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Authors

Weinstein, Robert A
Huang, Susan S

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Health Care–Associated Infection: Assessing the Value and Validity of Our Measures

Susan S. Huang

Division of Infectious Diseases and Department of Epidemiology and Infection Prevention, University of California Irvine School of Medicine, Irvine, California; and Channing Laboratory, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts

National recommendations for health care–associated infection and transmission metrics have arisen to address the diversity of health care measures in use today. Many of these recommendations include valuable proxy measures, which are simplifications of formal epidemiologic definitions. These proxies provide feasible real-time metrics for ongoing infection control programs. However, the maximum value of these measures is derived from understanding their benefits and limitations when applied to specific populations. Proxy measures should not be dismissed solely because they are imprecise; rather, the source and magnitude of imprecision should be evaluated on the basis of the likelihood that they adversely affect interpretive judgment and subsequent action. This review provides examples of common proxies used in infection control and prevention programs to discuss differences between proxies and exact epidemiologic measures, the value of those differences, and how to assess when exact measures should be used to supplement or replace proxy measures.

There is a critical need to measure events and outcomes in health care today. Hospital administrators and infection prevention programs are keenly interested in assessing the burden of infectious pathogens at their facilities. This interest is driven by the desire to know the microbial burden, to identify clusters, and to assess quality improvement initiatives intended to reduce spread. Measures also help attribute infections to community or health care origins. Although local phenomena are the most relevant for specific patient populations, there is also a desire to compare local measures with measures at other health care systems. National guidelines and legislative mandates have heightened the need for standardized measures and interpretations.

The choice of which measure to use is driven by several necessities. Functionally, measures should be simply defined and rapidly obtainable. They should be useful enough to drive further investigation and accurate enough to justify action or inaction. Unfortunately, the need for simplicity and for real-

time feedback are often in conflict with the acquisition of a highly accurate measure.

PROXY MEASURES VERSUS EXACT MEASURES

This conflict between simplified proxy measures and “exact” measures is not easily resolved. Table 1 details common—but not infallible—distinguishing attributes. Proxy measures are both widely used and broadly useful. A common example is the use of a pathogen case count to inform whether a nosocomial problem exists. An infection control program may note an increase in the number of nosocomial cultures that yield multidrug-resistant *Acinetobacter* species from 5 cases in the prior year to 10 cases in the current year. This case count is used as a proxy for an increase in the percentage of patients acquiring this pathogen, even though no denominator is considered. If denominators are stable, such proxy measures may sufficiently represent the exact measure. Furthermore, case counts are valuable for rare diseases of public health importance. For example, a single case of measles is sufficient to warrant action.

Proxy measures provide qualitative data that influence the next course of action. They are quick and intuitive assessment tools, although they are not entirely precise. Although imprecision leaves room for misinterpretation, it is important not to dismiss proxy measures solely because they are inexact; rather,

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Reprints or correspondence: Dr. Susan S. Huang, Div. of Infectious Diseases, University of California Irvine Medical Center, Bldg. 53, Ste. 215, 101 The City Drive, Orange, CA 92868 (susan.huang@uci.edu).

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Table 1. Common characteristics of health care–associated infection and transmission measures.

Characteristic	Proxy measure	Exact measure
Definition	Simple	Often complex
Acquisition	Rapid	Often time consuming
Accuracy	Variable	Exact
Interpretation	Qualitative	Quantitative
Usefulness	Preliminary	Confirmatory
Response	Real time	Often retrospective

we need to understand whether the degree of inaccuracy matters for the decision that needs to be made. Often, what is needed is a trend assessment. In these situations, proxy measures that provide relative accuracy can sufficiently inform action [1].

In contrast, exact measures provide certainty. They are consistently accurate, irrespective of hospital population characteristics; thus, they direct appropriate action. However, acquisition of exact measures comes at a cost. Often, there is a limited ability to collect the most accurate denominator. For example, in assessing rates of central-line infection, the collection of data on the number of days in which a central line was in place presents a hardship to many hospitals. Nevertheless, use of patient-day denominators in lieu of central line–days may lead to incorrect conclusions about the infection risk, particularly if the fraction of patients with central lines in place varies substantially month to month.

An important situation in which exact measures should be favored is when the intent is to disseminate results and guide policy. Qualitative and quantitative results for research and publication should be accurate or should provide ample proof that proxy measures are likely to reflect exact values.

Additional limitations apply to both exact and proxy measures. The small size of hospital wards can produce instability in monthly, quarterly, and even annual estimates if numerators (and especially denominators) are small [2]. This instability highlights the need for serial estimates and statistical methods to confirm whether initial trends represent meaningful change [3].

RECOMMENDED STANDARDIZED METRICS

The opposing benefits of proxy versus exact measures have led to a diversity of implemented measures across health care institutions. This has led to confusion regarding data collection, interpretation, and comparison. In an attempt to decrease confusion, several prior [4–6] and recent [7–8] guidelines have been published. The recent Society for Healthcare Epidemiology of America (SHEA)–Healthcare Infection Control Practices Advisory Committee (HICPAC) position paper on multidrug-resistant organism (MDRO) metrics provides detailed recommendations on standardized measures [7]. Recom-

mended measures address disease surveillance, nosocomial acquisition (incidence), and overall pathogen burden (prevalence). Similar categories will be used here to provide examples of the advantages and disadvantages of proxy measures across a variety of health care–associated infections.

SPECIFIC EXAMPLES AND APPLICATIONS

Disease measures. Disease measures are often considered the most critical, because outcomes are associated with morbidity, mortality, and health care costs. Thus, it is particularly important that standardized measures exist so that infection control and prevention programs can confidently react to assessments of improvement or decline. Desirable criteria include easy capture, standardized clinical detection, and specificity for infection versus colonization.

Easy capture is a major reason why proxy measures are widely used. Real-time measurement should not be delayed in favor of more-accurate measures unless currently used proxy measures have a substantial potential to mislead.

Standardized clinical detection is another desired criterion for disease measures. Standardization requires not only a clear definition of the condition, but also consistency in acquisition. One difficulty in identifying ventilator-associated pneumonia (VAP) relates to the subjective nature of proposed definitions. This leads to a lack of specificity and limits the accuracy and utility of VAP measurements [9, 10]. A second difficulty arises from differences in the way in which providers order chest radiographs or sputum cultures [11]. Clinical practice variation affects key elements of the definition of VAP [4] and leads to variable ascertainment. VAP measures can differ substantially just because different physicians are on duty at different times.

In contrast, measures of nosocomial bloodstream infection are more useful, because blood cultures are routinely performed for persons who have a temperature $\geq 38^{\circ}\text{C}$. This standardized testing across physicians reduces the likelihood that practice variation explains changes in bloodstream infection rates. The higher likelihood that a positive blood culture result indicates infection, compared with a positive sputum culture result, also improves the measures' specificity when bloodstream infection is compared with VAP.

Nevertheless, even with uniform clinical practice, it is necessary to understand the value and limitations afforded by proxy measures. One recommended metric for bloodstream infection is monthly incidence, defined on the basis of case count for bacteremia (1 case per person per pathogen, excluding recurrences) occurring ≥ 4 calendar days after hospital admission, divided by the total monthly number of hospital admissions [7].

The first question one should ask is whether this bloodstream infection measure is an exact or proxy measure. As defined, it is a proxy measure. Incidence is defined as the number of cases

among the population at risk of acquiring a bloodstream infection. Because patients who have been hospitalized for <4 days are not eligible to become a case in the measure, all such short-stay patients should be excluded from the denominator. Other advanced considerations would involve excluding patients whose entire hospital stay occurs within 14 days after the patient has experienced a previous confirmed bloodstream infection due to the same pathogen (table 2).

After understanding these considerations, the second—and more important—question should be whether these corrections need to be addressed. Is the direction and magnitude of error incurred by the proxy measure enough to invalidate it? If a hospital has few short-stay patients, then the denominator correction will have a small effect, and the proxy will approximate the exact measure. Similarly, if the number of bloodstream infections is small or if readmissions are uncommon, then the 14-day correction will have minimal effect.

An additional important consideration is the direction of the error. Often, all that is desired is an accurate assessment of a trend. In that scenario, the ability to trust a proxy measure depends on whether the magnitude and direction of errors are similar across serial measurements. In the above example, all proxy simplifications inflate the denominator and thus underestimate risk. If this underestimation is fairly uniform, then findings of improvement or decline based on the proxy measure will provide the desired information to guide action. If the magnitude and direction of the error are not uniform, then proxy measures can widely differ from exact measures [12] and lead to an inappropriate infection control response. Supplementation of proxy measures with periodic validations using exact measures can confirm the usefulness of proxy measures, especially if action has been frequently incurred on the basis of values from proxy measures.

Acquisition measures. Acquisition measures are important for detecting nosocomial transmission, regardless of whether acquisition represents colonization or infection. They are most commonly used for routine surveillance of MDRO spread. These measures serve to identify MDRO clusters in a timely manner, to trigger rapid response, to track containment, and to provide confidence in resolution.

For MDROs, nosocomial acquisition measures commonly are based on clinical cultures that indicated first-time identification of an MDRO in a patient. The recent health care-associated infection compendium and SHEA/HICPAC position paper on metrics for methicillin-resistant *Staphylococcus aureus* (MRSA) suggest the use of incidence density, which is defined as the number of patients with a newly identified MRSA culture >4 days after hospital admission divided by the total number of patient-days [7, 13].

This recommended measure is also a proxy. Because incidence density is defined as the number of cases divided by the

time that a person is at risk of acquiring a case, hospital-days of patients who cannot acquire a case should be excluded from the denominator (table 2). Ineligible patient-days that should be excluded include (1) all hospital-days for patients who have been hospitalized for <4 days; (2) the first 3 days of any hospitalization that lasts ≥ 4 days; (3) all hospital-days for patients who are already known to harbor MRSA, because they are ineligible to be a newly identified case; and (4) all patient-days after a patient is newly identified as being positive for MRSA, because the person cannot acquire a case a second time.

Both individually and collectively, these exclusions present a formidable task for real-time surveillance. For this reason, simpler proxy measures are used for ongoing assessment and response. Nevertheless, surrogate denominators can substantially underestimate nosocomial MRSA transmission rates. Furthermore, the number of short-stay patients, the number of hospitalized patients already known to harbor MRSA, and the number of monthly nosocomial cases are likely to vary. Large variations in the deductions attributable to the 4 exclusion criteria can produce different amounts of underestimation each month and may lead to inaccurate findings regarding pathogen burden and trends.

Given these caveats, it is critical for infection control programs to know the impact of using proxies in their specific patient populations and to assess whether more-robust measures are needed routinely or periodically to corroborate simpler measures. As mentioned above, this is particularly important if the proxy measure triggers labor-intensive investigations or interventions. Hospitals with minimal or stable fractions of short-stay patients, stable numbers of monthly admissions, and stable numbers of patients per month who were previously known to have MRSA are more likely to have a stable proportional correction to the denominator. Although this proxy may produce a fairly sizeable deviation from the absolute value of the exact measure, the simplifications might not adversely impact trend assessment. On balance, a periodic validation across a small retrospective or prospective series of months (whichever is easiest) is wise if several factors can produce error. Even if infrequent, such validation can provide reassurance that proxy results can adequately guide infection control response.

In some cases, published data exist on the direction and magnitude of errors incurred by proxy measures. For example, prior evaluations of intensive care unit measures of nosocomial MRSA acquisition have demonstrated that proxy measures underestimate actual incidence density by $\sim 30\%$ [14]. Naturally, the absolute degree of underestimation is more meaningful at a higher incidence density (figure 1) [14]. Another example is the strategy to estimate central line-days on the basis of findings from periodic sampling [15]. These studies provide some reassurance that proxy measures can perform relatively well in certain situations, but they do not obviate the need to verify

Table 2. Common distinctions between proxy and exact hospital-associated infection measures.

Characteristic	Numerator	Denominator	Advantage
Hospital-associated bloodstream infection risk (incidence)			
Simple proxy	Number of events occurring ≥ 4 days after hospital admission until discharge	Total number of admitted patients	Simple denominator
Complex proxy	Number of events occurring ≥ 4 days after hospital admission until discharge	Total number of admitted patients minus all patients who had been hospitalized for < 4 days	More accurate denominator; may produce substantial correction if hospital has many short-stay patients
Exact measure	Number of events occurring ≥ 4 days after hospital admission until discharge; also includes readmission events occurring ≤ 3 days after hospital discharge	Total number of admitted patients minus all patients who had been hospitalized for < 4 days and minus all patients whose entire hospitalization occurred ≤ 14 days after a prior bloodstream event involving the same pathogen	Accurate
Hospital-associated MRSA acquisition rate (MRSA incidence density)			
Simple proxy	Number of events occurring ≥ 4 days after hospital admission until discharge	Total number of patient-days	Simple denominator
Complex proxy 1	Number of events occurring ≥ 4 days after hospital admission until discharge	Total number of patient-days minus patient-days for patients who had been hospitalized for < 4 days	More accurate denominator; may produce substantial correction if hospital has many short-stay patients
Complex proxy 2	Number of events occurring ≥ 4 days after hospital admission until discharge	Total patient-days minus patient-days of those hospitalized for < 4 days and the first 3 days of those hospitalized for ≥ 4 days	More accurate denominator; likely substantial corrective effect
Exact measure	Number of events occurring ≥ 4 days from admission until discharge; also includes readmission events occurring within 3 days of discharge	Total number of patient-days minus patient-days (1) for persons who had been hospitalized for < 4 days; (2) for the first 3 days for persons who had been hospitalized for ≥ 4 days; (3) for patients already known to harbor MRSA; and (4) subsequent to new MRSA detection	Accurate; substantial corrective effect if MRSA prevalence high.

NOTE. MRSA, methicillin-resistant *Staphylococcus aureus*.

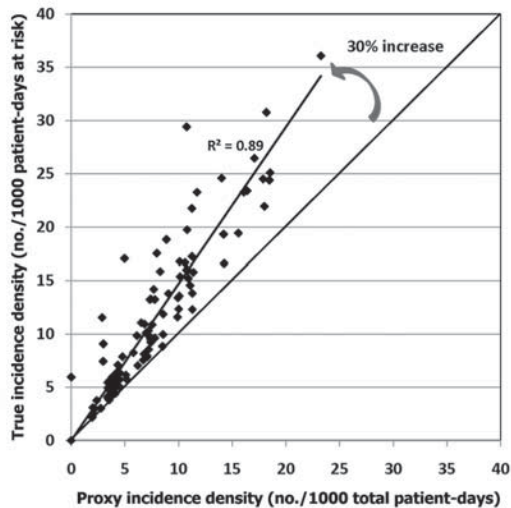


Figure 1. Increase in calculated monthly nosocomial acquisition rates for methicillin-resistant *Staphylococcus aureus* in the intensive care unit when total patient-day denominators are corrected to more-accurate denominators limited to hospital-days in which patients remain at risk of acquiring a case. The x-axis displays the proxy measure incidence density using total patient-day denominators, and the y-axis displays the actual incidence density after denominator correction. (Figure was modified from a previously published figure [14].)

the quality of proxy measures at some point at the individual facility level. In the majority of cases, deviations associated with surrogate denominators are unlikely to affect the detection of large or persistent trend effects, allowing proxy measures to remain the most reasonable and expeditious means of obtaining qualitative (possibly quantitative) evaluations of health care-associated infection and pathogen transmission.

Numerator considerations. Generally speaking, proxy measures use denominator surrogates, leaving case counts (numerators) unaffected. However, numerators still can be affected by differential clinical practice, such that physicians who are more likely to perform cultures (e.g., sputum and wound cultures) will have a higher chance of detecting VAP, surgical site infection, and MDRO carriage. A key example is active screening for MDROs, for which uniform, directed testing produces a rapid increase in case detection and reduces misclassification of prevalent cases as incident ones. This reduction in misclassification can be upwards of 17% [14, 16].

An additional issue specific to MDRO case ascertainment is the bias that arises because infection control programs have tracked MDRO cases for different lengths of time. Programs with long-standing tracking of MDRO cases will benefit from knowing the status of readmitted carriers. Programs that have only recently started tracking MDRO-infected patients are more likely to incorrectly classify prevalent cases as new nosocomial cases, unless great effort is made to preload the line list with

prior positive culture results from historical microbiology databases. Fortunately, this effect is temporary and should be noted as a caveat during this transition period.

Measures of overall burden. Prevalence measures are generally the least susceptible to error, because the ease of obtaining total population denominators leads to the use of exact measures. However, prevalence measures are less frequently used, because they do not distinguish between community-associated and health care-associated acquisition. Despite this, prevalence measures provide several advantages that should encourage their increased use for assessing hospital transmission risk.

Although they do not measure nosocomial spread, prevalence measures quantify contagious patients and the potential for transmission. For example, it stands to reason that hospitals with a high prevalence of MRSA carriers would have a higher risk of MRSA transmission. Similarly, hospitals with a very low prevalence of carriers should have little to no risk of transmission. Thus, importation of prevalent disease or carriage is important in understanding the risks of nosocomial spread. Because importation is beyond the control of hospitals and is heavily dependent on patient populations, prevalence measures may be useful to stratify hospitals by inherent risks of transmission.

As pressure mounts to reduce health care-associated infections to minimal levels, prevalence measures also serve as a metric for the success of interventions to reduce overall infectious burden. In the example of MRSA and other MDROs, total burden has been steadily increasing for several decades. The practice of infection control programs to compare current performance to the prior year's performance may only identify small blips in incidence while failing to detect a steady increase in the prevalence over time (figure 2). From a population standpoint, there may be a stronger need to evaluate interventions that reduce total burden and not just nosocomial episodes, which may be too few to indicate a significant increase in burden.

Interhospital comparisons. Feasibility and expediency drive recommendations for proxy measures in routine health care-associated infection surveillance. These proxy measures are important contributors to the rapid assessment of health care-associated infection and are invaluable to infection control and prevention programs if the benefits and limitations are well understood. In the context of a single program serving a well-understood patient population, health care-associated infection proxy measures can be validated and properly interpreted. However, use of proxy measures for interfacility comparisons raises several concerns that should be addressed before comparisons are made.

Caveats related to proxy measures are greatly increased if metrics are compared between institutions. First, interfacility differences in admission rates, the number of short-stay patients, and colonization pressure associated with prevalent cases

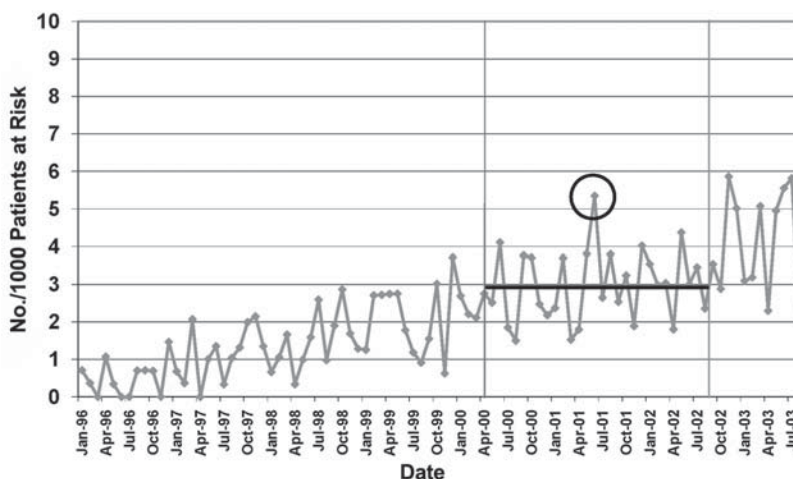


Figure 2. Display of the incidence of nosocomial methicillin-resistant *Staphylococcus aureus* bacteremia at a single hospital highlighting an 18-month period (between the vertical lines) in which the temporary stability of bacteremia cases (*horizontal line*) belies a persistent increase when longer periods of analysis are considered. The common practice of consistently comparing current risk to values solely within the prior year may capture small blips in values (*circle*) while causing broader concerning trends to be missed.

will impact the accuracy of proxy measures and make measures difficult to compare. Often, hospitals cannot dedicate resources to vet these differences to assure that meaningful interfacility interpretations are possible.

Second, facilities have different clinical practices. Many have institution-specific clinical pathways. Examples include the choice whether to perform peripheral blood cultures versus blood cultures through a central line or whether to order sputum cultures for patients with pneumonia versus to commence empirical antibiotic therapy without performing a culture. Third, infection control and prevention programs have different policies and quality-improvement activities, such as tracking of MRSA carriers and implementation of isolation practices. Beyond the presence of certain policies, the duration of certain policies, such as MDRO tracking or screening, can reduce misclassification of MDRO carriers with time as more prevalent cases are appropriately identified. Finally, variations in the case mix across institutions produces differential infection risks [17, 18]. This occurs because age, nutritional status, and chronic illnesses (e.g., diabetes, renal failure, and cancer) have large effects on infection risks in hospitals [17–22]. Similarly, varying severity of acute illness and complex issues surrounding socio-economic status also impact infection risk and preventability [23].

The ability to adjust for interfacility differences is a critical issue with regard to the validity of interfacility comparisons. This is true both for the ranking of facilities by health care-associated infection rates and the ability to be certain about the applicability of interventions across different hospitals. These issues are magnified if proxies are used in public reporting in which extensive explanation of the varying precision

of these measures across facilities is neither desirable nor feasible. Additional research is needed to understand how best to select proxy or exact measures for interfacility comparison and how best to stratify and provide valid interpretations for both programmatic evaluation and public consumption.

SUMMARY

National consensus recommendations for health care-associated infection measures provide much-needed guidance on metrics for health care-associated infection and pathogen spread. The provision of uniform definitions provides a vital foundation for infection control programs to assess and respond to levels of and trends in contagious events in hospitals. However, it is critically important to understand the difference between commonly used and recommended proxy measures and exact measures based on epidemiologic principles. On one hand, proxy measures are simpler to obtain and provide real-time qualitative evaluations that can be implemented among institutions with variable resources. On the other hand, proxy measures can be misleading if differences between proxy and exact measures are not well understood.

This review provides examples of such proxy measures and evaluates their deviation from exact epidemiologic measures. Most proxy measures underestimate actual risk. Problems in the interpretation of proxy measures arise when inaccuracy varies across time and wards. This review emphasizes the need for infection control programs to understand the magnitude and direction of error that occurs when proxy measures are applied to their patient populations. Periodic assessment is recommended to confirm that surrogates sufficiently reflect exact

values, especially if estimates suggest the need for resource-intensive infection control response. Additional research is needed to quantify the relationships between recommended proxy and exact measures and to assess whether stable relationships exist.

Finally, the limitations of health care-associated infection proxy measures are magnified when used to rank or compare institutions, because the direction and magnitude of error varies widely across diverse institutions. Urgent research is needed to guide reporting and interpretation of proxy measures, because widespread use of exact measures is impractical, and yet the inherent inaccuracies of proxy metrics can lead to erroneous conclusions with high-risk public repercussions.

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