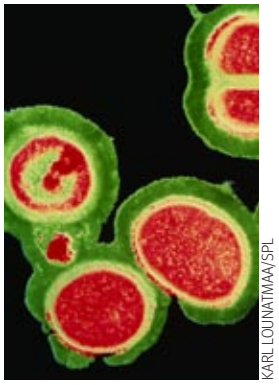
Rapid screening for MRSA

Is no more effective at reducing acquisition than conventional screening



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Controversy about the effectiveness of screening for meticillin resistant *Staphylococcus aureus* (MRSA) stems from the scarcity of robust data from controlled studies. Typically, studies supporting screening have used multiple control measures to curtail hospital outbreaks of MRSA and have lacked control groups.[1] The effectiveness of screening depends on key factors including compliance with and sensitivity of screening, capacity to isolate or form cohorts out of identified MRSA carriers, efficacy of decolonisation regimens, and compliance with standard infection control precautions (such as hand hygiene, aseptic procedures when handling vulnerable sites or devices, and prophylaxis).[2] In the accompanying study, Jeyaratnam and colleagues report a randomised controlled trial of the effect of rapid screening for MRSA on acquisition of MRSA on hospital general wards in the United Kingdom.[3]

In some healthcare systems—for example, in the Netherlands—MRSA screening has helped maintain low MRSA colonisation and infection rates. However, in MRSA endemic settings in the UK, the demand for isolation facilities (either to segregate known MRSA carriers or those at high risk) often exceeds availability.[4] This compromises one of the main principles of controlling the spread of healthcare associated pathogens.

Furthermore, the efficacy of MRSA decolonisation is suboptimal and may be exacerbated by resistance to mupirocin, the main agent used for nasal clearance, particularly if used repeatedly or for long periods.[2 5 6] A systematic review of randomised controlled trials of the efficacy of nasal mupirocin to reduce MRSA colonisation and prevent infection concluded that insufficient evidence exists to support the widespread use of topical or systemic antimicrobials for eradicating MRSA.[5] Short course mupirocin for selected patient groups, such as those about to undergo major surgery, may be helpful. UK guidelines advocate that MRSA screening should be targeted at patients at high risk of MRSA colonisation (for example, patients being transferred or re-admitted and previously known carriers) or infection (people being admitted to intensive care, cardiothoracic, orthopaedic, trauma, and vascular surgery wards).[2] Such categories will inevitably vary from hospital to hospital, which compounds the lack of standardisation of approach.

Screening on discharge can measure the prevalence of MRSA colonisation or acquisition, but it increases costs and does not guide the targeted use of measures to reduce the risk of infection. MRSA carriage is not a valid reason to delay discharge of people to their own homes or for exclusion from residential or nursing homes. Also, labelling a patient as MRSA positive at discharge may cause undue anxiety and have medicolegal implications. Despite the lack of supportive evidence for universal screening,[2] the Department of Health in England has recently stipulated that MRSA screening of all elective admissions should be in place by March 2009, and provision for screening of emergency admissions as soon as is practical.[7]

A valid criticism of most MRSA screening studies has been that the delay in obtaining a result means that transmission of MRSA from colonised patients may occur before carriage has been detected. There are two approaches to laboratory screening for MRSA—conventional culture based testing, which can give a provisional result in 24 (but more usually 48) hours, and the newer "rapid" nucleic acid amplification methods. Although these newer techniques can produce results within two to four hours, in reality sampling, transport, receipt, recording, and reporting increase this figure substantially and may make even same day results difficult to achieve for some patients. Two important recent studies are notable for their size (over 4000 and 20 000 patients) and rigour of evidence concerning the effectiveness of MRSA screening.[3 8] Both were crossover studies and used a rapid test to detect MRSA. The most recent of these is reported by Jeyaratnam and colleagues, who found no benefit of rapid versus conventional screening in terms of rates of MRSA acquisition by contacts of positive patients on 10 wards of a London teaching hospital.[3] Inappropriate isolation or cohorting of patients awaiting a screening result decreased significantly, but the authors conclude that the additional expense associated with rapid screening is unlikely to be justifiable. Laboratory costs associated with rapid screening are about three or four times higher than for conventional testing, although this difference is likely to narrow.

Jeyaratnam and colleagues' study was well designed and importantly controlled for the effects of key confounding factors, such as other MRSA control measures and antibiotic use.[3] The findings do not preclude a benefit of rapid screening for admissions to specialised units (such as intensive care), which were not studied. However, these units probably have robust infection control measures already in place, which would limit any added value of rapid screening. Four other reports on the effectiveness of rapid MRSA screening were subject to confounding as they used historical controls, so their results are unreliable.[9-12]

A Swiss study examined the effectiveness of MRSA screening of all surgical admissions compared with standard control measures.[8] While the rate of MRSA infection was low, the prevalence of MRSA colonisation was similar to that measured by Jeyaratnam and colleagues (5% *v* 7% of those screened).[3 8] Neither the rate of MRSA surgical site infection nor MRSA acquisition changed significantly when all admissions were screened.[8] More than half of the patients who developed MRSA infection on intervention wards were MRSA negative when screened on admission, and therefore probably had hospital acquired infection, despite generally good adherence to infection control precautions. Notably, the median time for "rapid" screening results to be reported was around 22 hours in both studies.[3 8] Acting on a positive result takes even longer.

MRSA infection in hospitals can be reduced by rigorous application of standard control principles, as shown by recent precipitous decreases in the incidence of bloodstream infections in England.[13] Such approaches have the added benefit of reducing risk for other healthcare associated infections. Targeted MRSA screening has a potential role as an adjunct to other infection control measures. Further large studies should investigate which patient groups benefit most from screening at admission in MRSA endemic settings, crucially when compliance with standard control measures can be demonstrated. Current evidence does not support the effectiveness of rapid as opposed to conventional MRSA screening. The cost effectiveness of MRSA screening should be compared with rigorously enforced standard control measures.

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How to improve surgical outcomes

Data should be monitored and acted on at local and national levels

RESEARCH, pp 931, 934

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Surgical outcomes are increasingly being scrutinised through national audit and publication of unadjusted league tables.[1] Two accompanying studies report different ways of measuring surgical outcomes and performance—one in groin hernia repair and the other in percutaneous coronary intervention.[2 3] Public scrutiny of surgical outcomes should be encouraged, but the data and statistical analysis should be robust, meaningful, and accurate. Unadjusted league tables are often misleading because they take insufficient account of the patients' risk factors. Commercial organisations can also produce in-depth analyses of NHS data, but many clinicians argue that the accuracy of the raw data is questionable and that such analyses are expensive and of unknown utility.

Encouraging clinicians to take responsibility for data analysis at local and national levels could improve our understanding of surgical results and help develop ways to improve outcomes. The outcomes studied should be important and easy to measure—for example, postoperative death or disease specific recurrence rates. Studies on "benefit" need further development before risk-benefit analyses can be used to plan health services.

Healthcare organisations in North America have suggested that variability in surgical outcomes is caused by factors other than cost and investment. Similar observations have been reported in the United Kingdom; this suggests that the identification and modification of risk factors at hospital level is important for improving patient outcomes. Several specialties, including arterial and hepatopancreatobiliary surgery, have focused on the relation between hospital annual workload (volume) and outcome.[4-7] The results show that units doing a higher volume of work produce significantly better outcomes. This association must be acknowledged when services are commissioned, and complex surgery should not be performed in low volume centres but should be centralised to larger units.[8]

Similar associations between volume and outcome

are apparent for procedures with a low surgical risk, such as groin hernia repair. In the first of the accompanying papers, Nordin and colleagues report that in Sweden re-operation rates were significantly higher for surgeons who performed fewer than five procedures each year.[2] They also report that almost half of hernia surgeons in Sweden are low volume operators and they performed only 8% of hernia repairs.

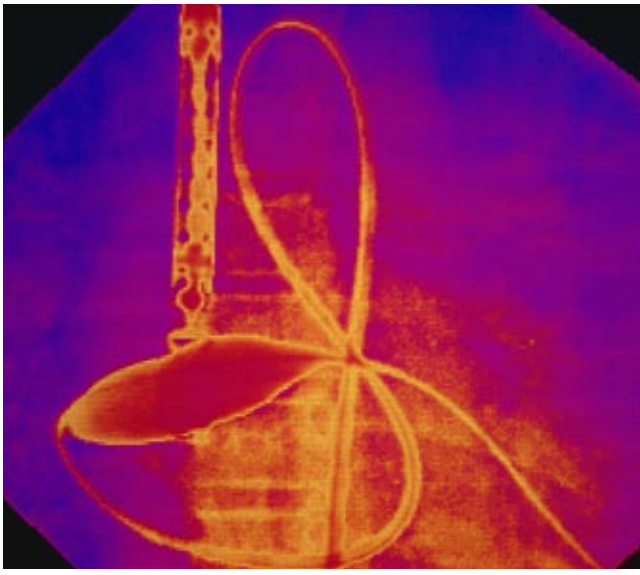
Service reconfiguration might also be facilitated by the publication of "safety charts" in complex procedures where mortality is an appropriate outcome measure.[9] This method allows the comparison of individual procedures on a national level. The technique provides a graphical output that distinguishes between hospitals with statistical evidence of safety, those with evidence of danger, and those with insufficient evidence of either. Using this technique, low volume centres were often unable to provide evidence of safety because of low case volume and consequent lack of statistical power. Therefore, not only are low volume centres associated with a worse outcome, but the appropriateness of performing high risk surgery in such centres is questionable, because outcomes cannot be assessed in terms of safety.

In a second accompanying paper, Kunadian and colleagues used funnel plots to show risk adjusted adverse outcome rates for percutaneous coronary intervention for individual operators and the overall unit.[3] The plots allowed the concurrent representation of observed and expected adverse outcome rates. They showed that the overall in-hospital rates of major adverse cardiovascular and cerebrovascular events were lower than the predicted event rate. The authors suggest that the plots could be used for internal monitoring and that individual operators could monitor their own performance in a way that is compatible with benchmarking to colleagues.

Analyses of national data have an important role in planning the delivery of services and in comparing peers, but they may be less useful at a local level. Local data must be used to understand individual unit outcomes, identify areas for improvement, and guide local commissioning. Local monitoring is of immediate importance to patients because divergent results can be identified and investigated. One way that this can be achieved is through the formation of mortality monitoring groups that meet on a monthly basis.[10] These groups use local data and statistical techniques, including cumulative sum techniques such as cumulative risk adjusted mortality charts or moving average charts, to detect change.[9 11] Individual death reports should be produced for every death to try to identify problems with care.

It is through robust local monitoring that the greatest improvements in outcomes may be seen. Too many clinicians and trusts defer responsibility for assuring outcomes to the analysis of the minimum data sets required by national bodies. This is not ideal because regular and prompt processing of local data encourages an early reaction to divergence.

Finally, analyses of local data will be of interest to healthcare commissioners. Access to these data may help commissioners to decide where surgical procedures should be performed. Centres could be selected on the basis of the demonstration of safety, a sufficient case volume, and a commitment to the ongoing assessment of local outcomes.



MEHAU KULYK/SPL

Coloured angiogram of an inflated ballon catheter during cardiac angioplasty

The analysis of surgical outcomes must remain a priority at both local and national levels. Trusts and clinicians have an obligation to be aware of local outcomes and to detect and investigate changes promptly. National data must be analysed with relevant clinical input and be of a high enough standard to provide evidence to facilitate service reconfiguration.

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Sentinel lymph node biopsy in malignant melanoma

Is unnecessary as clinically important micrometastases can be identified by ultrasound

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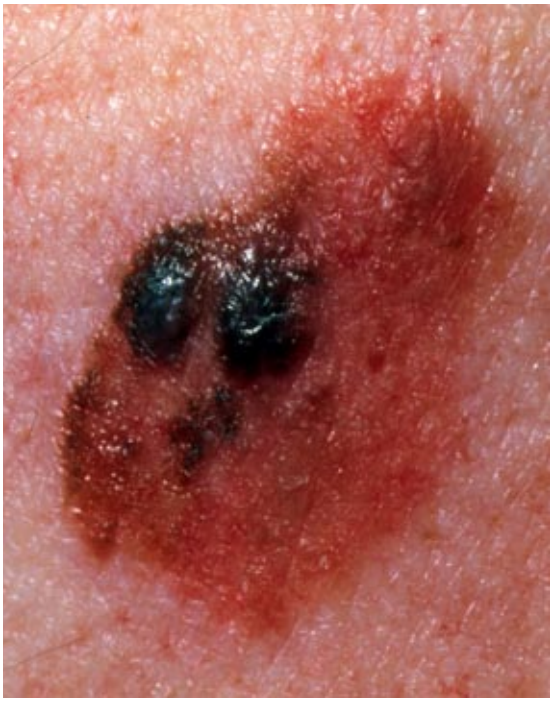
When melanoma spreads, it invariably does so by the lymphatic system. The first lymph node to be affected is called the sentinel node, and this node can be identified by injecting dye and a radioactive tracer at the primary tumour site. During sentinel lymph node biopsy, the sentinel node is located by a hand held γ probe and confirmed as the sentinel node using blue dye staining; it is then removed for histology. About 80% of patients have no melanoma in the sentinel node. In the remaining patients, the tumour burden varies from tiny deposits of melanoma in the subcapsular sinus to complete replacement of several sentinel nodes with extracapsular spread. Patients who are sentinel node negative have a better prognosis than those who are sentinel node positive, and the prognosis worsens as the tumour burden increases. But evidence is accumulating that some tiny deposits of melanoma in the sentinel node have no prognostic relevance and will not progress or disseminate further as determined by the patient's immune system and other host factors. Attributing a poorer prognosis to the presence of these tiny deposits in the sentinel node is called prognostic false positivity. This can lead to patients being mistakenly upstaged, given inaccurate prognostic information, undergoing unnecessary completion lymphadenectomy and unnecessary adjuvant therapy, or inappropriately being entered into trials of adjuvant therapy.

So what does the evidence say about the therapeutic advantage of sentinel lymph node biopsy? The multicenter selective lymphadenectomy trial (MSLT-1) randomised 2001 patients with clinically localised primary melanoma either to the control arm where they were treated by delayed lymphadenectomy if they developed palpable regional node metastases or to the biopsy arm, where they were treated by early lymphadenectomy if the sentinel node was positive for metastatic melanoma. No significant difference in melanoma specific survival was seen between the groups at five years.[1] This result was surprising because two retrospective studies had shown a 22% and a 12% survival advantage for early lymphadenectomy at five years.[2 3] In otherwise matched patients, these two studies compared the survival of sentinel node positive patients having early lymphadenectomy with those having delayed lymphadenectomy for palpable nodal recurrence. This large difference in survival between a randomised controlled trial and two similar but non-randomised studies can be explained by prognostic false positivity within the sentinel nodes of patients in the non-randomised studies.



DR P MARAZZI/SPL

Biopsy of the sentinel lymph node offers no survival advantage for patients with malignant melanoma

Other evidence exists for prognostic false positivity. Firstly, studies have reported that patients with tiny deposits of melanoma within the sentinel node—such as those that can be detected by immunohistochemistry only or deposits in the subcapsular sinus alone that are smaller than 0.1 mm—have a similar prognosis to patients who are sentinel node negative.[4 5] Secondly, the incidence of sentinel node positivity decreases with increasing age even though the incidence of melanoma and mortality from melanoma increase with age, as do tumour thickness and ulceration, which are both adverse prognostic factors. For instance, in a study of 3075 patients undergoing sentinel lymph node biopsy,[6] the incidence of sentinel node positivity was 23.1% in patients under 30 but only 12% in patients aged 61-70 ($P<0.001$). Meanwhile, mortality from melanoma rises from about 3 per 100 000 to 33 per 100 000 population between these ages. In the absence of evidence that melanomas spread more readily in the bloodstream of older patients, prognostic false positivity in younger patients is the most likely explanation, with some micrometastases being eliminated by the more competent immune systems of younger patients.[6] Thirdly, extrapolations of the results of MSLT-1 suggested that the incidence of prognostic false positivity is about 24% in patients with intermediate thickness tumours and 34% for all patients.[7]

If early lymphadenectomy has no therapeutic advantage, and in the absence of effective adjuvant therapy, is it justified to continue with sentinel lymph node biopsy for its prognostic value, other than perhaps to identify patients for entry into trials of adjuvant therapy? If the answer is no then do viable alternatives exist?

The greatest challenge to sentinel lymph node biopsy comes from ultrasound assessment of the at-risk regional node basins, which can identify up to

a third of patients ultimately found to be sentinel node positive.[8] Positivity of the sentinel node can be confirmed by ultrasound guided cytology. The ability of ultrasound to identify positive sentinel nodes rises to 50% (with 100% specificity) if the sentinel node has been located by lymphoscintigraphy.[9] Sentinel lymph node biopsy was well established before it was realised that high resolution ultrasound (which can also identify neovasculature) could identify deposits of melanoma as small as 3-4 mm in lymph nodes.[10] Ultrasound assessment of regional node basins is a neglected technique and is not used routinely to screen at-risk nodal basins at the time of diagnosis of the primary tumour. It has never been shown that sentinel node status has any prognostic value in ultrasound negative patients. Another alternative to sentinel lymph node biopsy is the use of algorithms of histological factors relating to the primary tumour, which is almost as accurate at determining prognosis as sentinel node status.[11]

So how does the evidence relate to clinical practice? Other national guidelines vary but in the UK, the National Institute for Health and Clinical Excellence guidelines on skin cancer state, "Sentinel lymph node biopsy should only be undertaken in centres where there is clinical experience of the procedure and normally only within the context of ethics-committee-approved clinical trials. However, to maintain their already established expertise, centres may continue to offer sentinel lymph node biopsy between trials."[12] In reality, sentinel lymph node biopsy is increasingly practised in the UK outside the context of clinical trials and on a "postcode" basis. In some regions, the procedure is offered as routine treatment by enthusiastic dermatologists and surgeons, and in other regions, not at all. Few British patients have been entered into randomised controlled trials as envisaged by NICE.

The sentinel lymph node biopsy procedure offers no survival advantage and no systemic adjuvant therapy is available that can benefit sentinel node positive patients. It is therefore difficult to justify the surgical morbidity incurred. Ultrasound screening and surveillance will identify clinically relevant micrometastases before they become palpable. Extrapolating from the results of MSLT-1, patients do not seem to be disadvantaged by this alternative method of management. On the contrary, patients with prognostically false positive sentinel nodes will be protected from unnecessary lymphadenectomy.

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Patient and public involvement in clinical trials

Is established worldwide, but encouragement is needed to promote institutional collaboration and avoid duplication of effort

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Patient and public involvement in clinical trials has been defined as "experimenting with" as opposed to "experimenting on" patients.[1] It is founded on the belief that a collaborative approach to testing treatments is vital if the uncertainties that matter most to patients are to be reduced.[2] In 1994, the ethicist Raanon Gillon proposed that not only morality but also scientific interest should combine to urge a "brave new partnership between clinical trialists and patients."[3]

It is difficult to be precise about the origin of patient and public involvement but several early examples exist. Rose Kushner—a pioneer of patient involvement in the United States in the 1970s—was a freelance writer who also had breast cancer. She wrote a book, which was based on a thorough review of evidence of the effects of radical mastectomy. Her influence and attitude was such that she eventually reviewed new research proposals for the US National Cancer Institute.[4] Her achievements helped inspire the work of the US National Breast Cancer Coalition.

Another early example of well organised and influential involvement occurred in the 1980s in the United Kingdom. The Association for Maternity Services convened a meeting of interested voluntary organisations and patient groups to encourage them to support the Medical Research Council's proposals for a

randomised controlled trial of chorionic villus sampling in pregnancy. Representatives of these groups were involved in conducting and promoting this important trial.[5] Another example is provided by well organised groups of people with AIDS—first in the US and then in the UK—who challenged researchers' approaches to conducting trials, which had overlooked patients' preferred outcomes.[2 6]

In 1997, the first international conference on breast cancer advocacy, attended by people from 44 countries and six continents, took place in Brussels. It was led by the US National Breast Cancer Coalition and supported by organisations from Panama, Belgium, the UK, and Israel. This meeting helped shift the balance towards consumer participation, which was becoming a reality at that time.[7] The Cochrane Collaboration (www.cochrane.org/), an international organisation that puts strong emphasis on consumer participation, also took part in the meeting.

After a UK government inquiry in March 1995, in which patient involvement in the whole research process had been advocated,[8] the Health Select Committee report on breast cancer services devoted a section to "Involving patients in research." On the basis of written and oral evidence, ministers recommended that patient involvement at all stages of a trial, including the initial design, is essential and that initiatives such as the Consumers Advisory Group for Clinical Trials should be welcomed.[6 9] Ministers believed that their recommendations would help to improve the standard of care for women with breast cancer in the UK. They also hoped that "as other specialties follow the lead, they may help to raise the standard of care for all cancer patients." Subsequently, the Standing Advisory Group on Consumer Involvement in the NHS R&D Programme was formed in April 1996 to advise the Central Research Development Committee on how to boost patient involvement in the UK NHS research and development programme. The group included representatives of consumer bodies, health professionals, managers, and information specialists.

Patient and public involvement now goes beyond clinical trials. For example, an appointed group of 30 well motivated and informed lay members, the Citizens Council of the National Institute for Health and Clinical Excellence (www.nice.org.uk/page.aspx?o=citizenscouncil), contributes to decisions about the prioritisation of healthcare resources on the basis of evidence from clinical trials. They help to decide whether interventions should be approved or rejected, or whether treatments should be available only in randomised controlled trials and not in clinical practice. Within the James Lind Alliance, lay people form part of a support and information group that works with health professionals to prioritise research questions.[10] In both of these examples, professional and lay members focus on improving research processes and seeking fair systems that consider the needs of patients.

Since the recognition and acceptance of patient and public involvement, and the rapid accumulation of evidence regarding its worth,[11] patient and public involvement has been implemented here in the UK and in Europe, the United States, Canada, and Australia. In the UK, the National Institute for Health Research (NIHR) is now established as part of the government's strategy, "Best research for best health." The NIHR wants patients and the public to be involved in all stages of research, and, together with its partners—the UK Clinical Research Collaboration and Involve—has put structures in place to achieve and facilitate this.

Healthy development of the partnership between patients and the medical profession will depend on firm policy directives that encourage institutional collaboration to avoid wastage of resources and duplication of effort. It will be important to record and understand the social and cultural history of patient and public involvement, compile comprehensive databases, and undertake ongoing reviews of the effect of public involvement if we are to make progress and maintain balance and equality within this new partnership.

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