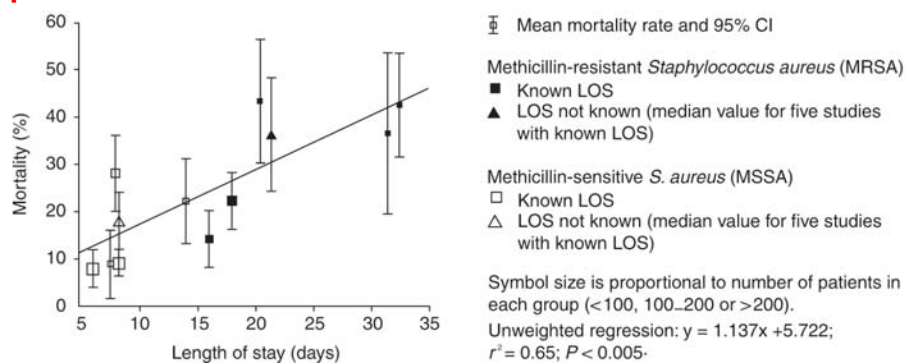


Mortality rate versus hospital length of stay before bacteraemia (LOS) in patients with MRSA or MSSA bacteraemia



group status (MRSA or MSSA) failed to achieve significance in any iteration of the regression, while LOS remained a significant predictor of mortality risk.

This suggests that, with *S. aureus* bacteraemia, mortality rate increases with length of time in hospital before the bacteraemia. The likely explanation is that patients residing in hospital for longer periods are sicker. Moreover, they are more likely to have been exposed to antibiotics, leading to increased risk of acquiring an *S. aureus* strain that is methicillin-resistant. The mortality risk is no different for MRSA versus MSSA bacteraemia if LOS, a surrogate marker for severity of patient illness, is taken into account. The difference that Whitby et al observed between the groups of patients with MRSA and MSSA bacteraemia could be accounted for by the difference in LOS between these groups.

1. Whitby M, McLaws M-L, Berry G. Risk of death from methicillin-resistant *Staphylococcus aureus* bacteraemia: a meta-analysis. *Med J Aust* 2001; 175: 264-267. □

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IN REPLY: We thank Hurley for his comments on our meta-analysis.¹ However, we strongly dispute that our analytical technique is flawed, and argue that we have been extremely cautious in drawing our conclusions. Hurley's contention is that hospital length of stay before bacteraemia (LOS) is a surrogate for severity of underlying disease and risk for colonisation with methicillin-resistant *Staphylococcus aureus* (MRSA), and that these factors explain the higher mortality in patients with MRSA.

We agree that LOH may be a confounder. It may be an effect modifier, whereby patients in hospital for longer may be more ill, and therefore more susceptible to infection with and death from MRSA. Both are intuitive and biologically plausible conclusions. In fact, we referred to these possibilities in our Discussion, writing that "patients who ultimately become infected with MRSA are more seriously ill than those who become infected with MSSA [methicillin-sensitive *S. aureus*]" and "separating the effect of the bacteraemia *per se* from the effects of patients' underlying disease and treatment is a major problem when comparing outcomes". We also cautioned readers that available published data on mortality made it impossible for us to adjust for numerous potential confounders, including LOH, as the information given did not link these potential confounders with the outcome in individual patients.

Hurley has not, as he suggests, undertaken an analysis that would allow him to control correctly for the potential confounder, LOH. He, like us, used "group-as-a-unit" data, but, although the groups are homogeneous for MRSA or MSSA, they are heterogeneous for LOH. Adequate examination of and control for potential confounders requires either individual patient data or data from homogeneous groups. Hurley has attempted to use analysis normally reserved for individual data.⁴ His analysis was analogous to treating the data as though from an ecological study, a design in which control of confounding is difficult,⁵ and thus does not permit him to draw his conclusions.

Our analysis (not presented in our original article) of only those studies where the authors attributed mortality to bacteraemia⁶⁻⁸ found that the magnitude of effect remained (fixed-effect relative risk, 2.27; 95% CI, 1.75-2.96; $P < 0.001$; test for heterogeneity, $\chi^2 = 6.14$, $df = 4$, $P = 0.19$).

As MRSA bacteraemia is a rare event and published studies are small, the statistical ability to control for confounding and effect modification is limited. Until sufficient suitable data for individual patients are available for analysis, we have remained restrained in our assessment. Mindful that MRSA bacteraemia is associated with increased mortality, regardless of the cause, we hold with our original conclusion that "our findings justify ongoing surveillance and proactive management of MRSA in healthcare facilities".

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PBS/RPBS cost implications of trends and guideline recommendations in the pharmacological management of hypertension

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TO THE EDITOR: The article by Nelson et al¹ estimates Pharmaceutical Benefits Scheme and Repatriation Pharmaceutical Benefits Scheme (PBS/RPBS) savings if hypertensive patients on monotherapy were prescribed the agents recommended in guidelines; however, the analysis contains algebraic errors and insufficient sensitivity analyses. The question of excessive costs through the use of expensive agents for which there is no evidence of increased benefit for most patients is an important one, but the estimates of extent of overuse should be methodologically sound. The

three main concerns we have with the paper's estimates are as follows:

■ The total number of patients on monotherapy in Box 3 of the article adds to 1.1 million, whereas elsewhere the authors state that 60% of all 1.2 million Australian patients treated for hypertension are on monotherapy, giving an estimate of 0.72 million. (These estimates of 60% and 1.2 million are not referenced in the article.) One reason for this discrepancy is that the authors have treated the sum of column 4 in Box 2 as patients, not patient-years of treatment (some patients are on dual or triple therapy), leading to a 40% overestimate of numbers of patients on monotherapy reported in Box 3.

■ Utilisation of prescription drugs is recorded by PBS/RPBS only if the cost to patient is subsidised. Therefore, PBS/RPBS expenditure divided by total patient numbers (Box 2) underestimates consumer cost for diuretics and β -blockers, both of which cost less than the non-concessional copayment. Of total PBS/RPBS scripts, 16% are for non-cardholders,² and the cost per script to these patients is about three to four times the prevailing 1998 cardholder copayment. As a rough estimate, total consumer cost for these agents may need to be doubled, and their omission is therefore material. Although non-concessional patients still have a saving, it is less than that estimated in the article.

■ Sensitivity analysis should have been performed on the following critical assumptions: (1) proportion of use for hypertension for each class of drugs, (2) the number of unsubsidised users of diuretics and β -blockers, and (3) the proportion of patients on each agent who are on monotherapy.

It is vital that the current scrutiny by all stakeholders of PBS/RPBS expenditure be informed by reasonable estimates of inappropriate utilisation. The contribution made by the authors in developing a technique to estimate appropriate use for this group of drugs is valuable. However, use of unreferenced estimates of key variables, insufficient application of sensitivity analyses, algebraic errors and inappropriately combining PBS with non-PBS data may cloud rather than shed light on this issue.

1. Nelson MR, McNeil JJ, Peeters A, et al. PBS/RPBS cost implications of trends and guideline recommendations in the pharmacological management of hypertension in Australia, 1994–1998. *Med J Aust* 2001; 174: 565–568.

2. PBS expenditure and prescriptions. January 2000 to December 2000. Canberra: Commonwealth Department of Health and Aged Care, 2001. Available at <http://www.health.gov.au/pbs/pubs/pbbexp/pbdec00/index.htm>. □

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IN REPLY: We thank Pekarsky and Ewald for their comments.

It is difficult to estimate the percentage of patients on monotherapy from any source. We used data from IMS Health (<http://www.ims-global.com/>) to determine the number of person-years of exposure to drugs prescribed with a principal indication of hypertension. Some of these drugs were prescribed as a sole agent if the script was for this single drug alone. Exposure for such agents was expressed as a percentage of the total exposure of this drug. For example, angiotensin-converting enzyme (ACE) inhibitors were sole agents in 63.9%. In the other 36.1%, the co-prescribed drugs may have been another antihypertensive drug or another type of drug altogether. Corresponding figures for calcium-channel blockers were 61.3%, for diuretics 53.6%, and for β -blockers 60.0%. As an approximation, we used the estimation that 60% of patients were likely to have been on monotherapy for hypertension. Adding the number on monotherapy for each drug gives an estimate of 1.2 million for the total population on monotherapy for hypertension. Therefore, the total number on drugs is likely to be greater than the 1.2 million as estimated in our article. However, the essential figure is that of 1.2 million for monotherapy, which we stand by.

It is true that a minority of prescriptions (16%) are written for people without a concession card and that these are more likely to pay the full cost of a cheaper drug. Our economic perspective was that of the PBS/RPBS. Hence, consumer costs were only included where the government made a copayment. It is acknowledged in the Methods section that “with some drugs, the patient copayment covers the total cost; in

these instances the Commonwealth makes no contribution to the cost and these prescriptions are not recorded in the PBS/RPBS data” (page 566). It is also stated in the Discussion that the PBS/RPBS captures “much more of the cost of the newer, more expensive agents than thiazide diuretics or β -blockers” (page 567).

We chose to limit our sensitivity analysis to the key issue of redistribution of agents after initiation of monotherapy. The data we presented allow interested parties to conduct their own further sensitivity analyses, such as those suggested by Pekarsky and Ewald. □

MEDicine or MADness

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TO THE EDITOR: In his recent Commentary on hastening death in terminally ill patients,¹ Hunt may not have fully appreciated a very cogent point made in the research by Douglas and colleagues.² The surgeons surveyed clearly reported the intent of their prescribing. This is contrary to Hunt's assertion that “Intention is inherently subjective...complex [and] ambiguous”. Some surgeons gave a dose appropriate to the symptoms, others deliberately increased the dose beyond direct symptomatic control, and a few deliberately ended life, at times with no explicit request. As Douglas points out, the dose of a medication given will be an important clue in this. Good clinical practice is about minimum effective dose (MED), not maximum administrable dose (MAD). This is the case for all patients, whether they are near the end of life or not.

Hunt also states that “The duty of doctors is to strive to satisfy the wishes and interests of their patients and their patients' loved ones”.¹ This is a disturbing comment if left unqualified. There is a broader accountability for doctors to the community through the registration process, quality assurance and continuing education, and the criminal code. If the article by Douglas et al highlights nothing else, it should be clear that there are certain members of the medical profession who believe that they are above the law and have control over the life and death of their patients, with no external review.² It is frightening that such paternalism still exists. Unfortunately, the Dutch experience of tolerating euthanasia does not appear to

Correction

Re: “Impairment bible” [book review of Guides to the evaluation of permanent impairment], by Ganora A, in the 21 January issue of the Journal (Med J Aust 2002; 176: 82). By editorial error, the reviewer's name was misspelled Gandora.

We apologise to Dr Ganora for the error.