LUND UNIVERSITY
School of Economics and Management

Publically funded ART-treatment in Sweden

Introducing a medical screening program

Master Thesis I, NEKN01
Department of Economics
Authors: Hanna Norrlid & Sofie Larsson
Supervisor: Carl-Hampus Lyttkens
October 2013

ABSTRACT

Background

The trend of postponed reproduction to late in life has increased demand for fertility treatment. The current program of subsidized ART-treatment in Sweden is thoroughly debated and critiqued. The Swedish National Council on Medical Ethics has highlighted the ethical shortcomings of the current system and called for a program change. This thesis expands on the proposal and introduces a medical screening program as a qualification aid for subsidized fertility.

Method and Data

To compare the current Strict Age Limited Program with the Medical Screening Program a cost-effectiveness analysis is conducted. The results are presented as incremental cost-effectiveness ratios (ICER). Data is collected from the RMC clinic and supplemented with national data (National Quality Register for ART-treatment) in the age groups where RMC data is lacking.

Results

Introducing the Medical Screening Program with the current Strict Age Limited Program generated a cost increase of SEK 2 244 (SEK 20 058) and a rise in the number of live births by 62 (48) for the RMC (Q-IVF) data set. Thereby the analysis resulted in an ICER of SEK 36 (SEK 429). The ICER is thus fairly unaffected while the number of live births rises significantly. A sensitivity analysis shows expected results and the overall effect seems negligible. It is also noteworthy that approximately three fourths of the societal costs of publically funded ART-treatment fall on the health care region, while the rest is divided between the patients and their employers.

Conclusion

Increased availability of publically funded ART-treatment may induce counter-productive behavior but the trend of increased demand is most likely related to shifting social norms. It is essential for western countries to promote fertility rate, due to the economic implications of an aging population, and the Medical Screening Program has potential to do so.

ACKNOWLEDGEMENT

First and foremost, we would like to express our sincere gratitude to our advisor Professor Carl Hampus Lyttkens for his support and pointers. His expertise has been vital to our work.

We would also like to extend our deepest appreciation to our contacts at the Reproductive Medicine Centre in Malmö, Aleksander Giwercman, Margareta Kitlinski and Mona Bungum, for their enthusiastic support and guidance throughout the project.

ABBREVATIONS

ART	Assisted Reproductive Technology
CEA	Cost-Effectiveness Analysis
CUA	Cost-Utility Analysis
ET	Embryo transfer
HC	Human Capital
HRQoL	Health Related Quality of Life
ICER	Incremental Cost-Effectiveness Ratio
ICSI	Intra-Cytoplasmic Sperm Injection
IVF	In-Vitro Fertilization
NICE	National Institute for Health and Clinical Excellence (The UK equivalent to NBHW)
NBHW	National Board of Health and Welfare
OH	Overhead costs
Q-IVF	National quality register for ART-treatment
RMC	Reproductive Medicine Centre (fertility clinic in Malmö)
SEK	Swedish Kronor
SRC	Skåne Regional Council
TLV	Swedish Dental and Pharmaceuticals Benefit Board
WHO	World Health Organization
WTP	Willingness To Pay

CONTENTS

1. INTRODUCTION

Declining fertility rates have been observed for several decades in most industrialized countries (McDonalds, 2006). During the last century the average number of children born per woman in Sweden has decreased from approximately 4 to 1.9 children per woman. For the population to reproduce itself, without the help of immigration, every woman needs to give birth to an average of 2.1 children during her lifetime, usually referred to as the replacement rate of fertility (Statistics Sweden, 2012:I). If the downward fertility trend continues, it will cause an ageing of the average population, which will have negative spillover effects on the pension system. We can already see changes in the population pyramid compared to the early 20th century, and prognosis predicts that the population pyramid might even turn upside-down in the future (Statistics Sweden, 2012:II). This demographic trend indicates negative economic consequences for countries with low levels of reproduction and hence calls for actions to increase, or even stabilize, fertility rates (Rainer et al, 2011).

One way for the welfare state to influence the levels of reproduction is through strategies and regulations regarding assisted reproduction technology (ART) treatments, such as IVF or ICSI. Involuntary childlessness is an increasing problem, especially in the western world, primarily caused by the societal trend to have children at a higher age. The average age of both men and women at time of birth of their firstborn has increased. In 1970 the average age of a woman having her first child was 24 years old, while the man was 27 years old. By 2011 the same ages had risen to 28.9 for women and 31.5 for men (Statistics Sweden, 2012:I).

Still, most people take reproduction for granted. We often view reproduction as the natural way of life even though it might not be as unproblematic as one may think. In Sweden approximately 15% of all couples in reproductive ages experience some fertility problems (Barnlängtan, 2013; McQuillan, 2012). Involuntary childlessness occurs when a couple has tried to get pregnant in the natural way for at least one year without succeeding, and are thus in need of medical assistance to reproduce (WHO, 2013). In 1997 involuntary childlessness, or more accurately infertility, was classified as a disease by the World Health Organization, WHO (WHO, 2011).

Evidence presented by de la Rochebrochard (2001) suggests that in the ages 35-39 and 40-44 respectively, it is almost 20% and 50% less likely for a woman to naturally conceive compared to 25-29 year-old women. This problem increases as reproduction is put forth to later in life. According to Swedish data, every fourth woman between 34 and 40 years old have used some kind of fertility aid (Statistics Sweden, 2009), and approximately 3.3 percent of the annual births in Sweden are results of ART-treatment.

This thesis aims to highlight the effect of age on fertility and evaluate the current subsidy program for ART-treatment. This leads us to the main question; *Would it be* *cost-effective to implement a medical screening system to determine eligibility for ART-treatment, for women aged 35-43, instead of retaining the current fixed age limit of <39?* We aim to clarify the existing regulations of publically funded ART-treatment in Sweden, and compare it with a proposed regulation change of a lower age limit of 35 years, accompanied with individual medical screening of women aged 35-42. The different treatment programs will be studied through a cost-effectiveness analysis.

The remainder of this thesis will be structured as follows; section 2 contains the outlines of the current ART-treatment program, its restrictions and critique as well as a proposed program change with which it will be compared throughout the thesis. Section 3 describes the methodological framework, motivates the choice of method and explains how it is applied. In section 4 presents the data sets used in the thesis and depicts what alterations have been made. In section 5 thorough descriptions of the cost calculation process is presented. Section 6 presents the results of the thesis, which are then discussed in section 7. Finally, section 8 presents the conclusions drawn.

2. BACKGROUND

2.1. Current Swedish legislation

Assisted reproduction in Sweden is primarily regulated by the Genetic Integrity Act (SFS 2006:351), in addition to guidelines from the National Board of Health and Welfare (NBHW) and international consensus (i.e. the EU directive 2004/23/EG and the UN convention on children's rights) (SMER, 2013). Currently, fertility treatment is provided under the following restrictions. First, both heterosexual and lesbian couples are eligible for fertility treatment (SoU26, 2011/12). Meanwhile, couples where the woman is unable to carry a child, HBT couples (see the fourth restriction) and singles are not offered treatment.[1] Secondly, both egg and sperm donation is legalized in Sweden. However they are not allowed simultaneously as the forthcoming child has the right to a biological tie to at least one of his/her parents. If donated sperm or eggs are used the couple receiving the donation has to undergo a suitability evaluation to ensure that the prospective child will grow up under favorable conditions. The evaluation takes medical, psychological and social circumstances into account. Couples who use their own gametes (eggs and sperm) in ART-treatment do not undergo any evaluation. Thirdly, donors cannot be anonymous but are usually unknown to the prospect parents. Information about the donor's identity is kept in a database so that the child is able to find his or her biological heritage when reaching adulthood. However, the donor has no legal obligation to the child. Fourthly, surrogacy is not allowed in Sweden. Fifth and final, there is no legislated age limit to fertility treatment (SMER, 2013).

2.1.1. Regional ART-treatment regulations

Even though there is no legislated age restriction of ART-treatment in Sweden, the reality is somewhat different. Sweden's democratic system relies on regional autonomy and is divided into independent county councils (SMER, 2013). Sweden has universal health care and each county council has the authority and obligation to make prioritizations and budgetary decisions. Therefore, and because there are scientific evidence of decreasing fertility with increasing age all county councils have endorsed age restrictions to publically funded ART-treatment. The age restrictions, however, vary between regions. The primary focus is female age in all county councils, as males stay fertile later in life, and the limits vary from 37-41 years for women and 54-56 years for men (SMER, 2013). For further details on age-restrictions, see appendix table 22.

[1] It is nationally regulated that both heterosexual and lesbian couples are eligible for reproductive treatment. A decision in the Swedish Parliament in 2012 also suggested that single women should be allowed fertility treatment and that a commission should be put together to draw out a legislative proposal as soon as possible (SoU26, 2011/12). To this day no such proposal has been presented.

Most county councils have developed regional collaboration units in order to fully utilize the medical expertise in the area to provide its inhabitants with optimal health care. Fertility clinics are fairly scarce and there is often only one publically funded medical unit providing ART treatment per health care region. Consequently, these health care regions have unified restrictions regarding fertility treatment. As shown in table 1 there are multiple criteria that vary across regions, however this study will solely focus on the female age restriction.

Table 1. Regional ART-treatment regulations

	South	Southeast	West	Stockholm-Gotland	Uppsala-Örebro	North
County Councils, included in Health Care Region	Skåne, Blekinge, Kronoberg, South Halland	Östergötland, Jönköping, Kalmar	Västra Götaland, North Halland	Stockholm, Gotland	Gävleborg, Dalarna, Uppsala län, Värmland, Örebro, Västmanland	Norrbotten, Jämtland, Västerbotten, Västernorrland
Experienced infertility to qualify for treatment	Medical indication required	> 2 years	> 1 year	> 1 year, unless documented reproduction challenges	> 1 year	> 1 year
Maximum age, women	< 39	25-38 (<39)	< 39	< 40	< 40	< 37
Maximum age, men	< 55	25-55 (<55)	< 55	< 56	< 55	< 55
Existing children	No mutual children, includes adoptees	No mutual children, excludes adoptees	No mutual children, includes adoptees	No mutual children, includes adoptees	No mutual children	At least one of the parents is childless
BMI, women	< 30	< 30	< 35	< 35	<35	<30

Source: Information retrieved from each regions official website, see separate reference list in references.

2.1.2. Critique of the current strict age limit programs

As Sweden has a publically funded universal health care system with a restricted budget, prioritizations are required. The Swedish health care system rules under the following statutory ethical prioritization preferences:

- *The principle of human dignity*
  All people are of equal value and have equal rights regardless of personal characteristics and societal functions
- *The need and solidarity principle*
  Resources should primarily be allocated to areas where the need is greater
- *The cost-effectiveness principle*

> Choices between various activities or actions should seek a reasonable relationship between cost and effect, in terms of health and quality of life.

It is incompatible with the ethical principles to neglect a person's medical need due to characteristic such as age. However, in particular cases, circumstances that are limiting the benefits of a medical intervention can be taken into reconsideration (RiR 2004:9). For example, if age is an obvious reason for negative outcomes from a specific treatment, age-regulations are entitled. However, since fertility is individual and not strictly age-related, a medical screening system could improve the agreement with the ethical principles compared to the current age-restricted system.

The second paragraph of the Health and Health Care Law (SFS 2010:243, §2) states that the health care's objective is to provide good health and health care on equal terms for the whole population. The legislation indicates that health care should be distributed in respect of all people's equal worth and the individuals' dignity. Those in greater need of health care should be prioritized. Therefore a system of four prioritization categories has been developed and every possible condition is classified thereafter. Prioritization group I, II and III was included in the universal health care system while the conditions in class IV were viewed as the individual's own obligation and treatment of which was thus not subsidized. ART-treatments are classified in prioritization group III and thereby included in the universal health care benefits (SMER, 2013). This in turn means that ART-treatment should be allocated according to the recommendations by the Health and Health Care Law, and thus be supplied on equal terms for the whole population. A critique of today's system is thus that it does not follow the equality restriction if a woman of 39 is allowed publically funded fertilization treatment in one county but is referred to out-of-pocket treatment in another. It is noteworthy that it is the regional regulations that establishes what treatment a couple can seek and it is thus not possible for a discriminated couple to seek subsidized ART-treatment elsewhere.

Furthermore, in a survey directed towards the county councils regarding fertility treatment, 9 out of 21 county councils found the situation so challenging that they called for a nationwide harmonization of the ART-treatment restrictions. The primary motivation was that an equalization of health care benefits patients (SKL 2012; SMER, 2013). The current inequality argument is also the strongest argument of the interest organizations for reproductively challenged individuals in Sweden called Barnlängtan (Child Longing). They argue that the age limits are randomly set across the nation and lack scientific ground. As a consequence of the varied treatment and availability across the nation, multiple cases of discrimination and indignity charges have risen (Barnlängtan, 2013).

2.2. ART-treatment in Skåne Regional Council

As this study will focus on the situation in Skåne, the current regulations for subsidized treatment in the county council of Skåne, (Skåne Regional Council, SRC), is presented in more detail in this section. All information about the treatment procedures were retrieved from the Reproductive Medicine Center's (RMC) website (RMC, 2013) and by direct communication with medical professionals at the clinic[2].

As previously stated the age limits to qualify for ART-treatment in SRC is for the woman to not have turned 39 and for the man to not have turned 55. In addition, the couple (heterosexual or lesbian) cannot have any mutual children and the treated woman has to have a BMI below 30 (see table 1). To further limit the treatment utilization, the number of fully reimbursed treatment cycles per couple is limited. The limited number of publically funded treatment cycles is related to an increasing incremental cost, but also to an increasing cost per cycle with each attempt. For each ART-treatment cycles, the probability for the treatment to be successful decreases (Griffiths et al., 2010).

SRC use a point system, where each couple entering RMC is assigned a pool of six points. Each therapy is worth a fixed amount of points and the couple's points can then be freely allocated between therapies. For example, one hormone stimulation, including egg aspiration, resulting in an embryo transfer (ET) is worth 2 points. Thus each couple is provided with a maximum of three full treatment cycles free of charge. If the ET does not result in a live birth, and more than one egg was retrieved and fertilized in the first hormone stimulation cycle, these have been kept frozen and can be thawed and transferred into the uterus at a cost of 1 point (see figure 2 in appendix). If, at any point, the treatment results in a live birth all of the couple's remaining points are exhausted. If the couple runs out of free points they can choose to proceed with treatment with out-of-pocket payment at a private clinic (RMC, 2012:II).

2.2.1. Treatment schedule

To adequately comprehend the ART-treatments, a more detailed description of the medical practice is needed. Therefore this section present the RMC treatment schedule. All information presented here is retrieved from RMC (2012:I), unless otherwise stated.

To start ART-treatment the couple is either remitted to RMC by a gynecologist or has filled out a private referral form online. During the first visit blood tests and sperm samples are given, as well as a full gynecological examination including ultrasound. When the test results comes back an individual treatment plan is drawn out and

[2] Personal comunication with Aleksander Giwercman, Mona Bungum and Margareta Kitlinski

hormone ordinations are discussed between the couple and a physician. A nurse will then instruct the couple on how to dose the hormones, as exact compliance is essential for a successful treatment outcome. The first hormone injection is the actual starting point of the treatment.

There are several steps in the hormone stimulation. Before the actual stimulation can start, a down-regulation of the female's natural hormones is sometimes required. This makes it easier to control the active hormone treatment and thus to determine the exact time of egg aspiration. When the woman's natural hormones are under control active hormone treatment is initiated. The hormone stimulation is individually adjusted and aims to get the ovarian follicles to grow. The follicles contain the oocytes that mature into eggs and in the natural menstrual cycle the follicle development culminates in ovulation. In a natural menstrual cycle only one egg matures, but to increase the chances of getting pregnant the hormone stimulation aims to produces multiple oocytes. Six days after the hormone stimulation is initiated, the hormone values are controlled through a blood sample. The blood tests tell the physician whether the stimulation is well adjusted or needs alteration. In three additional days a vaginal ultrasound is performed to examine whether the hormones have stimulated a desirable oocyte production.

The hormone stimulation aims to optimize the egg aspiration. When most of the follicles have a diameter of approximately 18 millimeters and blood tests show an appropriate hormone level, it is time for the aspiration. This usually occurs 12 to 16 days after the hormone stimulation is initiated, depending on treatment protocol. However, the exact time of egg aspiration cannot be determined until two to three days before the intervention due to the risk of insufficient follicles growth. Exactly 36 hours prior to egg aspiration special hormone stimulation is injected to help the eggs mature. The egg aspiration is performed vaginally with the aid of an ultrasound. On average, eight eggs are collected per hormone stimulation cycle.

Simultaneous to the egg aspiration the man gives a sperm sample. To maximize the result, the sample is refined in the lab by extracting the sperm with the highest quality before inseminated into the egg.

Two to five hours after the eggs are retrieved they are ready for fertilization. There are two different techniques to fertilize eggs, the choice of which depends on the quality of the sperm.

- In vitro fertilization (IVF): approximately 150,000 sperms are united with each egg. A single sperm will find its own way into the egg.
- Intra-cytoplasmic sperm injection (ICSI): a single sperm is collected and injected straight into the egg.

IVF is the technique used when the sperm quality is good while ICSI is used to treat sperm defects. As a precaution all retrieved eggs are inseminated.

After insemination, the eggs are put in a nutrient liquid and kept at 37 degrees. If the eggs have been fertilized it will split into two cells after 24 hours. The cells continue to multiply and eventually create an embryo. Medical experts at RMC estimate that 60-70% of the eggs will develop into embryos[3].

Two to five days after the egg is inseminated, the embryo is developed enough to be transferred into the woman's uterus. This is simply called an embryo transfer (ET). The perfect time for ET vary between couples and depend on the embryos' development pace. In Sweden a single embryo is usually transferred at the time, according to recommendations by NBHW introduced in 2003 (Granberg, 2004). Single ETs reduces the chance of initial pregnancy but increases the odds for a confirmed pregnancy to result in a live birth. Multiple ETs increases the probability for multiple pregnancies, which causes significant health care risks for both the fetuses and the mother (Kjellberg et al., 2006). Multiple ETs are still performed in Sweden, but are an exception to the rule. (Ferraretti et al., 2012).

Following the ET, hormone treatment continues to provide an optimal growth-environment for the embryo. The treatment proceeds until pregnancy can be confirmed two weeks after ET. If the pregnancy test is negative, new treatment is scheduled as soon as possible if the couple wishes to try again. If the pregnancy test is positive an early ultrasound is performed after 6 weeks to ensure the health of both the fetus and the mother.

2.3. Proposed regulatory changes

Due to the objections of different age limitations across the country several propositions for change has been presented over the years. There are two main propositions relevant for consideration in this study.

First, the Swedish National Council on Medical Ethics presented a report in January 2013 on ethical aspects of assisted reproduction, including a discussion on the current age limits. The council found the current legislation insufficient in several aspects. Specifically the increased demand for ART-treatment and the change in public opinion were held as two main arguments for reconsideration. Moreover, the council found the current treatment supply to be suboptimal in relation to the medical development in the area. As no statutory age limits exist and because there are good medical prospects even for older women to become pregnant under the right circumstances, the Swedish National Council on Medical Ethics argues that general age limits are inappropriate, and unethical. Instead the best interest of the prospective child should be prioritized simultaneous with consideration of the woman's medical prospects. Therefor the Swedish National Council on Medical Ethics recommends an abolition of the general age limit in the county councils in favor of individual

[3] Personal communication with Margareta Kitlinski

assessment (SMER, 2013).

Second, medical professionals at RMC in the Southern Health Care Region have alerted us to the potential deficiencies of the current strict age-limit program. In their professional opinion, a strict age limit is not necessarily the most efficient treatment allocation as ageing is individual. For example, it might not be the case that a 37-year-old female has superior biological prerequisites to achieve a live birth compared to a 41-year-old woman, on an individual level. In some cases it would be more efficient to allocate the medical resources towards the older woman. Therefore, RMC wishes to implement a medical screening system to determine who is eligible for treatment[4]. Apart from the medical differences in ageing, a further argument for RMC proposal is that Sweden's universal health care system rules under the statutory ethical prioritization preferences previously listed.

There are strong medical indications of severe and accelerating deterioration of the reproductive ability in women over the age of 35 (Piette et al., 1990). In contrast to the Swedish National Council on Medical Ethics, RMC professionals argue that 35 would be a suitable age limit under which universal reproductive treatment should be supplied[5]. However, the biological ageing is individual and there are studies suggesting that some women are able to reproduce well over 39 (Suchartwatnachai et al., 2000; SBU, 2012; SMER, 2013). Couples who do not qualify for publically funded ART-treatment have the option of seeking care at private clinics, which is then funded out-of-pocket. However, it is very unusual that ART-treatments are offered to woman >42 in any clinic in Sweden.[6] The proposal from RMC is to supply universal ART-treatment for women under 35 and to welcome women aged 35-42to undergo medical assessment in order to decide whether they are viable for further treatment.

This study will henceforth focus on evaluating the RMC proposal, instead of the Swedish National Council on Medical Ethics proposal, and compare its cost-effectiveness with today's strictly age-limit program. The medical experts at RMC states that the ratio of women under 35 who would be proven not suited for further treatment after a medical screening is marginal, even though female reproductive qualities start to decline as early as at the age of 25 (Piette et al., 1990). The cost of pursuing the screening process for all ages, is assumed to be more costly, or at least equal the cost of supplying treatment for the women under 35 where it lacks effect.

2.3.1. The medical screening process

The RMC proposal includes a medical screening of women aged 35-42. However, even though using a medical screening process the couple still need to pass the

[4] Personal communication with Aleksander Giwercman, Mona Bungum and Margareta Kitlinski

[5] Personal communication with Aleksander Giwercman and Margareta Kitlinski

[6] Personal communication with Aleksander Giwercman

original qualification criteria of BMI, mutual children and age restrictions. The couple will follow the previously described treatment schedule until egg aspiration, then satisfactory treatment response will be evaluated.

The screening process was defined by medical expertise at RMC to consist of hormone stimulation where the resulting egg production constitutes the qualification criteria. The treshold for satisfactory treatment response is defined as retrieving at least four eggs at egg aspiration. Four eggs is assumed to be the cut off to make ET, the next treatment step, probable[7]. This is in line with the European consensus of a poor response to hormone stimulation treatment (Ferraretti et al., 2011). If less than four eggs has been retrieved after hormone therapy then the couple will not be approved for further ART treatment at a publically founded clinic.

The proposed treatment regimen will hereafter be referred to as the Medical Screening Program (MS program in tables).

2.4. Previous literature

Previous economic evaluations of ART-treatment have held different perspectives, mainly due to the complexity in defining the target outcome. In general, health economic evaluations weigh a health intervention's costs against its benefits in an attempt to evaluate whether it brings a positive net gain and thus is worth pursuing. It evaluates where and how to allocate limited budgets earmarked for health care to maximize health outcomes. In order to compare the costs of a health intervention to its benefits in monetary or other comparable terms, the first step is to define what those costs and benefits are. There is a generally accepted methodology within the field of health economic evaluations to follow (Drummond et al., 2005; Evers et al., 2005; Philips et al., 2004). However, evaluating ART-treatments aggravates the definitions. Primarily, the definition of the ART-treatments' benefits is somewhat ambiguous. While the extent of most treatment outcomes can be measured in gained quality adjusted life years (QALYs), a successful ART-treatment creates a new life in addition to treating the infertility in the prospective parents.

The purpose of the treatment is to help infertile couples to reproduce. But is it a pregnancy that we wish to attain, or a live birth? Most people argue that the medical goal with ART-treatment is a live birth (Garceau et al., 2002). However, a live birth means that a new person is brought to life and to determine the economic value or benefits of an additional human life is a complicated matter, to say the least (Simon, 1975; Rice et al., 1967).

[7] Personal correspondence with Aleksander Giwercman and Margareta

Previous economic evaluations have mainly defined the benefits of ART-treatment in three different ways. First, some have limited the benefits to a live birth and thus ignored what the creation of an additional person is worth in monetary terms (Suchartwatnachai et al., 1999; Hirshfeld-Cytron et al., 2012; Neumann et al., 1994; Wølner-Hanssen et al., 1998; Griffiths et al., 2010). Instead of monetary values, these studies concentrate on estimating the cost per live birth and leaving it to decision makers to evaluate whether or not the benefit of a live birth is worth the cost. Some even disregard the outcome of ART-treatment and simply estimate the cost per treatment cycle, however successful (Bouwermans, 2008), or present multiple cost-estimates such as cost per cycle and per live birth (Van Voorish et al., 1998). Secondly, a number of studies have considered the economic interaction between the additional person and the state (Svensson et al., 2008; Connolly et al., 2008). Calculating the present value of both ART-treatment plus other governmental expenses that a person is accredited during a lifetime, such as schooling and health care, and the governmental income from taxation paid by an average individual during a lifetime. The net present value (NPV), the present value of governmental income minus governmental expenditures during an average lifetime, is calculated and considered as an investment bringing a return equivalent to the NPV. Third and final, some previous studies have chosen to consider what a child is worth to its infertile parents, who generally have spent years in agony prior to its birth. Here health effect of infertility, mental as well as physical, is estimated and the increased quality of life assumed to credit the child's parents is considered (Granberg et al., 1995; Neumann et al., 1994; Ryan, 1998).

Generally, economic evaluations aim to include a time perspective long enough for both costs and benefits to fully show. In this way the chosen time horizon will not affect the end result through missing data (Drummond, 2005). Considering that the benefit is a person, who contributes to the economy in production and consumption and who in turn may reproduces and thus start another production/consumption cycle, such time horizons are hard to fixate.

This study will limit the benefit-side of the evaluation to a live birth, which is an approach used in most previous studies (Neumann et al, 1994; Wølner-Hanssen et al., 1998; Griffiths et al., 2010). The argument for this is that the infertility, the initial diagnosis, is cured at childbirth. As curing the patient is the ultimate goal of any health care intervention we choose childbirth as our endpoint.

3. THEORY AND METHOD

3.1. Methods of economic evaluation

There are four main methodologies to consider when conducting an economic evaluation. Each methodology evaluates the costs of implementing a health care innovation; three of them also consider its health benefits. What diverges the methodologies is primarily the way they measure and value the benefit-side of the innovation (Drummond et al., 2005), see table 2, and are thus suited for different evaluations depending on the study-specific objective and data availability.

In an attempt to justify our choice of methodology each of the four alternatives are presented below, including a declaration of its suitability to our material and study objective. This study evaluates the provision of publically founded ART-treatment, which, for compliance, will be referred to as *the treatment* in this section.

Table 2. Characteristics of evaluation methods

Type of study	Measurement / valuation of costs in both alternatives	Identification of health benefits	Measurement / valuation of health benefits
Cost analysis (CA)	Monetary units	None	None
Cost-effectiveness analysis (CEA)	Monetary units	Single effect of interest, common to both alternatives, but achieved to different degrees	Natural units (e.g. life-years gained, number of live births etc.)
Cost-utility analysis (CUA)	Monetary units	Single or multiple effects, not necessarily common to both alternatives	Healthy years (typically measured in quality-adjusted life years)
Cost-benefit analysis (CBA)	Monetary units	Single or multiple effects, not necessarily common to both alternatives	Monetary units

Source: Drummond et al. 2005

The first economic evaluation method is the Cost Analysis (CA), which exclusively evaluates the cost-side of a treatment. The CA is only applicable when the compared treatment effects can be proven, or assumed, equivalent (Drummond et al., 2005). As it is assumed that a reallocation of fertility treatments would affect the outcome, CA was not an appropriate method for our analysis. The following methodologies, however, all include the evaluated treatment's health benefits.

The second evaluation method is the Cost-Effectiveness Analysis (CEA), which identifies and presents the most appropriate natural measure of the treatment's benefits. Examples of such natural measures include the number of gained life years, deterred heart attacks or live births. A monetary value of the health benefits is disregarded, but the outcome of the treatment is considered beneficial and desirable.

A CEA requires that the evaluated treatments bring the same kind of health benefits, but allows for a varied extent (Drummond et al., 2005). In other words, there is a single treatment effect of interest mutual to both treatment alternatives, this, considering the information in table 2, suggests that we apply a CEA in our evaluation.

Thirdly, there is the Cost-Utility Analysis (CUA) that measures the treatment benefits with a generic utility measure. This means that, in addition to the number of life years gained, the health related quality of the gained life years are considered. In other words both morbidity and mortality is included in the output value. The most common health output measure used in CUAs is QALYs. A CUA is a refined version of a CEA with a unified output measure enabling comparison of cost-effectiveness from a variation of diagnostic areas. Most often the result is presented as cost per gained QALY (Drummond et al., 2005). However, QALYs are rarely used when considering the benefits of a live birth, as it is vastly complex to estimate. Furthermore, the CEA is a better fit to our objective than the CUA as the endpoint is common for both treatment alternatives considered.

The fourth and final evaluation method is the Cost –Benefit Analysis (CBA). CBAs differ from CEAs and CUAs as the former concentrate on health effects in themselves, while the CBA convert the health effects into monetary values. Hence, both the costs and the benefits of a treatment are expressed in monetary terms and enables the deduction of a net benefit value. A CBA is the most exhaustive form of economic evaluation of health care programs, allowing comparison (and thus prioritization) with investments in other societal areas, such as construction or education. However, assigning a monetary value to a particular health state is not without complexity and the risk of measurement errors are therefore considerable. In the context of this thesis, it is too complex to estimate the monetary value of a child, an additional human life. Therefore no attempt of such calculations will be made which eliminates the CBA for this study.

In conclusion, this thesis applies the CEA methodology.

3.2. Cost-Effectiveness Analysis

In the following sections the CEA is described with more precision. The presented methodology is based on *Methods for the Economic Evaluation of Health Care Programmes* by Drummond et al. (2005), unless otherwise stated.

As stated, the CEA is an elaborate economic evaluation that considers both the cost-side and the benefit-side of the treatment. A CEA is most suitable when decision makers face prioritizations between two treatment alternatives and operate under a budget restriction. The CEA aims to provide information on what alternative maximizes the relevant output. For example, it is the decision maker's responsibility to supply the population with fertility treatment and the aim is to maximize the number of live births with a limited budget.

3.2.1. Perspective

The first quest is to determine what perspective to apply. The chosen time horizon affects what treatment costs and health benefits are included in the evaluation. A societal perspective is usually preferred, which is in line with recommendations for economic evaluations by the Swedish Dental and Pharmaceutical Benefits Agency (TLV) (LFN, 2003).

3.2.2. Costs

When a perspective is determined the relevant costs and health benefits should be identified, measured and valued. When valuing individual costs it is important to consider that the true cost might not be equivalent to its market price. This is true for most input items, especially in universal health care systems where prices are monopolistically projected in addition to often being heavily subsidized. A reasonable evaluation of found unit prices should thus be conducted before used in the calculations. Moreover, costs that are not specific to the treatment per se, but to the overall health care organization should be considered. These are called overhead (OH) costs and include entries such as electricity, facilities, administrative costs etc.

3.2.3. Health benefits

The effectiveness data used in a CEA can be abstracted from existing, quality assured, clinical studies or directly withdrawn trough statistical registers. It is of importance to consider the inclusion criteria of the clinical trial if such effectiveness data is used. If there is uncertainty regarding the quality of the effectiveness data, the efficacy variables should be varied in a sensitivity analysis.

When retrieving effectiveness data from existing studies, a different endpoint from what we are interested of might be used. In assisted reproduction many studies focus on cost per IVF cycle or cost per pregnancy. However, the present study is interesting in cost per live birth as a live birth is the actual purpose with fertility treatment. If the correct endpoint is missing one can turn to other studies to extract a link between two health stages, or the intermediate and final endpoint. For example, there can be other existing studies that present usable information regarding how many clinical pregnancies following ART-treatment result in a live birth.

3.2.4. Discounting

In economic evaluations of projects with long time horizons, or with spillover health benefits or include costs for years to come costs and benefits are discounted in order to obtain the present value of the project. Discounting aggregates costs and benefits that occur in different time periods (Boardman et al., 2011). One cycle of fertility treatment, including a 9-month pregnancy, takes about a year. And as discounting is a year-to-year adjustment discounting is not applicable to the calculations of this study.

3.3. Incremental cost-effectiveness ratios

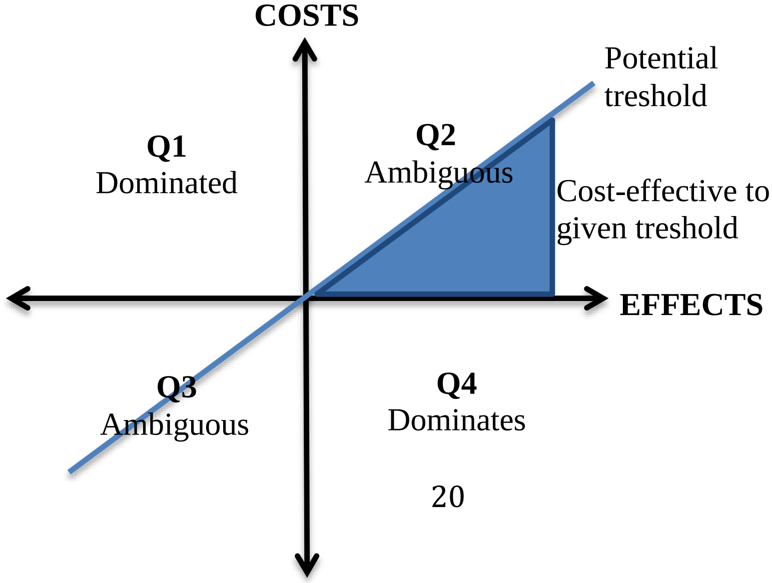
CEAs compare two treatment alternatives and often use incremental cost-effectiveness ratios (ICER) to present its results. An ICER presents the new treatments cost, treatment A, relative to the cost of the old treatment, treatment B, as well as treatment A's health effect relative to that of treatment B. The ICER is calculated through the following formula;

$$ICER = \frac{Costs_A - Costs_B}{Effects_A - Effects_B} = \frac{\Delta C}{\Delta E}$$

Additionally, it is a requirement that the two treatments included in an ICER are *mutually exclusive*, which means that if a patient receives one of the treatments, he/she cannot receive the other, also treatments are assumed to be *independent* of each other. These characteristics ensure that the costs and effects of another treatment do not affect costs and effects of a treatment, which is vital for this type of analysis.

There are four potential outcomes of a ICER demonstrated in the ICER plane in figure 1; (Q1) treatment A has higher costs but lower effects than treatment B and is dominated by treatment B, (Q2) treatment A has higher costs and higher effects than treatment B, (Q3) treatment A has lower costs and lower effect than treatment B, and (Q4) treatment A has lower costs but higher effects, then it dominates treatment B. In case (Q1) and (Q4), one treatment dominates the other and the relative cost-effectiveness is given. The implication of case (Q2) and (Q3) however, is ambiguous and the cost-effectiveness depends on what given monetary treshold is considered cost-effective (Drummond et al., 2005).

Figure 1. ICER plane



The monetary threshold for cost-effectiveness represents the willingness to pay (WTP) for the achieved health improvement. Ideally the WTP is equivalent to the opportunity cost of implementing the treatment, i.e. the economic value of the treatment already in place from which the new treatment would draw resources if implemented. Hence, a new treatment would be implemented due to cost-effectiveness if it brings more health than an already existing treatment with the same cost (SBU, 2013). Whether a treatment is regarded cost-effective depends on which side of the illustrated threshold-slope (figure 1) the ICER estimates end up. The threshold slope represents the highest acceptable ICER, i.e. the highest acceptable WTP, for a specific treatment. Better health effects allows for higher costs.

In some countries national guidelines state a fixed monetary value of the ICER-threshold when conducting CUAs and using QALYs as the health effect estimate. For example, in England the National Institute for Health and Clinical Excellence (NICE) has used an ICER-threshold in the range SEK 200 000 – 300 000[8] since 1998 (NICE, 2008). However, there is no official ICER-threshold in Sweden even though SEK 655 000 has been discussed as an appropriate limit. The NBHW has published an indicatory guideline presented in table 3, describing what is viewed as a low or a high price per QALY gained (Socialstyrelsen, 2008). In practice, the ICER-limits rather depend on the severity of the disease as well as its prevalence in the population.

Table 3. Discussed ICER thresholds

Amount (SEK)	Indication
< 100 000	Low cost per QALY gained
100 000 – 499 999	Moderate cost per QALY gained
500 000 – 999 999	High cost per QALY gained
> 1 000 000	Very high cost per QALY gained

Source: Socialstyrelsen, 2008

3.4. The applied method

As the objective of this study is to establish which allocation of ART treatment is most cost-effective an economic evaluation will be pursued. The health benefits of the two treatment alternatives evaluated is mutual to both treatment alternatives and measured in the natural unit *live births*. Therefore it is natural to apply the CEA method. The CEA is suitable when decision makers face a prioritization between two treatment alternatives and operate under a budget restriction, which is the case in this study. The results of the evaluation will be presented as cost per live birth for both treatments, which in turn will be compared in an ICER.

Treatment costs are collected from a public price list published by SRC, which includes specific numbers for the RMC clinic. The costs are assumed to equal the true

[8] An approximation after converting the original interval £20.000-£30.000 using the equivalent to, using the exchange rate of July 1st 2013 being SEK 10.1379/£1 (www.riksbank.se)

treatment costs and include OH costs, and are therefore left unadjusted. Some indirect costs in the form of transportation costs and production loss under treatment are identified and included. All costs will be presented in 2013 SEK.

The effectiveness data are retrieved from RMCs internal statistical database and supplemented with national information collected from the Swedish Quality Register Q-IVF (2013). The target treatment outcome was a live birth, which was the sole focus of the analysis. HRQoL measures were excluded, as they were argumentatively redundant.

4. DESCRIPTIVE STATISTICS

To study the relationship between age and cost-effectiveness of ART-treatment we have reviewed data from the Reproductive Medicine Center in Malmö, RMC. The data is non-experimental and collected for statistical purposes for the clinic. The collection period stretches from 1st of January 2011 to 30th of June 2012, and refer to the time of initiated treatment cycle. Even though the included data covers a relatively short time span, the inclusion choice is motivated by the lack of qualitative data prior to 2011 and that the outcome of treatment occur nine months after a full treatment cycle (i.e. late spring 2013 for the cycles started at the end of our observation period). Therefore the chosen duration period brought the most consistent and reliable data set. Only treatments with the couples' own gametes were included in the data set, while cycles with donated eggs or sperm (e.g. lesbian couples) were excluded. This was done in an attempt to separate the effect of age on fertility from that of other aspects, such as sexual orientation or a medical diagnosis.

Furthermore, the original data set contained couples where the woman is aged 21-41. Current regulations at RMC, however, state that only females under the age 39 are provided with treatment. Therefore, and because the sample is very small in the older age groups, women aged 39-41 are excluded from our data set. Average female age in our remaining sample is 32.4 years old.

Table 4. Treated patients

Female age	Observed patients [a]	Patients per year
<35	764	509
35	79	53
36	87	58
37	79	53
38	84	56
Total	1 093	729

[a] after exclusions

In the original data set possible ART-treatments consists of *IVF*, *ICSI* or *a combination of both*. Since it is impossible to know the allocation between ICSI and IVF in the treatment type *combination* these cycles (n=11) were excluded from our sample in order to maximize the accuracy on the most common treatments alternatives, ICSI and IVF.

These exclusions reduces our sample from 1200 couples to 1093. For the remaining patients a total of 2103 treatment cycles were observed (1.93 treatments per couple), out of which 97.8% (n=2057) reached egg aspiration. The live births counted 364 and generated a success rate of 17,3% per initiated treatment cycle.

A majority of the couples had more than one treatment. However, it is important to note that our limited duration for data collection implies that couples may have started their ART-treatment before and may continue with their treatment after, our observed time period. Therefore we are from our own data alone unable to state the average number of cycles per couple.

As the proposed treatment regime, the Medical Screening Program, include females up to 42 years old and the reliable RMC data only stretches to age 38, we turn to a national registry for assistance. The national quality register of fertility treatments (Q-IVF, 2013) gathers information from all fertility clinics in Sweden. The data includes age-specific information, it explicitly specifies how far along in the treatment individual cycles get and it is divided between treatments with donated or own gametes. These details enable a comparison between RMC data and the national data. However, there are some divergences between the data sets regarding the inclusion criteria of the fertility centers, as previously shown in table 1. Additionally, the Q-IVF data includes both public and private clinics. This implies that couples who are declined publically funded ART-treatment can turn to a private clinic and fund the treatment out-of-pocket. If a couple already has mutual children it generally increases the chances for ART-treatment to work, thus improving the success rate for private clinics compared to public ones such as RMC. Yet, the Q-IVF is the only available complement to our RMC data and is therefore used where the RMC data is lacking (i.e. for females aged 39-42). However, to be explicit about the differences of the data sets a simultaneous analysis on pure Q-IVF data will accompany the RMC based analysis throughout the thesis.

An overview of both data sets is presented in table 5 below. The RMC data has a lower success rate for both ICSI and IVF treatments than the national statistics. Although the relation between ICSI and IVF is pointing in the same direction, i.e. IVF has a slightly higher success rate than ICSI in both samples.

Table 5. Success rate per treatment type and data set

Data set	Treatment type	Number of treatments	Live births	Success rate
RMC				
	IVF	1 220	203	16,6%
	ICSI	883	161	18,2%
	Total	2 103	364	17,3%
Q-IVF				
	IVF	8 054	1 628	20,2%
	ICSI	8 806	1 852	21,0%
	Total	16 860	3 480	20,6%

Note that the endpoint of this study is live births, as the cure when treating infertility is a child. Therefore we will not make any difference between single ETs and double ETs, or multiple or single births. This implies that a twin birth will count as one childbirth, i.e. one successful treatment. This assumption is partly made due to the risks of a twin birth after the first cycle generating a success rate of 200%, but the primary reason is that we aim to explore the cost of treating infertility for a couple irrespective of how many children they conceive.

Success rates show the possibility of having a live birth per started treatment, which means that if treatments are repeated the cumulative success rate will be higher. Olivius et al. (2002) studied the relationship between numbers of treatment cycles and cumulative success rate, showing that more than 50% of all couples undergoing at least three ART-treatments would get pregnant. Due to the limited duration of our observed period we were unable to follow individual couples throughout their whole treatment process to determine the success rate per treated couple. The solution is to estimate the success rate per cycle and then use the number of subsidized treatment cycles (three) to determine the overall success rate per couple. The cumulative success rate after three cycles was estimated using Kaplan-Meier product limit estimate;

$$[1-(1-p_1)(1-p_2)(1-p_3)] * 100\%$$

where p_x is the probability of achieving live birth in cycle x (Olivius et al. 2002). As mentioned there was no data on cycle-specific success rate and the average success rate for each female age was therefore used for each p_x.

The use of three cycles in the cumulative success rate estimation, even though clearly not all couples utilize all provided cycles, is motivated by the assumption that the couples who do not pursue the third cycle are those who have already achieved a live birth. There is a portion of patients who opt out of treatment due to other reasons than a live birth, but those cases were assumed marginal and thus disregarded. Adding up the success rates for each cycle leaves us with the success rate per couple. The results are presented in table 6 and show a declining cumulative success rate with increasing age.

Table 6. Observed and cumulative success rates

Female age	Observed success rate				Cumulative success rate			
	Strict age limit (<39)		MS program		Strict age limit (<39)		MS program	
	RMC	Q-IVF	RMC [a]	Q-IVF	RMC	Q-IVF	RMC [a]	Q-IVF
<35	19,1%	26,2%	19,1%	26,2%	47,0%	59,7%	47,0%	59,7%
35	17,9%	21,0%	22,8%	22,0%	44,6%	50,8%	54,0%	52,5%
36	12,7%	21,0%	15,4%	22,0%	33,4%	50,8%	39,5%	52,5%
37	11,3%	21,0%	13,2%	22,0%	30,1%	50,8%	34,6%	52,5%
38	11,5%	15,3%	14,8%	16,2%	30,6%	39,3%	38,2%	41,2%
39	-	-	16,2%	16,2%	-	-	41,2%	41,2%
40	-	-	16,0%	16,0%	-	-	40,7%	40,7%
41	-	-	16,0%	16,0%	-	-	40,7%	40,7%
42	-	-	7,5%	7,5%	-	-	20,8%	20,8%

[a] Success rate data for women aged 39-42 was drawn from Q-IVF due to lack of RMC clinic data

The point of the proposed Medical Screening Program, including medical screening for women aged 35-42, is to improve the success rate of the individual couples that qualify for subsidized ART-treatment. As the end point of the suggested medical screening is whether or not the treatment reaches satisfactory egg aspiration the observed success rate for the Medical Screening Program refer to success rates per egg aspiration, which was then used to calculate the cumulative success rate for the Medical Screening Program. As shown in table 6 the cumulative success rate, except for the 42-year olds, vary between 30-60%. This range corresponds to the findings of previous studies where the success rate over three consecutive ART-cycles varied from 34 to 65% (Witsenburg et al., 2005; Malizia et al., 2013; Mol et al., 2000; Stewart et al., 2011; Elizur et al., 2006), the most relevant being a Swedish study conducted by Olivius et al. (2002) presenting a cumulative success rate rate of 63% for the overall population.

Additionally, table 6 illustrates the common problem of higher age on fertility rates. Several studies suggest that the female age is negatively correlated to success rates (Kenny 1994; Griffiths et al., 2010; Broekmans et al., 2004; Wright et al., 2005; Templeton et al., 1996; Olivius 2009). A regression analysis of our RMC data confirms the implications of the table above and shows a significant negative relationship between female age and live births.

Table 7. Regression analysis for success rates

Probit model		
Live birth	Coefficient	Robust std. errors
Age	-0.032***	0.008
ICSI=1, IVF=0	-0.023	0.068
Fresh=1, Frozen=0	0.501***	0.079
Interruption pre-egg asrationpi=1, no interruption=0	*omitted*	-
Interruption pre-ET=1, no interruption=0	*omitted*	-
Constant	-0.132	0.264
Chi squared-statistic	0.000	
Pseudo R^2	0.031	
Number of observations	1839	

Note: * = α< 10%, ** = α< 5%, *** = α<1%

The regression analysis, in table 7, is conducted through using models for binary dependent variables since our outcome, live birth, can only take the value 1 for *live birth* or 0 for *no live birth*. For this reason we have used a probit regression model. The independent variable *age* is the only variable that is not binary in our regression. All of the other variables are binary to test if the outcome is depending on difference between IVF/ICSI, fresh/frozen embryos, if egg aspiration or not and if ET or not. The results from the probit model suggest that, as previously stated, age has a negative impact on live births. It also concludes that fresh cycles has a positive impact on live births (compared to thawed) and that the treatment type, ICSI or IVF, is irrelevant to the outcome of a live birth. These results are equivalent to the statistics for each parameter in our sample. The variables of failed treatment pre-egg aspiration or pre-ET is omitted from the regression since both predicts failure perfectly. Data matching these variables =1 are excluded from the regression data.

Another factor affecting female fertility is BMI. However, one of the treatment conditions at RMC is for the woman to have a BMI below 30. The BMI restriction will be included the Medical Screening Program too, and the BMI effect will thus be equivalent for the two treatment alternatives. The effect of BMI on success rate is hence dealt with in the inclusion criteria for treatment and is therefore not further discussed in this thesis.

Our RMC sample of 2103 individual cycles is divided according to table 8 below, and as shown, success rate is higher for fresh treatments than for treatments with thawed embryos. The success rate for fresh cycles, both IVF and ICSI treatments are equivalent between our sample and the national register data. Although, in our sample there is a large difference between fresh and thawed cycles, while the difference is much smaller in the national data set. In the regression analysis (table 7) the results for fresh or frozen embryos are significant, which suggests that whether the cycle is fresh or thawed has a significant impact on live births. Remember however that even though the results are significant in the RMC sample that might not be the case for the Q-IVF data.

Table 8. Success rate per type of treatment

Data set			Cycles	Live births	Success rate
RMC					
	IVF	Fresh	632	134	21.2%
		Thawed	251	27	10.8%
	ICSI	Fresh	827	164	19.8%
		Thawed	393	39	9.9%
Q-IVF					
	IVF	Fresh	5838	1330	22.8%
		Thawed	2426	441	18.2%
	ICSI	Fresh	5754	1301	22.6%
		Thawed	3094	607	19.6%

Sourse: Q-IVF, 2013

As this thesis aims to study the economic consequences of implementing a new treatment regimen in the ART field we have to calculate the expected outcome of the new proposal, the Medical Screening Program. The main difference from today's structure is the additional medical screening for the couples where the woman is above 35 years, from which only those suitable for treatment will be selected to continue ART-treatment. Additionally, the Medical Screening Program would introduce publically funded ART-treatment for women aged 39-42.

Table 9. Yearly demand for ART-treatment

Female age	Observed	Extrapolated	Total
<35	509		509
35	53		53
36	58		58
37	53		53
38	56		56
39		53	53
40		51	51
41		50	50
42		49	49
Total			931

To be able to calculate the cost per live birth for each treatment program the age allocation of the population group is of interest. The age allocation is important as older women have lower success rates and thus face diverging cost structures from that of younger women. Since our sample only contains couples where the woman is <39 years old we had to extrapolate the demand of ART-treatments for women aged 39 and above. The demand was extrapolated using a linear relationship with a R^2 of 0.369, and adjusted to a yearly demand (see table 9).

For couples to qualify for treatment in the Medical Screening Program the woman need to have at least four oocytes for retrieval after hormone therapy (i.e. the pre-egg aspiration ultrasound has to testify of at least four maturing oocytes). To estimate the portion of patients per age group who will qualify for further treatment in the Medical Screening Program we rely on data from Ferraretti et al (2011). The study is based on Italian data, but after consulting the medical experts at RMC[9] we find it reasonable to apply in a Swedish setting, and thus we proceed using the medical screening qualification rates presented in table 10. If combining the yearly demand with the qualification rate, we find the qualified demand for the Medical Screening Program (see results).

Table 10. Qualification rates of medical screening

Female age	<4 oocytes (disqualified in Medical Screening)	MS qualification rate
<30	8%	92%
30-35	11%	89%
36-39	14%	86%
40-42	23%	77%
>42	38%	62%

Source: Ferraretti et al.,2011

In the forthcoming calculations we keep using both RMC and Q-IVF data to enable comparisons and inference about possible differences, as previously announced in this section.

[9] Personal correspondence with Aleksander Giwercman and Mona Bungum

5. COSTS AND COST CALCULATIONS

Couples undergoing fertility treatment at RMC in Malmö are allocated between a long and a short treatment protocol. Approximately 60% of the couples are treated according to the long protocol while the remaining 40% follow the short protocol. There are no age differences in the protocol allocation[10].

Each protocol follow its respective treatment steps listed in table 11 below. The main difference is that females treated with the long protocol undergo a down-regulation of her natural hormones before starting hormone stimulation, in order to neutralize the natural hormones and facilitate a positive treatment outcome. This step is ruled unnecessary for some women that are therefor referred to the short protocol. The short protocol, on the other hand, includes antagonist medication, preventing the maturing eggs from being released prematurely. Both treatment protocols include an ovulation trigger that promotes ovulation at the ideal time for the scheduled egg aspiration (RMC, 2012:I).

Table 11. Treatment schedule

LONG PROTOCOL			SHORT PROTOCOL	
	Description		Step	Description
1	Examination including ultrasound (F) [a]	MEDICAL SCREENING (steps 1–6)	1	Examination including ultrasound (F) [a]
	Andrological examination (M) [a]			Andrological examination (M) [a]
	Sperm sample			Sperm sample
2	Consultation, treatment planning (physician) and treatment information (nurse)		2	Consultation, treatment planning (physician) and treatment information (nurse)
3	Down regulation		3	Hormone stimulation
4	Hormone stimulation		4	Antagonist
5	Estradiol blood test (F)[a]		5	Estradiol blood test (F)[a]
6	Ultrasound (1-3)		6	Ultrasound (1-3)
7	Ovulation trigger		7	Ovulation trigger
8	Egg retrieval, incl. sperm sample and analysis		8	Egg retrieval, incl. sperm sample and analysis
9	ICSI or IVF		9	ICSI or IVF
10	Embryo transfer		10	Embryo transfer
11	Follow up treatment - hormone stimulation		11	Follow up treatment - hormone stimulation
12	Pregnancy test		12	Pregnancy test
13	Early pregnancy ultrasound (if positive pregnancy test)		13	Early pregnancy ultrasound (if positive pregnancy test)

[a] F indicates female patient; M indicates male patient

The protocols and their treatment steps help to identify what resources are used in the treatment and at what point they occur, which is why the protocols are presented yet again. In the next sections the resource units and their corresponding costs will be explored as well as how they are estimated and included in the treatment cost calculations.

[10] Personal correspondence with Margareta Kitlinski

Henceforth, the allocation of 60% of patients to the long protocol and the remaining 40% to the short protocol is included in all cost calculations and not further mentioned in detail.

5.1. Unit costs

The perspective of this analysis is societal, i.e. all costs and consequences, no matter to whom they accrue (patient/health care/society), are included (Drummond, 2005; Morris, 2012; Boardman 2011). On the cost-side this implies that both direct and indirect costs are identified and calculated. For example, direct medical costs include doctor time, equipment and OH costs (administration, facilities etc). Moreover cost of pharmaceuticals and the societal cost of production loss is calculated as well as direct transportation costs at RMC visits.

Table 12. Unit costs in 2013 SEK

Cost Category	Cost	Unit	Source
Direct health care costs			
Physician examination including ultrasound	3 134	Per visit	SHCR pricelist
Initial blood work [a]	610	Per patient	SHCR pricelist
Andrological examination (M)	4 740	Per visit	SHCR pricelist
Sperm sample	1 438	Per sample	SHCR pricelist
Sperm analysis	1 700	Per sample	SHCR pricelist
Physician consultation	1 714	Per visit	SHCR pricelist
Nurse consultation	1 419	Per visit	SHCR pricelist
Nurse visit	493	Per visit	SHCR pricelist
Estradiol blood test	36	Per test	SHCR pricelist
Ultrasound (HyCoSy)	2 180	Per visit	SHCR pricelist
IVF, completed	22 176	Per treatment	SHCR pricelist
IVF, aborted pre-embryo transfer	1 758	Per treatment	SHCR pricelist
IVF, aborted pre-egg aspiration	481	Per treatment	SHCR pricelist
ICSI, completed	28 325	Per treatment	SHCR pricelist
ICSI, aborted pre-embryo transfer	2 976	Per treatment	SHCR pricelist
ICSI, aborted pre-egg aspiration	481	Per treatment	SHCR pricelist
Thawed embryo transfer	12 529	Per treatment	SHCR pricelist
Pregnancy test	45	Per test	SHCR pricelist
Ultrasound visit (physician)	1 420	Per visit	SHCR pricelist
Cost of Pharmaceuticals			
Down regulation [a]	1 135	Per patient	FASS
Hormone stimulation [a]			
<35	3 344	Per patient	FASS
>35	7 443	Per patient	FASS
Antagonist [a]	1 977	Per patient	FASS
Ovulation trigger [a]	342	Per patient	FASS
Pharmaceutical use at egg retrieval [a]	26	Per egg retrieval	FASS
Follow-up treatment, fresh cycle [a]	506	Per patient	FASS
Follow-up treatment, thawed cycle [a]	877	Per patient	FASS
Direct non-medical costs			
Transportation cost, RMC round trip	210	Per round-trip	Google Maps, Swedish Tax Agency
Indirect costs			
Production loss [b]	263	Per hour	Statistics Sweden, Ekonomifakta

[a] For more details on pharmaceuticals and cost calculations, see appendix 11.3.
[b] Social benefit costs of 42% (Ekonomifakta) was added to average wage (Statistics Sweden, 2013). 160 work hours per month was assumed.

The unit costs are presented in table 12. All costs found in another currency than Swedish Kronor or presented in a price level other than SEK 2013 were firstly converted through the applicable exchange rate and then adjusted to the 2013 price levels through CPI.

The direct health care unit costs were gathered from the official 2013 price list of the Southern Health Care Region, where prices include OH costs. As mentioned, it is not necessarily the case that official prices translate into actual costs, especially for publically funded health care units. However, since these are the only prices available and they are used within the universal health care system to debit other regions (when health care services are utilized across regions) we view them as accurate cost estimates.

The pharmaceutical unit costs were found at FASS (2013) while information on the indirect costs was collected from Statistics Sweden (2013) and the statistical platform website Ekonomifakta (2013). Transportation costs were calculated with help from distance searches at Google Maps and current reimbursement levels of the Swedish tax Agency.

5.1.1. Pharmaceuticals

Medical professionals at RMC identified the pharmaceuticals, and quantities, used throughout ART-treatment[11]. Unit costs were found after converting package costs retrieved from the private-public partnership FASS, the Swedish Medicines Information Engine. The hormone stimulation-doses vary with age, which makes the use of some pharmaceuticals age dependent[12]. See appendix table 22 for a more detailed description.

5.1.2. Direct medical costs

The direct costs of publically founded ART-treatment are related to medical visits at RMC. A small portion of these costs fall on the patients with out-of-pocket payments per visit (approximately SEK 200 per visit) while the majority is publically funded by the health care system (Vårdguiden, 2013). This cost division of medical visits will not be discussed further since it is the total societal cost per live birth that is of interest in this analysis.

5.1.3. Direct non-medical costs

For the couple to attend the medical appointment they have to take time off work and transport themselves to the visit, implying two types of costs accrued to the treated couple. Production loss will be further dealt with in the following section.

[11] Personal correspondence with Margareta Kitlinski
[12] Personal correspondence with Margareta Kitlinski

Transportation costs are, although non-medical, direct costs paid by the couple. To estimate the transportation costs per RMC visit, geographical distance, population distribution in the Southern Health Care Region and governmental travel refunding levels were considered. The distance from Malmö to the largest city in each county was established using Google Maps and works as a proxy for the average distance for that county's inhabitants. In Skåne County the second largest city Helsingborg used to calculate average distances for the Skåne population. This was done since Malmö, hosting the RMC clinic, would generate a distance of zero kilometers for all enrolled Skåne couples, which was held as unlikely. The geographical distribution of couples seeking ART-treatment was assumed to follow the population distribution between the counties in the Southern Health Care Region, as no details regarding actual residence was available. Using the weighted county-population, an average distance of 104km to the RMC clinic was found.

To specify the cost per travel distance (km) the couple was assumed to drive, and share, a car. As an estimation of the average travel cost per distance (km), the amount deductible per commute-kilometer in the income declaration according to the Swedish Tax Agency was adopted; SEK 18.50 per 10km (Skatteverket, 2013). This brought a lower average cost than with travel by public transportation and was thus applies in our calculations in order to preclude overestimation of the transportation costs. The transportation costs were found to be SEK 210 per couple and visit, i.e. the cost per round-trip.

The transportation cost was only included in the treatment costs when the medical visit is located at RMC. Some physician visits per full ART-treatment-cycle can be placed in the local primary care (such as the pregnancy test), in case of which the transportation cost was assumed to be negligible and therefore set to zero.

5.1.4. Production loss

When the couple takes time off work to attend treatment visits, there is an indirect loss both to the couple themselves and to their employer. The couple looses income and the employer looses the production the employee would have produced if remaining at work. A generally accepted method to calculate production loss in health economic evaluations is the human capital (HC) approach. The HC approach is recommended for economic evaluations by Swedish authorities and is thus the natural methodological choice of this analysis (LFN, 2003). The HC approach estimates the monetary value time to equal the cost of an employee to an employer. Wages and other costs, such as pension fees, are included (Boardman et al., 2011; Drummond et al., 2005).

It is assumed that both the man and the woman in a couple undergoing ART-treatment take the same amount of time off work, as RMC stretches the importance of the treatment being a shared effort and thus the couple is assumed to be equally dedicated to the treatment (RMC, 2012:II). The man is therefore assumed to accompany the woman to the egg aspiration appointment and so on. Therefore the hourly production loss is held gender neutral.

In agreement with the recommendation by Drummond et al. (2005) the general wage rate for both men and women was used. The average monthly income from work in Sweden 2012 was adjusted to 2013 numbers using CPI. The adjusted average monthly income was SEK 29 805 (Statistics Sweden, 2013). Assuming 160 work hours per month, the average hourly wage rate in 2013 was SEK 186. In addition, payroll taxes of 42 percent were added including an average of pension fees for different types of employees (Ekonomifakta, 2013). These calculations generated an hourly cost of an employee of SEK 263, which was then set equivalent to the production loss according to the HC approach.

Production loss occurs at every medical visit, both for the actual visit and for the traveling time to and from the clinic. The RMC visits were assumed to take one hour on average and a one-hour travel to and from the appointment was assumed (2h round trip). Adding up that makes three-hours per RMC visit and person, generating a six-hour production loss per RMC visit and couple. For visits to a local primary care center a one-hour visit was again assumed but the traveling distance, and therefore also the traveling time, was viewed as negligible and set to zero.

5.2. Resource use

In order to convey the resource consumption in ART-treatment a list of resource use is presented in the table below. The indicated quantity consumed of each resource refers to a full (completed) cycle. As previously stated there are several points in a treatment cycle where disturbance can occur forcing discontinuation of treatment. This has not been taken into consideration in table 13 below. For a more detailed example of the calculations of an average cycle cost including discontinuation probabilities, see appendix table 30.

Table 13. Resource use in a full ART-treatment cycle

Resource	Units used, full cycle		
	C1	C2&C3 (fresh)	C2&C3 (thawed)
Physician examination including ultrasound	1	0	0
Initial blood work	1	0	0
Andrological examination (M)	1	0	0
Sperm sample	2	0	0
Sperm analysis	2	0	0
Physician consultation	1	1	1
Nurse consultation	1	0	0
Nurse visit	2	2	1
Estradiol blood test	1	1	0
Ultrasound (HyCoSy)	1,925	1,925	0
IVF	0,43	0,43	1
ICSI	0,57	0,57	1
Thawed embryo transfer	0	0	1
Pregnancy test	1	1	1
Ultrasound visit (physician)	1	1	1
Nafarelin	0,6	0,6	0
Hormone stimulation [f]	1	1	0,4
Ganirelix	0,4	0,4	0
Chorionic gonadotrophin alpha	1	1	0
Pharmaceutical use at egg retrieval	1	1	0
Transportation to RMC, round trip	8,925	5,925	3
Patient production loss, hours	60,55	54,55	22

5.3. Cost of medical screening

As the proposed change in the subsidized ART-treatment program contains a medical screening in order to determine whether a female aged 35-42 qualifies for state-funded treatment it is of interest to determine the cost of said screening process.

The Medical Screening Program would cover treatment steps 1 through 6 as presented in the protocol overview in table 11. The cost of a medical screening thus follows the cycle up to the point of the ultrasound where the ovarian growth is examined and the responsiveness to treatment is determined. When calculating the costs of medical screening only the patient groups >35 were considered, as they are the ones affected by the proposed program change. The cost of medical screening, regardless if the women qualifies for further treatment or not, is SEK 40 070.

Table 14. Cost of medical screening

Female age	Age neutral costs				Hormone stimulation	Total
	Direct medical costs	Pharmaceuticals	Transportation cost	Production loss		
<35	20 386	1 472	1 050	9 211	4 344	36 463
>35	20 386	1 472	1 050	9 211	7 951	40 070

5.4. Cycle variations

The Southern Health Care Region provides a maximum of three fresh ART-treatment cycles. Thawed cycles are offered if there are frozen embryos available from a previous cycle. In the age-dependent treatment cost calculations all treatment outcomes and costs are weighed after treatment type – fresh IVF, fresh ICSI and thawed IVF or ICSI – and their respective success rates. Calculations are also adjusted for long or short protocol costs.

Additionally, the corresponding cycle costs for each treatment step may vary between the first, second and third cycle. The main reason being the availability of thawed cycles but also because there is less need for informative meetings with medical professionals when the treatment is repeated. These variations are included in the treatment cost calculations.

All age-related variations – success rates, cycle type and protocol continuation – result in an age-dependent variation in cost per live birth. The success rates affect how many treatments are required to attain a live birth, the cycle type determines the cost of said cycle and the protocol continuation determines how far along into the protocol the treatment is interrupted (discontinued). All of these factors are included in the treatment costs.

It is noteworthy that the age-related cost difference may not be as straightforward as one might initially think. The fact that younger patients have higher success rates is not the only aspect influencing the cost per live birth. Older patients have higher discontinuation rate for each treatment step, and thus face a lower cost per started treatment cycle, counteracting the fact that younger patients have higher success rates. For example, a woman aged 34 has a higher chance of having a successful treatment than a woman of 40, but she also has a higher probability of getting relatively far in the treatment protocol without actually reaching a live birth, whereas the older woman has a higher risk of early treatment discontinuation which is a less costly treatment attempt.

5.5. Calculating cost per live birth

When calculating the cost per live birth following ART-treatment there are two sides to consider; the treatment cost and the number of live births.

As we are interested of the total treatment cost of each couple the cost per each specific cycle type was calculated, weighted and summed. The first cycle was assumed to be a fresh cycle, as thawed cycles require a frozen embryo from previous cycles. In the first cycle the age-specific allocation between the IVF and the ICSI method and their respective success rates and discontinuation rates were implemented and the corresponding costs were weighted accordingly. The same method was used in calculating the cost of cycle two and three, although with the inclusion of thawed cycles. In cycle two and three the fresh cycles were made less costly than in cycle one, as consultative medical visits and sperm sample analysis were viewed as redundant.

Further, an average of 2.39 cycles per couple was employed according to the findings of a study of ART-treatment at Sahlgrenska University hospital (Olivius et al., 2002). Other previous studies have found the average number of treatment cycles in the 2 to 3 range (Witsenburg et al., 2005; Malizia et al., 2013; Mol et al., 2000; Stewart et al., 2011; Elizur et al., 2006), verifying the validity of the 2,39 estimate. Consequently the weighted cost of the first cycle was then summed with 1.39 times the weighted cost of cycle two and three.

Additionally, costs of the medical screenings for patients who disqualify for further treatment in the Medical Screening Program are incorporated in the program specific cost per live birth.

5.6. Exclusions

This analysis does not include costs of delivery (child birth), nor does it explore the possible increase in health care utilization of children conceived through ART-treatment (Ericson et al., 2002). This implies an assumption of children conceived through ART-treatment not being overrepresented in hospital utilization, i.e. not being more costly, than naturally conceived children after the conception itself.

These exclusions are verified by the objective of ART-treatment to cure infertility. Thus the costs occurring after a child is conceived is irrelevant for the purpose of this thesis.

6. RESULTS

6.1. Base case analysis

The described calculation methods generated the results presented in tables 15 and 16 below. The results contain calculations based on both the RMC and the Q-IVF data set discussed in section 4. The results corresponding to each data set is presented separately.

As previously stated there is an overall societal trend to have children later in life (Statistics Sweden, 2012:I). The fact that more couples wish to reproduce at an older age implies a high demand for ART-treatment even in ages well above 35. This assumption is supported by the extrapolated demand that shows rather consistent levels of demand throughout the age groups (table 9). However, it is also well-known that fertility decreases with age, especially for women (de la Rochebrochard, 2001; Suchartwatnachai et al., 2000; SBU, 2012; SMER, 2013). Hence, when introducing the Medical Screening Program, we expect the qualification rate to be negatively correlated with age. This expectation is also confirmed in the results, showing a declining medical screening qualification rate with age (Ferraretti et al., 2011). This trend is universal in our analysis.

For the same reason as we expected the medical screening qualification rate to fall with age it is logical to assume that the cumulative success rate is negatively related to age. The declining success rate with age that can be observed for both data sets supports this assumption. Remember, however, that the original RMC data lacked satisfactory observations for females aged 39-42 and therefore the success rates for these age groups were extracted from the Q-IVF data set. This mixture of data in the RMC case somewhat confuses the age- success rate relation, as Q-IVF generally has higher success rates.

Table 15. Base case results using RMC data

Female age	Treatment demand (couples) [a]		Cumulative success rate		Expected live births		Cost per live birth	
	Unrestricted demand	Qualified in MS program	Strict age limit (<39)	MS program [b]	Strict age limit (<39)	MS program [b]	Strict age limit (<39)	MS program [b]
<35	509	509	0,47	0,47	239	239	280 739	280 739
35	53	47	0,45	0,54	24	25	309 934	265 167
36	58	50	0,33	0,40	19	20	404 326	357 745
37	53	45	0,30	0,35	16	16	455 846	415 115
38	56	48	0,31	0,38	17	18	445 432	373 550
39	53	45	-	0,41	-	19	-	331 153
40	51	40	-	0,41	-	16	-	351 117
41	50	39	-	0,41	-	16	-	351 117
42	49	37	-	0,21	-	8	-	678 754
Total	931	860	0,43 [c]	0,45 [c]	315	377	308 270	310 514

[a] Demand was observed at RMC in the time period Jan 2011- June 2012 for female patients aged <39, for 39-42 the presented demand is extrapolated. To attain the yearly ART-treatment demand for SHCR the observed demand was divided by 1,5.
[b] As the RMC's supply of treatment is age-restricted to females <39 the RMC data set only contained reliable success rates for the females up to 38 years of age. The success rates for females 39-42 are extracted from Q-IVF.
[c] Total success rates refer to a weighted population average.

Table 16. Base case results using Q-IVF data

Female age	Treatment demand (couples) [a]		Cumulative success rate		Expected live births		Cost per live birth	
	Unrestricted demand	Qualified in MS program	Strict age limit (<39)	MS program	Strict age limit (<39)	MS program	Strict age limit (<39)	MS program
<35	509	509	0,60	0,60	304	304	217 368	217 368
35	53	47	0,51	0,53	27	25	261 166	261 814
36	58	50	0,51	0,53	29	26	256 216	264 804
37	53	45	0,51	0,53	27	24	258 178	264 804
38	56	48	0,39	0,41	22	20	328 111	331 152
39	53	45	-	0,41	-	19	-	331 152
40	51	40	-	0,41	-	16	-	351 118
41	50	39	-	0,41	-	16	-	351 118
42	49	37	-	0,21	-	8	-	678 754
Total	931	860	0,56 [b]	0,53 [b]	409	457	231 646	251 704

[a] Demand was observed at RMC in the time period Jan 2011- June 2012 for female patients aged <39, for 39-42 the presented demand is extrapolated. To attain the yearly ART-treatment demand for SHCR the observed demand was divided by 1,5.
[b] Total success rates refer to a weighted population average.

Introducing the Medical Screening Program translates into excluding patients with unsatisfactory response to hormone stimulation, from further treatment. These patients' biological prerequisites are suboptimal for reproduction to be probable, even with the assistance of ART-treatment. Hence we expect the success rates to be higher, per age group (>35), for patients in the qualified sample than for patients in the Strict Age Limit Program where little attention is paid to individual biological and medical suitability. These expectations are confirmed in the data but does not eliminate the negative correlation between age and success rate, but rather increases each age groups internal success rate. The improved success rates are valid for both data sets.

Female patients of age 42 show a significantly lower success rate than the other patient groups. The success rate diversion affects the weighted success rate on a population level for the Medical Screening Program. In spite of this, and because of the lower proportion of patients who qualify for treatment in the older age groups, the Medical Screening Program shows a higher population success rate for the RMC data set. For the Q-IVF data set, however, the Medical Screening Program brings a too small improvement in success rate per age group to compensate for the inclusion of older patients and the population success rate is thus lower with the Medical Screening Program than with the Strict Age Limit Program.

Additionally, the tables clearly states that the Medical Screening Program is superior to the Strict Age Limit Program regarding live births generated. This is a natural effect as the Medical Screening Program allows for a larger number of treatments, an increase from 729[13] to 860 for both data sets, and has a similar, if not higher, population success rate.

So far the results are equivalent, or very similar, for the two data sets. Regarding cost per live birth, however, there are some differences worth noting. Firstly, the RMC data set analysis testifies that introducing the Medical Screening Program would increase the average cost per live birth with nearly SEK 3 000 (308 000-311 000) in comparison to the Strict Age Limit Program. The corresponding number for the Q-IVF data set is SEK 20 000 (232 000 – 252 000). An increased number of live births thus seem to correspond to a higher cost per live birth. The data sets both state that argument even though the results differ in magnitude. These results are expected as the couples with the highest probability of reproducing (i.e. younger women with a higher medical suitability in general) are already allowed treatment before introducing the Medical Screening Program.

To combine the effects of costs and benefits of introducing the Medical Screening Program, the results are preferably presented as ICER values. Remember from section 3.3. that the ICER value presents the change in cost in relation to the change in effect. Thus, the ICER value demonstrating the effects of a switch from the Strict Age Limit Program to the Medical Screening Program, is defined as;

$$ICER = \frac{Costs_{MS} - Costs_{Age\_limit}}{Effects_{MS} - Effects_{Age\_limit}}$$

And the corresponding ICER values for the RMC and Q-IVF data sets, respectively, are;

$$ICER_{RMC} = \frac{310\ 514 - 308\ 270}{377 - 315} = 36$$

$$ICER_{Q-IVF} = \frac{251\ 704 - 231\ 646}{457 - 409} = 420^{14}$$

[13] The sum of unrestricted ART-treatment demand for women <39: 509+53+58+53+56=729

As stated both analyses show a rise in cost per live birth and a significant increase in number of live births. The increase in the number of live births is 20% (377/315) and 12% (457/409) for the data sets respectively The interpretation of the $ICER_{RMC}$ 36 per additional live birth is such that the average cost per live birth increases with SEK 36 for each additional child brought to life by the new program. The resulting ICER from applying the Q-IVF data set generates a positive value with magnitude 420, confirming a cost increase per live birth.

As an increase in the number of live births a the constant aim with ART-treatment, while one wishes to keep costs down, the full interpretation of these results will depend on what monetary threshold is held cost-effective. Nevertheless, ICER values of 36 or 420 state that each additional live birth increases the average cost per live birth. But the rise is arguably negligible, especially considering the price tag per live birth.

6.2. Cost effects accrued to the Southern Health Care Region

Above the main results of this thesis, the Medical Screening Program's effect on cost per live birth, were presented while the following section regards the cost effect of the Medical Screening Program on the health care region. These subresults are of interest for regional decision makers when considering the Medical Screening Program. As our target population is the inhabitants of the Southern Health Care Region and the evaluated treatment program is that of RMC Malmö, these results are primarily of use to decision makers of that particular region.

In an attempt to depict the costs of the Southern Health Care Region, societal costs such as production loss and transportation costs are excluded.

Table 17. Costs to the Southern Health Care Region using the RMC data set

Female age	Strict age limit (<39)					MS program				
	Per live birth			Expected live births	Cumulative cost	Per live birth			Expected live births	Cumulative cost
	Hospital costs	Pharma-ceuticals	Total			Hospital costs	Pharma-ceuticals	Total		
<35	182 111	26 285	208 396	239	49 860 840	182 111	26 285	208 396	239	49 860 840
35	191 768	42 046	233 814	24	5 494 886	158 396	39 393	197 789	25	5 008 551
36	248 556	55 705	304 260	19	5 885 859	209 774	55 410	265 184	20	5 227 373
37	280 565	62 814	343 379	16	5 442 664	243 899	64 191	308 090	16	4 831 004
38	273 651	61 529	335 180	17	5 744 062	219 010	57 923	276 932	18	5 099 720
39						190 206	52 047	242 253	19	4 525 026
40						193 838	60 084	253 922	16	4 087 896
41						193 838	60 084	253 922	16	3 981 717
42						372 361	88 223	460 583	8	3 582 897
Total	196 842	33 021	229 863	315	72 428 311	191 662	37 225	228 886	377	86 205 024

[14] The resulting ICER-values refer to exact calculations

As stated by table 17 and 18, the RMC data set reveals an additional cost to the Southern Health Care Region of SEK 13 776 713 for the 62 additional live births as a result from implementing the Medical Screening Program, i.e. SEK 222 205 per live birth[15]. The corresponding numbers using the Q-IVF data set are a cost increase of SEK 14 663 166, 48 additional live births and a cost increase of SEK 305 483 per live birth[16]. Out of the total costs of implementing the Medical Screening Program, the medical screening of females aged 35-42 correspond to SEK 8 602 892 in both data sets (not shown in tables).

Table 18. Costs to the Southern Health Care Region using the Q-IVF data set

Female age	Strict age limit (<39)					MS program				
	Per live birth			Expected live births	Cumulative cost	Per live birth			Expected live births	Cumulative cost
	Hospital costs	Pharmaceuticals	Total			Hospital costs	Pharmaceuticals	Total		
<35	138 277	20 918	159 195	304	48 435 180	138 277	20 918	159 195	304	48 435 180
35	167 227	35 878	203 105	27	5 429 269	162 156	39 468	201 625	25	4 963 743
36	154 545	35 751	190 296	29	5 602 001	162 123	40 990	203 113	26	5 321 123
37	155 547	36 218	191 765	27	5 126 134	162 176	40 990	203 166	24	4 833 074
38	196 708	46 606	243 314	22	5 354 245	190 890	52 047	242 937	20	4 825 010
39						190 933	52 047	242 980	19	4 538 616
40						194 681	60 084	254 765	16	4 101 478
41						194 704	60 084	254 788	16	3 995 299
42						374 106	88 223	462 329	8	3 596 473
Total	145 482	25 344	170 954	409	69 946 829	156 941	30 608	185 160	457	84 609 995

In the base case analysis, the total cost of the Strict Age Limit Program added up to SEK 97 105 050 using the RMC data set and 94 743 214 using the Q-IVF, while the Medical Screening Program cost summed to SEK 117 063 778 and SEK 115 028 728, for the RMC and Q-IVF data sets respectively[17]. When focusing solely on costs that fall on the Southern Health Care Region the same costs are numbers are SEK 72 428 311 and SEK 69 946 829 under the Strict Age Limit Program and SEK 86 205 024 and SEK 84 609 995 under the Medical Screening Program, using the RMC and Q-IVF data sets respectively. In other words, the costs of the Southern Health Care Region correspond to approximately 74%[18] of the societal cost of ART-treatment. The remaining 26% fall on the patients in the form of lost income and transportation costs, and their employers in lost production due to sick leave.

If we assume that all couples who seek ART-treatment will do so irrespective of what program is in use, it is the pure hospital costs that are of interest. This assumption states that the demand for ART-treatment is constant irrespective but the allocations

---

[15] 86 205 024 - 72 428 311; 377 - 315; (86 205 024 - 72 428 311) / (377-315)
[16] 84 609 995 - 69 946 829; 457 - 409; (84 609 995 - 69 946 829) / (457-409)
[17] 308 270*315=97 105 050; 310 514*377=117 063 778; 231646*409=94 743 214; 251704*457=115 028 728 (see tables 15 and 16)
[18] 72 428 311/97 105 050=0.746 ; 69 946 829/94 743 214=0.738 ; 86 205 024/117 063 778=0.736 ; 84 609 995/115 028 728=0.736

between private and public clinics will vary between the programs (i.e. couples will demand the same level of ART-treatment whether it is reimbursed or not). The hospital costs then represent the additional cost that will fall under the subsidy and be reimbursed by the region, if the Medical Screening Program is introduced. The pure hospital costs equal the additional costs of the Medical Screening Program because hormone stimulation drugs fall under the high-cost threshold [19], and is hence ascribed the Southern Health Care Region for all ART-treatment patients, irrespective of clinic type. Consequently, the only cost for the Southern Health Care Region that can be fully controlled through the choice of subsidy program is hospital costs.

Table 17 and 18 translate into an increase of hospital costs by SEK 10 251 344 and SEK 12 219 899 when introducing the Medical Screening Program, for the RMC and Q-IVF data respectively[20]. These results correspond to a cost increase per live birth of SEK 165 344 for the RMC data, and SEK 254 581 for the Q-IVF[21].

6.3. Sensitivity analysis

To deal with possible inconsistency in our base case results we have conducted a sensitivity analysis by varying the uncertain variables and assumptions; demand for ART-treatment, medical screening qualification rate and success rate. These variables have significant influence in our evaluation of the new proposal from RMC. We applied a variation of +/- 30% to assess the effect on the base case results.

The demand for treatment and the medical screening qualification rate are uncertain parameters as they depend on non-observed data; extrapolation and non-Swedish data. The success rate for RMC includes uncertainty due to a small number of observations, especially in the older age groups, while the national Q-IVF register is inconsistent with our target population. The same goes for what types of cycles are included in success rate calculations. The Q-IVF includes private reproductive clinics that accept a wider range of patients than do publically funded treatment centers and the nationwide coverage hides regional variations in treatment supply. These variables are included in the first part of the sensitivity analysis, the results of which are shown in table 19.

The outcome of the sensitivity analysis varies somewhat between the data sets. While the effect on the RMC results is sparse, the Q-IVF results show large variation around the base case results.

When applying the RMC data set the sensitivity analysis show expected results. Varying the demand for treatment downwards is in favor of the Medical Screening

[19] The high-cost threshold refers to the system where a medicine is subsidized, and the state pays a portion of the costs.
[20] (191 662*377)-(196 842*315)=10 251 344; (156941*457)-(145 482*409)=12 219 899
[21] 10 251 344/62=165 344; 12 219 899/48=254 581

Program and brings a dominant ICER of -203 (found in Q4 in the ICER plane in figure 1) while an upward variation show very little affect (ICER 72). This is not surprising as a lower demand means fewer disqualified patients and thus fewer unsatisfactory hormone stimulations to fund. Varying the qualification rate, however, show the opposite results and are more in favor of Medical Screening Program with an upward variation of 30%. This implies that a more generous qualification rate would benefit the Medical Screening Program, which in turn speaks in favor of the older patient population. Additionally a decrease in success rate generates a poorer result while an increase has the opposite effect, both of which are expected. In sum higher success rates, lower treatment demand combined with a more generous age limit improves the objective of the Medical Screening Program. The results on the ICER-value vary from -203 to 541 and are still fairly small.

Table 19. Sensitivity analysis

Data	Variables	-30 %	Base case	+30 %
DEMAND, NUMBER OF PATIENTS				
RMC	C1	304 143	310 514	315 629
	E1	335	377	418
	C2	308 270	308 270	308 270
	E2	315	315	315
	ICER	**- 203**	**36**	**72**
Q-IVF	C1	244 082	251 704	257 938
	E1	411	457	503
	C2	231 646	231 646	231 646
	E2	409	409	409
	ICER	**6 259**	**420**	**281**
MS QUALIFICTION RATE				
RMC	C1	319 267	310 514	306 257
	E1	335	377	403
	C2	308 270	308 270	308 270
	E2	315	315	315
	ICER	**541**	**36**	**-23**
Q-IVF	C1	256 420	251 704	249 822
	E1	411	457	486
	C2	231 646	231 646	231 646
	E2	409	409	409
	ICER	**12 470**	**420**	**236**
SUCCESS RATE				
RMC	C1	343 496	310 514	286 062
	E1	340	377	409
	C2	308 270	308 270	308 270
	E2	315	315	315
	ICER	**1388**	**36**	**-237**
Q-IVF	C1	275 418	251 704	234 118
	E1	418	457	491
	C2	231 646	231 646	231 646
	E2	409	409	409
	ICER	**5177**	**420**	**30**

Note that only variables for woman aged 35-43 is varied in this sensitivity analysis

Considering the Q-IVF data set, however, the variations in the sensitivity analysis have greater impact on the results. Varying all factors (demand, qualification rate and success rate) upwards move the results in favor of the Medical Screening Program as it decreases the ICER value. A downward regulation of the same has the opposite effect. The results of varying the demand differ somewhat from those of the RMC sensitivity analysis, but this is expected. Even though a decreased demand implies fewer unsatisfactory medical screenings greater results, as previously argued, that mainly affects the cost structure of the treatment, which is not the only factor in an ICER. For the Q-IVF data set the effect side of the analysis seem to be more effected, which is expected as it has higher live birth rates initially, while the effects of demand on the cost side is more affected for the RMC data that also show the higher cost structure of the two. The sensitivity analysis regarding qualification rate have higher effects on the Q-IVF data but they move in the same direction as for the RMC and, again, the effect the success ratevariation is self-explanatory.

Still, the ICER for the Q-IVF data shows a higher variation around the base case outcome (SEK 30 – 12 470 and SEK -237 – 1 388 respectively). However, it is noteworthy that when new treatments, with improved treatment effect, are implemented with an ICER below SEK 100 000 it is viewed as a low cost per QALY or a life year (Socialstyrelsen, 2008). One might argue that a live birth cannot be valued in QALY-terms or life years gained, but the ICER of a live birth, using Q-IVF data set, are still comparatively low.

It is also important to note that varying the medical screening qualification rate upward by 30% it implies that all patients in all age groups will qualify, which is highly unlikely and makes the proposed program redundant.

Table 20. Sensitivity analysis using RMC data excluding thawed cycles

Female age	Treatment demand (couples) [a]		Incremental success rate		Expected live births		Cost per live birth	
	Unrestricted demand	Qualified in MS program	Strict age limit (<39)	MS program [b]	Strict age limit (<39)	MS program [b]	Strict age limit (<39)	MS program [b]
<35	509	509	0,47	0,47	239	239	280 739	280 739
35	53	47	0,45	0,59	24	28	309 934	242 775
36	58	50	0,33	0,46	19	23	404 326	304 943
37	53	45	0,30	0,40	16	18	455 846	359 368
38	56	48	0,31	0,41	17	20	445 432	346 804
39	53	45	-	0,43	-	19	-	317 394
40	51	40	-	0,41	-	16	-	347 513
41	50	39	-	0,41	-	16	-	347 513
42	49	37	-	0,17	-	6	-	831 690
Total	931	860	0,43 [c]	0,45 [c]	315	386	308 270	303 024

[a] Demand was observed at RMC in the time period Jan 2011- June 2012 for female patients aged <39, for 39-42 the presented demand is extrapolated. To attain the yearly ART-treatment demand for SHCR the observed demand was divided by 1,5.
[b] As the RMC's supply of treatment is age-restricted to females <39 the RMC data set only contained reliable success rates for the females up to 38 years of age. The success rates for females 39-42 are extracted from Q-IVF.
[c] Total success rates refer to a weighted population average.

In the tables 20 and 21, the type of cycles included when estimating the success rates for the Medical Screening Program are varied. In the base case fresh cycles that reached egg aspiration as well as all thawed cycles were included. It is thereby assumed that all thawed cycles are given to patients who would qualify for treatment in the Medical Screening Program. This assumption states that none of the patients disqualified in the screening process would later end up in the thawed-cycle data and thus not affect its success rate. However, there is no indication in the data stating whether the ratio of patients in the thawed cycle data would qualify in the Medical Screening Program. Therefore, the alternative assumption would be to exclude all thawed cycles when estimating the age-dependent success rate. Both assumptions are extremes, and draw the result in opposite directions, with the base case inclusion being the more restrictive one. Thus the effect of which assumption is used in the analysis is of interest.

Table 21. Sensitivity analysis using Q-IVF data excluding thawed cycles

Female age	Treatment demand (couples) [a]		Incremental success rate		Expected live births		Cost per live birth	
	Unrestricted demand	Qualified in MS program	Strict age limit (<39)	MS program	Strict age limit (<39)	MS program	Strict age limit (<39)	MS program
<35	509	509	0,60	0,60	304	304	217 368	217 368
35	53	47	0,51	0,54	27	25	261 166	253 078
36	58	50	0,51	0,54	29	27	256 216	255 969
37	53	45	0,51	0,54	27	25	258 178	255 969
38	56	48	0,39	0,43	22	21	328 111	317 634
39	53	45	-	0,43	-	19	-	317 634
40	51	40	-	0,41	-	16	-	347 448
41	50	39	-	0,41	-	16	-	347 448
42	49	37	-	0,17	-	6	-	835 595
Total	931	860	0,56 [b]	0,53 [b]	409	460	231 646	250 013

[a] Demand was observed at RMC in the time period Jan 2011- June 2012 for female patients aged <39, for 39-42 the presented demand is extrapolated. To attain the yearly ART-treatment demand for SHCR the observed demand was divided by 1,5.
[b] Total success rates refer to a weighted population average.

Tables 20 and 21 present the full effects of excluding thawed ART-cycles in the success rate estimation but the concluding effect is better explained by the ICER-values presented below. Remember that the ICERs were 36 and 420 in the base case for the RMC and Q-IVF data set respectively.

$$ICER_{RMC} = \frac{303\,024 - 308\,270}{386 - 315} = -74$$

$$ICER_{Q-IVF} = \frac{250\,013 - 231\,646}{460 - 409} = 360$$

The RMC data generates a negative ICER-value when excluding thawed cycles from the success rate estimate and the Medical Screening Program is thus, by definition, a dominant alternative (found in Q4 in the ICER plane in figure 1). Excluding thawed cycles from the success rate decrease the ICER-value for the Q-IVF as well, but the value remains positive but decreases to 360. Although excluding thawed cycles undeniably benefits the Medical Screening Program, the success rates hold similar levels and the ICER-effect is arguably marginal.

In sum, the sensitivity analysis moves the results in expected directions and the overall effect seems negligible. Since the Medical Screening Program is often more expensive while it always results in more live births than the Strict Age Limit Program the result remain open to interpretation for both data sets. However, the RMC data set show more promising results in regards of the Medical Screening Program than the Q-IVF data, and that the results are even dominant at times.

7. DISCUSSION

ART-treatment is already publically supplied and the question is thus not whether to supply treatment but rather to whom it should be supplied. The age limit for the proposed Medical Screening Program was set in agreement with clinical experts at RMC[22]. The age limit was set at <43 as it is equivalent to the highest age limits in the nation today (Barnlängtan, 2011), and because it is rare for patients >42 to receive treatment even at private clinics. The age limit is further supported by previous research stating that reproduction is possible for females well over 40 if they have the right biological qualities (Broekmans et al, 2004; Haebe et al., 2002). The objective of the proposed treatment regimen was to deter from the age fixation and rather focus on medical suitability, hence it is preferable to keep the age limit generous to better isolate the effect on cost-effectiveness of the medical screening from that of the chosen age limit.

As shown in the results, 42-year-olds have a significantly lower success rate than younger women. These lagging success rate brings about vast cost differences per live birth for 42-year-olds compared to all other age groups included in our analysis. One reason for the low success rates is that they are retrieved from Q-IVF, where the success rates are presented in age groups and where the oldest group includes all 42+ women (Q-IVF, 2013). Even though the >42 women included in the age group probably have a negative effect on the success rate of 42-year-olds, the Q-IVF is the only available source of Swedish data for this age category and there is thus no reliable alternative. Nevertheless, international studies have shown higher comparable cumulative success rates for 42-year-olds (Witsenburg et al., 2005), indicating that the cost per live birth may be overestimated in our results.

Both data sets show promising results for the Medical Screening Program, especially considering its effects on the number of live births, but incorporate different absolute numbers. The cost per live birth with the Strict Age Limit Program is 33% higher based on the RMC data compared to the Q-IVF (SEK 308 000 / SEK 232 000), and show significantly fewer expected live births in the target population of the Southern Health Care Region (315 compared to 409). When introducing the Medical Screening Program the corresponding numbers are a 23% higher cost per live birth with the RMC data (SEK 311 000 / SEK 252 000), and 80 fewer live births (377-457). These substantial differences bring about the question of what results to focus on. The RMC data set deals with the specific target population of the thesis. Furthermore, the more costly ART-treatment, with the RMC data, make those results more conservative, and underestimation of social costs per live birth are thus less likely. Therefore, the RMC results are most trustworthy, at least when considering the Southern Health Care Region. Nationwide interpretation, however, should rather be based on the Q-IVF data as it includes its target population. In other words, what result is more important depends on the chosen perspective.

[22] Personal correspondence with Aleksander Giwercman and Margareta Kitlinski

Even though introducing the Medical Screening Program show promising implications, the most cost-effective treatment program would be to combine a medical screening with the current age limit. It would reduce costs for medical screenings leading to disqualification, as fewer individuals would be screened compared to the Medical Screening Program. It would also raise the success rate per treatment compared to the current program, as the unsuitable treatment candidates would be disqualified. The number of live births, however, would either decrease or remain constant depending on if all patients with potential to achieve live birth would qualify for treatment in the screening process. Combined it would result in a lower ICER and further reduce the cost per live birth.

Nonetheless, introducing the Medical Screening Program for the suggested age group show relatively low variation in the ICER-values. This is the result of the decreased cost in the age group 35-38 as some patients are disqualified from treatment being met by the cost increase from allowing treatment for medically suitable women aged 39-42. In a sense, the Medical Screening Program holds the ICER-value constant while increasing live births. The purpose of implementing the Medical Screening Program is to allocate health care resources towards patients where it has the greatest effect. Treating more patients independent of age and reallocate resources to improve probability to reproduce will reduce the relative cost of a live birth even though the absolute costs might rise.

As this thesis compares different allocations of ART-treatment with the common target outcome being live births, the CEA methodology is a natural choice. Previous studies have pointed out that infertility/childlessness can have significant effect on quality of life and that HRQoL measures therefore could be beneficial to evaluate. For example, one can argue that a child will contribute to an increased number of societal QALYs (Svensson et al., 2008), or that miscarriages can lead to reduced mental health for the prospective parents (van Balen et al., 2008; Hujit et al., 2011). Further, a resent Danish study suggests that involuntarily childless couples suffer a greater risk of dying in early age (Agerbo et al., 2012). However, this thesis evaluates a proposed change in ART-treatment and despite the side effects of infertility its main goal is to treat childlessness. The exclusion of HRQoL estimates is therefore legitimate, as implementing the Medical Screening Program will evidently increase the number of live births, implying a decrease in negative side effects of infertility. Therefore an inclusion of HRQoL measures would be redundant in this study.

We have also avoided any monetary evaluations of live births. Partly due to the hardship in evaluating a life in monetary terms and partly as the value of a live birth, in the perspective of this thesis, refers to the benefit of the child’s parents. It is clear, however, that a child born also has a value to the welfare state, for example due to the effect on taxation revenues. At the same time there is a risk with conducting willingness-to-pay (WTP) studies or time-trade-off (TTO) studies among couples that receive ART-treatment as they might over-value a child compared to the overall population. When considering a live birth to primarily be the cure of infertility, such monetary valuations are redundant.

What is of utter importance, however, is the economic burden on couples treated for infertility. According to the WHO 16,96%[23] of total health care expenditures in Sweden were paid out-of-pocket in 2011 (WHO statistics, 2013), but a majority of fertility treatments are performed at private clinics (Socialstyrelsen, 2013) and 32% of costs are funded through out-of-pocket payment (Svensson et al., 2008). In other words, almost twice as much of the total expenses for fertility treatment are paid out-of-pocket compared to overall health care. Since infertility is defined as a disease by the WHO (WHO, 2013), and treated as such in the Swedish system, the high economic burden on fertility patients is hard to legitimize. With the Medical Screening Program, more couples would receive subsidized treatment and the divergence from the general ratio of publically funded treatment would decrease.

The disproportionate private funding of treatment implies an excess demand for ART. This conclusion is further supported by the interest organization Barnlängtan (Child Longing) that primarily works to induce more generous national treatment guidelines. The fact that there are private treatment alternatives for couples with monetary resources causes political problems. The universal health care system in Sweden was designed to provide equal health care to all (Diskrimineringsombudsmannen, 2012; SFS 2010:243). However, ART-treatment is expensive and not all couples denied subsidized treatment could find private financing. International studies have shown that income rates affect the utilization of ART (Ordovensky Staniee et al., 2007; Connolly et al., 2010) and that more treatments are pursued when financial aid is provided (Connolly et al., 2010). Consequently, the current access to fertility treatment depends on socioeconomic status, which calls for improvement of the current system.

Furthermore, the unmet demand for ART-treatment creates a market for private actors. Our societal perspective leads us to the question whether private or public health care supplies the most cost-effective treatment, regardless of who pays the bill. An international meta-analysis concluded that public health care providers are on average more cost-effective, primarily due to economics of scale such as regional procurement (Dahlgren, 2010; Hollingsworth, 2008). On the same note an Australian study showed that private clinics lacked in cost-effectiveness in small clinics while the relationship was reversed for large entities (Austrailian government, 2009). Reproductive clinics are generally fairly small, thus private clinics are likely to be less cost-effective compared to public clinics. This support an implementation of the Medical Screening Program as the new treatment regimen would reallocate couples from private to

[23] Private expenditure on health represented 19.1% of total expenditure on health in 2011, out of which 88.8% were out-of-pocket expenditures. Thus, 16,96% (19,1*0,888=16,96) of total expenditure on health was paid out of pocket.

public clinics. Although, the mere existence of competition to the public monopolistic market can be assumed to increase cost-effectiveness, which speaks against the Medical Screening Program based on the same reallocation argument (Svenskt Näringsliv, 2010). But it is unreasonable to expect the Medical Screening Program to eliminate all demand for private reproductive clinics. For example, couples that already have a mutual child will still be denied publically funded treatment. Thus we conclude that public clinics are preferable in a societal perspective, which further supports the introduction of the Medical Screening Program.

Although ART-treatment can be of great help for infertile couples, both positive and negative side effects have been found. When evaluating the effects of the development of ART-treatment on fertility Rainer et al. (2011) found that improvements in ART have a directly positive effect on fertility rates. However, they also found that the increased fertility rates could cause indirect changes in behavior, potentially counteracting the positive ART-effects. Such behavioral changes include women who would otherwise have tried to have children to postpone childbirth to later in life when the success rate of conceiving is lower, despite ART-treatments (Rainer et al, 2011). National statistics show that the average age of both women and men having their first child has increased rapidly in Sweden during the last 40 years (Statistics Sweden, 2012:I). If ART is reliable alternative it may induce this trend as it supplies a type of reproductive insurance. It is important to remember, however, that although ART-treatments constantly improve and show good success rates, there is no guarantee of a successful outcome. It is still a fact that the success rate of ART-treatments, as well as natural fertility, decline with age. This argumentation speaks against implementing the Medical Screening Program.

An additional aspect of the increase in parental age is the changing societal structures. Instead of the family being the center of most female lives, education and careers have become increasingly important. Today, more than half the student population at university level is female (Högskoleverket, 2012). Simultaneously, the norm of what is expected of a young woman in terms of reproduction also shifts. We consider it likely to be the norm shift that has the larger influence on the average maternal age at first births than the availability of ART. However, one cannot deny that a too extensive safety net may induce a behavior that, counterproductively, increases the problem of infertility and thus the demand for treatment by more couples waiting to reproduce late in life (Rainer et al., 2011). One solution could be to promote a wider knowledge of the age-dependence of fertility to deter young people from waiting to long to reproduce (Mac Dougall et al, 2013). If the age-dependence of fertility was more acknowledged individuals might make more favorable decisions regarding reproduction and, if so, treatment would be allocated towards those of non self-induced needs.

Previous studies have also suggested a positive correlation between maternal education and ART-treatments utilization. The results show that ART treatments increase along with educational level (Socialstyrelsen, 2013). Additionally, Lundberg et al (2012) has shown a positive relationship between children's skills and health status and maternal education. These results combined imply a higher value of a child conceived through ART than for an average child. Therefore it is not unreasonable to assume a high societal WTP for ART-treatments due to women seeking treatment being disproportionally well educated. At the same time this finding implies that our use of average wage rates to estimate production loss for the women receiving ART-treatment, and their spouses, are underestimated resulting in too low treatment cost results. However, there is no socioeconomic data included in any of the data sets and any conclusion on the subject therefore requires further investigations.

Moreover, it is of vital importance for western countries to find paths to promote reproduction (Conolly et al., 2010). The current demographic trend of the developed world should welcome any boost to fertility rates (Statistics Sweden, 2012:I). The negative economic consequences for countries with low levels of reproduction are evident and there is a great need for any investment that increases, or even stabilizes, fertility rates (Rainer et al., 2011; Ds 2013:8).

Presently, over 3% of children born in Sweden are the product of ART, a number that is likely to increase if the trend continues. Thereby, ART-treatment may contribute with a considerable number of future taxpayers with spillover effects for generations to come (Conolly et al., 2010). Preserving an adequate number of taxpayers in relation to the total population is an ongoing struggle in developed countries, not the least in order to solve impending pensions system difficulties (Ds 2013:8). To that background Svensson et al. (2008) evaluated the effects of ART-treatment on the Swedish nation. The net present value (NPV) of an IVF-child was estimating by the prognostic economic interaction between the child and the Swedish government over a lifetime. The study estimated a positive NPV for IVF-treatment and assessed a break-even point at age 41 (Svensson et al., 2008). Thus making public funding of fertility treatment a sound investment if the child lives at least 41 years, making the profitability of ART undeniable in this perspective.

Even though this thesis argues that ART-treatment should be promoted it is noteworthy that there are other available solutions to childlessness, such as adoption, surrogacy and foster care. However, surrogacy is not yet legal in Sweden forcing couples to seek such treatment abroad, which in turn complicates monitoring health care quality and the potential exploration of the surrogate mother (SMER, 2013). Adoption is available through Swedish agencies, but getting approved involves an extensive and exhausting process. According to Swedish guidelines the recommended maximum age is 42 years old for both parents (SOSFS 2008:8), which further validating the age limit of the Medical Screening Program as both solutions results in prospective parenthood. Today the cost of adopting is completely born by the prospective parents, causing a negative incentive to adopt compared to pursuing subsidized ART-treatment. Foster care is a risky solution to childlessness as the child's biological parents retain legal rights to the child if they can prove themselves able. However, foster parents receive governmental aid to care for the child, which causes a different structure of incentives than ART-treatment and adoption. Regardless, the most important difference between ART-treatment and adoption or foster parenting is that they do not result in a biological child. Therefore, and because surrogacy is still illegal in Sweden, there are no perfect substitutes to ART-treatment to reproductively challenged couples even though the suggested alternatives in fact cures childlessness.

Finally, the recent report from the Swedish National Council on Medical Ethics proposed an introduction of a medical assessment as the basis of qualification for ART-treatment, and argued its ethical superiority to a fixed age limit (SMER, 2013). However, the Swedish National Council on Medical Ethics refrained to present details regarding how the medical assessment should be constructed. The Medical Screening Program brought to light in this thesis was partly inspired by the Swedish National Council on Medical Ethics report. Thus, one of the objectives of this thesis was to complement the Swedish National Council on Medical Ethics report and draw the attention of decision makers to the inadequacy of the current ART-treatment program.

8. CONCLUSION

Introducing the Medical Screening Program results in more performed treatments, higher success rate and more live births relative to the current Strict Age Limit Program. At the same time the proposed program would increase the cost per live birth. However, the cost increase with the Medical Screening Program may be motivated as Medical Screening Program generates more live births and the monetary differences per live birth are fairly small. What is clear, however, is that the Medical Screening Program will generate a higher total cost of publically funded ART-treatments.

The majority, around three fourths, of the societal cost of publically funded ART-treatment is paid by the universal health care system (i.e. the county council) while the remaining fourth fall on the patients and their employers.

There are some indications that increased availability of publically funded ART-treatment induces counterproductive behavior. However, the greater effect on when in life people chooses to reproduce is likely related to shifting social norms. It is essential for western countries to promote fertility rate, due to the economic implications of an aging population.

In sum, the proposed Medical Screening Program show promising potential for cost-effectiveness from a societal perspective.

9. FURTHER RESEARCH

The largest shortcoming of this thesis is the lack of a reliable data set that covers the target region and includes all relevant age groups. A longer monitoring period, where patients were followed from their first visit to the end of all available treatment cycles, would also be preferable. Moreover, the optimal data set would reveal follicle count prior to egg aspiration so that qualification rates could be determined. The limited data sets used in this thesis thus calls for further research within the area, in order to retrieve results closer to the real outcomes of implementing the Medical Screening Program.

If a program shift is executed, close monitoring is of essence for future reliable evaluation. If the program shift shows suboptimal results, evaluations of additional program propositions should be conducted.

10. REFERENCES

Agerbo E, Mortensen PB, Munk-Olsen T (2012), *Childlessness, parental mortality and psychiatric illness: a natural experiment based on in vitro fertility treatment and adoption,* Journal of Epidemiology and Community Health Vol. 67, No. 4, pp. 374-376

Austrailian government (2009), *Public and Private Hospitals*, Productivity Commission Research Report, Available at; <http://www.pc.gov.au/projects/study/hospitals/report> [Accessed at: 2013-09-24]

Barnlängtan (2011), *Health care on unequal terms - County council rules for the treatment of infertility*, Available at: <http://www.barnlangtan.com/images/stories/PDF_filer/barnlangtan-landstingen2011.pdf> [Accessed at: 2013-09-24]

Barnlängtan (2013), *Child Longing*, <http://www.barnlangtan.com/> [Accessed at: 2013-03-14]

Boardman AE (2011), *Cost-benefit analysis: concepts and practice*, 4. ed., Upper Saddle River, N.J.: Prentice Hal

Bouwmans CA, Lintsen BM, Eijkemans MJ, Habbema JD, Braat DD, Hakkaart L (2008), *A detailed cost analysis of in vitro fertilization and intracytoplasmic sperm injection treatment,* Fertility and Sterility, Vol. 89, No. 2, pp. 331-341.

Broekmans FJ, Klinkert ER (2004), *Female Age in ART: When to Stop?*, Gynecologic and Obstetric Investigation, Vol. 58, No. 4, pp. 225–234.

Connolly MP, Pollard MS, Hoorens S, Kaplan BR, Oskowitz SP, Silber SJ (2008), *Long-term Economic Benefits Attributed to IVF-conceived Children: A Lifetime Tax Calculation*, American Journal of Managed Care, Vol. 14, No. 9, pp. 598-604.

Connolly MP, Ledger W, Postma MJ (2010), *Economics of assisted reproduction: Access to fertility treatments and valuing live births in economic terms*, Human Fertility, Vol 13, No. 1, pp. 13–18.

Dahlgren G (2010), *Health care on equal terms - driving forces and counter forces (Sv.)*, Socialmedicinsk tidskrift, Vol 87, Nr 1, pp. 5-48.

De la Rochebrochard E (2001), *Sterility, Fecundity: What about the Men?*, Population et Sociétés No. 371, Paris

Diskrimineringsombudsmannen, DO (2012), *The right to health care on equal terms*, Available at: <http://www.do.se/Documents/rapporter/Rätten%20till%20sjukvård%20på%20lika%20 villkor.pdp> [Accessed at: 2013-09-24]

Drummond M (2005), *Methods for the economic evaluation of health care programmes*, 3., [updated and rev.] ed., Oxford: Oxford University Press

Ds 2013:8, *Future welfare and population aging (Sv.)*, Stockholm: Framtidskommisionen, Available at: <http://www.regeringen.se/content/1/c6/21/04/91/ef26b14d.pdf> [Accessed at: 2013-09-24]

Ekonomifakta (2013), *Social Security Charges (Sv.)*, Available at: <http://www.ekonomifakta.se/sv/Fakta/Arbetsmarknad/Arbetsgivaravgift/Sociala-avgifter/> [Accessed at: 2013-09-19]

Elizur SE, Lerner-Geva L, Levron J, Shulman A, Bider D, Dor J (2006), *Cumulative live birth rate following in vitro fertilization: study of 5,310 cycles,* Gynecological Endocrinology, Vol. 22, No. 1, pp. 25–30.

Ericson A, Nygren KG, Olausson PO, Källén B (2002), *Hospital care utilization of infants born after IVF*, Human Reproduction, Vol. 17, No. 4, pp. 929-932.

Evers S, Goossens M, de Vet H, van Tulder M, Ament A (2005), *Criteria list for assessment of methodological quality of economic evaluations: Consensus on health economic criteria*. International Journal of Technology Assessment in Health Care, Vol. 21, No. 2, pp. 240-245.

FASS (2013), *Pharmaceutical facts*, Available at: <www.fass.se> [Accessed at: 2013-09-14]

Ferraretti AP, La Marca A, Fauser BC, Tarlatzis B, Nargund G, Gianaroli L; ESHRE working group on Poor Ovarian Response Definition (2011), *ESHRE consensus on the definition of 'poor response' to ovarian stimulation for in vitro fertilization: the Bologna criteria*, Human Reproduction, Vol. 26, No. 7, pp. 1616-1624.

Ferraretti AP, Goossens V, de Mouzon J, Bhattacharya S, Castilla JA, Korsak V, Kupka M, Nygren KG, Nyboe Andersen A; European IVF-monitoring (EIM); Consortium for European Society of Human Reproduction and Embryology (ESHRE) (2012) *Assisted reproductive technology in Europe, 2008: results generated from European registers by ESHRE*, Human Reproduction, Vol. 27, No. 9, pp. 2571–2584.

Garceau L, Henderson J, Davis LJ, Petrou S, Henderson LR, McVeigh E, Barlow DH, Davidson LL (2002), *Economic implications of assisted reproductive techniques: a systematic review,* Human Reproduction, Vol.17, No.12, pp. 3090-3109.

Granberg M, Wikland M, Nilsson L, Hamberger L (1995), *Couples' willingness to pay for IVF/ET*, Acta Obstetricia et Gynecologica Scandinavia, Vol. 74, No. 3, pp. 199-202.

Granberg M (2004), *Economic aspects of infertility treatment,* Intellecte DocuSys AB, Västra Frölunda

Griffiths A, Dyer SM, Lord SJ, Pardy C, Fraser IS, Eckermann S (2010), *A cost-effectiveness analysis of in-vitro fertilization by maternal age and number of treatment attempts*, Human reproduction, Vol. 25, No. 4, pp. 924-931.

Haebe J, Martin J, Tekepety F, Tummon I, Shepherd K (2002), *Success of intrauterine insemination in women aged 40–42 years*, Fertility and Sterility, Vol. 78, No. 1, pp. 29–33.

Hirshfeld-Cytron J, Grobman WA, Milad MP (2012), *Fertility preservation for social indications: a cost-based decision analysis,* Fertility and Sterility, Vol. 97, No. 3, pp. 665-670.

Hollingsworth B (2008), *The measurement of efficiency and productivity of health care delivery*, Health Economics, Vol. 17, No. 10, pp. 1107-1128.

Hujit T, Kraaykamp G, Subramanian SV (2011), *Childlessness and Psychological Well-Being in Context: A Multilevel Study on 24 European Countries*, European Sociological Review, Vol. 29, No. 1, pp.32–47.

Högskoleverket (2012), *University and college - Higher Education Authority yearly report 2012 (Sv.)*, Available at: <http://www.hsv.se/download/18.8b3a8c 21372be32ace80003121/1210R-universitet-hogskolor-arsrapport.pdf> [Accessed at: 2013-09-25]

Kenny DT, (1994) *The Impact of Maternal Age on Clinical Pregnancy and Spontaneous Abortion in Women Undergoing In Vitro Fertilization and Gamete Intra-Fallopian Transfer*, Australian and New Zeeland journal of Obstetrics and Gynaecology, Vol. 34, No. 4, pp. 443-448.

Kjellberg AT, Carlsson P, Bergh C (2006), *Randomized single versus double embryo transfer: obstetric and paediatric outcome and a cost effectiveness analysis*, Human Reproduction, Vol.21, No.1, pp. 210–216.

LFN (2003), *General guidelines for economic evaluations from the Pharmaceutical Benefits Board (LFNAR 2003:2) (Sv.),* Available at: <http://www.tlv.se/Upload/ Lagar_och_foreskrifter/LAG-lfnar-2003-2.pdf> [Accessed at: 2013-08-15]

Lundberg P, Nilsson A, Rooth DO (2012) *Parental education and offspring outcome: evidence from Swedish compulsory schooling reform,* IZA Discussion Papers 6570.

Mac Dougall K, Beyene Y, Nachtigall RD (2013), *Age shock: misperceptions of the impact of age on fertility before and after IVF in women who conceived after age 40*, Human Reproduction, Vol.28, No.2, pp. 350–356.

Malizia BA, Dodge LE, Penzias AS, Hacker MR (2013), *The cumulative probability of liveborn multiples after in vitro fertilization: a cohort study of more than 10,000 women*, Fertility and Sterility, Vol. 99, No. 2, pp. 236–243.

McDonald P, (2006) *Low Fertility and the State: The Efficacy of Policy,* Population and Development Review 32, pp. 485-510.

McQuillan J, Greil A, Shreffler K, Wonch-Hill P, Gentzler K, Hatcoat J (2012) *Does the Reason Matter? Variations in Childlessness Concerns Among U.S. Women*, Journal of Marriage and Family, Vol. 74, pp.1166 – 1181.

Mol BW, Bonsel GJ, Collins JA, Wiegerinck MA, van der Veen F, Bossuyt PM (2000), *Cost-effectiveness of in vitro fertilization and embryo transfer,* Fertility and Sterility, Vol. 73, No. 4, pp. 748 –754.

Morris S, Devlin N, Parkin D (2012), *Economic analysis in health care,* 2. ed., Chichester, John Wiley & Sons

Neumann PJ, Gharib SD, Weinstein MC (1994), *The cost of a successful delivery with in vitro fertilization*, New England Journal of Medicine, Vol. 331, No. 4, pp. 239-243.

Neumann PJ, Johannesson M (1994) *The willingness to pay for in vitro fertilization: a pilot study using contingent valuation*, Medical Care, Vol. 32, No. 7, pp. 686–699.

NICE – National Institute for Health and Clinical Excellence (2008), *Guide to the methods of technology appraisal*, London: National Institute for Health and Clinical Excellence (NICE)

Olivius C, Fridén B, Lundin K, Bergh C (2002), *Cumulative probability of live birth after three in vitro fertilization/intracytoplasmic sperm injection cycles*, Fertility and Sterility, Vol. 77, No. 3, pp. 505-510.

Olivius C (2009), *Cumulative Live Birth Rates after In Vitro Fertilization*, Department of Obstetrics and Gynaecology Institute of Clinical Sciences Sahlgrenska Academy, University of Gothenburg, Sweden

Ordovensky Staniec JF, Webb NJ (2007), *Utilization of infertility services: how much does money matter?*, Health services research, Vol. 42, No. 3p1, pp. 971-989.

Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R, Woolacoot N, Glanville J (2004), *Review of guidelines for good practice in decision-analytic modelling in health technology assessment*, Health Technology Assessments, Vol. 8, No. 36, pp. 1-158.

Piette C, de Mouzon J, Bachelot A, Spira A (1990), *In-vitro fertilization: influence on women's age on pregnancy rates*, Human Reproduction, Vol. 5, No. 1, pp. 56-59.

Q-IVF – The national quality register of fertility treatments (2013), *Open comparisons 2010*, Available at: <http://www.ucr.uu.se/qivf/index.php/behandlingsresultat> [Accessed at: 2013-07-01]

Rainer H, Selvaretnama G, Ulpha D (2011), *Assisted Reproductive Technologies (ART) in a Model of Fertility Choice*, Journal of Population Economics, Vol. 24, No. 3, pp. 1101-1132.

Rice, D.P., & Cooper, B.S. (1967). The economic value of human life. *American Journal of Public Health*, 57, 1954–1966.

RiR 2004:9, *Guidelines for prioritization in Health Care*, Stockholm: The Swedish National Audit Office, Available at: <http://www.riksrevisionen.se/ PageFiles/560/RiR_2004_9.pdf> [Accessed at: 2013-07-10]

RMC – Reproductive Medical Center (2012:I), *Patient information – IVF-treatment (Sv.)*, Available at: <http://www.skane.se/Public/SUS_extern/Verksamheter/ RMC/Dokument/Patientinfo%20IVF%20dec%202012.pdf> [Accessed at: 2013-09-19]

RMC – Reproductive Medical Center (2012:II), *IVF-school*, Available at: <http://www.skane.se/sv/Webbplatser/Skanes-universitetssjukhus/Organisation-A-O/Reproduktionsmedicinskt-centrum/For-patienter/SjukdomarFakta/IVF-enheten/IVF-skolan/> [Accessed at: 2013-08-01]

RMC – Reproductive Medical Center (2013), *Reproductive Medical Center*, Available at: <http://www.skane.se/sus/rmc> [Accessed at: 2013-07-04]

Ryan, M (1998) *Valuing psychological factors in the provision of assisted reproductive techniques using the economic instrument of willingness to pay*, Journal of Economic Psychology, Vol. 19, Issue 2, pp. 179–204.

SBU (2012), *Is the possibility of a successful IVF treatment reduced with increasing age or increasing BMI?*, Available at: <http://www.sbu.se/sv/Publicerat/ Upplysningstjanst/IVF-BMI-alder/> [Accessed at: 2013-07-09]

SBU (2013), *Evaluations of methods in health care. A handbook (Sv.)*, Version 2013-05-16, Available at: <http://www.sbu.se/upload/ebm/metodbok/SBUsHandbok.pdf> [Accessed at: 2013-08-16]

SFS 2006:351, *The Genetic Integrity Act*, Stockholm: The National Board of Health and Welfare

SFS 2010:243, *Health and Health Care Law*, Stockholm: The National Board of Health and Welfare

SHCR pricelist (2013), *Regional rates and allowances South Health Care Region*, Available at: <http://www.skane.se/Upload/Webbplatser/Sodra%20 regionvardsnamnden/prislista/2013/ helaprislistan2013.pdf> [Accessed at: 2013-08-20]

Simon JL (1975), *The welfare effect of an additional child cannot be stated simply and unequivocally,* Demography, Vol. 12, No. 1, pp. 89-105.

Skatteverket (2013), *Deductions - Travel to and from work (Sv.),* Available at: <http://www.skatteverket.se/privat/svarpavanligafragor/avdrag/privatarbetsresorfaq/jagkorbiltillmittarbetevilketavdragkanjagfa.5.10010ec103545f243e80001517.html> [Accessed at: 2013-07-26]

SKL (2012), *Assisted reproduction – mapping and Council offers (Sv.),* Version 2.

SMER (2013), *Assisted reproduction – ethical aspects. Summary of a report*, The Swedish national council on medical ethics (SMER) Available at: <http://www.smer.se/wp-content/uploads/2013/03/Slutversion-sammanfattning-eng-Assisted-reproduction.pdf> [Accessed at: 2013-07-04]

Socialstyrelsen (2008), *National guidelines for cardiac care (Sv.),* Available at: <http://www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/8592/2008-102-7_20081027_bilaga_8.pdf> [Accessed at: 2013-09-08]

Socialstyrelsen (2013), *Pregnancys, childbirth and newly born children (Sv.),* Available at: <http://www.socialstyrelsen.se/publikationer2013/2013-3-27> [Accessed at: 2013-08-16]

SOSFS 2008:8, The National Board of Health and Welfare's guidelines on social welfare casework about adoption (Sv.), Available at: <http://www.socialstyrelsen.se/sosfs/2008-8> [Accessed at: 2013-08-22]

SoU26 (2011/12), *Assisted reproduction (Sv.),* Social Committee, Swedish Parliament, Available at: <http://www.riksdagen.se/sv/Dokument-Lagar/Utskottens-dokument/Betankanden/201112Assisterad-befruktning-_GZ01SoU26/> [Accessed at: 2013-07-04]

Statistics Sweden (2009), *Having children or not? Results from a questionnaire survey about women´s and men´s attitudes towards having children*, <http://www.scb.se/Pages/PublishingCalendarViewInfo____259923.aspx?PublObjId =11740> [Accessed at: 2013-02-26]

Statistics Sweden (2012:I), *Decreased childbearing (Sv.)*, Available at: <http://www.scb.se/Pages/Article____333981.aspx> [Accessed : 2013-02-26]

Statistics Sweden (2012:II), *The future population of Sweden 2012–2060*, Available at: <http://www.scb.se/statistik/_publikationer/BE0401_2012I60_BR_ BE51BR1202ENG.pdf> [Accessed at: 2013-09-24]

Statistics Sweden (2013), *Average salary, SEK by region, sector, occupation, gender and time, 2012*, <http://www.scb.se/Pages/SSD/SSD_TablePresentation____ 340486.aspx?layout=tableViewLayout1&rxid=d19fcd22-fafa-4cc5-801a-b2b41c64afa4> [Accessed at 2013-07-08]

Stewart LM, Holman CD, Hart R, Finn J, Mai Q, Preen DB (2011), *How effective is in vitro fertilization, and how can it be improved?*, Fertility and Sterility, Vol. 95, No. 5, pp. 1677–1683.

Suchartwatnachai C, Wongkularb A, Srisombut C, Choktanasiri W, Chinsomboon S, Rojanasakul A (2000), *Cost.effectiveness of IVF in women 38 years and older*, International Journal of Gynecology and Obstetrics, Vol. 69, No. 2, pp. 143-148.

Svenskt Näringsliv (2010), *Private initiativ within Health care – Motivations, not counter forces*, Available at: <http://www.svensktnaringsliv.se/multimedia/archive/ 00023/Privata_initiativ_in_23980a.pdf> [Accessed at: 2013-09-24]

Svensson A, Connolly M, Gallo F, Hägglund L (2008), *Long term fiscal implications of subsidizing in vitro fertilization in Sweden: a lifetime tax perspective*, Scandinavian Journal of Public Health, Vol. 36, No. 8, pp. 841-849.

Templeton A, Morris JK, Parslow W (1996), *Factors that affect outcome of in-vitro fertilization treatment*, The Lancet Vol. 348, No. 9039, pp. 1402–1406.

van Balen F (2008), *Involuntary childlessness: a neglected problem in poor-resource areas,* Oxford University Press on behalf of the European Society of Human Reproduction and Embryology, Vol. 2008, No. 1, pp. 25-28.

Van Voorhis BJ, Stovall DW, Allen BD, Syrop CH (1998), *Cost-effective treatment of the infertile couple*, Fertility and Sterility, Vol.70, No.6, pp. 995-1005.

Vårdguiden (2013) *Patient fees in Skåne (Sv.)*, Available at: <http://translate.google.se/#sv/en/Patientavgifter%20i%20Sk%C3%A5n> [Accessed at: 2013-09-28]

WHO – World Health Organization (2011), *The International Statistical Classification of Diseases and Related Health Problems,* Available at: <http://www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/18172/2010-11-13.pdf> [Accessed at: 2013-07-16]

WHO – World Health Organization (2013), *Infertility definitions and terminology*, Available at: <http://www.who.int/reproductivehealth/topics/infertility/definitions/en/index.html> [Accessed at: 2013-09-26]

WHO statistics (2013), *Health financing: Health expenditure ratios by country*. Available at: <http://apps.who.int/gho/data/node.main.75?lang=en> [Accessed at: 2013-09-24]

Witsenburg C, Dieben S, Van der Westerlaken L, Verburg H, Naaktgeboren N (2005), *Cumulative live birth rates in cohorts of patients treated with in vitro fertilization or intracytoplasmic sperm injection*, Fertility and Sterility, Vol. 84, No. 1, pp. 99–107.

Wright VC, Chang J, Jeng G, Macaluso M (2005), *Assisted reproductive technology Surveillance – United* States, *2005,* MMWR Surveillance Summaries, Vol. 57, pp. 1-23.

Wølner-Hanssen P, Rydhstroem H (1998). *Cost-effectiveness analysis of in-vitro fertilization: estimated costs per successful pregnancy after transfer of one or two embryos,* Human Reproduction, Vol. 13, No. 1, pp. 88-94.

Reference for Tabel 1, *Treatment restrictions in each Health Care Regions*, page 9, Available at:
<http://www.akademiska.se/sv/Verksamheter/Reproduktionscentrum/Fertilitetsbevarande-atgarder/>
<http://www.akademiska.se/sv/Verksamheter/Reproduktionscentrum/Information-till-inremitterande-lakare/>
<http://www.karolinska.se/Verksamheternas/Kliniker--enheter/Kvinnokliniken/Fertilitetsenheten/Remisser/Regler-och-grundkrav/>
<http://www.lj.se/infopage.jsf?nodeId=32784&childId=6203>
<http://www.sahlgrenska.se/sv/SU/Omraden/1/Verksamhetsomraden/Gynekologi-och-reproduktionsmedicin/Enheter/Reproduktionsmedicin/Behandling/Provrorsbefruktning-IVF/>
<http://www.sahlgrenska.se/sv/SU/Omraden/1/Verksamhetsomraden/Gynekologi-och-reproduktionsmedicin/Enheter/Reproduktionsmedicin/Behandling/Assisterad-befruktning-/>
<http://www.skane.se/sv/Webbplatser/Skanes-universitetssjukhus/Organisation-A-O/Reproduktionsmedicinskt-centrum/For-patienter/SjukdomarFakta/IVF-enheten/Vem_erbjuds_IVF-behandling/>
<http://www.vll.se/default.aspx?id=28231&refid=28232&parid=28224>

<http://webbutik.skl.se/bilder/artiklar/pdf/7164-882-2.pdf?issuusl=ignore>
[All accessed at: 2013-05-23]

Interviews/Personal correspondence

Bungum, Mona
Laboratory Manager at The Reproductive Medical Center, Malmö

Giwercman, Aleksander
Professor of Reproductive Medicine at Lund University, Operations Manager at The Reproductive Medical Center, Malmö

Kitlingki, Margareta
Cheif Physician, Section Manager IVF at The Reproductive Medical Center, Malmö

11. APPENDIX

11.1. Age restriction of ART

Table 22. Age restrictions per county council

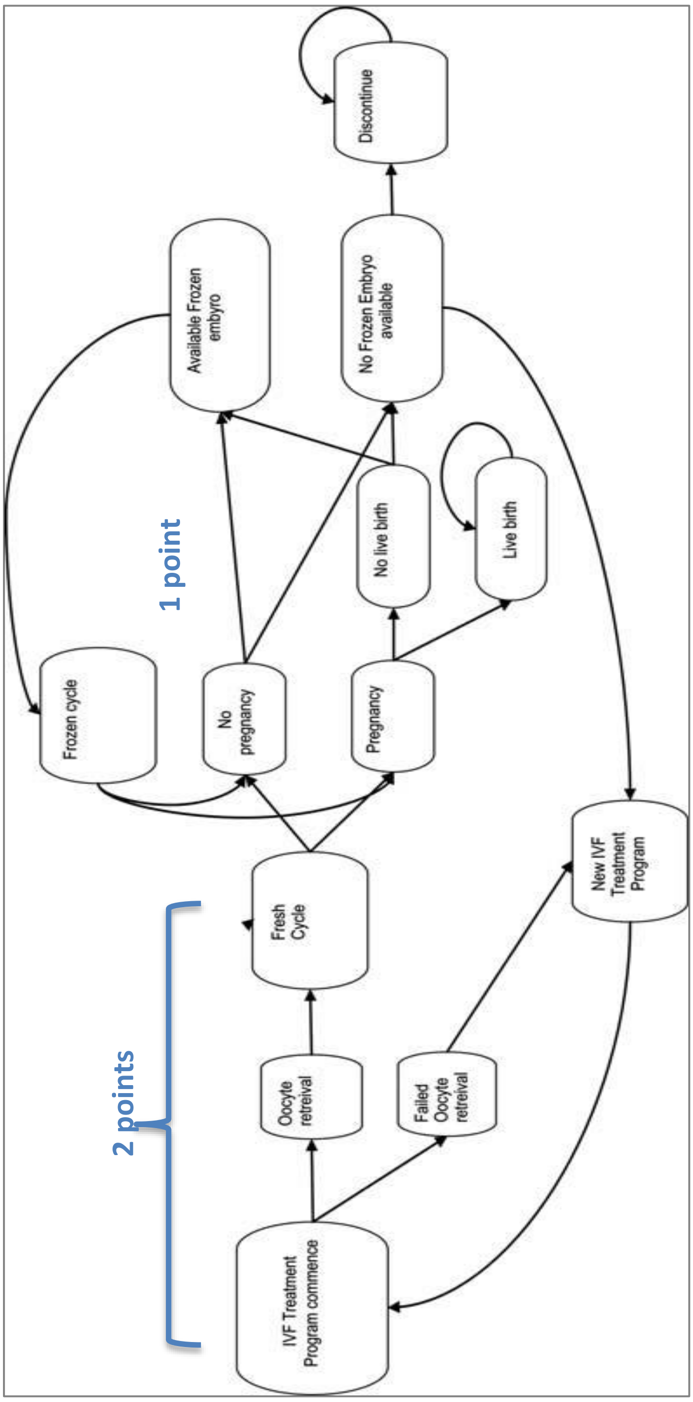
County Council	Evaluation		IVF		Egg donation	
	Women	Men	Women	Men	Women	Men
Skåne			39	55	39	55
Blekinge			39	55	39	55
Kronoberg	43	55	39	55	39	55
Halland [a]						
Götaland [a]						
Jönköping						
Kalmar			38	55	38	55
Stockholm	40	56	40	56	40	56
Gotland	41	55	40	55	40	55
Gävleborg			38	55	38	55
Dalarna	40	55	40	55	40	55
Sörmland	38	55	38	55	38	55
Östergötland	41	54	38	55	38	55
Värmland	43	55	40	55	40	55
Uppsala	40	55	40	55	40	55
Örebro	42	55	40	55	40	55
Västmanland	40	55	40	55	40	55
Uppsala	40	55	40	55	40	55
Norrbotten	40	56	37	55	37	55
Jämtland	40		37	55	37	55
Västerbotten	23-37	23-54	24-37	24-55	24-37	24-44
Västernorrland [a]						

Source: Barnlängtan (Child Longing) interest organization.
[a] Information about these county councils is absent because they are divided between different Health Care Regions. For example, the north part of Halland goes under the Western Region while the southern parts belong to the South Region.

11.2. Treatment schedule

Figure 2. ART-treatment cycle

Source: Griffiths et al. 2010 (A CEA of IVF by maternal age and number of treatment attempts



11.3. Cost calculations

Table 23. initial blood work

Type of test	Cost	Unit	Reference
FSH	30	per test	SHCR pricelist
LH	30	per test	SHCR pricelist
TSH	21	per test	SHCR pricelist
Infectious sample (HTLV) [a]	216	per test	SHCR pricelist
Rubella	97	per test	SHCR pricelist
Infectious sample [b]	216	per test	SHCR pricelist
Total	610	per patient	

[a] Only for female patients
[b] Only for male patients

Table 24. Pharmaceuticals

Drug therapy	Active substance	Pharmaceutical	Type	Concen-tration	Unit	Package size (number of units)	Package price	Price per unit	Weighted use, portion of patients	Average dose (if in use)	Average treatment days	Treatment cost
Down regulation	Nafarelin	Synarela	Nasal spray	200 µg/dose	Dose	60	1134,5	18,91	1	60		**1134,5**
Hormone stimulation[a]								2,83	1	Age-dep. [b]	11,7	
	Follitropin alfa	Gonal-f [c]	Injection fluid	900 IE / 1,5ml	IE	900	2662	2,96	0,25		11,7	
	Follitropin beta	Puregon	Injection fluid	900 IE / 1,08ml	IE	900	2662	2,96	0,25		11,7	
	Menotropin	Menopur	Powder and injection fluid	1200 IE	IE	1200	3534	2,95	0,25		11,7	
	Urofollitropin	Fastimon	Powder and injection fluid	150 IE	IE	1500	3673	2,45	0,25		11,7	
Antagonist	Ganirelix	Oraglutran	Injection fluid	0,25 mg/0,5 ml	mg	5	1521	304,20	1	6,5		**1977,3**
Ovulation trigger	Koriongonatropin alfa	Ovitrelle	Injection pen	250 µg	µg	1	342			1	1	**342**
At egg aspiration									1			**26**
	Paracetamol	Panodil	Tablet	1g	tablet	50	134	2,68	1	1		3
	Meklozin	Postafen	Tablet	25mg	tablet	100	85,5	0,855	1	1		1
	Fentanyl	Fentanyl B. Braun	Ampoule	50 µg /ml	ml	100	209	2,09	1	1,25		3
	Midazolam	Midazolam Actavis	Ampoule	1 mg/ml	ml	50	141	2,82	1	0,75		2
	Propofol	Propofol-®Lipuro	Injection fluid	10 mg/ml	ml	1000	1526	1,526	0,1	1,5		0
	Mevipakain	Carbocain ®	Injection fluid	10mg/ml	ml	100	171	1,71	1	10		17
Follow-up treatment	Progesteron	Crinone®	Vaginal gel	8%	dose	15	506	33,73	1			
Fresh cycles										1	15	506
Stimulated thawed cycles										2	13	877
Additional stim. thawed cycles if clin.preg.										2	49	2429

[a] The hormone stimulation drugs are assumes to be used in 25% of patients each, thus an average of SEK 2,83/IE was used in the treatment cost calculations
[b] See table 25 below
[c] New market price from October 1st 2013 according to TLV decision.

Table 25. Hormone stimulation

Age	Portion of patients	Dose (E/day)	Weighted dose	Cost per dose	Average treatment days		Treatment cost		
					LP [a]	SP [a]	LP [a]	SP [a]	Weighted
<35	0,66			2,83	12,5	10,5	4641	3898	4344
<31	0,33	112,5	37	2,83	12,5	10,5			
31-35	0,33	150	50	2,83	12,5	10,5			
>35	0,34	225	76	2,83	12,5	10,5	7952	6680	7443
Total	1		163	2,83	12,5	10,5			

[a] LP stands for long protocol and represents 60% of the patients irrespective of age, while SP stands for short protocol and represents the remaining 40% of patients.

Table 26. Consumer Price Index (CPI)

Year	CPI (yearly average)	CPI conversion into 2013 (SEK)
2000	260,7	1,203
2001	267,1	1,175
2002	272,8	1,150
2003	278,1	1,128
2004	279,2	1,124
2005	280,4	1,119
2006	284,22	1,104
2007	290,51	1,080
2008	300,61	1,044
2009	299,66	1,047
2010	303,46	1,034
2011	311,43	1,007
2012	314,2	0,998
2013*	313,722	1,000

*Average of the published CPI-indicatorscovering Jan-May 2013
Source:http://www.scb.se/Pages/TableAndChart____272151.aspx

Table 27. Average wage rates

	Monthly wage 2012	CPI conversion from 2012 to 2013	Monthly wage 2013	Work hours per month	Hourly wage, 2013
Men	32100	1,0015	32051	160	**200**
Women	27600	1,0015	27558	160	**172**
All	29800	1,0015	29755	160	**186**

Source: Wages were retrieved from Medlingsinstitutet (www.mi.se/lonestatistik/) and CPI information were retrieved from Statistics Sweden (http://www.scb.se/Pages/Product____33783.aspx)

Table 28. Social benefits

Benefit	Percentage of wage		
	Workers	Officials	Average*
Statutory payroll tax	31,42	31,42	31,42
Pension and insurance payments in agreement with labor unions	5,2	15	10,1
Total	36,62	46,42	**41,52**

*a 50/50 division between workers and officials is assumed
Source: All benefit information was retrieved from the statistics collector Ekonomifakta (www.ekonomifakta.se)

Table 29. Hourly production loss

	Hourly wage	Employee benefits (%)	Total hourly production loss
Men	200	41,52	**283**
Women	172	41,52	**244**
All	186	41,52	**263**

Table 30. Population and distances in SHCR

County	Population	Population weight	Largest city	Distance from largest town to RMC (km) [a]	Weighted distance (km)
Halland [b]	168 064	0,10	Halmstad	140	13
Kronoberg	185 695	0,11	Växjö	243	26
Blekinge	152 452	0,09	Karlskrona	207	18
Skåne	1 262 028	0,71	Helsingborg [c]	66,7	48
Total	1 768 239	1,00			57

[a] The distance from the largest town is used as a proxy for the average distance in the county
[b] Only the municipalities that belong to the Southern Health Care Region is included in the population
[c] Helsingborg is the second largest town in Skåne. Helsingborg is used because RMC is located in Malmö and an average distance for the whole Skåne population of zero kilometers would largely underestimate the true average distance in the county.
Source: Population information was retrieved from the Swedish Association of Local Authorities and Regions (www.skl.se). The distances from each region's largest city was retrieved from Google Maps (www.maps.google.com).

Table 31. Transportation costs

Weighted distance	57
Cost, SEK/km [a]	1,85
Transportation cost, one way	105
Transportation cost, per visit	210

[a] Amount reimbursed per km by the Swedish Tax Agency (www.skatteverket.se)

11.4. Example of treatment cost calculation

Table 32. Treatment cost calculations, <35, cycle 1, long protocol

Treatment step	Visit no	Visit Entity (RMC/PC /home)	Detailes and comments	Unit cost	Indirect costs			Treat. cost	Prev.	Total cost per cycle
					Transp. cost	**Hours off work**	**Prod. loss**			
Physician visit	1	RMC	Examination including ultrasound and blood tests (F)	3134	210	6	1579	4923	1	4923
			FSH	30				30	1	30
			LH	30				30	1	30
			TSH	21				21	1	21
			Infectious samples (HTLV, F)	216				216	1	216
			Rubella	97				97	1	97
			Andrological exam including blood test and (M)	4740				4740	1	4740
			Infectious samples (M)	216				216	1	216
	2		Sperm samples	1438	210	5	1316	2964	2	5928
			Sperm analysis	1700				1700	2	3400
Physician visit	3	RMC	Consultation	1714	210	8	2105	4029	1	4029
Nurse visit			Consultation and treatment information	1419				1419	1	1419
Down regulation		Home	Pharmaceutical. Supressing woman's normal fertility cycle	1135				1135	1	1135
Hormone stimulation		Home	Pharmaceuticals	4641				4641	1	4641
Nurse visit	4	PC		493		5	1316	1809	1	1809
			Blood test (F) - estradiol	36				36	1	36
Doctor visit	5	RMC	Ultrasound 1	2180	210	6	1579	3969	1	3969
Doctor visit	5.2	RMC	Ultrasound 2 - only in case of inadequate follicle maturity at ultrasound 1	2180	210	6	1579	3969	0,85	3374
Doctor visit	5.3	RMC	Ultrasound 3 - only in case of inadequate follicle maturity at ultrasound 2	2180	210	6	1579	3969	0,075	298
Cost of Medical screening										**40310**
		Home	Ovulation trigger	342				342	1	342
Egg aspiration	6	RMC	Pharmaceutical use at egg aspiration	26	210	16	4211	4446	0,975	4334
			Sperm sample	1438				1438	0,975	1402
			Sperm analysis	1700				1700	0,975	1657
ICSI or IVF			IVF	18252				18252	0,404	7380
			ICSI	23430				23430	0,596	13956
Embryo transfer	7	RMC			210	6	1579	1789	0,809	1448
Follow up treatment		Home	Hormone stimulation	506				506	0,809	410
Nurse visit	8	PC		493		2	526	1019	0,809	825
			Pregnancy test (hCG blood test)	45				45	0,809	36
	9	RMC	Ultrasound (if clinical pregnancy)	1420	210	6	1579	3209	0,295	946
Total protocol cost										**73047**