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(Accepted 7 June 2006)

doi 10.1136/bmj.38891.681215.AE

Mortality after *Staphylococcus aureus* bacteraemia in two acute hospitals in Oxfordshire, 1997-2003: cohort study

David H Wyllie, Derrick W Crook, Tim E A Peto

Abstract

Objective To determine the incidence of methicillin resistant and methicillin sensitive *Staphylococcus aureus* (MRSA and MSSA) bacteraemia in inpatients and associated mortality within 30 days after diagnosis.

Design Anonymised record linkage study of data from hospital information systems and microbiology databases.

Setting Teaching hospital and district general hospital in Oxfordshire.

Participants Inpatients aged 18 or over admitted to a teaching hospital between 1 April 1997 and 31 March 2004 and to a district general hospital between 1 April 1999 and 31 March 2004. The main part of the study comprised 216 644 inpatients; patients admitted to haematology, nephrology, or oncology services were not included because most were managed as outpatients.

Outcome measures Nosocomial MSSA and MRSA bacteraemia; death in hospital within 30 days after bacteraemia.

Results Rates of *S aureus* bacteraemia rose between 1997 and 2003, and MRSA was responsible for this increase. Overall mortality 30 days after bacteraemia was 29%. The crude odds ratio for death after MRSA bacteraemia compared with MSSA bacteraemia was 1.49 (95% confidence interval 0.99 to 2.26).

Conclusion The spread of MRSA has greatly increased the overall number of cases of *S aureus* bacteraemia and has contributed to short term mortality after *S aureus* bacteraemia.

Introduction

Rapidly rising rates of infection with methicillin resistant *Staphylococcus aureus* (MRSA) led to the revision of United Kingdom national infection control guidelines in 1998. Previously, an MRSA search and destroy

method was used; afterwards, patients were stratified according to risk, and targeted prevention measures recommended.¹ However, rates of MRSA bacteraemia have continued to rise.^{2 3}

Our understanding of the impact of the high rate of MRSA in the UK on death after *S aureus* bacteraemia is limited. Analyses of death certificates have suggested rising MRSA associated mortality, but analysis of death certificates can result in biased estimates of disease associated mortality.^{4 5} We describe secular trends in nosocomial methicillin sensitive *S aureus* (MSSA) bacteraemia, MRSA bacteraemia, and survival 30 days after bacteraemia in inpatients in acute care hospitals in Oxfordshire after the search and destroy policy changed, and we discuss the impact of the MRSA epidemic on mortality after nosocomial *S aureus* bacteraemia.

Methods

Data sources, linkage, and statistical analysis

Our study took place in a teaching hospital and a district general hospital in Oxfordshire, which together provide acute clinical and bacteriology services to 600 000 people.

We used anonymised record linkage.⁶ We generated a database of all patient admissions, excluding outpatients, between 1 January 1997 and 31 March 2004. In addition to admission data, the database had information on all isolates of MSSA and MRSA detected between 1 January 1995 and 31 March 2004.

Editorial by Paul

Nuffield
Department of
Clinical Laboratory
Sciences, University
of Oxford, John
Radcliffe Hospital,
Oxford OX3 9DU
David H Wyllie
clinical lecturer in
microbiology
Derrick W Crook
consultant
microbiologist

Nuffield
Department of
Medicine,
University of
Oxford

Tim E A Peto
professor of infectious
diseases

Correspondence to:
D Wyllie
david.wyllie@
ndcls.ox.ac.uk

BMJ 2006;333:281-4



This is the abridged version of an article that was posted on bmj.com on 23 June 2006: <http://bmj.com/cgi/doi/10.1136/bmj.38834.421713.2F>

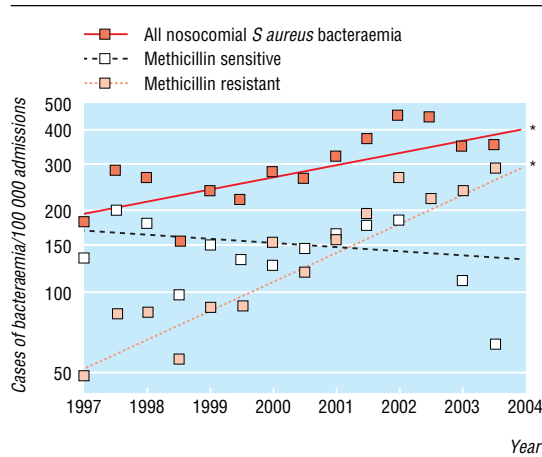


Fig 1 Changes in rates of nosocomial bacteraemia over time in two Oxfordshire hospitals (n=144 134). Regression lines indicate change over time. Asterisks indicate that the slope of the line is significant (P<0.01; P>0.20 for the others)

Cohort studied

Patients were admitted between 1 April 1997 and 31 March 2004; they were aged 18 or over on the day of admission. We restricted our analysis to patients who stayed in hospital for two or more days, as these patients are at risk of nosocomial bacteraemia.⁷ We excluded patients admitted to renal, haematology, and oncology services, as few admissions lasted two or more days (see bmj.com).

Screening policies and microbiology

Our MRSA screening policies were based on national guidance. Microbiological processing used standard techniques.⁶

Statistical analysis

We analysed correlations between *S aureus* bacteraemia, inpatient death, and previous isolation of MRSA. We used linear and logistic regression to relate the variables of interest to date of admission. We built two sets of multivariate regression models: one described *S aureus* bacteraemia, and the other described inpatient death according to patient characteristics. We compared inpatient mortality 30 days after bacteraemia among patients with MSSA and MRSA (see bmj.com).

Results

The cohort was made up of 216 644 admissions. We identified 461 cases of nosocomial *S aureus* bacteraemia—232 cases of MRSA and 229 cases of MSSA. Of these 461 cases, 441 (96%) occurred in the 144 134 admissions to medical, surgical, or trauma

services. Only 20 cases (4%) occurred in the other 72 510 patients. We restricted our further analyses to medical, surgical, and trauma specialties.

Rates of MRSA and MSSA bacteraemia

During the seven years from 1997, overall rates of *S aureus* bacteraemia per admission rose; this was due to an increase in MRSA bacteraemia—rates of MSSA bacteraemia did not alter (fig 1). Case mix also changed over this time, with the age, duration of stay, and proportion of admissions with prior isolation of MRSA all increasing (see bmj.com).

Increase in *S aureus* bacteraemia and isolation of MRSA

The table shows a multivariate logistic regression model for all types of *S aureus* bacteraemia; we constructed similar models for MSSA and MRSA bacteraemia (not shown). These models show that the increase in overall *S aureus* bacteraemia is not explained by changes in case mix alone (adjusted increase each year 1.06, 1.01 to 1.12; P=0.02; table). The estimated rates of change per annum for MRSA and MSSA bacteraemia were 1.22 (1.13 to 1.31) and 0.93 (0.87 to 1.00; P=0.05). Thus, the increase in overall rates of *S aureus* bacteraemia is due to MRSA; although unadjusted rates of MSSA bacteraemia have stayed constant over time, when correlates of increased risk, ageing hospital population, and increasing stay are adjusted for, the rate of MSSA bacteraemia may have fallen.

The model in the table also shows a significant interaction between age and duration of stay, indicating that the increased risk associated with a longer period of inpatient stay depends on age and previous length of stay. We built more complex models that included specialty and examined multiple interactions. Results were similar to those presented in the table.

Mortality associated with *S aureus* bacteraemia

Staphylococcus aureus bacteraemia identifies a group at high risk of inpatient death; bacteraemia associated mortality could not be explained by age, date of admission, previous isolation of MRSA, or specialty (see bmj.com).

We investigated the association between MRSA and MSSA bacteraemia and death during the following 30 days. Among the 441 cases of *S aureus* bacteraemia, 130 (29%) patients died within 30 days. The death rate was 34% (76/227) for MRSA and 27% (58/214) for MSSA. The crude odds ratio for mortality within 30 days with isolation of MRSA versus MSSA was 1.49 (0.99 to 2.26). To identify groups in which MRSA was more likely to cause death than MSSA, we stratified by age, isolation of MRSA before admission, stay on an intensive care unit or renal ward before bacteraemia, specialty admitted to, specialty from which last

Risk of nosocomial *Staphylococcus aureus* bacteraemia (both MRSA and MSSA) in two Oxfordshire hospitals 1997-2003 (n=144 134)

Variable	Univariate analysis					Multivariate analysis	
	Odds ratio (95% CI)	Wald χ^2	df	P value	Odds ratio (95% CI)	Wald χ^2 (1 df)	
Secular trend, per year	1.11 (1.05 to 1.17)	18.2	1	<0.01	1.06 (1.01 to 1.12)	5.1	
Specialty, overall	–	3.6	3	0.30	Not entered	–	
Log (length of stay in weeks)	4.33 (3.99 to 4.70)	1251	1	<0.01	11.3 (8.10 to 15.6)	210	
Age, per decade	1.19 (1.12 to 1.25)	38.8	1	<0.01	1.09 (1.01 to 1.18)	4.3	
Previous isolation of MRSA	2.86 (2.01 to 4.06)	34.2	1	<0.01	1.53 (1.07 to 2.21)	5.4	
Log (duration of stay) \times age	1.18 (1.17 to 1.20)	1169	1	<0.01	0.87 (0.83 to 0.91)	34	

MRSA=methicillin resistant *S aureus*, MSSA=methicillin sensitive *S aureus*.

What is already known on this topic

Mortality is high in inpatients who develop methicillin resistant *Staphylococcus aureus* (MRSA) bacteraemia—short term mortality is 12-25%

What this study adds

From 1997 to 2003, hospital acquired *S aureus* bacteraemia rates and post-bacteraemia mortality rose because of an increase in the number of MRSA cases

Mortality after MRSA bacteraemia was at least as high as after MSSA bacteraemia

discharged, and year of admission (fig 2). We found no significant heterogeneity within the strata examined, indicating that the risk of death after MRSA bacteraemia is similar to (or higher than) that after MSSA bacteraemia in many patient groups.

Discussion

We found that about 30% of patients with *S aureus* bacteraemia died within 30 days after diagnosis, a result similar to other studies.⁸⁻¹⁰ From 1997 to 2003, instead of displacing MSSA as the cause of nosocomial *S aureus* bacteraemia, MRSA added to it, thereby increasing the rates of *S aureus* bacteraemia. This increase cannot be explained by ageing of the hospitalised population or increased hospital stay in the group studied, although both occurred. Comparison of short term outcome (mortality within 30 days) after MRSA and MSSA bacteraemia suggests that the outcome of MRSA bacteraemia was at least as bad as that from MSSA bacteraemia. There may be an MRSA associated excess in the order of 50%, although this excess is not conventionally significant in our study. A small MRSA associated excess in mortality would fit in with the findings of a UK based study of a larger number of risk factors and with a recent meta-analysis.^{11 12} Thus, the emergence of MRSA seems to be associated with an increase in inpatient mortality soon after *S aureus* bacteraemia.

Limitations

We did not consider long term outcomes, such as readmission or relapse. We lack information on antibiotic treatment, which is a determinant of outcome in bloodstream infection in general and *S aureus* in particular.^{9 13 14} A key issue is whether bacteraemia was the underlying cause of death in these patients. It is difficult to attribute the cause of death in cases of *S aureus* bacteraemia because of the many coexisting risk factors for death, such as acute and chronic illness, and the high degree of medical intervention.¹⁵ Because we have limited information on comorbidity, we did not try to assess the fraction of deaths attributable to *S aureus* bacteraemia. Multivariate methods yielded estimates of 25% in a Belgian intensive care unit and 15% in older patients in a study from the United States^{8 16}; a UK study produced an estimate of 12%.¹¹

Implications

The contribution of MRSA to overall *S aureus* bacteraemia combined with the high mortality associated with

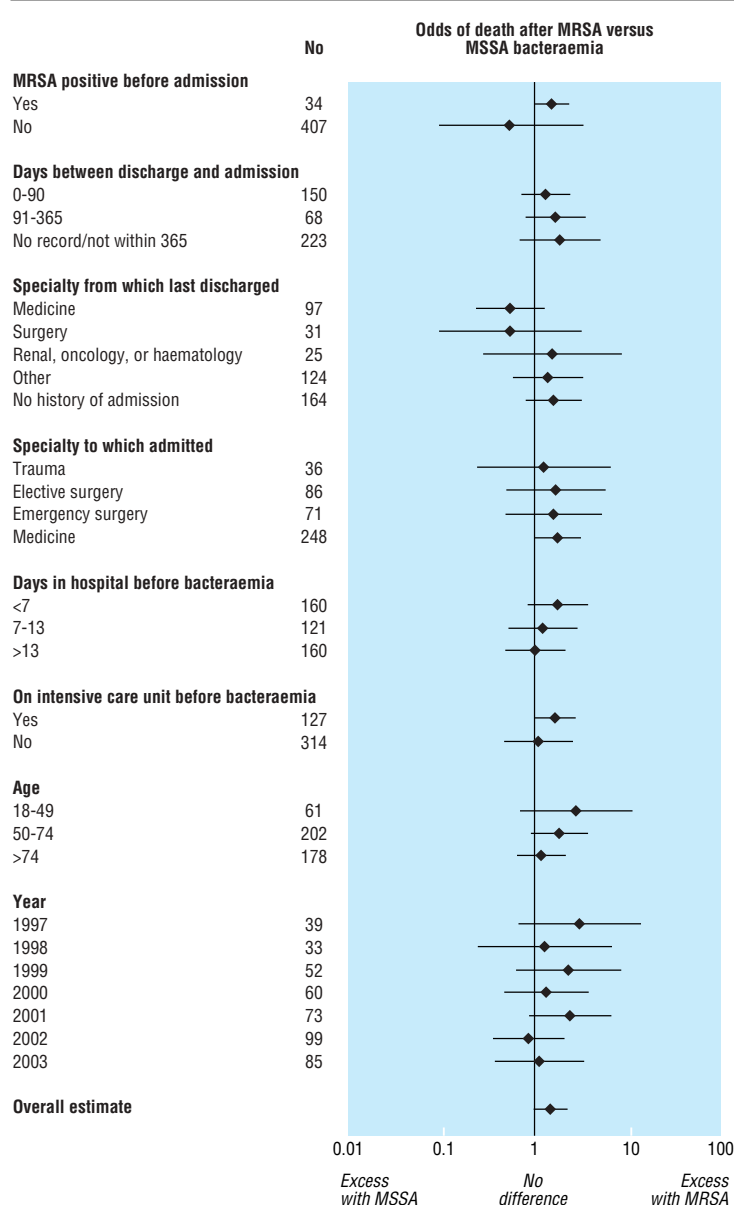


Fig 2 Risk of death 30 days after diagnosis of *Staphylococcus aureus* bacteraemia in two Oxfordshire hospitals (n=144 134)

the condition supports current attempts to reduce the spread of MRSA. It would be useful to carry out studies with a similar design to ours that systematically collect hospital based, patient centred data on cases of MSSA and MRSA and controls. If implemented over a sufficient patient base, this would allow investigation of reasons for MRSA associated excess mortality, estimation of the effect of treatment protocols, and ecological and individual studies of determinants of outcome.^{11 12} It would also allow planning of intervention trials of the options available to prevent the spread of MRSA and treat bacteraemia.

We thank the reviewers for their helpful comments.

Contributors: See bmj.com.

Funding: None.

Competing interests: None declared.

Ethical approval: Not needed.

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(Accepted 13 April 2006)

doi 10.1136/bmj.38834.421713.2F

Health professionals' and service users' interpretation of screening test results: experimental study

Ros Bramwell, Helen West, Peter Salmon

Abstract

Objective To investigate the accuracy of interpretation of probabilistic screening information by different stakeholder groups and whether presentation as frequencies improves accuracy.

Design Between participants experimental design; participants responded to screening information embedded in a scenario.

Setting Regional maternity service and national conferences and training days.

Participants 43 pregnant women attending their first antenatal appointment in a regional maternity service; 40 companions accompanying the women to their appointments; 42 midwives; 41 obstetricians. Participation rates were 56%, 48%, 89%, and 71% respectively.

Measures Participants estimated the probability that a positive screening test result meant that a baby actually had Down's syndrome on the basis of all the relevant information, which was presented in a scenario. They were randomly assigned to scenarios that presented the information in percentage ($n=86$) or frequency ($n=83$) format. They also gave basic demographic information and rated their confidence in their estimate.

Results Most responses (86%) were incorrect. Obstetricians gave significantly more correct answers (although still only 43%) than either midwives (0%) or pregnant women (9%). Overall, the proportion of correct answers was higher for presentation as

frequencies (24%) than for presentation as percentages (6%), but further analysis showed that this difference occurred only in responses from obstetricians. Many health professionals were confident in their incorrect responses.

Conclusions Most stakeholders in pregnancy screening draw incorrect inferences from probabilistic information, and health professionals need to be aware of the difficulties that both they and their patients have with such information. Moreover, they should be aware that different people make different mistakes and that ways of conveying information that help some people will not help others.

Introduction

Extensive psychological research has shown that most people, including health professionals, incorrectly interpret probabilistic information from screening tests.¹ Laboratory research suggested extreme overestimation or underestimation of the probability that a positive screening result indicated that the relevant condition was present. Scenarios describing medical screening produced more overestimation than did ones describing screening of machine parts.² The suggestion that evolution and experience equip people better to understand probabilistic information expressed as frequencies in a population, rather than

Division of Clinical Psychology,
University of Liverpool,
Liverpool L69 3GB
Ros Bramwell
senior lecturer
Helen West
research student
Peter Salmon
professor

Correspondence to:
R Bramwell
rosb@liv.ac.uk

BMJ 2006;333:284-6



This is the abridged version of an article that was posted on bmj.com on 13 July 2006: <http://bmj.com/cgi/doi/10.1136/bmj.38884.663102.AE>