Cost-Effectiveness of replacing culture test by Xpert

MRSA screening test for patients at high risk of MRSA

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FOREWORD

As a Chinese student in an international Master program of Health Economics, Policy and Management, I was assigned internship at Oslo University Hospital, Ullevål in 2009. At that time, a project about rapid screening test for Methicillin-Resistant *Staphylococcus aureus* (MRSA) was about to be implemented. MRSA is a type of bacteria which has developed resistance to certain types of antibiotics. It has accounted for considerable proportions of nosocomial infections all over the world in the recent few decades. To combat this pathogen, one of the most effective strategies has been to screen high-risk patients accompanied with preemptive contact isolation. Among all techniques used to detect MRSA, the conventional culture test has been the most accurate one. The use of this test, however, means that it takes 24-48 hours to verify the presence of the organism. More recently, new screening techniques based on molecular biology have been developed and may allow the detection of MRSA within a couple of hours. Oslo University Hospital, Ullevål (Oslo, Norway) introduced a screening test in 2009 — Xpert MRSA. This screening method could reduce the verification time of the pathogen to approximately 75 minutes. Certainly, while the new screening tests may save use of hospital resources, speed up treatment for which the patient is admitted and increase patient satisfaction, it costs far more than the culture test. The question is therefore whether the additional costs of Xpert MRSA are reasonable in relation to the benefits. After six months of collecting cost and outcome data, through interviews, questionnaires and hospital information system, I tried to answer this question in the context of Oslo University Hospital, Ullevål.

I am grateful for all assistance I have received from Kim Ulvin, at Oslo University Hospital, Ullevål, and Henrietta Biboh, in the same internship program with me, during the data collection period.

My supervisor was Ivar Sønbø Kristiansen, MD PhD MPH, at The Department of Health Management and Health Economics, University of Oslo.

ABBREVIATIONS

BSI	Bloodstream Infection
CA-MRSA	Community-Associated Methicillin-Resistant *Staphylococcus aureus*
EAC	Equivalent Annual Cost
HADS	Hospital Anxiety and Depression Scale
HA-MRSA	Healthcare-Associated Methicillin-Resistant *Staphylococcus aureus*
HRQOL	Health-Related Quality of Life
MRSA	Methicillin-Resistant *Staphylococcus aureus*
MSSA	Methicillin-Sensitive *Staphylococcus aureus*
NOK	Norwegian kroner
PFGE	Pulsed-field gel electrophoresis
PVL	Panton-Valentine Leucocidine
QALD	Quality-Adjusted Life Day
QALY	Quality-Adjusted Life Year
QWB	The Quality of Well-Being index
SCC	Squamous cell carcinoma
SSI	Surgical Site Infection
US$	United States Dollar
VAT	Value Added Tax

ABSTRACT

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a type of bacteria that does not react to certain antibiotics and has become the major cause of nosocomial infections. Both the treatments and precautions of MRSA add to the burden of infections caused by *S. aureus*. To reduce the costs, Oslo University Hospital, Ullevål introduced the GeneXpert system to help accelerating the procedure of screening.

Objective: The aim of the study was to estimate the additional costs and outcomes of replacing the current used screening strategy with new strategies which involved the GeneXpert system in patients at high risk of MRSA.

Methods: We developed a decision model to represent the current strategy and two new strategies with the GeneXpert system, and measured costs and outcomes (length of preemptive isolation, number of unavailable room-hours, quality of life) for each of them.

Results: While the cost of the current strategy was NOK16,984, the results showed that the new strategies were much less costly than the current used one (NOK7,360 and NOK3,690). The new strategies reduced the length of preemptive isolation and the number of unavailable room-hours and improved patients' quality of life. The sensitivity analyses indicated that these results were not sensitive to reasonable changes in the model parameters.

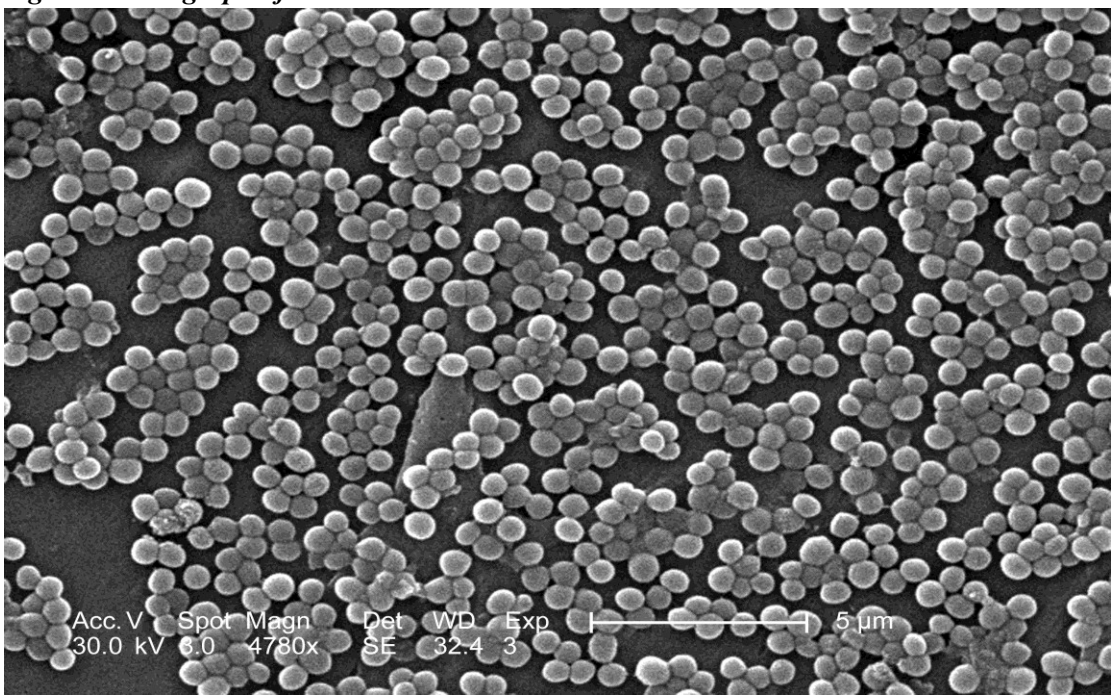
Conclusions: The new GeneXpert system represents a dominant strategy in that it reduces costs and improves outcomes under reasonable assumptions.

1. INTRODUCTION

As far as human history is recorded, infections have been a threat to human health. After the introduction of penicillin during last century, *Staphylococcus aureus* became spread in hospitals worldwide and replaced haemolytic streptococci as the major infecting organism. That started a long-term combat of antibiotic-resistant *Staph. atreus*.

1.1. Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Figure 1 SEM graph of MRSA



Source: Centers for Disease Control and Prevention, Public Health Image Library, USA

MRSA, abbreviation of Methicillin-resistant *Staphylococcus aureus*, appeared first in the 1960s soon after the introduction of new semi synthetic beta-lactamase-resistant penicillins such as methicillin and cloxacillin, which were developed to treat *Staph. aureus*. The multi-resistant nature of MRSA made the new generation of antibiotics lose their effectiveness far more quickly than imagined. As the time went by, the spread of MRSA withdrew for a while in the 1970s but soon came back dramatically in the 1980s.

During the recent decades, MRSA has become a major cause of nosocomial infection

throughout the world but not replaced more susceptible *Staph. aureus* as a pathogen (Lowy 1998). Consequently, MRSA infections represent an addition to the infections caused by methicillin-sensitive strains. Thus, a high incidence of MRSA adds to the overall burden of infections caused by *S. aureus* in hospitals (Herwaldt 1999).

MRSA could be classified in two categories – healthcare associated MRSA (HA-MRSA) and community associated MRSA (CA-MRSA). HA-MRSA strongly indicates previous contact with healthcare settings and long-term antibiotic use. CA-MRSA differs from HA-MRSA in risk factors, high-risk populations, SCC type, PFGE type, toxins, PVL, antibiotic resistance pattern and associated clinical syndromes (Safdar, et al. 2008). For a long time, HA-MRSA was the main concern on MRSA with rare exceptions. However, several studies have documented the increasing danger of CA-MRSA recently (Kazakova, et al. 2005) (Herold, et al. 1998) (Anonymous 2003) (Campbell, et al. 2004) (Anonymous 2006).

Infections with MRSA could start as small, red skin "bumps" that resemble pimples. Generally, the bacteria remain on the skin, but they can also cause potentially life-threatening infections in bones, joints, surgical wounds, the bloodstream, heart valves, and lungs (Itani 2008). Moreover, CA-MRSA, unlike HA-MRSA, can produce a type of toxin, which is capable of causing severe, often fatal skin infections (necrotizing fasciitis) and pneumonia. According to the report from the SENTRY Antimicrobial Surveillance Program from United States and Canada in 2000, MRSA is responsible for 30% of surgical site infections (SSIs) (Rennie, et al. 2003). Up to 30% of skin isolates from diabetic foot ulcers are confirmed as MRSA and lead to worse diabetic outcomes and longer hospital stay (Rogers, et al. 2008). Furthermore, diabetes is associated with persistent bacteremia in patients with MRSA, and MRSA bacteremia is associated with increased mortality compared with MSSA (methicillin sensitive *Stahpylococcus aureus*) bacteremia (Brunsvold, et al. 2008).

In order to explore the association between MRSA and outcome, some researchers performed a meta-analysis to compare mortality rates among patients with bloodstream infection (BSI) caused by MRSA and MSSA. Here, the odds for a fatal outcome are

consistently higher among patients with MRSA (odds ratio 1.56-2.20) and the association between MRSA and mortality persisted even when adjustments were made for severity of illness (Cosgrove, et al. 2003). Although with some doubts (Zahar, et al. 2005), other studies have also reported excess mortality with MRSA infections (Chang, et al. 2003) (Ridenour, et al. 2006).

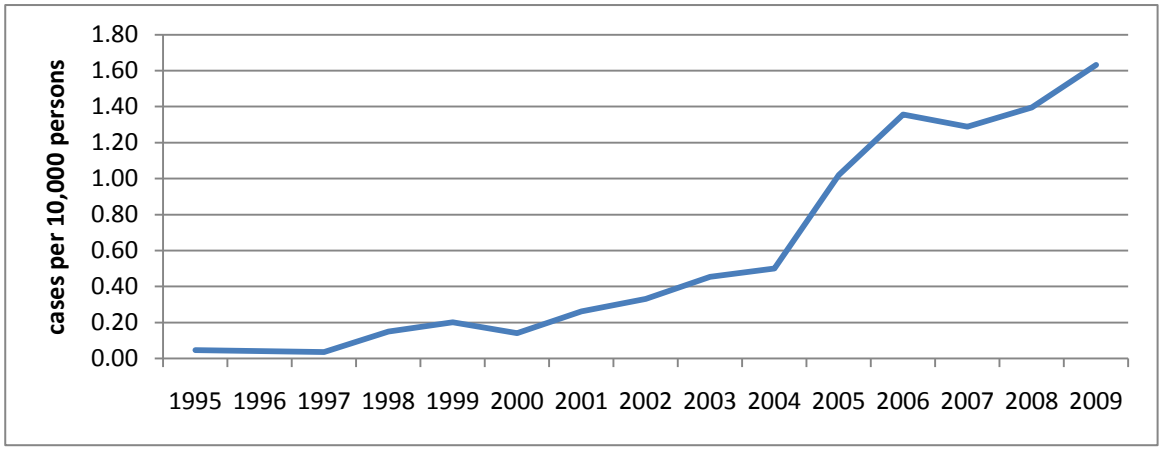
The impact of MRSA on mortality is still controversial, but the costs of MRSA treatment are undoubtedly high, primarily due to the long hospital stays. In one study, hospital costs attributable to MRSA bacteremia was almost twice as those of MSSA bacteremia (US$21,577 vs. US$11,668) (Lodise, et al. 2005).

2. EPIDEMIOLOGY

MRSA may be spread in different ways: a) having direct contact with another person's infection; b) sharing personal items, such as towels or razors, which have touched infected skin; c) touching surfaces or items, such as used bandages, contaminated with MRSA. In a healthcare setting, the media of transmission could be hands, equipment and apparel of healthcare workers, and colonized patients are the main reservoir (Safdar, et al. 2008).

Compared with countries elsewhere, the Scandinavian countries have had relatively low prevalence of MRSA due to intensive control (Fluit, et al. 2001). In Norway, it has been under 1% for about 10 years (Anonymous 2009a). However, according to the reported data from Norwegian Public Health Institute (Folkehelseinstituttet), even though the number of reported cases of MRSA is still relatively low, it has increased from 20 in 1999 to 783 in 2009, including both colonization and clinical infection. Converting these numbers to incidence, it becomes a growth trend of MRSA in Norway (Figure 2).

Figure 2 Incidence of MRSA in Norway (per 10,000 population)

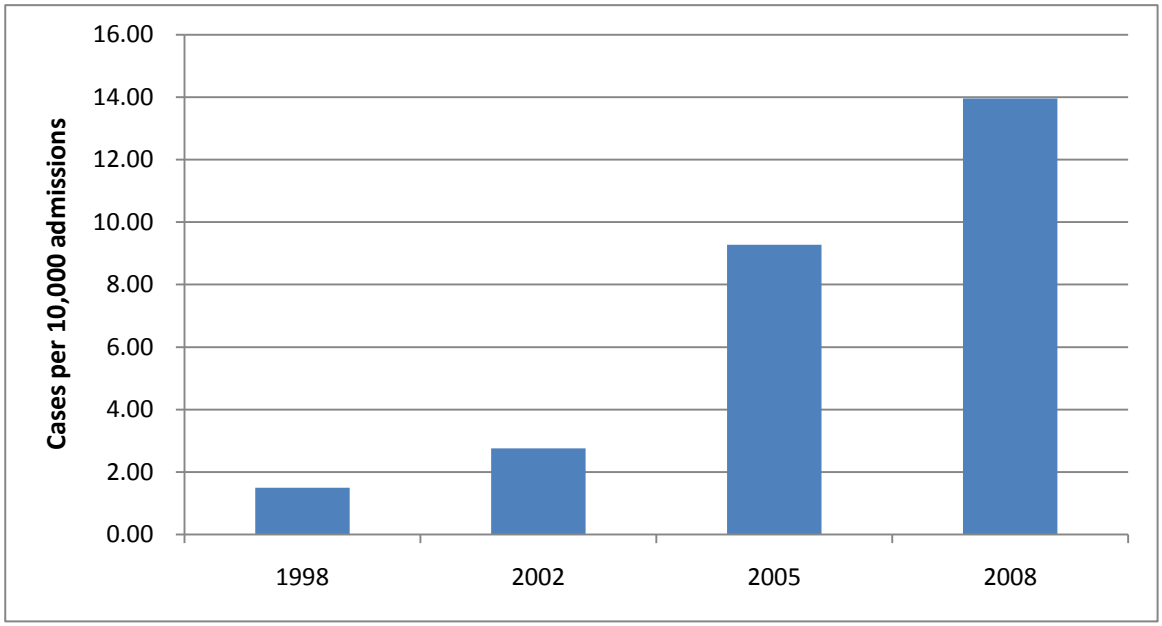


Sources: MRSA cases from Meldingssystem for smittsomme sykdommer (MSIS) and Population in Norway from Statistisk sentralbyrå

Among patients admitted to hospital, there were approximately 14 persons with MRSA infection or colonization per 10,000 hospital admissions in 2008. This number was approximately 10 times greater than the corresponding measure 10 years ago (Figure 3).

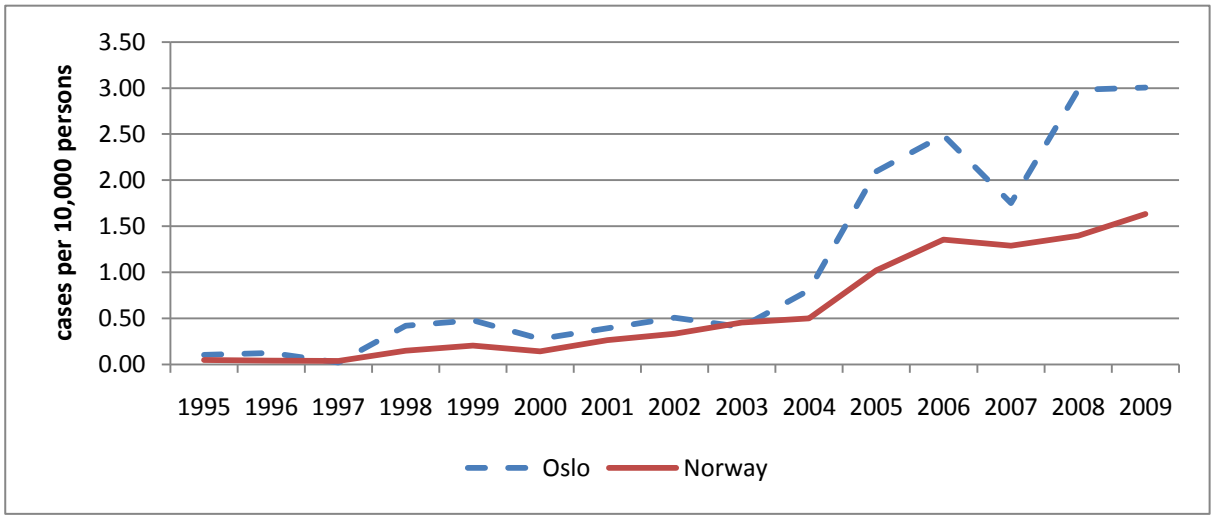
The incidence of MRSA has been higher in the capital city of Oslo than the rest of the country (Figure 4).

Figure 3 Incidence of MRSA (per 10,000 admissions) in Norway



Source: MRSA cases from Meldingssystem for smittsomme sykdommer (MSIS) and Population admitted in the last 12 months in Norway from Statistisk sentralbyrå

Figure 4 Incidence of MRSA (cases per 10,000 population) in Oslo and the whole Norway

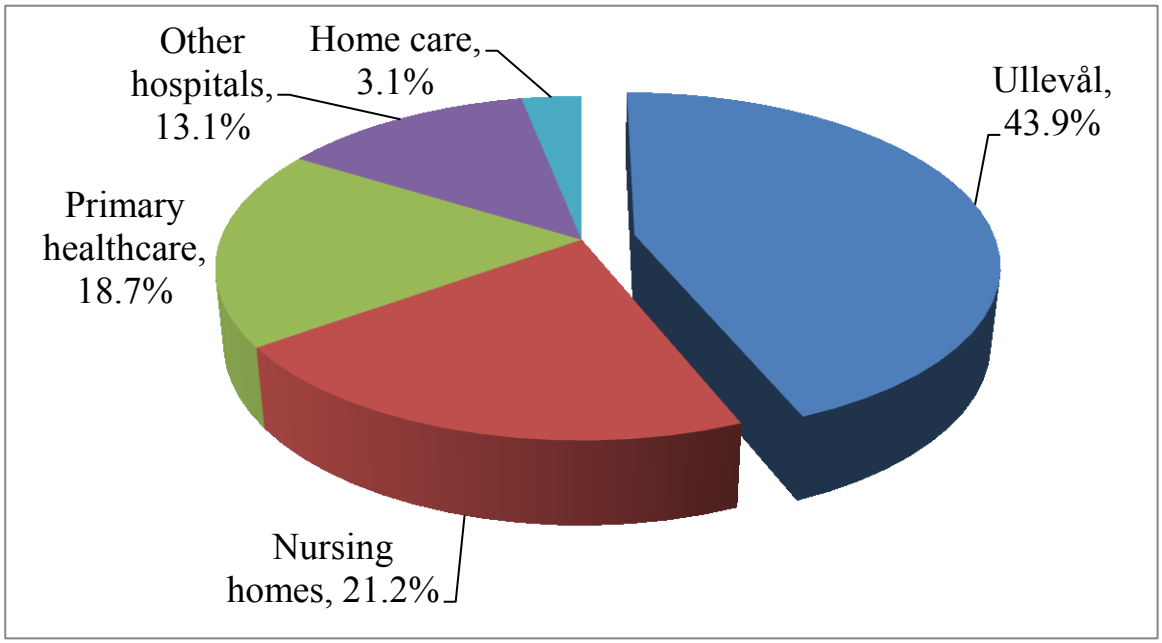


Sources: MRSA cases from Meldingssystem for smittsomme sykdommer (MSIS) and Population from Statistisk sentralbyrå

During 1993-2006, 358 MRSA cases were registered in Oslo, of which 43.9% were detected at Oslo University Hospital, Ullevål, 21.2% in nursing homes, and 18.7% in primary

health care (Figure 5) (Andersen, et al. 2007). The high number of reported MRSA cases at Oslo University Hospital, Ullevål mostly resulted from an increase of import-associated cases, and cases from primary healthcare. With regard to the low prevalence and the preemptive isolation policy implemented in Norway, the fact that almost half of the cases were discovered at one hospital indicated much more pressure on controlling infectious diseases and utilizing health care resources at that hospital. Referring the information system of the hospital, 11803 MRSA tests were performed in 2009 but only 44 new MRSA cases were verified. This indicated that a considerable amount of resources were occupied by unnecessary preemptive isolation.

Figure 5 Proportion of MRSA cases in Oslo, Norway



(Andersen, Rasch and Syversen, Is an increase of MRSA in Oslo, Norway, associated with changed infection control policy? 2007)

3. MRSA IDENTIFYING PROCEDURES

The way MRSA is transmitted implies that it is possible to break the infection chain by contact isolation. Identification of patients likely to be colonized or infected with MRSA on admission is the key to promptly deploying contact isolation. According to the guidelines for preventing MRSA at Oslo University Hospital, Ullevål (Anonymous 2009b), all patients that:

- Have had contact with health care settings abroad during the last 12 months; or
- Have had experience as health care personnel abroad during the last 12 months; or
- Worked or stayed in orphanages, refugee camps or prisons abroad during the last 12 months; or
- Worked or stayed in asylums during the last 12 months; or
- Have had a history of infected or colonized by MRSA,

have to be preemptively isolated and screened for MRSA although in practice not all of them are isolated at hospital.

While healthcare personnel take the medical history on admission, they are supposed to ask the questions above to identify patients at high risk of MRSA infection or colonization. Once a patient at high risk is identified, he or she takes MRSA detection test immediately. Nurses working in wards are responsible for collecting samples from patients, labeling them and ordering tests. Based on indicators such as severity of underlying diseases, risk of severe infections and availability of home-care, some patients are sent home and self-isolated, and others are admitted to hospital and isolated in wards.

Samples can be collected from several sites of human body, including nares, throat, hands and wrists, perineum, wounds/scars/eczema/skin lesions and all types of catheters.

Generally, samples from four different sites of the body are collected for each patient. The sample from nares is always one of them. The responsible personnel send the samples to the central laboratory for microbiologic examination. The conventional way to verify MRSA is using culture test. Routinely, culture plates are examined after 24 hours to give a preliminary result. If the laboratory technician believes that the result will be positive, he or she can call the patient's ward. MRSA treatment will start immediately. When the preliminary test reading indicates that the result will be negative, no call to the wards is made.

When MRSA cases are confirmed, the rooms in which the patients have stayed must be disinfected. Even for unconfirmed cases, the patient rooms have to be disinfected each time the patients change room until they are declared as MRSA free. The disinfection procedure is performed by cleaning robots and cleaning personnel. It is complicated, taking approximately seven hours. Two hours are for pre- and after-preparation by personnel, including transporting and cleaning the robots and sealing the rooms. During the other five hours cleaning is performed automatically by robots (Table 1).

Table 1 Time used to disinfect one hospital room

Item	Transport time	Preparing time	Disinfecting by robot	Cleaning the robot
Time (hour)	0.5	1	4~5	1

Preemptive isolation does not completely cut patient's contact with those outside the room. Since the reason for referral to hospital may not be MRSA infection, certain kinds of laboratory tests or physical examinations may be performed as appropriate. Especially in the case of emergency cases, a patient will never stay in the emergency department for more than six hours unless the patient may die if he or she is moved out. For these reasons, some patients may stay in more than one room, department or clinical examination unit during the whole period of isolation. Such moves add to the number of rooms that eventually will need disinfection. In some urgent cases, the therapy to the principle diagnosis keeps going and leads to several transfers and stays within a probably huge area.

There are also screening procedures for healthcare personnel who have exposed to

contaminated environments. Those procedures don't include preemptive isolation. Instead, personnel are screened for MRSA risk factors and stay at home until bacteriologic result is known. This practice is not evaluated in this study.

4. SCREENING STRATEGIES

In consideration of potential harm of MRSA infections, preventive strategies are undoubtedly essential. Preemptive isolation and screening test represent one of the most effective strategies to stop the spread of MRSA. Nevertheless, considerable costs are incurred, and clinical facilities cannot be used to produce health benefits. The costly efforts in MRSA negative patients have no impact on the spread of MRSA. Because health care resources are limited, the optimal preventive strategy for MRSA depends on costs as well as benefits. In order to reduce unnecessary consumption of resources, Oslo University Hospital, Ullevål started to adopt the use of Xpert MRSA method to screen patients at high risk of MRSA in July, 2009.

4.1. Xpert MRSA test

The rapid method Xpert MRSA test took use of the GeneXpert System. It is a real-time PCR-based molecular testing system, which is highly automatic and needs only 75 minutes to produce the test result. The system can provide PCR results by a connected computer without human injection. Anyone can operate it after a brief learning period because of its integration and automation.

The sensitivity and specificity, according to the limited data (n=410) at Oslo University Hospital, Ullevål, were 99% and 100% respectively. In other studies, the sensitivity of Xpert MRSA test varied between 75% and 100% while the specificity varied from 92% to 100% (Andersen, et al. 2010) (Stürenburg 2009) (Kelly, et al. 2009) (Wolk, et al. 2009a) (Wolk, et al. 2009b) (Rossney, et al. 2008). Although this screening test is not perfect, it is believed to be sufficiently effective in ruling out true negative cases and thus saves unnecessary costs and shortens the period of isolation. Furthermore, this new method is supposed to increase the satisfaction of patients as well. Accordingly, we designed three screening strategies to explore the additional costs and benefits of the Xpert MRSA test in this study.

4.1.1. Day-time Xpert strategy

At Olso University Hospital, Ullevål, the GeneXpert system is operated by staff at the microbiology laboratory. With the day-time Xpert strategy, the Xpert MRSA test is operated from 8.00 to 14.15 o'clock on weekdays (Anonymous 2009c). Patients who are admitted before or after this time period have to be isolated immediately but tested in the next working day. Each Xpert test is accompanied by a corresponding culture test. Only when the Xpert test result is negative, the patient can be released from isolation. Otherwise, patients are isolated until culture tests are negative.

4.1.2. 24-hour Xpert strategy

With the 24-hour Xpert strategy, the Xpert test was assumed to be performed 24 hours and 365 days. Thus, waiting time would be avoided and the corresponding time and resource costs could possibly be reduced. The microbiology laboratory considered that it had no capacity to perform more tests without expanding its staff. A report from the department concluded that 7-9 additional full-time and part-time positions, equivalent to 4.25 full-time positions, were needed to offer a 24 hours service. This increased staffing would imply not only 24 hours Xpert test service, but also 24 hours culture test service. Improved staffing would not be confined to run MRSA tests once it were implemented. The additional staff members would also perform other tasks.

4.2. Culture test

The gold standard test for detecting MRSA is the conventional culture test, for which it takes on average 48 hours to receive the final result. Nurses take the samples from the patients, while laboratory technicians handle the rest of the working process. Working hours for the laboratory technicians is from 8.00 until 15.00 on weekdays. No tests are performed during weekends.

Compared with the culture test, the Xpert test entails higher capital and material costs.

Additionally, the 24-hour Xpert strategy requires additional laboratory work. The advantage of the rapid screening test is the earlier availability of test results, which leads to reductions in the length of preemptive isolation among MRSA-negative patients. In that way, resources may be saved. The extent of cost savings will depend on how long the time of preemptive isolation is avoided with different strategies.

5. AIM

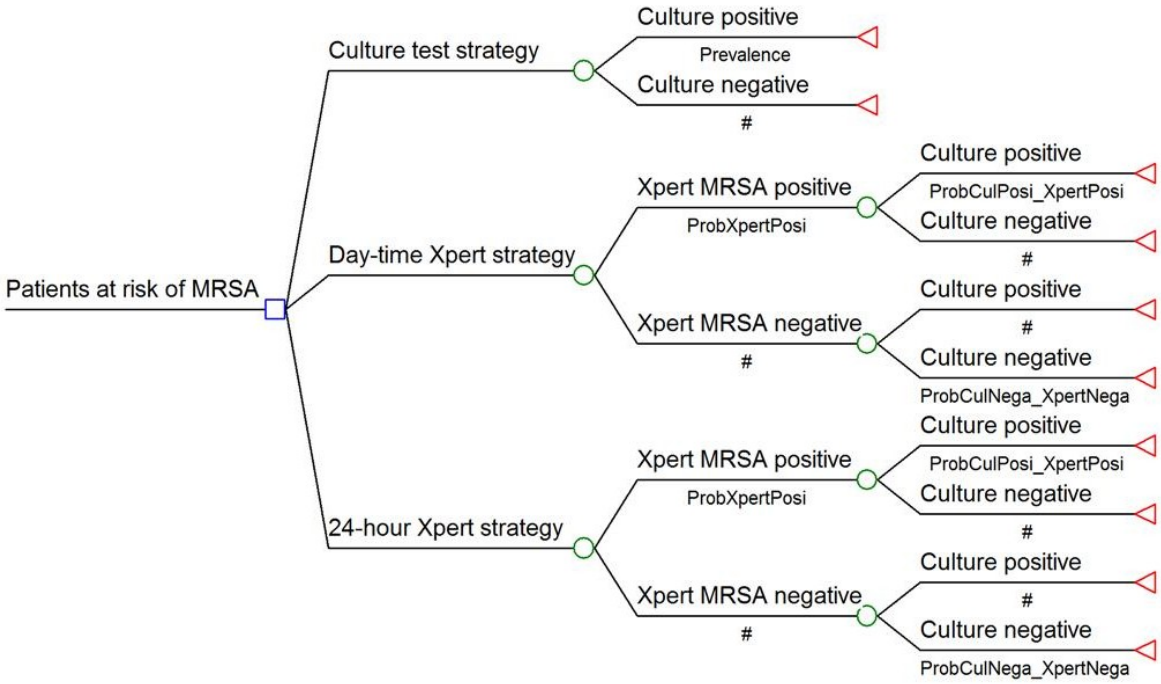
Adopting a health care perspective, the aim of this study was to explore the additional costs, health-related consequences and other consequences of replacing culture test alone with culture test plus either day-time Xpert test or 24-hour Xpert test in patients at high risk of MRSA.

6. METHODS

6.1. Model

We developed a decision tree model with the computer program TreeAge Pro 2009. The model starts with patients at high risk of MRSA and has three strategies: 1) Culture test strategy; 2) Day-time Xpert strategy; and 3) 24-hour Xpert strategy (Figure 6).

Figure 6 Decision Tree for Cost-Effectiveness Analysis



With the culture test strategy, two branches, indicating positive result and negative result, are presented secondary to the chance node. This is the conventional and current strategy.

With the day-time Xpert strategy, the first chance node was followed by positive and negative results of the Xpert test. Each of the two braches is followed by the results of confirmatory culture test. If the Xpert test result is negative, the patient is released from isolation immediately. Thus, time and costs of preemptive isolation are reduced, possibly also the cost of disinfection, without any adverse effect when the test result is true negative. If the Xpert test result is false negative (the corresponding culture test result is positive),

however, the risk of infecting other persons increases. In that case, all persons who have had contact with the infected patient have to be isolated preemptively and screened, incurring additional costs.

With the 24-hour Xpert strategy, the tree structure is the same as in the day-time Xpert strategy, but the model parameters are different (see Appendix 10.1). The main difference is that, with the day-time Xpert strategy, patients suspected of MRSA who arrive in hospital during the evening and night, have to wait till next morning to have the tests. Consequently, there is more waiting time and isolation with this strategy, but less laboratory labour costs.

6.2. Probabilities

The crucial test characteristics are sensitivity and specificity. According to data collected at Oslo University Hospital, Ullevål during the period July 22nd, 2009 ~ Sept 15th, 2009 and using culture test as the confirmatory test, the sensitivity of the Xpert test is 99% and the specificity is 100%. We searched Medline using the keywords "Xpert" and "MRSA" to identify published studies of the Xpert MRSA test characteristics. In total six studies were identified (Table 2, also see Appendix 10.2) (Rossney, et al. 2008) (Wolk, et al. 2009a) (Wolk, et al. 2009b) (Kelly, et al. 2009) (Anonymous n.d.) (Andersen, et al. 2010). These data on sensitivity and specificity of the Xpert test were based on the comparison with culture tests using different kinds of agar. Although culture tests may also produce false results, such tests are considered to represent valid verification of MRSA. Given that the aim of this study was to explore the additional costs and consequences of replacing the culture test alone strategy with the Xpert strategies, the costs related to false negative or false positive results of culture test were disregarded because they are inevitable and occur with the same probability in all three strategies.

Table 2 Sensitivities and Specificities from different studies

Sources	Sensitivity	Specificity
Andersen, et al. 2010	87%	100%
Anonymous n.d.	86%	95%
Kelly, et al. 2009	87%	94%
	75%	95%
Wolk, et al. 2009a	94%	93%
	86%	95%
Wolk, et al. 2009b	97%	96%
	98%	99%
Rossney, et al. 2008	88%	92%
	79%	94%
	90%	97%

The mean sensitivity and specificity were 89% and 95%, respectively. We used SPSS (Explore description) to estimate the 95% confidence intervals, which were 84%~94%, 94%~97% respectively.

The probability parameters used in the model were ProbXpertPosi, ProbCulNega_XpertNega and ProbCulPosi_XpertPosi. ProbXpertPosi represents the probability of positive Xpert test result. ProbCulNega_XpertNega and ProbCulPosi_XpertPosi are the predictive value negative and the predictive value positive. They were calculated by following formulas:

Formula 1

$$\text{ProbXpertPosi} = (1 - \text{Specificity}) \times (1 - \text{Prevalence}) + \text{Sensitivity} \times \text{Prevalence}$$

Formula 2

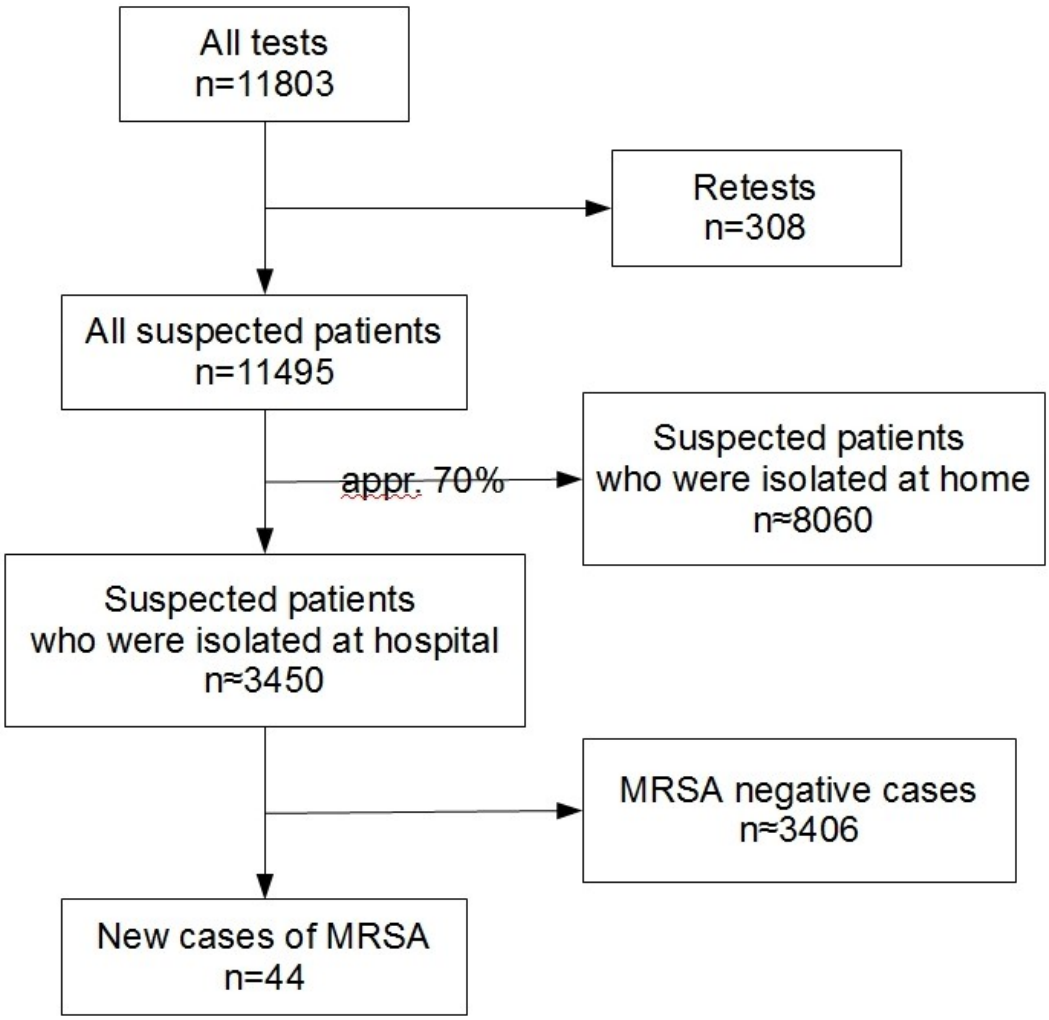
$$\text{ProbCulNega\_XpertNega} = \frac{(1 - \text{Prevalence}) \times \text{Specificity}}{\text{Specificity} \times (1 - \text{Sensitivity} - \text{Specificity}) \times \text{Prevalence}}$$

Formula 3

$$\text{ProbCulPosi\_XpertPosi} = \frac{\text{Sensitivity} \times \text{Prevalence}}{(1 - \text{Specificity}) \times (1 - \text{Prevalence}) + \text{Sensitivity} \times \text{Prevalence}}$$

The prevalence of MRSA in this study was defined as the proportion of MRSA cases among the patients who were isolated preemptively at hospital for suspected MRSA. In 2009, 11,803 tests were ordered for patients at Oslo University Hospital, Ullevål according to the laboratory register system, among which 308 tests were ordered for retesting patients. In 11,459 MRSA suspects, approximately 70% were sent home and self-isolated, although exact figures are not available. This left approximately 3,450 patients isolated preemptively at hospital. Among these isolated patients, there were 44 new MRSA cases detected (Figure 7). The estimated prevalence of MRSA among MRSA suspects who were admitted to Oslo University Hospital, Ullevål, was therefore 1.3%. Considering the uncertainty in the proportion of self-isolated patients among all suspected ones, we used 0.6%~2.0% as an uncertainty interval of the prevalence.

Figure 7 Use of culture test (MRSA) in 2009 at Oslo University Hospital, Ullevål



6.3. Costs

The costs related to the tests, preemptive isolation and disinfection were identified, quantified and valued. The MRSA treatment is constant no matter which strategy is carried out. Switching screening strategies won't change the treatment. The costs of treating MRSA were therefore omitted from the model.

The main cost components of the strategies were: labour costs, material costs and capital cost. At the end of this section, for the purpose of easy understanding, they are presented by means of two tables: one for the cost of the tests and one for the cost of preemptive isolation. All costs were measured in 2009 Norwegian Kroner (NOK) (US$1.00 = NOK6.28).

6.3.1. Labour Costs

Labour costs encompassed laboratory technicians who operated either of the tests, nurses who collected samples for the tests and cared for patients during the isolation period in the wards, and cleaning personnel who disinfected rooms. We assumed that the preemptive isolation did not influence the physicians' use of time, and therefore, physician costs were not included in this analysis. Data on the relevant wage rates including social security and holiday payments were collected from the hospital accounts. Where appropriate, we added 45% of the salary for out-of-hours working according to Norwegian labour payment agreements.

As the culture test always accompanied the Xpert test, the labour costs of the tests in the Xpert strategies were the sum of the labour costs of the Xpert test and the labour costs of the culture test. In order to obtain estimates of the use of time for the tests, we interviewed the director of the microbiology laboratory and two of his staff. They provided information on the average working time for each of the tests (Table 3). The mean wage rate of laboratory technicians was NOK289 including overtime payment, social security and holiday payment.

Table 3 Working time used by technicians for each of the tests in the microbiology laboratory

Procedure	Culture test	Xpert MRSA test
Preparing work before tests operating	2-5 min	20 min
Predicting results after 24 hours	5-15 min	—
Getting results after 48 hours	5 min	0 min

We interviewed three doctors and five nurses to obtain information on the use of nurse manpower during the isolation. They stated that one nurse could only care for one single isolated patient and no other patients. We therefore assumed that the labour costs of one-hour isolation was the full cost of one-hour nurse costs, and the total nurse costs increased linearly with the increasing number of hours of isolation. There are hundreds of nurses at the hospital, and they have different work schedules. Even in one department, their

payments may vary for several reasons. It was not feasible to track specific individuals' payments for this study. We therefore used the average cost of a nurse within the whole hospital (NOK217 per hour including overtime payment and other costs), and this estimate was used to value the labour costs in the wards. The director of the cleaning department informed that the cleaning personnel used on average 2.5 hours in preparation for the robot cleaning and other work related to disinfecting potentially infected rooms. The cleaning personnel never worked at night. The average wage rate of cleaning personnel was NOK207 per hour including social security and holiday payment, and this amount was adopted to value the labour costs of disinfection.

6.3.2. Material Costs

Material costs encompassed materials used during the sample collecting process and disposable materials used by healthcare personnel during the isolation period and during disinfections.

With respect to sampling for MRSA tests, we based the cost data on the hospital's guidelines. We consequently assumed that four swabs and four tubes were used for each suspected patient, in addition to one set of gown, gloves and respirators (Figure 8), which nurses have to wear when they collect samples. The unit prices were taken from the hospital accounts.

Figure 8 Nurse wearing gown, gloves and respirator

A wide range of materials are used in the microbiology laboratory for MRSA tests. It was not feasible to collect information on all details here, and we only included the cost of the selective culture plate and the Xpert MRSA test package. With respect to other materials, the costing was based on aggregate cost item in the hospital accounts, named disposable materials. This item was NOK135,000 in 2009. The cost of disposable materials for the tests in the Xpert strategies was the sum of the cost of disposable materials for the culture test and the Xpert test. In order to allocate the costs to each test, working time was used as distribution factor by means of the following formula:

Formula 4

$$\text{Disposable materials cost per test} = \frac{\text{Total disposable materials cost}}{\text{Annual personhours in the microbiology laboratory}} \times \text{Working time used on one test}$$

The annual person-hours were based on the number of full-time positions (31.5 in 2009) assuming 1,950 working hours per position per year. With the 24-hour Xpert strategy, the total amount of disposable materials costs might increase but the disposable materials for each test would be the same as with the day-time Xpert strategy.

According to the isolation rules, all persons entering an isolated room have to wear gloves, gowns and respirators as shown in Figure 8. Each time this happens, a set of those materials are used. We assumed that the physician see his/her patient twice per day while in isolation. With respect to nurses, based on interviewing a nurse from orthopedic ward, we assumed 16 times of entering rooms per day including serving meals, helping personal hygiene, giving necessary medicine and other essential visits due to isolation.

Disinfection requires considerable use of materials. First, cleaning personnel has to wear cap, gloves, gown and respirator once they enter the room. If they leave the room and later return, another set of suits is required. The director of the cleaning department informed that the cleaning personnel uses 16 pairs of gloves, 2 caps, 2 gowns and 2 respirators when cleaning one room. For sealing the rooms prior to the robot cleaning, 1

roll of plaster, 1 roll of tape, 2 black and 4 yellow plastic bags, certain amount of soap and disinfection gas are consumed each time. One bottle of soap could be used for 105 rooms. One bottle of disinfection gas could cover 320 m^2. All these items were accounted for material costs of disinfection.

The costs of all types of materials listed above were valued according to market prices (NOK) as stated in the financial accounts of the hospital. A detailed price list was presented in Appendix 10.3.2.

6.3.3. Capital Cost

Capital cost in this study encompassed the incubators for the culture test, the GeneXpert system and the robot for disinfection. At Oslo University Hospital, Ullevål, an incubating room is used instead of several incubating boxes. Because the number of MRSA culture tests is limited comparing with the total number of culture tests, the capital cost of the culture test was assumed to be zero. The hospital has two GeneXpert Systems, one for patients and one for personnel. In this study, only the system for patients was considered. The price of this machine was stated in the purchase contract as NOK990,000 excluding VAT (Anonymous 2009d). It was assumed that the life time of the machine is 10 years. The price of cleaning robots used for disinfection was NOK190,000 for each according to the records of the cleaning department. The life time of the robots was assumed to be 3 years. A 4% discount rate was adopted in the calculation of capital costs (Anonymous 2009e). After depreciation, we got the equivalent annual cost (EAC), which was NOK152,572 for the GeneXpert system and NOK68,466 for the robots. Capital cost per test = EAC/Annual number of MRSA tests. Capital cost per disinfection = EAC/Annual number of times of using robots. Details about depreciation are presented in the Appendix 10.3.3.

6.3.4. Summary of Costs

Based on the methods presented in section 6.3.1 – 6.3.3, the cost per culture test was NOK387, the cost per day-time Xpert test was NOK2,151 and the cost per 24-hour Xpert test

was NOK2,339 (Table 4). With respect to the costs of preemptive isolation including disinfection, the cost per patient was NOK16,596 with the culture test strategy. The cost per patient of preemptive isolation was NOK16,596 when the day-time Xpert test result was positive and NOK4,477 when it was negative. With the 24-hour Xpert strategy, the cost per patient was NOK12,759 when the Xpert test result was positive while it was NOK639 when the result was negative (Table 5). Details about the calculation of costs are presented in the Appendix 10.3.4.

Table 4 Cost of tests (2009 Norwegian Kroner (NOK)) according to screening strategy

	Culture test (NOK)	**Day-time Xpert (NOK)**	**24-hour Xpert (NOK)**
Labour cost per test	**321**	**628**	**817**
Material cost per test	**67**	**1,510**	**1,510**
Capital cost per test	**0**	**13**	**13**
Cost per test	**387**	**2,151**	**2,339**

Table 5 Costs per patient of preemptive isolation and disinfection (2009 Norwegian Kroner (NOK)) according to screening strategy

	Culture test (NOK)	**Day-time Xpert (NOK)**		**24-hour Xpert (NOK)**	
Result		Positive	Negative	Positive	Negative
Labour cost of preemptive isolation	**13,642**	**13,642**	**3,538**	**10,718**	**614**
Disinfection cost of preemptive isolation	**2,365**	**2,365**	**788**	**1,577**	**0**
Material cost during preemptive isolation	**589**	**589**	**150**	**464**	**25**
Cost of preemptive isolation	**16,596**	**16,596**	**4,477**	**12,759**	**639**

6.4. Measure of Outcomes

Three types of outcomes were used as measures of benefits: reduction in the length of the preemptive isolation, reduction in unavailable room-hours and quality–adjusted life.

6.4.1. Time of preemptive isolation

The time period of preemptive isolation started when samples were collected and ended when the test results were available. This period of time encompassed collecting samples in wards, conveying samples to the microbiology laboratory, performing the tests and additionally, waiting time because the tests were not performed during night time.

The time of collecting samples is same for all strategies because nurses in the wards use double pre-wet swabs (Figure 9) to collect samples for both tests simultaneously. Given that there was no record on the length of this time period, we assumed it to be 10 minutes based on interviewing four nurses.

Figure 9 Double pre-wet swabs

Because of deficiencies of the laboratory register system, the information on the transport time from individual departments to the microbiology laboratory was not complete. According to the best register data we could get, the average time of transport was 3-7 minutes.

Operating time of the tests encompassed time of preparation, time of bacteria growing (the culture test) or reacting (the Xpert test) and time of verification (the culture test). The director of the microbiology laboratory and two of his staff informed that it takes 2-5 minutes to prepare the culture test. The time for the bacteria to grow is 48 hours. The culture plate

is read twice during the 48 hours, the first after 24 hours and the second after 48 hours. The first reading takes 5-15 minutes while the second one takes approximately 5 minutes. The staff also informed that it takes approximately 20 minutes to prepare an Xpert test. The reacting time for Xpert test is 75 minutes. The verification report is presented automatically by a computer linked to the GeneXpert system so that there is no verification time. When the Xpert test produced a positive result, however, the operating time of culture test was used to calculate the total time in the model instead of that time of the Xpert test. In that case, all patients who got positive test results from the Xpert test continued to be isolated until the 48-hour culture test result was available. Given that the culture test and the Xpert test were performed simultaneously, the longer period of time was used to value the length of the preemptive isolation period.

Waiting time was applied for the strategies of the culture test and the day-time Xpert test, but not for the 24-hour Xpert strategy. In the former two strategies, samples were sent to the laboratory the next morning if they were collected later than 14.15 o'clock. Estimates of waiting time were based on the laboratory registration system of Oslo University Hospital, Ullevål. In 2009, 11,803 MRSA tests were ordered. Although 4,724 of those tests had no record on ordering time, the rest were registered every hour throughout the day (see Appendix 10.4.1). We analyzed the distribution of the length of waiting time in SPSS (Explore description) and got the mean (13.4 hours) of the length of waiting time. The 95% confidence interval was 13.23-13.57.

Based on the methods described in this section, the length of preemptive isolation was 63.0 hours with the culture test strategy, 63.0 hours with the day-time Xpert strategy when the Xpert test result was positive and 16.3 hours when the result was negative. The 24-hour Xpert strategy produced the shortest preemptive isolation period, which lasted 49.5 hours when Xpert test result was positive and 2.8 hours when result was negative (Table 6).

Table 6 The length of preemptive isolation (hours) according to screening strategy

	Culture test (hours)	**Day-time Xpert (hours)**		**24-hour Xpert (hours)**	
Result		Positive	Negative	Positive	Negative
Working time per test (nurse)	0.2	0.2	0.2	0.2	0.2
Transport time	0.1	0.1	0.1	0.1	0.1
Time of test	49.2	49.2	2.6	49.2	2.6
Waiting time for having test performed	*13.5*	*13.5*	*13.5*	*0.0*	*0.0*
Time of preemptive isolation	**63.0**	**63.0**	**16.3**	**49.5**	**2.8**

6.4.2. Unavailable Room-Hours

As a standard approach to controlling infectious diseases, isolation rooms were supposed to be disinfected after each period of isolation. In the case of preemptive isolation for preventing MRSA, if a room was used as an isolation room, either the patient was verified as MRSA positive or he/she was transferred to another room before being declared as MRSA free, the room has to be disinfected after the patient moved out. The total unavailable room-hours due to preemptive isolation were defined as the sum of time of preemptive isolation and time of disinfection, during which period the room was occupied and not available to other patients. The time of preemptive isolation was presented in the previous section. The time of disinfection encompassed time of transporting the robots to the rooms, time of sealing the rooms and preparing the robots, time of disinfection by robots, and time of cleaning the robots after disinfection (Table 1). While the robots worked, the cleaning staff performed other tasks.

In a busy department, such as the emergency department, most patients are transferred to other departments within 6 hours. That means that it's impossible to receive the culture test results before the MRSA suspects are moved to another ward or department. All rooms used for isolating the suspected patients must be disinfected. In addition, certain kinds of clinical

examinations and tests for the underlying diseases are performed during the isolation period. These facts in practice lead to more than one room disinfection during preemptive isolation. Generally, the longer a patient is isolated, the more rooms are used and the more disinfections are needed. Based on the interviews with five doctors from different departments, we preliminarily assumed that the frequency of disinfection was once every 24 hours. With reference to the director of the cleaning department, it takes on average 7 hours to disinfect one room. Considering the time of preemptive isolation, the unavailable room-hours were 84.0 hours (3.5 bed-days) with the culture test strategy. The unavailable room-hours were 84.0 hours (3.5 bed-days) with the day-time Xpert strategy when the Xpert test result was positive and 23.3 hours (1 bed-day) when the result was negative. With the 24-hour Xpert strategy, the unavailable room-hours were 63.5 hours (2.6 bed-days) when the Xpert result was positive and only 2.8 hours (0.1 bed-days) when the result was negative.

Table 7 Number of unavailable room-hours according to screening strategy

	Culture test (hours)	**Day-time Xpert (hours)**		**24-hour Xpert (hours)**	
Result		Positive	Negative	Positive	Negative
Time of preemptive isolation	**63.0**	**63.0**	**16.3**	**49.5**	**2.8**
Time of room disinfection by robot	4.5	4.5	4.5	4.5	4.5
Working time per disinfection	2.5	2.5	2.5	2.5	2.5
Number of room disinfection	*3 times*	*3 times*	*1 times*	*2 times*	*0 times*
Unavailable room-hours	**84.0**	**84.0**	**23.3**	**63.5**	**2.8**

In Table 7, “Time of room disinfection by robot” was the time that one robot used to disinfect a room. “Working time per disinfection” encompassed time of transporting the robots to the rooms, time of sealing the rooms and preparing the robots before and after disinfection. The number of room disinfection was dependent upon the length of preemptive

isolation and was assessed in sensitivity analyses.

6.4.3. Quality-Adjusted Life

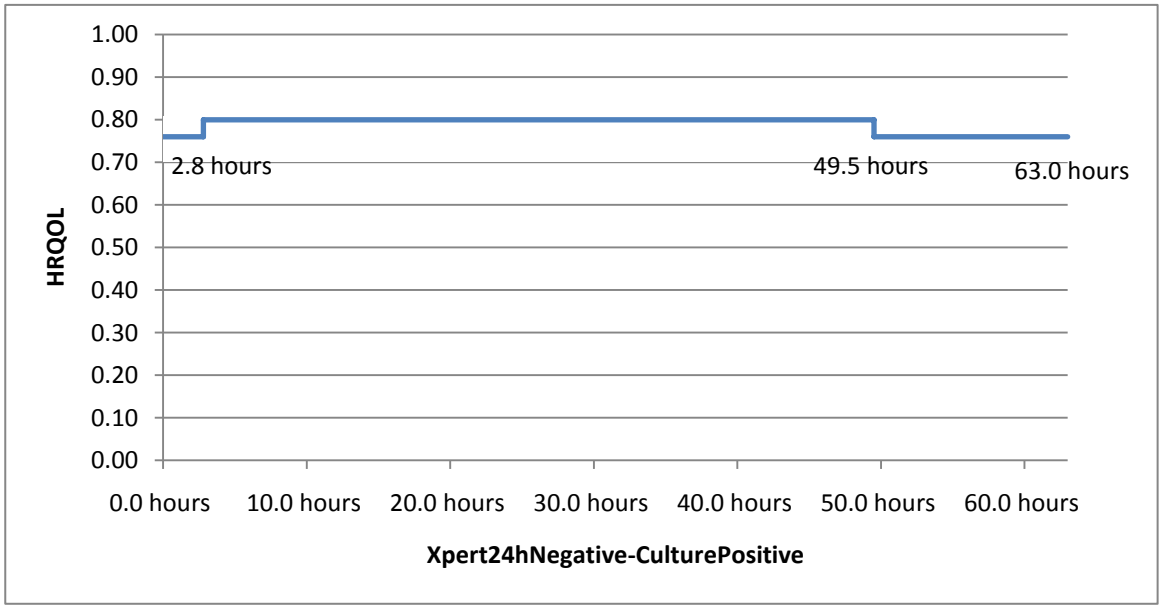
In the base case, we assumed that isolation had no adverse effect on patients' diagnosis and treatment. With reference to the interviews with five doctors from different hospital departments, treatment of underlying diseases was postponed only if it was considered unharmful to patients' health. Contact isolation may however affect patients' feelings and well-being to a smaller or greater extent. Consequently, we assumed that preemptive isolation may have an impact on mental health and health-related quality of life (HRQOL). Due to time and resource constraints of this study, we were unable to measure preferences for preemptive isolation. Consequently, we chose to use data from published studies.

We searched PubMed with the keywords "isolation AND utility", "seclusion AND utility", "isolation AND preference" "seclusion AND preference" and "isolation AND quality of life AND infection", and identified three articles about HRQOL in patients in isolation due to infection. One article explored the impact of isolation in an older adult population (Tarzi, et al. 2001). The other two measured levels of anxiety and depression in patients in isolation, one for long-term (Catalano, et al. 2003) and the other for short-term isolation (Wassenberg, et al. 2010). Because the target population in this study was not constrained to older adult and the isolation period was approximately two or three days, we discarded the former two articles and took advantage of the last one (Wassenberg, et al. 2010). The authors adopted the Hospital Anxiety and Depression Scale (HADS) to measure the anxiety and depression the patients experienced in isolation and compared them with common patients. HADS is a questionnaire containing 14 questions with four levels of points for each one (0-3). Half of the questions are about anxiety and the rest are about depression. The maximum of the points for each section is 21. The results of HADS for isolated patients and non-isolated patients were 5.0 (3.0-7.0) and 4.5 (2.0-6.0) for anxiety while 5.0 (3.0-7.0) and 4.0 (3.0-7.3) for depression. Taking use of the formula that HRQOL = 1 – points / 21, we calculated the HRQOLs which were 0.76 (both anxiety and depression) for isolated patients and 0.79

(anxiety) and 0.81 (depression) for non isolated patients.

On the basis of this study, we assumed that the HRQOL was 0.80 of non-isolated patients and of isolated patients was 0.76. In order to make all strategies comparable, we adopted the time scale from 0 to 63 hours for all strategies to measure HRQOL. Based on these assumptions, Quality-Adjusted Life Days (QALDs) and subsequently Quality-Adjusted Life Years (QALYs) were calculated under different conditions. Loss of QALDs and QALYs was presented with minus value. For example, when the Xpert test produced a false negative result in the 24-hour Xpert strategy, the value of HRQOL was 0.76 from 0 to 2.8 hours because of preemptive isolation and suspected MRSA. The Xpert test produced a false negative result in 2.8 hours so that HRQOL went back to and remained 0.80 from 2.8 to 49.5 hours. The culture test produced a positive result after 49.5 hours, and therefore HRQOL became 0.76 again from 49.5 to 63.0 hours (Figure 10). In this case, the total value of HRQOL was $\text{HRQOL} = 0.76 \times 2.8 + 0.80 \times (49.5 - 2.8) + 0.76 \times (63.0 - 49.5) = 49.7$. QALDs were $49.7/24 = 2.07$ QALDs and QALYs were $49.7/24/365 = 5.7 \times 10^{-3}$ QALYs.

Figure 10 Health-Related Quality of Life (HRQOL) when Xpert test produced a false negative result in the 24-hour Xpert strategy



According to the calculation process above, with the culture test strategy, 1.99 QALDs

($5.5*10^{-3}$ QALYs) were gained, regardless of the result. With the day-time Xpert strategy, 1.99 QALDs ($5.5*10^{-3}$ QALYs) were gained when the Xpert test result was positive, regardless of the culture test result. Similarly, when the day-time Xpert test produced negative results, 2.07 QALDs ($5.7*10^{-3}$ QALYs) were gained, regardless of the culture test results. When the 24-hour Xpert test produced a true result, 1.99 QALDs ($5.5*10^{-3}$ QALYs) (true positive) and 2.09 QALDs ($5.7*10^{-3}$ QALYs) (true negative) were gained respectively. 2.02 QALDs ($5.5*10^{-3}$ QALYs) were gained when the 24-hour Xpert test produced a false positive result. 2.07 QALYs ($5.7*10^{-3}$ QALYs) were gained when the 24-hour Xpert test produced a false negative result (Table 8, also see Appendix 10.4.2).

Table 8 The number of Quality Adjusted Life Days (QALDs) and Quality Adjusted Life Years (QALYs) during the 63 hours observation period, according to test result

Test Results	QALDs	QALYs
Culture test positive	1.99	$5.5*10^{-3}$
Culture test negative	1.99	$5.5*10^{-3}$
True positive daytime Xpert test	1.99	$5.5*10^{-3}$
False positive daytime Xpert test	1.99	$5.5*10^{-3}$
False negative daytime Xpert test	2.07	$5.7*10^{-3}$
True negative daytime Xpert test	2.07	$5.7*10^{-3}$
True positive 24-hour Xpert test	1.99	$5.5*10^{-3}$
False positive 24-hour Xpert test	2.02	$5.5*10^{-3}$
True negative 24-hour Xpert test	2.09	$5.7*10^{-3}$
False negative 24-hour Xpert test	2.07	$5.7*10^{-3}$

The threshold for willingness-to-pay per QALY in Norway was NOK 500,000, and this value was adopted in this study if applicable.

6.5. Data Sources

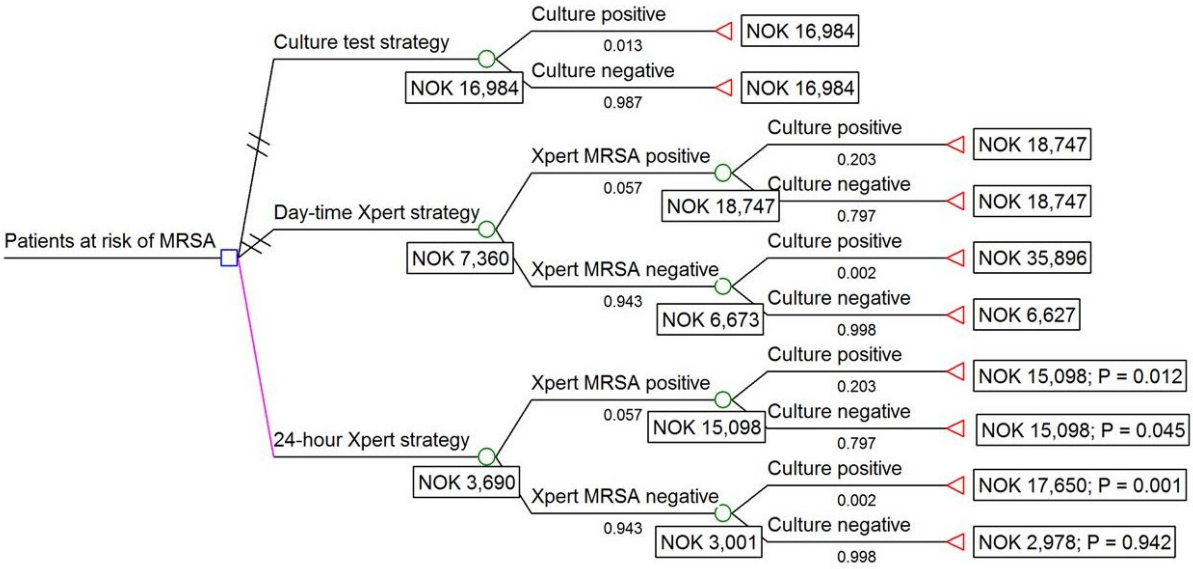
All the data on costs were taken from the accounts of the Oslo University Hospital, Ullevål, including the hospital's information system, contracts, etc. The data on wage rates and full-time positions were referred to the accounts and the annual report of Oslo University Hospital, Ullevål. All the data on time was collected through interviewing relevant personnel, by face-to-face interview and questionnaire.

7. RESULTS

7.1. Costs

The expected total cost of the strategies were NOK16,984, NOK7,360 and NOK3,690 per patient with the culture test, the day-time and the 24-hour Xpert strategies, respectively (Figure 11). Although the costs per patient were high when the Xpert MRSA test result was false negative (NOK35,896 with the day-time Xpert strategy and NOK17,650 with the 24-hour Xpert strategy), the total costs of the Xpert strategies were still lower than those of the culture test strategy because of the low probability of a false negative test (0.1%).

Figure 11 Costs according to screening strategy



With respect to the cost of the culture test strategy, out of NOK16,984, NOK13,963 represented labour costs. The next largest cost component was disinfection (NOK2,365) followed by material (NOK656), and there was no capital cost. In the Xpert strategies, labour costs represented NOK4,769 for day-time testing and NOK2,018 for 24-hour testing. Here, material costs represented NOK1,695 and NOK1,569, respectively. Disinfection costs appeared to be smaller in the Xpert strategies (NOK883 and NOK90, respectively). Capital cost was NOK13 per patient in both of the Xpert strategies (Table 9).

Table 9 Cost components of the three strategies

Costs	Culture test (NOK)	Daytime Xpert (NOK)	24-hour Xpert (NOK)
Labour costs	13,963	4,769	2,018
Material costs	656	1,695	1,569
Disinfection costs	2,365	883	90
Capital cost	0	13	13
Total	**16,984**	**7,360**	**3,690**

7.2. Outcomes

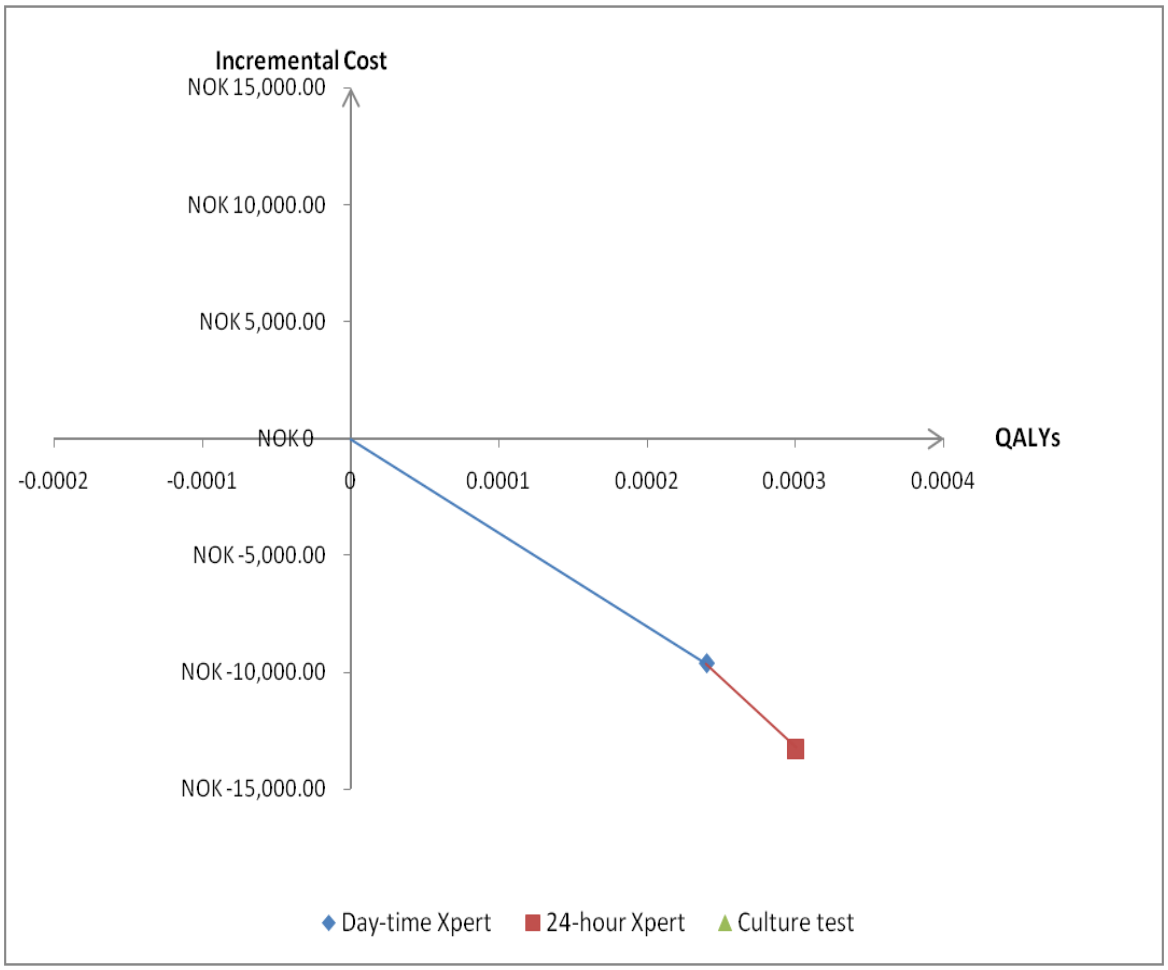
The average time of preemptive isolation was shortest (5.5 hours) with the 24-hour Xpert strategy while it was longest (63.0 hours) with the culture test strategy, representing reductions in the length of the preemptive isolation of 57.5 hours with the 24-hour Xpert strategy and 43.9 hours with the day-time Xpert strategy. The number of unavailable room-hours was 6.3 hours with the 24-hour Xpert strategy, 26.9 hours with the day-time Xpert strategy and 84.0 hours with the culture test strategy. The QALYs gained by replacing the strategy of culture test alone with the 24-hour Xpert strategy was $3.0*10^{-4}$ QALYs (0.11 QALDs), while it was $2.4*10^{-4}$ QALYs (0.09 QALDs) with the day-time Xpert strategy.

7.3. Cost-Effectiveness

The culture test strategy had the highest costs and the least favorable outcome for all three outcomes, and it was thus dominated by the day-time Xpert strategy. This however, had higher costs and worse outcomes than the 24-hour Xpert strategy. By replacing the culture test strategy with the 24-hour Xpert strategy, NOK13,294 could be saved, 57.5 hours unnecessary preemptive isolation could be avoided, 77.7 room-hours could be freed and $3.0*10^{-4}$ QALYs (0.11 QALDs) could be gained. In conclusion, the 24-hour Xpert strategy was dominant in the base case analysis (Figure 12, also see Appendix 10.5). Assuming that 3,500 patients were screened and isolated preemptively per year, NOK46,529,000 might be saved by replacing the culture test strategy with the 24-hour Xpert strategy. In addition, on average 271,950 unavailable room-hours (11,331 bed-days) might be saved and 1.05

additional QALYs could be produced during one year.

Figure 12 Cost-effectiveness plane using QALYs as the measure of effectiveness (the culture test strategy is in the origin of the graph)



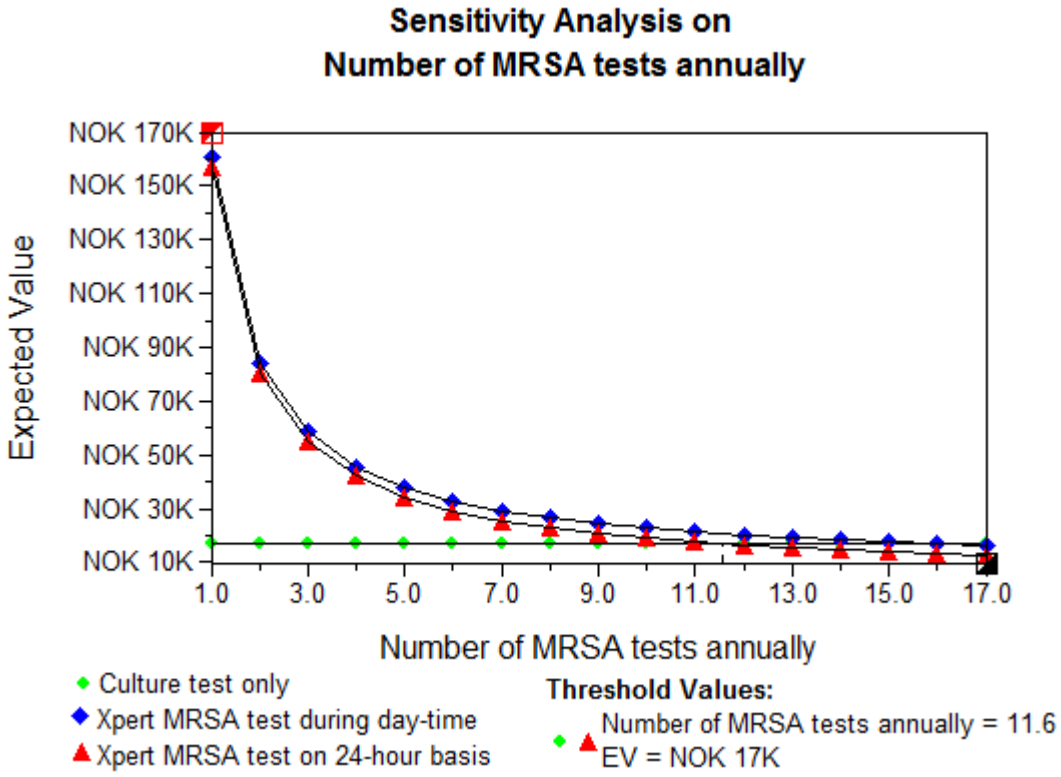
7.4. Sensitivity Analysis

One-way sensitivity analyses were performed on all model parameters, and the most important findings are presented in Table 10. Only changing the annual number of MRSA suspects could change the conclusion that the Xpert strategies dominated the culture test strategy (Figure 13). Except for this parameter, in all other cases, the 24-hour Xpert strategy dominated over the daytime Xpert strategy, and the culture test strategy was dominated by both of the others.

Table 10 Some important parameters for sensitivity analyses

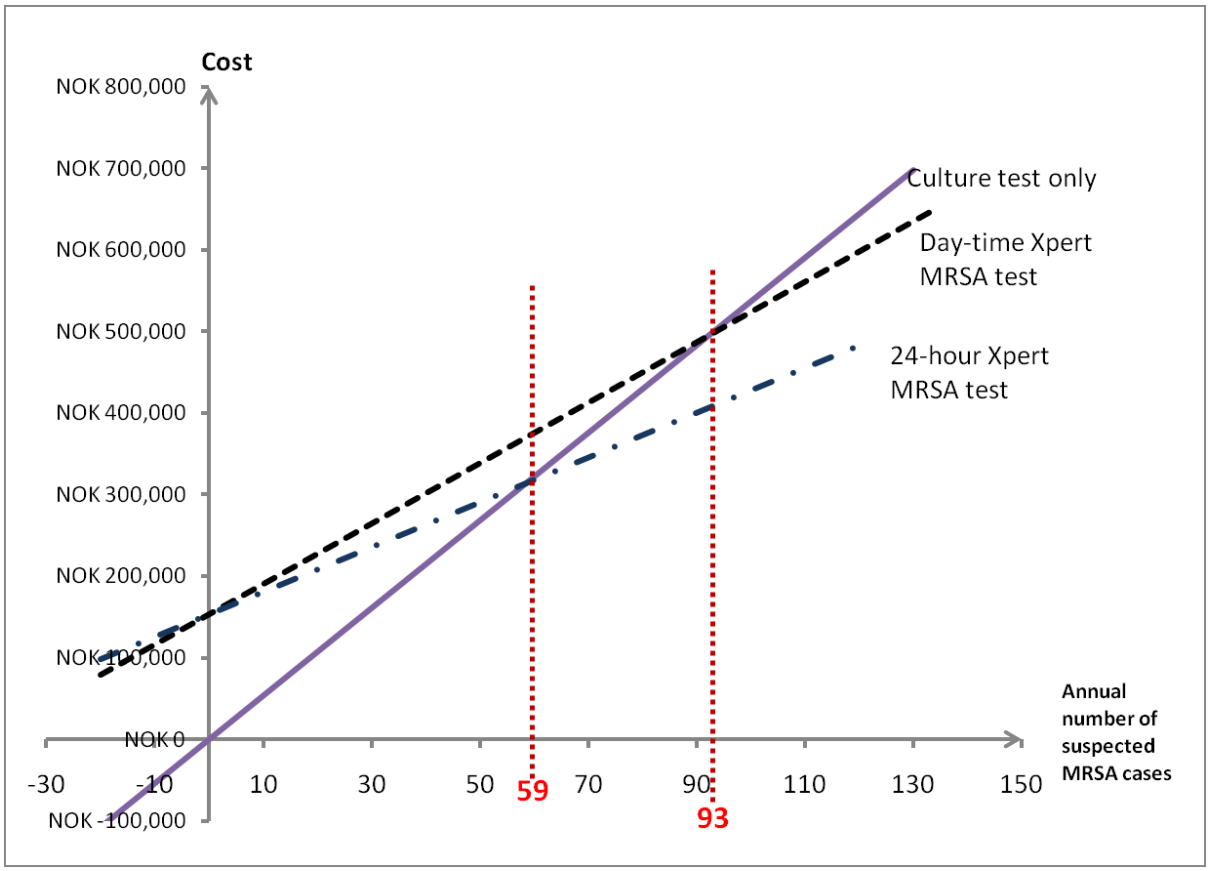
Parameter Description	Base Case Value	Lower Bound	Upper Bound	ICER (Lower Bound)	IECR (Upper Bound)
Number of times of doctors' visits per day per patient	1	2	6	24-hour Xpert dominant	24-hour Xpert dominant
Number of samples per patient	2	4	10	24-hour Xpert dominant	24-hour Xpert dominant
Annual number of suspected MRSA cases	11803	1	15000	Day-time Xpert: NOK756,989,474 per QALY gained 24-hour Xpert: NOK609,382,609 per QALY gained	Day-time Xpert: NOK-50,668,421 per QALY gained 24-hour Xpert: NOK-57,817,391 per QALY gained
Number of times of disinfection according to culture test strategy	3	2	6	24-hour Xpert dominant	24-hour Xpert dominant
Number of times of nurses' visits per day per patient	16	8	24	24-hour Xpert dominant	24-hour Xpert dominant
Number of persons have contact with MRSA patients who get false negative results	4	1	30	24-hour Xpert dominant	24-hour Xpert dominant
Prevalence of MRSA	0.013	0.006	0.02	24-hour Xpert dominant	24-hour Xpert dominant
Proportional nurses working time during isolation	1	0.3	1	24-hour Xpert dominant	24-hour Xpert dominant
Health-related quality of life of non-isolation	0.8	0.85	0.76	24-hour Xpert dominant	24-hour Xpert dominant
Health-related quality of life of isolation	0.76	0.8	0.68	24-hour Xpert dominant	24-hour Xpert dominant
Sensitivity of Xpert MRSA test	0.8875	0.8424	0.938	24-hour Xpert dominant	24-hour Xpert dominant
Specificty of Xpert MRSA test	0.954	0.9411	0.973	24-hour Xpert dominant	24-hour Xpert dominant
Waiting time for patients having tests performed	13.5	13.23	100	24-hour Xpert dominant	24-hour Xpert dominant

Figure 13 Sensitivity Analysis: Expected cost per patient according to the annual number of MRSA suspected patients



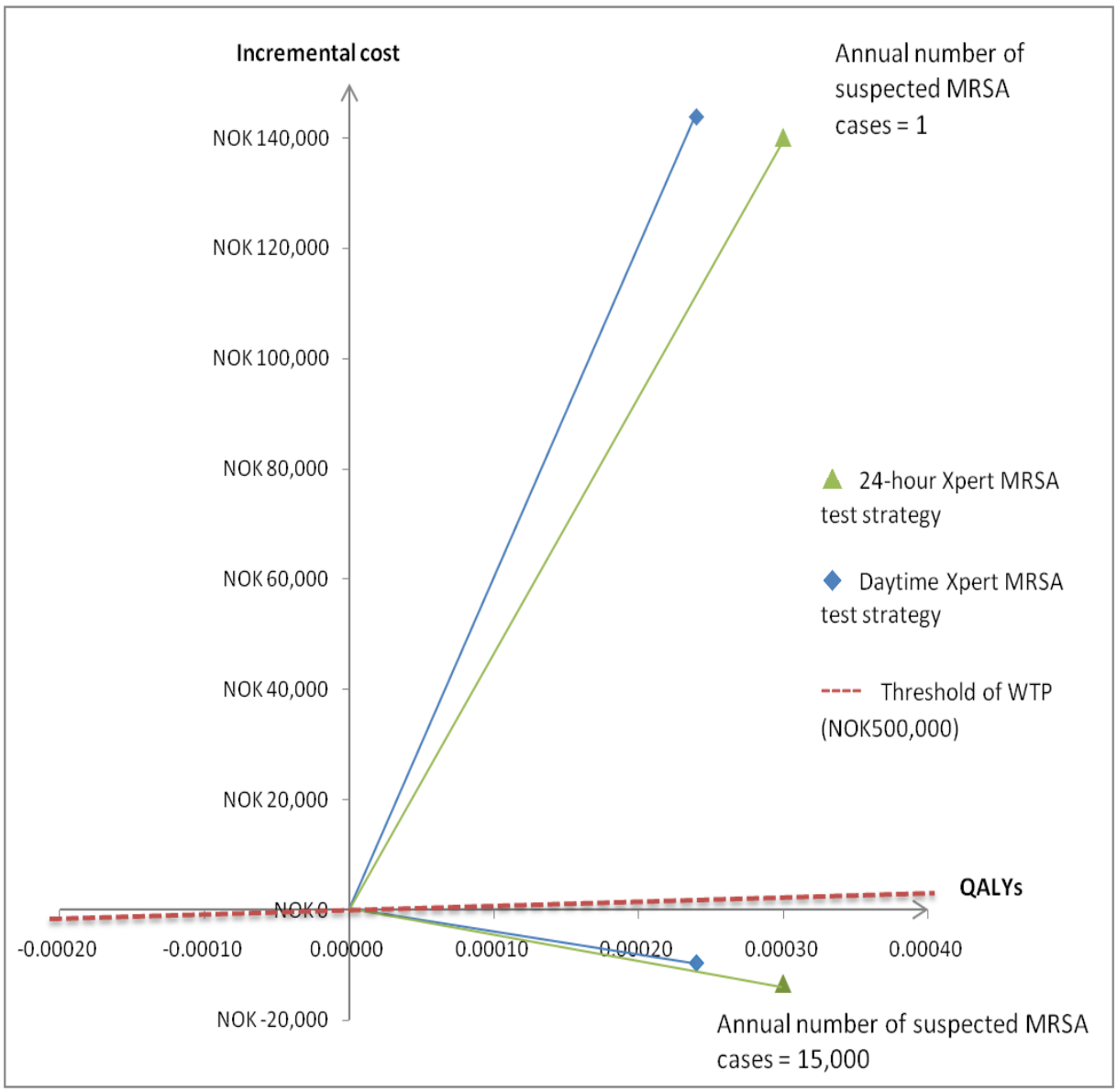
If the annual number of suspected MRSA cases was below 12 per year and all of them were isolated at hospital, the costs of both Xpert strategies outnumbered the costs of the culture test only strategy, but produced more favourable outcomes. With more than 12 suspected MRSA patients annually, the 24-hour Xpert strategy appeared to be less costly than the culture test alone strategy but produced better outcomes. The equivalent threshold for the day-time Xpert strategy was 16. In reality, 70% of the patients with suspected MRSA infection or colonization were isolated at home which is much less costly. Taking account of 70% home isolation, the 24-hour Xpert strategy would be less costly than the culture test strategy when the annual number of suspected MRSA cases was more than 59 (Figure 14).

Figure 14 Sensitivity analysis: The total costs according to the number of suspected MRSA cases



With only one MRSA suspects per year, the cost per QALY would be much greater than the commonly recommended threshold for willingness-to-pay in Norway (NOK500,000) (Figure 15). Only if the annual number of suspected MRSA cases were more than 59 for the 24-hour Xpert strategy or more than 93 for the day-time Xpert strategy, these strategies would be considered cost-effective.

Figure 15 Sensitivity analysis: Cost-effectiveness with one and with 15,000 suspected cases of MRSA per year (the culture test strategy is in the origin of the graph)



8. DISCUSSION

The results of this study indicate that the 24-hour Xpert strategy has lower costs and better outcomes than the two others under a wide range of assumptions.

8.1. Strengths and weaknesses

This study was based on a wide range of input data, most of which were uncertain. In fact, the Treeage model had 39 parameters. In the following, we will focus on some parameters that are particularly uncertain.

It is difficult to value the labour costs during preemptive isolation partly because we lack accurate records on type, wage rate and amount of relevant staff. As far as we know, nurses usually take responsibility for more than only one patient when he or she is on duty. That means that the labour costs we used in the base case analysis may be overestimated, but the sensitivity analysis indicate that realistic changes in labour costs will not change the conclusion keeping the other parameters constant.

Although MRSA may be overlooked even by use of culture test (Struelens, et al. 2009), the risk of false negative test results is believed to be greater with the Xpert MRSA test. False negative results may mean spread of MRSA and increased burden of the disease. The uncertainty of such effects may have been underestimated in the current model which means that the benefits from the Xpert strategies could be overestimated.

Because our model was static, we did not account for the fact that preemptive isolation may reduce the prevalence of MRSA carrying in the population. To the extent that the isolation reduces the prevalence, we have underestimated the effectiveness of the rapid screening test. In contrast, if the sensitivity of the GeneXpert system were much less than 100%, we have overestimated the effectiveness. In the appendix we present a dynamic model that could be used to estimate herd effects.

There is no direct information about how many times of disinfection are performed for each patient with suspect of MRSA infection or colonization. We assumed that the number of disinfections depends on the length of preemptive isolation. In reality, the number of disinfections depends on the patients' medical condition and its treatment and diagnostics. The number can vary considerably across, which makes the number of disinfections quite uncertain.

There is evidence that contact isolation influences patients' quality of life (Gammon 1999). Because we lack own data on quality of life, we used data from a previous study (Wassenberg, et al. 2010). Here, the data are uncertain, but fortunately, the sensitivity analyses indicate that the conclusion is not sensitive to the assumptions we made in this respect.

The analysis included costs and benefits related to patients, but not to staff members. Even staff members are isolated (at home) when they are suspected of having MRSA infection or colonization. Using Xpert MRSA test implies shorter isolation periods for them as well, but this benefit was omitted from the analysis, and this will bias the total benefits from the Xpert strategies down.

There is some evidence that doctors avoid contacting patients who are suspected of MRSA infection or colonization (Halcomb, et al. 2002). There is even evidence that such patients have poorer outcomes than others (Chang, et al. 2003) (Ridenour, et al. 2006). Reduced isolation time could therefore improve patients' outcomes. Lacking hard evidence, such aspects were omitted from the model.

A strength of this study is the large number of information pieces that were collected through interviews and through hospital records. It is impossible to overview all the data, and a decision model is a tool to handle all the data in a logic way.

8.2. Discussion of own findings

The base case analysis indicated that the most important cost-driver in all three strategies was labour costs. In the culture test strategy, approximately 83% of the total costs were attributable to labour costs. This proportion appeared to be lower in the Xpert strategies (65% with the day-time Xpert strategy and 54% with the 24-hour Xpert strategy). The reduction was associated with the length of isolation period because the labour costs of caring patients during isolation represented a large proportion of the total labour costs. With the culture test strategy, disinfection costs were the second largest component. In contrast, disinfection costs and material costs were the second largest cost component with both Xpert strategies. Labour costs and material costs accounted for 98% of the total costs of the 24-hour Xpert strategy. Even though the material costs of the Xpert strategies were approximately three times that of the material costs of the culture test strategy, the large reduction of other components, mainly labour costs, still made the Xpert strategies less costly. This fact indicates that the relative magnitude of staff costs versus material costs determines whether the culture test or the Xpert strategies are most cost-effective. However, regarding the costs saving, what should be kept in mind is that those costs will not be saved literally because nurses and laboratory technicians are still there and get paid. What we called ‘save’ here actually means that the human power resources are freed from one job and can do other presumably beneficial work. The hospital budget will not be reduced, but treatment capacity will be higher.

The interviews indicate that the reduction of unavailable room-hours could be more important in practice than we have imagined. If patients with suspected MRSA infection or colonization need to be isolated at hospital while there is no available room, the patients have to lie on a bed in the hallway. If such patients test positive, the whole area will be blocked and disinfected, and all the persons who have stayed there and can be traced will be screened and isolated. Such interventions not only increase unavailable room-hours but impact the whole prevention system. It implies that, to some extent, using Xpert MRSA test can produce more positive outcomes than what we identified in this study.

During the information collection phase we realized that other factors can influence the overall effect of all the strategies. The first one is the number of patients at high risk of MRSA infection or colonization which are isolated preemptively. According to the guidelines, personnel in patient reception unit are responsible for preliminarily selecting patients for MRSA screening. However, no matter how strict the guidelines are, there is always a possibility that MRSA cases are lost due to carelessness or system deficiencies. If the quality of the preliminary selection is poor, it will weaken the strength of any strategy preventing MRSA. The compliance of contact isolation is another factor related to the effect of prevention. We assumed in this study that both patients and healthcare personnel were 100% compliant with the isolation rules. In practice, however, the level of compliance fluctuates from hospital to hospital and varies with the length of the isolation period. Although the conclusion of this study is unlikely to change for this reason, the overall effect of the prevention of MRSA is probably influenced. Furthermore, we also realized that not everyone agrees on the great importance of MRSA. Some insist that it's important to keep the low prevalence in Norway and it will be too late when it rises up. But some doctors feel the hospital and the government have paid too much attention on MRSA, and resources could have been spent better elsewhere. As the prevalence of MRSA in Norway has increased during last two decades, one may questions if it is realistic to only protect Norway in the current globalized environment. The argument is still out there and that is beyond the extent of this study.

The conclusion of this study is relevant primarily for Norway, or more specifically, for Oslo University Hospital, Ullevål. This is because differences in prevalence of MRSA, policies of preventing MRSA, wage rates and environments of health settings impact the results. Any change in these factors will make differences on the components and the amounts of costs and outcomes. For example, if there were no preemptive isolation accompanied with screening tests, the total costs would be far lower than in this study so that the conclusion could be completely different. In countries such as the Nordic ones with similar prevalence, health care systems and cost structure, the GeneXpert system is likely to represent dominant strategies.

8.3. Findings in other studies

We identified six studies that reported the sensitivity and specificity of the Xpert MRSA test. One of them was a review and one included not only the Xpert MRSA test but also other rapid tests. These studies used traditional culture growth method as the gold standard and classified sensitivities and specificities by which location of body the samples coming from. The studies generally showed that the specificities lie in the range 92%-99.6% while the sensitivities lie in the range 75%-98.3% (Andersen, et al. 2010) (Anonymous n.d.) (Kelly, et al. 2009) (Wolk, et al. 2009a) (Wolk, et al. 2009b) (Rossney, et al. 2008). Five of them only focused on the evaluation of Xpert MRSA assays but one also concerned cost.

One cost study of day-time Xpert MRSA test from Oslo University Hospital, Ullevål measured costs for patients as well as healthcare workers (Andersen, et al. 2010). The period of isolation (for patients) and leave (for healthcare personnel) were both assumed to be three days. Among 41 healthcare workers and 51 patients with suspected MRSA infection or colonization, the Xpert MRSA test saved €895 per healthcare personnel and €502 per patient. The study did not present details of the cost estimates, and no outcome data were included.

With respect to quality of life, three studies targeting psychological impact of isolation due to infection were identified (Tarzi, et al. 2001) (Catalano, et al. 2003) (Wassenberg, et al. 2010). One of them targeted older adult population and used the Abbreviated Mental Test Score, the Barthel Index, The Geriatric Depression Scale-Short form and the Profile of Mood States to measure the impact (Tarzi, et al. 2001). The mean score of the isolated group was 15 and 8.6 of the non-isolated group (Catalano, et al. 2003). Another study targeted hospitalized patients and used Hamilton Anxiety Rating Scale and Hamilton Depression Rating Scale. The authors performed a study with 1-week and 2-week follow-up. The study showed that patients in isolation had significantly higher scores on both the anxiety and depression scales at the time of follow-up than did patients who were not isolated but the difference was not significant. The third study measured psychological impact of short-term

isolation in hospital patients with Hospital Anxiety and Depression Scale (Wassenberg, et al. 2010). This study indicated that the short-term isolation do not influence the hospitalized patients' levels of anxiety and depression.

8.4. Policy implications

The results of this study indicate that hospitals with more than 59 MRSA suspected patients per year may do well in using Xpert MRSA test on 24-hour basis accompanied with the culture test. It should be noted, however, that this conclusion rest on labour savings from less preemptive isolation, and the budget impact of the Xpert strategies may be small if the hospital management does not reduce nurse staffing.

Even though this study concluded that a switch to the Xpert strategies may be favourable for larger hospitals, still some pieces of information are uncertain. Further research in the area should therefore focus on the sensitivity and specificity of the Xpert MRSA test and the impact of contact isolation for hospitalized patients on HRQOL.

8.5. Conclusion

The results of this study indicate that using the Xpert MRSA test on 24-hour basis accompanied with the culture test is more effective and less costly than using the culture test alone even for low number of MRSA suspected patients.

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10. APPENDIX

10.1. Parameters Used in the Model

Table 11 Parameters in Decision Tree

Name	Description	Formula	Value	Low	High
CCapital_Culture	Capital cost of culture test	-	0	-	-
CInstrumentDisinfect	Cost of instruments used in disinfection per time	-	270.95	-	-
CLabourDisinfect	Labour cost of disinfection per hour	-	207.01	-	-
CLabourIsolation	Labour cost of isolation time per hour	-	216.59	-	-
CLabourLab	Labour cost per hour of technician in laboratory	-	230.61	-	-
CMaterialCultureLab	Material costper culture plate	-	11.1	-	-
CMaterialDisposable	Cost of disposable materials per person-hour	135000/31.5/1950	2.2	-	-
CMaterialRoomVisit	Material cost of one time of room visit during isolation	-	12.54	-	-
CMaterialTestNurse	Material cost per test by nurses	1.77*Number_Samples+CMaterial RoomVisit	19.62	19.62	30.24
CMaterialXpertLab	Material cost per Xpert MRSA package	-	360	-	-
DoctorVisit	Number of doctor visits per day	-	2	2	6
EAC_Xpert	Equivalent annual cost of GeneXpert System	-	152572	-	-
HRQOL_1	Health-related quality of life of non-isolation	-	0.8	0.85	0.76
HRQOL_2	Health-related quality of life of isolation	-	0.76	0.8	0.68
Number_Samples	Number of samples per test	-	4	4	10
Number_TestAnnual	Annual number of MRSA tests	-	11803	1	15000
NumDisinfect_Culture	Number of times of disinfection according to culture test strategy	-	3	2	6
NumDisinfect_Xpert24hNega	Number of times of disinfection according to 24-hour Xpert MRSA test strategy when Xpert result is negative	-	0	-	-
NumDisinfect_Xpert24hPosi	Number of times of disinfection according to 24-hour Xpert MRSA test strategy when Xpert result is positive	NumDisinfect_Culture-1	2	1	5
NumDisinfect_XpertDaytimeNega	Number of times of disinfection according to day-time Xpert MRSA test strategy when Xpert result is negative	NumDisinfect_XpertDaytimePosi-2	1	0	4
NumDisinfect_XpertDaytimePosi	Number of times of disinfection according to day-time Xpert MRSA test strategy when Xpert result is positive	NumDisinfect_Culture	3	2	6
NurseVisit	Number of nurse visits per day	-	16	8	24
PersonAtRisk	Persons have contact with MRSA patients	-	4	1	30
Prevalence	Prevalence of MRSA	-	0.013	0.006	0.02
ProbCulNega_XpertNega	Probability of culture negative in Xpert MRSA negative	(1-Prevalence)*Spec/(Spec+(1-Sens-Spec)*Prevalence)	0.9989	-	-
ProbCulPosi_XpertPosi	Probability of culture positive in Xpert MRSA positive	Sens*Prevalence/((1-Spec)*(1-Prevalence)+Sens*Prevalence)	0.1904	-	-

ProbXpertPosi	Probability of Xpert MRSA positive	(1-Spec)*(1-Prevalence)+Sens*Prevalence	0.0470	-	-
PropWorkLoadIsolation	Proportion of working load used in isolation by nurses	-	1	0.3	1
Sens	Sensitivity of Xpert MRSA test	-	0.8941	0.856	0.933
Spec	Specificty of Xpert MRSA test	-	0.9616	0.948	0.976
TimeLabourDisinfect	Working time used by personnel in disinfetion per time	-	2.5	-	-
TimeMachineDisinfect	Working time used by machine alone in disinfection per time	-	4.5	-	-
Time_CultureGrowing	Growing time of culture test	-	48	-	-
Time_Transport	Transport time from units to laboratory	5/60	0.08	-	-
Time_XpertReacting	Reacting time of Xpert test	75/60	-	-	-
WaitingTime	Waiting time for patients for having tests performed	-	13.5	13.23	13.57
WT_CultureLab	Working time per culture test in laboratory	18.5/60	0.31	-	-
WT_TestNurse	Working time per test by nurses	10/60	0.17	-	-
WT_XpertLab	Working time per Xpert test in laboratory	20/60	0.33	-	-

Table 12 Calculation formulas for payoffs according to the culture test strategy

		Payoff				
	Branch	Cost	Time of Isolation	Number of Unavailable Room-hour	QALD	QALY
Culture test only	Both Culture positive and Culture negative	WT_TestNurse*CLabourIsolation+WT_CultureLab*CLabourLab*Number_Samples+CMaterialTestNurse+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+CLabourIsolation*PropWorkLoadIsolation*(WT_TestNurse*CLabourIsolation+WT_CultureLab*CLabourLab*Number_Samples+CMaterialTestNurse+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WaitingTime)+(CInstrumentDisinfect+CLabourDisinfect*TimeLabourDisinfect)*NumDisinfect_Culture+CMaterialRoomVisit*Round((DoctorVisit+NurseVisit)*(WT_TestNurse*CLabourIsolation+WT_CultureLab*CLabourLab*Number_Samples+CMaterialTestNurse+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WaitingTime)/24)	WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CultureGrowing	WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+(TimeLabourDisinfect+TimeMachineDisinfect)*NumDisinfect_Culture	(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing)*HRQOL_2/24/365	(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing)*HRQOL_2/24

Table 13 Calculation formulas for payoffs according to the day-time Xpert strategy

	Payoff				
Branch	Cost	Time of Isolation	Number of Unavailable Room-hour	QALD	QALY
Xpert MRSA positive - Culture positive	WT_TestNurse*CLabourIsolation+WT_CultureLab*CLabourLab*Number_Samples+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WT_XpertLab*CLabourLab*Number_Samples+CMaterialTestNurse+CMaterialXpertLab*Number_Samples+CMaterialDisposable*WT_XpertLab*Number_Samples+EAC_Xpert/Number_TestAnnual+CLabourIsolation*PropWorkLoadIsolation*(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)+(CInstrumentDisinfect+CLabourDisinfect*TimeLabourDisinfect)*NumDisinfect_XpertDaytimePosi+CMaterialRoomVisit*Round((DoctorVisit+NurseVisit)*(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)/24)	WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime	WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime+(TimeLabourDisinfect+TimeMachineDisinfect)*NumDisinfect_XpertDaytimePosi	(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)*HRQOL_2/24	(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)*HRQOL_2/24/365
Xpert MRSA positive - Culture negative	WT_TestNurse*CLabourIsolation+WT_CultureLab*CLabourLab*Number_Samples+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WT_XpertLab*CLabourLab*Number_Samples+CMaterialTestNurse+CMaterialXpertLab*Number_Samples+CMaterialDisposable*WT_XpertLab*Number_Samples+EAC_Xpert/Number_TestAnnual+CLabourIsolation*PropWorkLoadIsolation*(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)+(CInstrumentDisinfect+CLabourDisinfect*TimeLabourDisinfect)*NumDisinfect_XpertDaytimePosi+CMaterialRoomVisit*Round((DoctorVisit+NurseVisit)*(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)/24)	WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime	WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime+(TimeLabourDisinfect+TimeMachineDisinfect)*NumDisinfect_XpertDaytimePosi	(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)*HRQOL_2/24	(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)*HRQOL_2/24/365

Xpert MRSA negative - Culture positive	(ProbXpertPosi*(WT_TestNurse*CLabourIsolation+WT_CultureLab*CLabourLab*Number_Samples+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WT_XpertLab*CLabourLab*Number_Samples+CMaterialTestNurse+CMaterialXpertLab*Number_Samples+CMaterialDisposable*WT_XpertLab*Number_Samples+EAC_Xpert/Number_TestAnnual+CLabourIsolation*PropWorkLoadIsolation*(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)+(CInstrumentDisinfect+CLabourDisinfect*TimeLabourDisinfect)*NumDisinfect_XpertDaytimePosi+CMaterialRoomVisit*Round((DoctorVisit+NurseVisit)*(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)/24))+(1-ProbXpertPosi)*(WT_TestNurse*CLabourIsolation+WT_CultureLab*CLabourLab*Number_Samples+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WT_XpertLab*CLabourLab*Number_Samples+CMaterialTestNurse+CMaterialXpertLab*Number_Samples+CMaterialDisposable*WT_XpertLab*Number_Samples+EAC_Xpert/Number_TestAnnual+CLabourIsolation*PropWorkLoadIsolation*(WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime)+(CInstrumentDisinfect+CLabourDisinfect*TimeLabourDisinfect)*NumDisinfect_XpertDaytimeNega+CMaterialRoomVisit*Round((DoctorVisit+NurseVisit)*(WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime)/24)))*PersonAtRisk+WT_TestNurse*CLabourIsolation+WT_CultureLab*CLabourLab*Number_Samples+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WT_XpertLab*CLabourLab*Number_Samples+CMaterialTestNurse+CMaterialXpertLab*Number_Samples+CMaterialDisposable*WT_XpertLab*Number_Samples+EAC_Xpert/Number_TestAnnual+CLabourIsolation*PropWorkLoadIsolation*(WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime)+(CInstrumentDisinfect+CLabourDisinfect*TimeLabourDisinfect)*NumDisinfect_XpertDaytimeNega+CMaterialRoomVisit*Round((DoctorVisit+NurseVisit)*(WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime)/24)	(ProbXpertPosi*(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)+(1-ProbXpertPosi)*(WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime))*PersonAtRisk+WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime	(ProbXpertPosi*(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime+(TimeLabourDisinfect+TimeMachineDisinfect)*NumDisinfect_XpertDaytimePosi)+(1-ProbXpertPosi)*(WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime+(TimeLabourDisinfect+TimeMachineDisinfect)*NumDisinfect_XpertDaytimeNega))*PersonAtRisk+WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime+(TimeLabourDisinfect+TimeMachineDisinfect)*NumDisinfect_XpertDaytimeNega	(ProbXpertPosi*(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)*HRQOL_2/24+(1-ProbXpertPosi)*((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime)*HRQOL_2+(WT_CultureLab*Number_Samples+Time_CulureGrowing-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1)/24)*PersonAtRisk+((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime)*HRQOL_2+(WT_CultureLab*Number_Samples+Time_CulureGrowing-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1)/24	(ProbXpertPosi*(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)*HRQOL_2/24/365+(1-ProbXpertPosi)*((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime)*HRQOL_2+(WT_CultureLab*Number_Samples+Time_CulureGrowing-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1)/24/365)*PersonAtRisk+((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime)*HRQOL_2+(WT_CultureLab*Number_Samples+Time_CulureGrowing-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1)/24/365

Xpert MRSA negative - Culture negative	WT_TestNurse*CLabourIsolation+WT_CultureLab*CLabourLab*Number_Samples+CMaterialTestNurse+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WT_TestNurse*CLabourIsolation+WT_XpertLab*CLabourLab*Number_Samples+CMaterialTestNurse+CMaterialXpertLab*Number_Samples+CMaterialDisposable*WT_XpertLab*Number_Samples+EAC_Xpert/Number_TestAnnual-CMaterialTestNurse-WT_TestNurse*CLabourIsolation+CLabourIsolation*PropWorkLoadIsolation*(WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime)+(CInstrumentDisinfect+CLabourDisinfect*TimeLabourDisinfect)*NumDisinfect_XpertDaytimeNega+CMaterialRoomVisit*Round((DoctorVisit+NurseVisit)*(WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime)/24)	WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime	WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime+(TimeLabourDisinfect+TimeMachineDisinfect)*NumDisinfect_XpertDaytimeNega	((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime)*HRQOL_2+(WT_CultureLab*Number_Samples+Time_CulureGrowing-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1)/24	((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+WaitingTime)*HRQOL_2+(WT_CultureLab*Number_Samples+Time_CulureGrowing-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1)/24/365

Table 14 Calculation formulas for payoffs according to the 24-hour Xpert strategy

		Payoff				
	Branch	Cost	Time of Isolation	Number of Unavailable Room-hour	QALD	QALY
Xpert MRSA test on 24-hour basis	Xpert MRSA positive - Culture positive	WT_TestNurse*CLabourIsolation+WT_CultureLab*(CLabourLab*7/24+CLabourLab*1.45*17/24)*Number_Samples+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WT_XpertLab*(CLabourLab*7/24+CLabourLab*1.45*17/24)*Number_Samples+CMaterialTestNurse+CMaterialXpertLab*Number_Samples+CMaterialDisposable*WT_XpertLab*Number_Samples+EAC_Xpert/Number_TestAnnual+CLabourIsolation*PropWorkLoadIsolation*WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+(CInstrumentDisinfect+CLabourDisinfect*TimeLabourDisinfect)*NumDisinfect_Xpert24hPosi+CMaterialRoomVisit*Round((DoctorVisit+NurseVisit)*WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing/24)	WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing	WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+(TimeLabourDisinfect+TimeMachineDisinfect)*NumDisinfect_Xpert24hPosi	((WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)*HRQOL_2)/24	((WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)*HRQOL_2)/24/365
	Xpert MRSA positive - Culture negative	WT_TestNurse*CLabourIsolation+WT_CultureLab*(CLabourLab*7/24+CLabourLab*1.45*17/24)*Number_Samples+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WT_XpertLab*(CLabourLab*7/24+CLabourLab*1.45*17/24)*Number_Samples+CMaterialTestNurse+CMaterialXpertLab*Number_Samples+CMaterialDisposable*WT_XpertLab*Number_Samples+EAC_Xpert/Number_TestAnnual+CLabourIsolation*PropWorkLoadIsolation*WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+(CInstrumentDisinfect+CLabourDisinfect*TimeLabourDisinfect)*NumDisinfect_Xpert24hPosi+CMaterialRoomVisit*Round((DoctorVisit+NurseVisit)*WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing/24)	WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing	WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+(TimeLabourDisinfect+TimeMachineDisinfect)*NumDisinfect_Xpert24hPosi	((WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing)*HRQOL_2+WaitingTime*HRQOL_1)/24	((WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing)*HRQOL_2+WaitingTime*HRQOL_1)/24/365

Xpert MRSA test on 24-hour basis	Xpert MRSA negative - Culture positive	(ProbXpertPosi*(WT_TestNurse*CLabourIsolation+WT_CultureLab*(CLabourLab*7/24+CLabourLab*1.45*17/24)*Number_Samples+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WT_XpertLab*(CLabourLab*7/24+CLabourLab*1.45*17/24)*Number_Samples+CMaterialTestNurse+CMaterialXpertLab*Number_Samples+CMaterialDisposable*WT_XpertLab*Number_Samples+EAC_Xpert/Number_TestAnnual+CLabourIsolation*PropWorkLoadIsolation*WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+(CInstrumentDisinfect+CLabourDisinfect*TimeLabourDisinfect)*NumDisinfect_Xpert24hPosi+CMaterialRoomVisit*Round((DoctorVisit+NurseVisit)*WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing/24))+(1-ProbXpertPosi)*(WT_TestNurse*CLabourIsolation+WT_CultureLab*(CLabourLab*7/24+CLabourLab*1.45*17/24)*Number_Samples+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WT_XpertLab*(CLabourLab*7/24+CLabourLab*1.45*17/24)*Number_Samples+CMaterialTestNurse+CMaterialXpertLab*Number_Samples+CMaterialDisposable*WT_XpertLab*Number_Samples+EAC_Xpert/Number_TestAnnual+CLabourIsolation*PropWorkLoadIsolation*WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+(CInstrumentDisinfect+CLabourDisinfect*TimeLabourDisinfect)*NumDisinfect_Xpert24hNega+CMaterialRoomVisit*Round((DoctorVisit+NurseVisit)*WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting/24)))*PersonAtRisk+WT_TestNurse*CLabourIsolation+WT_CultureLab*(CLabourLab*7/24+CLabourLab*1.45*17/24)*Number_Samples+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WT_XpertLab*(CLabourLab*7/24+CLabourLab*1.45*17/24)*Number_Samples+CMaterialTestNurse+CMaterialXpertLab*Number_Samples+CMaterialDisposable*WT_XpertLab*Number_Samples+EAC_Xpert/Number_TestAnnual+CLabourIsolation*PropWorkLoadIsolation*WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+(CInstrumentDisinfect+CLabourDisinfect*TimeLabourDisinfect)*NumDisinfect_Xpert24hNega+CMaterialRoomVisit*Round((DoctorVisit+NurseVisit)*WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting/24)	(ProbXpertPosi*WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+(1-ProbXpertPosi)*WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting)*PersonAtRisk+WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting	(ProbXpertPosi*(WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+(TimeLabourDisinfect+TimeMachineDisinfect)*NumDisinfect_Xpert24hPosi)+(1-ProbXpertPosi)*(WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+(TimeLabourDisinfect+TimeMachineDisinfect)*NumDisinfect_Xpert24hNega))*PersonAtRisk+WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+(TimeLabourDisinfect+TimeMachineDisinfect)*NumDisinfect_Xpert24hNega	((ProbXpertPosi*(((WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)*HRQOL_2)*ProbCulPosi_XpertPosi+((WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing)*HRQOL_2+WaitingTime*HRQOL_1)*(1-ProbCulPosi_XpertPosi))+(1-ProbXpertPosi)*(ProbCulNega_XpertNega*((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting)*HRQOL_2+(WT_CultureLab*Number_Samples+TimeCultureGrowing+WaitingTime-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1)+(1-ProbCulNega_XpertNega)*((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting)*HRQOL_2+(WT_CultureLab*Number_Samples+TimeCultureGrowing-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1+WaitingTime*HRQOL_2)))*PersonAtRisk+((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting)*HRQOL_2+(WT_CultureLab*Number_Samples+TimeCultureGrowing-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1+WaitingTime*HRQOL_2))/24	((ProbXpertPosi*(((WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing+WaitingTime)*HRQOL_2)*ProbCulPosi_XpertPosi+((WT_TestNurse+Time_Transport+WT_CultureLab*Number_Samples+Time_CulureGrowing)*HRQOL_2+WaitingTime*HRQOL_1)*(1-ProbCulPosi_XpertPosi))+(1-ProbXpertPosi)*(ProbCulNega_XpertNega*((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting)*HRQOL_2+(WT_CultureLab*Number_Samples+TimeCultureGrowing+WaitingTime-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1)+(1-ProbCulNega_XpertNega)*((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting)*HRQOL_2+(WT_CultureLab*Number_Samples+TimeCultureGrowing-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1+WaitingTime*HRQOL_2)))*PersonAtRisk+((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting)*HRQOL_2+(WT_CultureLab*Number_Samples+TimeCultureGrowing-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1+WaitingTime*HRQOL_2))/24/365

Xpert MRSA test on 24-hour basis	Xpert MRSA negative - Culture negative	WT_TestNurse*CLabourIsolation+WT_CultureLab*(CLabourLab*7/24+CLabourLab*1.45*17/24)*Number_Samples+CMaterialCultureLab*Number_Samples+CMaterialDisposable*WT_CultureLab*Number_Samples+CCapital_Culture+WT_XpertLab*(CLabourLab*7/24+CLabourLab*1.45*17/24)*Number_Samples+CMaterialTestNurse+CMaterialXpertLab*Number_Samples+CMaterialDisposable*WT_XpertLab*Number_Samples+EAC_Xpert/Number_TestAnnual+CLabourIsolation*PropWorkLoadIsolation*WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+(CInstrumentDisinfect+CLabourDisinfect*TimeLabourDisinfect)*NumDisinfect_Xpert24hNega+CMaterialRoomVisit*Round((DoctorVisit+NurseVisit)*WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting/24)	WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting	WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting+(TimeLabourDisinfect+TimeMachineDisinfect)*NumDisinfect_Xpert24hNega	((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting)*HRQOL_2+(WT_CultureLab*Number_Samples+TimeCultureGrowing+WaitingTime-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1)/24	(((WT_TestNurse+Time_Transport+WT_XpertLab*Number_Samples+Time_XpertReacting)*HRQOL_2+(WT_CultureLab*Number_Samples+TimeCultureGrowing+WaitingTime-WT_XpertLab*Number_Samples-Time_XpertReacting)*HRQOL_1)/24/365

10.2. Probabilities

From July 22nd to Sept 15th, there were 410 pairs of tests (both culture and rapid tests for each person). As the culture test was regarded as the golden standard, the results of culture tests were used as the reference. Then, the specificity of the rapid test was 98.77% and sensitivity was 100.00%.

Table 15 Xpert test results using culture test as the reference

	Culture positive	Culture negative	Total
Xpert MRSA positive	2	5	7
Xpert MRSA negative	0	403	403
Total	2	408	410

Table 16 Statistics of sensitivities and specificities from 6 identified studies and data collected at Oslo University Hospital, Ullevål

			Statistic	Std. Error
Sensitivity	Mean		.88749	.021711
	95% Confidence Interval for Mean	Lower Bound	.84238	
		Upper Bound	.93795	
	Median		.87500	
	Variance		.006	
	Std. Deviation		.075207	
	Minimum		.750	
	Maximum		1.000	
Specificity	Mean		.954029	.0072292
	95% Confidence Interval for Mean	Lower Bound	.941147	
		Upper Bound	.972970	
	Median		.949000	
	Variance		.001	
	Std. Deviation		.0250426	
	Minimum		.9200	
	Maximum		.9960	

10.3. Original Costs Data

10.3.1. Labour Costs

Table 17 Cost of microbiologist in laboratory

Konto	Beskrivelse	Sum
	Årslønn	347,097
	Forventet økning vedr lønns	0%
	Antall timer pr år	1,950
	Årslønn	347,097.00
5000	Grunnlønn 10,88 måneder	314,701.28
5095	Feriepenger	37,764.15
5415	Pensjon	41,651.64
5400	Arb avgift grunnlønn	44,372.88
5408	Arb avgift feriepenger	5,324.75
5409	Arb avgift Pensjon	5,872.88
	Total Lønnskostnad	**449,687.58**
	Årlig lønnskostnad inkl sos	**449,687.58**
	Timelønn	**230.61**
	1 årsverk =1950 timer	
	Dagsverk pr måned: 21,6667	

Table 18 Cost of nurses

Konto	Beskrivelse	Sum
	Årslønn	326,000
	Forventet økning vedr lønns	0%
	Antall timer pr år	1,950
	Årslønn	326,000.00
5000	Grunnlønn 10,88 måneder	295,573.33
5095	Feriepenger	35,468.80
5415	Pensjon	39,120.00
5400	Arb avgift grunnlønn	41,675.84
5408	Arb avgift feriepenger	5,001.10
5409	Arb avgift Pensjon	5,515.92
	Total Lønnskostnad	**422,354.99**
	Årlig lønnskostnad inkl sos	**422,354.99**
	Timelønn	**216.59**
	1 årsverk =1950 timer	
	Dagsverk pr måned: 21,6667	

10.3.2. Material Costs

Table 19 Material cost of tests

Name	Per unit
Swab & Tube	NOK1.77
Selective culture plate	NOK11.10
MRSA package	NOK360.00

Table 20 Unit cost of respirator, gown, gloves and cap

Name	Per unit
Respirators	NOK 1.11
Gowns	NOK 5.77
Gloves	NOK 5.66
Caps	NOK 0.50

Table 21 Material cost of disinfection

Material for disinfection	
1 plaster + 1 tape	NOK1,018.75
Number of rooms covered	105
Cost per room	**NOK9.70**
1 bottle of gas	NOK500.00
m^3 covered	320
m^3 per room	48
Cost per room	**NOK75.69**
1 role of black plastic bag	NOK56.73
1 role of yellow plastic bag	NOK43.75
Units per role	48
Units of black plastic bag per room	2
Units of yellow plastic bag per room	4
Cost per room	**NOK6.01**
1 bottle of soap	NOK14.80
Number of rooms covered	105
Cost per room	**NOK0.14**
2 gowns per room	NOK11.54
2 masks per room	NOK2.21
2 caps per room	NOK1.00
16 pairs of gloves per room	NOK90.56
Cost per room	**NOK105.31**
Total cost per room	**NOK196.85**

10.3.3. Capital cost

GeneXpert System was accounted a technical installment in building in this study. According to the Budget 2009 (Anonymous 2009), it was in group j which gained a 10% depreciation rate. The discount rate has kept being 4% in the last few years in Norway. Finally, mva (market value added) is 25% in Norway.

Table 22 Cost of GeneXpert System

GeneXpert System		
Price	NOK	1,980,000.00
Volume		2
Price per unit	NOK	990,000.00
mva		25%
Cost per unit	NOK	1,237,500.00

EAC = 1237500/8.1109 = NOK152,572.46

Capital cost per test = $\frac{\text{EAC}}{\text{Annual amount of MRSA tests}} = \frac{152572.46}{11803}$ = NOK12.93

Price of each cleaning robot = NOK190,000.00

EAC = 190000/2.7751 = NOK68,466.00

Quoting the director of cleaning department at Oslo University Hospital, Ullevål, the average number of using robots was approximately 77 per month. Even though not all of them resulted from MRSA-related isolation, the average share was the same. Capital cost per disinfection = $\frac{\text{EAC}}{12\times77} = \frac{68466}{924}$ = NOK74.10

10.3.4. Summary of Cost Calculations

Table 23 Detail numbers used in the cost calculations of tests

	Culture test	Day-time Xpert	24-hour Xpert	
Working time per test (laboratory)	1.233 hours	2.567 hours	2.567 hours	
Cost per working hour (laboratory)	NOK 230.61	NOK 230.61	NOK 230.61	NOK 334.38
Cost per test (laboratory)	**NOK 284.42**	**NOK 591.90**	**NOK 780.56**	
Working time per test (nurse)	0.167 hours	0.167 hours	0.167 hours	
Cost per working hour (nurse)	NOK 216.59	NOK 216.59	NOK 216.59	
Cost per test (nurse)	**NOK 36.10**	**NOK 36.10**	**NOK 36.10**	
Labour cost per test	**NOK 321**	**NOK 628**	**NOK 817**	
Material cost per test (nurse)	NOK 19.62	NOK 19.62	NOK 19.62	
Culture plate/MRSA package	NOK 44.40	NOK 1,484.40	NOK 1,484.40	
Disposable materials cost (laboratory)	NOK 2.71	NOK 5.64	NOK 5.64	
Material cost per test	**NOK 67**	**NOK 1,510**	**NOK 1,510**	
Capital cost per test	**NOK 0**	**NOK 13**	**NOK 13**	
Cost per test	**NOK 387**	**NOK 2,151**	**NOK 2,339**	

The extra number under "Xpert MRSA test (24-hour)" was the labour cost per working hour of night duty in the laboratory. Cost per test (laboratory) = $({}^{7}/_{24} \times 231 + {}^{17}/_{24} \times 334) \times 2.6$ = NOK781

Table 24 Detail numbers of cost calculations of preemptive isolation

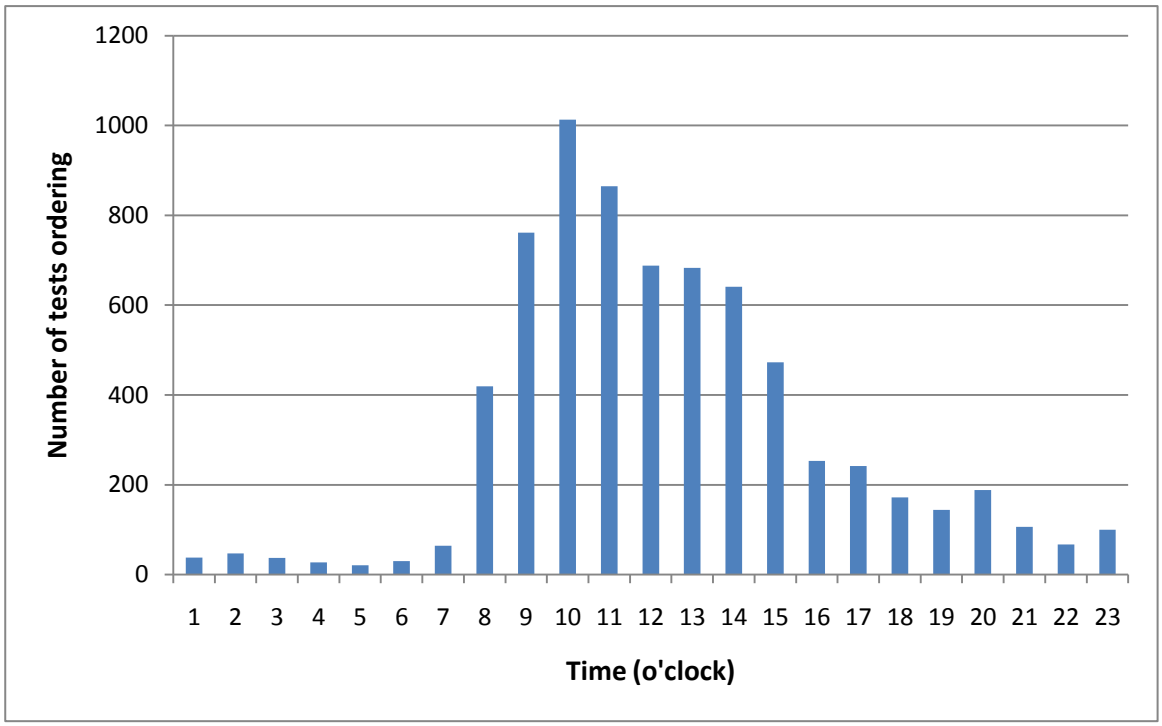
	Culture test	Day-time Xpert		24-hour Xpert	
Result		Positive	Negative	Positive	Negative
Cost per working hour (nurse)	NOK 216.59	NOK 216.59	NOK 216.59	NOK 216.59	NOK 216.59
Working time per isolation (nurse)	62.983 hours	62.983 hours	16.333 hours	49.483 hours	2.833 hours
Proportion of working load used in isolation by nurses	*100%*				
Labour cost of preemptive isolation	**NOK 13,642**	**NOK 13,642**	**NOK 3,538**	**NOK 10,718**	**NOK 614**
Capital cost of disinfection	NOK 74.10	NOK 74.10	NOK 74.10	NOK 74.10	NOK 74.10
Material cost of room disinfection per time	NOK 196.85	NOK 196.85	NOK 196.85	NOK 196.85	NOK 196.85
Cost per working hour (cleaning staff)	NOK 207.01	NOK 207.01	NOK 207.01	NOK 207.01	NOK 207.01
Times of room disinfection	*3*	*3*	*1*	*2*	*0*
Disinfection cost of preemptive isolation	**NOK 2,365**	**NOK 2,365**	**NOK 788**	**NOK 1,577**	**NOK 0**
Material cost during preemptive isolation	**NOK 589**	**NOK 589**	**NOK 150**	**NOK 464**	**NOK 25**
Cost of preemptive isolation	**NOK 16,596**	**NOK 16,596**	**NOK 4,477**	**NOK 12,759**	**NOK 639**

10.4. Original Health Benefits Data

10.4.1. Time of Preemptive Isolation

According to the laboratory register system, 11,803 MRSA tests were ordered in 2009 for patients. Among these tests, 4,724 tests were not registered by time they were ordered. The graph following showed the distribution of the rest 7,079 tests according to ordering time.

Figure 16 Distribution of MRSA tests ordering at Oslo University Hospital, Ullevål (2009)



In the rest 7,079 tests, 4,589 tests were ordered within working time (8.00~14.15), leading to 2,490 tests would maintain waiting time from 0.5 hours to 17.375 hours.

Figure 17 Distribution of cases according to how long they waited for tests

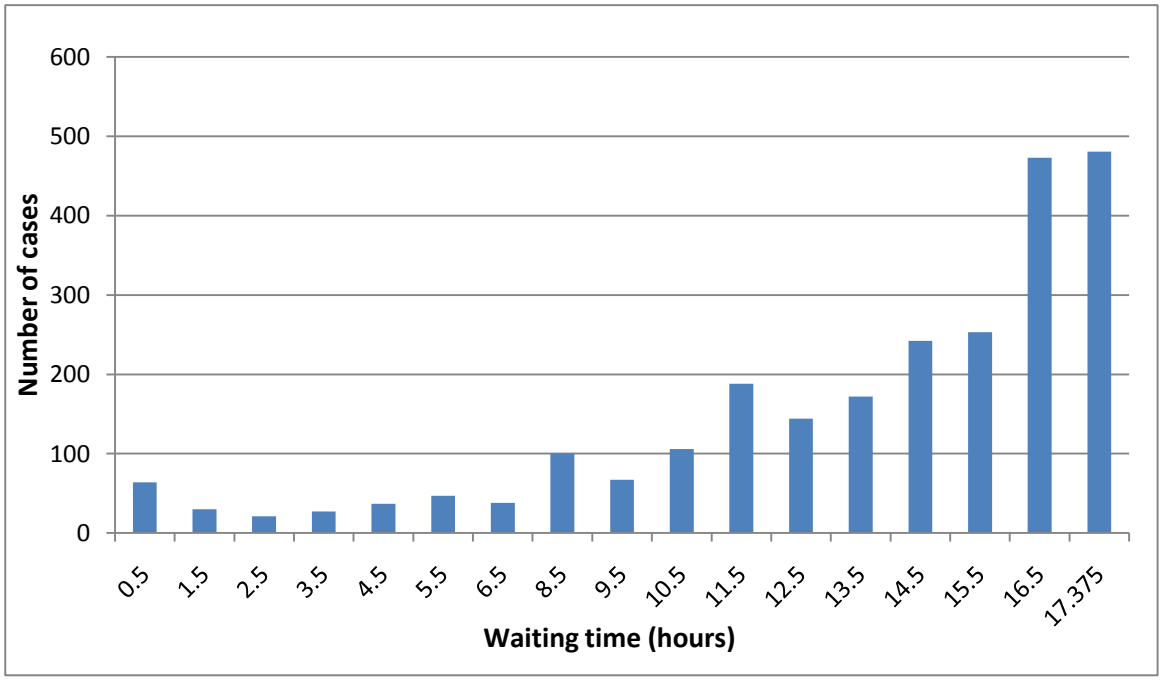


Table 25 Frequency of cases according to waiting hours

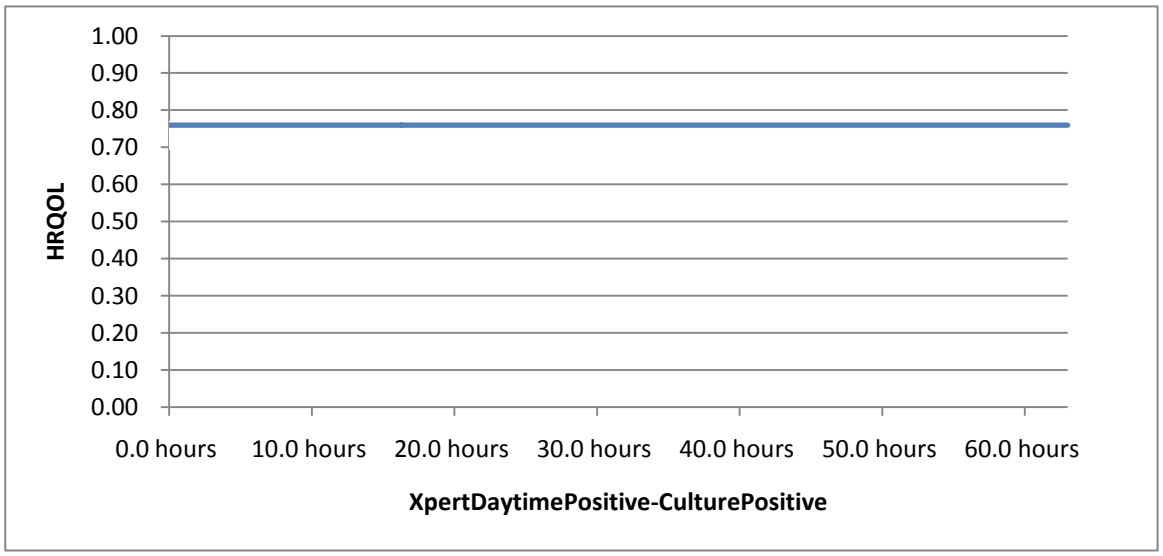
Waiting time (hours)	Number of cases
17.375	481
16.5	473
15.5	253
14.5	242
13.5	172
12.5	144
11.5	188
10.5	106
9.5	67
8.5	100
6.5	38
5.5	47
4.5	37
3.5	27
2.5	21
1.5	30
0.5	64
Total	**2490**

Table 26 Statistics of waiting time

Statistics		Value
Mean of waiting time		13.40
	Lower bound	13.23
	Higher bound	13.57
Variance		18.63229
S.D		4.316514
Median		14.5
	25%	11.5
	75%	16.5

10.4.2. Health-Related Quality of Life

Figure 18 Health-Related Quality of Life (HRQOL) when Xpert MRSA test produced a true positive result in the day-time Xpert strategy



HRQOLs of the culture test strategy (regardless of results) were the same as Figure 18.

Figure 19 Health-Related Quality of Life (HRQOL) when Xpert MRSA test produced a false positive result in the day-time Xpert strategy

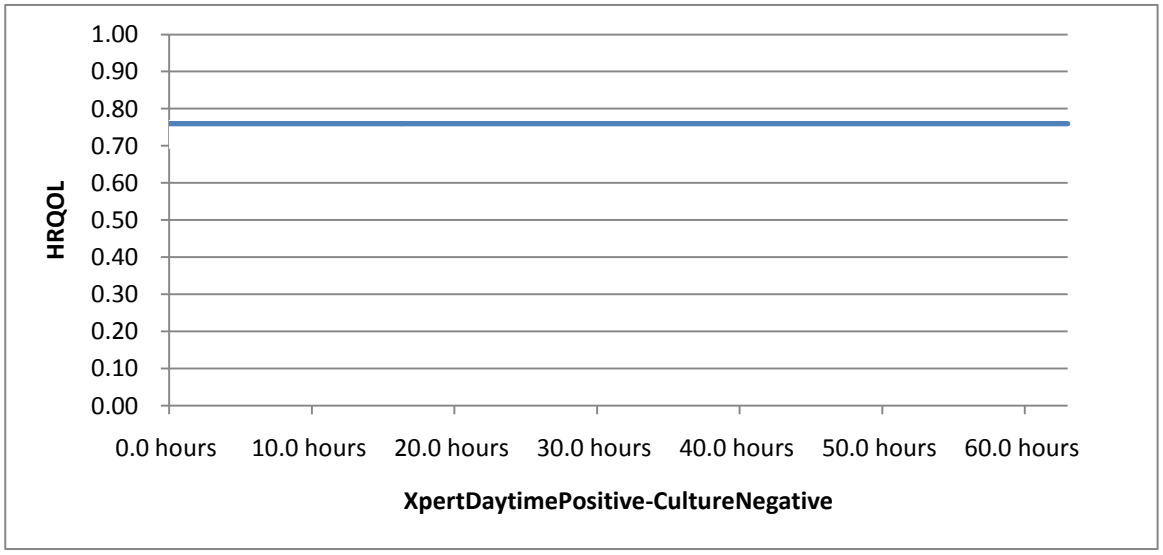


Figure 20 Health-Related Quality of Life (HRQOL) when Xpert MRSA test produced a false negative result in the day-time Xpert strategy

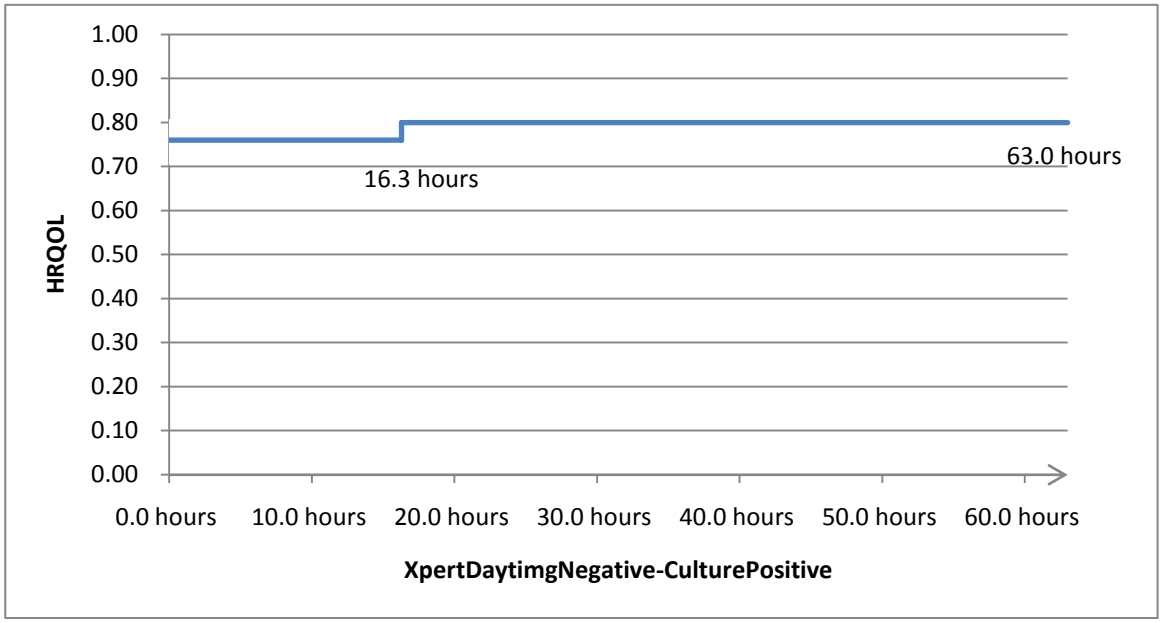


Figure 21 Health-Related Quality of Life (HRQOL) when Xpert MRSA test produced a true negative result in the day-time Xpert strategy

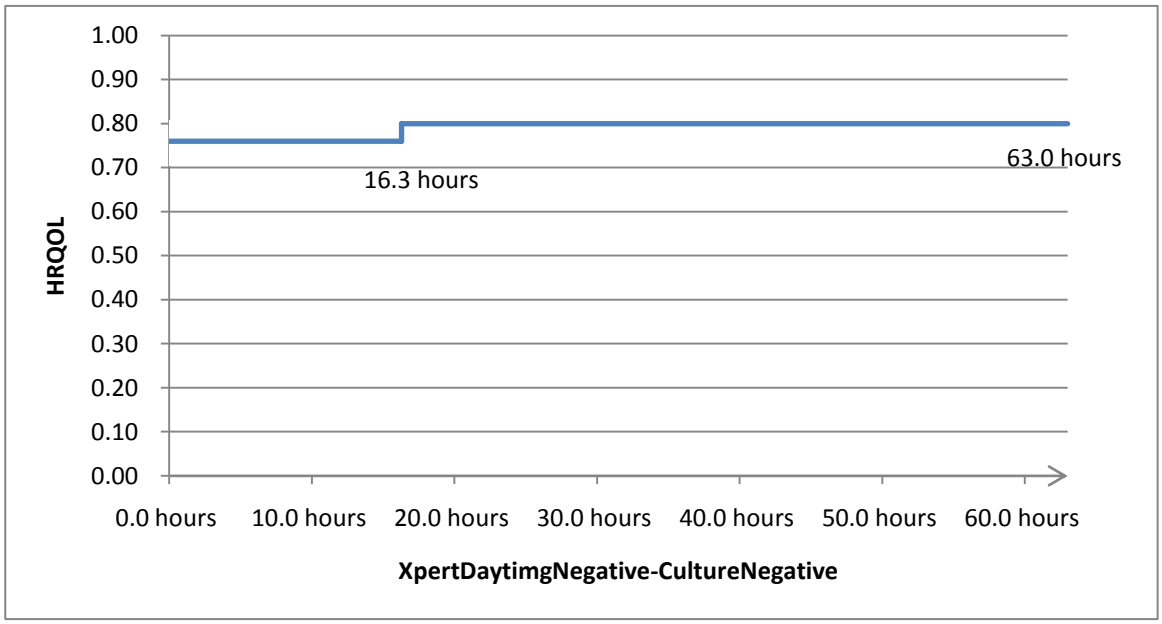


Figure 22 Health-Related Quality of Life (HRQOL) when Xpert MRSA test produced a true positive result in the 24-hour Xpert strategy

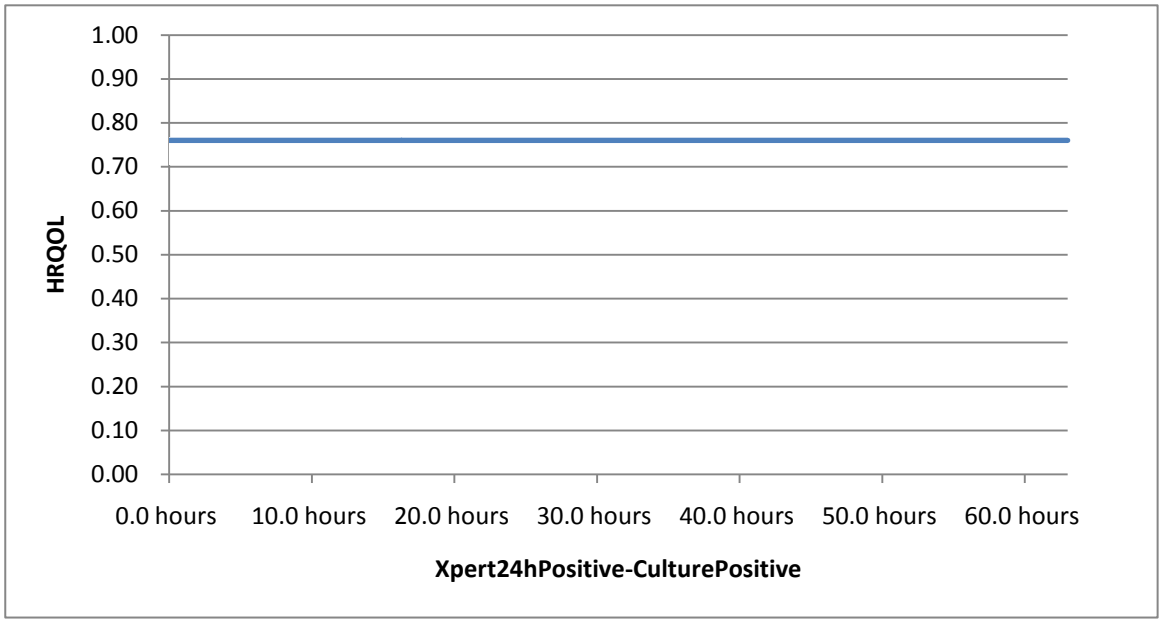


Figure 23 Health-Related Quality of Life when Xpert MRSA test produced a false positive result in the 24-hour Xpert strategy

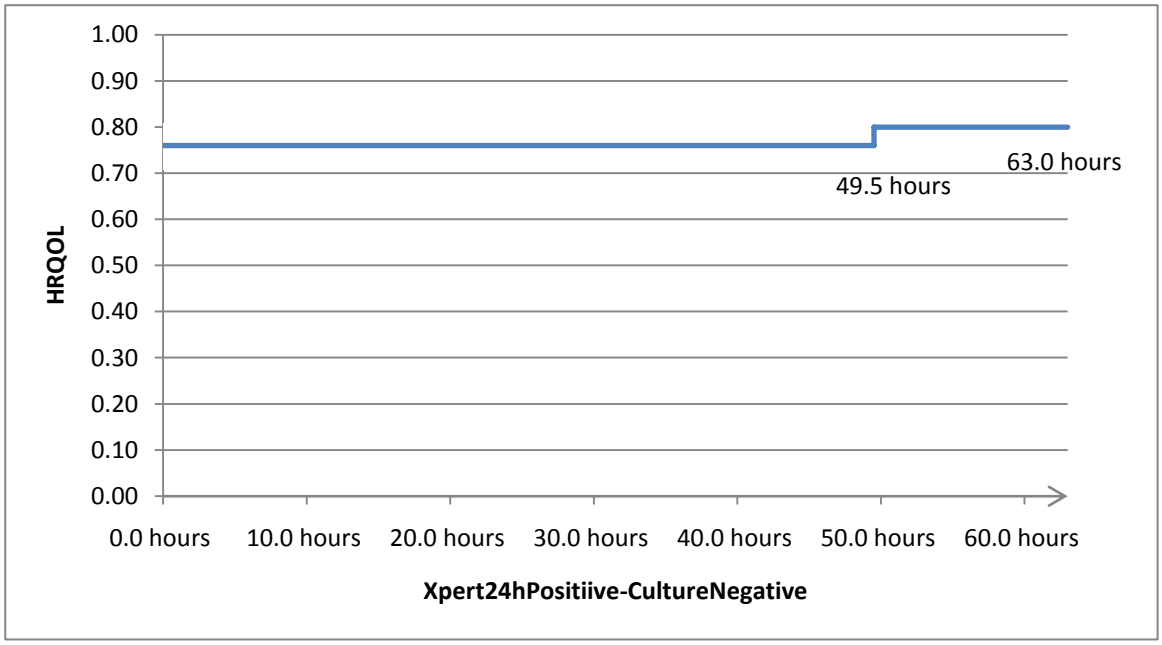


Figure 24 Health-Related Quality of Life (HRQOL) when Xpert MRSA test produced a false negative result in the 24-hour Xpert strategy

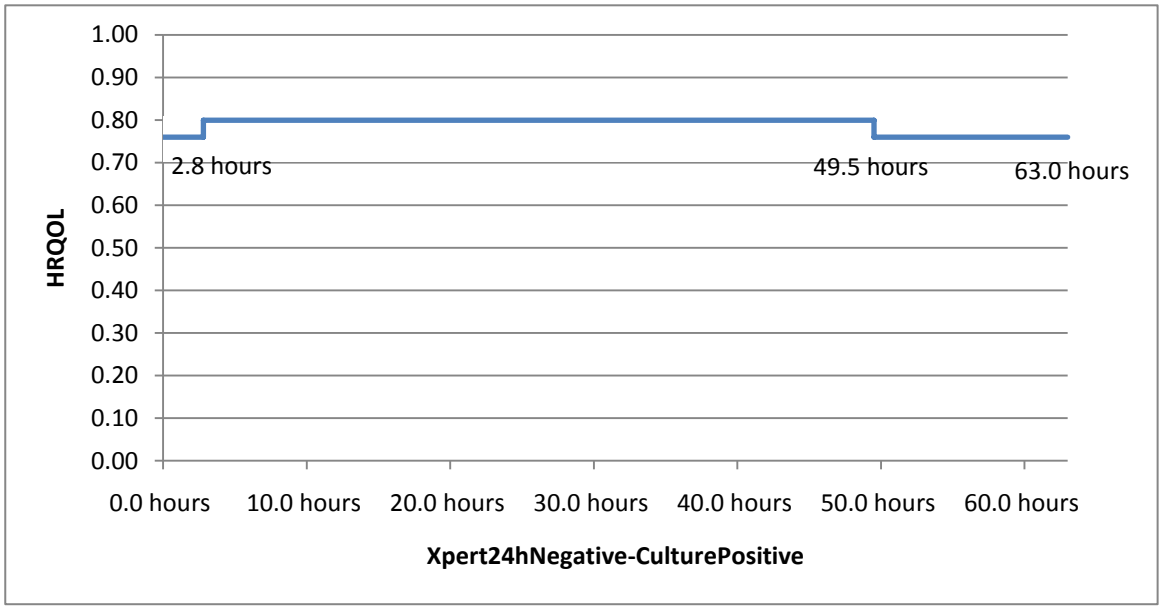
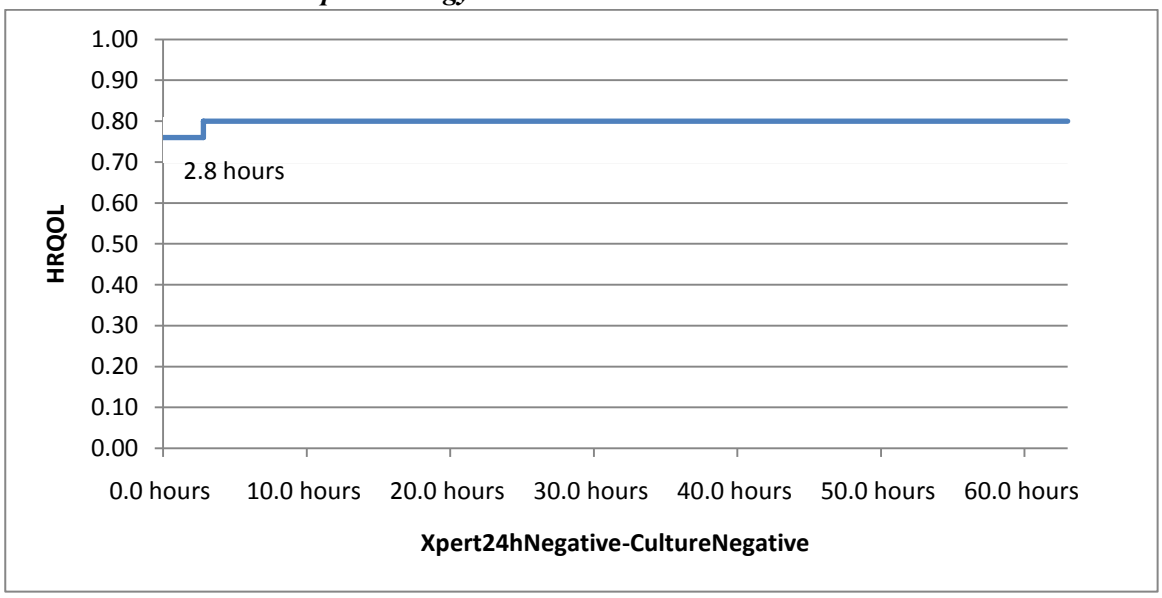


Figure 25 Health-Related Quality of Life (HRQOL) when Xpert MRSA test produced a true negative result in the 24-hour Xpert strategy



QALYs were calculated as:

Formula 5

$$\text{QALDs gained} = \frac{\sum[(\text{HRQOL}) \times \text{Corresponding period of time}]}{24}$$

Formula 6

$$\text{QALYs gained} = \frac{\sum[(\text{HRQOL}) \times \text{Corresponding period of time}]}{24 \times 365}$$

10.5. Results in detail

Table 27 Cost-Effective Analysis when all options referred to the option "culture test " as a common baseline with time of preemptive isolation as outcome

Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
24-hour Xpert	NOK 3,690	NOK -13,294	5.5 hours	-57.5 hours	NOK 671	NOK 231
Day-time Xpert	NOK 7,360	NOK -9,624	19.1 hours	-43.9 hours	NOK 385	NOK 219
Culture test	NOK 16,984		63.0 hours		NOK 265	

Table 28 Cost-Effective Analysis when all options referred to the option "culture test " as a common baseline with unavailable room-hours as outcome

Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
24-hour Xpert	NOK 3,690	NOK -13,294	6.3 hours	-77.7 hours	NOK 586	NOK 171
Day-time Xpert	NOK 7,360	NOK -9,624	26.9 hours	-57.1 hours	NOK 274	NOK 169
Culture test	NOK 16,984		84.0 hours		NOK 198	

Table 29 Cost-Effective Analysis when all options referred to the option "culture test " as a common baseline with QALYs gained as outcome

Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
24-hour Xpert	NOK 3,690	NOK -13,294	0.00576 QALYs	0.00030 QALYs	NOK 640,625	NOK -44,313,333
Day-time Xpert	NOK 7,360	NOK -9,624	0.00570 QALYs	0.00024 QALYs	NOK 1,291,228	NOK -40,100,000
Culture test	NOK 16,984		0.00546 QALYs		(Undefined)	

Table 30 Cost-Effectiveness Analysis when all options referred to the option "culture test " as a common baseline with QALDs gained as outcome

Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
24-hour Xpert	NOK 3,690	NOK -13,294	2.10 QALDs	0.11 QALDs	NOK 1,757	NOK -120,855
Day-time Xpert	NOK 7,360	NOK -9,624	2.08 QALDs	0.09 QALDs	NOK 3,538	NOK -106,933
Culture test	NOK 16,984		1.99 QALDs		(Undefined)	

To calculate the threshold of annual number of MRSA tests, we assumed that of all patients with suspected MRSA infection or colonization, 30% were isolated preemptively at hospital. We hypothesized that the annual number of MRSA suspects was X and built three functions of X.

Formula 7 Function of Annual number of MRSA tests in the culture test only strategy

$$f(x) = 5365.8 \times \mathrm{X}$$

Formula 8 Function of Annual number of MRSA tests in the Day-time Xpert MRSA test strategy

$$f(x) = 3709.1 \times \mathrm{X} + 153518$$

Formula 9 Function of Annual number of MRSA tests in the 24-hour MRSA test strategy

$$f(x) = 2741.1 \times \mathrm{X} + 153518$$

10.6. Sketch of a dynamic model

In the discussion section, we suggested to use a dynamic model to estimate the herd effect resulting from the new screening strategy. Hereby, we presented the preliminary version of the model (Figure 26). In the model, the general population in community was categorized as two groups. Group one (A persons) was population who were free of MRSA infection and colonization. Group two (B persons) was population who were infected or colonized with MRSA. We assumed that the admission rates among the two groups were the same (a). Therefore, among the patients who were admitted to hospital, A*a people were free of MRSA infection and colonization, and B*a people were infected or colonized with MRSA. According to the protocol, part of the patients was identified as suspects of MRSA. We assumed the proportion of being identified as suspects of MRSA was b1 among the non-MRSA patients, and b2 among the MRSA patients. That lead to A*a*b1+B*a*b2 patients were identified as suspects of MRSA and therefore isolated preemptively at hospital. The rest of the patients (A*a*(1-b1) + B*a*(1-b2) patients) were classified as MRSA-free and received no preventive measure. When the patients under preemptive isolation received a screening test, some of them got a negative test result and were released from isolation, and others got a positive result and continued to be isolated. Among the patients who were free of MRSA, all positive results were false positive (A*a*(1-d1) patients). In contrast, all positive results among the patients who were infected or colonized with MRSA were true positive (B*a*b2*d2 patients). The patients with a false positive result ended up being

isolated until the confirmatory test declared they were free of MRSA. The patients with a true positive result ended up receiving MRSA treatment. All patients who were free of MRSA and admitted to the hospital plus those who received MRSA treatment became a new group of patients. This group of patients was free of MRSA at hospital (A*a + B*a*b2*d2 patients). The patients who got a false negative test result (B*a*b2*(1-d2) patients) were released improperly. Those patients and the patients, who were infected or colonized with MRSA but not identified on admission, formed the new group of MRSA patients at hospital (B*a*(1-b2*d2) patients). At that point, both groups might have contact with each other directly or indirectly, which lead to the transmission of the bacteria. We assumed that during the contact, r persons out of 100 people would be infected. That made the number of the patients with MRSA increase to B*a*(1-b2*d2) + r/100*(A*a + B*a*b2*d2) people and the number of the patients who were free of MRSA decreased to (1-r/100)*(A*a + B*a*b2*d2) persons. When the confirmatory test results verified those with false negative screening test results, these patients were supposed to be treated and isolated. However, in practice, some of them were discharged from hospital before the result coming out. Therefore, it's possible that not all of them received treatment. On the other side, during the treatments for other diseases, some MRSA cases would be found out without screening and preemptive isolation. Based on these facts, we used a parameter 'e' to estimate the difference between new discovered cases and missing cases. 'e' was valued a random number varying from –B*a*b2*(1-d2) to r/100*(A*a + B*a*b2*d2). At the end, both groups went back to community with or without MRSA infection or colonization.

Figure 26 The dynamic model of transmission of MRSA

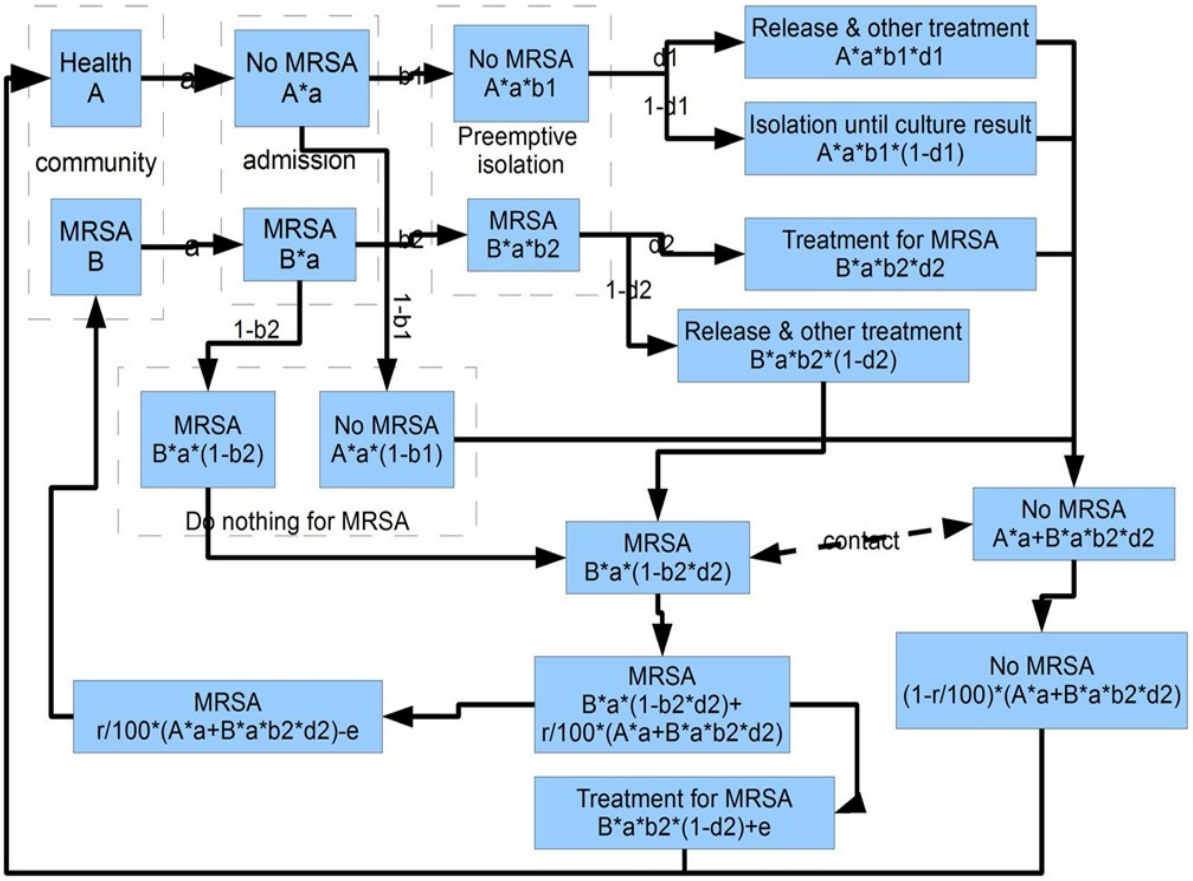


Figure 27 Variables used in the dynamic model of transmission of MRSA

A = Population without MRSA in community

B = MRSA infected or colonized population

a = Admission rate

b1 = Proportion of patients receiving isolation among MRSA-free patients

b2 = Proportion of patients receiving isolation among MRSA patients

d1 = True negative rate of rapid MRSA test

d2 = True positive rate of rapid MRSA test

$-B*a*b2*(1-d2) \leq e \leq r/100*(A*a+B*a*b2*d2)$, random number, number of patients with MRSA are discovered or missed

r/100 = r persons per 100 people will be infected or colonized during contact with MRSA patients, $0 \leq r \leq 100$