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Infection in the critically ill—questions we should be asking

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Best practice in infection control and management in the critically ill continues to generate considerable debate. The wide variation in current practice is witness to this continuing uncertainty. In large part this is due to the lack of a decent evidence base and to an over-reliance on deep-set dogma. Data that go against the grain are often conveniently overlooked and political imperatives frequently supervene. This article highlights some of these discrepancies and argues for a more balanced, scientific approach. In this time of financial restraint, we need to identify true priorities from both health and economic perspectives, and to see what practices can safely and effectively be modified or abandoned.

Keywords: infection control, bacteraemia, antibiotic treatment, intensive care, critical illness

Introduction

Optimal prevention and management of infection in the critically ill continues to be vexatious. As a consequence, practices vary markedly, even within geographically proximal locations. The aim of this article is to take a few potshots at some of the current dogma in this area, aiming to puncture a few balloons. We will highlight the lack of supportive data, potential mis-extrapolations, overblown claims and the non-consideration of contrary findings. These blinkered views enable conclusions and recommendations to be drawn that often fall well short on closer scrutiny. We will focus on some specific examples of infection treatment and control measures in the intensive care unit (ICU) that illustrate these issues.

We do stress that our article should not impel a change in practice but rather provoke debate. Beliefs and guidelines are often based upon what appears, at least within current therapeutic paradigms, as common sense. History often shows that what appeared obvious turns out to be misguided. The contrary views and implications presented herein may also turn out to be incorrect. They may simply represent an alternative spin based on selective cherry-picking of articles that we use to support our arguments. If so, we are as guilty as those taking the establishment view or who promote their own particular bandwagons. However, we do hope that they gently provoke the reader into reconsidering his/her current stance and perhaps motivate well-designed, prospective investigations that provide the definitive data upon which better recommendations can—and should—be based at both health and economic levels.

Evidence-based medicine—worshipping at the high altar

We are certainly in thrall to the notion of evidence-based medicine. Unfortunately, distillation of evidence is also prone to bias, as amusingly graded by Bleck[1] (Figure 1). The myriad ways of performing meta-analysis which change the likelihood of deriving a 'positive' result, trial protocols that load the odds unfairly against the control group, and extrapolation of data from specific patient subsets to whole populations are but three examples of 'evidence-biased' medicine. We are also recognizing that overall benefit applied to a population may not necessarily help an individual. Subsets may be either benefited, unaffected or disadvantaged by specific treatments and stratagems, so the net result of a wide population study will often fail to reflect an individual's response. Recent studies on pharmacogenomics[2] and the marked severity-related differences in survival with activated protein C in severe sepsis[3] highlight this fact.

Ignaz Philipp Semmelweis (1818–1865) is often considered a founder of clinical microbiology and evidence-based medicine. He observed that adoption of hand hygiene in medical attendants during childbirth reduced mortality rates due to puerperal fever by a factor of 10. While ridiculed at the time, these observations have become regarded as one of the seminal events in the development of modern medicine. Seen in this quasi-religious light, and with additional pressure from media shock–horror exposés and governmental/insurer threats of 'naming and shaming', financial penalties and senior administrator dismissal and litigation, it is easy to see why a perceived rise in

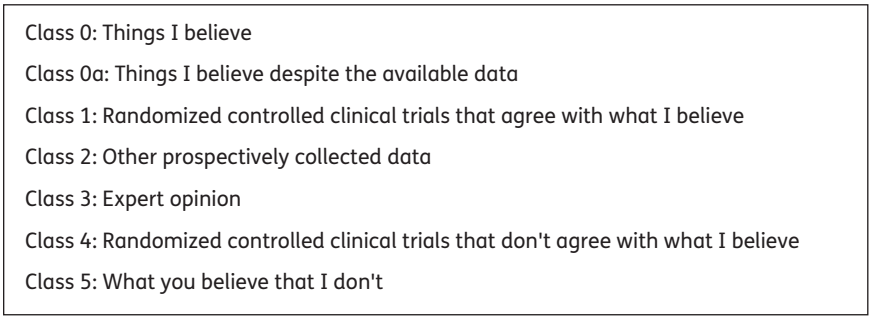

Figure 1. Evidence-biased medicine—a classification (from Bleck[1]).

hospital-acquired infection instinctively provokes calls for more assiduous hand disinfection, increased use of barrier precautions and institution of diagnostics and therapies that offer dubious cost- or outcome-benefit. Practices such as the use of gown and gloves, isolation of selected patients and alcohol gel hand sterilization have been rapidly established as standards of care but without specific high-level proof of efficacy. Subsequent efforts at grant funding, formal testing and/or publication may then be impeded by a lack of equipoise, especially when experts who promote the orthodoxy tend to be the 'go-to' reviewers.

To take an extreme example, the death rate from primary surgical amputations (some going as high as the hip) during the American Civil War, carried out in field hospitals usually without any form of hand hygiene or instrument disinfection, was only 28%, of which only a proportion would have been related to infection.[4] In short, many patients will do well even in the face of the poorest practice, an inconvenient truth that greatly impedes scientific evaluation of care improvements as proper trial design often requires very large sample sizes and/or use of valid surrogate endpoints.

Numerous interventions have been championed with the aim of improving patient outcomes in the treatment and prevention of ICU-acquired infections. Judging the evidence base for these treatments is complex. For example, is Level 1 evidence from prospective randomized controlled trials required to justify the use of every intervention, or would such a requirement prevent the uptake of many potentially beneficial interventions? Is it ethical to formally test by prospective randomized controlled trial the benefits of interventions long established as standard of care? Even if this were possible, would sufficient equipoise exist? In the absence of such evidence, how valid are findings culled from retrospective database analyses and historical studies that suggest benefit? This is particularly pertinent when the practice and process of critical care has changed dramatically in the last 10–20 years. Stress ulcer bleeding was a major cause of morbidity and mortality in ICU patients in the early 1970s; now it is a relatively unusual phenomenon regardless of the use (or not) of gastric protectants. The unwanted consequences of the continued (over)use of proton pump inhibitors and H_2 antagonists, e.g. impairment of neutrophil bactericidal activity[5] and *Clostridium difficile* overgrowth,[6] may no longer be outweighed by their direct therapeutic benefit. Is it now time to have a moratorium on these agents except in well-defined patient populations (perhaps concurrent peptic ulcer disease)?

In recent years, focus has shifted from single treatments towards an emphasis on packages of interventions or 'care bundles'. The evidence base underpinning each bundle component is often worryingly thin. Should we therefore not demand confirmation that the package works as a whole? If confirmed, should we then determine which components become superfluous or offer only minimal added benefit to save valuable effort, cost and resource. Should we be opposing changes in clinical practice that are motivated by political or financial priorities merely because they lack a clear evidence base? Or are such changes occasionally essential for public confidence? Yet again, why have interventions with a good evidence base from prospective randomized controlled trials not been widely adopted?

Does delay in initiating inappropriate antibiotic therapy really matter?

The Surviving Sepsis Campaign[7] strongly recommends (1B grading) that intravenous antibiotic therapy be started as early as possible, ideally within the first hour of recognition of severe sepsis, and that initial empirical anti-infective therapy include one or more drugs that have activity against likely causative pathogens (bacterial and/or fungal) and that penetrate in adequate concentrations into the presumed source of sepsis. The rationale is that 'patients with severe sepsis or septic shock have little margin for error in the choice of therapy, so the initial selection of antimicrobial therapy should be broad enough to cover all likely pathogens. There is ample evidence that failure to initiate appropriate therapy (i.e., therapy with activity against the pathogen that is subsequently identified as the causative agent) correlates with increased morbidity and mortality'. The most frequently quoted paper[8] in support of this claim was based, like most others, on a retrospective data analysis. The authors of the paper indeed found a strong relationship between delay in effective antimicrobial initiation and in-hospital mortality in patients with septic shock. Appropriate treatment within the first hour of documented hypotension was associated with a survival rate of 79.9%; however, survival decreased by 7.6% for each hour of delay thereafter over the next 6 h. Delay exceeding 36 h increased the risk of death 100-fold with less than 5% surviving. Clearly, these data are surprising given that bacterial culture and susceptibility results are often not available until after 36 h, not infrequently prompting

a belated change of antibiotics, and that many such patients do survive.

Other retrospective analyses have likewise claimed the overriding prognostic importance of antibiotics within the early resuscitation bundle promulgated by the Surviving Sepsis Campaign.[7,9,10] However, an equivalent-sized literature showing *no* relationship between antibiotic appropriateness and outcome has received remarkably little airing. Indeed, some studies have even reported a trend, approaching statistical significance, in the *opposite* direction.[11] A systematic review published in 2007 highlighted 21 of 49 reported studies in bacteraemic patients that failed to detect any association between inappropriate antibiotic prescription and mortality.[12] The authors were highly critical of the methodologies used to assess whether true differences actually existed, or whether unrecognized sources of confounding or biases affected the observations and conclusions, e.g. determination as to whether mortality is attributable or not to the infection. They concluded that 'without adequately designed research studies in this area, there is little evidence for or against recommendations regarding aggressive empiric therapy with broad-spectrum antibiotics'.

In a recently published study,[13] logistic regression analysis performed on data prospectively collected on 1702 bacteraemic ICU patients in 132 ICUs from 26 countries found age, illness severity and immunosuppression were independent predictors for mortality. However, *no* variable associated with antibiotic policy was significantly associated with death. If the maximum severity of the bacteraemic illness was removed from the model, effective first-line antibiotic therapy did reduce mortality, but only when started early as empirical treatment (odds ratio 0.58; 95% confidence interval 0.39–0.87). The benefit would thus appear to be derived from early treatment but only when commenced *before* the patient becomes critically ill. These data support the conclusion made in an excellent review by Harbarth and colleagues[14] that 'the detrimental effects of inadequate antibiotic therapy seem to become weaker in the most severely ill patients with short life expectancies'. They too were critical of the methodological aspects of reported studies.

Clearly, the definitive trial comparing antibiotics versus no antibiotics could not now be ethically performed to formally confirm or refute benefit. However, this was actually done in 1938 by Evans and Gaisford in Dudley Road Hospital, Birmingham.[15] They compared outcomes in 200 patients with lobar pneumonia (mainly pneumococcal) either treated or not with a sulphonamide. Randomization was performed on the basis of whether or not they, or their colleagues on other wards, managed the patients. The control group received the 'usual routine non-specific treatment', though what this constitutes was not stated. At that time intravenous fluid administration was unusual and positive pressure ventilation had not yet been invented, though facemask oxygen therapy was likely to have been available. Of note, the sulphonamide, given on average for just 5–7 days, reduced mortality from 27% to 8%. While clearly an impressive effect from the short-term sulphonamide treatment, also striking is the fact that three-quarters survived often-confirmed pneumococcal pneumonia *without* antibiotics and with minimal other intervention. What the outcomes would have been had intravenous fluid resuscitation, non-invasive or invasive ventilation and other organ support been available must remain speculative. As a challenging reflection on our progress (or lack of), overall mortality rates from pneumococcal pneumonia are no better to this day. For example, a Spanish multicentre study recently reported a 30 day mortality of 15.1%.[16] The mantra must remain that clinicians should strive to administer antibiotics both promptly and effectively to patients with suspected infection, but it is reasonable to question the absolute impact on outcomes.

How long should a course of antibiotic therapy last?

The Surviving Sepsis Campaign recommends (Grade 1D) that the duration of therapy should typically be 7–10 days and that longer courses may be appropriate in patients with a slow clinical response, an undrainable focus of infection, or immunological deficiencies, including neutropenia.[7] Their grading of 1D reflects a strong recommendation: '1' is when an intervention's desirable effects clearly outweigh any negatives, but 'D' reflects a very low quality of evidence to support the recommendation. It is a sad indictment of the specialties of intensive care, microbiology and infectious diseases, as well as governmental bodies and industry, that after 40 years or more of critical care we still do not know the optimal duration of a course of antibiotics for a 'standard' infection. Clearly, deep-seated infections such as osteomyelitis and endocarditis warrant a prolonged antibiotic course but, even in these cases, the chosen duration is largely empirical. Is there any evidence that neutropenics or patients with a 'slow clinical response' benefit from a longer course of antibiotics? Or do patients simply suffer the consequences of microbial overgrowth with (often multiresistant) hospital flora, *C. difficile* and fungi? Data from the USA suggest that fungal causes of sepsis rose by 207% between 1979 and 2000;[17] how much of this rise was caused by better identification, sicker patient cohorts or antibiotic (over)use is unknown.

Antibiotic courses thus tend to be empirical, often lasting 7 or 14 days, and are likely to be chosen to coincide with a weekly multiple. Prospective randomized controlled trials (PRCTs) are few and far between. Chastre *et al.*[18] did show that comparable clinical effectiveness was achieved with 8 day or 15 day treatment regimens for ventilator-associated pneumonia, but there was a significant reduction in the emergence of multiresistant pathogens in those receiving the shorter course. Two recently published PRCTs have used the pro-inflammatory blood marker procalcitonin to guide discontinuation of antibiotics. The multicentre PRORATA trial,[19] performed in 321 patients in eight French ICUs, showed a reduction in antibiotic course duration from 14.3 ± 9.1 days to 11.6 ± 8.2 days ($P < 0.0001$) with no change in mortality. The predominant type of infection treated was of the respiratory tract and nearly half the patients had septic shock. Similar patients were treated and similar outcomes were achieved by Nobre *et al.*[20] in a single-centre trial from Geneva; they, however, showed a median reduction in antibiotic use from 9.5 days to 6 days ($P = 0.15$). A reasonable argument can be made that ongoing inflammation is not a direct surrogate of ongoing bacterial activity, so the procalcitonin measure could be merely acting as a comfort blanket to support the clinician's decision to stop antibiotics. Indeed, the practice in our ICU, reported in 2004,[21] showed a median duration of treatment for bacteraemia of 5–5.5 days, without the use of procalcitonin monitoring, and with very low relapse rates. If anything, our current practice is even shorter, although this has not been

formally measured. The extent to which an antibiotic course can be safely truncated requires many more prospective, randomized studies in different infections affecting different patient populations. A trial comprising Dutch adults with mild to moderate/severe community-acquired pneumonia who had improved after 3 days of treatment with intravenous amoxicillin, involved randomization to either placebo ($n=56$) or a further 5 days of oral amoxicillin ($n=63$).[22] Outcomes (clinical and radiological success rates) were similar in both groups. From Auckland, Briggs *et al.* [23] reported a case series of 90 patients with proven ($n=72$) or probable ($n=16$) meningococcal disease who received just 3.1 ± 0.5 (mean $\pm$ SD) days of intravenous benzylpenicillin. Of the six who died, four did so soon after admission while still on treatment, with the other two dying of late complications resulting from the initial multi-organ failure. No microbiological relapses were seen, either in the short or long term. Even more extreme, at least in a Western context, was the study by Nathan *et al.*[24] performed in health clinics in Niger, where patients with meningococcal meningitis were randomized to receive a single intramuscular dose of either ceftriaxone or chloramphenicol. In cases of clinical failure, a second single dose was given after 24–48 h and, if failure persisted at 72 h, rescue treatment was intravenous ceftriaxone for a minimum of a further 4 days. Only 7% required a second dose at 24–48 h, and the rate of treatment failure at 72 h was 9% (mortality 5%). Using multiple logistic regression analysis, they found that only impaired consciousness at baseline, or diagnosis of another disease (alone or in association with meningococcal meningitis), remained significant risk factors for treatment failure at 72 h.

Staphylococcus aureus bacteraemia is another example of a condition for which prolonged treatment (2–4 weeks, or even longer) is traditionally mandated for fear of relapse and deep-seated infections.[25] Although prospective randomized trials are lacking, more recent data show that short courses appear as effective provided no ongoing focus of infection (e.g. an infected prosthesis) remains and clinical response is prompt.[26–28]

Hand hygiene—old wine in a new bottle?

Hand hygiene and use of hand barrier precautions has been heavily promoted to reduce nosocomial infection rates. Data from a Hong Kong teaching hospital during the outbreak of the severe acute respiratory syndrome (SARS) coronavirus during 2002–03 demonstrated that use of strict barrier precautions involving use of gown and gloves for each patient was associated with an 8-fold *increase* in acquired methicillin-resistant *S. aureus* (MRSA) infection in the ICU.[29] Bacterial contamination is more readily transferred by gloved than by bare hands.[30] Perhaps increased and/or inappropriate use of gloves, while offering a perceived increase in security to the wearer, led to an increased spread of microorganisms. Studies have also shown an outbreak traced to a contaminated blood gas analyser[31] and that pathogenic bacteria are carried on healthcare workers' mobile phones.[32] Would these be facilitated by glove transfer?

Alcohol antibacterial hand rubs have also been widely advocated as a method of improving hand hygiene and thus lowering rates of healthcare-associated infection.[33] These products are undoubtedly effective at killing a range of microorganisms, but they have little sporicidal activity. Tellingly, widespread uptake of these products in the UK in the early 2000s, as well as the introduction of proton pump inhibitors for gastric acid suppression,[6] was temporally associated with an increase in nationally reported mortality related to *C. difficile* infection.[34] Only once this became a highlighted problem did guidelines stress the need to use soap and water and avoid alcohol gel in cases of diarrhoea. Notably, 2008 was the first year in the UK that *C. difficile* death rates fell since reporting began in 1999.[34]

Thus, indiscriminate use of gloves and hand gels may have potentially deleterious consequences in routine clinical practice. Effective hand hygiene should undoubtedly remain a cornerstone of modern medicine and we would not suggest otherwise. However, the evangelical zeal to adopt new methods should perhaps be tempered by measured reflection on their true efficacy and the unintended consequences of real-world implementation. Frequent handwashing can cause cracked skin and dermatitis and an increased risk of colonization with hospital flora.[35] The effect on depleting natural bactericidal skin oils that represent an important part of the dermal immune system[36] is also unknown.

Physical isolation—barrier to bacteria or barrier to care?

Barrier precautions and hand hygiene are commonly augmented with use of physical isolation in a single room or cohorting when colonization with high-risk microorganisms such as MRSA is proven or suspected. UK Department of Health guidance recommends 'When a patient is identified as MRSA positive, either because they have an MRSA infection or because they have been identified as an asymptomatic carrier by screening, they should be isolated, if possible, to reduce the risk of transmission to other patients'.[37] However, the available evidence supporting such an approach is anecdotal and inconclusive.[38] Much of the published data is methodologically weak[39] and inadequate to demonstrate the adequacy of isolation over standard barrier precautions and hand hygiene.[40] In a prospective study that included our ICU, cohorting or side-room isolation of MRSA-colonized patients had no effect on rates of MRSA acquisition.[41] Indeed, in the ICU, cross-infection with MRSA seems to be a relatively infrequent method of MRSA acquisition,[42] as does MRSA acquisition from a contaminated environment.[43] These findings undermine the rationale for physical isolation in this environment, especially when there are increased nursing costs, an increased lack of visibility and reduced medical/nursing caregiver input, with an attendant increase in adverse events.[44] These results are not necessarily generalizable outside the ICU setting or across different patient populations but they do suggest, at least for MRSA colonization, that practice recommendations may be motivated perhaps more by dogma and political impetus than by quality evidence or plausible biological rationale. These policies undoubtedly cater to public concerns about the rising incidence of healthcare-acquired infection and the need to demonstrate clearly visible attempts at infection control. This is nevertheless a perfect illustrative example of a policy led principally by a desire to be seen be taking action, despite unproven benefits and the potential to harm.

Selective decontamination of the oral and digestive tract—evidence without uptake?

Selective digestive decontamination (SDD) is a method of infection control principally used in mechanically ventilated patients in the ICU, aimed at prevention of autoinfection with potentially pathogenic microorganisms normally resident in the oral and digestive tracts. These strategies involve application of topical antimicrobials to the pharynx and gastrointestinal tract with or without parenteral antibiotics to combat infections occurring at the time of ICU admission and on endotracheal intubation. Bizarrely, in contrast to the evidence base for many other infection control methods in intensive care, a wealth of evidence exists for this strategy, with over 50 randomized controlled trials performed. Meta-analyses show SDD is associated with significant reductions in lower airway and bloodstream infection rates and offers an overall survival benefit.[45–47] The fear that this approach encourages bacterial resistance does not appear to be borne out; indeed, the reduction in infection has often led to an overall decrease in antibiotic use.

Given this apparent weight of evidence, why is SDD not widely used or even recommended by international guidelines when many other, less evidence-based infection control measures are advocated as standard of care? The latest iteration of the Surviving Sepsis Campaign guidelines[7] acknowledged the evidence base yet reserved judgement on the use of SDD, with the panel evenly split and none strongly advocating its use. A valid criticism is that many of the SDD studies are generally small, heterogeneous, largely single-centre, of low quality and not blinded. The recent large Dutch multicentre randomized controlled trial[48] employed a cluster-randomized design crossing over between SDD, selective oral decontamination (topical antibiotics without prophylactic parenteral agents) and standard care in over 5000 patients expected to stay in the ICU for longer than 48 h. In this study, survival benefit only became evident after statistical correction for differences in illness severity arising from imbalanced randomization. Use of such adjustments must be questionable, especially when the effects of the intervention under investigation would be expected to act late in the ICU stay, when severity scoring may poorly predict outcome.

In short, despite the numerical weight of data suggesting benefit and safety, the majority of intensivists and microbiologists remain unpersuaded. Whether this is due to a lack of commercial drivers or high-profile advocates, the relative difficulty in administering the topical agents or an unassailable conviction of non-benefit or even harm, notwithstanding the data, remains uncertain.

Catheter insertion protocols

A recent systematic review of 200 prospective studies estimated that incidence rates of catheter-related bloodstream infections (CR-BSIs) expressed per 1000 catheter days was 1.7 for arterial catheters and 2.7 for short-term central venous catheters (CVCs).[49] Edgeworth[50] makes the important point that identification of the source of infection in an ICU patient is notoriously difficult and, despite the use of strict criteria, identification retains a degree of subjectivity in patients who are acutely unwell for other reasons. He reviewed five representative large ICU studies and demonstrated a wide variation (19–62%) in the proportion of hospital-acquired bloodstream infections assigned to CR-BSI, highlighting likely differences in local interpretation. National Nosocomial Infections Surveillance guidelines recommend that the use of multiple lines in a single patient should still be counted as 1 catheter day. Thus, a rate of 2.7 per 1000 catheter days would equate to approximately *one* CR-BSI per ICU bed per year. The health and economic impact of reducing CR-BSIs has not been assessed in the UK but would fall far short of numbers claimed for the USA. In 2006 Pronovost *et al.*[51] asserted that an estimated 80000 CR-BSIs occurred per annum in the USA, with up to 28000 deaths among ICU patients. With an average cost of care of US$45000 per infection, they claimed the annual cost could be up to US$2.3 billion. This staggering amount equates to more than the entire UK critical care budget for 2008/9![52]

The Michigan Keystone project sought to implement five simple procedures to follow during venous catheter insertion, namely, hand washing, use of full-barrier precautions during the insertion of CVCs, cleansing the skin with chlorhexidine, avoiding the femoral site if possible, and removing unnecessary catheters. These five procedures were chosen on the basis of being recommended by the CDC and identified as having the greatest effect on the rate of CR-BSI and the lowest barriers to implementation.[53] The strength of the evidence base does not, however, actually hold up on closer scrutiny.[33] Pronovost *et al.* studied the impact of this five-step intervention in a before/after study performed in 2004 in 103 Michigan ICUs.[51] They reported a dramatic fall in CR-BSIs from a median rate of 2.7 CR-BSIs per 1000 catheter/days at baseline to 0 at 3 months post-implementation, with low rates being maintained at 18 months. This was, however, an open study with diagnosis being made by an infection control practitioner. The authors did acknowledge some limitations, including the potential for under-reporting (no validity checks were made), non-evaluation of protocol compliance and, surprisingly, non-collection of any microbiological data. In addition, any impact on length of ICU stay, survival rates and antibiotic use were not recorded, nor were the numbers of blood culture samples taken in the different periods.

Of note, the last few years have seen ever-increasing external pressure by governmental quality bodies, insurance companies and media/public pressure groups on US hospitals to avoid 'never events', including CR-BSI and ventilator-associated pneumonia. Indeed, several US states have now enacted laws mandating disclosure of 'never events' and introduced remunerative or punitive measures for failure. Consumer (e.g. www.ConsumerReportsHealth.org) and business (e.g. www.leapfroggroup.org) groups now name and shame hospitals that are either poorly performing or who decline to release their data. Clearly, this has had an impact. Many hospitals now report zero infection rates. The Leapfrog Group found that roughly half of 1285 hospitals responding to a survey waived fees for 'never events', those that waived fees being much more likely to have perfect scores on the Leapfrog Safe Practices Score. The Michigan Health and Hospital Association Keystone:ICU (www.mhakeystonecenter.org) stated that a series of interventions to improve ICU safety, with daily goals and elimination of CR-BSI and ventilator-associated pneumonia, has resulted over a 5 year

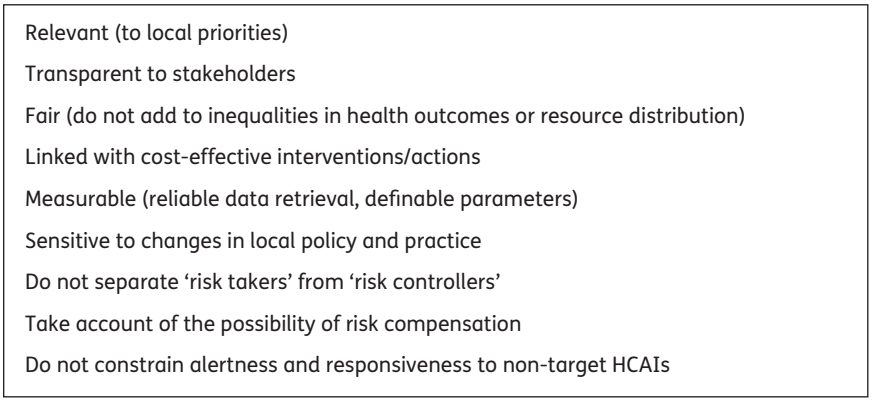

Figure 2. Ideal properties of infection targets (from Millar;[57] HCAI, healthcare-associated infection).

period (2004–09) in 1830 lives saved, 140 700 excess hospital days avoided and US$271 million in healthcare dollars rescued in the state of Michigan alone.[54] The validity of these claims has not, to our knowledge, been substantiated, yet the UK Department of Health has been so impressed that the National Health Service is attempting to follow suit with the Matching Michigan project.[55] However, Edgeworth[50] has pointed out how estimates of excess length of stay due to CR-BSI (claimed to be 10–20 days) are predominantly based on case–control studies, a design fraught with difficulties in both selecting controls and adjusting for potential confounders. Similar difficulties surround attributable mortality due to CR-BSI, which is reported to vary from 0 to 35%. Studies that employed more sophisticated approaches to correct for confounders have generally been unable to show a significant effect of CR-BSI upon mortality. This applies not only when all organisms are included but also holds when coagulase-negative staphylococci are excluded.[56]

Conclusions

Having examined a range of policies for control and treatment of infection in the ICU setting, we are struck by the paucity of high-level evidence underpinning decision making and the often contradictory data that receive minimal airing. Paradoxically, an intervention with a large evidence base, SDD, is largely rejected while interventions with little evidence of efficacy are promoted through either dogma and/or political imperative. Indeed, the lack of consistency in infection control and treatment policies between hospitals highlights the weakness of this evidence base and the vagaries of our behaviour. Millar[57] argues that the particular circumstances and environment of any healthcare facility predisposes to differing microbiological hazards, reducing the generalizability of practice recommendations and research findings. He rightly contends that government-driven targets to reduce specific infections (for instance MRSA bacteraemia, which accounts for just 2% of healthcare-associated infection in the UK) inevitably encourage deprioritization of other, non-targeted infections. Some of these (e.g. Gram-negative bacteraemias) are associated with an equal if not larger burden of adverse outcomes and yet, despite the huge increase in expenditure, staff effort and resource spent on infection control, are inexorably increasing. Furthermore, these targets and the procedures instituted to control them may distract from other, arguably more important, patient outcomes that may not be related to infection. His list of ideal properties for an infection target is reproduced in Figure 2.

We thus need to have a more focused and objective approach to these questions, leading to a balanced debate. We should address and prioritize the definitive studies needed to address current major deficiencies in our knowledge base. We need to identify the true outcome- and cost-effectiveness of an intervention, and not rely on headline-grabbing 'telephone' numbers to spark media interest and subsequent governmental activity and funding. We do recognize that benefit may be difficult to assess. This is especially pertinent when baseline rates of infection are low (such as CR-BSI) and when directly attributable mortality from such infections may represent perhaps only a small component of the overall cause of death in critical illness. With the financial crises currently besetting most healthcare systems, it is incumbent upon us to maximize the utility of our interventions, particularly when a bundled package is promoted with minimal scrutiny. Given that unequivocal evidence is unlikely to become available for many interventions, we would not suggest their immediate abandonment, but we should recognize their limitations and be prepared to modify practice as this changes. We also need to carefully assess the effect of real-world implementation of any change to detect unanticipated harm and understand the true cost–benefit balance.

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