Evidence-based model for hand transmission during patient care and the role of improved practices. WHO Global Patient Safety…

Article *in* The Lancet Infectious Diseases · November 2006

DOI: 10.1016/S1473-3099(06)70600-4 · Source: PubMed

7 authors, including:

Didier Pittet
Hôpitaux Universitaires de Genève

Hugo Sax
University of Zurich

Liam J Donaldson
London School of Hygiene and Tropical Medi…

John Boyce
Yale-New Haven Hospital

Evidence-based model for hand transmission during patient care and the role of improved practices

Didier Pittet, Benedetta Allegranzi, Hugo Sax, Sasi Dharan, Carmem Lúcia Pessoa-Silva, Liam Donaldson, John M Boyce; on behalf of the WHO Global Patient Safety Challenge, World Alliance for Patient Safety

Hand cleansing is the primary action to reduce health-care-associated infection and cross-transmission of antimicrobial-resistant pathogens. Patient-to-patient transmission of pathogens via health-care workers' hands requires five sequential steps: (1) organisms are present on the patient's skin or have been shed onto fomites in the patient's immediate environment; (2) organisms must be transferred to health-care workers' hands; (3) organisms must be capable of surviving on health-care workers' hands for at least several minutes; (4) handwashing or hand antisepsis by the health-care worker must be inadequate or omitted entirely, or the agent used for hand hygiene inappropriate; and (5) the caregiver's contaminated hand(s) must come into direct contact with another patient or with a fomite in direct contact with the patient. We review the evidence supporting each of these steps and propose a dynamic model for hand hygiene research and education strategies, together with corresponding indications for hand hygiene during patient care.

Lancet Infect Dis 2006; 6: 641–52

Infection Control Programme, University of Geneva Hospitals, Geneva, Switzerland (Prof D Pittet MD, H Sax MD, S Dharan Dip HIC); **WHO Global Patient Safety Challenge** (Prof D Pittet, H Sax, S Dharan), **and World Alliance for Patient Safety** (L Donaldson MD), **Geneva; Department of Infectious Diseases, University of Verona, Verona, Italy** (B Allegranzi MD); **Epidemic and Pandemic Alert and Response, WHO, Lyon, France** (B Allegranzi); **Healthcare-Associated Infections Programme, Department of Epidemic and Pandemic Alert and Response, WHO, Geneva, Switzerland** (C L Pessoa-Silva MD); **and Infectious Diseases Section, Hospital of Saint Raphael, New Haven, CT, USA** (J M Boyce MD)

Correspondence to: Prof D Pittet, Infection Control Programme, University of Geneva Hospitals, 24 Rue Micheli-du-Crest, 1211 Geneva 14, Switzerland. Tel: +41-22-372-9828; fax: +41-22-372-3987 ; **didier.pittet@hcuge.ch**

For further information on the **World Alliance** or the **Global Patient Safety Challenge**, see http://www.who.int/patientsafety/en

Introduction

Hand hygiene is considered the most important measure for preventing health-care-associated infections and the spread of antimicrobial resistant pathogens.[1] However, non-compliance with hand hygiene remains a major problem in health-care settings. Following recent improvements in our understanding of the epidemiology of hand hygiene compliance, new approaches for promotion have been suggested. Guidelines for hand hygiene have been revisited and should improve standards and practices, and help to design successful intervention strategies.[1,2] A clear understanding of the process of hand transmission is also crucial for the success of education strategies.[1,2] We review the evidence for hand transmission of microbial pathogens during patient care, and propose a model to help develop strategies for education and to support the recently reviewed,[2] recognised indications for hand hygiene practice. A related research agenda detailing areas where there is a lack of knowledge or a paucity of data is also proposed to help guide future studies.

Transmission of pathogens on hands

Transmission of health-care-associated pathogens from one patient to another via health-care workers' hands requires five sequential steps (panel 1). Evidence supporting each of these steps is given below.

Organisms present on patients skin or immediate environment

Health-care-associated pathogens can be recovered not only from infected or draining wounds, but also from frequently colonised areas of normal, intact patient skin.[3–14] The perineal or inguinal areas tend to be the most heavily colonised, but the axillae, trunk, and upper extremities (including the hands) also are frequently colonised (figure 1).[6,7,9,10,12,14,15] The number of organisms, such as *Staphylococcus aureus, Proteus mirabilis, Klebsiella* spp, and *Acinetobacter* spp, present on intact areas of some patients' skin can vary from 100 to 10^6 colony forming units (CFU)/cm^2.[7,9,13,16] People with diabetes, patients undergoing dialysis for chronic renal failure, and those with chronic dermatitis are particularly likely to have areas of intact skin colonised with *S aureus*.[17–24] Since nearly 10^6 skin squames containing viable microorganisms are shed daily from normal skin,[25] it is not surprising that patient gowns, bed linen, bedside furniture, and other objects in the immediate environment of the patient become contaminated with patient flora.[14,26–29] Such contamination is probably caused by staphylococci or enterococci, which are resistant to desiccation.

Organism transfer on health-care workers' hands

Few data are available regarding the types of patient-care activities that result in transmission of patient flora to health-care workers' hands (figure 2).[10,28–34] In the past, attempts have been made to stratify patient-care activities into those most likely to cause hand contamination,[35] but such stratification schemes were never validated by quantifying the level of bacterial contamination that

Panel 1: **The five sequential steps for cross-transmission of microbial pathogens.**

1. Organisms are present on the patient's skin or have been shed onto inanimate objects immediately surrounding the patient.
2. Organisms must be transferred to the hands of health-care workers.
3. Organisms must be capable of surviving for at least several minutes on health-care workers' hands.
4. Handwashing or hand antisepsis by the health-care worker must be inadequate or omitted entirely, or the agent used for hand hygiene inappropriate.
5. The contaminated hand(s) of the caregiver must come into direct contact with another patient or with an inanimate object that will come into direct contact with the patient.

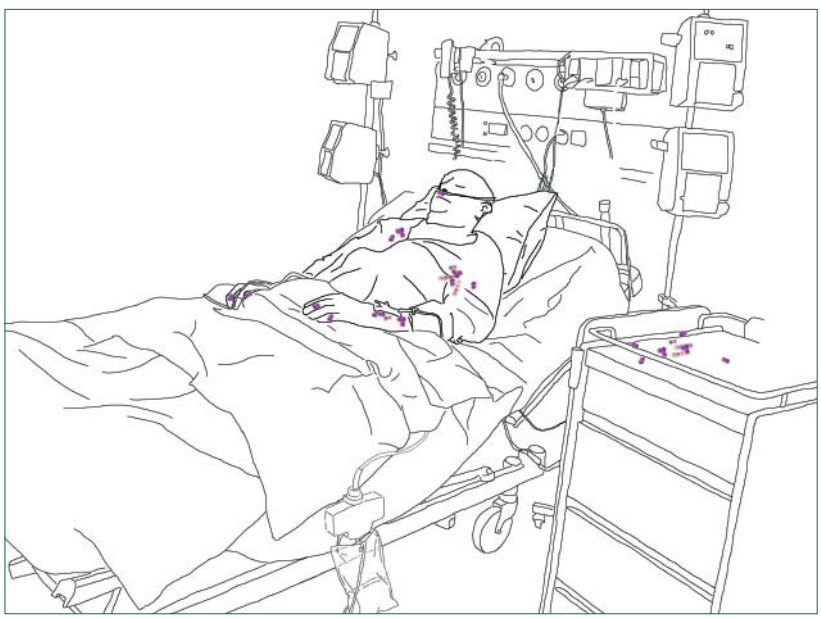

Figure 1: **Organisms present on patient skin or immediate environment**
Bedridden patient colonised with Gram-positive cocci, in particular at nasal, perineal, and inguinal areas (not shown), as well as axillae and upper extremities. Some environment surfaces close to the patient are contaminated with Gram-positive cocci, presumably shed by the patient.

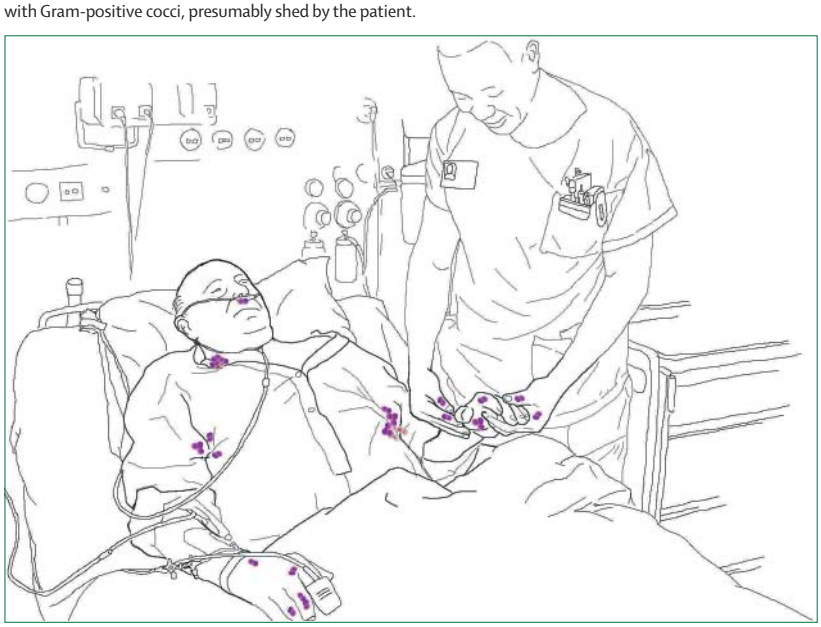

Figure 2: **Organism transfer from patient to health-care worker's hands**
Contact between the health-care worker and the patient results in cross-transmission of microorganisms. In this case, Gram-positive cocci from the patient's own flora.

occurred. Casewell and Phillips[31] showed that nurses could contaminate their hands with 100–1000 CFU of *Klebsiella* spp during "clean" activities such as lifting patients, taking the patient's pulse, blood pressure, or oral temperature. Similarly, Ehrenkranz and Alfonso[9] cultured the hands of nurses who touched the groin of patients heavily colonised with *P mirabilis* and found 10–600 CFU/mL in glove juice samples.

Assessment of the contamination of health-care workers' hands before and after direct patient contact, wound care, intravascular catheter care or respiratory tract care, or before and after handling patient secretions, showed that the number of bacteria recovered using agar fingertip impression plates ranged from 0 to 300 CFU.[34] Direct patient contact and respiratory tract care were most likely to contaminate the fingers of caregivers. Gram-negative bacilli accounted for 15% (54/372) of isolates, and *S aureus* accounted for 11% (39/372). Importantly, duration of patient-care activity was strongly associated with the intensity of bacterial contamination of health-care workers' hands. A similar study of hand contamination during routine neonatal care defined skin contact, nappy change, and respiratory care as independent predictors of hand contamination.[36] In this study, the use of gloves did not fully protect health-care workers' hands from bacterial contamination and glove contamination was almost as high as naked hand contamination after patient contact.

Other studies have shown that health-care workers can also contaminate their hands with Gram-negative bacilli, *S aureus*, enterococci, or *Clostridium difficile* by doing clean procedures or touching intact areas of skin of hospitalised patients.[10,28,29,37] Furthermore, as expected, hands could be contaminated after contact with body fluids or waste.[38]

McBryde and colleagues[39] estimated the frequency of health-care workers' glove contamination with meticillin-resistant *S aureus* (MRSA) after contact with a colonised patient. Health-care workers were intercepted after a patient-care episode and cultures were taken from their gloved hands before handwashing took place; 17% (95% CI 9–25) of contacts with patients, patient clothing, or patient beds resulted in transmission of MRSA from a patient to the health-care worker's gloves. Furthermore, health-care workers caring for infants with respiratory syncytial virus (RSV) infections have acquired RSV by doing activities such as feeding infants, nappy change, and playing with the infant.[32] Caregivers who had contact only with surfaces contaminated with the infants' secretions also acquired RSV; thus, health-care workers contaminated their hands with RSV and inoculated their oral or conjunctival mucosa.

Additional studies have documented contamination of health-care workers' hands with potential pathogens, but did not relate their findings to the specific type of preceding patient contact.[40–48] In studies done before glove use was common among health-care workers, Ayliffe and colleagues[46] found that 15% of nurses working in an isolation unit carried a median of 10^4 CFU of *S aureus* on their hands. 29% of nurses (53/180) working in a general hospital had *S aureus* on their hands (median count, $3 \cdot 8 \times 10^3$ CFU), as did 78% (37/46) of those working in a hospital for dermatology patients (median count, $14 \cdot 3 \times 10^6$ CFU). The same survey revealed that 17–30% of nurses carried Gram-negative bacilli on their hands

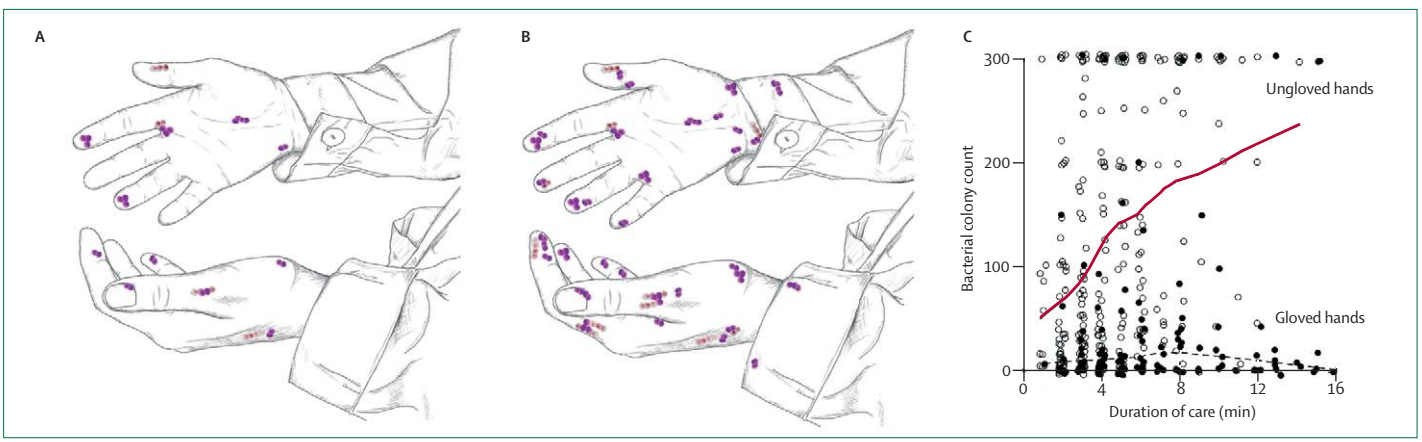

Figure 3: **Organism survival on health-care workers' hands**
(A) Microorganisms, in this case Gram-positive cocci, survive on hands. (B) When growing conditions are optimal (temperature, humidity, absence of hand cleansing, or friction), micoorganisms can continue to grow. (C) Bacterial contamination increases linearly over time during patient contact. Adapted with permission from reference 34.

(median counts ranged from $3 \cdot 4 \times 10^3$ CFU to 38×10^3 CFU). Daschner[44] found that *S aureus* could be recovered from the hands of 21% (67/328) of intensive care unit (ICU) staff, and that 21% (69/328) of doctors and 5% (16/328) of nurse carriers had more than three CFU of the organism on their hands. Maki[49] found lower levels of colonisation on the hands of health-care workers working in a neurosurgery unit, with an average of three CFU of *S aureus* and 11 CFU of Gram-negative bacilli. Serial cultures revealed that 100% of health-care workers carried Gram-negative bacilli at least once, and 64% (16/25) carried *S aureus* at least once. Gram-negative bacilli were recovered from the hands of 38% (45/119) of nurses in neonatal ICUs.[48]

Hands (or gloves) of health-care workers could also be contaminated after touching inanimate objects in patient rooms.[29,36–39,50–53] Similarly, laboratory-based studies have documented that touching contaminated surfaces can transfer *S aureus* or Gram-negative bacilli to the fingers.[54] Unfortunately, none of the studies dealing with health-care worker hand contamination were designed to determine whether the contamination resulted in the transmission of pathogens to susceptible patients.

Organism survival on hands

Microorganisms can survive on hands for different lengths of time (figure 3). In a laboratory study, *Acinetobacter calcoaceticus* survived better than *Acinetobacter lwoffi* 60 min after an inoculum of 10^4 CFU per/finger.[55] Similarly, epidemic and non-epidemic strains of *Escherichia coli* and *Klebsiella* spp showed a 50% survival after 6 min and 2 min, respectively.[56] Both vancomycin-resistant *Enterococcus faecalis* and *Enterococcus faecium* survived for at least 60 min on gloved and ungloved fingertips.[57] *Pseudomonas aeruginosa* and *Burkholderia cepacia* were transmissible by handshaking for up to 30 min when contaminated with organisms suspended in saline, and up to 180 min with organisms suspended in sputum.[58] *Shigella dysenteriae* type 1 can survive on hands for up to 1 h.[59]

Ansari and colleagues[60,61] studied rotavirus, human parainfluenza virus 3, and rhinovirus 14 survival on hands and potential for cross transfer. Survival percentages for rotavirus 20 min and 60 min after virus inoculation were 16·1% and 1·8 % of the initial inoculum, respectively. When a clean hand was pressed against a contaminated disk, the virus transfer was much the same: 16·8% and 1·6 %, respectively. Contact between a contaminated and a clean hand 20 min and 60 min after virus inoculation resulted in the transfer of 6·6% and 2·8% of the viral inoculum, respectively.[61] Therefore, contaminated hands could be vehicles for the spread of certain viruses.

Health-care workers' hands become progressively colonised with commensal flora as well as with potential pathogens during patient care.[34,36] Bacterial contamination increases linearly over time (figure 3C).[34] In the absence of hand hygiene action, the longer the duration of care, the higher the degree of hand contamination. Whether care is provided to adults or neonates, both the duration and the type of patient care affect health-care workers' hand contamination.[34,36] Furthermore, gloves do not provide complete protection against hand contamination.[33,38,43,62] The dynamics of hand contamination are much the same on gloved versus ungloved hands; while gloves protect hands from acquiring bacteria during patient care, the glove surface is contaminated,[34,36] making cross-transmission via contaminated gloved hands probable.

Defective hand cleansing results in hands remaining contaminated

Only a few studies have attempted to show the adequacy or inadequacy of hand cleansing by microbiological proof. From these, it can be assumed that hands remain contaminated with the risk of transmitting organisms

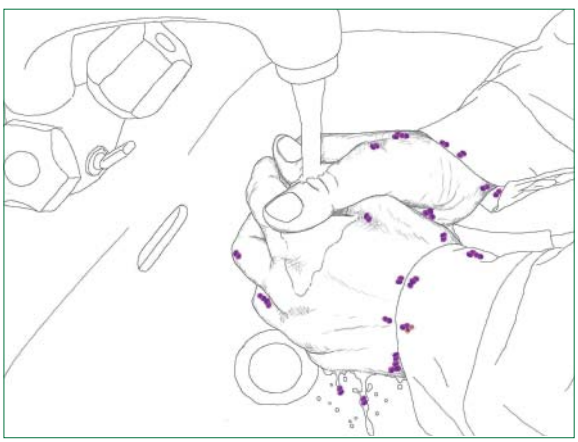

Figure 4: **Incorrect hand cleansing**
Inappropriate handwashing can result in hands remaining contaminated; in this case, with Gram-positive cocci.

via hands (figure 4). In a laboratory-based study, Larson and colleagues[63] found that using only 1 mL of liquid soap or alcohol-based handrub yielded lower log reductions (greater number of bacteria remaining on hands) than using 3 mL of the product to clean hands. The findings have clinical relevance since some health-care workers use as little as 0·4 mL of soap to clean their hands. In a comparative cross-over study of microbiological efficacy of handrubbing with an alcohol-based solution and handwashing with an unmedicated soap, 15% (15/100) of health-care workers' hands were contaminated with transient pathogens before hand hygiene;[64] no transient pathogens were recovered after handrubbing, whereas two cases were found after handwashing. Trick and colleagues[65] did a comparative study of three hand hygiene agents (62% ethyl alcohol handrub, medicated hand wipe, and handwashing with plain soap and water) in a group of surgical ICU nurses. Hand contamination with transient organisms was significantly ($p=0·02$) less likely after the use of an alcohol-based handrub compared with a medicated wipe and soap and water. They also showed that ring-wearing increased the frequency of hand contamination with potential nosocomial pathogens. Wearing artificial fingernails can also result in hands remaining contaminated with pathogens after use of either soap or alcohol-based hand gel,[66] and has been associated with infection outbreaks.[67]

In a study by Sala and colleagues,[68] an outbreak of food poisoning caused by norovirus was traced to an infected food handler at the hospital cafeteria. Most of the foodstuffs consumed during the outbreak were handmade, thus supporting the evidence that inadequate hand hygiene resulted in viral contamination of the food. Noskin and colleagues[57] showed that a 5 s handwash with water alone had no effect on contamination with vancomycin-resistant enterococci (VRE); 20% of the initial inoculum was recovered on unwashed hands, and a 5 s wash with two soaps did not completely remove the organisms, with nearly 1% recovery. A 30 s wash with either soap was necessary to completely remove the organisms from hands.

Obviously, when health-care workers fail to clean their hands between patient contact (figure 5) or during the sequence of patient care, in particular when hands move from a microbiologically contaminated to a cleaner body site in the same patient (figure 6), microbial transfer could occur.

Contaminated hands cross-transmit organisms

Cross-transmission of organisms occurs through contaminated hands (figure 5 and figure 6). Factors that influence the transfer of microorganisms from surface to surface and affect cross-contamination rates are type of organism, source and destination surfaces, moisture level, and size of inoculum. Contaminated hands can cross-transfer bacteria from a clean paper towel dispenser and vice versa[69] with transfer rates ranging from 0·01% to 0·64% and 12·4% to 13·1%, respectively.

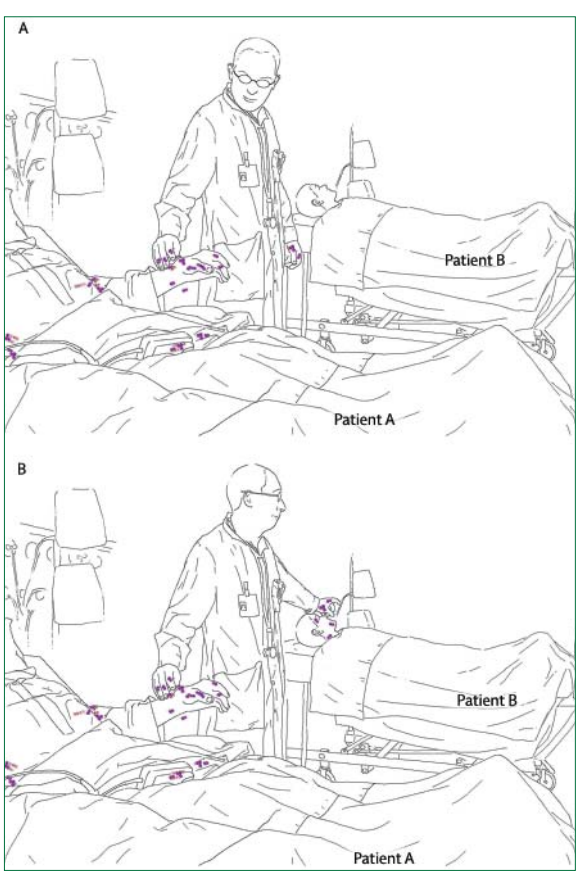

Figure 5: **Failure to cleanse hands results in between-patient cross-transmission**
(A) The doctor had a prolonged contact with patient A colonised with Gram-positive cocci and contaminated his hands. (B) He is now going to have direct contact with patient B without cleansing his hands in between. Cross-transmission of Gram-positive rods from patient A to patient B through the health-care worker's hands is likely to occur.

Norovirus-contaminated fingers have been shown to sequentially transfer the virus to up to seven clean surfaces, and novovirus has also been shown to transfer from a contaminated cleaning cloth to clean hands and surfaces.[70] During an outbreak of multidrug-resistant *Acinetobacter baumannii*, strains from patients, health-care workers' hands, and the environment were identical.[71] The outbreak was terminated when remedial measures were taken. *Serratia marcescens* was transmitted from contaminated soap to patients via health-care wokers' hands.[72] Another study showed that VRE could be transferred from the contaminated environment or patients' intact skin to clean sites via health-care workers' hands or gloves in 10·6% of contacts.[73] Finally, several studies have shown that pathogens can be transmitted from out-of-hospital sources to patients via health-care workers' hands—eg, an outbreak of postoperative *S marcescens* wound infections was traced to a contaminated jar of exfoliant cream in a nurse's home. An investigation suggested that the organism was transmitted to patients via the hands of the nurse who wore artificial fingernails.[74] In another outbreak, *Malassezia pachydermatis* was probably transmitted from a nurse's pet dogs to infants in a neonatal unit via the nurse's hands.[75]

Many parameters are associated with patient colonisation, and include exogenous and endogenous factors. The presence of medical devices, the disruption of normal mechanical and other host defence mechanisms, patient comorbidities, and exposure to medication—in particular broad spectrum antimicrobials—are some factors that might facilitate successful patient colonisation. It is important to say, however, that colonisation can occur in the normal host and that poor patient underlying conditions are not a prerequisite for either exogenous or endogenous colonisation.

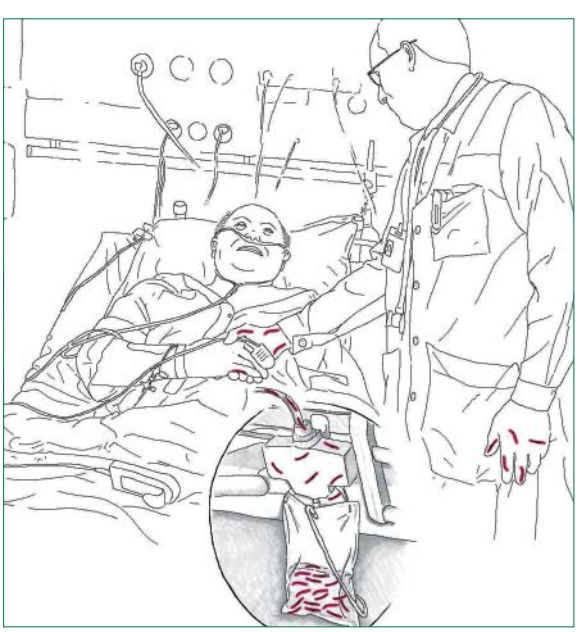

Figure 6: **Failure to cleanse hands during patient care results in within-patient cross-transmission**
The doctor is in close contact with the patient. He touched the urinary catheter bag previously and his hands are colonised with Gram-negative rods from touching the bag and lack of subsequent hand cleansing. Direct contact with patients or patients' devices would probably result in cross-transmission.

Experimental and mathematical models of hand transmission

Experimental models

Several investigators have studied the transmission of infectious agents with different experimental models. Ehrenkranz and Alfonso[9] asked nurses to touch a patient's groin for 15 s as though they were taking a femoral pulse. The patient was known to be heavily colonised with Gram-negative bacilli. Nurses then cleansed their hands by washing with plain soap and water, or by using an alcohol-based handrub. After cleansing their hands, they touched a piece of urinary catheter material with their fingers and the catheter segment was cultured. The study revealed that touching patients' intact areas of moist skin transferred enough organisms to the nurses' hands to allow subsequent transmission to catheter material despite handwashing with plain soap and water. Conversely, alcohol-based handrubbing was effective.

Marples and Towers[76] studied the transmission of organisms from artificially contaminated donor fabrics to clean recipient fabrics via hand contact and found that the number of organisms transmitted was greater if the donor fabric or the hands were wet. Overall, only 0·06% of the organisms obtained from the contaminated donor fabric were transferred to the recipient fabric via hand contact. Using the same experimental model, *Staphylococcus saprophyticus, P aeruginosa,* and *Serratia* spp were transferred in greater numbers than *E coli* from a contaminated to a clean fabric following hand contact.[77] In another study, organisms were transferred to various types of surfaces in much larger numbers (>10^4) from wet hands than from hands that had been dried carefully.[78] Similarly, the transfer of *S aureus* from fabrics commonly used for clothing and bed linen to fingerpads occurred more frequently when fingerpads were moist.[79]

Mathematical models

Mathematical modelling has been used to examine the relations between the multiple factors that influence the transmission of pathogens in health-care facilities. These factors include hand hygiene compliance, nurse staffing levels, frequency of introduction of colonised or infected patients onto a ward, whether or not cohorting is practised, patient characteristics, and antibiotic stewardship practices, to name but a few.[80] Most reports describing mathematical modelling of health-care-associated pathogens have attempted to quantify the influence of various factors on a single ward, such as an ICU.[81–84] Given that such units tend to

house a small number of patients at any one time, random variations (stochastic events), such as the number of patients admitted with a particular pathogen during a short time period, can have a substantial effect on transmission dynamics. As a result, stochastic models seem to be the most appropriate for estimating the effect of various infection control measures, including hand hygiene compliance, on colonisation and infection rates.

In a mathematical model of MRSA infection in an ICU, the number of patients who became colonised by strains transmitted from health-care workers was one of the most important determinants of transmission rates.[81] Of interest, the authors found that increasing hand hygiene compliance rates had only a modest effect on the prevalence of MRSA colonisation. Their model estimated that if the prevalence of MRSA colonisation was 30% without any hand hygiene, it would decrease to only 22% if hand hygiene compliance increased to 40%, and colonisation would decrease to 20% if hand hygiene compliance increased to 60%. Antibiotic policies had little effect in this model.

Austin and colleagues[82] used daily surveillance cultures of patients, molecular typing of isolates, and monitoring of compliance with infection control practices to study the transmission dynamics of VRE in an ICU. Hand hygiene and staff cohorting were predicted to be the most effective control measures: for a given level of hand hygiene compliance, adding staff cohorting would lead to better control of VRE transmission. The rate at which new VRE cases were admitted to the ICU had an important role in the level of VRE transmission in the unit.

In a study using a stochastic model of transmission dynamics, Cooper and colleagues[85] predicted that improving hand hygiene compliance from very low levels by 20% or 40% significantly ($p<0·05$) reduced transmission, but that improving compliance to levels above 40% would have little effect on the prevalence of *S aureus*. Grundmann and colleagues[84] did an investigation that included cultures of patients at the time of ICU admission and twice-weekly observations of the frequency of contact between health-care workers and patients, cultures of health-care workers' hands, and molecular typing of MRSA isolates. A stochastic model predicted

Reference	Hospital setting	Results	Duration of follow-up
Casewell and Phillips (1977)[31]	Adult ICU	Significant reduction (p<0·001) in the percentage of patients colonised or infected by *Klebsiella* spp	2 years
Conly et al (1989)[95]	Adult ICU	Significant reduction (p=0·02) in health-care-associated infection rates immediately after hand hygiene promotion (from 33% to 12% and from 33% to 9%)	6 years
Simmons et al (1990)[96]	Adult ICU	No effect on health-care-associated infection rates (no significant [p<0·05] improvement of hand hygiene adherence)	11 months
Doebbeling et al (1992)[90]	Adult ICUs	Significant (p<0·02) difference between rates of health-care-associated infection using two different hand hygiene agents	8 months
Webster et al (1994)[91]	NICU	Elimination of MRSA, when combined with multiple other infection control measures. Reduction of vancomycin use. Significant p<0·02 reduction of nosocomial bacteraemia (from 2·6% to 1·1%) using triclosan compared with chlorhexidine for handwashing	9 months
Zafar et al (1995)[92]	Newborn nursery	Control of a MRSA outbreak using a triclosan preparation for handwashing, in addition to other infection control measures	3·5 years
Larson et al (2000)[94]	MICU/NICU	Significant (85%, p=0·02) relative reduction of VRE rate in the intervention hospital; insignificant (44%) relative reduction in control hospital; no significant change in MRSA	8 months
Pittet et al (2000)[93]	Hospital-wide	Significant (p=0·04 and p<0·001) reduction in the annual overall prevalence of health-care-associated infections (41·5%) and MRSA cross-transmission rates (87%). Active surveillance cultures and contact precautions were implemented during same time period	5 years
Hilburn et al (2003)[99]	Orthopaedic surgical unit	36·1% decrease in infection rates (from 8·2% to 5·3%)	10 months
MacDonald et al (2004)[97]	Hospital-wide	Significant (p=0·03) reduction in hospital-acquired MRSA cases (from 1·9% to 0·9%)	1 year
Swoboda et al (2004)[98]	Adult intermediate care unit	Reduction in health care-associated infection rates (not significant, p value not reported)	2·5 months
Lam et al (2004)[100]	NICU	Reduction (not significant, p=0·14) in health-care-associated infection rates (from 11·3 per 1000 patient-days to 6·2 per 1000 patient-days)	6 months
Won et al (2004)[101]	NICU	Significant reduction (p=0·003) in health care-associated infection rates (from 15·1 per 1000 patient-days to 10·7 per 1000 patient-days), in particular of respiratory infections	2 years
Zerr et al (2005)[102]	Hospital-wide	Significant (p=0·01) reduction in hospital-associated rotavirus infections	4 years
Rosenthal et al (2005)[103]	Adult ICUs	Significant (p<0·001) reduction in health-care-associated infection rates (from 47·5 per 1000 patient-days to 27·9 per 1000 patient-days)	21 months
Johnson et al (2005)[104]	Hospital-wide	Significant (p=0·01) reduction (57%) in MRSA bacteraemia	36 months

ICU=intensive care unit, NICU=neonatal ICU, MRSA=meticillin-resistant *Staphylococcus aureus*, MICU=medical ICU, VRE= vancomycin-resistant enterococci.

Table: **Association between adherence with hand hygiene practice and health-care-associated infection rates: hospital-based studies, 1975–2005**

that a 12% improvement in adherence to hand hygiene policies or in cohorting levels might have compensated for staff shortages, and prevented transmission during periods of overcrowding and high workloads.

Although the above studies have provided new insights into the relative contribution of various infection control measures, all have been based on assumptions that might not be valid in all situations. For example, most studies assumed that the transmission of pathogens occurred only via health-care workers' hands, and that contaminated environmental surfaces had no role in transmission. The latter might not be true for some pathogens that can remain viable in the inanimate environment for prolonged periods. Moreover, practically all mathematical models were based on the assumption that when health-care workers did clean their hands, 100% of the pathogens of interest were eliminated from the hands,[86] which is unlikely to be true in many instances.[85] Importantly, all the mathematical models described above predicted that improvements in hand hygiene compliance could reduce pathogen transmission. However, the models did not agree on the level of hand hygiene compliance that is necessary to halt transmission of pathogens. In reality, the level might not be the same for all pathogens and in all clinical situations. Finally, no model used direct observation of health-care workers' practices with further validation of the observed actions. Further use of mathematical models of transmission of health-care-associated pathogens is warranted. Potential benefits of such studies include assessing the benefits of various infection control interventions, and understanding the effect of random variations in the incidence and prevalence of various pathogens.[80]

Relations between hand hygiene and acquisition of health-care-associated pathogens

Despite a paucity of appropriate randomised controlled trials, there is substantial evidence that hand antisepsis reduces the incidence of health-care-associated infection.[1,87,88] In what would be considered now as an intervention trial using historical controls, Semmelweis[86] demonstrated in 1847 that the mortality rate in mothers who delivered children at the First Obstetrics Clinic at the General Hospital of Vienna was substantially lower when hospital staff cleansed their hands with an antiseptic agent than when they washed their hands with plain soap and water.

In the 1960s, a prospective, controlled trial sponsored by the USA National Institutes of Health and the Office of the Surgeon General compared the effect of no handwashing with that of antiseptic handwashing on the acquisition of *S aureus* in infants in a hospital nursery.[89] The investigators showed that infants cared for by nurses who did not wash their hands after handling an index infant colonised with *S aureus* acquired the organism significantly ($p<0\cdot05$) more often and more rapidly than did infants cared for by nurses who used hexachlorophene to cleanse their hands between infant contacts. This trial provided compelling evidence that hand cleansing with an antiseptic agent between patient contacts reduces transmission of pathogens when compared with no handwashing between patient contacts.

Several studies have shown the effect of hand cleansing on health-care-associated infection rates or reduction in antimicrobial resistant pathogen cross-transmission (table).[31,90–104]

In addition to these studies, outbreak investigations have underscored the role of organism cross-transmission through health-care workers' hands.[67,105–113] Some of these investigators have shown an association between infection and understaffing or overcrowding that was consistently linked with poor adherence to hand hygiene.[110–113] These findings show indirectly that an imbalance between workload and staffing leads to relaxed attention to basic control measures—such as hand hygiene—and spread of microorganisms.

Implications for hand hygiene practices

Indications for hand cleansing during patient care are closely related to the sequential steps involved in cross-transmission of microbial pathogens. Figure 7 illustrates the sequential steps and highlights the indications for hand hygiene according to the most recent expert recommendations.[2] In particular, the current review of the dynamics of microbial pathogen hand transmission validates indications for hand hygiene after contact with inanimate objects in the immediate vicinity of the patient, after contact with body fluids or excretions, mucous membranes, non-intact skin, or wound dressings, after contact with the patient and immediately before next patient contact, as well as when moving from a contaminated body site to a clean body site during patient care. The latter indication is frequently unrecognised by health-care workers in their daily practices,[93,114,115] and fails to be recorded in most studies on the epidemiology of hand hygiene compliance.[2] Although cross-transmission of microbial pathogens from patient-to-patient is likely to be reduced by increased compliance before and after contact with the patient, endogenous infections acquired through inappropriate patient-care practices mostly result from inappropriate glove use (or absence of glove removal at appropriate times), or the absence of, or insufficient, hand cleansing before handling an invasive device or during the sequence of patient care when hands are moving from a contaminated to a clean body site.

Impact of improved hand hygiene

13 hospital-based studies of the effect of hand hygiene on the risk of health-care-associated infection have been published between 1977 and 2005 (table).[31,90–104]

Despite study limitations, most reports showed a temporal relation between improved hand hygiene practices and reduced infection rates.

The hand hygiene promotion campaign at the University of Geneva Hospitals constitutes the first reported

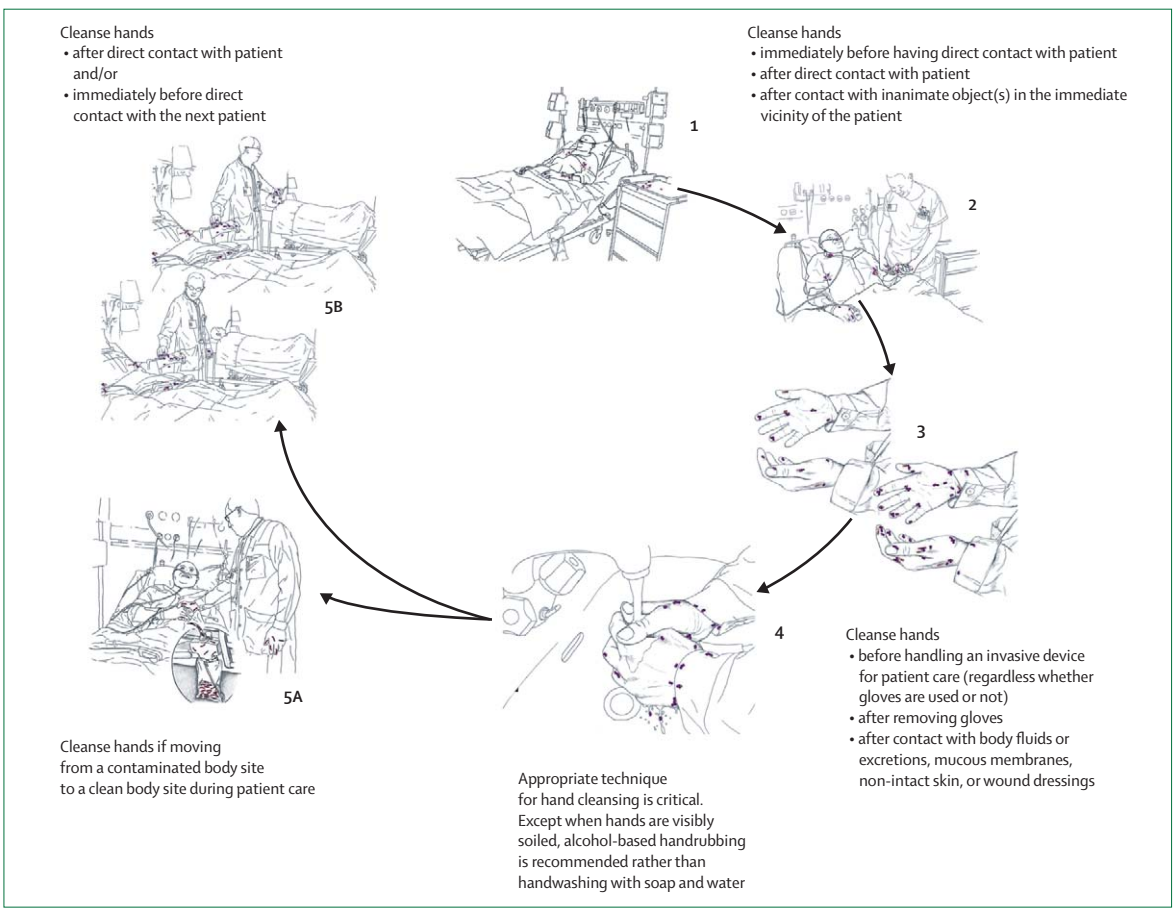

Figure 7: **Summary of hand transmission and indications for hand hygiene during patient care**

experience of a sustained improvement in compliance with hand hygiene, coinciding with a reduction of nosocomial infections and MRSA transmission.[93] The multimodal strategy that contributed to the success of the promotion campaign included repeated monitoring of compliance and hand hygiene performance feedback, communication and education tools, constant reminders in the work environment, active participation and feedback at both individual and organisational levels, senior management support, and involvement of institutional leaders. The use of waterless hand antisepsis was largely promoted and facilitated throughout the institution. The promotion of bedside, alcohol-based handrub largely contributed to the increase in compliance. Including both direct costs associated with the intervention and indirect costs associated with health-care worker time, the promotion campaign was cost effective.[116]

Subsequently, several small-sized studies done over shorter periods have also shown that hand hygiene promotion programmes that included introduction of an alcohol-based handrub led to increased hand hygiene compliance among health-care workers and a decrease in health-care-associated infections.[101,117] In several other studies in which hand hygiene compliance was not monitored, multidisciplinary programmes that involved the introduction of an alcohol-based handrub were associated with a decrease in infection rates.[97,99,118,119] The beneficial effects of hand hygiene promotion on the risk of cross-transmission have also been reported in surveys done in schools or day-care centres,[120–126] as well as in community settings.[127–131]

Although none of the studies done in the health-care setting were randomised controlled trials, they provide substantial evidence that increased hand hygiene compliance is associated with reduced cross-transmission and infection rates. Methodological and ethical concerns make it difficult to set up randomised controlled trials with appropriate sample size that could establish the relative importance of hand hygiene in the prevention of health-care-associated infection. Thus, the studies so far conducted could not determine a definitive causal relation because of the lack of statistical significance, the presence of confounding factors, or the absence of randomisation. However, a large, randomised, controlled trial to test the effect of hand hygiene promotion clearly showed a reduction of upper respiratory pulmonary infection, diarrhoea, and impetigo in children in a Pakistani community, with a positive effect on child health.[130,131]

Although the generation of additional scientific and causal evidence for the effect of enhanced adherence with hand hygiene on infection rates in health-care settings remains important, these results indicate that improved hand hygiene practices reduce the risk of transmission of pathogens.

Perspectives and future research

Heath-care worker education, in particular regarding indications for hand cleansing during patient care, is a crucial step within multimodal intervention strategies targeted to improve hand hygiene. We encourage educational materials to strongly consider steps in hand transmission to help promote hand hygiene practices (figure 7). Timing of hand hygiene indications is based on the dynamics of cross-transmission summarised here in accordance with the best current evidence. This review of the literature has identified some unexplored aspects and methodological weaknesses of the available studies and, therefore, helps to pinpoint priority areas for future research (panel 2). Investigation of these issues is warranted to make the evidence basis of the model even stronger. In particular, research should consider the entire spectrum of hand transmission at the time of study design.

Panel 2: Priority research topics according to steps of cross-transmission

- Investigate the level of health-care workers' hand contamination subsequent to exposure to patient and/or fomite (*steps 1 and 2*)
- Study the effect of different surface features (eg, tissue, skin, moisture-level) on hand contamination (*steps 1 and 2*)
- Develop further research on optimum hand hygiene agents and techniques (*step 4*)
- Assess the effect of inadequate hand hygiene technique on microbial hand transmission (*steps 4 and 5*)
- Delineate the relative risk of cross-transmission according to the type of patient-care activity (*step 5*)
- Assess the relative importance of between-patient and within-patient cross-transmission (*step 5*)
- Determine the relative importance of different hand hygiene indications and their effect on cross-transmission and/or infection (*steps 1, 2, 3, and 5*)
- Investigate the correlation between the level of hand hygiene compliance increase and the degree of hand transmission reduction (*steps 1–5*)
- Establish the benefit of hand hygiene versus other infection control measures on pathogen cross-transmission and infection rates by the development of specific experimental and mathematical models (*steps 1–5*)
- Demonstrate the effectiveness of hand hygiene to reduce health-care-associated infections through carefully planned randomised controlled trials (*steps 1–5*)

Search strategy and selection criteria

Data for this review were identified by a Medline search and references taken from relevant articles; numerous articles were identified through a search of the extensive files of the authors. Search terms included "hand hygiene", "handwashing", "alcohol-based handrub", "cross-infection", "dynamics", "modelling", and "microbial pathogens". English and French language papers were reviewed from January 1975–March 2006.

Conflicts of interest

JMB is a consultant for Gojo Industries Inc. and Advanced Sterilization Products, and has acted as a consultant for Dial Corp and Woodward Laboratories. He has also received an honorarium from Johnson & Johnson. All other authors declare that they have no conflicts of interest.

Acknowledgments

We are indebted to the group of international experts and WHO members who worked on the development of the Global Patient Safety Challenge, in particular for their participation in the two international WHO consultations, review of the available scientific evidence, writing of the WHO draft Guidelines on Hand Hygiene in Health Care, and fostering discussion among authors and members of the different task forces and working groups. The complete list of participants in the development of the guidelines documents is available at http://www.who.int/patientsafety/events/05/HH_en.pdf. We also thank the Patient Safety team and other WHO staff from all the departments involved at headquarters and in the regional offices for their work.

Didier Pittet thanks the members of the Infection Control Programme at the University of Geneva Hospitals, Rosemary Sudan for providing editorial assistance and outstanding support, and Florian Pittet for the preparation of the figures.

References

1 Boyce JM, Pittet D. Guideline for hand hygiene in health-care settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. *MMWR Recomm Rep* 2002; **51:** 1–45.

2 WHO. WHO Guidelines for Hand Hygiene in Health Care (Advanced Draft). Geneva: WHO, 2006. http://www.who.int/patientsafety/challenge/en (accessed Sept 5, 2006).

3 Lowbury EJL. Gram-negative bacilli on the skin. *Br J Dermatol* 1969; **81:** 55–61.

4 Noble WC. Distribution of the Micrococcaceae. *Br J Dermatol* 1969; **81** (suppl 1): 27–32.

5 McBride ME, Duncan WC, Bodey GP, McBride CM. Microbial skin flora of selected cancer patients and hospital personnel. *J Clin Microbiol* 1976; **3:** 14–20.

6 Casewell MW. The role of hands in nosocomial gram-negative infection. In: Maibach HI, Aly R, eds. Skin microbiology relevance to clinical infection. New York: Springer-Verlag, 1981: 192–202.

7 Larson EL, Cronquist AB, Whittier S, Lai L, Lyle CT, Della Latta P. Differences in skin flora between inpatients and chronically ill patients. *Heart Lung* 2000; **29:** 298–305.

8 Larson EL, McGinley KJ, Foglia AR, Talbot GH, Leyden JJ. Composition and antimicrobic resistance of skin flora in hospitalized and healthy adults. *J Clin Microbiol* 1986; **23:** 604–08.

9 Ehrenkranz NJ, Alfonso BC. Failure of bland soap handwash to prevent hand transfer of patient bacteria to urethral catheters. *Infect Control Hosp Epidemiol* 1991; **12:** 654–62.

10 Sanderson PJ, Weissler S. Recovery of coliforms from the hands of nurses and patients: activities leading to contamination. *J Hosp Infect* 1992; **21:** 85–93.

11 Coello R, Jiminez J, Garcia M, et al. Prospective study of infection, colonization and carriage of methicillin-resistant *Staphylococcus aureus* in an outbreak affecting 990 patients. *Eur J Clin Microbiol* 1994; **13:** 74–81.

12 Sanford MD, Widmer AF, Bale MJ, Jones RN, Wenzel RP. Efficient detection and long-term persistence of the carriage of methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis* 1994; **19:** 1123–28.

13 Bertone SA, Fisher MC, Mortensen JE. Quantitative skin cultures at potential catheter sites in neonates. *Infect Control Hosp Epidemiol* 1994; **15:** 315–18.

14 Bonten MJ, Hayden MK, Nathan C, et al. Epidemiology of colonisation of patients and environment with vancomycin-resistant enterococci. *Lancet* 1996; **348:** 1615–19.

15 Polakoff S, Richards ID, Parker MT, Lidwell OM. Nasal and skin carriage of *Staphylococcus aureus* by patients undergoing surgical operation. *J Hyg (Lond)* 1967; **65:** 559–66.

16 Leyden JJ, McGinley KJ, Nordstrom KM, Webster GF. Skin microflora. *J Invest Dermatol* 1987; **88** (suppl 3)**:** 65s–72s.

17 Tuazon CU, Perez A, Kishaba T, Sheagren JN. *Staphylococcus aureus* among insulin-injecting diabetic patients. An increased carrier rate. *JAMA* 1975; **231:** 1272.

18 Kaplowitz LG, Comstock JA, Landwehr DM, Dalton HP, Mayhall CG. Prospective study of microbial colonization of the nose and skin and infection of the vascular access site in hemodialysis patients. *J Clin Microbiol* 1988; **26:** 1257–62.

19 Aly R, Maibach HI, Shinefield HR. Microbial flora of atopic dermatitis. *Arch Dermatol* 1977; **113:** 780–82.

20 Kirmani N, Tuazon CU, Murray HW, Parrish AE, Sheagren JN. *Staphylococcus aureus* carriage rate of patients receiving long-term hemodialysis. *Arch Intern Med* 1978; **138:** 1657–59.

21 Goldblum SE, Ulrich JA, Goldman RS, Reed WP. Nasal and cutaneous flora among hemodialysis patients and personnel: quantitative and qualitative characterization and patterns of staphylococcal carriage. *Am J Kidney Dis* 1982; **11:** 281–86.

22 Boelaert JR, Van Landuyt HW, Gordts BZ. Nasal and cutaneous carriage of *Staphylococcus aureus* in hemodialysis patients: the effect of nasal mupirocin. *Infect Control Hosp Epidemiol* 1996; **17:** 809–11.

23 Zimakoff J, Pedersen FB, Bergen L, Baago-Nielsen J, Daldorph B. *Staphylococcus aureus* carriage and infections among patients in four haemo- and peritoneal-dialysis centres in Denmark. *J Hosp Infect* 1996; **33:** 289–300.

24 Bibel DJ, Greenbert JH, Cook JL. *Staphylococcus aureus* and the microbial ecology of atopic dermatitis. *Can J Microbiol* 1997; **23:** 1062–68.

25 Noble WC. Dispersal of skin microorganisms. *Br J Dermatol* 1975; **93:** 477–85.

26 Walter CW, Kundsin RB, Shilkret MA, Day MM. The spread of staphylococci to the environment. *Antibiot Annu* 1958–1959; **6:** 952–57.

27 Boyce JM, Opal SM, Chow JW, et al. Outbreak of multidrug-resistant *Enterococcus faecium* with transferable *vanB* class vancomycin resistance. *J Clin Microbiol* 1994; **32:** 1148–53.

28 McFarland LV, Mulligan ME, Kwok RY, Stamm WE. Nosocomial acquisition of *Clostridium difficile* infection. *N Engl J Med* 1989; **320:** 204–10.

29 Samore MH, Venkataraman L, DeGirolami PC, Levin E, Karchmer AW. Clinical and molecular epidemiology of sporadic and clustered cases of nosocomial *Clostridium difficile* diarrhea. *Am J Med* 1996; **100:** 32–40.

30 Lidwell OM, Towers AG, Ballard J, Gladstone B. Transfer of micro-organisms between nurses and patients in a clean air environment. *J Appl Bacteriol* 1974; **37:** 649–56.

31 Casewell M, Phillips I. Hands as route of transmission for Klebsiella species. *Br Med J* 1977; **2:** 1315–17.

32 Hall CB, Douglas RG. Modes of transmission of respiratory syncytial virus. *J Pediatr* 1981; **99:** 100–02.

33 Olsen RJ, Lynch P, Coyle MB, Cummings J, Bokete T, Stamm WE. Examination gloves as barriers to hand contamination in clinical practice. *JAMA* 1993; **270:** 350–53.

34 Pittet D, Dharan S, Touveneau S, Sauvan V, Perneger TV. Bacterial contamination of the hands of hospital staff during routine patient care. *Arch Intern Med* 1999; **159:** 821–26.

35 Fox MK, Langner SB, Wells RW. How good are hand washing practices? *Am J Nurs* 1974; **74:** 1676–78.

36 Pessoa-Silva CL, Dharan S, Hugonnet S, et al. Dynamics of bacterial hand contamination during routine neonatal care. *Infect Control Hosp Epidemiol* 2004; **25:** 192–97.

37 Ojajarvi J. Effectiveness of hand washing and disinfection methods in removing transient bacteria after patient nursing. *J Hyg (Lond)* 1980; **85:** 193–203.

38 Lucet JC, Rigaud MP, Mentre F, et al. Hand contamination before and after different hand hygiene techniques: a randomized clinical trial. *J Hosp Infect* 2002; **50:** 276–80.

39 McBryde ES, Bradley LC, Whitby M, McElwain DLS. An investigation of contact transmission of methicillin-resistant *Staphylococcus aureus*. *J Hosp Infect* 2004; **58:** 104–08.

40 Larson E. Effects of handwashing agent, handwashing frequency, and clinical area on hand flora. *Am J Infect Control* 1984; **11:** 76–82.

41 Larson EL, Norton Hughes CA, Pyrak JD, Sparks SM, Cagatay EU, Bartkus JM. Changes in bacterial flora associated with skin damage on hands of health care personnel. *Am J Infect Control* 1998; **26:** 513–21.

42 Bauer TM, Ofner E, Just HM, Just H, Daschner FD. An epidemiological study assessing the relative importance of airborne and direct contact transmission of microorganisms in a medical intensive care unit. *J Hosp Infect* 1990; **15:** 301–09.

43 Tenorio AR, Badri SM, Sahgal NB, et al. Effectiveness of gloves in the prevention of hand carriage of vancomycin-resistant enterococcus species by health care workers after patient care. *Clin Infect Dis* 2001; **32:** 826–29.

44 Daschner FD. How cost-effective is the present use of antiseptics? *J Hosp Infect* 1988; **11** (suppl A)**:** 227–35.

45 Knittle MA, Eitzman DV, Baer H. Role of hand contamination of personnel in the epidemiology of gram-negative nosocomial infections. *J Pediatr* 1975; **86:** 433–37.

46 Ayliffe GAJ, Babb JR, Davies JG, Lilly HA. Hand disinfection: a comparison of various agents in laboratory and ward studies. *J Hosp Infect* 1988; **11:** 226–43.

47 Strausbaugh LJ, Sewell DL, Ward TT, Pfaller MA. High frequency of yeast carriage on hands of hospital personnel. *J Clin Microbiol* 1994; **32:** 2299–300.

48 Waters V, Larson E, Wu F, et al. Molecular epidemiology of gram-negative bacilli from infected neonates and health care workers' hands in neonatal intensive care units. *Clin Infect Dis* 2004; **38:** 1682–87.

49 Maki DG. Control of colonization and transmission of pathogenic bacteria in the hospital. *Ann Intern Med* 1978; **89:** 777–80.

50 Boyce JM, Potter-Bynoe G, Chenevert C, King T. Environmental contamination due to methicillin-resistant *Staphylococcus aureus*: possible infection control implications. *Infect Control Hosp Epidemiol* 1997; **18:** 622–27.

51 Hayden MK, Blom DW, Lyle EA, et al. The risk of hand and glove contamination by healthcare workers after contact with a VRE (+) patient or the patient's environment. 41st Interscience Conference on Antimicrobial Agents and Chemotherapy; Chicago, IL, USA; December 16–19, 2001. Abstract 424.

52 Ray AJ, Hoyen CK, Taub TF, Eckstein EC, Donskey CJ. Nosocomial transmission of vancomycin-resistant enterococci from surfaces. *JAMA* 2002; **287:** 1400–01.

53 Bhalla A, Pultz NJ, Gries DM, et al. Acquisition of nosocomial pathogens on hands after contact with environmental surfaces near hospitalized patients. *Infect Control Hosp Epidemiol* 2004; **25:** 164–67.

54 Scott E, Bloomfield SF. The survival and transfer of microbial contamination via cloths, hands and utensils. *J Appl Bacteriol* 1990; **68:** 271–78.

55 Musa EK, Desai N, Casewell MW. The survival of *Acinetobacter calcoaceticus* inoculated on fingertips and on formica. *J Hosp Infect* 1990; **15:** 219–27.

56 Fryklund B, Tullus K, Burman LG. Survival on skin and surfaces of epidemic and non-epidemic strains of enterobacteria from neonatal special care units. *J Hosp Infect* 1995; **29:** 201–08.

57 Noskin GA, Stosor V, Cooper I, Peterson LR. Recovery of vancomycin-resistant enterococci on fingertips and environmental surfaces. *Infect Control Hosp Epidemiol* 1995; **16:** 577–81.

58 Doring G, Jansen S, Noll H, et al. Distribution and transmission of *Pseudomonas aeruginosa* and *Burkholderia cepacia* in a hospital ward. *Pediatr Pulmonol* 1996; **21:** 90–100.

59 Islam MS, Hossain MZ, Khan SI, et al. Detection of non-culturable *Shigella dysenteriae 1* from artificially contaminated volunteers' fingers using fluorescent antibody and PCR techniques. *J Diarrhoeal Dis Res* 1997; **15:** 65–70.

60 Ansari SA, Sattar SA, Springthorpe VS, Wells GA, Tostowaryk W. Rotavirus survival on human hands and transfer of infectious virus to animate and nonporous inanimate surfaces. *J Clin Microbiol* 1988; **26:** 1513–18.

61 Ansari SA, Springthorpe VS, Sattar SA, Rivard S, Rahman M. Potential role of hands in the spread of respiratory viral infections: studies with human Parainfluenza virus 3 and Rhinovirus 14. *J Clin Microbiol* 1991; **29:** 2115–19.

62 Doebbeling BN, Pfaller MA, Houston AK, Wenzel RP. Removal of nosocomial pathogens from the contaminated glove. Implications for glove reuse and handwashing. *Ann Intern Med* 1988; **109:** 394–98.

63 Larson EL, Eke PI, Wilder MP, Laughon BE. Quantity of soap as a variable in handwashing. *Infect Control* 1987; **8:** 371–75.

64 Kac G, Podglajen I, Gueneret M, Vaupre S, Bissery A, Meyer G. Microbiological evaluation of two hand hygiene procedures achieved by healthcare workers during routine patient care: a randomized study. *J Hosp Infect* 2005; **60:** 32–39.

65 Trick WE, Vernon MO, Hayes RA, et al. Impact of ring wearing on hand contamination and comparison of hand hygiene agents in a hospital. *Clin Infect Dis* 2003; **36:** 1383–90.

66 McNeil S, Foster C, Hedderwick S, Kauffman C. Effect of hand cleansing with antimicrobial soap or alcohol-based gel on microbial colonization of artificial fingernails worn by health care workers. *Clin Infect Dis* 2001; **32:** 367–72.

67 Gupta A, Della-Latta P, Todd B, et al. Outbreak of extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* in a neonatal intensive care unit linked to artificial nails. *Infect Control Hosp Epidemiol* 2004; **25:** 210–15.

68 Sala MR, Cardenosa N, Arias C, et al. An outbreak of food poisoning due to a genogroup I Norovirus. *Epidemiol Infect* 2005; **133:** 187–91.

69 Harrison WA, Griffith CJ, Ayers T, Michaels B. Bacterial transfer and cross-contamination potential associated with paper-towel dispensing. *Am J Infect Control* 2003; **31:** 387–91.

70 Barker J, Vipond IB, Bloomfield SF. Effects of cleaning and disinfection in reducing the spread of Norovirus contamination via environmental surfaces. *J Hosp Infect* 2004; **58:** 42–49.

71 El Shafie SS, Alishaq M, Leni Garcia M. Investigation of an outbreak of multidrug-resistant *Acinetobacter baumannii* in trauma intensive care unit. *J Hosp Infect* 2004; **56:** 101–05.

72 Sartor C, Jacomo V, Duvivier C, et al. Nosocomial *Serratia marcescens* infections associated with extrinsic contamination of a liquid nonmedicated soap. *Infect Control Hosp Epidemiol* 2000; **21:** 196–99.

73 Duckro AN, Blom DW, Lyle EA, Weinstein RA, Hayden MK. Transfer of vancomycin-resistant enterococci via health care worker hands. *Arch Intern Med* 2005; **165:** 302–07.

74 Passaro DJ, Waring L, Armstrong R, et al. Postoperative *Serratia marcescens* wound infections traced to an out-of-hospital source. *J Infect Dis* 1997; **175:** 992–95.

75 Chang HJ, Miller HL, Watkins N, et al. An epidemic of *Malassezia pachydermatis* in an intensive care nursery associated with colonization of health care workers' pet dogs. *N Engl J Med* 1998; **338:** 706–11.

76 Marples RR, Towers AG. A laboratory model for the investigation of contact transfer of micro-organisms. *J Hyg (Lond)* 1979; **82:** 237–48.

77 Mackintosh CA, Hoffman PN. An extended model for transfer of micro-organisms via the hands: differences between organisms and the effect of alcohol disinfection. *J Hyg (Lond)* 1984; **92:** 345–55.

78 Patrick DR, Findon G, Miller TE. Residual moisture determines the level of touch-contact-associated bacterial transfer following hand washing. *Epidemiol Infect* 1997; **119:** 319–25.

79 Sattar SA, Springthorpe S, Mani S, et al. Transfer of bacteria from fabrics to hands and other fabrics: development and application of a quantitative method using *Staphylococcus aureus* as a model. *J Appl Microbiol* 2001; **90:** 962–70.

80 Bonten MJ, Austin DJ, Lipsitch M. Understanding the spread of antibiotic resistant pathogens in hospitals: mathematical models as tools for control. *Clin Infect Dis* 2001; **33:** 1739–46.

81 Sebille V, Chevret S, Valleron AJ. Modeling the spread of resistant nosocomial pathogens in an intensive-care unit. *Infect Control Hosp Epidemiol* 1997; **18:** 84–92.

82 Austin DJ, Bonten MJ, Weinstein RA, Slaughter S, Anderson RM. Vancomycin-resistant enterococci in intensive-care hospital settings: transmission dynamics, persistence, and the impact of infection control programs. *Proc Nat Acad Sci USA* 1999; **96:** 6908–13.

83 Hotchkiss JR, Strike DG, Simonson DA, Broccard AF, Crooke PS. An agent-based and spatially explicit model of pathogen dissemination in the intensive care unit. *Crit Care Med* 2005; **33:** 168–76; discussion 253–54.

84 Grundmann H, Hori S, Winter B, Tami A, Austin DJ. Risk factors for the transmission of methicillin-resistant *Staphylococus aureus* in an adult intensive care unit: fitting a model to the data. *J Infect Dis* 2002; **185:** 481–88.

85 Cooper BS, Medley GF, Scott GM. Preliminary analysis of the transmission dynamics of nosocomial infections: stochastic and management effects. *J Hosp Infect* 1999; **43:** 131–47.

86 Semmelweis I. The etiology, concept and prophylaxis of childbed fever. Pest, Wien und Leipzig: C.A.Hartleben's Verlag-Expedition, 1861. (In German)

87 Larson E. A causal link between handwashing and risk of infection? Examination of the evidence. *Infect Control Hosp Epidemiol* 1988; **9:** 28–36.

88 Larson E. Skin hygiene and infection prevention: more of the same or different approaches? *Clin Infect Dis* 1999; **29:** 1287–94.

89 Mortimer EA, Lipsitz PJ, Wolinsky E, et al. Transmission of staphylococci between newborns. *Am J Dis Child* 1962; **104:** 289–95.

90 Doebbeling BN, Stanley GL, Sheetz CT, et al. Comparative efficacy of alternative hand-washing agents in reducing nosocomial infections in intensive care units. *N Engl J Med* 1992; **327:** 88–93.

91 Webster J, Faoagali JL, Cartwright D. Elimination of methicillin-resistant *Staphylococcus aureus* from a neonatal intensive care unit after hand washing with triclosan. *J Paediatr Child Health* 1994; **30:** 59–64.

92 Zafar AB, Butler RC, Reese DJ, Gaydos LA, Mennonna PA. Use of 0.3% triclosan (Bacti-Stat) to eradicate an outbreak of methicillin-resistant *Staphylococcus aureus* in a neonatal nursery. *Am J Infect Control* 1995; **23:** 200–08.

93 Pittet D, Hugonnet S, Harbarth S, et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. *Lancet* 2000; **356:** 1307–12.

94 Larson EL, Early E, Cloonan P, Sugrue S, Parides M. An organizational climate intervention associated with increased handwashing and decreased nosocomial infections. *Behav Med* 2000; **26:** 14–22.

95 Conly JM, Hill S, Ross J, Lertzman J, Louie TJ. Handwashing practices in an intensive care unit: the effects of an educational program and its relationship to infection rates. *Am J Infect Control* 1989; **17:** 330–39.

96 Simmons B, Bryant J, Neiman K, Spencer L, Arheart K. The role of handwashing in prevention of endemic intensive care unit infections. *Infect Control Hosp Epidemiol* 1990; **11:** 589–94.

97 MacDonald A, Dinah F, MacKenzie D, Wilson A. Performance feedback of hand hygiene, using alcohol gel as the skin decontaminant, reduces the number of inpatients newly affected by MRSA and antibiotic costs. *J Hosp Infect* 2004; **56:** 56–63.

98 Swoboda SM, Earsing K, Strauss K, Lane S, Lipsett PA. Electronic monitoring and voice prompts improve hand hygiene and decrease nosocomial infections in an intermediate care unit. *Crit Care Med* 2004; **32:** 358–63.

99 Hilburn J, Hammond BS, Fendler EJ, Groziak PA. Use of alcohol hand sanitizer as an infection control strategy in an acute care facility. *Am J Infect Control* 2003; **31:** 109–16.

100 Lam BC, Lee J, Lau YL. Hand hygiene practices in a neonatal intensive care unit: a multimodal intervention and impact on nosocomial infection. *Pediatrics* 2004; **114:** e565–71.

101 Won SP, Chou HC, Hsieh WS, et al. Handwashing program for the prevention of nosocomial infections in a neonatal intensive care unit. *Infect Control Hosp Epidemiol* 2004; **25:** 742–46.

102 Zerr DM, Allpress AL, Heath J, Bornemann R, Bennett E. Decreasing hospital-associated rotavirus infection: a multidisciplinary hand hygiene campaign in a children's hospital. *Pediatr Infect Dis J* 2005; **24:** 397–403.

103 Rosenthal VD, Guzman S, Safdar N. Reduction in nosocomial infection with improved hand hygiene in intensive care units of a tertiary care hospital in Argentina. *Am J Infect Control* 2005; **33:** 392–97.

104 Johnson PD, Martin R, Burrell LJ, et al. Efficacy of an alcohol/chlorhexidine hand hygiene program in a hospital with high rates of nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infection. *Med J Aust* 2005; **183:** 509–14.

105 Boszczowski I, Nicoletti C, Puccini DM, et al. Outbreak of extended spectrum beta-lactamase-producing *Klebsiella pneumoniae* infection in a neonatal intensive care unit related to onychomycosis in a health care worker. *Pediatr Infect Dis* 2005; **24:** 648–50.

106 Zawacki A, O'Rourke E, Potter-Bynoe G, Macone A, Harbarth S, Goldmann D. An outbreak of *Pseudomonas aeruginosa* pneumonia and bloodstream infection associated with intermittent otitis externa in a healthcare worker. *Infect Control Hosp Epidemiol* 2004; **25:** 1083–89.

107 Weber S, Herwaldt LA, McNutt LA, et al. An outbreak of *Staphylococcus aureus* in a pediatric cardiothoracic surgery unit. *Infect Control Hosp Epidemiol* 2002; **23:** 77–81.

108 Mermel LA, McKay M, Dempsey J, Parenteau S. Pseudomonas surgical-site infections linked to a healthcare worker with onychomycosis. *Infect Control Hospital Epidemiol* 2003; **24:** 749–52.

109 Boyce JM, Potter-Bynoe G, Opal SM, Dziobek L, Medeiros AA. A common-source outbreak of *Staphylococcus epidermidis* infections among patients undergoing cardiac surgery. *J Infect Dis* 1990; **161:** 493–99.

110 Fridkin S, Pear SM, Williamson TH, Galgiani JN, Jarvis WR. The role of understaffing in central venous catheter-associated bloodstream infections. *Infect Control Hosp Epidemiol* 1996; **17:** 150–58.

111 Vicca AF. Nursing staff workload as a determinant of methicillin-resistant *Staphylococcus aureus* spread in an adult intensive therapy unit. *J Hosp Infect* 1999; **43:** 109–13.

112 Harbarth S, Sudre P, Dharan S, Cadenas M, Pittet D. Outbreak of *Enterobacter cloacae* related to understaffing, overcrowding, and poor hygiene practices. *Infect Control Hosp Epidemiol* 1999; **20:** 598–603.

113 Pessoa-Silva CL, Toscano CM, Moreira BM, et al. Infection due to extended-spectrum beta-lactamase-producing *Salmonella enterica* subsp. *enterica* serotype infantis in a neonatal unit. *J Pediatr* 2002; **141:** 381–87.

114 Pittet D, Mourouga P, Perneger TV. Compliance with handwashing in a teaching hospital. *Ann Intern Med* 1999; **130:** 126–30.

115 Pittet D, Simon A, Hugonnet S, Pessoa-Silva CL, et al. Hand hygiene among physicians: performance, beliefs, and perceptions. *Ann Intern Med* 2004; **141:** 1–8

116 Pittet D, Sax H, Hugonnet S, Harbarth S. Cost implications of successful hand hygiene promotion. *Infect Control Hosp Epidemiol* 2004; **25:** 264–66.

117 Brown SM, Lubimova AV, Khrustalyeva NM, et al. Use of an alcohol-based hand rub and quality improvement interventions to improve hand hygiene in a Russian neonatal intensive care unit. *Infect Control Hosp Epidemiol* 2003; **24:** 172–79.

118 Gopal Rao G, Jeanes A, Osman M, Aylott C, Green J. Marketing hand hygiene in hospitals—a case study. *J Hosp Infect* 2002; **50:** 42–47.

119 Ng PC, Wong HL, Lyon DJ, et al. Combined use of alcohol hand rub and gloves reduces the incidence of late onset infection in very low birthweight infants. *Arch Dis Child Fetal Neonatal Ed* 2004; **89:** F336–40.

120 Early E, Battle K, Cantwell E, et al. Effect of several interventions on the frequency of handwashing among elementary public school children. *Am J Infect Control* 1998; **26:** 263–69.

121 Butz AM. Occurrence of infectious symptoms in children in day care homes. *Am J Infect Control* 1990; **6:** 347–53.

122 Kimel LS. Handwashing education can decrease illness absenteeism. *J Sch Nurs* 1996; **12:** 14–16.

123 Master D, Hess Longe SH, Dickson H. Scheduled hand washing in an elementary school population. *Fam Med* 1997; **29:** 336–39.

124 Roberts L, Smith W, Jorm L, et al. Effect of infection control measures on the frequency of upper respiratory infection in child care: a randomized, controlled trial. *Pediatrics* 2000; **105**(4 Pt 1)**:** 738–42.

125 Roberts L, Jorm L, Patel M, et al. Effect of infection control measures on the frequency of diarrheal episodes in child care: a randomized, controlled trial. *Pediatrics* 2000; **105:** 743–46.

126 Hammond B, Ali Y, Fendler E, Dolan M, Donovan S. Effect of hand sanitizer use on elementary school absenteeism. *Am J Infect Control* 2000; **28:** 340–46.

127 Khan MU. Interruption of shigellosis by handwashing. *Trans R Soc Trop Med Hyg* 1982; **76:** 164–68.

128 Shahid NS, Greenough WB, Samadi AR, Huq MI. Hand washing with soap reduces diarrhoea and spread of bacterial pathogens in a Bangladesh village. *J Diarrhoeal Dis Res* 1996; **14:** 85–89.

129 Stanton BF, Clemens JD. An educational intervention for altering water-sanitation behaviors to reduce childhood diarrhea in urban Bangladesh. II. A randomized trial to assess the impact of the intervention on hygienic behaviors and rates of diarrhea. *Am J Epidemiol* 1987; **125:** 292–301.

130 Luby SP, Agboatwalla M, Painter J, et al. Effect of intensive handwashing promotion on childhood diarrhea in high-risk communities in Pakistan: a randomized controlled trial. *JAMA* 2004; **291:** 2547–554.

131 Luby SP, Agboatwalla M, Feikin DR, et al. Effect of handwashing on child health: a randomised controlled trial. *Lancet* 2005; **366:** 225–33.