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Review Article

A Systematic Review on Prevention of Methicillin-Resistant *Staphylococcus aureus* Infection by Pre-Admission Screening: The Cost Effectiveness and Practicality

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ABSTRACT

Background: Methicillin Resistant *Staphylococcus aureus* (MRSA) is a common source of nosocomial infection, which is spreading through the community and hospitals across the countries. The performance of screening program really needs major effort related to laboratory capacity and ethical consideration, among other costly components. Significant literature research was conducted to review the cost, effectiveness and practicality of different methods of pre-admission MRSA screening in the hospital setting. A systematic literature review was conducted with search strategy using the PubMed Medline, Scopus and the Science Direct databases. The relevant data was abstracted from all studies based on various countries which in line with the finalized eligibility criteria. **Results:** PCR method was reported to have high sensitivity with low turnaround time as compared to culture method. A review of selected studies found the increasing annual costs of screening from standard culture, chromogenic agar to rapid PCR. In the meantime, other studies reported the total costs for labor and materials was lower for rapid PCR screening compared to culture methods. The culturing method offers a high level of variability due to time consumption and additional costs. Whereas PCR was reported as advantageous in term of saving time to identify MRSA positive patients, which involved isolation, thus increase the effectiveness of screening programs. It can pick up false negative results by conventional methods in the early condition of disease. **Conclusion**: Most studies verified that PCR is the most accurate method for detection of MRSA with Xpert MRSA having the best performance. Otherwise, oxacillin agar screen was revealed as a good alternative method to PCR. Targeted screening on high risk patients using rapid PCR may be the best choice to be implemented, in order to balance the economic and practicality of screening. We recommend that further clinical studies should be done to provide a sharp evidence of MRSA screening.

Key words: Prevention, MRSA, Pre-Admission, Screening, Cost-Effectiveness.

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INTRODUCTION

A common source of nosocomial infection is spreading through the community and hospitals across the countries.[1,2] This particular of superbug is called Methicillin Resistant *Staphylococcus aureus* (MRSA) has been found in the nose, throat, axillae, groin and perineum of a person, in surgical patients and patients with a catheter and intravenous lines.[3] Previous studies have shown that ineffective antimicrobial therapy will lead to excess mortality and significantly prolonged hospitalization.[4-6] Hospital acquired infections increases morbidity, mortality and health care costs.[7] There was a little research regarding the cost implications of implementing MRSA screening programs.[8-11] The performance of screening program really needs major effort related to laboratory capacity and ethical consideration, among other costly components.[12] Though some studies find ambiguous effects of MRSA infection, these findings may provide useful answers in balancing the potential economic costs and benefits of pre-admission screening as one of the control measures. Selected parameters that are considered to be significant are summarized. A selection of these factors is identified as an overview using a systematic literature research. The objective of this study is to review the cost and effectiveness of different methods of pre-admission MRSA screening with respect to the cost, practical and ethical issues concerning the screening to be implemented in Malaysia. This study was conducted in particular to review in hospitals setting and to find possible solutions to potential problems that may arise from the implementation of the MRSA screening. This study aims to bring up adequate evidence-based information on the cost and effectiveness of the testing.

MATERIALS AND METHODS

Data Sources and Search Strategy: A systematic literature review regarding the implementation of pre-admission screening of MRSA was conducted after the ethical approval from Medical Research and Ethics Committee of Malaysian Ministry of Health (MREC: NMRR-14-1539-20975). The search strategy included electronic database searches using keyword and text word combinations in the PubMed Medline database (1-1-2005-28-2-2015), the Scopus (1-1-2005-28-2-2015) and the Science Direct (1-1-2005-28-2-2015) which were organized using Revman Software. The search terms included "MRSA screening" and "cost" or "MRSA screening" and "cost comparison" or "MRSA screening" and "economics" or "MRSA" and "economics" or "MRSA" and "cost comparison" or "MRSA" and "cost".

Study Selection: Inclusion and exclusion criteria were applied to the exploratory search of the literature. No limitations were placed on geographical location. Generally, the irrelevant titles and abstracts were excluded, and the potentially eligible articles were retrieved with full text for a detailed assessment. The specific criteria for a systematic literature

research included irrelevant comparator, irrelevant and inappropriate studies or outcome. Meanwhile, the selection date was limited to, articles published between 2005 and onwards. The duplicate record studies were also excluded. The remaining eligible articles were included in the review after double filter screening. More emphasis was placed on studies that were well designed and aligned with the specific objectives. The primary outcome chosen was the comparison of polymerase chain reaction (PCR) and culture for the pre-admission screening of MRSA. The relevant data was abstracted from all studies which in line with the finalized eligibility criteria. A flow diagram (Figure 1) illustrates the process used to select the final review.

RESULTS

Study Characteristics: The literature review resulted in 47 studies, which met all inclusion and exclusion criteria. Selected studies were identified from various countries, such as England, India, Iran, Germany, Canada, United Kingdom, Spain and United States. Generally, most of the studies emphasized on the cost effectiveness of MRSA screening implementation. 37 studies focused on the most reliable methods, either rapid test, polymerase chain reactions or conventional culture methods. In specific, 8 studies were investigating the performance of culture methods, 9 studies were investigating the performance of PCR methods, and 20 studies were comparing the performance of culture and PCR methods. Other than that, 21 studies focused on the most effective screening policy, either universal or targeted screening. In specific, 8 and 13 studies were found to investigate universal and targeted screening, namely the risk patients for MRSA. Others focused on the practicality and ethicality of MRSA screening, which involved clinically valuable, eligibility, patients' acceptance and experience. Several studies, designs were identified which are quite different. There were prospective and retrospective study, case control, cross sectional, observational, decision analytic models, review and systematic analysis which involved comparative and convenience samples. The health economic studies include used of analytical methods such as decision tree analysis, decision modeling tree, decision analytic model, the micro-costing approach of Markov models and retrospective cost calculations. Eleven studies were identified which provided information about costs per MRSA case. All of these studies reviewed direct and indirect costs of MRSA screening, including the laboratory costs, supplies and products, isolation costs and additional costs for the prolonged length of hospital stay. The compilation of studies which provides the characteristics of MRSA screening in global settings (Table 1).

Performance Criteria of Screening Methods: Emergence of technology has revolved the transformation in scientific methods. This explains the revolution of screening methods from conventional culture into rapid polymerase chain reaction. The performance of both screening methods (PCR and culture) which consist of sensitivity, specificity and turnaround time from selected studies (Tables 2 and 3). Based on studies that investigated culture methods (Table 2), the averages sensitivity and specificity were 94.03% and 94.5% respectively. Mean turnaround time was assumed to be 48-72 hours as it was not reported in several studies. Oxacillin E-test has been one of the highlighted conventional culture methods with the highest specificity and sensitivity of 100% value.[40] Cefoxitin disk diffusion and oxacillin screen agar test were also reported to have 100% value for specificity and sensitivity.[39] The lowest sensitivity and specificity for conventional culture methods were chromogenic agar (83%) and oxacillin disk diffusion (56%) respectively.[12,32] Furthermore, studies that investigated PCR methods (Table 3) reported that the averages sensitivity and specificity were 94.0% and 96.8% respectively. Mean turnaround time was identified by an average of 20 h. The highest value was determined by the study with 100% value for both sensitivity and specificity by using Multiplex PCR methods.[14] The low sensitivity and specificity of PCR methods were Xpert MRSA assay with 75% and Quantitative PCR with 91%.[12,43,44] According to another study "PCR for mecA gene is the best method for detecting methicillin resistance in S. aureus with respect to accuracy, sensitivity, specificity, speed, and cost effectiveness".[37]

Costs Effectiveness

Overall costs regarding MRSA screening were abstracted from selected studies and represented (Table 4). Generally, the average costs for each study were different resulting from international settings, which based on wide-ranging currencies, exchange rates, years of investigations, the total mean of patients monthly or annually and different methods employed. Cost evaluations of conventional methods and rapid PCR were focused in this systematic review. Based on one study, annual costs of MRSA screening were increasing from standard culture, chromogenic agar to rapid PCR, which were US$126,788 (RM388,562.24), US$135,906 (RM416,505.81) and US$192,709 (RM590,587.75), respectively.[35] The total of expenses includes laboratory supplies, laboratory technician time, nurse collection time, costs per test, variable costs of tests overhead and management. The expected costs of the intervention per admitted hospital patient were also increased from standard culture, chromogenic agar to rapid PCR, which were $22.22 (RM68.10), $23.33 (RM71.50) and $30.20 (RM92.55).[35]

Another study reported that the cost of preventing one MRSA infection by introducing conventional culture screening policy was measured to be £3200 (RM20,818.44) in England with additional costs that achieved £13 972 (RM90,898.53) per patient to treat MRSA infection.[34] The other requirements involved the costs of the length of prolonged admission.[34] One more study calculated the total costs of labor and materials was lower for rapid PCR screening with cost of US$3.74 (RM12.37), compared to conventional culture methods which cost US$4.90 (RM16.20) for oxacillin disk diffusion, US$13.76 (RM45.50) for E-tests oxacillin and US$5.91 (RM19.54) for MRSA screen latex.[14] The cost avoidance of unnecessary isolation of US$108,940.08/year (RM357,216.98) was obtained with total annual cost savings of US$101,230.21 (RM331,936.14) resulting from screening program implementation. Screening of all admissions would become cost-effective if at least a quarter of patients screened were MRSA-positive.[45] Implementation of MRSA screening by automated PCR was estimated to save a total of €7.3 million (RM13,897,000.98) in hospital costs for patients over the years 2006 to 2009.[47] Another research investigated the costs of targeted screening in high risk units using rapid PCR and identified that monthly costs of screening program was US$3,475 (RM13,132.95).[17] They found the cost avoidance of $19,714/month (RM74,504.45) for ICUs after implementation of screening.[17] Meanwhile, an alternative study suggested targeted screening using conventional culture screening program with the annual cost of €10261 (RM274.95).[22] The economic burden caused by MRSA infections achieved €101,000/year (RM2,706.34) with the mean estimated the cost of a single infection of €2730 (RM73.16). The costs include the infection control nursing (infection control nursing for patients screened and visits to patients in isolation), screening and follow-up cultures, isolation and decolonization procedures (staff contacts with gloves and gown).[22] A review study explored that universal MRSA screening strategies are far expensive than the targeted screening approaches. But, all targeted screening strategies turn out lower costs than not performing a screening at all.[42] The same outcome was also determined by another study stated that screening all patients at high risk units and those previously detected with MRSA or screening of flagged patients only bring the cost effectiveness in hospital viewpoint.[26]

Practical and Ethical Issue: Culturing method offers a high level of variability due to time consumption and additional costs. Whereas PCR was reported as advantageous in term of saving time to identify MRSA pos

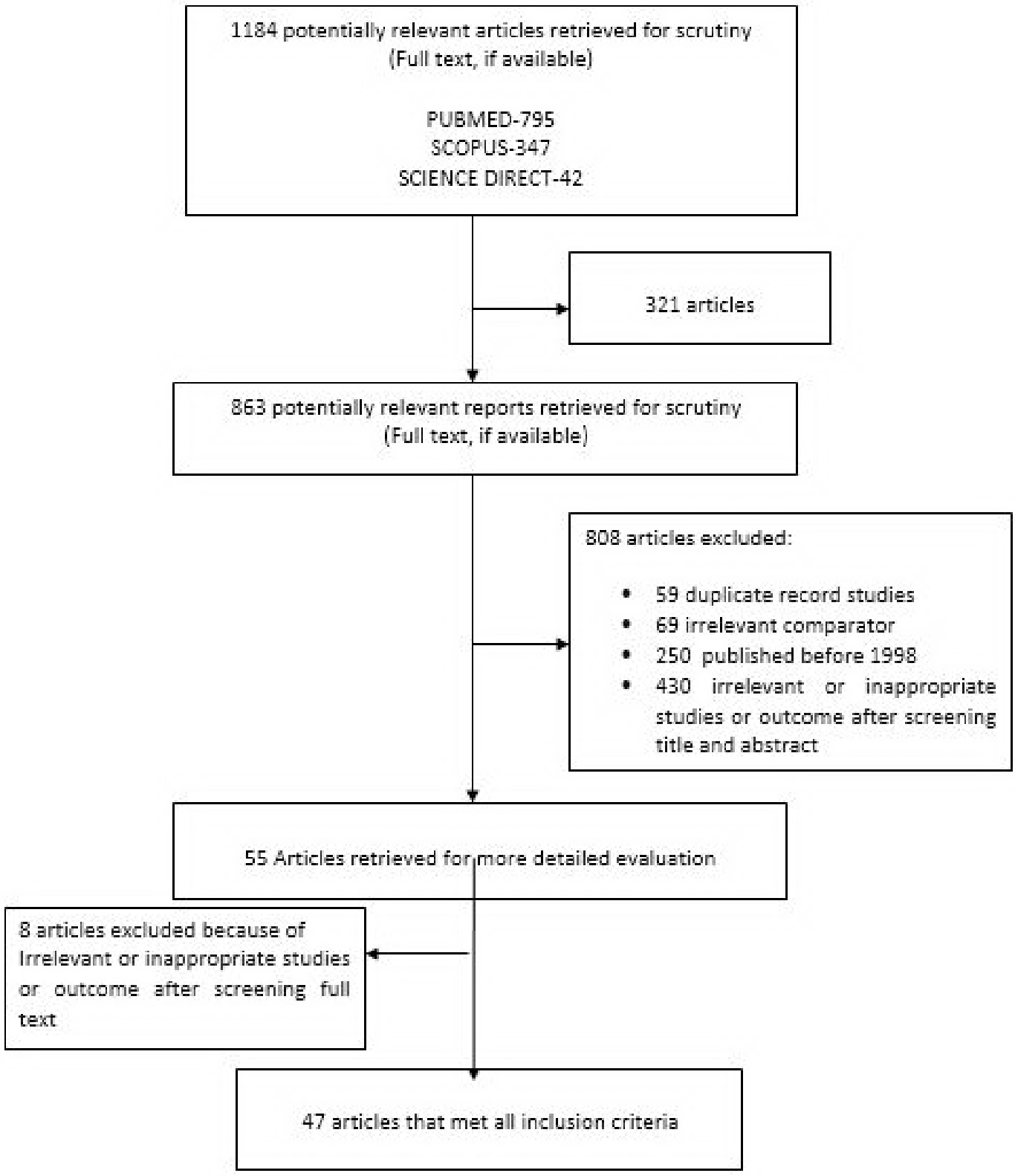

Figure 1: The Flow Diagram for Study Selection Process.

Table 1: Characteristics of MRSA screening in worldwide settings

Study	Setting	Type of study	Aim of study	Universal vs Targeted	Sites of swab
Adaleti *et al*, 2007[13]	Clinics of the HaydarpasaNumune Teaching and Research Hospital, Istanbul, Turkey	Cross sectional studies	Comparison of polymerase chain reaction and conventional methods in detecting methicillin-resistant *Staphylococcus aureus*	Universal	Nasal swabs
Akpaka *et al*., 2008[14]	Three regional hospitals in Trinidad and Tobago, Spain		Evaluation of Methods and Costs for Detecting Methicillin-resistant *Staphylococcus aureus* isolates from Clinical Specimens at Regional Hospitals in Trinidad and Tobago	Universal	n.r.
Barkataly *et al*, 2013[15]	Orthopaedic surgery, East Lancashire Hospital Trust (ELHT), England	A prospective analysis	MRSA screening in orthopaedic surgery: Clinically valuable and cost effective?	Universal	Nasal nose, groin and superficial skin & wound
Boyce and Havill, 2008 [16]	Hospital of Saint Raphael, Yale University School of Medicine, New Haven		Comparison of BD GeneOhm Methicillin-Resistant *Staphylococcus aureus* (MRSA) PCR versus the CHROMagar MRSA Assay for Screening Patients for the Presence of MRSA Strains	n.r.	Nares , nasal swabs
Buhlmann *et al*, 2008[11]	University Hospital of Berne, Switzerland		Rapid Screening for Carriage of Methicillin-Resistant *Staphylococcus aureus* by PCR and Associated Costs	n.r.	Nasal and groin swabs
Clancy *et. al*, 2006[17]	Denver Health Medical Center, Colorado, United States	Cross sectional (Prospective)	Active Screening in High-Risk Units Is an Effective and Cost-Avoidant Method to Reduce the Rate of Methicillin-Resistant *Staphylococcus aureus* Infection in the Hospital	Targeted	Anterior nares
Creamer and Humphreys, 2012[18]	Hospital, Dublin Ireland		The Value of Universal versus Targeted Screening for Methicillin-Resistant *Staphylococcus aureus* among Admission Patients	Targeted	n.r.
Cunha *et al*, 2013[19]	Winthrop-University Hospital, United States		Clinical- and cost-ineffectiveness of targeted methicillin-resistant *Staphylococcus aureus* screening of high-risk patients admitted to a low-prevalence teachinghospital	Targeted	Nasal swabs
Danial *et al*, 2011[20]	Microbiology lab Royal Infirmary of Edinburgh, United Kingdom		Real-time evaluation of an optimized real-time PCR assay versus Brilliance chromogenic MRSA agar for the detection of methicillin-resistant *Staphylococcus aureus* from clinical specimens	Targeted	Nasal swabs nose, throat, groin or ulcer site swab.

Table 1: Characteristics of MRSA screening in worldwide settings (Contd.)

French, 2009[21]	Hospital, London United Kingdom	Cross sectional study	Methods for screening for methicillin-resistant *Staphylococcus aureus* carriage	n.r.	n.r.
Gavalda *et. al*, 2006 [22]	Dr. JosepTrueta Hospital, Girona, Catalonia, Spain	Retrospective cohort study	Comparative Cost of Selective Screening To Prevent Transmission of Methicillin-Resistant *Staphylococcus aureus* (MRSA), compared with Attributable Costs of MRSA Infection	Targeted	n.r.
Giese *et al*, 2013[23]	The University Hospital Marien hospital Herne, Medical centre of the Ruhr-University Bochum, German North Rhine-Westphalia (NRW).	Retrospective	Postponing elective hospitalizations for pre-admission MRSA screening and decolonization. A study evaluating eligibility and acceptance among patients of a German university hospital	Targeted	Nasal, pharyngeal, wounds
Girou *et al*, 2000[24]	Henri Mondor Hospital, Créteil, France	Prospective Cohort Study	Comparison Of Systematic Versus Selective Screening For Methicillin-Resistant *Staphylococcus aureus* Carriage In A High-Risk Dermatology Ward	Both	Nasal mucosa, perineum, and skin lesions
Goldsack *et al*, 2014[25]	Cristiana Hospital, Newark Delaware	Mixed-method retrospective study	Clinical, patient experience and cost impacts of performing surveillance on known methicillin-resistant Staphylococcus positive patients admitted to medical-surgical units	Targeted	Anterior nares
Gurieva *et al*,2013[26]	Hospital, Netherlands		Cost and Effects of Different Admission Screening Strategies to Control the Spread of Methicillin resistant*Staphylococcus aureus*	Both	n.r.
Hombach *et al*., 2010[27]	Luzerner Kantonsspital (LUKS), Switzerlands	Prospective cohort study	Detection of Methicillin-Resistant *Staphylococcus aureus* (MRSA) inSpecimens from Various Body Sites: Performance Characteristics of the BD Gene Ohm MRSA Assay, the Xpert MRSA Assay, and Broth-Enriched Culture in an Area with a Low Prevalence of MRSA Infections.	Universal	Nose, groin, wounds, axilla, vagina, and throat
Hubner *et al*, 2012[28]	Hospital, Germany	Decision analytic Model and Review	Cost-analysis of PCR-guided pre-emptive antibiotic treatment of *Staphylococcus aureus* infections: an analytic decision model	n.r.	n.r.

Table 1: Characteristics of MRSA screening in worldwide settings (Contd.)

Huletsky *et al*., 2005[29]	McGill University Health Center; Montreal, Canada		Identification of Methicillin-Resistant *Staphylococcus aureus* Carriage in Less than 1 Hour during a Hospital Surveillance Program	Targeted	Nasal swabs
Kang *et al*, 2012[30]	Academic Hospital, North Carolina		Cost-Effectiveness Analysis of Active Surveillance Screening for Methicillin-Resistant *Staphylococcus aureus* in an Academic Hospital Setting	Both	Nasal samples
Leonhardt *et al*, 2011[31]	Two community hospitals in Wisconsin, Scotland		Clinical Effectiveness and Cost Benefit of Universal versus Targeted Methicillin-Resistant *Staphylococcus aureus* Screening upon Admission in Hospitals	Both	Nasal swabs
Mathews *et al*, 2010[32]	Department of Microbiology, PSG Institute of Medical Science and Research, Coimbatore, India		Evaluation and comparison of tests to detect methicillin resistant *S. aureus*	n.r.	Blood, pus, surgical site, diabetic wounds, burn wounds, fracture sites, sputum, tracheal aspirates, central venous pressure tips, urine
McGinigle *et. al*, 2008 [33]	Adult Intensive Care Units, North Carolina, United States	A systematic Review	The Use of Active Surveillance Cultures in Adult Intensive Care Units to Reduce Methicillin-Resistant *Staphylococcus aureus*–Related Morbidity, Mortality, and Costs: A Systematic Review	Targeted	n.r.
Murthy *et al*, 2010 [12]	Swiss Teaching Hospital, Switzerland	A prospective cohort study	Cost-effectiveness of universal MRSA screening on admission to surgery	Universal	n.r.
Nixon *et. al*, 2006 [34]	Orthopedic wards, Glenfield Hospital, Leicester, England	Case-control	Methicillin-resistant *Staphylococcus aureus* on orthopedic wards	Universal	Nose, perineum and sites such as wounds, sputum, tracheostomies or urinary catheters
Nyman *et al*, 2011 [35]	Minneapolis Veterans Affairs Medical Center, United States	Intervention	Cost of screening intensive care unit patients for methicillin-resistant *Staphylococcus aureus* in hospitals	Targeted	Nasal swabs
Ornskov *et al*., 2008 [36]	Six hospitals in the Country of Vejle (Kolding, Fredericia, Horsens, Braedstrup, Give and Vejle Hospitals)		Screening for methicillin-resistant *Staphylococcus aureus* in clinical swabsusing a high-throughput real-time PCR-based method	n.r.	Nose, throat, skin, wounds, perinium

Table 1: Characteristics of MRSA screening in worldwide settings (Contd.)

Pillai, *et al* 2012 [37]	Hospital Based observational Study, India	A comparative study	Detection of Methicillin Resistance in *Staphylococcus aureus* by Polymerase Chain Reaction and Conventional Methods: A Comparative Study	n.r.	Pus samples, urine samples, blood samples, ear swab samples and umbilical swab
Polisena *et al*, 2011 [38]	Hospital, Canada	Systematic Review	Clinical effectiveness of rapid tests for methicillin resistant *Staphylococcus aureus* (MRSA) in hospitalized patients: a systematic review	n.r.	n.r.
Pramodhini *et al*, 2011 [39]	Tertiary Care Hospital, South India	Prospective study	Comparison of Various Phenotypic Methods and mecA Based PCR for the Detection of MRSA	Targeted	Superficial and deep abscesses
Shariati et al, 2010 [40]	Cellular and Molecular Research , University of Medical Sciences, Shahrekord, Iran	A comparative study	Comparison of Real-Time PCR with Disk Diffusion, Agar Screen and E-test Methods for Detection of Methicillin-Resistant *Staphylococcus aureus*	n.r.	Routine clinical specimens including deep and superficial wounds, blood, urine, CSF, and venous catheter etc
Tubbicke et al, 2012 [41]	Hospital, Germany	Systematic Literature Review	Transmission rates, screening methods and costs of MRSA—a systematic literature review related to the prevalence in Germany	Both	n.r.
Tubbicke et al, 2013 [42]	Hospital, Germany	Systematic Literature search	Cost comparison of MRSA screening and management – a decision tree analysis	n.r.	n.r.
Uckay et al, 2008 [43]	Uni of Geneva Hospital, switzerland	Cohort study, cost analysis	Effect of Screening for Methicillin-Resistant *Staphylococcus aureus* Carriage by Polymerase Chain Reaction on the Duration of Unnecessary Preemptive Contact Isolation	Targeted	Anterior nares and groin
Wassenberg et al, 2010 [44]	14 Dutch Hospital, Netherlands	Prospective cohort study	Rapid screening of methicillin-resistant *Staphylococcus aureus* using PCR and chromogenic agar: a prospective study to evaluate costs and effects	Universal	Anterior nares, throat, perineum, wounds, catheter insertion sites, sputum and urine samples
Wernitz et al, 2005 [45]	Hospital, Berlin Germany	Prospective cohort study	Cost analysis of a hospital-wide selective screening programme for methicillin-resistant *Staphylococcus aureus* (MRSA) carriers in the context of diagnosis related groups (DRG) payment	Targeted	Nose and throat
Wolk et al, 2009 [46]	Clinical Microbiology Laboratories, University of Arizona, Tucson, AZ	Active surveillance convenience sample	Comparison of MRSA Select Agar, CHROMagar Methicillin-Resistant *Staphylococcus aureus* (MRSA) Medium, and Xpert MRSA PCR for Detection of MRSA in Nares: Diagnostic Accuracy for Surveillance Samples with Various Bacterial Densities	Universal	Nares
Zee et al, 2013 [47]	Hospital, Netherlands	Review	Review of a major epidemic of methicillin-resistant *Staphylococcus aureus*: The costs of screening and consequences of outbreak management	n.r.	Nose, throat, perineum, wounds, sputum and catheters

Table 2: Performance of Culture Methods

Study	Studied culture method	Outcome		
		Sensitivity	Specificity	Mean turn-around time
Adaleti *et al*, 2007 [13]	Oxacillin disk diffusion	100	89	n.r.
	Oxacillin agar screening	99.5	100	n.r.
	Cefoxitin disk diffusion	99.5	100	n.r.
Barkataly *et al*, 2013 [15]	Chromogenic medium	89	97.1	24-48
French, 2009 [21]	chromogenic medium	90	96	48
Gurieva *et al*,2013 [26]	Conventional culture method	100	100	96
Mathews et al, 2010 [32]	Oxacillin disk diffusion	n.r.	56	24-48
Murthy *et al*, 2010 [12]	Chromogenic agar	83	98	28
Pillai, *et al* 2012 [37]	Oxacillin disk diffusion	93.5	83.5	48
	Manitol Salt Agar with Oxacillin	87.1	89.3	48
Pramodhini *et al*, 2011 [39]	Oxacillin disk diffusion	90	100	n.r.
	Cefoxitin disk diffusion	100	100	n.r.
	Oxacillin screen agar test	100	100	n.r.
Shariati *et al*, 2010 [40]	Oxacillin disk test	95	93	n.r.
	Oxacillin E-test	100	100	n.r.
	Oxacillin agar screen	98	99	n.r.
Tubbicke *et al*, 2012 [41]	Culture	89.01	93.21	48-72
Wassenberg *et al*, 2010 [44]	chromogenic agar	85.7	96.6	12-168
Wolk *et al*, 2009 [40]	MRSA Select agar	97.1	99.2	24-48
	CHRO Magar MRSA	90.3	100	24-48

Table 3: Performance of PCR Methods

Study	Studied PCR method	Outcome		
		Sensitivity	Specificity	Mean turn-around time
Akpaka *et al*., 2008 [14]	Multiplex PCR	100	100	5.3
Boyce and Havill, 2008 [16]	BD GeneOhm MRSA PCR	100	98.6	14.5
Bühlmann *et al*., 2008 [11]	Geno Type MRSA Direct	92.6	98.9	24
Danial *et al*, 2011 [20]	PCR	98.6	99.4	7
French, 2009 [21]	PCR	88-95	92-99	22
Gurieva *et al*,2013 [26]	PCR	93	96	24
Hubner *et al*, 2012 [28]	PCR	91.09	95.79	24
Huletsky *et al*., 2005 [29]	Multiplex PCR	100	98.4	24
Hombach *et al*., 2010 [27]	BD GeneOhm MRSA PCR	100	98.5	17
	Xpert MRSA	100	98.2	7.8
Murthy *et al*, 2010 [12]	PCR	96	91	22.5
Ornskov *et al*., 2008 [36]	Multiplex real-time PCR	100	94	24
Tubbicke *et al*, 2012 [41]	PCR	91.09	95.79	7
Uckay *et al*, 2008 [43]	Qpcr	96	91	24
Wassenberg *et al*, 2010 [44]	BD GeneOhm MRSA PCR	85.2	96.5	13-23
	Xpert MRSA assay	75	94.5	13-23
Wolk *et al*, 2009 [46]	Xpert MRSA assay	84.3	100	24-48

Table 4: Costs of MRSA Screening

Author (Year)		Screening method	Costs preventing MRSA case	Associated costs
Akpaka *et al*., 2008 [14]		PCR vs culture	Total costs for labor and materials : Rapid PCR screening -US$ 3.74 (exchange rate 2011:1USD = RM3.306976) = RM12.37 Oxacillin disk diffusion -US$4.90 (exchange rate 2011:1USD = RM3.306976) = RM16.20 E-tests oxacillin - US$13.76 (exchange rate 2011:1USD = RM3.306976) = RM45.50 MRSA Screen latex test -US$5.91 (exchange rate 2011:1USD = RM3.306976) = RM19.54 Oxacillin salt agar plate -US$10.34 (exchange rate 2011:1USD = RM3.306976) = RM34.19	
Barkataly *et* al, 2013 [15]		Culture	Annual costs of screening programme: minimum of £ 184,170 (exchange rate 2013:1GBP = RM4.943879) = RM910,514.27	Not screening orthopedic patients who are not having any metalwork inserted could potentially save 168 × £ 94,307 = £ 15,843,576 (exchange rate 2013:1GBP = RM4.943879) = RM78,328729.43
Clancy *et. al*, 2006 [17]		PCR	Monthly costs of screening programme : $3,475 (exchange rate 2006: 1USD = RM3.779266) = RM13,132.95	Costs avoidance for ICUs after implementation of screening : $19,714/month (exchange rate 2006: 1USD = RM3.779266) = RM74,504.45
Gavalda *et. al*, 2006 [22]		Culture	Annual costs of screening programme : €10261 (exchange rate 2006: 1ESP = RM0.026796) = RM274.95	The economic burden caused by MRSA infections: €101,000/year (exchange rate 2006: 1ESP = RM0.026796) = RM2706.34, The mean estimated cost of a single infection : €2730 (exchange rate 2006: 1ESP = RM0.026796) = RM73.16
Goldsack *et al*, 2014 [25]		Culture	Annual costs of screening programme :$7,709.87 (exchange rate 2014:1USD = RM3.279023) = RM25,280.84	The costs of unnecessary isolation was $108,940.08 /year. (exchange rate 2014:1USD = RM3.279023) =357216.98 Total annual cost savings of $101,230.21 resulting from program implementation. (exchange rate 2014:1USD = RM3.279023) = 331,936.14
Hubner *et al*, 2012 [28]		PCR	The total costs per MRSA case: €1780 per case. (exchange rate 2012:1DEM = RM2.099109) = RM3736.42	
Murthy *et al*, 2010 [12]	PCR vs culture	PCR	apid PCR screening - CHF 41.36 (exchange rate 2010:1CHF = RM3.324751) = RM137.51 Standard chromogenic agar culture - CHF 18.63 (exchange rate 2010:1CHF = RM3.324751) = RM61.94	

Table 4: Costs of MRSA Screening (Contd.)

Nyman *et al*, 2011 [35]	PCR vs culture	Annual costs of screening ICU patients : Standard culture - $126,788 (exchange rate 2011:1USD = RM3.064661) = RM38,8562.24 Chromogenic agar - $135,906 (exchange rate 2011: 1USD = RM3.064661) = RM41,6505.81 PCR - $192,709 (exchange rate 2011:1USD = RM3.064661) = RM59,0587.75 The expected costs of the intervention per admitted hospital patient : Standard culture - $22.22 (exchange rate 2011: 1USD = RM3.064661) = RM68.10 Chromogenic agar - $23.33 (exchange rate 2011: 1USD = RM3.064661) = RM71.50 PCR - $30.20 (exchange rate 2011: 1USD = RM3.064661) = RM92.55	The total annual costs of isolating the colonized cases identified by the intervention : $56,908 (exchange rate 2011: 1USD = 3.064661) = RM17,4403.73
Tubbicke *et al*, 2012 [41]	PCR vs Culture	The total costs per MRSA case: €9,261. (exchange rate 2012: 1DEM = RM2.099109) = 19439.83	
Tubbicke *et al*, 2013 [42]	PCR vs Culture	Costs for a single culture test with positive result - € 24.10 (exchange rate 2013:1DEM = RM2.062909) =49.71 Costs for a single culture test with negative result - €6.40 (exchange rate 2013:1DEM = RM2.062909) = 13.19 Costs for a single PCR test - € 20.50 (exchange rate 2013:1DEM = RM2.062909) = 42.28	
Uckay *et al*, 2008 [43]	PCR vs Culture	Admission screening costs : culture - US$10 (exchange rate 2008:1USD = RM3.306976) = RM33.07 in-house qPCR - US$15 (US$5 and US$7.50 per test, respectively) (exchange rate 2008:1USD = RM3.306976) = RM49.60	The use of qPCR resulted in an overall reduction in the number of isolation-days (422 [22.1%] of 1,909 isolation-days were saved) and in total cost (US$5,450 [17.9%] of US$30,395 were saved) (exchange rate 2008:1USD = RM3.306976) =RM18.02

Table 4: Costs of MRSA Screening (Contd.)

Wassenberg *et al*, 2010 [44]	PCR vs culture	The cost per test: BD GeneOhm MRSA PCR - €56.22 (exchange rate 2010:1NLG = RM2.238316) = RM125.83 Gene Xpert - €69.62 (exchange rate 2010:1NLG = RM2.238316) = RM155.82 chromogenic agar - €2.08 (exchange rate 2010:1NLG = RM2.238316) = RM4.64 Annual costs of screening programme : €16 ,573.58 (exchange rate 2005:1DEM = RM2.646437) = 43,860.94	Costs per isolation day avoided : IDI - €95.77 (exchange rate 2010:1NLG = RM2.238316) = RM214.37 Gene Xpert - €125.43 (exchange rate 2010:1NLG = RM2.238316) = RM280.76 PCR-based decision-making (IDI) - €153.64 (exchange rate 2010:1NLG = RM2.238316) = RM343.90 PCR-based decision-making (GeneXpert) - €193.84 (exchange rate 2010:1NLG = RM2.238316) =433.87 per patient to overall costs chromogenic testing would have saved €30.79 per patient. (exchange rate 2011:1NLG = RM2.238316) = RM68.91
Wernitz *et al*, 2005 [45]		The screening costs : MRSA-negative - €39.96 (exchange rate 2005:1DEM = RM2.646437) = 105.75 MRSA-positive - €82.33 (exchange rate 2005:1DEM = RM2.646437) = 217.86	Net saving of €110 236.56 annually after implementation of screening programme. (exchange rate 2005:1DEM = RM2.646437) = 291,734.07
Zee *et al*, 2013 [47]	PCR vs culture	Costs of screening: Rapid PCR screening - €19. (exchange rate 2013:1NLG = RM1.830867) = RM34.78 Culture screening - €7 (exchange rate 2013:1NLG = RM1.830867) = RM12.83	Implementation of MRSA screening by automated PCR was estimated to save a total of €7.3 million in hospital costs for patients over the years 2006 to 2009 (exchange rate 2013:1NLG = RM1.830867) = RM 13 897 000.98

Table 5: Outcome of MRSA Screening

Study	Aim of study	Outcome
Adaleti *et al*, 2007 [13]	Comparison of polymerase chain reaction and conventional methods in detecting methicillin-resistant *Staphylococcus aureus*	Detection of mecA gene by PCR is considered to be the gold standard test but not practical for a routine clinical laboratory. Combining the ODD and CDD methods could be a good choice for detecting methicillin resistance in S. aureus strains where mecA PCR cannot be performed.
Akpaka *et al*., 2008 [14]	Evaluation of Methods and Costs for Detecting Methicillin-resistant *Staphylococcus aureus* isolates from Clinical Specimens at Regional Hospitals in Trinidad and Tobago	Latex agglutination test had the advantage of giving a reliable, rapid and most cost effective result that compares well to PCR in this environment.
Barkataly *et al*, 2013 [15]	MRSA screening in orthopedic surgery: Clinically valuable and cost effective ?	MRSA "screening" program should be re-assessed by the DOH, to include only high risk groups of patients which could result in substantial saving. MRSA screening program should fulfill the ideal screening criteria set out by Wilson and Junger (WHO 1968).
Boyce and Havill, 2008 [16]	Comparison of BD GeneOhm Methicillin-Resistant *Staphylococcus aureus* (MRSA) PCR versus the CHROMagar MRSA Assay for Screening Patients for the Presence of MRSA Strains.	Compared to C-MRSA agar, the BD GeneOhm MRSA PCR assay was more sensitive, provided significantly faster turnaround times, and resulted in more-prompt isolation of MRSA-colonized patients.
Buhlmann et al, 2008 [11]	Rapid Screening for Carriage of Methicillin-Resistant *Staphylococcus aureus* by PCR and Associated Costs	PCR tests are valuable for the rapid detection of MRSA carriers, but high costs require the careful evaluation of their use. In patient populations with low MRSA endemicity, the broad use of PCR probably is not cost-effective.
Clancy *et. al*, 2006 [17]	Active Screening in High-Risk Units Is an Effective and Cost-Avoidant Method to Reduce the Rate of Methicillin-Resistant *Staphylococcus aureus* Infection in the Hospital	Active MRSA screening as part of a multi-factorial intervention targeted to high-risk units may be an effective and cost-avoidant strategy for achieving a sustained decrease of MRSA infections throughout the hospital.
Creamer and Humphreys, 2012[18]	The Value of Universal versus Targeted Screening for Methicillin-Resistant *Staphylococcus aureus* among Admission Patients	Universal screening is used in a strong case for using molecular methods, which reduce the turnaround time and facilitate early isolation of MRSA-positive patients or the release from preemptive isolation of suspected MRSA-positive patients after a negative result. It may increase the rate of detection, the additional expense probably does not justify its widespread implementation in most institutions.

Table 5: Outcome of MRSA Screening

Cunha *et al*, 2013 [19]	Clinical- and cost-ineffectiveness of targeted methicillin-resistant *Staphylococcus aureus* screening of high-risk patients admitted to a low-prevalence teaching hospital	MRSA screening via PCR is unnecessary as the cost is much higher for and MRSA infection rates remained constant. It was not clinically effective or cost-effective to perform targeted MRSA screening to detect MRSA nasal carriage in patients
Danial *et al*, 2011 [20]	Real-time evaluation of an optimized real-time PCR assay versus Brilliance chromogenic MRSA agar for the detection of methicillin-resistant *Staphylococcus aureus* from clinical specimens	This optimized, in-house, inexpensive, real-time PCR test maintained a very high sensitivity and specificity. The TAT of this real-time PCR assay was substantially lower than that of chromogenic culture. It was also maintained throughout the entire process, which can be taken as an indirect measure of test performance.
French, 2009 [21]	Methods for screening for methicillin-resistant *Staphylococcus aureus* carriage	An effective culture screening method is direct inoculation of pooled nose, throat and perineal swabs on a well-performing MRSA-selective chromogenic agar. In comparison with culture-based methods, PCR tests are costly, and some have relatively high false-positivity rates; definitive evidence of their clinical cost effectiveness is lacking.
Gavalda *et. al*, 2006 [22]	Comparative Cost of Selective Screening To Prevent Transmission of Methicillin-Resistant *Staphylococcus aureus* (MRSA), compared with Attributable Costs of MRSA Infection	The cost of the screening program would be covered if it only prevented 4 infections per year in the hospital. Policies for screening high-risk patients can be considered in healthcare facilities where MRSA is a relevant nosocomial pathogen.
Giese *et al*, 2013 [23]	Postponing elective hospitalizations for pre-admission MRSA screening and decolonization. A study evaluating eligibility and acceptance among patients of a German university hospital	A relevant number of affected admissions to our tertiary referral hospital is eligible for an MRSA-PreASD. The majority of patients with proven MRSA-colonization eligible for a pre-admission decolonization treatment would prefer such an approach over being isolated at the hospital. The implementation of an MRSA-PreASD-protocol may reduce costs.
Girou *et al*, 2000 [24]	Comparison Of Systematic Versus Selective Screening For Methicillin-Resistant *Staphylococcus aureus* Carriage In A High-Risk Dermatology Ward	A screening strategy targeted to patients at risk of harboring MRSA has similar sensitivity and is more cost-effective than a strategy of systematic screening to identify MRSA carriers on admission
Goldsack *et al*, 2014 [25]	Clinical, patient experience and cost impacts of performing surveillance on known methicillin-resistant Staphylococcus positive patients admitted to medical-surgical units	Chromogenic agar is less sensitive than PCR and require a longer turnaround time. Patients in MRSA isolation report feeling worried about their MRSA status, stigmatized, neglected, and contaminated indicate that unnecessary isolation should be avoided wherever possible to reduce the potential negative impact on clinical outcomes and unnecessary distress for patients. A screening program targeting patients with a history of MRSA who would otherwise be placed in isolation has the potential to improve outcomes and patient experience and reduce costs.

Table 5: Outcome of MRSA Screening

Gurieva *et al*, 2013 [26]	Cost and Effects of Different Admission Screening Strategies to Control the Spread of Methicillin-resistant *Staphylococcus aureus*	Screening all patients at ICU admission and those previously detected with MRSA or screening of flagged patients only are likely to be the most effective and cost-saving from a hospital perspective. These strategies should be seriously considered by hospitals that aim to control the nosocomial spread of MRSA.
Hombach *et al*., 2010 [27]	Detection of Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Specimens from Various Body Sites: Performance Characteristics of the BD GeneOhm MRSA Assay, the Xpert MRSA Assay, and Broth-Enriched Culture in an Area with a Low Prevalence of MRSA Infections.	(i) Both PCR methods performed equally well regarding sensitivity, specificity, PPV, and NPV, as well as the probability of producing results discrepant from the results of culture. (ii) Combining swabs from nose and groin increases the rate of detection of MRSA carriers. (iii) Taking swabs from body sites other than the nares and groin may not be advisable because of higher inhibition rates and a significantly increased likelihood of discrepant results. (iv) The NPV was exceptionally high (100%) for both PCR methods, demonstrating that back-up cultures are unnecessary if PCR is negative. For PCR-positive specimens, back-up cultures may, however, be useful because of the low PPV even after the resolution of discrepancies. (v)The low PPV of both PCR methods might be due to PCR rather than culture being the actual gold standard. Culture, in all likelihood, produces false-negative results and, therefore, is not a true gold standard. (vi) Concerning rapid availability of PCR results, the Xpert MRSA was superior to the BDGO.
Hubner *et al*, 2012 [28]	Cost-analysis of PCR-guided pre-emptive antibiotic treatment of *Staphylococcus aureus* infections: an analytic decision model	Early verification and adaptation of an initial pre-emptive antimicrobial treatment using PCR-based tests for S. aureus infections is an economically efficient approach.
Huletsky *et al*., 2005 [29]	Identification of Methicillin-Resistant *Staphylococcus aureus* Carriage in Less than 1 Hour during a Hospital Surveillance Program	MRSA carriers can be identified rapidly and reliably by direct molecular testing of nasal specimens. The use of this test should facilitate MRSA surveillance programs.
Kang *et al*, 2012 [30]	Cost-Effectiveness Analysis of Active Surveillance Screening for Methicillin-Resistant *Staphylococcus aureus* in an Academic Hospital Setting	Targeted active surveillance screening for MRSA is the most cost-effective screening strategy in an academic hospital setting.
Mathews *et al*, 2010 [32]		Results of cefoxitin disk diffusion test are in to PCR for detection of MRSA in resource constraint settings.
McGinigle *et. al*, 2008 [33]	The Use of Active Surveillance Cultures in Adult Intensive Care Units to Reduce Methicillin-Resistant *Staphylococcus aureus*–Related Morbidity, Mortality, and Costs: A Systematic Review	The most cost-effective screening method is to inoculate a single nasal sample directly onto ciprofloxacin Baird-Parker agar without the use of broth and then confirm the result with a staphylococcal latex test. The value of PCR remains unclear, because there are concerns about test sensitivity, high cost, and the need for technically skilled laboratory workers.

Table 5: Outcome of MRSA Screening

Murthy *et al*, 2010 [12]	Cost-effectiveness of universal MRSA screening on admission to surgery	Settings with a higher prevalence of MRSA colonization may find universal screening cost-effective and, in some cases, cost-saving.
Nixon *et. al*, 2006 [34]	Methicillin-resistant *Staphylococcus aureus* on orthopaedic wards	The cost of care for such patients greatly exceeds the cost of introducing a policy to prevent MRSA infection. Introducing a surveillance and treatment policy is a cost-effective way of reducing its incidence.
Nyman *et al*, 2011 [35]	Cost of screening intensive care unit patients for methicillin-resistant *Staphylococcus aureus* in hospitals	The intervention was cost saving compared with no intervention. Because of the high cost of caring for a MRSA patient, interventions that reduce the spread of infections—such as screening intensive care unit patients upon admission studied here—are likely to pay for themselves.
Ornskov *et al.*, 2008 [36]	Screening for methicillin-resistant *Staphylococcus aureus* in clinical swabs using a high-throughput real-time PCR-based method	Semi-automated, high throughput, real-time PCR-based screening method for MRSA has good reproducibility, 100% sensitivity and high specificity.
Pillai, *et al* 2012 [37]	Detection of Methicillin Resistance in *Staphylococcus Aureus* by Polymerase Chain Reaction and Conventional Methods: A Comparative Study	PCR for mecA gene is the best method for detecting methicillin resistance in S. aureus with respect to accuracy, sensitivity, specificity, speed, and cost effectiveness. Increasing the number of samples for PCR on a regular basis will decrease the cost of a single PCR.
Polisena *et al*, 2011 [38]	Clinical effectiveness of rapid tests for methicillin resistant *Staphylococcus aureus* (MRSA) in hospitalized patients: a systematic review	Some studies found lower MRSA colonization and acquisition, infection, and transmission rates in screening with PCR versus screening with chromogenic agar, and the turnaround time for screening test results was lower for PCR.
Pramodhini *et al*, 2011 [39]	Comparison of Various Phenotypic Methods and mecA Based PCR for the Detection of MRSA	Conventional MRSA detection assays like the cefoxitin disc diffusion test and the oxacillin screen agar test are simple and relatively cheap and can be used as alternatives to PCR for the detection of MRSA in resource constraint settings.
Shariati *et al*, 2010 [40]	Comparison of Real-Time PCR with Disk Diffusion, Agar Screen and E-test Methods for Detection of Methicillin-Resistant *Staphylococcus aureus*	Although more expensive, real-time PCR is even more efficient than the conventional PCR as far as time is concerned. Reliable and rapid detection of patients infected by MRSA strains is pre-requisite to the successful prevention and control of MRSA infection outbreak in hospitals. Oxacillin E-test is proposed as the best phenotypic method. For economic reasons, the oxacillin agar screen method (6.0 lg/ml), which is suitable for the detection ofMRSA, is recommended due to its accuracy and low cost.
Tubbicke *et al*, 2012 [41]	Transmission rates, screening methods and costs of MRSA—a systematic literature review related to the prevalence in Germany	PCR methods show a higher sensitivity and specificity than the culture methods, which exhibit more statistical spread. Furthermore, a much faster turn-around time of PCR methods was detected, so test results are available within a day. This is balanced by the higher costs.

Table 5: Outcome of MRSA Screening

Tubbicke *et al*, 2013 [42]	Cost comparison of MRSA screening and management – a decision tree analysis	Universal MRSA screening strategies are far more cost-intensive than the targeted screening approaches. All targeted screening strategies produce lower costs than not performing a screening at all. A combination of PCR and culture method or performing the MRSA test via PCR is advantageous in comparison to the application of the culture method alone.
Uckay *et al*, 2008 [43]	Effect of Screening for Methicillin-Resistant *Staphylococcus aureus* Carriage by Polymerase Chain Reaction on the Duration of Unnecessary Preemptive Contact Isolation	The replacement of culture on chromogenic agar with rapid quantitative polymerase chain reaction for readmission screening reduces the number of unnecessary preemptive isolation-days and related costs for patients who test negative for MRSA.
Wassenberg *et al*, 2010 [44]	Rapid screening of methicillin-resistant *Staphylococcus aureus* using PCR and chromogenic agar: a prospective study to evaluate costs and effects	Rapid diagnostic testing safely reduces the number of unnecessary isolation days, but only chromogenic screening, and not PCR-based screening, can be considered as cost saving.
Wernitz *et al*, 2005 [45]	Cost analysis of a hospital-wide selective screening programme for methicillin-resistant *Staphylococcus aureus* (MRSA) carriers in the context of diagnosis related groups (DRG) payment	The screening programme became cost-effective at a low MRSA incidence rate, meaning that it can be recommended for most hospitals with an MRSA problem.
Wolk *et al*, 2009 [46]	Comparison of MRSA Select Agar, CHROMagar Methicillin-Resistant *Staphylococcus aureus* (MRSA) Medium, and Xpert MRSA PCR for Detection of MRSA in Nares: Diagnostic Accuracy for Surveillance Samples with Various Bacterial Densities	In active-surveillance convenience sample, the use of broth enrichment followed by subculture to MS offered a low-cost but sensitive method for MRSA screening, with performance similar to that of Xpert MRSA PCR.

tive patients, which involved isolation, thus increase the effectiveness of screening programs.[33] PCR can pick up false negative results by conventional methods in the early condition of the disease. It could accurately detect the presence of mecA gene rapidly with only 5 hours of bacterial isolation. Whereas, the time taken in diagnosing MRSA by the conventional method is 48-72 hours, which is twice longer than PCR method.[37] In order to identify the best solution that leads to cost benefit in terms of practicality and ethicality, an MRSA screening program should be re-evaluated by the DOH. The MRSA screening program should accomplish the ideal screening criteria set out by Wilson and Junger (WHO 1968).[15] The University Hospitals of Leicester NHS Trust develop MRSA policy in October 2003 to manage and reduce the increasing incidence of MRSA among trauma patients. The plans involved deep cleaning of wards, staff education program and providing alcohol gel dispensers in each patient's bed.[34] Moreover, screening swabs should be taken from multiple sites in order to enhance the performance. PCR was reported to have a tendency to yield false-positive rates compared to culture method. Due to this, quality assurance systems should be taken to maintain the reliability of results.[21]

A research found that almost half percentage patients that were admitted to MRSA contact isolation did not favor the isolation and quarter of them resulting in having emotional distress.[25] In order to improve patients experience and reduce costs, their studies suggested that screening with isolation should be done by targeting patients with a history of MRSA only. Several responses were recorded from patients, included feeling contaminated, inconvenient and uncomfortable. Patients that suffer emotional distress believe that isolation disturbed the privacy, and their rights were limited. In addition, some of them find that they have different treats from nurses and fewer visitors because of the gap restriction, which increase the level of uncertainty of their MRSA status.[25]

DISCUSSION

The practicality and cost effectiveness of different MRSA screening methods have become an extended debate in the medical area. The emergence of technology, conventional methods were mostly replaced by rapid screening PCR. However, the traditional method was still preferred in the first place for certain area worldwide. The main causes of the debate include the accuracy, turnaround time, cost per test, overall costs and workforce availability. Another study found that the high cost of PCR can be neutralized and cost effective in higher prevalence settings of MRSA.[12] The cost of workload per PCR can be decreased by increasing the daily number of MRSA screening tests. Even the whole costs for PCR greatly exceed the cost of the conventional method; it is revealed as the best option.[37]

PCR methods were said to have excellent sensitivity and specificity with minimum time to obtain results of 2 hours. Alternatively, conventional method maintained popularity as it offers, lower costs compared to PCR. Direct agar cultures were reported as relatively insensitive in comparison to PCR. Broth enrichment cultures were required to improve sensitivity.[48-51] Another study suggested that the addition of enrichment culture for culture method.[64] In the meantime, advancement would lead the increasing of TAT, while a PCR method was able to perform well without enrichment or any extraction.[65,66] Most studies verified that PCR is the most accurate method for detection of MRSA.[52-56] Otherwise, oxacillin agar screen was revealed as a good alternative method to PCR. It was proved to have high sensitivity and specificity for detection of MRSA with reasonable economic reasons. The results were confirmed with those of other studies that used the presence of the mecA gene as the "gold standard".[3,13,15,20,22,29,33] Any laboratory performing tests for MRSA needs to weigh up the patient benefit in relation to MRSA prevalence and the advantage of rapid results".[20]

Another research stressed that two parameters which must be taken seri-

ously to choose the reasonable screening strategy were MRSA prevalence and rate of MRSA of transmission per day of non-isolated patients.[42] Transmission rates of MRSA were reported to be higher in isolation compared to vice versa. "The costs that carried by isolation include personnel protective equipment for workers and visitors (extra gowns, gloves, masks, and caps, cleaning costs and time for nurses and physicians attributable to isolation precautions)".[41] "The use of PCR resulting in a reduction of a median 4 isolation days per patient, which directly reduce costs for previous MRSA carriers that tested positive at readmission".[43]

In this new era, quality of time has been a high demand. PCR method was said to have clear boundaries compared to culture methods with the advancement of turnaround time which balanced the high costs. The number of inappropriate isolation days (nursed patients under MRSA precautions, but were not MRSA positive on admission) was lower in rapid screening PCR compared to culture method. Whereas, the inappropriate open days (patients not under MRSA precautions, but MRSA positive on admission) were also lower for PCR compared to conventional method.[67] Xpert MRSA was said to have the best performance, which reduces isolation hours, followed by BD Gene Ohm MRSA and doubled duration with chromogenic agar (30 hours versus 16.1 hours).[44]

Our systematic review consists of several limitations. First, the costs were varied for different studies. Some studies were limited to direct costs and indirect costs. Several studies calculate costs based on annual and monthly costs, which involved different scopes of patients. Studies from a wide-ranging countries provide different perceptions in analyzing costs. Second, the selection of studies was conducted independently, which include different qualities. Publication bias might occur due to a large number of poor quality studies. However, the studies were already filtered with some stages in order to maintain the reliability of this review.

Indeed, the costs of MRSA screening using PCR are much higher than the costs of traditional culture. However, the higher costs clearly outweigh the clinical and economic benefits of saving time.[47] The outcome and effectiveness of MRSA screening from several studies were clearly summarized (Table 5). Based on the holistic review, our findings provide that PCR offers an excellent package of maintaining high sensitivity and specificity throughout the process, with lower turnaround time and isolation days. As a conclusion, targeted screening using rapid PCR may be the best choice to be implemented in Malaysia. The targeted screening of high-risk patients is a good strategy in order to balance the economic and practicality of testing due to demand for cost effectiveness. This research recommends that further clinical studies should be done in Malaysia, to provide a definite evidence of MRSA screening.

CONCLUSION

As a conclusion, targeted screening using rapid PCR may be the best choice to be implemented in the hospital setting. Due to the demand of cost effective, targeted screening of high risk patients is a good strategy in order to balance the economic and practical of screening. We recommend that further clinical studies should be done to provide a sharp evidence of MRSA screening.

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COMPETING INTERESTS

Authors possesses no competing interest. Authors have no financial competing interests with a person, institution or company.

ABBREVIATIONS

MRSA: Methicillin-Resistant *Staphylococcus aureus*; **PCR:** Polymerase Chain Reaction; **NHS:** National Health Service; **ICU:** Intensive care unit.

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