuals infected. According to the description outlined in the section Framework of Scenario Analysis, the following table depicts the effect of varying the SA infection rate:

Table 15. Effect of varying SA infection rate on cost and benefit and IRR.

SA Infection Rate (Number of Individuals)	Benefit of Individuals' Production (ISK in millions)	Intangible Benefit (ISK in millions)	Benefit of Health Care System (ISK in millions)	Benefit of Households (ISK in millions)	Other Benefit Created (ISK in millions)	Cost of SDP (ISK in millions)	Net Social Benefit (ISK in millions)	IRR
383.4	2,208	676	967	70	666	-3,754	**833**	**11%**
405.4	4,353	676	1,038	75	1,401	-3,754	**3,789**	**82%**
427.5	6,499	676	1,109	80	2,135	-3,754	**6,746**	**153%**
449.6	8,645	676	1,181	85	2,870	-3,754	**9,702**	**224%**
471.6	10,790	676	1,252	90	3,605	-3,754	**12,658**	**295%**
493.7	12,936	676	1,323	95	4,340	-3,754	**15,614**	**366%**
515.7	15,081	676	1,394	100	5,074	-3,754	**18,571**	**437%**
537.8	17,227	676	1,465	104	5,809	-3,754	**21,527**	**508%**
559.8	19,372	676	1,536	109	6,544	-3,754	**24,483**	**579%**

By increasing the SA infection rate by 176.4 individuals, or by 217.3%, the NSB increases by more than 29 times, mainly due to high rises in the benefit of individuals' production values and other benefits created. This indicates that the "elasticity" of the NSB is positively correlated to increases in the SA infection rate, i.e., the NSB raises relatively faster than the increases in the number of SA of infected individuals. Consequently, if it is likely that the rate/prevalence of SA increases in absence of the SDP, the CBA supports the position that such a policy change should be reconsidered. Furthermore, IRR is positive by more than 10.0% in all scenarios.

Varying the number of individuals infected by SA results in decreasing patterns on the benefit of each healthy life year and each saved life year as per the following table:[25]

Table 16. Effect of varying SA infection rate on cost and benefit of healthy and saved life years.

SA Infection Rate (Number of Individuals)	Benefit of each Healthy Life Year (ISK in millions)	Benefit of each Saved Life Year (ISK in millions)	Cost of each Healthy/Saved Life Year (ISK in millions)	NSB of each Healthy Life Year (ISK in millions)	NSB of each Saved Life Year (ISK in millions)	NSB of each Healthy and Saved Life Year (ISK in millions)
383.4	18.0	2.0	-2.2	15.7	-0.2	**0.5**
405.4	17.6	1.8	-1.1	16.5	0.7	**1.1**
427.5	17.3	1.8	-0.7	16.6	1.0	**1.3**
449.6	17.2	1.7	-0.5	16.6	1.2	**1.4**
471.6	17.0	1.7	-0.4	16.6	1.3	**1.4**
493.7	16.9	1.7	-0.4	16.5	1.3	**1.5**
515.7	16.7	1.7	-0.3	16.4	1.4	**1.5**
537.8	16.6	1.7	-0.3	16.4	1.4	**1.5**
559.8	16.5	1.7	-0.2	16.3	1.4	**1.5**

The main reason for this result is that the number of healthy and saved life years increases at a higher rate than the number of SA infected individuals, or almost 9.5 times more, when changing the number of SA infected individuals by 217.3%

[25] Please note that all decimals are approximate. Therefore, there seems to be a small measure of inaccuracy in the numbers of NSB of each Healthy Life Year or NSB of each Saved Life Year.

4.1.1.2 Varying the MRSA Infection Rate

One of the variables that is varied in the scenario analysis is the MRSA infection rate. The following table depicts the effect of varying MRSA infection rates on the cost, the benefit, and the IRR as described:

Table 17. Effect of varying MRSA infection rate on cost and benefit and IRR.

MRSA Infection Rate (Ratio of Total SA Infections)	Benefit of Individuals' Production (ISK in millions)	Intangible Benefit (ISK in millions)	Benefit of Health Care System (ISK in millions)	Benefit of Households (ISK in millions)	Other Benefit Created (ISK in millions)	Cost of SDP (ISK in millions)	Net Social Benefit (ISK in millions)	IRR
7.0%	661	676	166	12	212	-3,754	**-2,028**	**<0%**
10.5%	1,022	676	353	26	318	-3,754	**-1,360**	**<0%**
14.0%	1,383	676	540	39	424	-3,754	**-693**	**<0%**
17.5%	1,744	676	727	53	530	-3,754	**-25**	**<0%**
21.0%	2,105	676	914	66	636	-3,754	**642**	**8%**
24.5%	2,466	676	1,101	80	742	-3,754	**1,310**	**22%**
28.0%	2,826	676	1,288	93	848	-3,754	**1,977**	**38%**
31.5%	3,187	676	1,475	107	954	-3,754	**2,645**	**55%**
35.0%	3,548	676	1,662	121	1,060	-3,754	**3,312**	**71%**
38.5%	3,909	676	1,849	134	1,166	-3,754	**3,980**	**87%**
42.0%	4,270	676	2,036	148	1,271	-3,754	**4,647**	**103%**

As shown above, the preventive program is not socially beneficial for MRSA infection rates lower than approximately 17.5% to 18.0% out of 383.4 SA infected individuals. In this scenario, three sources of increased NSB are due to hindering higher rates of MRSA infection, i.e., the benefit from higher individuals' production, the benefit from lower costs in the health care system, and the increased benefits created by the elderly. Thereof increases the benefit of the health care system by more than 12 times while the increases of the other two are similar by the increases in the rate of MRSA infection or around 6 times. The IRR increases with higher rates of MRSA infection. The NSB per healthy and saved life years is depicted in the following table:

Table 18. Effect of varying MRSA infection rate on cost and benefit of healthy and saved life years.

MRSA Infection Rate (Ratio of Total SA Infections)	Benefit of each Healthy Life Year (ISK in millions)	Benefit of each Saved Life Year (ISK in millions)	Cost of each Healthy/Saved Life Year (ISK in millions)	NSB of each Healthy Life Year (ISK in millions)	NSB of each Saved Life Year (ISK in millions)	NSB of each Healthy and Saved Life Year (ISK in millions)
7.0%	18.7	2.9	-7.2	11.5	-4.3	**-3.9**
10.5%	18.4	2.5	-4.7	13.6	-2.3	**-1.7**
14.0%	18.2	2.3	-3.5	14.7	-1.3	**-0.7**
17.5%	18.1	2.1	-2.8	15.3	-0.7	**-0.0**
21.0%	18.0	2.1	-2.3	15.7	-0.3	**0.4**
24.5%	17.9	2.0	-2.0	15.9	-0.0	**0.7**
28.0%	17.9	1.9	-1.8	16.1	0.2	**0.9**
31.5%	17.9	1.9	-1.6	16.3	0.4	**1.1**
35.0%	17.8	1.9	-1.4	16.4	0.5	**1.2**
38.5%	17.8	1.9	-1.3	16.6	0.6	**1.4**
42.0%	17.8	1.8	-1.2	16.6	0.7	**1.4**

According to the table above, preventive programs are not socially beneficial for MRSA infection rates lower than around 17.5% to 18.0%. The SDP program leads to increasing benefits of each healthy life year if MRSA infection rates increase, but notably decreases the benefit of each saved life year in the scenario because saved life years increase at higher rates than does the benefit of the SDP.

4.1.1.3 Varying MRSA Mortality Rate

The MRSA mortality rate is changed from 28.2% (same as the estimated MSSA mortality rate) by 10% up to 56.4%. The result and effect on cost, benefit, and IRR is depicted in the following table:

Table 19. Effect of varying MRSA mortality rate on cost and benefit and IRR.

MRSA Mortality Rate	Benefit of Individuals' Production (ISK in millions)	Intangible Benefit (ISK in millions)	Benefit of Health Care System (ISK in millions)	Benefit of Households (ISK in millions)	Other Benefit Created (ISK in millions)	Cost of SDP (ISK in millions)	Net Social Benefit (ISK in millions)	IRR
28.2%	281	676	964	70	0	-3,754	**-1.764**	**<0%**
31.0%	1,052	676	965	70	266	-3,754	**-725**	**<0%**
33.8%	1,822	676	967	70	533	-3,754	**314**	**3%**
36.7%	2,593	676	968	70	799	-3,754	**1,352**	**23%**
39.5%	3,364	676	969	70	1.066	-3,754	**2,391**	**48%**
42.3%	4,135	676	971	70	1.332	-3,754	**3,429**	**73%**
45.1%	4,906	676	972	70	1.598	-3,754	**4,468**	**98%**
47.9%	5,677	676	973	70	1.865	-3,754	**5,506**	**123%**
50.8%	6,447	676	975	70	2.131	-3,754	**6,545**	**148%**
53.6%	7,218	676	976	70	2.398	-3,754	**7,584**	**173%**
56.4%	7,989	676	977	70	2.664	-3,754	**8,622**	**198%**

The main effect of a hindered higher mortality rate by current SDP on NSB is in the benefit of individuals' production and other benefits created as expected when production is lower from the age of 65 to 70 and the benefit of the elderly is foregone. Notably, the benefit of other values created is zero because in the base case the excess mortality rate caused by MRSA compared to the mortality rate of MSSA is zero. Therefore, there is also no benefit to the item "Benefit of Individuals' Production" due to the excess mortality rate, i.e., ISK 281m is merely lost benefit from the production by inpatients.

As expected, the benefit of each saved life year and the cost of each saved life year are both zero when the MRSA mortality rate is 28.2; no excess life year compared to MSSA mortality rate is saved at that rate as the following table depicts:

Table 20. Effect of varying MRSA mortality rate on cost and benefit of healthy and saved life years.

MRSA Mortality Rate	Benefit of each Healthy Life Year (ISK in millions)	Benefit of each Saved Life Year (ISK in millions)	Cost of each Healthy/Saved Life Year (ISK in millions)	NSB of each Healthy Life Year (ISK in millions)	NSB of each Saved Life Year (ISK in millions)	NSB of each Healthy and Saved Life Year (ISK in millions)
28.2%	26.9	-	-50.8	-23.9	-	**-23.9**
31.0%	18.6	2.6	-5.2	13.4	-2.7	**-1.0**
33.8%	18.1	2.1	-2.8	15.4	-0.6	**0.2**
36.7%	17.9	2.0	-1.9	16.0	0.1	**0.7**
39.5%	17.7	1.9	-1.4	16.3	0.5	**0.9**
42.3%	17.6	1.8	-1.1	16.4	0.7	**1.0**
45.1%	17.5	1.8	-1.0	16.5	0.8	**1.1**
47.9%	17.4	1.8	-0.8	16.5	1.0	**1.2**
50.8%	17.3	1.8	-0.7	16.5	1.0	**1.3**
53.6%	17.2	1.7	-0.6	16.5	1.1	**1.3**
56.4%	17.1	1.7	-0.6	16.5	1.2	**1.3**

The calculations also show that the preventive program is not beneficial except if the mortality rate of MRSA is more than 10.0% higher than the mortality rate by MSSA for the given scenario. Furthermore, the table demonstrates that the cost of each life year and the cost of each saved life year decreases substantially, or at least at faster rate, than the benefit changes, due to changes in the mortality rate by MRSA.

4.1.1.4 Varying MRSA Average Dying Age

In the base case the average age of death of MRSA infected individuals was set 65 years old. If the average age of MRSA infected patients is lowered, the benefit of the program increases substantially as shown in the following table:

Table 21. Effect of varying MRSA average dying age on cost and benefit and IRR.

Average Age of Dying by MRSA	Benefit of Individuals' Production (ISK in millions)	Intangible Benefit (ISK in millions)	Benefit of Health Care System (ISK in millions)	Benefit of Households (ISK in millions)	Other Benefit Created (ISK in millions)	Cost of SDP (ISK in millions)	Net Social Benefit (ISK in millions)	IRR
65	2,208	676	967	70	666	-3,754	**833**	**11%**
60	4,356	676	967	70	897	-3,754	**3,213**	**50%**
55	6,752	676	967	70	1,085	-3,754	**5,796**	**90%**
50	9,423	676	967	70	1,239	-3,754	**8,621**	**135%**
45	12,401	676	967	70	1,369	-3,754	**11,730**	**184%**

The origin of NSB of lowering the average age of death of MRSA infected individuals is primarily in the benefit of individuals' production, where the benefit increases almost 6 times when lowering the average age of death by MRSA from 65 years old to 45 years old.

The NSB also substantially increases each healthy and saved life year due to lower average age of death by MRSA in the scenario, depicted as follows:

Table 22. Effect of varying MRSA average dying age on cost and benefit of healthy and saved life years.

Average Age of Dying by MRSA	Benefit of each Healthy Life Year (ISK in millions)	Benefit of each Saved Life Year (ISK in millions)	Cost of each Healthy/Saved Life Year (ISK in millions)	NSB of each Healthy Life Year (ISK in millions)	NSB of each Saved Life Year (ISK in millions)	NSB of each Healthy and Saved Life Year (ISK in millions)
65	18.0	2.0	-2.2	15.7	-0.2	**0.5**
60	17.9	2.7	-1.7	16.2	1.0	**1.5**
55	17.8	3.2	-1.4	16.4	1.8	**2.2**
50	17.8	3.6	-1.2	16.6	2.4	**2.8**
45	17.8	4.0	-1.0	16.7	3.0	**3.2**

The benefit of each saved life year doubles. This result can mainly be explained by the fact that even though the number of life years saved increases because of lower average age of death by MRSA, the value of lost production increases at a faster rate. Furthermore, the calculated benefit of each healthy life year decreases minimally with a lower average age of death because the number of healthy life years changes relatively little when the mortality variable is varied. When the number of healthy and saved years increases, the cost of each healthy year and each saved year drops by more than 50%.

4.1.1.5 Varying the Difference in ALOS between MRSA and MSSA

The increasing difference in the ALOS of inpatients infected by MRSA compared to inpatients infected by MSSA affects both the benefit of individuals' production and the benefit of the health care system due to lost active time at work and more cost in the health care system, respectively. This is depicted in the following table:

Table 23. Effect of varying difference in ALOS between MRSA and MSSA on cost and benefit and IRR.

Difference in ALOS between MRSA and MSSA	Benefit of Individuals' Production (ISK in millions)	Intangible Benefit (ISK in millions)	Benefit of Health Care System (ISK in millions)	Benefit of Households (ISK in millions)	Other Benefit Created (ISK in millions)	Cost of SDP (ISK in millions)	Net Social Benefit (ISK in millions)	IRR
2	2,067	676	513	35	666	-3,754	**203**	**1%**
3	2,138	676	740	53	666	-3,754	**518**	**6%**
4	2,208	676	967	70	666	-3,754	**833**	**11%**
5	2,278	676	1,194	88	666	-3,754	**1,148**	**18%**
6	2,348	676	1,422	105	666	-3,754	**1,463**	**26%**
7	2,418	676	1,649	123	666	-3,754	**1,778**	**34%**
8	2,488	676	1,876	140	666	-3,754	**2,092**	**42%**
9	2,559	676	2,103	158	666	-3,754	**2,407**	**49%**
10	2,629	676	2,330	175	666	-3,754	**2,722**	**57%**
11	2,699	676	2,557	193	666	-3,754	**3,037**	**65%**
12	2,769	676	2,785	210	666	-3,754	**3,352**	**72%**
13	2,839	676	3,012	228	666	-3,754	**3,667**	**80%**
14	2,909	676	3,239	246	666	-3,754	**3,982**	**87%**
15	2,980	676	3,466	263	666	-3,754	**4,297**	**95%**

The main source of NSB is originated in the health care system or about ISK 2,953m out of ISK 4,093m increases of NSB given that the difference in ALOS of inpatients infected by MRSA compared to inpatients infected by ALOS is changed from two days to 15 days.

Consequently, increases in the NSB of each healthy and saved life year are considerable as following table reveals:

Table 24. Effect of varying difference in ALOS between MRSA and MSSA on cost and benefit of healthy and saved life years.

Difference in ALOS between MRSA and MSSA	Benefit of each Healthy Life Year (ISK in millions)	Benefit of each Saved Life Year (ISK in millions)	Cost of each Healthy/Saved Life Year (ISK in millions)	NSB of each Healthy Life Year (ISK in millions)	NSB of each Saved Life Year (ISK in millions)	NSB of each Healthy and Saved Life Year (ISK in millions)
2	18.7	2.0	-2.3	16.4	-0.3	**0.1**
3	18.2	2.0	-2.3	16.0	-0.2	**0.3**
4	18.0	2.0	-2.2	15.7	-0.2	**0.5**
5	17.8	2.0	-2.2	15.6	-0.2	**0.7**
6	17.7	2.0	-2.2	15.5	-0.2	**0.9**
7	17.7	2.0	-2.2	15.5	-0.1	**1.0**
8	17.6	2.0	-2.1	15.5	-0.1	**1.2**
9	17.6	2.0	-2.1	15.4	-0.1	**1.4**
10	17.5	2.0	-2.1	15.4	-0.1	**1.5**
11	17.5	2.0	-2.1	15.4	-0.1	**1.7**
12	17.5	2.0	-2.1	15.4	-0.0	**1.8**
13	17.4	2.0	-2.0	15.4	-0.0	**2.0**
14	17.4	2.0	-2.0	15.4	-0.0	**2.1**
15	17.4	2.0	-2.0	15.4	0.0	**2.3**

The primary reason for this is that the difference in the ALOS of inpatients infected by MRSA compared to inpatients infected by MSSA creates the most benefit for individuals who gain healthy lives, i.e., are on the labour market if they survive the MRSA infection.

4.1.1.6 Varying the Discount Rate

Finally, the effect of varying the discount rate on the cost, benefit, and IRR of the program is examined. The following table reveals the result of the scenario when the discount rate is changed by 0.5% increments from 1.0% to 6.5%:

Table 25. Effect of varying discount rate on cost and benefit and IRR.

Discount Rate	Benefit of Individuals' Production (ISK in millions)	Intangible Benefit (ISK in millions)	Benefit of Health Care System (ISK in millions)	Benefit of Households (ISK in millions)	Other Benefit Created (ISK in millions)	Cost of SDP (ISK in millions)	Net Social Benefit (ISK in millions)	IRR
1.0%	3,574	1,029	1,460	114	520	-5,666	**1,030**	**14%**
1.5%	3,082	903	1,285	98	590	-4,988	**970**	**13%**
2.0%	2,673	797	1,137	85	634	-4,414	**912**	**12%**
2.5%	2,329	708	1,012	74	660	-3,928	**855**	**11%**
3.0%	2,041	631	905	65	672	-3,513	**801**	**11%**
3.5%	1,797	567	814	57	673	-3,158	**749**	**10%**
4.0%	1,591	511	735	51	667	-2,853	**701**	**10%**
4.5%	1,415	463	667	45	655	-2,590	**656**	**9%**
5.0%	1,266	422	609	40	639	-2,362	**614**	**9%**
5.5%	1,137	386	557	36	621	-2,163	**575**	**8%**
6.0%	1,027	355	513	33	601	-1,990	**538**	**8%**
6.5%	932	328	474	30	580	-1,839	**504**	**7%**

As expected, the NSB decreases gradually with the raises in the discount rate. Note that the IRR is around 7% when the discount rate is 6.5%.

The scenario for benefit and cost for each healthy life year and each saved life year is shown as follows:

Table 26. Effect of varying discount rate on cost and benefit of healthy and saved life years.

Discount Rate	Benefit of each Healthy Life Year (ISK in millions)	Benefit of each Saved Life Year (ISK in millions)	Cost of each Healthy/Saved Life Year (ISK in millions)	NSB of each Healthy Life Year (ISK in millions)	NSB of each Saved Life Year (ISK in millions)	NSB of each Healthy and Saved Life Year (ISK in millions)
1.0%	27.7	2.9	-3.4	24.3	-0.5	**0.6**
1.5%	24.2	2.6	-3.0	21.2	-0.4	**0.6**
2.0%	21.3	2.3	-2.6	18.7	-0.3	**0.5**
2.5%	18.9	2.1	-2.3	16.5	-0.2	**0.5**
3.0%	16.8	1.9	-2.1	14.7	-0.2	**0.5**
3.5%	15.0	1.7	-1.9	13.1	-0.1	**0.4**
4.0%	13.5	1.6	-1.7	11.8	-0.1	**0.4**
4.5%	12.2	1.5	-1.5	10.6	-0.1	**0.4**
5.0%	11.0	1.3	-1.4	9.6	-0.1	**0.4**
5.5%	10.1	1.2	-1.3	8.8	-0.0	**0.3**
6.0%	9.2	1.2	-1.2	8.0	-0.0	**0.3**
6.5%	8.5	1.1	-1.1	7.4	-0.0	**0.3**

Notably, the NSB of each saved life year is a negative value in all scenarios in the table, which is explained by the fact that the rate of MRSA infected people needs to be higher than 22.0% (the value used as a base ratio for the scenario).

4.1.1.7 Varying Several Variables in Contemporary Analysis

To estimate the effect of contemporary changes in variables, the following scenarios are displayed:

Table 27. Assumptions in contemporary variance analysis.

Variables	Best Case Scenario	Middle Case Scenario	Worst Case Scenario
Variables in the Variance Analysis			
SA Infection Rate	383.4	471.6	559.8
MRSA Infection Rate	7.0%	24.5	42.0%
MRSA Mortality Rate	28.2%	42.3%	56.4%
MRSA Average Dying Age	65	55	45
Difference in ALOS between MRSA and MSSA	2	7	15
Discount Rate	1.0%/6.5%	1.0%/6.5%	1.0%/6.5%
Fixed Variables			
MSSA Mortality Rate	Fixed	Fixed	Fixed
Economic Growth	Fixed	Fixed	Fixed
Real Interest Rate of Private Pension Funds	Fixed	Fixed	Fixed
Growth of Population	Fixed	Fixed	Fixed

*Average Growth of 65 Years and Older next 50 Years

As shown in Table 27, four scenarios are created: best case scenario, middle case scenario, and worst scenario with two calculations by different discount rates. The results of these cases are presented in Table 28 below:

Table 28. Effect of contemporary changes in variables on cost, benefit and IRR.

Scenario	Benefit of Individuals' Production (ISK in millions)	Intangible Benefit (ISK in millions)	Benefit of Health Care System (ISK in millions)	Benefit of Households (ISK in millions)	Other Benefit Created (ISK in millions)	Cost of SDP (ISK in millions)	Net Social Benefit (ISK in millions)	IRR
Best Case (1.0%)	39	1,029	0,131	10	0	-5,666	**-4,457**	**<0%**
Middle Case (1.0%)	73,662	1.029	3,636	288	8,065	-5,666	**81,014**	**1069%**
Worst Case (1.0%)	388,262	1,029	16,688	1,351	35,853	-5,666	**437,518**	**5368%**
Best Case (6.5%)	10	328	43	3	-0	-1,839	**-1,455**	**<0%**
Middle Case (6.5%)	19,204	328	1,180	75	4,308	-1,839	**23,256**	**796%**
Worst Case (6.5%)	101,224	328	5,415	352	10,391	-1,839	**115,873**	**4134%**

The above model estimates that the preventive program against MRSA is not socially beneficial for the best case scenario, i.e., lowest infection rate (SA and MRSA), lowest mortality rate by MRSA, highest average age of death by MRSA, lowest difference in ALOS between MRSA inpatients and MSSA inpatients, and lowest discount rate. It is noted that a higher discount rate makes the NSB less negative.

The NSB of the program is extreme when evaluated in an extreme situation, i.e., if all the variables that have effects on cost and benefit are at their worst. Specifically meaning, highest infection rate (SA and MRSA), highest mortality rate by MRSA, lowest average age of death by MRSA, highest difference in ALOS between MRSA inpatients and MSSA inpatients, and lowest discount rate all lead to a NSB of up to ISK 437,518m. As before, the cost and benefit of healthy and saved life years is depicted in the following table:

Table 29. Effect of contemporary changes in variables on cost and benefit of healthy and saved life years.

Scenario	Benefit of each Healthy Life Year (ISK in millions)	Benefit of each Saved Life Year (ISK in millions)	Cost of each Healthy/Saved Life Year (ISK in millions)	NSB of each Healthy Life Year (ISK in millions)	NSB of each Saved Life Year (ISK in millions)	NSB of each Healthy and Saved Life Year (ISK in millions)
Best Case (1.0%)	191.6	166.4	-898.0	-706.4	-731.6	**-706.4**
Middle Case (1.0%)	25.5	4.6	-0.3	25.2	4.3	**4.5**
Worst Case (1.0%)	24.7	6.1	-0.1	24.6	6.0	**6.2**
Best Case (6.5%)	60.8	54.9	-291.4	-230.6	-236.4	**-230.6**
Middle Case (6.5%)	7.8	1.3	-0.1	7.7	1.2	**1.3**
Worst Case (6.5%)	7.5	1.6	-0.0	7.5	1.6	**1.7**

From the data in Table 29, it seems that the benefit of healthy and saved life years develops abnormally. From the best-case scenario to the middle-case scenario, the

benefit per healthy life year decreases but from the middle case scenario to the worst-case scenario these benefits increase. The explanation is that the base case to the middle case increases the number of healthy years at a higher rate than would occur from the middle case to the worst case.

4.2 Discussion

The object of this sub-section is to discuss and recognize the strengths and the weaknesses of the applied method by reviewing the data and the structure of the model in relation with calculated result and scenario analysis and the analysis of limitations above. Finally the validity of the results will be examined.

4.2.1 The Data

The section Limitations in the Data Collection Process and Variables, discusses how the data on price of resources (labour, operational goods, and medicine) were assumed to be reliable and are therefore also expected to be credible. However, the data from LUH on cost can hardly be said to reflect the market value of the resources. The reason is that the hospital is a dominant buyer in the health-care "market". The state, for example, negotiates centrally regarding the wage for all health-care employees (a very minimal share of the total wage can be negotiated within each health-care institution) and is the main buyer of their services in the Icelandic health care market. Additionally, LUH is the only byer of many medicines and medical devices in Iceland due to its role and size within the health care system. Therefore, I conclude that the price of resources is correctly estimated in the model, but it is also possible that the cost is estimated at a minimum level where the prices may not reflect the opportunity cost of the resources used in the preventive program.

The data on market wages, pension, social benefits, real interest rates, economic growth, population growth, and distribution of the population is regarded as credible and reliable. The reason being that this data are collected and published by Statistics Iceland and/or Central Bank of Iceland and nothing has come along to question the reliability of the data.

The data on LUH's/Iceland's activity or use of resources "within" each preventive program/process, medication process, and profile of epidemiology/distribution are

questionable in terms of credibility and reliability due to the lack of verification and validation with the exception of the data based on the literature.

First, no activity/process/medication difference in ALOS (or such variable) was quantified by gauging real time or by reading medical records; LUH's experts' descriptions were taken as accurate. Unfortunately, there was a difference when the experts' descriptions were compared and when they were compared to the real use of resources in the prevention processes, but these differences was minor.

Second, there was a lack of review of the medical and medicine data by the hospitals' physicians on a number of hospitalization codes by ICD codes. Third, data on the profile of epidemiology/distribution in the base case was developed by an "educated guess" and data from the ECDC used to modify variance analysis also has its flaws as previously discussed. Therefore, the reliability of the data regarding the use of resources "within" each preventive program/process, medication process, and epidemiology cannot be fully judged as reliable, but with the notice provided above one can reason that the data on the whole are at least credible because there is no reason to believe that experts are giving intentionally wrong information. Furthermore, the process of forming the profile of epidemiology/distribution was done by using the available data from the literature.

4.2.2 The Method

The structure of the model and scenario analysis is based on the "hypothesis" that resources can be utilized in lowering the rate of hospital-acquired MRSA, which leads to benefits that are higher than the cost of resources used. The method is therefore based on two assumptions. Assumption one is that it is possible to utilize resources to lower the incidence of MRSA or hinder MRSA infections and assumption two is that there is a benefit of lower MRSA infection rates compared to MSSA infection rates.

I conclude that the method and, therefore, the model and scenario analysis, is based on a sufficient cause-effect relationship. First, by referring to Holzknecht et al. (2010, p. 4221), Iceland, Nordic countries, and the Netherlands apply the search and destroy method against MRSA within their health care institutions, but these countries have consistently had low incidence of MRSA compared to other European countries that do not apply SDP. Tacconelli (2009, p. 32) refers to Bootsma et al. who concluded that screening for MRSA and isolating carriers is effective and could in fact reduce

prevalence of MRSA below 1% in high endemic settings. Therefore, I conclude that the first assumption is accurate, i.e., it is possible to utilize resources to lower the incidence of MRSA or hinder MRSA infections. Second, it was found in the literature that MRSA infection is more costly than MSSA infection in terms of longer ALOS, higher mortality rate, and higher cost of treatment. This was supported in the Literature Review by referring to Rubio-Terrés et al. (2009), Cosgrove et al. (2003), Köck et al. (2010) and Resch, Wilke and Fink (2009), and Nulens et al. (2008). Therefore, I conclude that the second assumptions is also accurate, i.e., lower incidence of MRSA out of all SA infections creates benefits due to shorter ALOS, lower mortality rate, and lower treatment cost.

The modelling of the cost can be criticized in part. The direct cost items included in each prevention process is fully recorded as cost, but the indirect cost of the program is not included. This means that all of the direct cost items are regarded as a marginal cost, for example, the time of the nurses and other health care professionals who would very likely work at the hospital whether the SDP is active or not. In contrast, the indirect cost such as that attributed to the Department of Infectious Control and Disease is omitted. One might say that a possible overestimation in direct cost and lack of indirect cost out weight each other, but I conclude that the cost is estimated as a minimum cost of running the program.

The benefit in the model was defined as more production due to a higher number of healthy individuals, some value for society's certainty of having infection control, lower cost in the health-care system due to fewer people infected, lower cost of the households and other values created estimated as a benefit for individuals by facilitating them in reaching an older age. The integrity of the model's benefit relies on the appropriate demographic of each group and appropriate changes in the growth of the population, as well as wages and cost. In the model the age group was broken up into two demographic groups: younger than 70 years in one group and 70 years and older in the other. Individuals in the younger group were supposed to be active on the labour market and did not receive pensions or social benefits, but the older group was expected to receive pensions, social benefits, and wages. This formation is a bit

ambiguous but because the average numbers were used for wages, social benefits and wages, possible bias according to this simplification was modified at some level.

A change in population growth was estimated by data from Statistics Iceland and its medium forecast for the growth in the group 65 years and older. By doing this, the burden of higher age for the health care system was included in the estimated. This is quite justifiable because infection of SA is highly correlated with higher age as discussed in the Literature Review by referral to the work of Laupland et al. (2003, p. 1454). The estimation of the growth of wages and social benefits are based on estimated economic growth since 1945 and the growth of private pensions is estimated by real interest rates over the last 15 years. There is an implicit uncertainty about the validity of these assumption from now through the next 50 years, but this estimation is as accurate a measure as possible. The cost in the model is not expected to increase or decrease in real value.

As discussed above, there is the lack of a method to value (social) programs to decrease negative externalities, i.e., diminishing contagious diseases is a weakness of the model. This is true even though the estimation of other values created, such as the cost and benefit attributed to the elderly, can at least partly met this critique.

4.2.3 Validity of the Results

The method applied is non-parametric but deals with a subject that is parametric in its nature, meaning that the underlying variables follow some distribution(s) that was/were not estimated or not known. To overcome this aspect of the method, a scenario analysis was applied to gain some insight into the magnitude and effect of the used variables. Where the CB of the SDP implicitly relies on variables' distributions, there are plenty of reasons to raise scepticism about the validity of the results.

In the Literature Review, by referring to Marcel et al. (2008, p. 897), Wenzel and Perl (1995, p. 13), Gorwitz et al. (2008, pp. 1226,1229) and den Heijer et al. (2013), it became evident that the prevalence of SA (and therefore MRSA) is not known and depends on many interrelated factors. This raises the serious question of whether the result is generally valid. According to Gudlaugsson (personal communication, 2012) the SDP is developed with new knowledge, for example, when the ratio of community-acquired MRSA increases. Specifically, even as the prevalence of MRSA in Iceland

increases, the eradication therapy is not applied in each case. This changes the profile of the current SDP from one time to another. According to Asgeirsson et al. (2011, p. 339), the antibiotic treatment to deal with SA bacteraemia was judged inadequate in 53% of episodes, while appropriate treatment was associated with lower relapse rate and mortality. This reveals that the practice in medicine affects the CB of the program and it is likely that the medicinal practice or newly developed drugs changes the CB in the end.

4.3 Reflection of the Results

The results of the CBA of Iceland's SDP against MRSA is based on many unknown and uncertain variables which is mainly because the spread of the bacteria depends on many factors such as prescriptions, surveillance culture, genetic adaptation, and possibly even the general infrastructure of the health care system. Even though, the result will be reflected by comparing it to the actual data in the literature. Firstly the estimated cost of preventive programs and secondly the estimated benefit (as it is possible). In the following comparisons, amounts noted in the relevant literature are converted to ISK at a price level for 2012. Then they are indexed by the price level of 2012 and converted by the average exchange rate supplied by the Central Bank of Iceland (Exchange rate: Time series, 2013). In order to index these amounts, information on the changes in the appropriate price level was retrieved from Eurostat (HICP - inflation rate, 2013), also by use of an online inflation calculator that uses data from the U.S. Department of Labour Bureau of Labour Statistic (US Inflation Calculator, 2013) and from Statistics Canada (Home-Summary-tables, 2013).

4.3.1 Estimated Cost of Preventive Programs

An evaluation of the estimated cost of LUH's prevention program against MRSA can be completed by making comparisons of the estimated screening cost against MRSA in this study to the estimated screening cost against MRSA in other research studies. One can then make inferences as to whether the estimate of the screening cost against MRSA in this study appears to be realistic. As noted previously, the average cost of each individual who undergoes some of the preventive process is ISK 47,516 per individual and the average cost of finding one person carrying or infected by MRSA is ISK

3,251,770. Furthermore, the average cost of each preventive process in the base case is shown in the following table:

Table 30. Estimated average cost of each preventive process.

Process	Cost in ISK
P_1 via Accident and Emergency	235,913
P_1 via Admission Centre	199,333
P_1*P_2	257,477
P_3	36,580
P_3*P_4	58,144
P_5	9,110
P_5*P_6	30,674

Chaix et al. (1999, p. 1745) found that the total cost of the control program ranged from ISK 55,561 to ISK 241,852 per patient in the intensive care unit which is comparable to P_1, both via Accident and Emergency and the Admission Centre. Papia et al. (1999, p. 473) estimated that laboratory and nursing costs were ISK 1,417 per sample obtained which is similar to the number used in the cost estimation of that item in this dissertation.

Van Rijen and Kluytmans (2009, pp. 1245, 1248) estimated the prevention cost per admission at ISK 1,013, the daily isolation costs for individuals suspected of being colonised/infected by MRSA at ISK 17,471, and the daily isolation cost for MRSA-positive individuals at ISK 79,802. These figures are in similar "ranges" compared to the results of this study when the cost of building isolation rooms is subtracted, which was not included in the estimation of this study.

Murthy et al. (2010, p. 1749) estimated the cost of decolonization treatment to be ISK 2,558 and the incremental cost per day of infection control for suspected carriers was estimated to be ISK 25.169. The incremental cost per day is similar to that of LUH, which is ISK 22,426.

Wernitz et al. (2005, p. 466) estimated that a total of ISK 5,104,962 was spent for the 539 patients screened during a two day isolation period, or ISK 4,736 per day; a comparable number in this study is at a maximum ISK of 24,916 per day.

The comparison of estimated screening costs against MRSA between this study and others noted above shows that the estimate in this study is at a level of cost that other research indicates as a normal level for costs of screening against MRSA. Therefore, I conclude that the cost estimation of the screening program in this study is judged rather credible.

4.3.2 Estimated Incremental Cost of MRSA

The evaluation of incremental costs caused by MRSA compared to MSSA can be done by comparing the estimated cost level caused by MRSA to the cost level of MSSA between this study and others. To calculate the cost level in this study, I reverse estimated benefit, which was shown in the former sections. In the base case, the incremental cost per MRSA infected patient compared to MSSA infected inpatient is calculated by dividing the benefit numbers in year one by the number of additional MRSA infections in the base case. The result is shown in the following table:

Table 31. Incremental cost of each MRSA infection compared to MSSA infection in base case.

Incremental Cost of Lost Production per MRSA Infection	Incremental Cost of Lost Intangible Benefit per MRSA Infection	Incremental Cost of Health Care System per MRSA Infection	Incremental Cost of Households per Indiviudal	Incremental Cost of each Individual related to Other Benefit	Incremental Total Cost of Each MRSA Infection	Cost of per MRSA Infection Hindered
379,945	219,053	287,807	12,072	369,239	1,268,116	1,078,542

Köck et al. (2010, p. 3) outlined the burden of MRSA infections. In their overview, the health care cost for patients infected by MRSA compared to patients infected by MSSA was estimated to be from 38% (ISK 1,237,936) higher to 170% (ISK 11,632,129) higher for MRSA infected patients compared to MSSA infected patients, which is a considerably higher incremental cost compared to what the results of this study indicates.

Van Rijen and Kluytmans (2009, p. 1245) estimated the cost and the benefit of SDP for a 1,370 bed hospital in the Netherlands. The estimated total cost per prevented MRSA infection is ISK 1,094,398 and the estimated total benefit due to hindered MRSA infection cases for the hospital is estimated to be ISK 2,169,695 per MRSA infection. By comparing this finding to the result of this study, the estimated total cost per hindered MRSA infection is similar between LUH and the Dutch hospital or ISK 1,078,542 compared to ISK 1,094,398, respectively. In contrast, there seems to be some difference

between the costs saved by the Icelandic hospital and the Dutch hospital. The Icelandic hospital saves incremental costs per MRSA infection compared to MSSA infection of ISK 287,807. This figure is slightly lower than the 38% minimum incremental ratio (Köck et al. above) of the Dutch base number of saved incremental treatment costs of MRSA compared to MSSA (ISK 2,169,695 to ISK 2,169,695/1,38 = ISK 597,452).

Resch, Wilke and Fink (2009, p. 291) estimated that the incremental cost for MRSA infected patients was ISK 1,557,258 compared to patients in the control group (the control group was other inpatients but not MSSA inpatients).

Rubio-Terrés et al. (2009, p. 726) found that the incremental cost per patient with MRSA bacteraemia compared to patient with MSSA bacteraemia was ISK 239,286 or 12% higher than for MSSA bacteraemia. This level of cost accords with the result of this study (ISK 287,807). The range of the incremental costs of MRSA was estimate to be from ISK 58,183 to 1,030,220.

Chaix et al. (1999, p. 1745) estimated the incremental mean cost and incremental median cost of MRSA infection to be ISK 1,525,663 and ISK 961,690, respectively. The comparison was made to the control group of inpatients' for the intensive care unit in a 1,000-bed, referral university hospital in France (the control group was other inpatients but not MSSA inpatients).

Generally, the SDP against MRSA is recommended in the literature based on the reflected results for the cost and benefit of the program for hospitals. Chaix et al. (1999, p. 1745) concluded that a 14% reduction in MRSA infection made the examined control program beneficial. Van Rijen and Kluytmans (2009, p. 1245) concluded that the application of SDP in a hospital in a country with a low rate of endemic MRSA incidence saves money and lives. Naber (2009, p. 234) explores several studies and concludes that treatment costs of MRSA bacteraemia can be up to 24% higher compared to the treatment of MSSA bacteraemia. Finally, Simoens, Ophals and Schuermans (2009, p. 1853) found that the cost-benefit ratio of SDP was 1:17 in the intensive care unit and 1:16 in the gerontology unit. Notably, Graves et al. (2007, p. 280) concluded that the cost attributed to health care infections might be overstated because many other variables, which have been excluded, are related to length of stays and variable costs along with health care infections.

A comparison of the estimated cost avoided (or benefit) in this study indicates that the cost level of the incremental cost of the Icelandic health care system is underestimated. At what level it is actually at is hard to determine because one study shows similar costs and Graves et al. (2007, p. 280) has given notice of the overestimation of costs regarding health care infections. In addition, the cost estimation is not fully comparable between studies, amongst other reasons, due to differing accuracy in counting cost items. For these reasons, I conclude that the evaluation of incremental cost caused by MRSA compared to MSSA in the Icelandic health care system is sparsely estimated.

It should be noted that some of the studies uses the word benefit. As shown above, some of studies use the word "benefit" for the hindered cost to the hospital due to SDP and, therefore, this is the only comparable variable in Table 31, for the incremental cost of each MRSA infection compared to MSSA infection in base case. However, recall Drummond et al. (2004, p. 212) who points out that some studies are mislabelled as CBA, where they are in fact cost analyses. This "mislabelling" can also be recognised in the comparison above, where these studies do not fully recognise, report, and calculate **all** costs and **all** benefits of their subjects, respectively.

5 Conclusion

The aim of this study has been to estimate the cost-benefit of the SDP against MRSA that is implemented at LUH (or at a similar health care institution in Iceland). In the previous sections, the prerequisites for completion of a CBA were modified, relevant data was composed and screened, and calculations were executed. The result was then presented, analysed, and discussed. This section contains conclusions regarding the CB of the SDP in Iceland and provides recommendations on subjects related to this field of study and its limitations. Finally, I provide a short self-generated estimation on what this study adds to knowledge related to the research topic and I reflect on the work completed.

5.1 Summary of Findings and Conclusion

The calculations reveal that the current value of the present and future *benefit* of the SDP in Iceland equals an NSB[26] that is worth a total of ISK 833m with IRR of approximately 11% for the base case. Specifically, the benefit of deterring loss of production is ISK 2,208m, the intangible benefit for the inhabitants of Iceland created by controlling infection is worth of ISK 676m, and the total benefit of cost saved in the health care system is worth of ISK 967m. In addition, the benefit of prolonging life by deterring death caused by MRSA is estimated to be ISK 666m.

The current value of the present and future *cost* of the preventive program against MRSA is ISK 3,754m. Furthermore, it was estimated that the NSB of each healthy and saved life year is worth ISK 0.5m. This result was obtained from a more in-depth analysis. The benefit of each healthy life year was estimated to be worth ISK 16.3m, the benefit of each saved life year was estimated to be worth ISK 2.0m, and the cost of each healthy and saved life year was estimated to be ISK 2.2m. Therefore, the NSB of each healthy life year was estimated to be worth ISK 14.1m and the NSB of each saved life year was estimated to be worth ISK -0.2m.

The scenario analysis confirmed some predictable and logical findings. A higher rate of SA infection, a higher rate of MRSA infections (measured as the number of infected

[26] All numbers are NPV of the program for 50 years, as explained previously.

individuals by MRSA), a higher mortality rate from MRSA (measured as the number of individual deaths from MRSA) all contributed to a higher NSB of the SDP. This finding was also valid for the following: a lower average age of death due to MRSA infection, longer differences in ALOS between MRSA infected inpatients and MSSA infected inpatients, and a higher discount rate for the calculation of NPV of the NSB for the SDP. The scenario analysis also revealed that the MRSA infection rate, measured as ratio of MRSA infections out of all SA infections, "needs" to be at least higher than 17.5% in order for the NSB of the SDP to be positive. Furthermore, for a positive NSB the mortality rate for MRSA infected patients needs to be at least approximately 15.0% to 20.0% higher than for MSSA infected patients. Finally, out of three defined scenarios, Best Case, Middle Case and Worst Case, the Best Case scenario was found to be slightly more unbeneficial to society.

From the summary of findings above, I conclude that the NSB of the SDP against MRSA that is applied in Iceland is overall positive, meaning that it is worth applying. This conclusion relies on the minimum conditions noted above that are required for a positive NSB finding under the current prevalence rates of SA infections

It is important to note that the local epidemiology of MRSA plays a significant role in the strategy (concluded after performing a scenario analysis). Wernitz et al. (2005, p. 466) concluded that a sensitivity analysis of the break-even points for different screening frequencies and different MRSA incidence rates indicated that the screening program became cost-effective, even at a low MRSA incidence rate. In other words, it can be recommended for most hospitals with an MRSA problem.

5.2 Recommendations

Based on the findings and conclusions, recommendations are provided relating to some limitations of the method used and the need for further research in this field. In examining the model's accuracy, a valid consideration is the fact that the sacrificed benefit in the absence of SDP is an estimation. The criteria for the model was to use only measureable data as much as possible to determine the sacrificed benefit in the absence of the SDP, which could be attributed to some degree to the gainers and losers

of the policy. This criteria was based on Pareto's principle,[27] although this was not strictly applied when the model was developed. For example, the *only* financial value created by private pension funds is the real interest rate. Moreover, the private pension funds and their social benefits are only transfers of values between gainers and losers, i.e., the elderly, the inheritors, and the taxpayers. Although not expressly stated in the creation of the model, this Pareto Principle is relevant and accurate in discussing the purpose of the model. Therefore, I recommend that when a CBA analysis is executed, one compares models with different methods of estimating the gain of the gainers and loss of the losers according to the Pareto rule.

In analysing the results, it is important to recognize that the method of data collection is not without some criticisms. The information on cost items and the use of resources was collected by interviewing medical experts and not through systematic overview of resources used in the described processes and activities, for example, by classifying medical records into target group (MRSA) and control group (MSSA). Part of the reason this was not completed was to keep the research at an appropriate and manageable level. However, it is generally recommended that medical records are used to collect and confirm information on the use of resources when describing and estimating clinical programs/processes within the health care system.

The cost of capital (housing, etc.) was intentionally not specified in the analysis of cost nor was there some estimation of the effect created by a non-market situation in the health care sector as discussed in the section Limitation. Therefore, it is recommended that if a scenario analysis is executed it should include some estimation of the cost of capital and/or some undefined cost or effect of non-market situations in the health care sector.

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[27] According to Drummond et al. (2004, p. 217), the Pareto Principle assumes that the social welfare is made up of utilities of each individual in the society and each one is the best judge of his/her own welfare. Therefore, to make an actual Pareto improvement by way of a social program, one applies a policy that puts one or more individuals into a better position but no one into a worse position. Additionally, to make a potential Pareto improvement (Kaldor-Hicks criterion) you have gainers and losers, but the gainers compensate the losers and the gainers are still put in a better position, i.e., the society as a whole is better off.

Again regarding the data collection process, the author of this dissertation is aware that information regarding resources' prices seems to be easily accessible. However, there was a problem in attempting to gather data from the medical laboratory system despite significant efforts on the part of the laboratory clinical staff. Therefore, it is recommended that LUH's directors improve their hospital's clinical records systems.

Turning now to the specific subject matter, a worthy question in this field is whether the use of CBA to evaluate activity within the health care sector is a suitable method by which to prioritize the supply of services and assess the effectiveness of activities/programs (based on the cost and benefit created by the activity). The simple answer is that CBA should be used. I highly recommend, based on this study, that the Icelandic health care authorities use academic knowledge and accepted research methods in economics in order to select and prioritize beneficial projects within the health care system.

Finally, this study raises other noteworthy questions. For example, the incidence of MRSA within hospitals is very low in Iceland compared to some other countries, which is possibly due to the applied SDP. If this low incidence rate can be attributed to the SDP then is it cost-effective to monitor and control MRSA in smaller societies/communities?

5.3 Contribution to Knowledge

As noted above, no study on the NSB of the SDP against MRSA seems to have been executed from the societal perspective. All of the studies completed to date appear to be (more or less) from the hospital point of view. Therefore, I conclude that this dissertation has contributed a "broader point of view" in the literature regarding the estimation of CB of the SDP against MRSA. Furthermore, in a country such as Iceland, where CBA has not traditionally been used very frequently in the health care sector, the number of such studies is limited and a study like this is at least a small contribution.

5.4 Self-Reflection

The modification and completion of this dissertation has not been a straightforward process, which I assume is not unusual in researching such a subject. The main challenge was building up the hypothetical base case in absence of the SDP, i.e., how

MRSA would be distributed if Iceland were not running the SDP. The difficulties notwithstanding, the search for knowledge to fulfil curiosities is a reward unto itself.

Glossary

Colonisation

According to Gudlaugsson (personal communication, 2004), colonisation indicates that bacteria have settled.

Community-acquired Infections (CAI)

According to Marcel et al. (2008, pp. 895-896), CAI refers to infections which arise outside of health-care systems.

Healthcare-Associated Infections (HAI)

According to Marcel et al. (Healthcare-Associated Infections: Think Globally, Act Locally, 2008, pp. 895-896), HAI means infections which arise within health-care systems.

Incidence

Gordis (2004, p. 33) explains that the incidence rate is measured as a ratio of the number of individuals who are developing designated (medical) condition out of the population in a defined time span. This includes an assessment of the risk of obtaining a disease that is given a designated diagnosis. The rate of incidence is expressed mathematically in the following equation:

$$\frac{\begin{array}{c}Number\ of\ new\ cases\ of\ disease\ occuring\ in\ the\ population\\ during\ a\ period\ of\ time\ from\ t\ to\ t+1\end{array}}{\begin{array}{c}Number\ of\ persons\ at\ risk\ of\ developing\ disease\\ during\ a\ period\ of\ time\ from\ t\ to\ t+1\end{array}}$$

Prevalence

According to Gordis (2004, p. 35), prevalence is measured as ratio of the number of individuals that are given designated (medical) condition out of the population in a defined time span. This prevalence rate measures the risk of being given a designated diagnosis:

$$\frac{Number\ of\ new\ cases\ of\ disease\ present\ in\ the\ population\ at\ time\ t}{Number\ of\ persons\ in\ the\ population\ at\ time\ t}$$

Interrelation between Incidence and Prevalence

Gordis (2004, pp. 35-36) defines a logical relationship between the variables of prevalence and incidence. The mathematical expression is:

$$Prevalence = Incidence - Number\ of\ Cured\ and\ Deaths$$

Search and Destroy Strategy

According to Tacconelli (2009), the Search and Destroy Strategy/Policy (SDP) includes: "contact isolation for MRSA-positive patients; pre-emptive isolation and screening for high-risk patients; screening of patients and personnel when an unexpected MRSA-positive is found; screening of all health care workers and keeping carriers away from work until decontamination is achieved; and closing wards to new admissions when there is more than one carrier among hospital patients" (p. 32).

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Appendix A: Biology of Bacteria and Its "Survival Capability"

The purpose of this section is to explain to readers how and why bacteria develops immunity against antibiotics at a relatively fast rate. As such, this appendix provides an overview of the discovery and the evolution of bacteria. The structure of bacteria cells and their adaptability are briefly described and the classification of different types of bacteria are provided. Lastly, SA traits are described and the "idea" of immunity is introduced.

In the following figure Huskey (2005) depicts a timeline commencing at when the earth began to form 4.5 billion years ago and how bacteria began to evolve approximately 3.5 to 4.0 billion years ago. Notably, it is estimated that homo sapiens have only existed for the past 120,000 years.

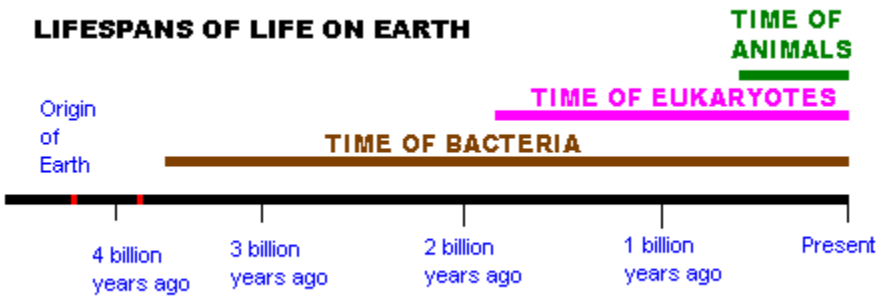

Figure A1. Lifespans of living creatures on earth.

The fact that bacteria can be found "everywhere" on earth further supports the conclusion that bacteria are organisms that have existed for centuries. Gudlaugsson, M.D. explained in an interview (personal communication, 2004) with author of this dissertation: bacteria can be found everywhere, for instance, at the bottom of the ice-cold ocean, in piping hot geysers, at the top of the world's highest mountains, and in the strata of the atmosphere. Furthermore, as supported by Huskey (People Virginia, 2005), the genetic varieties of bacteria are numerous and are evidence of its adaptability and survival.

According to Levy (2001, pp. 18-20), bacteria are independent, microscopic, single-cell organisms that multiply themselves by a process of division in which each cell creates a copy of its gene and passes this on to its progeny. Many types of bacteria can

divide within 20 minutes in favourable environments but, in nature, where energy may be limited and there is more competition, this process can take up to a few days.

Bacteria cells consist of several components including the plasma membrane (which forms the outer later and comprises the capsule), the cell wall, and the cytoplasm membrane. Inside the cell there is cytoplasm and ribosome. Davidson (2005) displays a bacterium cell in the following figure.

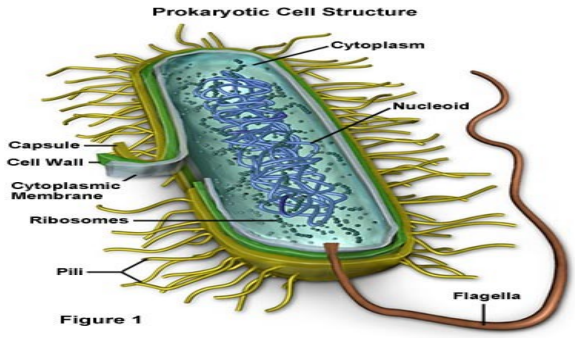

Figure A2. A bacterium cell.

As Levy (2001, pp. 18-20) explains, nutrition for bacteria can be as simple as carbon, oxygen, hydrogen, and/or nitrogen. The methods bacteria use to obtain these chemicals include ingestion from sugar found in the environment, incorporating elements, or by converting organic materials into nutrition as needed, i.e., some bacteria have proteins/enzymes which can break down or transform biological chemicals into nutrients such as fat, oil, etc. This natural ability is important because it also allows bacteria to break down toxins (chemicals that normally harm other organisms).

As noted previously, bacteria are extremely skilled adaptors. Levy (2001, pp. 82-88) described it, the process of adaption passes through by changes in the traits of the cells heredity. First, mutations occur and then the transfer of "traits" occurs by four ways. The first way to transfer "traits" between two bacterium is transformation wherein the donor bacterium gives away the genetic material a^+ and the accepting bacterium b^+ picks up a^+ and reorganises its gene chain so that a^+ becomes predominant. The second way to transfer genetic materials between two bacterium is transduction wherein the donor bacterium b puts genetic material a^+ into a virus. The virus transfers the genetic material to bacterium b^+ where the material is "spit" into b^+. Bacterium b^+ then reorganises its gene chain so a^+ "takes over". The third way to transfer genetic materials between two bacterium is conjugation wherein the donor bacterium b connects to the bacterium b^+,

which accepts the genetic material a^+. The genetic material is "injected" from b to b^+ and then they separate. Bacterium b^+ reorganises its gene chain so that a^+ takes over. The last way to transfer genetic materials between two bacterium is transposition. In this process the gene material a^+ is transferred by plasmid or a chromosome within the set of genes in bacterium b^+ and then it goes with the transferable gene material to the cell b. Bacterium b^+ reorganises its gene chain so that a^+ takes over.

Levy (2001, pp. 97-100) explained that the naturalness of heredity causes immunity against medicine for several reasons. First, it is possible that bacteria can block effective chemicals with the consequences that the chemicals cannot enter into the cell or the chemicals will be transferred out of the cell. Second, it is possible that the cell can neutralise effective chemicals by enzymes. Third, it is possible for bacteria to change the enzymes that the medicine is targeting by changing or, rather, mutating those enzymes so that they then become resistant against the medicine. Fourth, it is possible that a bacterium produces a new enzyme that is resistant towards a certain medicine. Because bacteria can reproduce themselves at high rates over a relatively short amount of time, medicine-resistant types of bacteria can also spread quickly.

According to Gudlaugsson, M.D. (personal communication, 2004), bacteria are separated by shape and by stain (i.e., by Gram stain). The most common shapes are cocci and bacilli.

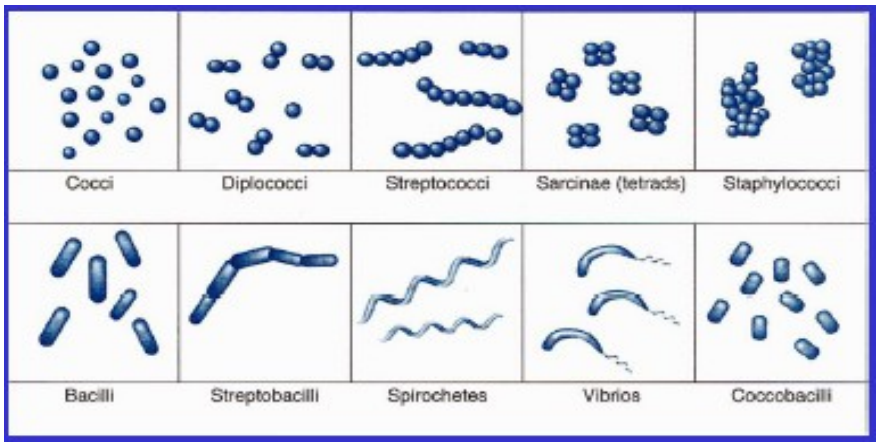

Figure A3. Common shapes of bacteria.

According to Levy (2001, p. 21), a Gram stain technique is used to make distinctions between bacterium by the differing composition of the bacterial cell walls. Gram-positive bacteria keep the colour through the colouring process, whereas Gram-negative bacteria recolor in the process. The reasons behind this is that the Gram-negative bacteria have three-layer cell walls, but the Gram-positive bacteria have only one-layer cell walls. Heritage at Leeds University (2003) depicts the staining process as follows:

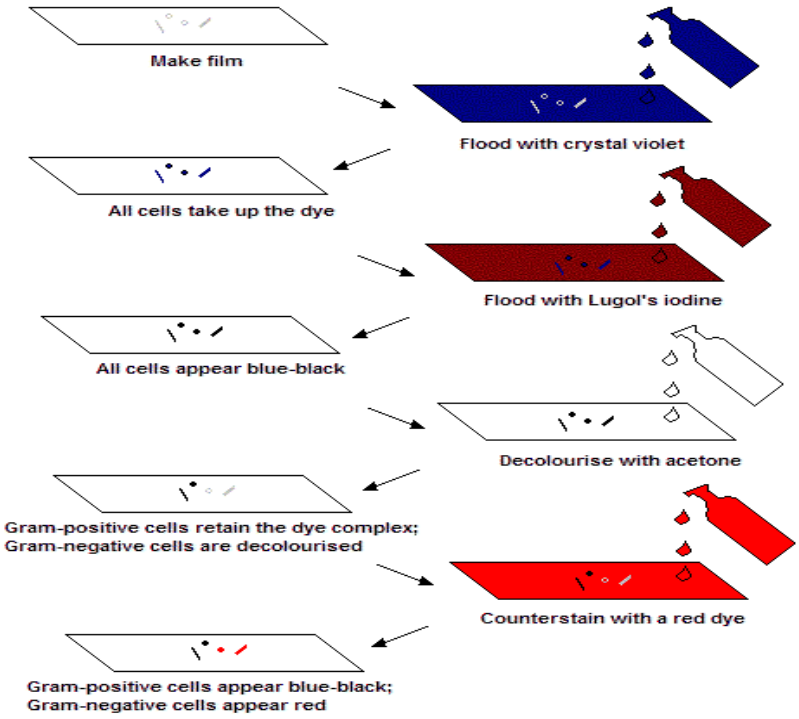

Figure A4. Method of classifying bacteria between Gram-negative bacteria and Gram-positive bacteria.

According to Mandell, Bennet and Dolin (2004, pp. 2321-2355), SA is a Gram-positive cocci which is found either single, in diplo (pairs), quarto, streptococcus (chains), or staphylococcus (clusters). The genus Staphylococcus has around 32 "species" and, of those, one can find 16 in/on the human body. Few of these stocks are pathogenic but one of the virulent types is SA; it is virulent for both human beings and animals. SA thrives on human skin but is mainly in the anterior nose where the environment is well suited to it. Biologically, SA has a unique capability to survive as this type of bacteria can live on/in several areas of the human body and can "easily" adapt to its environment. As Mandell, Bennet and Dolin (2004) describe it: "S. Aureus harbour a large number of mobilizable exogenous DNA stretches, including insertion sequences, transposing, bacteriophages and pathogenicity islands that contain specific determinants responsible

for disease and antibiotic resistance. The presence of these exogenous elements attest high capacity of S. Aureus to undergo horizontal gene transfer and exchange genetic elements with other organisms, including both staphylococcal and no staphylococcal genera. Because gene exchange is a key player of evolution, this peculiar genetic plasticity is a likely explanation for the success of S. Aureus as both a colonizer and disease-producing microbe" (pp. 2321-2355)

Levy (2001, pp. 7-8) explains that the discovery of penicillin began the evolution of antibiotics, which, according to some, has become out of control. Given bacteria's great ability to adapt, new strains evolved that were immune to common medicine. Alexander Fleming, the discoverer of penicillin, was already alerting the medical community to the dangers of misuse (and/or overuse) of penicillin in the year 1945. He pointed out that the misuse of penicillin could lead to selection and dissemination of mutated immunity against medicines. For example, it is necessary to finish (complete) treatments in order to decrease the risk of immunity, so consumption without control could increase the risk of immunity in cases where people do not finish their prescribed antibiotic treatment. As Fleming stated that "The greatest possibility of evil in self-medication is the use of too small doses so that instead of clearing up infection, the microbes are educated to resist penicillin and a host of penicillin fast organisms is bred out which can be passed to other individuals and from them to others until they reach someone who gets a septimia or a pneumonia which penicillin cannot save" (2001, p. 8).

Appendix B: Economics of the Immunity

Behind the spread of bacteria's immunity to medicine, are not only biological explanations, but also explanations focusing on economic infrastructures (or economic institutions) within health care arenas. That is, the economy and infrastructure of society and the health care system "include" decisions regarding the use of antibiotics and how they are executed; in turn affecting the level of immunity of bacteria flora. I refer to data and information from Stuart B. Levy who provides support in his book *The Antibiotic Paradox* (2001, p. 289) for the following statements.[28]

Statement 1: One of the most effective ways to control the use of antibiotics is to run well organized prescription-systems with some level of monitoring and control. In a well-organised prescription-system, educated and informed health care professionals are able to determine the patterns and frequency of antibiotics use. The intention is that with less widespread overuse of antibiotics, there will be less medicine immunity in bacteria. According to Levy (2001, pp. 216, 286), the number of medical doctors varies from one medical doctor per 520 inhabitants to one medical doctor per 17,000 inhabitants between the countries of the world. This ratio greatly affects how nations organize and control the supply of health care and medicines. In developing countries, where the number of medical doctors is relatively few, over-the-counter sales without prescriptions are common. As a result, consumers misuse medications in both quantity and "time-span". Furthermore, management and control of the use of antibiotics is in some ways a political matter in terms of structuring of the health care system and the interests of the producers.

Statement 2: The system of payment can indirectly influence the level of immunity of bacteria flora. Levy explains (2001, p. 117) that if a third party pays the bill for medications, then the incentive to "underuse" or limit medicine disappears. If a system

[28] It should be noted that socioeconomic status can affect the level of immunity of bacteria flora or, as Levy (2001, p. 289) points out, poverty causes or is related to the misuse of medicine. People living below the poverty line often suffer from a shortage of quantity and are unable to complete medication therapy. Furthermore, in some areas the insurance system is organized in such a way that the first day in a medical treatment program is free for the consumer but not the following days. This can lead to discontinuity in patients' medication therapies.

of controlling prescriptions is effective, then the likelihood of overuse (or over-prescription) decreases. Therefore, the responsibility of medical doctors may be below the effective level required to decrease antibiotic use if immunity is prevalent.

Statement 3: The cost of medicine and the amount of access to health care services can influence the level of immunity of bacteria flora. As Levy (2001, pp. 8,123) explains the first types of antibiotics, such as penicillin, were often introduced into the blood stream by primitive and expensive methods. Economic incentives induced development that made dosages cheaper for the health care system (i.e., the producers and administers) but not for the patients. Furthermore, from the advent of antibiotic use, there were predictions that such use would lead to the misuse of medicines. In addition, if access to medicine is open, it has been shown in research that people more frequently take medicine for the purposes of prevention. The prevention is often unnecessary or unfounded because knowledge and diagnosis is not necessarily the basis for the use of the medicine.

Because improper (and even proper) consumption of antibiotics increases the immunity of bacteria, the effect of the consumption can be classified as an external effect, i.e., all the costs are not included in the cost of antibiotic consumption. Therefore, by increasing the cost of antibiotics, it is possible to decrease bacteria's immunity against antibiotics as a result.

Several methods can be used to increase the cost of antibiotic consumption. Increased cost depends, among other things, on the economy and accessibility to antibiotics. One way is to raise the prices of antibiotics. This would be an effective way to reduce the misuse/overuse of antibiotics because, if a third party is paying the costs of the antibiotics, they will be more likely to demand explanations for the medication's use. However, there are drawbacks to this strategy if the consumer is paying for the medication. If the consumer is in a higher socioeconomic class, he/she would or could accumulate medicine and engage in symptom treatment. If the consumer struggles with financial difficulties, he/she would be less able to finish his/her antibiotic therapy.

Another method is to regulate the "sales and use" of medication. This would include requiring prescriptions, increasing control of what can be prescribed, and so on. This way demands a strong infrastructure including knowledge and information systems.

Therefore, this method is difficult to implement in developing countries where it is not possible to control the supply with the participation of medical doctors.

Appendix C: The Progress of SA Infection

The progress of infection by SA is described by Kristjansson M.D. (personal communication, 2005) and I have provided a brief overview. The early phase is interception on skin and abscess develops (phase 1). The second phase is cellulitis (phase 2). The third phase is blood infection/bacteraemia (phase 3) and the possible consequences of this latter phase are threefold: cardiac valve infection (phase 4.A), abscess in inner organs such as the brain, joints liver, bones, spleen, lungs, etc. (phase 4.B), and abscess in implants such as artificial hip joints (phase 4.C). The final phase of infection by SA is death. Graphically, these steps are displayed in Figure 1:

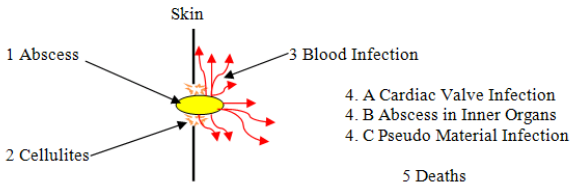

Figure C1. Biological consequences of infection by SA bacteria.

It should be noted that, according to Gudlaugsson M.D. (personal communication, 2011), the process and escalation of infection varies between clinical episodes, e.g., abscess does not necessary entail blood infection and there are clinical episodes where one does not diagnose abscess before blood infection.

Figure C2 is a photo from the website of the Centre for Disease Control and Prevention (MRSA Home>Symptoms of MRSA, 2010) which displays cutaneous abscess on a hand caused by MRSA:

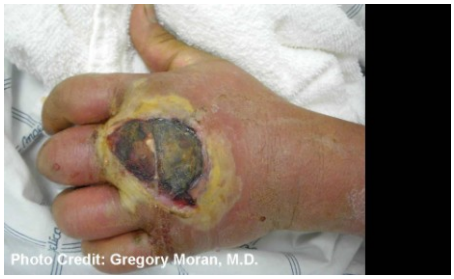

Figure C2. Cutaneous abscess on hand caused by MRSA.

Appendix D: Cost Items

Table D 1. Cost items used in the cost analysis of medication processes and preventive processes.

Cost Item	Measured by	Priced by
Medical Doctor	Hours	Average wage
Registered Nurse	Hours	Average wage
Nurse Assistant	Hours	Average wage
Medical Secretery	Hours	Average wage
Rubbing alcohol	Litre	Hospital price
Mask	Unit	Hospital price
Sterilized aater	Unit	Hospital price
Disposable gloves	Unit	Hospital price
Disposable apron	Unit	Hospital price
Chlorine	Litre	Hospital price
Virkon	Unit	Hospital price
Bed linen	Unit	Hospital price
Linen	Unit	Hospital price
MRSA samples	Unit	Hospital price
Bactrim	Unit/Millilitre	Hospital price
Dalacin	Unit/Millilitre	Hospital price
Ekvacillin	Millilitre	Hospital price
Keflex	Unit	Hospital price
Kefzol	Millilitre	Hospital price
Staklox	Units	Hospital price
Vancomycin	Millilitre	Hospital price
Klórhexitín	Milligram/Millilitre	Hospital price
Mobirozin	Milligram	Hospital price
Hibiscrub	Millilitre	Hospital price
Bactroban	Milligram	Hospital price

Appendix E: Ethical Approval by LUH's Ethical Research Governance Committee

LANDSPÍTALI
HÁSKÓLASJÚKRAHÚS

Guðmundur I Bergþórsson
Öldugranda 1
107 Reykjavík

Reykjavík, 17. mars 2011
Tilvísun 16 EE/ks

Varðar: Erindi 11/2005 til siðanefndar stjórnsýslurannsókna á LSH
" The Struggle of Keeping a Hospital free og Methicillin-Resistant Staphylococcus Areus – COST-BENEFIT ANALYSIS"

Siðanefnd stjórnsýslurannsókna hefur fjallað um endurnýjaða umsókn um ofangreint erindi frá 2005. Erindið var samþykkt en bent er á eftirfarandi:

1. Í markmiðslýsingu kemur ekki fram að verkefnið snúist að hluta til um að tryggja öryggi sjúklinga.
2. Bent er á að æskilegt er að formlegt samþykki lækningaforstjóra liggi fyrir með öðrum hætti en tölvupósti ef ætlunin er að birta niðurstöður opinberlega.

Siðanefnd stjórnsýslurannsókna óskar eftir því fyrir hönd LSH að fá rafrænt eintak af niðurstöðum úr rannsókninni að henni lokinni.

Virðingarfyllst fyrir hönd siðanefndar stjórnsýslurannsókna á LSH,

Erna Einarsdóttir, formaður

Afrit: Ólafur Guðlaugsson, yfirlæknir sýkingavarna

Siðanefnd stjórnsýslurannsókna,
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Appendix F: Approval by LUH's Chief Medical Executive

LANDSPÍTALI
HÁSKÓLASJÚKRAHÚS

Guðmundur I. Bergþórsson
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LSH Eiríksgötu 5

29.03.2006
Tilv. 16
ÞH/ei

Efni: The Struggle of Keeping a Hospital free of Methicillin-Resistant Staphylococcus Aureus – Cost Benefit Analysis

Ágæti Guðmundur.

Vísað er til bréfs þíns til lækningaforstjóra, dags. 28.03.2006 þar sem þú óskar heimildar til að framkvæma ofangreinda rannsókn á LSH. Fram kemur að rannsóknin er hluti af MS verkefni þínu við viðskipta- og hagfræðideild Háskóla Íslands en leiðbeinendur eru Þórólfur M.Matthíasson, prófessor viðskipta- og hagfræðideild HÍ, Ólafur Guðlaugsson, yfirlæknir og Már Kristjánsson, yfirlæknir sem báðir eru starfsmenn LSH.

Hér með er veitt heimild til að ofangr. rannsókn verði framkvæmd á LSH undir þinni stjórn. Leyfi þetta er háð því að fyrir liggi samþykki siðanefndar LSH og Persónuverndar þar sem leita þarf upplýsinga í sjúkraskrám sem tengjast rannsókninni.

Með kveðju og ósk um gott rannsóknargengi,

Þórður Harðarson
prófessor, yfirlæknir

Jóhannes M. Gunnarsson
framkvæmdastjóri lækninga

Afrit:
Jón Jóhannes Jónsson, formaður
Sigrún Jóhannesdóttir, forstjóri

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