**EXPLORING THE POTENTIAL OF ANTIMICROBIAL HAND**

**HYGIENE PRODUCTS IN REDUCING THE INFECTIOUS BURDEN IN LOW-INCOME COUNTRIES: AN INTEGRATIVE REVIEW**

**ABSTRACT**

**Objective:** The purpose of this review was to understand whether adding antimicrobial agents to hand hygiene products could increase the health benefits of handwashing with plain soap (HWWS) in low-income settings.

**Methods:** A review of experimental studies comparing the effects of HWWS to antimicrobial soap and waterless hand sanitizer on health and hand contamination in naturalistic conditions was conducted. In addition, an analysis of the evidence from laboratory studies examined the factors that may affect the impact of antimicrobial soap, taking into account the conditions in low-income settings.

**Results**: The review found no evidence for a superior effect of antimicrobial products compared to HWWS on disease incidence and limited evidence for an effect on hand contamination under naturalistic conditions. An analysis of the effectiveness of antimicrobial soap in laboratory settings suggested that it was only more effective than HWWS when handwashing frequency, duration and product concentrations were above levels that could be expected in low-income settings.

**Conclusions:** The limited available evidence suggests that under naturalistic conditions, antimicrobial products are no more effective than HWWS in removing pathogens from hands. Without significant improvement in efficacy, antimicrobial products are unlikely to produce greater health gains than HWWS in low-come settings.

**Keywords:** Hand hygiene; Antimicrobial soap, Waterless hand sanitizer, Antibacterial soap, Health, Low-income settings

Despite the great advances that have been made in reducing morbidity and mortality from infectious diseases during the 20th century, preventable diseases such as diarrhoea and pneumonia remain the two biggest causes of death in children under 5,1 leading to almost two million deaths each year.2 More than three quarters of these deaths occur in low-income settings across South Asia and sub-Saharan Africa.3

Contaminated hands play an important role in the transmission of pathogens4,5,6 and hand washing with plain soap (HWWS) has been found to be effective in reducing infectious diseases, with systematic reviews suggesting that handwashing promotion can reduce the risk of diarrheal disease by 23-40%7 and of respiratory infection by 16-21%.8,9

 It has been contended that HWWS may be the most cost-effective tool available to reduce the global infectious disease burden.10 Opportunities to further increase the impact of hand hygiene are worth exploring, particularly in low-income settings where the potential impact of handwashing on infectious diseases is higher. With rates of handwashing with soap in domestic settings globally estimated at only 19% after risk of contact with excreta7 there is work to be done in handwashing promotion. A further way of improving the impact of hand hygiene might be to add antimicrobial substances to hand hygiene products. Antimicrobial hand hygiene products in the form of soaps and waterless hand sanitizers are routinely used in health-care settings and the food industry and they are becoming increasingly available to consumers in high-income countries.11,12 However, in low-income settings where interrupting disease transmission is likely to have the biggest impact, the use of antimicrobial hand hygiene products has received limited attention. The present review aims to address this gap.

**The role of hand hygiene in disease transmission**

 HWWS is thought to be effective in interrupting disease transmission because the surfactants in soap and the rubbing of hands together enable water to solubilise and remove pathogenic microorganisms from hands.13 Adding active ingredients to soap to inhibit the growth of, or kill bacterial or viral pathogens on hands could potentially provide added health benefits. A range of antimicrobial agents are commonly used in hand hygiene products, including alcohols, chlorhexidine, gluconate, chlorine derivatives, iodine, parachlorometaxylenol, chlorxylenol, quaternary ammonium compounds, triclosan and triclocarban. Some antimicrobial agents such as chlorhexidine and triclosan can have a residual action; with repeated use they get absorbed into the upper layers of the skin and can prevent microbial recolonization.14 Waterless hand sanitizers (WHS) offer an alternative to antimicrobial soaps. Their efficacy lies predominantly in their ability to inhibit or kill pathogens, rather than in their mechanical removal from hands. As they do not require water, it has been suggested that they may be useful in low-income settings where limited water availability may impede regular HWWS.15,16

From a biological and practical perspective it is thus plausible that antimicrobials could have an important role to play in increasing the health effects of hand hygiene in low- income settings. However, it is still not clear as to whether such products used in ‘real-life’ conditions could reduce transmission in low-income settings more effectively than soap. To understand whether adding antimicrobial agents to hand hygiene products could further increase the health benefits reaped from handwashing with soap in low-income settings, this review examines three key questions about the impact of antimicrobials: 1) Are antimicrobial hand hygiene products more effective than plain soap at improving health in community settings? 2) Are antimicrobial hand hygiene products more effective than plain soap at reducing microbial hand contamination in community settings?; and 3) How effective are antimicrobial had hygiene products compared to plain soap under laboratory conditions and what factors determine their efficacy?, to uncover the factors that may affect the health impact of antimicrobial hand hygiene in real-world settings.

**METHODS**

*Search strategy.* We searched Web of Science, Medline, PubMed and Global Health databases for English-language articles published during the period January 1980- August 2014 and updated in March 2015, using the following keywords (combinations): ‘Antimicrobial’ ‘Medic\*’, ‘Antiviral’, ‘Disinfect\*’, ‘Alcohol\*’, ‘Sanitiz\*’, ‘Sanitis\*’, ‘Hand\*’, ‘Hygien\*’, ‘Soap’, ‘Gel’, ‘Intervention’, ‘Commun\*’, ‘Household’, ‘School\*’, ‘Centre’, ‘Laboratory’, ‘Experiment\*’. This time frame was chosen because consumer level antimicrobial hand hygiene products were introduced in the 1980s and it was therefore unlikely to find studies that had investigated effectiveness of antimicrobial products in community settings before 1980. In addition to the database search, the reference lists from the research articles and reviews found in this search were searched for relevant studies. A summary of the search process is illustrated in Figure 1. It should be noted that we did not conduct a full systematic review. Given the expected paucity of research on this topic, particularly in low-income settings, an integrative review evaluating all the available evidence for the impact of antimicrobial hand hygiene products in community settings while taking into account the conditions in low-income settings was deemed most appropriate to answer the current research question.

*Study selection*. For objectives 1 and 2, the review of the literature was limited to experimental studies that allowed comparison of the effectiveness of antimicrobial hand products with that of plain soap under ‘real-life’ conditions (henceforth referred to as ‘naturalistic conditions’) and focussed on community settings in both high- and low income countries. Articles were excluded if the setting was a health care or food handling facility or if the study subjects were health workers as the aims and frequency of handwashing in these contexts are different from community settings. For objective 3, to discern the conditions that may affect the efficacy of antimicrobials, we also looked for evidence from laboratory studies that had compared the efficacy of antimicrobial hand hygiene products with plain hand products under optimal conditions.

Studies that compared the effect of WHS to HWWS were included if the efficacy was compared to HWWS in a single hand hygiene episode or when they had been conducted in a low-income setting. In studies in high-income settings WHS is mostly used in addition to normal handwashing practices and thus it would be impossible to distinguish the independent effects of the microbial product from HWWS. However, as many low-income settings are water-constrained, WHS has been suggested as a replacement of HWWS and thus was more likely to have been used instead of -rather than in addition to- HWWS.15,16,17

Study outcomes for the health impact of antimicrobials included reported or diagnosed infections, symptoms of infections or infectious symptom related absences. Measures of hand contamination consisted of studies that reported microbial reductions on the hands under use conditions.

*Analysis*. After the articles meeting the inclusion criteria had been selected by two independent researchers, the first author extracted the relevant data from each article. For objective 1 this included information on population and sample size, setting, type of antimicrobial agent, type of soap (liquid vs bar), intervention, time span, measurement of health outcome and the reported risk ratios and confidence intervals. For objective 2, information on population type and sample size, setting, antimicrobial agent, study design and measurement, wash time and procedure, soap type (liquid vs. bar) and concentration, outcome organism, sampling procedure, the outcome measurements and the reported inference statistics were extracted. These data can be found in Tables 1 and 2. For objective 3, which analysed the results of a systematic review and meta-analysis of laboratory studies to identify potential factors that could influence the effectiveness of antimicrobials, information on the number of studies included, the antimicrobial agents surveyed, the population, the overall outcome and the factors that been identified as having an impact on this outcome were reviewed.

Using the available data, we first summarized and reviewed the evidence for the impact of antimicrobials on health outcomes in community settings and then did the same for hand contamination. Next, using the collated evidence from more controlled laboratory studies, we looked more closely at the factors that influence the efficacy of antimicrobial hand products, before sketching out if and under what conditions antimicrobial hand products can improve the impact of HWWS in low-income settings.

Figure 1: *Flow diagram for study selection*



\*Reports of individual laboratory studies were included in the initial search but not included in the final analysis as a meta-analysis and systematic review were used to analyse the factors that determine the efficacy of antimicrobials in laboratory settings.

**RESULTS**

**The effect of antimicrobial hand hygiene on health outcomes in community settings**

*Descriptives.* The search for experimental studies investigating the effect of antimicrobial soap on health outcomes identified four published research articles (Table 1), three of which have been previously reviewed in a meta-analysis by Aiello et al.9 Two of those four articles were based on the same randomised controlled trial (RCT) 18,19 and the results have been reported in two separate articles (one reporting general child health outcomes and one

focussing on diarrhoea specifically[[1]](#footnote-2)). Therefore, to date, only three studies have compared the health impact of antimicrobial soap to that of plain soap in community settings. All three studies were RCTs.

Of those three RCTs, two were in low income settings (both in Karachi, Pakistan)18,20 and one was conducted in a high income setting (USA).21 The trials investigated the effect of antimicrobial soap containing 0.2% triclosan21 or 1.2% triclocarban18,19,20 (SAFEGUARD by P&G). The outcomes recorded infectious illness symptoms such as cough, fever diarrhoea and skin infections as reported by study participants, 18,19,21 and physician-diagnosed impetigo.19,20 None of these studies included the collection of clinical samples for laboratory confirmation of the aetiology of the symptoms. All studies were conducted in households including at least one child under 5. Health outcomes were either measured among all household members20,21 or among the under 5s and under 15s only.18,19 The study duration was 6 months20 or a year.18, 19, 21 All studies were double-blinded. One RCT included a hygiene education component in the intervention.18,19

*Impact on health*. None of the four articles reported a meaningful reduction in illness symptoms among household members associated with the use of antimicrobial soap compared to plain soap.

The three studies that investigated the relative impact of soap (nonantimicrobial and antimicrobial) on gastrointestinal illnesses, respiratory infections or a combination of both18, 19,21 have previously been reviewed by Aiello et al.9 The resulting meta-analysis yielded pooled Rate Ratios (RR) of 0.99 (95% confidence interval (CI) 0.54-1.83) (2 studies), 1.00 (95%CI 0.84-1.19) (2 studies) and 0.96 (95%CI 0.71-1.30) (1 study) for use of antibacterial soap compared to use of nonantibacterial soap on rates of gastrointestinal illness, respiratory illnesses and combined symptoms respectively, i.e. no effect.

When looking at the effect of antimicrobial soap on general skin infections and impetigo, which were not included in the meta-analysis by Aiello et al.,9 none of the four articles reported that antimicrobial soap had a greater effect on skin infections than plain soap. The first study on impetigo by Luby et al.20 found impetigo incidence to be 23% lower among children living in households using antimicrobial soap than the incidence among children from households using plain soap after adjusting for clustering and covariates, but the small study size meant the confidence interval was wide and included 1 (95%CI 0.48-1.24). The 2005 study, which enrolled nearly four times as many households, found no significant difference in the reduction in impetigo incidence achieved by the use of antimicrobial soap (36%, 95%CI53%-18%) and plain soap (34%, 16%).19

*Interpretation*. Of the limited empirical evidence that has compared the effect of antimicrobial hand products with that of plain soap on infectious disease incidence in community settings, none of the studies indicated that antimicrobial soap has any effect over and in addition to regular soap in reducing gastrointestinal, respiratory and skin infections, with RRs all close to null. This review also makes clear that very few studies have investigated the health impact of antimicrobial soap in community settings, especially in low-income settings where all the available evidence is based on data from a single setting and research group.18,20

An explanation for the lack of supporting evidence for a health impact of antimicrobial soaps could be that in all studies that used antimicrobial soap, the antimicrobial agent was either 0,2% triclosan or 1.2% triclocarban. Triclosan (in low concentrations) and triclocarban are bacteriostatic agents that are effective at inhibiting the growth of gram positive bacteria and fungi, but have less activity against some gram negative bacteria and viruses or parasites.14,22 However, most common gastrointestinal and respiratory illness pathogens such as Shigella, Rotavirus, RSVs, Rhinovirus, Influenza, Adenovirus, *E. coli* and Hib23,24 are either viruses or gram-negative bacteria. Therefore, the antimicrobial agents used in these studies may not be effective against the majority of pathogens underlying the most common infectious diseases. Still, the studies also did not find convincing protective effects of antimicrobial soap on impetigo, which is most likely to be caused by gram-positive bacterial pathogens. As none of these studies gathered clinical isolates for laboratory confirmation of the biological agent associated with the illness symptoms*,* it was not possible to assess whether the reported symptoms were caused by bacteria or viruses.

The lack of evidence for a superior health effect of antimicrobial hand hygiene products raises the question whether antimicrobial hand hygiene products are in fact more effective than HWWS in interrupting disease transmission and reduce hand contamination more effectively than plain soap under naturalistic conditions. To answer this question, we will examine whether antimicrobial products are more effective than plain soap at reducing hand contamination under naturalistic conditions.

Table 1: *Studies comparing the impact of antimicrobial soap with that of plain soap on health* *outcomes in community settings*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Sample size and Setting** | **Antimicrobial wash agent** | **Plain soap** | **Intervention** | **Outcome** | **Results (antibacterial vs. plain soap)** |
| Luby et al. (2005)\*19 | 600 Households with at least 1 child <5 years old and 2 children <15 years old in Karachi, Pakistan | Bar (1.2% triclocarban) Wt/V(Safeguard) | Bar | Provision of either plain soap or antimicrobial soap and weekly handwashing promotion for a year vs. no intervention control | Self-reported infectious illness symptoms, including respiratory, gastrointestinal and physician confirmed Impetigo among children | No difference: RR of symptoms all approx. 1 |
| Larson et al. (2004)21 | 240 Households with at least 1 child <5 in NYC, USA.  | Liquid soap (0,2% triclosan) Wt/V | Liquid | Households were provided with either antimicrobial soap and household cleaning products or plain soap and household cleaning products for a year | Self-reported infectious illness symptoms, including respiratory, gastrointestinal and skin infections among household members | No difference: RR of 0.96 (95% CI 0.82-1.12) |
| Luby et al. (2004)\*18 | 600 Households with at least 1 child <5 years old and 2 children <15 years old in Karachi, Pakistan | Bar (1.2% triclocarban) Wt/V(Safeguard) | Bar | Provision of either plain soap or antimicrobial soap and weekly handwashing promotion for a year vs. no intervention control | Self-reported diarrhoea symptomsamong children | No difference: mean incidence was 2.02 (antimicrobial soap) vs. 1.91 (plain soap) |
| Luby et al. (2002)20 | 162 Households with at least 1 child <5 years old and 2 children <15 years old in Karachi, Pakistan | Bar (1.2% triclocarban) Wt/V(Safeguard) | Bar | Provision of either antimicrobial or plain soap for six months | Physician confirmed Impetigo among children | No difference: incidence density ratio of 0.77 (95% CI, 0.48-1.24) |

\*Luby 2004 and 2005 are based on the same trial

**The effect of antimicrobial hand hygiene on hand contamination under naturalistic conditions**

*Descriptives.* Four studies were found that compared the effect of antimicrobial agents and plain soap on hand contamination under naturalistic conditions, two of which were conducted in low-income settings, Tanzania15 and Bangladesh.17 The other two studies took place in the USA25,26 (Table 2). Two of the reported studies used a standard operating procedure (SOP) for hand hygiene and compared the immediate pre- and post-wash effects,15,25 one study used more naturalistic conditions by providing the study participants with either an antimicrobial hand hygiene product or plain soap and measured hand contamination before and after a prolonged period of use,17 and the fourth study used both single pre-post wash and longitudinal (1 year) comparisons.26 Two studies used alcohol-based WHS (62% ethanol),15,25 one study an organic acid-based WHS17 (chosen because an alcohol-based WHS was deemed inappropriate for the predominantly Muslim study population), and one study a 0,2% triclosan liquid soap.26 Outcome measures were faecal streptococci (two studies),15,17 *E. coli* and other thermotolerant coliforms (three studies),15,17,25 *C. perfringens* (1 study),17 or total bacterial counts (2 studies) on hands.25,26

*Impact on hand contamination under naturalistic conditions*. Only one of the studies reviewed reported a superior effect of the antimicrobial agent compared to plain soap on one of the outcome measures: Faecal streptococci; 0.64 vs. 0.25 log reductions per hand, *p* <.01. This study was conducted in Tanzania using a 62% ethanol WHS as antimicrobial product and hand contamination was measured immediately before and after an SOP.15 This was one of the two studies that detected faecal streptococci on hands. The other study using faecal streptococci as the measure of hand contamination did not provide a direct comparison between the WHS and water and soap usage. The data indicate that the availability of a WHS did not reduce contamination with faecal streptococci to any greater extent than a control group. In contrast, faecal streptococci counts were reduced by HWWS compared with a control. This suggests that an organic acid-based WHS may not have better long term effects on removal of faecal streptococci from hands than taking no action at all.17 It should be noted, however, that in this study faecal streptococci were measured at baseline and after 13 weeks of supply of the hand hygiene agent, but not necessarily after use. It is therefore possible that in the total outcomes some respondents had used the antimicrobial product and others had not, thereby obscuring the effect that the antimicrobial product itself could have on the organism. Thus, while the study by Luby et al.17 is a more realistic representation of antimicrobial use under everyday conditions, the study may not inform us on the effectiveness of the tested microbial compound on faecal streptococci contamination of hands per se.

None of the studies using *C. perfringens*, *E. coli* and coliforms as an outcome measure showed any effect of the use of antimicrobial agents, organic acid WHS and 62% ethanol WHS, on counts on hands, either after a single standard operationalized hand hygiene procedure15,25 or in a more naturalistic longitudinal measurement.17 Likewise, none of the studies looking at total bacterial count found a superior effect of the antimicrobial product compared to regular HWWS either after a before-after hand hygiene episode using 62% ethanol25 or 0,2% triclosan,26 or after a year of regular 0,2% triclosan use.26

*Interpretation*. Of the four studies that have directly compared the effect of different antimicrobial and non-antimicrobial hand hygiene products on levels of hand contamination under naturalistic conditions only one study showed a superior effect of WHS (62% ethanol) compared to plain soap on one of the two outcome measures (faecal streptococci).15 The other study that used faecal streptococci as an outcome organism did not find a superior effect of the antimicrobial product compared to plain soap. The review also highlights that only a handful of studies have directly compared the effects of antibacterial hand hygiene with HWWS under naturalistic conditions and that they vary greatly in their methods, thereby limiting any meaningful comparisons. As a result it is difficult to pinpoint the factor responsible for the diverging findings on faecal streptococci.

The antimicrobial agents used in the majority of these studies were either 62% ethanol solutions or 0.2% triclosan. Both these agents are assumed to be effective against both gram- positive and gram-negative bacteria used as the outcome organisms in these studies. Thus, unlike in the studies conducted on health outcomes, the antimicrobial agents used in these studies theoretically should be effective in reducing the indicator organisms. In spite of this, in these studies the use of antimicrobial hand hygiene products did not reduce levels of *E.coli* and thermotolerant coliforms, *c. perfringens*, and total bacterial counts more effectively than soap.

 In all studies Faecal Indicator Bacteria (FIB) were used as marker of microbial contamination rather than actual pathogens. The relationship between FIB counts and infectious disease transmission remains unclear. Two studies also used total bacterial counts as an outcome measure, and, assuming that pathogenic bacteria would be included in these total counts, one would expect a reduction in total bacteria counts if the antimicrobial agent effectively reduced pathogenic bacteria.

The results indicated that even when adopting a SOP for hand hygiene, the antimicrobial hygiene procedures were not more effective in reducing microbial counts on hands compared to plain soap under naturalistic conditions. Out of the three studies using an SOP and/or supervised hand hygiene procedure, only one study found an effect on one (but not all) of the outcomes. Also, the findings from the one-year follow up study using 0,2% triclosan26 did not find any support for the hypothesis that the effectiveness of some antimicrobial agents (including triclosan) lies in the gradual build-up of the antimicrobial compounds on the skin after repeated use.14

The reviewed evidence suggests that even use of the appropriate antimicrobial compounds, does not lead to a superior efficacy of antimicrobials in removing pathogens from the hands under naturalistic conditions. The observed lack of a health effect of antimicrobials therefore seems unlikely to be fully attributable to the use of antimicrobial agents that are ineffective for the targeted pathogens. A potential explanation why the *in vitro* efficacy does not translate to *in vivo* effectiveness may lie in the application process or other conditions that affect the impact of the antimicrobial agent under use conditions. Therefore, we will now turn to more controlled laboratory studies to uncover the factors that may affect the antimicrobial’s capacity to remove pathogens from hands.

Table 2: *Studies comparing the impact of antimicrobial soap with that of plain soap on microbial hand contamination under naturalistic conditions*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Sample size1  and Setting** | **Wash agents** | **Design/Follow-up period** | **Wash time** | **Soap vol. (ml or gr)** | **Outcome organism** | **Sampling method** | **Results (antimicrobial vs. regular soap)** |
| Larson (2003) 26 | 238 Primary care givers in NYC, USA | 0,2% triclosanliquid soap vs. plain liquid soap | -1 episode of hand hygiene-1 year of use | As usual | As usual | Mean log10 bacterial CFU  | Modified glove-juice technique | No difference after 1 episode of hand hygiene, 5.77 (antimicrobial soap) vs. 5.62 (plain soap) log10 CFU (P >.28).No difference after 1 year of use, 4.87 (antimicrobial soap) vs. 4.93 (plain soap) log10CFU (P >.28) |
| Davis (2006)25 | 100 animal handlers at a livestock event in the USA | 62% ethanol WHS vs. plain soap and water. | -1 episode of hand hygiene (SOP) | WHS: 60sHWWS: 10-20s | *WHS:* 1-3 ml*HWWS:* Not specified | Difference in reduction in mean log10  coliform and totalbacterial CFU | Hand rinse | No difference for coliforms (P >.69).No difference for total bacterial counts (P >.12) |
| Luby (2010)17 | 30 housing compounds with at least 4 children of which 1 <5 years in Dhaka, Bangladesh240 samples at each timepoint | WHS using organic acids to reduce the PH of the skin (*First Defence*) vs. plain bar soap | -Baseline- 23 weeks of availability  | Microbial hand samples were taken at key moment at baseline and one-year follow up, regardless of whether respondent had cleansed hands | As usual | Mean log10 counts of thermo-tolerant coliforms,faecal streptococci and *C. Perfringens* | Hand rinse | No direct comparison between antimicrobial soap and plain soap. Compared to the no intervention control group, the antimicrobial product significantly reduced *C. Perfringens* but did not differ from control on *E. coli* and faecal streptococci. |
| Pickering (2010)16 | 204 mothers and students in Dar-es-Salaam, Tanzania. | 62% ethanol WHS vs. plain liquid soap | -1 episode of hand hygiene (SOP) | No specified duration. Following WHO hand hygiene protocol | *WHS:* 2 ml*HWWS:* 1.4 gr non liquid bar soap | Mean difference in mean Log10 CFU of *E. coli* and faecal streptococci | Hand rinse | Statistically significant mean log reductions of faecal streptococci after using WHS 0.64 (WHS) vs. 0.25 (plain soap) mean log10 CFU, P <. 010.No difference for E. coli: 0.66 (WHS) vs 0.50 (plain soap) mean log10 CFU , p > .35 |

1 Antimicrobial vs antimicrobial only, except when no direct comparison

**An analysis of the effect of antimicrobial hand hygiene on hand contamination under laboratory conditions**

While the public health impact of antimicrobial hand hygiene products is best evaluated by their effect on health and hand contamination in real-life settings, studying them under more controlled laboratory conditions could give us more insight into the factors that determine their (lack of) effectiveness. However, as the results of laboratory studies investigating the effect of antimicrobials on hand contamination vary considerably depending on the methods used - such as type of antimicrobial, duration of wash, soap quantity and organism used - the comparison and interpretation of the results is difficult. In this section, we analyse the results of a systematic review27 and a meta-analysis28 of studies that have investigated whether handwashing with antimicrobial and non-antimicrobial soaps results in a difference in microbial reduction on hands in lab settings to identify the factors that might affect this difference.

*Impact on hand contamination under laboratory conditions.* Aiello et al.27 conducted a systematic review of studies examining the effectiveness of soap containing triclosan or triclocarban versus plain soap in reducing bacterial levels on the hands using similar inclusion criteria as the present review. Eight studies were identified that were conducted in a controlled laboratory setting. These mostly used resident skin flora as the outcome organism, whilst two studies inoculated the skin with *S. marcescens*. Five out of eight studies reported a significant reduction in bacterial counts with the use of triclosan containing soap compared with plain soap. Four of these five studies used soaps with triclosan levels of >1%, which is considerably higher than the triclosan levels of between 0.1 to 0.45% wt/vol that are found in most commercially available antimicrobial soaps.13,27 One study assessed the effect of triclosan at a level similar to the concentration levels of most consumer soaps (0.3%) and reported a significant reduction in total bacterial counts. This reduction was observed after five days of use at 18 hand washes for 30 seconds per day, but not after fewer days or lower levels of handwashing frequency.

The meta-analysis by Montville and Schaffner28 expanded on the systematic analysis by Aiello et al.27 by including antimicrobial compounds other than triclosan and specifically set out to identify the factors that may influence the effectiveness of antimicrobial hand hygiene agents. While no information was provided on whether this review excluded studies in health care settings or among health care workers, it did exclude data on surgical type hand wash with a contact time of over 3 minutes or the use of brushes and hand wash machines. A total of 25 publications, containing 375 observations, were included in the meta-analysis. Only 1 out of the 25 articles was also included in the systematic review by Aiello. The article is not clear on what caused this discrepancy. Antimicrobial compounds included chlorhexidine gluconate, parachlorometaxylenol, trichlorocarbanilide, benzalkonium cetylphosphate and triclocarban. Outcome organisms included resident flora, S*. marcescens*, *E. coli*, *Micrococcus*, *S. Aureus*, *Shigella,* *Staphylococcus* and others.

When comparing the effect of antimicrobial soap and plain soap *across* studies and thus without controlling for the study methods, the comparison suggests that soap containing an antimicrobial agent causes a similar reduction in bacteria as plain soap. However, when comparing the difference between the efficacy of antimicrobial soap and plain soap for individual observations or the means *within* all studies (and thus study factors were held constant), a small but significant difference in favour of antimicrobial soap was observed (Mean log CFU = 0.45, *p* <.0001).

When looking at the different study characteristics that may have had an impact on the outcome of the comparisons, the analysis showed that antimicrobial soaps were significantly more effective in reducing both resident and transient flora than plain soap, although the effect was considerably smaller in studies using resident flora (0.31 Log CFU) than those that used either gram-negative or gram-positive transient bacteria that had been inoculated onto the hands (1.93 log CFU). Inoculum size also had a significant effect on the reported efficacy of antimicrobial soaps compared to plain soaps, with the largest reductions observed at the highest inoculum levels. No difference in effectiveness of antimicrobial soap compared to plain soap was observed between gram negative and gram positive bacteria. The duration of the hand hygiene procedure also had a significant impact on the effectiveness of the antimicrobial agents. Hand wash times of 120 seconds had significantly higher reductions of microbial contamination than lower times for antimicrobial versus plain soap. This difference between antimicrobial soap and plain soap was also statistically significant at 30 seconds. No differences in effects compared to plain soap were found for type of antimicrobial compound or form (bar or liquid).

*Interpretation*. The literature suggests that antimicrobials can be more effective in reducing microbial load than soap in controlled laboratory conditions, but that the conditions required for their effectiveness are difficult to translate to everyday situations, particularly in low-income settings.

While higher levels of antimicrobial agent were more effective, these effects were no greater than handwashing with plain soap when using concentration levels commonly found in consumer antimicrobial soaps. Similarly, antimicrobial soaps were more effective than plain soap at handwashing durations of 30 seconds and longer. In reality however it is doubtful whether people wash their hands for at least 30 seconds. Indeed, an analysis of 27 observational studies yielded a mean wash times of approximately 9 seconds, even in settings where handwashing is heavily regulated such as in health care settings or food preparation areas.13 In the same vein, while the high frequencies of handwashing (>18) necessary for antimicrobials to achieve a superior impact over soap seem unlikely in any setting, they seem particularly unrealistic in low-income settings where water is usually collected from a communal point and use is often rationed.

Another factor of importance was whether the outcome organisms were resident or transient flora. In the context of the current review, the efficacy of antimicrobial agents in reducing or preventing the acquisition of transient flora is more relevant than their effect on resident flora, as the transient flora are more likely to contain pathogens. However, the studies included in the systematic review by Aiello et al.27 mainly included residential flora, and the meta-analysis by Montville and Schaffner28 revealed that antimicrobials are likely to have a bigger impact on transient flora. It could therefore be that the studies included in the review by Aiello et al. gave a conservative impression of the effectiveness of triclosan on transient organisms.

Inoculum size may also affect antimicrobial efficacy. The findings from Montville and Schaffner’s meta-analysis28 suggest that studies that use a high inoculum size make it possible to determine the full capacity of the antimicrobial agent to reduce bacterial populations on the hands. The article suggests that inoculum levels of 6> Log CFU might be the best. However, the three field studies suggest that even in highly contaminated settings such as squatter settlements in Pakistan the baseline levels of transient bacteria such as thermotolerant coliforms and *E. coli*, faecal streptococci and *C. perfringens* are between 1.57 and 4.47, and 5.07-5.75 for total bacterial counts.15,17, 26 It could therefore be that the bacterial hand contamination levels under natural conditions are too low to observe an effect of antimicrobial agents. However, for antimicrobial agents (or any hand hygiene agent) to have an effect on disease transmission, it is not the mean or relative reduction compared to soap that is the most important, but rather the residual level of microbial contamination after their use and whether this level of reduction is sufficient to prevent infection.

Finally, the quality of the studies was not reviewed and some of the studies used inadequate comparison conditions. In one of the included studies for example, the efficacy of water and soap was tested by merely dipping the contaminated finger in soapy solution, thereby omitting the mechanism that makes handwashing with soap effective: the removal of pathogens by lathering and scrubbing of the hands. Such omissions may have meant that the meta-analysis28 inflated the actual effectiveness of antimicrobials.

**DISCUSSION**

A review of the studies that compared the effect of antimicrobial hand hygiene products to plain soap found no evidence for a superior effect on the incidence of gastrointestinal, respiratory and skin infections in community settings and limited evidence for an effect on hand contamination under field conditions in one of four studies. Reviewing the factors that affect the impact of antimicrobial agents under controlled laboratory settings suggested that the efficacy of antimicrobial products is influenced by the type of organism measured (resident vs transient), inoculation level, duration of the hand hygiene procedure, frequency of hand hygiene occasions and the concentration of the antimicrobial agent. Antimicrobial soap was only found to be effective when the above factors were above levels that could be expected in real-life conditions. The current review therefore indicates that in community settings, antimicrobial products are no more effective than plain soap in removing pathogens from hands. If this is the case, we can conclude that, without significant improvement in efficacy, antimicrobial products will produce no greater health gains than that which can be achieved by handwashing with plain soap. When also taking into account concerns about the role that antimicrobials may have in the emergence of antibiotic resistant bacteria (e.g.12, 27), the recommendation would therefore be that the use of antimicrobial hand products as a public health tool should be not be encouraged until a proven superior effect over plain soap justifies their use.

This review has highlighted several routes by which antimicrobials could achieve a greater impact in community settings. Firstly, it is of prime importance that the antimicrobial agents used are effective against disease-relevant microorganisms. In our review of the evidence, none of the studies that investigated the health impact of antimicrobial hand hygiene used antimicrobial agents that are effective against the gram-negative bacterial and viral pathogens that underlie the most common infectious diseases. Therefore, for antimicrobial hand hygiene to have an impact on public health in vulnerable settings the antimicrobial agents used should be effective against the pathogens responsible for the most common infectious diseases in these settings such as Shigella, Rotavirus, RSVs, Rhinovirus, Influenza, Adenovirus, *E. coli* and Hib.23,24

A second factor that enhanced the efficacy of antimicrobial agents compared to plain soap under laboratory conditions was the duration of the handwashing episode. However, as noted before, it appears unlikely that under real-life conditions handwashing durations of at least 30 seconds can be achieved. The alternative solution would therefore be for the active agent to work faster; i.e. within the time scale of normal handwashing. Thirdly, in laboratory settings higher concentrations of the antimicrobial agents demonstrated greater efficacy compared to plain soap. However, in view of the risk of antibiotic resistance associated with antimicrobial use as well as the disruptive effect higher levels of antibacterial agents may have on the (protective) resident flora, increasing the concentrations of antimicrobials for consumer use may not be advisable for public health. Therefore, efforts should be made to develop a product that has higher specific activity and could demonstrate enhanced activity compared to plain soap even when used at lower levels such as those found in consumer soaps. A fourth route by which antimicrobials could improve the impact of hand hygiene is by increasing their residual effect and thereby decreasing recontamination, which can occur rapidly in heavily contaminated environments.29 This is especially important considering that current antimicrobial formulations may require daily handwashing frequencies of up to 18 times30 to attain greater efficacy than plain soap. Such high frequencies are unlikely in any setting and particularly in low-income settings where instilling handwashing with soap habits at the minimally required key moments still poses a challenge for public health practioners.31 By reducing recontamination, this limitation of antimicrobial soaps could be omitted. Finally, it is an open question as to whether WHS are a viable alternative to soap and water in low-income settings even if they were proven to be more effective. Soap is broadly available and cheap in low income settings 32 and can be used for other purposes such as bathing and laundry, which makes a multifunctional product such as soap the more attractive option for people with a limited disposable income. Likewise, while hand sanitizers may be effective in reducing bacterial contamination even on soiled hands,16 there may be a low incentive to use them as they do not leave the hands physically clean. The field study by Luby et al.17 where residents of low-income housing compounds in Bangladesh were provided with either WHS or soap suggested that the availability of a WHS did increase the frequency of hand hygiene behaviour, yet it did not do so to the same extent as providing regular soap. This suggests that WHS may not be preferred over the use of soap and water as method of hand hygiene in these settings.

The most important gap in our knowledge concerning hand hygiene products concerns the reductions required in the levels of key pathogens on hands that are needed to provide a measurable benefit to health. Without this it is hard to design hand hygiene products with that can interrupt pathogen transmission more effectively than plain soap.

To our knowledge this is the first review to compare the effectiveness of antibacterial hand products with plain soap under field conditions and that takes into account conditions in the low-income settings that carry the greatest disease burden. Previous reviews and studies investigating the effect of antimicrobial hand hygiene in community settings did not directly compare the effectiveness of antimicrobials with HWWS while the studies that did directly compare the effect of antibacterial products with plain soap were predominantly conducted in laboratory settings or only tested the effect of a single antimicrobial compound. Therefore, despite the empirical attention that antimicrobial hand products have generated, only a few studies fulfilled the criteria and could be included in the present review. Furthermore, because of the low number of studies that we could include, we did not explicitly take into account the quality of the studies as a selection criterion, which constitutes a further limitation. In addition, only very few of the reviewed studies had actually been conducted in low-income settings. As a result, it should be take into account that the present review is based mostly on indirect evidence from studies in high-income settings and laboratory settings.

 In conclusion, the limited available evidence suggests that in community settings antibacterial hand hygiene is no more effective in removing pathogens from hands than plain soap. It is therefore unlikely that without new product formulations that target disease-specific bacteria, act faster, have a higher activity in lower concentrations, and that have a measurable effect on recontamination, antibacterial products could have a more significant health impact in areas at highest risk from diarrhoea and other diseases preventable by handwashing than plain soap.

**ACKNOWLEDGEMENTS**

Discussions with Timothy Tobery (Unilever PLC) sparked the initial idea for this review and we thank him sincerely for his engagement and dialogue during this work. This study was funded by Unilever (PLC).

**REFERENCES**

[Liu L](http://www.ncbi.nlm.nih.gov/pubmed/?term=Liu%25252520L%2525255BAuthor%2525255D&cauthor=true&cauthor_uid=22579125), [Johnson H](http://www.ncbi.nlm.nih.gov/pubmed/?term=Johnson%25252520HL%2525255BAuthor%2525255D&cauthor=true&cauthor_uid=22579125), [Cousens S](http://www.ncbi.nlm.nih.gov/pubmed/?term=cousens%25252520s%2525255bauthor%2525255d&cauthor=true&cauthor_uid=22579125), et al. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *The Lancet*. 2012; 379: 2151- 2161.

Fischer-[Walker CL](http://www.ncbi.nlm.nih.gov/pubmed/?term=Walker%25252520CL%2525255BAuthor%2525255D&cauthor=true&cauthor_uid=23582727), [Rudan I](http://www.ncbi.nlm.nih.gov/pubmed/?term=rudan%25252520i%2525255bauthor%2525255d&cauthor=true&cauthor_uid=23582727), [Liu L](http://www.ncbi.nlm.nih.gov/pubmed/?term=Liu%25252520L%2525255BAuthor%2525255D&cauthor=true&cauthor_uid=23582727), et al. Global burden of childhood pneumonia and diarrhoea. *The Lancet*. 2013; 381: 1405-1416.

Boschi-Pinto C, Velebit L, Shibuyac K. Estimating child mortality due to diarrhoea in developing Countries. *Bulletin of the World Health Organization*. 2008; 86: 710–717.

Aiello A, Larson E. What is the evidence for a causal link between hygiene and infections? *Lancet Infect. Dis*. 2002; 2: 103–110.

Curtis V, Cairncross, S. Effect of washing hands with soap on diarrhoea risk in the community: a systematic review. *Lancet Infect. Dis.* 2003; 3: 275-281.

Larson E, Gomez-Duarte C, Lee V, Della-Latta P, Kain D, Keswick B. Microbial flora of the hands of homemakers. *Am J Infect Control*. 2003; 31: 72–79.

Freeman M, Stocks M, Cumming O, Jeandron A, Higgins J, Wolf J, et al. Hygiene and Health: Systematic review of handwashing practices worldwide and update of health effects. *Tropical Medicine and International Health*. 2014; 18: 906-916.

Rabie T, Curtis V. Handwashing and risk of respiratory infections: a quantitative

systematic review. *Tropical Medicine and International Health*. 2006; 11: 258–267.

Aiello A, Coulborn R, Perez, V, Larson E. Effect of Hand Hygiene on Infectious Disease Risk in the Community Setting: A Meta-Analysis. *Am J Public Health*. 2008; 98: 1372–1381.

 Jamieson, D, Breman, J, Measham, A, Alleyne, G, & Claeson, M, Evans, et al. Disease Control Priorities in Developing Countries. Oxford: The World Bank and Oxford University Press; 2006.

1. Perencevich E, Wong M, Harris A. National and regional assessment of the antibacterial soap market: a step toward determining the impact of prevalent antibacterial soaps. *Am J Infect Control*. 2001; 29: 281-283.

Halden R. On the Need and Speed of Regulating Triclosan and Triclocarban in the United States. *Environmental Science & Technology*. 2014; 48: 3603-3611.

Todd E, Michaels B, Smith D, Greig J, Bartleson C. Outbreaks where food workers have been implicated in the spread of foodborne disease. Part 9. Washing and drying of hands to reduce microbial contamination. *Journal of Food Protection*. 2010; 73: 1937-1955.

World Health Organization, WHO Patient Safety *WHO guidelines on hand hygiene in health care*.World Health Organization, Geneva (2009).

Pickering A, Boehm A, Mwanjali M, Davis, J. Efficacy of Waterless Hand Hygiene compared with Handwashing with Soap: A field Study in Dar es Salaam, Tanzania. *Am J Tropical Medicine*. 2010; 82: 270-278.

Pickering A, Davis J, Boehm A. Efficacy of alcohol-based hand sanitizer on hands soiled with dirt and cooking oil. *Journal of Water and Health*. 2011; 9: 429-433.

1. Luby S, Kadir M., Sharker M, Yeasmin F, Unicomb L, Islam M. A community-randomised controlled trial promoting waterless hand sanitizer and handwashing with soap, Dhaka, Bangladesh. *Tropical Medicine and International Health.* 2010; 15: 1508-1516.
2. Luby S, Abgoatwalla M, Painter J, Altaf A, Billhimer W, Hoekstra R.The effect of intensive handwashing promotion on childhood diarrhoea in high-risk communities in Pakistan. A randomized controlled trial. *Journal of the American Medical Association.* 2004;291: 2547- 2554.
3. Luby S, Agboatwalla M, Feikin , Painter J, Billhimer W, Altaf A, Hoekstra R,

The effect of handwashing on child health: a randomised controlled trial. *The Lancet.* 2005; 366: 225-233.

1. Luby S, Agboatwalla M, Schnell B, Hoekstra R, Rahbar M, Keswick B. The effect of antibacterial soap on impetigo incidence, Karachi, Pakistan. *American* *Journal of Tropical Medicine and Hygiene.* 2002; 76: 430- 435.
2. Larson E, Lin S, Gomez-Pichardo C, Della-Latta O. Effect of antibacterial home

cleaning and handwashing products on infectious disease outcomes: a randomized double blind trial. *Annals of Internal Medicine.* 2004*; 140*: 321-329.

1. Kampf G, Kramer A. Epidemiologic Background of Hand Hygiene and Evaluation of the Most Important Agents for Scrubs and Rubs. *Clin Microbiol Rev*. 2004; 17: 863-893.

Kotloff K, Nataro J, Blackwelder W, Nasrin D, Faras T, Panchalingam S,et al. (2013). Burden and aetiology of infants and young children in developing countries (the global enteric multicenter study, GEMS): a prospective, case control study. *The Lancet.* 2013; 382: 209-222.

1. Simoes E, Cherian T, Chow J, Shahid-Salles S, Laxminarayan R, John T. Acute Respiratory Infections in Children. In: Jamieson D, Breman J, Measham A, et al., ed. *Disease Control Priorities in Developing Countries. 2nd edition*. Washington (DC): World Bank; 2006.
2. Davis M, Sheng H, Newman J, Hancock D, Hovde, C. Comparison of a waterless hand-hygiene preparation and soap-and-water handwashing to reduce coliforms on hands in animal exhibit settings. *Epidemiology. Infect.* 2006; *143*: 1024-1028.
3. Larson E, Aiello A, Lee L, Delta-Latta O, Gomez-Duarte C, Lin S. Short-and long term effects of handwashing with antimicrobial or plain soap in the community. *Journal of Community Health.* 2003; *28*: 139-150.
4. Aiello E, Larson E, Levy S. Consumer antibacterial soaps: Effective or just risky? *Clinical Infectious Diseases.* 2007; *45:* 137-147.
5. Montville R, Schaffner D. A meta-analysis of the published literature on the effectiveness of antimicrobial soaps. *Journal of Food Protection.* 2011; *74*, 1875.

Devamani C, Norman G, Schmidt W-P. A simple microbiological tool to evaluate the effect of environmental health interventions on hand contamination. *Int J Environ Res Public Health*. 2014; 11: 11846-11859.

Larson E, Mayur K, Laughon B. Influence of two handwashing frequencies on reduction in colonizing flora with three handwashing products used by health care personnel. Am J Infect Control. 1989; 17: 83–8.

1. Biran A, Schmidt W-P, Varadharajan KS, et al. Effect of a behaviour-change intervention on handwashing with soap in India (SuperAmma): a cluster-randomised trial. *The Lancet Global Health.* 2014; 2: 145-154.
2. Curtis V, Schmidt W, Luby S, Florez R, Touré O, Biran A. Hygiene: new hopes, new horizons. *The Lancet Infectious Diseases.* 2011; 11: 312-321.
1. The results for diarrhoea are reported in both articles, yet will be treated as a single observation. [↑](#footnote-ref-2)