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REVIEW

The preventable proportion of nosocomial infections: an overview of published reports

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Summary The proportion of nosocomial infections potentially preventable under routine working conditions remains unclear. We performed a systematic review to describe multi-modal intervention studies, as well as studies assessing exogenous cross-infection published during the last decade, in order to give a crude estimate of the proportion of potentially preventable nosocomial infections. The evaluation of 30 reports suggests that great potential exists to decrease nosocomial infection rates, from a minimum reduction effect of 10% to a maximum effect of 70%, depending on the setting, study design, baseline infection rates and type of infection. The most important reduction effect was identified for catheter-related bacteraemia, whereas a smaller, but still substantial potential for prevention seems to exist for other types of infections. Based on these estimates, we consider at least 20% of all nosocomial infections as probably preventable, and hope that this overview will stimulate further research on feasible and cost-effective prevention of nosocomial infections for daily practice.

Introduction

For the last 30 years, there has been great interest in understanding the causes and impact of hospital-acquired infections.[1] Many experimental studies and randomized trials have examined various methods to prevent nosocomial infections.[2–5] Uncertainty remains, however, about the proportion of nosocomial infections that could potentially be prevented by infection control measures applied under routine working conditions.

Most estimates about the proportion of potentially preventable nosocomial infections were collected almost three decades ago during the SENIC study, which was performed between 1971 and 1976 and published 10 years later.[6] This interventional cohort study showed that about 6% of all nosocomial infections could be prevented by minimal infection control efforts, and that 32% of all nosocomial infections could be prevented by well-organized and highly effective infection control programmes.[6]

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It remains unclear whether these frequently mentioned results are still applicable today,[7] as no other systematic, nationwide cohort study has attempted to replicate these findings. However, several large-scale prevalence studies have suggested that great potential may exist to reduce the prevalence of nosocomial infections on a regional or national scale.[8–13] Moreover, a number of single-centre intervention studies published during the last decade compared infection rates during two consecutive observation periods before and after implementation of multi-modal intervention measures (hereafter called intervention studies) and demonstrated the impact of standardized infection control policies and procedures under real-life conditions.[14,15]

Due to advanced molecular biology and typing methods, it is possible to identify cross-transmission between patients and to distinguish endogenous from exogenous nosocomial infections. Transmission studies may enable conclusions to be drawn about the potential preventability of exogenous nosocomial infections by avoiding cross-transmission.

The aim of this paper was to conduct a systematic review of the published literature to describe multi-modal intervention studies and transmission studies performed during the last decade, in order to give a crude estimate of the proportion of potentially preventable nosocomial infections under current healthcare conditions.

Methods

To identify intervention studies, we performed a MEDLINE search using combinations of the index terms 'nosocomial, hospital, infection, intervention, incidence, survey and reduction' for the period between January 1990 and October 2002. The search for intervention studies focussed on studies applying a multi-modal prevention strategy under real-life working conditions. To search for transmission studies the index terms 'cross infection' or 'transmission' or 'typing' were used. We excluded studies on infection control in long-term care facilities,[16] outbreak reports,[17] studies describing hand hygiene promotion without giving information on infection rates,[5,18] studies investigating only one or two specific intervention measures such as one-day infection control courses or antibiotic prophylaxis,[4,19,20] and randomized trials of treatment or device innovations in infection control.[21,22] To be included, studies had to present crude, quantitative data and not focus on a single type of micro-organism.[23–26] Two reviewers independently assessed the relevance and validity of the included studies.

After completing the computer search for relevant articles, we manually scanned references and review articles. The following items were collected for each included intervention study: patient group, sample size, study design, observation period, infection rates and the documented reduction effect. For transmission studies, we collected information about patient group, observation period, type and number of isolates and estimated number of cross-transmission. Papers in English, French and German were reviewed. References of all identified publications were entered into a database using reference-managing software (EndNote 4.0; Niles Software, Inc., Berkeley, USA).

We expressed the results of each included intervention study showing the difference in the proportional frequency of nosocomial infections before and after an intervention or, in case of controlled studies, the difference in infection rates between intervention and control groups. Whenever provided, we added risk ratios or risk differences to our results. However, given the large heterogeneity of studies, interventions and outcomes, we did not attempt a formal quantitative synthesis by meta-analytic methods.[27,28] In particular, the mix of study designs (i.e., large proportion of uncontrolled before and after intervention trials), the heterogeneous type of infection control interventions, varying data collection methods and definitions of outcomes (i.e., clinically confirmed versus microbiologically confirmed nosocomial pneumonia), the different baseline rates of nosocomial infections and the frequent absence of individual patient-level data meant that formal meta-analysis was not possible. Instead, a qualitative review without generation of summary odds ratios was performed.

For two types of studies we were able to perform a pooled analysis of results: (1) cross-transmission studies; and (2) studies investigating multi-modal interventions for the prevention of catheter-related bacteraemia in critically ill patients. Randomized trials of technological innovations for the prevention of catheter-related bacteraemia have been pooled and discussed in previously published meta-analyses.[29–31]

Results

We identified 25 relevant intervention studies, which were performed in different parts of the

world. The settings and patient populations were extremely diverse, offering a sample of the multifarious nature of current medical care. Ten of the included studies investigated the influence of multi-modal interventions on all types of nosocomial infections (Table I),[11,14,32–39] whereas 15 studies focused on specific types of nosocomial infections (Table II).[15,40–53] Eight studies targeted catheter-related bacteraemia, four studies targeted ventilator-associated pneumonia, and three targeted specifically surgical site infections or urinary tract infections. Many different study designs were used, implicating a variety of methodological approaches, outcome definitions and data collection methods. Most studies used before–after comparisons. Only a few studies used concurrent control groups.[15,39,47] The interventions were equally diverse, including surveillance with feedback, algorithms, guidelines, educational programmes, posters and leaflets, quality circles, and other multidisciplinary approaches.

In those studies using a global intervention approach on all types of nosocomial infections, the reduction of the risk of nosocomial infections ranged from 11 to 55%.[36,37] Most studies used active surveillance and feedback as one of the main components. The study by Gastmeier et al.[39] added quality circles to the implemented intervention programme and reduced infection rates by 26%, whereas four control hospitals had only a minor reduction in infection rates. Pittet et al.[14] included an active campaign to promote alcohol-based hand hygiene into their efforts to prevent nosocomial infections and decreased hospital-wide infection rates from 16.9 to 9.9% within a 4-year period.

In the studies evaluating specific types of nosocomial infections, they were reduced by between 14 and 71% by multi-modal intervention measures.[15,44,45,53] The most important effect was found in studies attempting to decrease bloodstream infection rates in neonatal intensive care, with a potential risk reduction of up to 70%.[45] A pooled evaluation of four intervention studies examining catheter-related infections in critically ill adult patients revealed that the crude reduction effect was 56%, from 8.7 episodes of catheter-related bacteraemia per 1000 catheter-days to 3.8 episodes per 1000 catheter-days.[15,49,52,53] Conversely, studies looking at rates of ventilator-associated pneumonia or surgical site infections had a smaller, but still substantial, effect on risk reduction.[42,50,51]

Five studies were found that assessed exogenous cross-transmission for all types of nosocomial infections (Table III). These studies reported a proportion of nosocomial infections caused by exogenous cross-transmission from 11 to 35%.[54,55] The largest study ever performed on this subject assessed more than 1000 isolates retrieved from 1828 patients in five German intensive care units, and found the proportion of cross-transmitted infections was at least 11% (unpublished data, P. Gastmeier). When the results of all five cross-transmission studies were combined, the total proportion of microbiologically proven, exogenous cross-transmission was 14% (265/1893 isolates).

Discussion

By definition, any infection not present or incubating at the time of admission to the hospital is classified as a nosocomial infection.[58] To date, it remains unclear to what extent these nosocomial infections are avoidable under real-life hospital conditions and what represents the irreducible minimum.[59] The simplest way to answer this question is to document infection rates before and after a multi-modal quality improvement intervention, adopting standardized policies, and if necessary, mandatory practice changes. This was done in a number of intervention studies.[15,35,37,46,50] The evaluation of these reports suggests that great potential exists to decrease endemic nosocomial infection rates, from a minimum reduction effect of 10% to a maximum effect of 70%, depending on the setting, study design, baseline infection rates and type of nosocomial infection.

It is of note that the most important reduction effect was identified for nosocomial bloodstream infections related to the use of central venous catheters. This finding is in accordance with the SENIC data reporting an average reduction effect of 28% for hospital-acquired bacteraemia after implementing effective infection control programmes.[6] A lower potential for reduction seems to exist for surgical site infections or nosocomial pneumonia (average reduction effect in the SENIC study, 7%). Yet, independent of patients' underlying comorbidities and severity of illness, promising prevention approaches exist to decrease the frequency and impact of ventilator-associated pneumonia in the future.[60]

An interesting autopsy study from former East Germany, with an extremely high autopsy rate of 98%, provided crude estimates about the avoidable proportion of nosocomial infections by assessing case histories and autopsy records of 873 deaths occurring at two hospitals in 1990.[61] In the university hospital included, a total of 335 nosocomial

Table I Summary of intervention studies that aimed at prevention and surveillance of all types of nosocomial infections

Reference	Time period	Setting	Study design	Intervention	Infection rate 1st period	Infection rate 2nd period	Intervention effect
Greco et al., 1991[32]	1987–1989	12 hospitals	Before–after intervention study	Surveillance and multi-modal modification of patient care practices	12.9%	10.5%	19% reduction of infected patients (RR 0.81, CI 0.69–0.95)
Raine, 1991[33]	1978–1988	Hospital-wide study	Retrospective cohort study	Multi-modal infection control programme with surveillance	7.6%	3.9%	48% reduction of infections
Evaldson et al., 1992[34]	1988–1990	Obstetrics	Prospective cohort study	Surveillance, feedback, quality improvement programme	14.2%	9.5%	33% reduction of infections
Malone and Lasson, 1996[35]	1990–1994	Hospital-wide study	Retrospective study and prospective follow-up	Hospital-wide introduction of barrier precautions and body substance isolation	3.9%	2.6%	33% reduction of infections
Ng et al., 1998[36]	1993–1995	Neonatal ICU	Prospective study	Reduction of invasive procedures, introduction of a system of aseptic delivery of drugs	13.5 per 1000 patient-days	6.1 per 1000 patient-days	55% relative risk reduction
Hacek et al., 1999[37]	1992–1996	Hospital-wide study	Cohort study with longitudinal assessment	Enhanced infection control programme with rapid assessment of microbial clonality and weekly feedback with discussion	6.49 per 1000 patient days	5.79 per 1000 patient days	11% relative risk reduction
Pittet et al., 2000[14]	1994–1997	Hospital-wide study	Seven observational studies	Hand hygiene campaign (posters, alcohol-based handrubs), surveillance, active MRSA control programme	16.9%	9.9%	41% reduction of infections
Andersen et al., 2000[11]	1996–1998	14 hospitals	Repeated point-prevalence studies	General infection control and surveillance	7.7%	5.9%	23% reduction of infections
Delgado-Rodriguez et al., 2001[38]	1992–1997	General surgery	Surveillance study	Infection control programme and surveillance	18.4 per 1000 patient-days	14 per 1000 patient-days	24% reduction of infections (RR 0.56, CI 0.43–0.74, after adjustment for several confounders)
Gastmeier et al., 2002[39]	1996–1998	Surgical + ICU patients	Prospective, controlled study (8 hospitals)	Introduction of quality circles and ongoing surveillance during two intervention periods	Study hospitals: 7.5 (6.4–8.8) per 1000 patient-days. Control hospitals: 7.4 (6.2–8.8)	Study hospitals: 5.6 (4.6–6.7) per 1000 patient-days. Control hospitals: 6.7 (5.5–8.1)	1st intervention period: RR = 0.75 (0.58–0.97) 2nd intervention period: RR = 0.78 (0.60–1.01), adjusted for several confounders

ICU, intensive care unit; RR, relative risk; CI, confidence interval; MRSA, methicillin-resistant *Staphylococcus aureus*.

Table II Summary of intervention studies that targeted prevention and surveillance of specific types of nosocomial infections

Reference	Time period	Setting	Targeted nosocomial infection	Study design	Intervention	Infection rate 1st period	Infection rate 2nd period	Intervention effect
McConkey et al., 1999[50]	1991–1994	Cardiac surgery	SSI	Prospective cohort study	Surveillance and feedback, multi-modal intervention programme	12.4%	8.2%	34% reduction of SSI. Adjusted adds ratio = 0.37 (CI, 0.22–0.63)
Kelleghan et al., 1993[40]	1987–1990	ICU	VAP	Cohort study with longitudinal assessment	Multidisciplinary team approach (new guidelines, education)	NA	NA	57% reduction in incidence of VAP
Berg et al., 1995[41]	NA	ICU	VAP	Prospective study	Multi-modal educational programme	33%	16%	52% reduction in incidence of VAP
Joiner et al., 1996[42]	1992–1994	ICU	VAP	Prospective study	Introduction of a quality assurance process	26 VAP per 1000 ventilator-days	16 VAP per 1000 ventilator days	38% reduction in incidence of VAP
Kaye et al., 2000[51]	1997–1998	ICU	VAP	Cohort study with longitudinal assessment	Multidisciplinary team approach evaluating patient care processes and implementing multiple interventions	40 VAPs per 1000 ventilator-days	12 VAPs per 1000 ventilator-days	70% reduction in incidence of VAP
Civetta et al., 1996[43]	1992–1994	ICU	CVC-BSI	Sequential prospective study	Continuous quality management approach	15%	8.6%	43% reduction in incidence of CVC-BSI
Cohran et al., 1996[44]	1987–1992	Hospital-wide	CVC-BSI	Cohort study with longitudinal assessment	Surveillance and education programme	1.4 CVC-BSI per 1000 patient-days	1.2 CVC-BSI per 1000 pt-days	14% reduction in incidence of CVC-BSI (not significant)
Maas et al., 1998[45]	1988–1993	Neonatal ICU	CVC–BSI	Before–after comparison	Surveillance and feedback. Education programme.	42%	12%	71% reduction in incidence of CVC-BSI (RR, 0.27; P = 0.001)
Bishop-Kurylo, 1998[46]	1995–1997	Neonatal ICU	CVC-BSI	Cohort study with longitudinal assessment	Continuous quality improvement process by a multidisciplinary team	11.2 BSI per 1000 CVC days	7.0 BSI per 1000 CVC days	37% reduction in incidence of CVC-BSI
Bijma et al., 1999[49]	19-month period	Surgical ICU	CVC-BSI	Cohort study with longitudinal assessment	Five measures (hand hygiene, technical changes, surveillance)	13 BSI per 1000 CVC-days	8 BSI per 1000 CVC-days	38% reduction in incidence of CVC-BSI
Eggimann et al., 2000[15]	1995–1997	ICU	CVC-BSI	Cohort study with longitudinal assessment	Educational campaign for vascular-access insertion and on device use and care	6.6 per 1000 patient days	2.3 per 1000 patient days	65% reduction in BSI incidence (RR 0.33; CI, 0.20–0.56)
Yoo et al., 2001[52]	1998–1999	ICU	CVC-BSI	Cohort study with longitudinal assessment	Surveillance and active infection control interventions	4.2 BSI per 1000 CVC-days	1.3 BSI per 1000 CVC-days	69% reduction in CVC-BSI incidence
Coopersmith et al., 2002[53]	1998–2000	Surgical ICU	CVC-BSI	Cohort study with longitudinal assessment	Educational programme with feedback	10.8 CVC-BSI per 1000 CVC-days	3.7 CVC-BSI per 1000 CVC-days	66% reduction in CVC-BSI incidence
Pumigan et al., 1998[47]	1992–1997	Cardiac ICU	UTI	Cohort study with longitudinal assessment	Multidisciplinary team approach (new guidelines, education)	15.1 per 1000 catheter days	8.3 per 1000 catheter days	66% reduction in UTI incidence (no reduction in two other ICUs)
Goetz et al., 1999[48]	1995–1997	Hospital-wide	UTI	Cohort study with longitudinal assessment	Educational programme with feedback	32 per 1000 catheter days	17.4 per 1000 catheter days	46% reduction in UTI incidence

SSI, surgical site infections; VAP, ventilator-associated pneumonia; UTI, urinary tract infection; CVC-BSI; Central-venous catheter-associated bloodstream infection; ICU, intensive care unit; RR, relative risk; CI, confidence interval.

Table III Summary of cross-transmission studies (including all types of nosocomial infection)

Reference	Setting	Observation period (months)	Pathogens studied	Source of isolates	Number of isolates	Cross-transmissions (%)
Chetchotisakd et al., 1994[54]	5 ICUs	6	Enterobacteriaceae, *Pseudomonas* spp., *Enterococcus* spp., *Staphylococcus aureus*	Infected patients	177	13
Grundmann et al., 1999[56]	2 ICUs	12	Enterobacteriaceae, *Acinetobacter* spp., *Pseudomonas* spp., *S. aureus*	Infected and colonized patients	132	13
Webster and Towner, 2000[57]	1 ICU	12	Enterobacteriaceae, *Acinetobacter* spp., *Pseudomonas* spp.	Infected and colonized patients	215	23
Weist et al., 2002[55]	1 ICU	9	Enterobacteriaceae, *Enterococcus* spp., *S. aureus*	Infected patients	104	35
Gastmeier, unpublished data	5 ICUs	18	Enterobacteriaceae, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterococcus* spp., *S. aureus*, *Stenotrophomonas maltophilia*	Infected and colonized patients	1265	11

ICU, intensive care unit.

infections were documented in 212 out of 461 (46%) deceased adult patients, whereas 212 nosocomial infections were found in 147 of 412 (36%) deceased patients evaluated at the community hospital. Nosocomial infections were the direct cause of death in 88 patients (19%) in the university hospital and in 64 patients (16%) in the community hospital. After thorough case review, 41 nosocomial infections (12%) at the university hospital and 37 (17%) at the community hospital were classified as easily avoidable. Moreover, 185 nosocomial infections (55%) at the university hospital and 111 (52%) at the community hospital were considered avoidable under certain theoretical conditions, and 105 (31%) and 55 (26%), respectively, were regarded as unavoidable, even if care had been optimal. Based on these findings and our review, it seems both plausible and feasible that between 20 and 30% of all nosocomial infections occurring under current healthcare conditions can be prevented. As suggested by different expert groups,[62,63] an even larger proportion ($>50\%$) of device-associated bloodstream infections seems avoidable. Nevertheless, the 'theoretical minimum risk'[64] of acquiring a nosocomial infection remains unknown and needs further investigation. The cost-effectiveness of various strategies to prevent nosocomial infections also remains to be analysed formally, but the huge cost implications of nosocomial infections indicate that most prevention strategies are probably cost-attractive.[14,37]

Most of the included intervention studies used a multi-modal quality management approach to reduce nosocomial infection rates. We excluded national prevalence surveys from our review, as most of these studies did not implement regular feedback or standardized prevention policies and procedures.[8,10,12,65] Therefore, any reduction effect observed on a national scale may have been caused by factors unrelated to infection control. For instance, a study by Aavitsland et al.[65] showed the progressive fall in the prevalence of nosocomial infections in Norway, from 9% in 1979 to 6.3% in 1991. Unfortunately, no causal link with infection control or other reason is cited for the decrease in that study. The relative reduction of 27% in the prevalence of nosocomial infections observed in Denmark over a 20-year period may have been caused by a decrease in length of hospital stay and does not necessarily represent the impact of prevention efforts.[12] By contrast, the relative decrease in prevalence of nosocomial infections in Spain has been smaller (18%) over a eight-year period and may, at least in part, be associated with regular and systematic feedback of surveillance

data to the participating hospitals, stimulating further infection control efforts.[9]

While DNA fingerprinting techniques have been widely used in outbreak investigations to identify nosocomial cross-transmission, only a few studies have evaluated endemic cross-transmission of nosocomial infections. The reason may be that it is a time- and money-consuming method to prove occurrence of cross-transmissions. In our review, a proportion of exogenous cross-infections between 11 and 35% was noted. The included transmission studies tried to identify cross-infections directly from patient to patient or indirectly via vehicles like the environment, personnel or other patients. Therefore, the amount of cross-infections identified depends on the amount of samples taken from the environment (water, surfaces), personnel (e.g. throat swabs) and other patients (colonized, but not infected). According to the number of these samples, the transmission rate identified in the various studies is an 'at least' number. It can be assumed that further transmissions may have occurred, but were not identified due to the lack of recovery of environmental samples. Therefore, not only the number of cross-transmissions may be higher, but also the number of avoidable cross-infections.

Several sources of bias may have influenced our review. It is reasonable to assume that many small intervention trials with negative results remain unpublished.[66] Not surprisingly, we found only a few studies that reported negative results. For example, Cohran et al.[44] reported that the implementation of an intravascular surveillance and education programme without authority to mandate practice changes resulted neither in a significant reduction in the total rate of catheter-related bloodstream infections nor in a change in the proportion of potentially preventable bloodstream infections. A surveillance study from Denmark[67] documenting surgical site infections without specific interventions did not observe a preventive effect of the continuous monitoring programme in the surveyed surgical units. Hence, even after a comprehensive literature search, one might expect publication bias in this review, leading to an overestimation of the intervention effect on the potential preventability of nosocomial infections. Due to methodological limitations, we were not able to quantify this publication bias by analytical techniques.[68] Furthermore, most studies used an uncontrolled study design with a before–after assessment of the intervention effect. In general, these studies had only one or two time points before the intervention, often used questionable statistical tests to show a significant reduction effect and none used advanced time-series anlaysis.[20] Thus, bias due to the influence of sequential time effects cannot be excluded, potentially distorting the reported results.

Prevention is better than cure. Based on our review, we consider at least 20% of all nosocomial infections as probably avoidable, and hope that this paper will stimulate further research about feasible and cost-effective prevention of nosocomial infections. The time has come to bridge the gap between academic research and daily practice, and decrease the rates of nosocomial infections to the irreducible minimum.

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