# Evidence of hand hygiene to reduce transmission and infections by multi-drug resistant organisms in health-care settings

## INTRODUCTION

Infections by multidrug-resistant organisms (MDROs) are increasing worldwide (1). Prevention of spread and control of MDROs in health-care settings are critical and urgent as the number of antibiotics available to treat these infections is extremely limited and development of new antibiotics is not forthcoming in the foreseeable future. Worldwide, the most common bacteria causing health-care associated infections (HAIs) are:

- **MRSA** **M**ethicillin **r**esistant *Staphyloccous **a**ureus*
- **VRE** **V**ancomycin **r**esistant *Enterococci* spp.
- **ESBL** **E**xtended-**s**pectrum **b**eta (β)-**l**actamase gram-negative organisms
- **CRE** **C**arbapenems **r**esistant **E**nterobacteriaceae
- **MRAB** **M**ulti-**r**esistant *Acinetobacter **b**aumannii*

The emergence of resistance in these microorganisms has mainly been caused by an inappropriate use of antibiotics in general and use of broad spectrum antibiotics in particular. In addition the spread of MDROs in health-care settings is common and occurs mostly via health-care workers' (HCWs) contaminated hands, contaminated items/equipment and environment often leading to outbreaks and serious infections especially in critically ill patients. Therefore, implementation of standard precautions for *all* patients *all* the time is key to preventing spread of all microorganisms and MDROs in particular. Hand hygiene performance according to recommendations (2) is the most important measure among standard precautions.

## SUMMARY RESULTS OF A SYSTEMATIC LITERATURE REVIEW

Through a systematic literature review from January 1980 to December 2013 conducted using Medline, the WHO Clean Care is Safer Care team has evaluated the available evidence about the impact of hand hygiene improvement interventions to reduce transmission and/or infections by MDROs'.

The review primarily focused on studies where hand hygiene was the key intervention implemented in the study period and hand hygiene indicators (hand hygiene compliance and/or alcohol-based hand rub (ABHR) products consumption) were measured along with MDRO infection and/or transmission rates. The review identified 39 papers with these characteristics. Some relevant and higher quality papers were selected and summarized (see Table). Three non-systematic reviews also discussed this topic in the context of the role of hand hygiene to reduce HAIs (3-5). A further 60 papers included major hand hygiene interventions but in the context of a broader infection control programme or implementation of other measures aimed at reducing antimicrobial resistance (AMR).

Most of the published studies were "before and after" intervention studies (17/39); a limited number of randomized controlled trials (2/39) was available. In addition, a number of studies investigated the temporal association between hand hygiene indicators and MDRO infection trends (12/39) and some estimated the impact of hand hygiene interventions by applying mathematical models (4/39). The great majority of these papers offer convincing evidence that improved hand hygiene practices lead to a reduction of HAIs and/or transmission or colonization by MDROs. Four papers failed to demonstrate an impact of hand hygiene interventions or improvement in the MDRO's infection or colonization. However, one of these studies did not show any significant improvement of hand hygiene compliance (6) thus explaining the failure to reduce infections, while another study was a low/quality retrospective study (7). One cluster randomized controlled trials did not show any reduction in MRSA infection and colonization rate in the intervention compared to the control wards (8).

Pittet *et al* published the first landmark study using a multifaceted and multidisciplinary hand hygiene promotion strategy and showed significant and sustained hospital-wide compliance improvement associated with reduction of overall HAI prevalence and MRSA cross-transmission (9). The same approach of a multimodal culture-change campaign was adopted at state level in Victoria (Australia) and then at national level leading to significant sustained reductions of MRSA bacteremia and clinical MRSA isolates (10, 11).

Overall, in most studies, the intervention was based on a multimodal strategy including the introduction of ABHRs or an improvement of their location and provision, hand hygiene observation and performance feedback, HCWs education, use of reminders and various methods of communication (posters, memos,  poster-board communications, internal marketing campaign, etc.). It is important to highlight that most of the studies reported the implementation of such a strategy hospital-wide, and many were multicentre and even rolled out nationally. One cluster randomized study demonstrated significant reduction of MRSA infections in 18 long-term facilities, although the follow-up was short (four months) (12).

Only a handful of  studies evaluated the interesting question concerning the levels of hand hygiene compliance or of the  relative increase to observe MDRO rates reduce. A study by Song and colleagues showed that when hand hygiene compliance increased from poor (<60%) to excellent (90%), each level of improvement was associated with a 24% reduction in the risk of MRSA acquisition. This risk decreased significantly (by 48%) with hand hygiene compliance levels above 80%. Two additional clinical studies supported this data, showing lower incidence rates of MRSA (13), resistant *E. coli* and carbapenem resistant *P. aeruginosa* (14) in wards achieving compliance levels higher than 70% and the greatest degree of compliance increase.

Through time series analysis and other methods, a number of papers including a review with data pooling (3), reported a temporal association or correlation between increasing consumption of ABHR and decreasing MRSA infection or isolation rates. This effect was also reported for ESBL-producing Gram negative bacteria (15) and carbapenem resistant *P. aeruginosa* (16). In particular, two papers from Australia and England described this

association in the context of national hand hygiene campaigns (10, 17) with reductions of MRSA or *S. aureus* bacteremia nationwide.

Interestingly, some of these studies reported cost and cost-benefit data. According to Chen and colleagues (18) every US$1 spent on hand hygiene promotion could result in a US$ 23.7 benefit. Similarly, Pittet et al reported that the total cost of hand hygiene promotion corresponded to less than 1% of the costs associated with nosocomial infections (19). In another study by Carboneau and colleagues (20), the overall prevention of 41 MRSA infections resulted in a gross saving of US$ 354 276 with a net hard dollar saving of US$ 276 500. According to a stochastic mathematical model, a 200-bed hospital incurs US$ 1 779 283 in annual MRSA infection–related expenses attributable to hand hygiene noncompliance; in this setting the model estimated that a 1% increase in hand hygiene compliance would result in annual savings of US$ 39 650 (21).

## GAPS AND RESEARCH PERSPECTIVES
While bringing important information about the actual role of hand hygiene improvement in reducing the spread and infection by MDROs in healthcare, this review also identified some gaps and key areas where more research is needed. For example, the great majority of studies were conducted in high-income countries. Good quality surveillance data on AMR and the feasibility and impact of interventions based on hand hygiene promotion compliance are urgently needed from low- to- middle income countries. In addition, the study settings were hospitals apart from one study conducted in long term health care facilities. Given that AMR is a cross-cutting problem affecting all health-care settings and the community, it is important to acquire evidence from these settings too. Finally, most papers focused on the role of hand hygiene in preventing and controlling MRSA, while other MDROs such as VRE, ESBL-producing Gram negatives, CRE where rarely included as an outcome. We are aware that strategies to combat the spread of these microorganisms are more complex and comprehensive, but hand hygiene remains a cornerstone.
Patient education was included in only one study (22); the role of patients and the civil society in combating AMR is crucial at different levels and hand hygiene is one simple yet key measure that can be practiced and advocated for by them.

## CONCLUSIONS
Studies where hand hygiene was used as the main intervention and a significant  improvement in hand hygiene compliance and/or increased ABHR consumption were achieved, demonstrated substantial decrease of MDROs' infections and/or colonization rates, mainly for MRSA.
To be successful, these interventions need to be multimodal and sustained over time in the context of an improved patient safety climate; in addition, particular attention should be paid to embed hand hygiene in the care flow and within best practices for specific procedures. Finally, combating AMR spread and infections involves the implementation of other specific prevention and control measures too.

**Table:** Key studies assessing the effect of hand hygiene interventions on MDROs' transmission and/or infection

| Year Country | Setting | Effect on hand hygiene compliance and/or consumption of alcohol-based handrubs (ABHR) | Impact on MDROs' | Reference |
|---|---|---|---|---|
| 2000 Switzerland | Hospital-wide | Significant increase in HH compliance from 48% to 66%. Increased consumption of ABHR from 3.5 to 15.4 L/1000 patient-days | Significant reduction in the annual overall prevalence of HAI (42%) and **MRSA**\* cross-transmission rates (87%). Continuous increase in ABHR use, stable HAI rates and cost savings, in a follow-up study | Pittet D et al (9) |
| 2008 Australia | 1: 6 pilot hospitals 2: all public hospitals in Victoria (Australia) | 1) Increase of HH compliance 21% to 48% . Increased consumption of ABHR from 5.3 to 27.6 L/ 1000 bed-days<br><br>2) Increase of HH compliance from 20% to 53%. Mean ABHR supply increased from 6.0 to 20.9 L/1000 bed-days | 1) Significant reduction of **MRSA** bacteremia (from 0.05/1000 to 0.02/1000 pt-discharges per month) and of clinical MRSA isolates<br><br>2) Significant reduction of **MRSA** bacteremia (from 0.03/1000 to 0.01/1000 pt-discharges per month) and of clinical MRSA isolates | Grayson ML et al (11) |
| 2009 USA | Hospital-wide 7 acute care facilities | Significant increase of HH compliance from 49% to 98% with sustained rates greater than 90% | Significant reduction of **MRSA** rates from 0.52 to 0.24 episodes/1000 patient days | Lederer JW et al (23) |
| 2010 USA | 2 acute hospitals | Significant increase of HH compliance from 65% to 82% | 51% decrease in hospital-acquired **MRSA** cases during the 12-month\* | Carboneau C et al (20) |
| 2010 Canada | 3 tertiary care hospitals | Significant difference of HH compliance between the intervention group (48.2 %) and the control group (42.6%) | No reduction in **MRSA** colonization. Intervention group: 48.2%; control group: 42.6%; intervention group: 0.73 cases per 1,000 patient-days, mean in control group, 0.66 cases per 1,000 patient-days (statistically insignificant) | Mertz D et al (8) |
| 2011 Taiwan | Hospital-wide | Significant increase of HH compliance from 43.3% to 95.6%. | 8.9% decrease in HAIs and a decline in the BSI caused by **MRSA** and **extensively drug-resitant** *Acinetobacter baumannii*\*<br><br>Every US$1 spent on HH could result in a US$23.7 benefit | Chen Y-C et al (18) |

| Year Country | Setting | Effect on hand hygiene compliance and/or consumption of alcohol-based handrubs (ABHR) | Impact on MDROs' | Reference |
|---|---|---|---|---|
| 2011 Australia | Nationwide (521 hospitals) | In sites not previously exposed to the campaign, increase of HH compliance went from 43.6% to 67.8% | Significant reduction of overall **MRSA** BSI (from 0,49 to 0,3497 per 10,000 patients-days) but not of hospital-onset MRSA BSI | Grayson ML et al (10) |
| 2012 Hong Kong (China) | 18 LTCFs (4 months) | Significant increase of HH compliance in intervention arms (27% to 61% and 22% to 49%)<br><br>The proportions of ABHR usage among compliant actions increased from 33.9% - 53.2% to 90.3% - 94.6% | Significant decrease of respiratory outbreaks (IRR, 0.12; 95% CI, 0.01–0.93) and **MRSA** infections requiring hospital admission (IRR, 0.61; 95% CI, 0.38–0.97) | Ho M et al (12) |
| 2013 Saudi Arabia | Hospital-wide | Significant increase of HH compliance from 38% in 2006 to 83% in 2011<br><br>Significant increase in ABHR consumption over time from 10.3 to 57.3 L/1,000 patient-days. | Significant reduction of **MRSA** infections (from 0.42 to 0.08), VAP (from 6.1 to 0.8), CLA-BSI (from 8.2 to 4.8), catheter-associated UTI (from 7.1 to 3.5) | Al-Tawfiq AA et al (24) |
| 2013 Spain | Hospital-wide | Significant HH compliance increase from 57% to 85% | Significant reduction of **MRSA** infections/colonization/10 000 pt-days* | Mestre G et al (25) |
| 2013 Serbia, France, Spain, Italy, Greece, Scotland, Israel, Germany & Switzerland | Multicenter (33 surgical wards of 10 hospitals) | HH compliance improved in all centres with overall compliance increase from 49.3% to 63.8% | Immediate non-significant increase in nosocomial **MRSA** isolation rate (aIRR 1.44, 95% CI 0.96 to 2.15) with no change in the trend in rates over time in the HH arm of the study.<br><br>Enhanced HH promotion alone was not associated with changes in **MRSA** infection rates. | Lee AS et al (26) |

ABHR, alcohol-based handrub; BSI, bloodstream infection; CLA-BSI, central line-associated BSI; HAI, healthcare-associated infection; HH, hand hygiene; ICU, intensive care unit; LTCFs, long-term care facilities; MRSA, methicillin resistant *Staphylococcus aureus*; NA, not available; UTI, urinary tract infection; VAP, ventilator-associated pneumonia.
*Statistics not reported

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