

THIS WEEK'S RESEARCH QUESTIONS

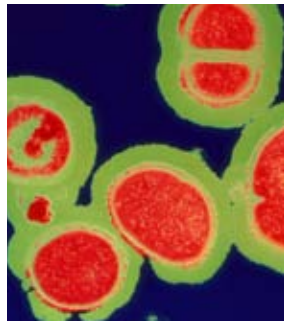
- 781** What is the most cost effective MRSA control strategy in intensive care units?
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- 783** What is the updating speed of authoritative point of care summaries—that is, the time between a relevant paper's publication and its citation in information summaries?
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Controlling MRSA infection in hospital

Infection with methicillin resistant *Staphylococcus aureus* (MRSA) has become a major cause of morbidity and mortality in patients admitted to hospital, particularly those in intensive care units. Isolation and decolonisation are the two main control measures, with screening of other patients for potential asymptomatic colonisation with MRSA a possible third. Without good evidence on the most effective combination of interventions or the optimal screening method, control strategies tend to vary from hospital to hospital.

This week Julie Robotham and colleagues describe how they used a hypothetical model of MRSA transmission in an attempt to determine the most cost effective MRSA control strategy in intensive care units (p 781). Their analysis indicated that a strategy of universal topical decolonisation, regardless of MRSA status, was the most cost effective in the short term. However, such untargeted use of antibiotics could encourage resistance, making the problem much worse in the long term. If decolonisation of all patients is excluded, the optimal strategy becomes targeted decolonisation based on the results of universal screening using polymerase chain reaction.

In their linked editorial (p 753), Jan Kluytmans and Stephan Harbarth consider the practical implications of this study and warn that the effectiveness of the suggested control strategies needs to be confirmed in clinical studies. For example, the practical difficulty of decolonisation in critically ill patients with endotracheal tubes, catheters, drains, and wounds increases the risk of treatment failure and could tip the balance more towards isolation.



DR KARI LOUNATMAA/SPL

Which is the best online resource? Time for a debate

The choice of point of care summaries is vast. The million dollar question for clinicians surfing the net for quality, up to date information is which one is choose? Few studies have compared the quality of point of care summaries, according to Rita Banzi and colleagues (p 783). In the absence of evidence, clinicians may rely on their instincts, recommendations, subscriptions, or the appealing marketing lines of such point of care resources, to guide them.

Banzi and colleagues begin to unpick one element of quality; the speed of updating content. They selected five point of care summaries (Clinical Evidence, Dynamed, EBM Guidelines, eMedicine, and UpToDate), that they judged to be of high quality on the basis of coverage of medical conditions (volume) and editorial quality and evidence based methodology, and measured how quickly they incorporated evidence

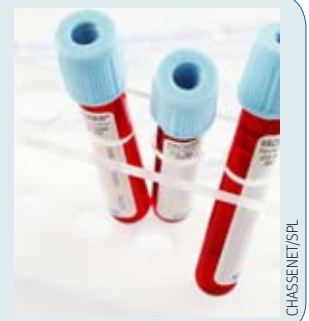
from certain systematic reviews. At nine months, Dynamed had cited 87% of the 128 eligible systematic reviews that had been published in that time, whereas the other summaries had cited less than 50%.

The authors conclude that Dynamed clearly dominates the other products in terms of speed but acknowledge that updating speed is only one aspect of the overall quality of a point of care product. In his rapid response to the full paper on bmj.com, Rubin Minhas, editor-in-chief of *BMJ Clinical Evidence*, widens the debate: "What is the 'need for speed'? How quick is too quick and how long is too long? Are priority based approaches better than time based ones? Should users of evidence based point of care tools expect publishers to be transparent about the quality of their products? And is it finally time we had a CONSORT-type framework for clinical decision support tools?"

LATEST RESEARCH: For these and other new research articles see www.bmj.com/research

Impact of late diagnosis and treatment on life expectancy in people with HIV-1 Margaret May and colleagues found that life expectancy in people treated for HIV infection in the UK has increased by over 15 years during 1996-2008 but is still about 13 years less than that of the general population, and a late start to antiretroviral therapy (CD4 cell count <200 cells/mm³) resulted in up to 15 years' loss of life (doi:10.1136/bmj.d6016).

Effect of multidimensional lifestyle intervention on fitness and adiposity in predominantly migrant preschool children (Ballabeina) In a group of predominantly migrant young children, who tend to have high levels of obesity and low fitness, J J Puder and colleagues found that a multidimensional, culturally tailored, lifestyle intervention programme improved fitness and body fat, though not body mass index (doi:10.1136/bmj.d6195).



CHASSENET/SPL

CME

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This is a summary of a paper that was published on *bmj.com* as *BMJ* 2011;343:d5694

EDITORIAL by Kluytmans and Harbarth

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Screening, isolation, and decolonisation strategies in the control of meticillin resistant *Staphylococcus aureus* in intensive care units: cost effectiveness evaluation

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STUDY QUESTION

How cost effective are screening combined with isolation or decolonisation strategies to control meticillin resistant *Staphylococcus aureus* (MRSA) in an intensive care unit (ICU) setting?

SUMMARY ANSWER

All decolonisation strategies improved health outcomes and reduced costs, and although universal decolonisation was most cost effective in the short term, strategies using screening with polymerase chain reaction (PCR) to target carriers may be preferred owing to the reduced risk of selecting for resistance. Of the strategies involving isolation, targeting patients at high risk of carrying MRSA is likely to be an efficient use of resources.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

RSA continues to cause a high burden of disease in ICUs yet which screening and intervention strategies are most effective and cost effective remains uncertain. Using a model based analysis, interventions based on screening and decolonisation were potentially cost saving in ICU settings provided strains were sensitive to the agents used, with universal PCR based screening likely to represent an efficient use of resources.

Main results

Control measures based on screening combined with decolonisation reduced infection rates by up to 50%, although reductions in mortality were small (<1%). While universal decolonisation had the highest probability (70%) of being the

most cost effective strategy at a willingness to pay of £30 000 (€34 000; \$48 000) per quality adjusted life year (QALY), the best targeted decolonisation strategy used universal PCR screening. Reduction in infection rates through screening and isolation strategies ranged from 8% (conventional culture) to 13% (PCR).

Design

We used a cost effectiveness analysis based on a dynamic transmission model. We calculated incremental cost effectiveness ratios for alternative strategies and carried out probabilistic sensitivity analyses to provide net monetary benefits with associated uncertainty. The perspective was of a healthcare decision maker at a regional or national level.

Source(s) of effectiveness

Estimates for intervention effectiveness and other model parameters (and associated uncertainty) were obtained through a combination of literature review, new analyses of primary data, and formal elicitation of expert opinion.

Data sources

Costs comprised direct intervention costs, infection related treatment costs, and extra bed days and their associated opportunity costs. Short run average costs were evaluated against health benefits summarised by changes in QALYs.

Results of sensitivity analysis

Universal decolonisation remained the most cost effective option in sensitivity analyses of varying ICU size, MRSA admission prevalence, and the proportion of high risk patients admitted, whereas universal polymerase chain reaction based screening remained the best targeted option. Results were largely insensitive to the effectiveness of decolonisation. For ICUs with less than 5% of patients colonised on admission, admission and weekly chromogenic agar screening of high risk patients with isolation of patients identified as MRSA positive was the optimal isolation based approach (£17 000 per QALY). At a 10% prevalence, universal PCR screening and isolation was optimal (£25 000 per QALY). Results were highly sensitive to the effectiveness of isolation.

Limitations

This analysis ignores longer term health consequences of MRSA infections. Therefore the results underestimate the health benefits and cost savings.

Study funding/potential competing interests

All researchers are independent of the funding body, the Department of Health policy research programme (PR-IP-0807-0410026). We have no competing interests.

SCREENING, ISOLATION, AND DECOLONISATION STRATEGIES TO CONTROL METICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA) IN INTENSIVE CARE UNITS

Decolonisation strategies

Do nothing (decolonisation of clinical cases only)

Pre-emptive decolonisation (with chlorhexidine)

Universal pre-emptive decolonisation

Pre-emptive decolonisation of high risk patients

Universal screening+decolonisation of MRSA positive patients (with nasal mupirocin)

Conventional culture+decolonisation

Chromogenic agar+decolonisation

Polymerase chain reaction+decolonisation

Screening of high risk patients

+decolonisation of MRSA positive patients (with nasal mupirocin)

Conventional culture+decolonisation

Chromogenic agar+decolonisation

Polymerase chain reaction+decolonisation

Isolation strategies

Do nothing (isolation of clinical cases only)

Pre-emptive isolation

Pre-emptive isolation of high risk patients

Universal screening+isolation of MRSA positive patients

Pre-emptive isolation (+amendment on results of conventional culture)

Conventional culture+isolation

Chromogenic agar+isolation

Chromogenic agar (24 and 48 hour result)

+isolation

Polymerase chain reaction+isolation

Screening of high risk patients+isolation of MRSA positive patients

Conventional culture+isolation

Chromogenic agar+isolation

Chromogenic agar (24 and 48 hour result)

+isolation

Polymerase chain reaction+isolation

This is a summary of a paper that was published on bmj.com as *BMJ* 2011;343:d5886

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Impact of CONSORT extension for cluster randomised trials on quality of reporting and study methodology: review of random sample of 300 trials, 2000-8

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STUDY QUESTION Has the reporting or methodological conduct of cluster randomised trials improved since the publication of the extension to CONSORT for cluster randomised trials?

SUMMARY ANSWER Improvements were seen in some aspects of reporting but not for any measured aspects of methodological conduct.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Cluster randomised trials are becoming more common and have particular risks for bias that must be addressed through unique methodology and transparent reporting. Previous reviews have found poor reporting of cluster randomised trials, and the extension of CONSORT for cluster randomised trials tried to address this. This review found that few aspects of reporting have improved over time, and the reporting and methodological conduct of cluster randomised trials remain suboptimal.

Selection criteria for studies

300 studies published in 2000-8 were randomly selected from a sensitive Medline search for cluster randomised trials. Two investigators independently abstracted data.

Primary outcomes

We abstracted 14 criteria related to quality of reporting and four methodological criteria specific to cluster randomised trials. Changes over time in reporting or methodological conduct of studies were evaluated from before (2000-4) to after (2005-6 and 2007-8) the CONSORT extension, with a test for trend.

Main results and role of chance

There was a significant trend for improvement in five of the 14 reporting criteria: identification as "cluster randomised" in title or abstract; providing a justification for the clustered design; reporting whether or not outcome assessors had been blinded; reporting of the number of clusters randomised; and reporting on cluster loss to follow-up. There was no evidence of a trend for any of the four criteria evaluating methodological conduct: allocating a minimum of four clusters per arm; use of restricted randomisation; accounting for clustering in sample size; and accounting for clustering in analysis. Trials conducted in clinical rather than non-clinical settings and studies published in higher impact factor or general medical journals were more likely to adhere to recommended reporting and methodological criteria overall, but there was no evidence that improvements after publication of the CONSORT extension were more likely in trials conducted in clinical settings nor in trials published either in general medical or in higher impact factor journals.

Bias, confounding, and other reasons for caution

The Medline search strategy for cluster randomised trials had a sensitivity of 90%, but if the 10% of cluster randomised trials not identified by the strategy were systematically different with respect to reporting or methodological quality, this could bias our results. Although the sample was large relative to previous methodological reviews, our sample size was determined by the objectives of a separate study focusing on ethical issues in cluster trials, and we were therefore not specifically powered to detect small improvements in reporting. Furthermore, there is a risk of spurious findings associated with multiple testing in our analyses. Finally, the extension to CONSORT for cluster randomised trials might have resulted in improvements for criteria other than those that we abstracted.

Study funding/potential competing interests

This study was been funded by the Canadian Institutes of Health Research. NMI and AMCR both hold a fellowship award from the Canadian Institutes of Health Research. JMG and CW both hold Canada Research Chairs.

ADHERENCE TO STANDARD CRITERIA FOR REPORTING AND METHODOLOGY FOR CLUSTER RANDOMISED TRIALS BEFORE AND AFTER PUBLICATION OF CONSORT EXTENSION FOR CLUSTER RANDOMISED TRIALS

| | No (%) of adherent studies (n=300) | P for trend* |
|---|------------------------------------|--------------|
| Criteria related to quality of reporting | | |
| Clearly identified as clustered in title or abstract | 145 (48) | 0.038 |
| Justification provided for using cluster design | 94 (31) | 0.038 |
| Reported on blinding of outcome assessors | 113 (38) | 0.019 |
| Reported on blinding of participants/administrators | 151 (50) | 0.292 |
| Primary outcome identified clearly | 141 (47) | 0.284 |
| Sample size calculation presented | 164 (55) | 0.483 |
| Identified who enrolled participants† | 134 (58) | 0.674 |
| Reported no of clusters randomised | 261 (87) | 0.035 |
| Reported no of clusters lost to follow-up | 235 (78) | 0.010 |
| Reported no of clusters that withdrew | 256 (85) | 0.078 |
| Reported size of clusters in each arm | 262 (87) | 0.081 |
| Reported no of individuals lost to follow-up | 228 (76) | 0.860 |
| Reported methods of analysis | 281 (94) | 0.456 |
| Reported intracluster correlation‡ | 35 (16) | 0.323 |
| Criteria relating to methodological quality | | |
| Used restricted randomisation | 167 (56) | 0.272 |
| Allocated minimum of four clusters per arm§ | 244 (86) | 0.867 |
| Accounted for clustering in sample size calculations¶ | 100 (61) | 0.662 |
| Accounted for clustering in analysis | 209 (70) | 0.474 |

*Comparing trials meeting criteria before (2000-4) to after (2005-6 and 2007-8) CONSORT.

†Excludes 67 trials with no participant enrolment.

‡Excludes 84 trials with pair matched designs or primary analysis at cluster level.

§Excludes 15 studies with unclear number of clusters.

¶Excludes 136 trials with no sample size calculation presented.

Speed of updating online evidence based point of care summaries: prospective cohort analysis

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STUDY QUESTION

What is the updating speed of authoritative point of care summaries—that is, the time between a relevant paper's publication and its citation?

SUMMARY ANSWER

Evidence relevant to practice is inserted at different speeds in point of care information summaries. The updating speed of Dynamed clearly leads the others.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Information summaries are increasingly used by doctors to support clinical decision making at the point of care. Few studies have compared the quality of such summaries and none their updating speed. Point of care summaries insert latest evidence relevant to practice at different speeds, with one product leading the others.

Participants and setting

We selected five point of care information summaries (Clinical Evidence, Dynamed, EBM Guidelines, eMedicine, and UpToDate) for their quality in terms of editorial policy, evidence based methodology, and coverage of medical conditions (volume). To measure updating speeds we examined the incidence of citations of newsworthy pieces of information in the chapter contents. This sample comprised 128 systematic reviews mentioned in the ACP Journal Club, Evidence-Based Medicine, and the Cochrane Library from

April to December 2009. These sources select reviews that meet basic validity criteria for quality and potential clinical implications for practice.

Design, size, and duration

The updating speed of point of care information summaries was measured with a prospective cohort design over a one year period, from June 2009 to May 2010. We assessed the cumulative updating rate using Kaplan-Meier survival analyses and citation was equivalent to death. We calculated the hazard ratios for comparing the top performer with the other summaries using a univariate random Cox model.

Main results and the role of chance

Dynamed has an updating process that markedly leads the others. For instance, the hazard ratios of citation of EBM Guidelines and Clinical Evidence compared with the top performer were 0.22 (95% confidence interval 0.17 to 0.29) and 0.03 (0.01 to 0.05), respectively. The median citation was around two months for Dynamed and around 10 months for EBM Guidelines but close to the limit of our follow-up (nine months). UpToDate, eMedicine, and Clinical Evidence were so slow that they exceeded the follow-up period so the median could not be computed. Overall, Dynamed cited 87% of the sampled systematic reviews and the others less than 50%.

Bias, confounding, and other reasons for caution

The updating speed of point of care summaries was measured with a citational approach, counting bibliographic references without going deeply into the content of the citation. We selected systematic reviews as samples of newsworthy and relevant evidence but did not directly assess how many of them called for a change in clinical practice. Finally, we did not consider the updating of results from studies with other designs (such as randomised clinical trials) as systematic reviews are preferable to support decision making at the point of care.

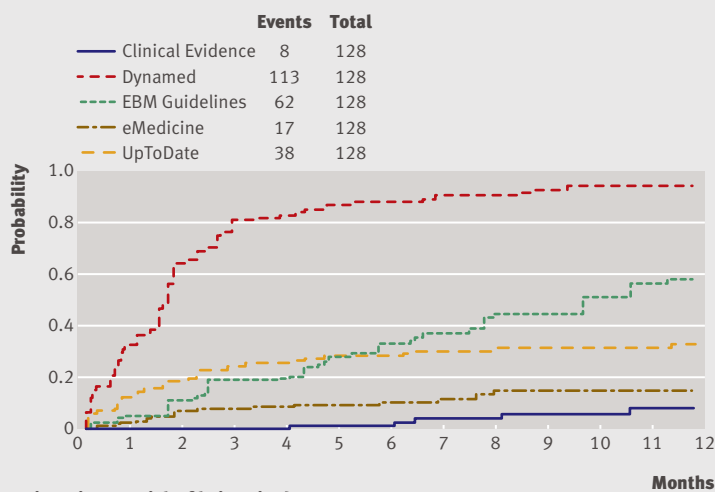
Generalisability to other populations

In an editorial market with rapidly evolving point of care summaries, our analysis reflects one quality dimension—speed of updating—of five authoritative point of care products over the period 2009-10.

Study funding/potential competing interests

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. In 2003-8 the Italian Cochrane Centre received grants from the Italian Medicines Agency (AIFA) for the Italian translations of one of the products assessed in the study (Clinical Evidence).

UPDATING CURVES FOR RELEVANT EVIDENCE (FROM 128 SYSTEMATIC REVIEWS) BY POINT OF CARE INFORMATION SUMMARIES



No of systematic reviews at risk of being cited

| | 128 | 118 | 106 | 103 | 102 | 101 | 98 | 92 | 61 | 53 | 45 | 31 | 25 |
|-------------------|-----|-----|-----|-----|-----|-----|-----|----|----|----|----|----|----|
| Clinical Evidence | 128 | 83 | 41 | 22 | 20 | 15 | 14 | 10 | 8 | 6 | 3 | 2 | 1 |
| Dynamed | 128 | 118 | 107 | 98 | 97 | 87 | 79 | 71 | 51 | 46 | 33 | 21 | 17 |
| EBM Guidelines | 128 | 117 | 108 | 107 | 106 | 105 | 103 | 98 | 68 | 62 | 53 | 38 | 32 |
| eMedicine | 128 | 108 | 96 | 89 | 89 | 84 | 83 | 79 | 51 | 49 | 43 | 30 | 27 |

Prevalence of financial conflicts of interest among panel members producing clinical practice guidelines in Canada and United States: cross sectional study

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EDITORIAL by Gale

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STUDY QUESTION

What is the prevalence of financial conflicts of interest among members of panels producing clinical practice guidelines on screening, treatment, or both for hyperlipidaemia or diabetes?

SUMMARY ANSWER

The prevalence of conflicts of interest is high among members of such clinical practice guideline panels and is significantly higher among panellists from non-government sponsored guidelines than among those from government sponsored guidelines.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Financial conflicts of interest among panel members are common in guidelines issued by certain specialty organisations on screening, treatment, or both for hyperlipidaemia or diabetes. The prevalence and under-reporting of conflicts of interest are high and transparency is incomplete among a wide range of guideline producing organisations, and an association exists between the source of sponsorship of guidelines and the presence of conflicts.

Participants and setting

We evaluated panel members of clinical practice guidelines released by national organisations in the United States and Canada between 2000 and 2010 that covered screening or treatment of hyperlipidaemia or diabetes for financial conflicts of interest (COI).

Design

This was a cross sectional study.

Primary outcome(s)

The primary outcome was the prevalence of COI among members of guideline panels.

Main results and the role of chance

Of a total of 288 panel members, 150 (52%) had COI. Of

REPORTED FINANCIAL CONFLICTS OF INTEREST (COI) AMONG PANEL MEMBERS BY CATEGORY OF GUIDELINE SPONSOR

| Guideline category | No of guidelines | No of panel members | No (%) panel members with COI |
|----------------------|------------------|---------------------|-------------------------------|
| Government sponsored | 6 | 92 | 15 (16) |
| Other | 8 | 196 | 135 (69)* |
| Total | 14 | 288 | 150 (52) |

*P<0.001, using two sided, 0.05 level ² test of significance.

these, 138 were declared and 12 were undeclared. Panel members from government sponsored guidelines were less likely to have COI than were panel members from non-government sponsored guidelines (16% v 69%; P<0.001). Twelve of the 14 guideline panels in the study identified chairs; six of these had financial COI.

Bias, confounding, and other reasons for caution

Our methods were deliberately conservative and may have underestimated COI among guideline panellists. We were unable to account for relations with industry that were not publicly available, and our sample size was limited to only two disease conditions.

Generalisability to other populations

Our results are more generalisable than are those of other recent studies of the same kind, because our study included guidelines from many different organisations, which provides a more realistic estimate of the prevalence of COI on guideline panels.

Study funding/potential competing interests

This project was not directly supported with any research funds. SK is funded by a Veterans' Administration HSR&D career development award. JSR is supported by the National Institute on Aging and by the American Federation of Aging Research through the Paul B Beeson Career Development Award Program.

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