



Comparative efficacy of hospital hand hygiene promotion interventions: a systematic review and network meta-analysis.

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3 **Comparative efficacy of hospital hand hygiene promotion interventions: a**
4 **systematic review and network meta-analysis.**
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Abstract

Objective: Many interventions have been proposed to improve hand hygiene compliance amongst healthcare workers, and in 2005 the World Health Organization launched a campaign promoting a 5-component strategy (WHO-5). We aimed to evaluate the relative efficacy of WHO-5 and other hand hygiene promotion interventions and to summarize associated resource-use information.

Design: A search strategy was developed and electronic databases searched for studies published between 1980 and February 2014. Random effects and network meta-analyses were performed on studies considered sufficiently homogeneous with regard to interventions, participants and outcome measures. Information on resources required for interventions was extracted, and graded into three levels.

Inclusion criteria: Studies implementing an intervention to improve hand-hygiene compliance amongst healthcare workers in hospital settings and measuring hand-hygiene compliance or appropriate proxies that met the Cochrane Effective Practice and Organisation of Care Group (EPoC) quality inclusion criteria were included. Where studies had not used appropriate analytical methods, we re-analysed primary data.

Results: Of 3,633 studies retrieved, 36 met the inclusion criteria (6 randomized controlled trials (RCTs), 26 interrupted time-series (ITSs), 2 controlled trials, and 2 controlled before-and-after studies). Meta-analysis of two RCTs showed the addition of goal-setting to WHO-5 was associated with improved compliance (pooled odds ratio [OR] = 1.39, 95% confidence interval 1.15 to 1.67; $I^2= 80.0\%$). Of the 13 ITS pairwise comparisons, 12 showed stepwise increases in hand-hygiene compliance and all but three showed a post-intervention trend for increasing hand-hygiene compliance. Network meta-analysis indicated considerable uncertainty in the relative efficacy of interventions, but nonetheless provided evidence that WHO-5 is effective, and that compliance can be further improved by adding interventions including goal-setting, reward incentives and accountability. The reported cost of interventions ranged from \$US 225 to 4,669 per 1,000 bed-days.

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5 **Conclusion:** Hand-hygiene promotion using WHO-5 is effective at increasing hand
6 hygiene compliance in healthcare workers. There is evidence that adding goal-setting,
7 reward incentives and accountability strategies can lead to further improvements.
8 Reporting of resources required for such interventions remains inadequate.
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13 **Keywords:** Hand hygiene, Cross infection, Review, Comparative effectiveness
14 Research, Meta-Analysis, Network meta-analysis
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Introduction

More than 1.4 million patients around the world suffer from healthcare associated infections (HAIs) at any point in time.^[1] HAI causes excess morbidity and is associated with increased mortality.^[2-3] Direct patient contact with healthcare workers (HCWs) who are transiently contaminated with nosocomial pathogens is believed to be the primary route of transmission for several organisms and can lead to patients becoming colonised or infected. Although hand hygiene is widely thought to be the most important activity for the prevention of nosocomial infections, a review of hand hygiene studies by the World Health Organization (WHO) found that baseline hand hygiene compliance among HCWs was on average only 38.7% (range: 5% to 89%).^[4]

In 2005, the WHO World Alliance for Patient Safety launched a campaign, the First Global Patient Safety Challenge, “Clean Care is Safer Care” aiming to improve hand hygiene in healthcare.^[4] This campaign promotes a multimodal strategy (WHO-5) consisting of five components: system change; training and education; observation and feedback; reminders in the hospital; and a hospital safety climate. More recently, additional strategies for improving hand hygiene have been evaluated, including those based on behavioural theory.

Evaluating the evidence for the efficacy of different interventions is complicated by three factors: first, most evaluations of hand hygiene promotion interventions use non-randomized study designs, and in many cases the reported analysis is inappropriate or methodological quality is too low to allow meaningful conclusions to be drawn;^[5-7] second, there is wide variation between studies in the hand-hygiene promotion activities used in the comparison group; third, direct head-to-head comparisons of most interventions are lacking.^[8]

In this review and meta-analysis we aimed to overcome these problems by: i) restricting attention to randomized trials and high quality non-randomized studies, re-analysing data where necessary; ii) explicitly accounting for hand hygiene promotion activities in the comparison group in each study; iii) using a network meta-analysis to allow indirect comparison between interventions.

Information on resources used in different interventions is essential for those wishing to implement such interventions or evaluate their cost-

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3 effectiveness.^[9 10] A secondary aim was therefore to document information on
4 resources used in hand-hygiene promotion interventions.
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8 **Methods**

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10 A protocol was developed and systematic methods were used to identify
11 relevant studies, screen study eligibility, and assess study quality. This review is
12 reported according to the Preferred Reporting Items for Systematic Reviews and
13 Meta-Analyses (PRISMA) guidelines.^[11]
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17 **Search strategy**

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19 A two-stage search strategy was used. First, all studies included in two
20 previous reviews (covering the period up to November 2009) were obtained.^[5 6]
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22 Second, we extended the search from these studies from December 2009 to
23 February 2014. The following electronic databases was searched: MEDLINE,
24 EMBASE, Cumulative Index to Nursing and Allied Health (CINAHL), Database of
25 Abstracts of Reviews of Effects (DARE), National Health Service Economic
26 Evaluation Database (NHS-EED), National Health Service Centre for Reviews and
27 Dissemination (NHS-CRD) and British Nursing Index (BNI), Cochrane Library
28 (Cochrane database of systematic reviews, Cochrane central register of
29 controlled trials, Cochrane methodology register, Database of abstracts of
30 reviews of effects, Health Technology assessment database), Clinical Trial.gov,
31 Current Clinical Control trial, EPOC register, ACP journal, and Evidence-based
32 medicine reviews. Results were limited to peer-reviewed publications. The
33 complete search strategy is provided in Appendix 1 (supplement).
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45 **Inclusion and Exclusion**

46 A study was considered to meet initial inclusion criteria if

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48 i) it evaluated one or more interventions intended to improve
49 hand hygiene compliance among HCWs in a hospital setting
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54 ii) it measured hand hygiene compliance either using opportunities
55 with pre-specified indications or using proxies linked to
56 compliance (eg soap and alcohol hand rub consumption).
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4 iii) it was either a randomized controlled trial (RCT), controlled
5 clinical trial (CCT), controlled before and after study (CBA), or
6 used an interrupted time series (ITS) design.
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11 No restrictions were placed on hand hygiene promotion in the
12 comparison group. Studies were excluded if they were retrospective, not
13 reported in peer-reviewed publications or not written in English.
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17 We then applied a methodological filter by excluding studies that failed
18 meet minimal quality criteria specified by the Cochrane Effectiveness
19 Practice and Organisation of Care Group (EPOC).^[12]
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24 25 **Data extraction and Quality assessment**

26 Two reviewers (NL and BSC) independently screened the titles and
27 abstracts of the citations obtained from the search to assess the eligibility.
28 Consensus was reached by discussion if initial assessments differed. Evaluation
29 of the full-text and data abstraction was conducted by NL and checked by BSC.
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32 The reviewers abstracted data on study design, population, interventions,
33 comparisons, outcomes, and settings. Interventions implemented in each study
34 were extracted and classified according to WHO guidelines on hand hygiene in
35 healthcare.^[4] Results and raw compliance data from each study were extracted
36 for further re-analyses. In addition, cost of hand hygiene interventions or
37 resource use data (materials and time spent on interventions) were extracted
38 where appropriate. Additional information was obtained from the authors if it
39 was not clear from the manuscript. For all included studies we recorded the level
40 of information (high, moderate, or low) about resources used for hand hygiene
41 promotion using pre-specified definitions (Appendix 2 in supplement).
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52 **Assessment of risk of bias in included studies**

53 Risk of bias was assessed using the Cochrane Collaboration's tool,^[13] Nine
54 standard criteria for RCTs, CCTs, and CBAs, and seven standard criteria for ITS
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3 studies were applied and used to classify each study's risk of bias as low, high or
4 not clear.
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8 **Data synthesis and Statistical analysis**

9 **Measurement of intervention effect**

10 Data synthesis was performed separately for different study designs. The
11 primary evidence synthesis was based on studies measuring hand hygiene
12 compliance (HHC%) by direct observation. We restricted our analysis to this
13 outcome because it reflects the opportunities for hand hygiene.
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18 For RCTs, the natural logarithm of the odds ratio and associated variance
19 were calculated and used to estimate the pooled odds ratio with a random effects
20 model,^[14] using Cochrane Review Manager (RevMan) version 5.1. The same
21 method was applied to CCTs and CBAs if applicable.
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25 For ITS studies, a two-step approach was used.^[15] First, we used a
26 generalized linear segmented regression analysis to estimate the stepwise
27 change in level and change in trend associated with the intervention. This
28 approach is similar to that proposed by Ramsey et al. and Vidanapathirana et al.
29 except that it accounts for the binomial nature of the data, appropriately
30 weighting each data point by the number of observations.^[16 17] If there was
31 evidence of autocorrelation, we accounted for this by using Newey-West
32 standard errors.^[18] Analysis was performed with STATA 13 (Statacorp LP,
33 College Station, TX, USA). In addition, we estimated two summary measures that
34 combined both effects. First, we calculated the mean natural logarithm of the
35 odds ratio for hand hygiene associated with the intervention, a measure of
36 relative improvement. Second, we calculated the mean percentage change in
37 hand hygiene compliance in the post-intervention period (compared to that
38 expected if there had been no intervention), an absolute measure of
39 improvement in hand hygiene compliance. Standard errors were derived using
40 the delta method using the *emdbook* package in R (Bolker, 2008).^[19 20] See
41 Appendix 3 in supplement for details.
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55 **Network meta-analysis**

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3 Network meta-analysis aims to combine all of the evidence, both direct
4 and indirect, in order to estimate the comparative efficacy of all the
5 interventions.^[21] Each intervention strategy is represented by a node in the
6 network. If a study directly compares two interventions they are directly
7 connected by a link on the network and a direct comparison is possible. If two
8 interventions are connected indirectly (for example, if there are studies
9 comparing each with a third intervention), then indirect comparison is possible.
10 Studies permitting a segmented regression analysis and with a clearly-defined
11 baseline intervention and directly observed hand hygiene compliance were
12 included in the network meta-analysis.^[22 23] Intervention activities were grouped
13 into eight components: 1) system change, 2) education, 3) feedback, 4)
14 reminders, 5) safety climate, 6) incentives, 7) goal-setting, and 8) accountability
15 (Table 1). This gave 12 hand hygiene strategies (T1-T12) (Table 2).
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25 The effect sizes obtained from each comparison were combined to
26 perform a network meta-analysis using a random effects model.^[15] Effect sizes
27 were taken as the mean of the natural logarithm of the odds ratio for the hand
28 hygiene intervention as estimated using the segmented regression model.
29 Intervention rankings and associated credible intervals were obtained. Model-
30 fitting was carried out within a Bayesian framework using WinBUGS.^[24]
31 Inconsistency checks were performed for closed loops in the network.^[25] Full
32 model details are provided in Appendix 4 (supplement).
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39 We performed a sensitivity analysis by excluding studies that
40 implemented multicomponent strategies in a stepwise manner without sufficient
41 data to evaluate individual components. This led to the exclusion of four
42 studies.^[26-29]
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47 Results

48 Overall description

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50 A summary of the review process is shown in Figure 1. Of 3,633 studies
51 screened, 136 studies met initial inclusion criteria and 36 of these met EPOC
52 criteria. Amongst these 36 studies, six were RCTs (including four cluster RCTs),
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3 [30-35] 26 were ITSs,^[26-29 36-57] two were CCTs^[58 59] and two were CBAs.^[60 61]
4 Reasons for exclusions are provided in Appendix 5 (supplement).

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6 15 studies applied interventions to the whole hospital while 17 studies
7 enrolled hospital wards. Four studies recruited the HCWs as the participant
8 units.^[30 32 35 61] 25 studies were conducted in either a hospital-wide setting or
9 combined ICU and general wards, while 11 were conducted in ICU or general
10 wards alone. Of eight studies conducted in more than one hospital, three studies
11 included two or more countries.^[40 46 48] Only six of the 36 studies were conducted
12 in low or middle income countries.^[32 35 44 47 49 62]

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18 Study periods ranged between 4 months and 6 years. In nine studies the
19 period was ≤ 1 year; in 16 studies it was >1 year and ≤ 3 years; and in 11 it was >3
20 years. Amongst the 26 ITS studies, only eight were longer than 12 months.

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24 In 30 studies hand hygiene was observed in all HCW types with patient
25 contact while four studies considered only hand hygiene in nurses and/or
26 nursing assistants.^[33 35 58 61] One study recruited only nursing students as
27 participants.^[52] Patients' relatives were also included in one study.^[38]

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30 In six studies a single-faceted intervention was employed: four
31 implemented education alone^[32 44 52 61] and two applied system change or
32 reminders.^[38 42] 14 studies employed interventions equivalent to WHO-5 and six
33 of these added supplemental interventions including goal-setting, incentives, and
34 accountability.^[26 33 39 43 54 59] 16 studies implemented two to four-modal
35 interventions; four of these applied components not in WHO-5 including goal-
36 setting and incentives.^[27 31 35 58]

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42 25 studies (4 RCTs, 19 ITS, and 2 CCTs) measured hand hygiene
43 compliance with direct observation. Two of these used a combination of video
44 recorders and external observers.^[36 37] Proxy measures were assessed in 16
45 studies including the rate of hand hygiene events, consumption of hand hygiene
46 products (alcohol hand rub or soap), and a hand hygiene score checklist (2 RCTs,
47 12 ITSs, and 2 CBAs). Finally, HAI or device-associated HAI rate were measured
48 as one of the outcomes in 10 studies.^[26 28 34 45 47 49 53-55 57] Study characteristics
49 including study design, setting, intervention and comparison groups are
50 reported in Table 3.
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Quality assessment

10 studies were considered to have a high risk of bias. 26 studies had either low or unclear risk. High risk of bias was present in all of four CCTs or CBAs, but only in six out of 26 ITS designs. No RCTs or CRCTs were thought to have a high risk of bias (Figure 2).

The two CBAs^[60 61] had high risks for inadequate allocation sequence and concealment, while both CCTs^[58 59] had high risks of dissimilarity in baseline outcome between experimental and control groups.

14 studies (39%) had a low risk of bias due to the knowledge of allocated intervention, as these studies either measured objective outcomes (eg. alcohol consumption or output from electronic counting devices) or stated that the observers were blinded to the intervention. The rest of the studies had unclear risk as they did not report whether the observers were blinded.

Risk of selective outcome reporting was unclear in 33 studies as pre-specified protocols were reported only in three RCTs.^[31 33 34] Two of the ITS studies had a high risk of selective outcome reporting as they reported on a non-periodical basis.^[26 57] Amongst the ITS studies, five had a high risk that outcomes were affected by other interventions such as a universal chlorhexidine body-washing program,^[40] reinforcement of standard precautions,^[40] screening and decolonization for multidrug-resistant micro-organisms,^[46] quality improvement program,^[44 57] and antibiotic use and HAI control policy implemented at the same time.^[55]

Level of information on resource use

Reporting of cost and resource use information was limited with 3, 25 and 8 studies classified as having high, moderate and low information respectively (Appendix 6 in supplement). Three studies reported costs associated with both materials and person time;^[33 50 59] in two cases these reports were in separate papers.^[63 64] The estimated cost of interventions ranged from \$US 225 to 4,669 per 1,000 bed-day (Table 4).

Meta analysis/Data synthesis

RCTs

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3 Four of six RCTs measured hand hygiene compliance by direct
4 observation with indications similar to WHO-5.^[31-34] In two of these studies,
5 WHO-5 was compared with WHO-5 with goal-setting.^[31 33] Meta-analysis showed
6 this additional intervention to be associated with improved hand hygiene
7 compliance. The pooled odds ratio (OR) was 1.35 (95% confidence interval 1.04
8 to 1.75; $I^2= 81\%$) (Figure 3). The other two studies also showed significant
9 improvement in hand hygiene compliance after implementing a bundle of
10 education, performance feedback, and visual reminders,^[34] and an education
11 program.^[32]

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13 Fisher et al. randomized individuals to either a control group where hand
14 hygiene was not actively promoted, or an intervention arm which used audio
15 reminders and individual feedback. Compliance was assessed using an
16 automated system at entry to and exit from patients' rooms. The intervention
17 was associated with a 6.8% (95% confidence interval 2.5 to 11.1) improvement
18 in compliance.^[30] Salmanti et al. randomized nursing personnel to either a
19 *Motivational Interviewing* intervention (a behaviour-modification approach
20 initially developed to treat patients with alcoholism) or a control group. Both
21 arms also received an educational intervention. The outcome measure was a
22 composite hand hygiene score, which was found to increase significantly in the
23 intervention arm. The scoring details, however, are unclear.^[35]

34 Interrupted Time Series Studies (ITsS)

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36 Of 26 ITS studies, 19 measured hand hygiene compliance. However, only
37 15 studies with direct observation reported the number of observations at each
38 time point making them eligible for re-analysis.^[26-29 36 37 39-41 43 44 46 48 52 54] As
39 some of these studies were conducted at multiple sites^[46] or had multiple
40 intervention phases,^[54] 19 pair-wise comparisons from these 15 studies were
41 available for re-analysis (Figure 4). In four studies there was evidence of positive
42 first order autocorrelation.^[36 37 39 54]

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44 The baseline compliance ranged between 7.6% and 91.3%. 11 of 19
45 comparisons showed a declining trend in compliance during the pre-
46 intervention period while 13 pair-wise contrasts showed a positive post-
47 intervention change in trend for hand-hygiene compliance (Table 5). All but
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3 three contrasts showed both stepwise increases in hand hygiene compliance
4 associated with the intervention and in increase in mean hand hygiene
5 compliance in the post-intervention period compared to that expected in the
6 absence of the intervention. However, the range was wide: the mean hand
7 hygiene change attributed to the intervention varied between a decrease of
8 14.8% and an increase of 83.3% (Table 5). Two studies had an intervention
9 period lasting at least two years; neither showed evidence for any decline in
10 compliance over this period.^[27 39] In only one study was there a net trend for
11 decreasing hand hygiene compliance over the post-intervention period (Figure
12 4).^[43]

21 CCTs and CBAs

22 Both CCT studies reported positive effects of hand hygiene interventions.
23 Mayer et al.,^[59] using an appropriate analysis, found that a bundle of
24 interventions, WHO-5 and reward incentive compared with a combination of
25 system change, education and feedback and a standard practice as control group
26 were associated with improved compliance (odds ratio 1.78, 95% confidence
27 interval 1.34 to 2.37).

28 Harne-Britner et al. reported that a combination of education, group
29 incentives and goal-setting were associated with an increase in mean compliance
30 of 21.7% while education and poster reminders were not associated with any
31 improvement (change in mean: -1.8%).^[58] Confidence intervals were not
32 reported.

33 Benning et al., using a CBA design, reported an increased hospital-wide
34 trend of soap and alcohol consumption in both intervention (package of system
35 change, reminders, and safety climate) and control (no intervention) groups but
36 found no evidence of an increased effect in the intervention group.^[60] Gould et al.
37 found no evidence of improvement in hand decontamination frequency in
38 surgical ICU wards resulting from a series of educational lectures compared to
39 no intervention (control).^[61]

56 Network meta-analysis

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3 Amongst 15 ITS studies, 11 had clear details about interventions and
4 similar indications for hand hygiene compliance amongst qualified HCWs. These
5 were eligible for network meta-analysis (see Appendix 7 for exclusion reasons in
6 supplement). 15 direct pairwise comparisons between interventions were
7 possible from 12 different hand hygiene intervention strategies (Figure 5). 10
8 strategies are connected in the network (Figure 6), making indirect comparisons
9 possible. The comparative efficacy amongst nine of these strategies in a
10 connected network was assessed compared with T1 (no intervention or
11 standard practice).
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14 The network meta-analysis showed that although there was large
15 uncertainty in effect size amongst the pairwise comparisons, all intervention
16 strategies were associated with an improvement in hand hygiene compliance
17 compared with T1 (Figure 7). For four strategies, T7 (WHO-5), T8 (system
18 change+education+feedback+reminders+incentive+goal-setting), T11 (WHO-
19 5+incentive+goal-setting), and T12 (WHO-5+incentive+goal-
20 setting+accountability), 95% credible intervals for odds ratios did not include
21 one (Table 2).
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24 Strategies T8, T9, T10, T11, and T12, which combined WHO-5 with
25 (respectively) incentives, goal-setting, and accountability, showed additional
26 improvement compared with T7 (WHO-5) alone. T8 (system
27 change+education+feedback+reminders+incentive+goal-setting) had the highest
28 probability (90%) and highest median rank of being the best strategy in
29 improving hand hygiene compliance (Figure 7).
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32 When excluding studies with multiple stepwise interventions in the
33 sensitivity analysis there was a decrease in the effect size of T2 (system change),
34 T6 (system change+education+feedback+reminders) and T7 (WHO-5). Other
35 interventions were not affected. As T8 (system
36 change+education+feedback+reminders+incentive+goal-setting) and T10 (WHO-
37 5+goal-setting) strategies were unavailable in the network structure, T12 (WHO-
38 5+incentive+goal-setting+accountability) became dominant with the highest
39 probability (57%) of being the best intervention, and the highest median rank of
40 being the most effective strategy (see Appendix 4 in supplement).
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Discussion

We found that a multi-faceted hand hygiene intervention, WHO-5, and single interventions including system change, training and education, or reminders alone are associated with improved hand hygiene compliance compared with standard practice. Results from both RCT and ITS designs provided consistent evidence that adding supplemental interventions including goal-setting, reward incentives, and accountability to the WHO-5 strategy led to additional improvements in compliance. Information about resources used in the interventions was not well-reported.

We are aware of four previous systematic reviews of hand-hygiene interventions in healthcare settings.^[5-8] One of these found only four studies of sufficient methodological quality to reliably evaluate hand hygiene promotion interventions and was unable to reach firm conclusions.^[5] Overlap between included studies in the other three and ours is small: respectively 1 (4.8%),^[7] 2 (4.9%),^[6] and 5 (11.1%)^[8] of studies included in our review were included in previous reviews, while 20 (95.2%), 39 (95.1%), and 40 (88.9%) of the studies in these reviews failed to meet the minimum quality threshold in ours.^[12] While high quality non-randomized studies can potentially play an important role in the evaluation of interventions if analysed using appropriate methods, there are many reasons for thinking that simple before-after studies (a design used by the majority of the studies included in previous reviews) do not provide a reliable basis for evaluating interventions.^[65-67] In contrast to ITS studies, a strong quasi-experimental design where multiple outcome measures are taken before and after the intervention, a before-after study compares a single outcome measure pre- and post-intervention and is vulnerable to distorting effects of pre-intervention trends.

We found an increasing number of “high quality” hand hygiene intervention studies after 2009. A systematic review conducted by Gould et al.^[5] examining the literature from 1980 to November 2009, found only four studies meeting the EPOC criteria (1 RCT, 2 ITSs and 1 CBA). With the same criteria, our review found 31 studies (5 RCTs, 13 ITSs, 2 CCTs and 1 CBA) published between December 2009 and May 2014. Most of them used an ITS design, possibly reflecting logistical difficulties in conducting RCTs.

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3 A particular strength of our study is that the network meta-analysis
4 allows us to quantify the relative efficacy amongst a series of different
5 intervention strategies with different baseline interventions, even where the
6 direct head-to-head comparisons were absent.
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10 Reporting on resource implications for interventions was generally very
11 limited with some notable exceptions. Most included studies reported only part
12 of the resources used and methodologies for collecting cost data were unclear.
13 Such resource-use information is important both for those wishing to implement
14 similar strategies and for economic evaluation of different interventions.^[10 68] A
15 good framework to collect such data has also been proposed.^[69] Cost-
16 effectiveness analysis of hand hygiene promotion is required to assess under
17 what circumstances these initiatives represent good value for money and when
18 resources might be better directed at supplemental interventions including care
19 bundles,^[70] ward cleaning,^[71] and screening and decolonization,^[72] to
20 complement well-maintained hand hygiene compliance.
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28 This study has several limitations. First, implementation details of
29 intervention components may vary substantially. For example, personal
30 feedback and group feedback were classified together but, in practice, the
31 impacts of these strategies may vary. Moreover, different studies may implement
32 the same program with different quality of delivery and level of adherence, so-
33 called intervention fidelity or Type III error.^[73] Both issues are common to many
34 interventions to improve the quality of care in hospital settings and are likely to
35 be responsible for much of the unexplained heterogeneity between studies.^[74 75]
36 Second, most direct pairwise comparisons between strategies in the network
37 meta-analysis were based on a single study. Third, publication bias may be
38 substantial, particularly for non-randomized studies, although a funnel plot of
39 ITS study results did not display obvious asymmetry (Appendix 7). There might
40 also be a low level of language bias because studies in languages other than
41 English were excluded. However, the magnitude of such bias is likely to be
42 small.^[76 77] Finally, linking improved compliance to clinical outcomes such as
43 number of infections prevented would provide more direct evidence about the
44 effectiveness of interventions.^[10] Such direct evidence is still limited in hospital
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3 settings, although the association is supported by a large body of indirect
4 evidence as well as biological plausibility.^[78 79]
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8 **Conclusion**

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10 While there is some evidence that uni-modal interventions led to
11 improvements in hand hygiene, there is strong evidence that the WHO-5
12 intervention can lead to substantial, rapid and sustained improvements in hand
13 hygiene compliance in HCWs. There is also evidence that goal-setting, reward
14 incentives and accountability provided additional improvements beyond those
15 achieved by WHO-5. Important directions for future work are to improve
16 reporting on resource implications for interventions, increasingly focus on
17 strong study-designs, and evaluate the long-term sustainability and cost-
18 effectiveness of improvements in hand hygiene.
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27 **What is already known on this topic**

- 28 - Hand hygiene amongst healthcare workers is widely believed to be one
29 of the most effective measures to reduce healthcare-associated
30 infections, but compliance remains poor in many hospital settings.
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- 32 - In 2005 the World Health Organization (WHO) launched a campaign to
33 improve hand hygiene in healthcare settings by promoting a multimodal
34 strategy consisting of five components: system change; training and
35 education; observation and feedback; reminders in the hospital; and a
36 hospital safety climate.
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- 38 - More recently, additional strategies for improving hand hygiene have
39 been evaluated.
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45 **What this paper add**

- 46 - These meta-analyses provide evidence that the WHO campaign is
47 effective at increasing hand hygiene compliance in healthcare workers.
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- 49 - We also found evidence that additional hand hygiene interventions
50 (used in conjunction with the WHO campaign elements) including goal-
51 setting, reward incentives and accountability can lead to further
52 improvements.
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- 57 - Reporting on resource implications of such interventions is limited.
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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

NL, BSC, YL, DL, NG, and ND contributed to the study conception and design. NL and BSC extracted data and NL performed the data analysis. NL wrote the first draft. DL, YL, MH, ASL, SH, NG, ND, and BSC critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Figures and Tables

Figure 1: Systematic review flow chart.

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Figure 2: Assessment of risk of bias in included studies.

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Figure 3: Forest plot of the associations between WHO-5 and goal setting compared with WHO-5 alone and hand hygiene compliance from RCTs.

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3 **Figure 4:** Re-analysis of studies involving interrupted time series where the
4 outcome was hand hygiene compliance. Points represent observations, solid
5 lines show expected values from fitted segmented regression models, and
6 broken lines represent extrapolated pre-intervention trends.
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8 *The last four studies (Jaggi et al., Armellino et al. (2012), Armellino et al. (2013),
9 and Salmon et al.) were not eligible for the network meta-analysis.
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3 **Figure 5:** Forest plot showing the effect size as mean log odds ratios for hand
4 hygiene compliance for all direct pair-wise comparisons from interrupted time
5 series studies.

6 Note that Lee H4, Lee H7, Lee H8, and Lee H9 all come from a multi-centre study.
7 In two of the hospitals (H7 and H9) the baseline strategy was already equivalent
8 to WHO-5.
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Figure 6: Network structure of indirect treatment comparison of 12 different hand hygiene intervention strategies from interrupted time series studies.

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3 **Figure 7:** Box-and-whiskers plot showing relative efficacy of different hand
4 hygiene intervention strategies compared with standard of care estimated by
5 network meta-analysis from interrupted time series studies. Lower and upper
6 edges represent 25th and 75th percentiles from the posterior distribution; the
7 central line represents the median. Whiskers extend to the 5th and 95th
8 percentiles. Intervention strategies were as follows: T2-System change; T3-
9 Education; T6-System change+Education+Feedback+Reminders; T7-WHO-5; T8-
10 System change+Education+Feedback+Incentives+Goal-setting; T9-WHO-
11 5+Incentives; T10-WHO-5+Goal-setting; T11-Incentives+Goal-setting; T12-
12 WHO-5+Incentives+Goal-setting+Accountability.
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Figure 8: Rankograms showing the probabilities of possible rankings for each intervention strategy (rank 1=best, rank 10=worst).

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Table 1: Description of hand hygiene intervention components.

Type of Hand hygiene intervention component	Description
1. System change ^a	Ensuring necessary infrastructure is available including a) access to water, soap and towels and b) alcohol-based handrub at the point of care.
2. Education and Training	Providing training or educational programme on the importance of hand hygiene and the correct procedures for hand hygiene, for healthcare workers.
3. Feedback	Monitoring hand hygiene practices among healthcare workers while providing the compliance feedback to staff.
4. Reminders at workplace	Prompting healthcare workers either through printed material, verbal reminders, electronic communications or other methods, to remind them about the importance of hand hygiene and the appropriate indications and procedures.
5. Institutional safety climate	Active participation at institutional level, creating an environment allowing prioritization of hand hygiene.
6. Goal-setting	Setting of specific goals aimed at improving hand hygiene compliance, which may both apply at the individual and group level and may include healthcare associated infection rates.
7. Reward incentives	Interventions involved with providing any reward incentive for the participants once they achieve a particular task or reach a certain level of hand hygiene compliance. Both non-financial and financial rewards are included.
8. Accountability	Interventions involved with improving healthcare workers' accountability both at an individual and unit level.

^a if the intervention period included changing the place or formulation or installing more dispensers of alcohol based handrub, the baseline intervention was counted as no intervention or standard practice (no system change component) although the alcohol-based handrub had been used during the baseline.

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Table 2: Mean odds ratios with 95% credible intervals for hand hygiene intervention strategies. Results are from random effects network meta-analysis model.

Code	Hand hygiene strategies	System change	Education	Feedback	Reminders	Safety climate	Incentives	Goal-setting	Accountability	Mean OR	95% Credible Interval	
T1	None/Current practice	×	×	×	×	×	×	×	×	Reference		
T2	System change	✓	×	×	×	×	×	×	×	3.50	0.12	100.38
T3	Education	×	✓	×	×	×	×	×	×	7.72	0.14	435.28
T4	Reminders	×	×	×	✓	×	×	×	×	Not in the network		
T5	Education+Feedback+Reminders	×	✓	✓	✓	×	×	×	×	Not in the network		
T6	System change+Education+Feedback+Reminders	✓	✓	✓	✓	×	×	×	×	4.52	0.18	112.51
T7	WHO-5 ^a	✓	✓	✓	✓	✓	×	×	×	6.65	1.33	33.41
T8	System change+Education+Feedback+Reminders +Incentives+Goal-setting	✓	✓	✓	✓	×	✓	✓	×	2,646.52	18.39	396,329.02
T9	WHO-5+Incentives	✓	✓	✓	✓	✓	✓	×	×	9.64	0.56	164.84
T10	WHO-5+Goal-setting	✓	✓	✓	✓	✓	×	✓	×	11.54	0.68	189.81
T11	WHO-5+Incentives+Goal-setting	✓	✓	✓	✓	✓	✓	✓	×	17.27	1.07	288.30
T12	WHO-5+ Incentives+ Goal-setting+Accountability	✓	✓	✓	✓	✓	✓	✓	✓	50.10	1.01	2578.60

Model fit statistic: posterior mean residual deviance= 13.82 and deviance information criterion (DIC)= 26.41
T1-T12: 12 hand hygiene intervention strategies. Refer to Table1 for details of components.
^aWHO-5 strategy contained five components: System change, Education, Feedback, Reminders, and Institutional safety climate.

Table 3: Summary of study characteristics.

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Author (year)	Study design	Study period/ duration	Settings and Details of the design	Unit of Participant	Population	Interventions	Comparison group	Methods of observation	Indication	Outcomes	Country
Fuller (2012)	CRCT (Stepped wedge)	Total: 39 months Baseline: approx. 20 months Intervention: approx. 20 months October 2006 to December 2009	60 wards from 16 hospital trusts Experimental: 33 mixed wards from 13 trusts Control: 27 mixed wards from 11 trusts	Ward	HCWs	WHO-5+GOAL+FED	WHO-5 (UK national campaign)	Direct observation by ward coordinators	Before and after patient contact	Hand hygiene compliance Soap and AHR consumption	England and Wales
Huis (2013)	CRCT	Total: 13 months Baseline: 1 month Intervention: 6 months Follow up (no intervention): 6 months September 2008 to November 2009	67 wards from 3 hospitals Experimental: 30 mixed wards Control: 37 mixed wards	Ward	Nurses	WHO-5+GOAL	WHO-5 (except SAF)	Direct observation by nursing student	Before and after patient contact, patient surroundings and use of gloves	Hand hygiene compliance	Netherlands
Mertz (2010)	CRCT	Total: 15 months Baseline: 3 months Intervention: 12 months October 2006 to December 2006 (Baseline) and June 2007 to May 2008 (Intervention)	30 wards from 3 acute care sites Experimental: 15 mixed wards Control: 15 mixed wards Randomized stratified by hospital site and type of hospital unit. (number of bed not reported)	Ward	HCWs	SYS+EDU+FED+REM	SYS (with AHR at point of care)	Direct observation by researchers	Before and after patient contact, skin wounds or mucous, insertion of an intravenous line and use of gloves	Hand hygiene compliance Incidence of hospital-acquired MRSA colonisation	Canada
Huang (2002)	RCT	Intervention: 4 months period (Pre and Post-test) September 2000 to January 2001	100 randomly selected nurses from a 1,300 bed hospital Experimental: 50 nurses Control: 50 nurses	Individual	Nurses	EDU	None (unclear AHR)	Direct observation by researchers	Before and after patient contact	Hand washing compliance	China
Fisher (2013)	RCT	Total: 24 weeks Baseline: 14 weeks Intervention I: 6 week Intervention II: 4 weeks Start from January 2012	233 participants from 3 wards from 2 hospitals Experimental: 119 participants Control: 114 participants	Individual	HCWs	SYS+REM+FED	SYS (with AHR at point of care)	Direct observation by trained nurses	Room entry and exit	Hand hygiene compliance AHR consumption	Singapore
Salamati (2013)	RCT	No data provided Year 2010	128 participants from a 109-bed hospital Experimental: 64 participants Control: 64 participants	Individual	Nurses, Anesthesiology, Technician, and Nurese-aid	SYS+EDU+FED	SYS+EDU	Direct observation by infection control supervisor	Unclear	Hand hygiene score with unclear details	Iran

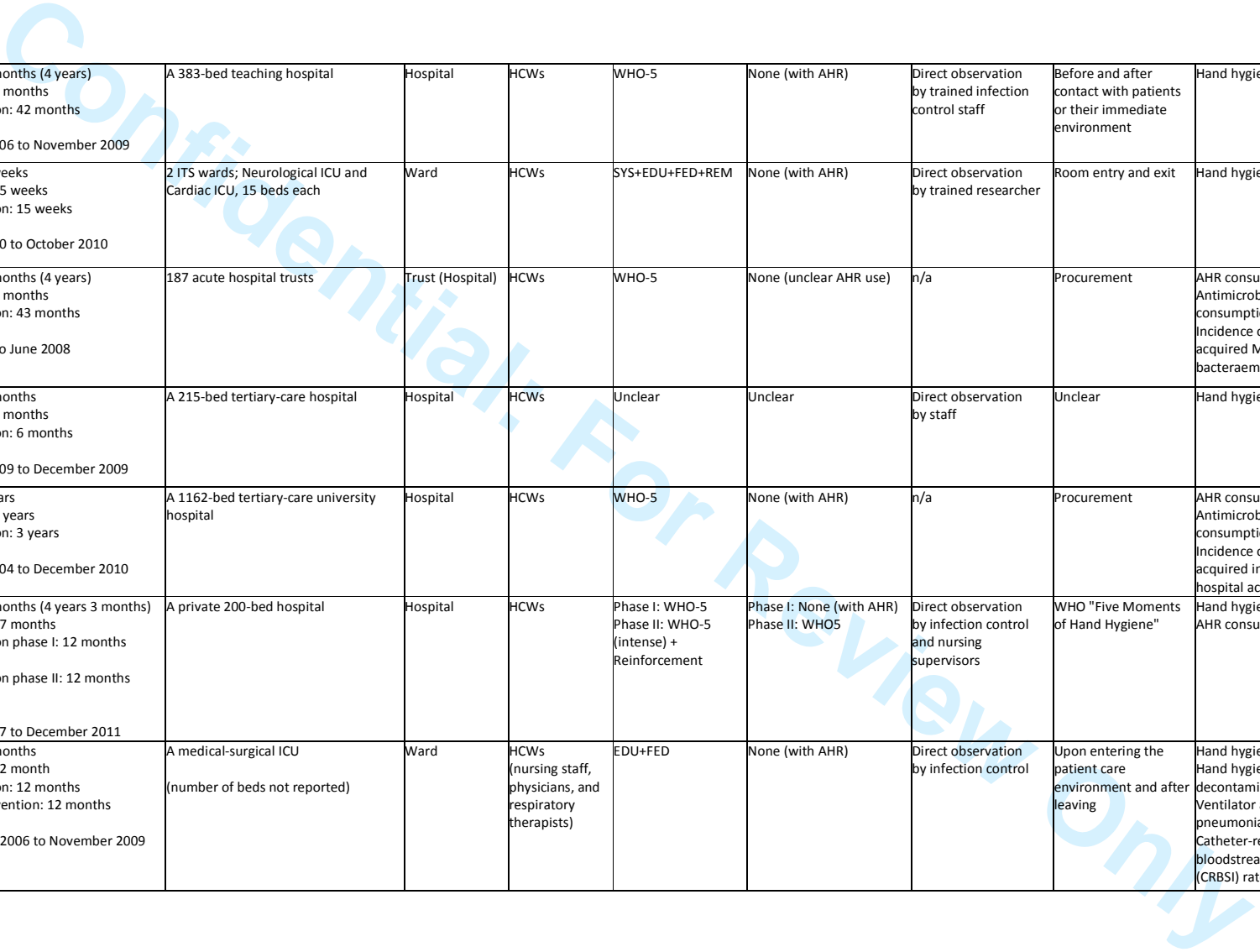
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Derde (2014)	ITS	Total: 36 months (3 years) Baseline: 6 months Intervention I: 18 months Intervention II: 12 months May 2008 to April 2011	13 European ICUs (all with least 8 beds)	Ward	HCWs	EDU+FED+REM	REM (unclear AHR use)	Direct observation by researchers	Before and after patient contact, before an aseptic task, and after contact with patients' body fluids and surroundings	Hand hygiene compliance	Multiple European countries
Lee (2013)	ITS	Total: 24 months (2 years) Baseline: 6 months Intervention: 12 months Post-Intervention (Wash out): 6 months March 2008 to July 2010	33 Surgical wards of 10 hospitals in 9 countries	Ward	HCWs	WHO-5	None (with AHR) in 1 hospital, SYS in 1 hospital and WHO-5 in 2 hospitals	Direct observation by researchers	Before and after patient contact, before an aseptic task, and after contact patients' body fluids and surroundings	Hand hygiene compliance	Multi-center 9 European countries including Germany, Israel, Serbia, Switzerland, France, Greece, Italy, Spain, Scotland
Marra (2013)	ITS	Total: 12 months Baseline: 3 months Intervention: 9 months August 2011 to July 2012	9 wards (8 ICUs and 1 general ward) from 7 tertiary hospitals in 2 countries	Ward	HCWs	WHO-5	None (with AHR)	Direct observation by trained nurses	WHO "Five Moments of Hand Hygiene"	Hand hygiene compliance	Brazil and Thailand
Al-Tawfiq (2013)	ITS	Total: 54 months (4 years 6 months) Baseline: 9 months Intervention: 42 months (implemented at multiple time points) Post-Intervention: 3 months October 2006 to December 2011	A 350-bed hospital	Hospital	HCWs	WHO-5+GOAL	None (with AHR)	Direct observation by infection control team	Before wearing gloves, after removing gloves, before and after patient contact, after leaving patient's room, before and after performing invasive procedures, and after contact with patient's body fluids.	Hand hygiene compliance AHR consumption Device-associated infection rate	Saudi Arabia
Armellino (2013)	ITS	Total: 17 months Baseline: 1 month Intervention: 16 months March 2010 to July 2011	An 18-bed surgical intensive care unit (SICU) from a 804-bed hospital	Ward	HCWs	FED + GOAL	None (unclear AHR use)	Electronic motion sensor and video recorders and sinks and dispensers. Review and audit by researchers	Room entry and exit	Hand hygiene compliance	USA
Armellino (2012)	ITS	Total: 25 months Baseline: 4 months Intervention: 4 months Maintenance: 17 months June 2008 to June 2010	A 17-bed medical intensive care unit from a 804-bed hospital	Ward	HCWs	FED + GOAL	None (unclear AHR use)	Electronic motion sensor and video recorders and sinks and dispensers. Review and audit by researchers	Room entry and exit	Hand hygiene compliance	USA

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Chan (2013)	ITS	Total: 7 months Baseline: 1 month Intervention: 6 months April 2009 to October 2009	A general medical unit with 10 single rooms	Ward	HCWs and others including patients and relatives	SYS	None (with AHR)	n/a	Dispenser count	Hand hygiene event per patient-day	USA
Crews (2013)	ITS	Total: 63 months (5 years 3 months) Baseline: 9 months Intervention: 15 months (implemented at multiple time points) Post-intervention: 39 months October 2006 to December 2011	A 46-bed children hospital	Hospital	HCWs	SYS+EDU+FED+REM+INC+GOAL	EDU (with AHR)	Direct observation by contracted certified infection control practitioner	Before and after contact patient or environment	Hand hygiene compliance	USA
Salmon (2013)	ITS	Total: 45 months (3 years 9 months) Baseline: 18 months Intervention: 3 month Post-Intervention: 24 months January 2009 to September 2012	A 1,032-bed hospital	Hospital	Nursing students	EDU	None (unclear AHR use)	Direct observation by infection control nurses	WHO "Five Moments of Hand Hygiene"	Hand hygiene compliance	Singapore
Falbot (2013)	ITS	Total: 68 months (5 years 8 months) Baseline: 29 months Intervention phase I: 18 months Intervention phase II: 21 months January 2007 to August 2012	A university medical center (support 65,000 inpatient admission, annually)	Hospital	HCWs Settings were inpatient, outpatient clinics and procedural areas	Phase I: WHO-5+INC+GOAL Phase II: WHO-5+INC+GOAL+ACC	Phase I: EDU (unclear AHR use) Phase II: WHO5+INC+GOAL	Direct observation by trained healthcare workers	WHO "Five Moments of Hand Hygiene"	Hand hygiene compliance Device-associated infection rate	USA
Higgins (2013)	ITS	Total: 30 months (2 years 6 months) Baseline: 15 months Intervention: 15 months November 2009 to April 2012	A tertiary referral private hospital (acute healthcare setting) (number of bed not reported)	Hospital	HCWs	WHO-5+INC	None (with AHR)	Direct observation by trained infection prevention control nurses	WHO "Five Moments of Hand Hygiene"	Hand hygiene compliance	Ireland
Helder (2012)	ITS (for hand hygiene event) BA (for HHC% observation) not eligible as no control group and inadequate data collection point	Total: 4 months Baseline: 2 months Intervention: 2 months January 2008 to May 2008	A 27-bed Neonatal Intensive Care Unit (NICU)	Ward	HCWs	(SYS+) REM	SYS (with AHR at POC)	Electronic dispensers counting Direct observation by medical students	Before and after touching a patient, before sterile procedures, before and after the use of gloves and after contact with body fluids	Hand hygiene compliance (pre-post test) Hand hygiene event per patient-day	Netherlands

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Kirkland (2012)	ITS	Total: 48 months (4 years) Baseline: 6 months Intervention: 42 months January 2006 to November 2009	A 383-bed teaching hospital	Hospital	HCWs	WHO-5	None (with AHR)	Direct observation by trained infection control staff	Before and after contact with patients or their immediate environment	Hand hygiene compliance	USA
Morgan (2012)	ITS	Total: 30 weeks Baseline: 15 weeks Intervention: 15 weeks March 2010 to October 2010	2 ITS wards; Neurological ICU and Cardiac ICU, 15 beds each	Ward	HCWs	SYS+EDU+FED+REM	None (with AHR)	Direct observation by trained researcher	Room entry and exit	Hand hygiene compliance	USA
Stone (2012)	ITS	Total: 48 months (4 years) Baseline: 5 months Intervention: 43 months July 2004 to June 2008	187 acute hospital trusts	Trust (Hospital)	HCWs	WHO-5	None (unclear AHR use)	n/a	Procurement	AHR consumption Antimicrobial consumption Incidence of hospital acquired MRSA and MSSA bacteraemia	England and Wales
Aggi (2012)	ITS	Total: 12 months Baseline: 6 months Intervention: 6 months January 2009 to December 2009	A 215-bed tertiary-care hospital	Hospital	HCWs	Unclear	Unclear	Direct observation by staff	Unclear	Hand hygiene compliance	India
Lee (2012)	ITS	Total: 6 years Baseline: 3 years Intervention: 3 years January 2004 to December 2010	A 1162-bed tertiary-care university hospital	Hospital	HCWs	WHO-5	None (with AHR)	n/a	Procurement	AHR consumption Antimicrobial consumption Incidence of healthcare acquired infection and hospital acquired-MRSA	Taiwan
Mestre (2012)	ITS	Total: 51 months (4 years 3 months) Baseline: 27 months Intervention phase I: 12 months (2010) Intervention phase II: 12 months (2011) March 2007 to December 2011	A private 200-bed hospital	Hospital	HCWs	Phase I: WHO-5 Phase II: WHO-5 (intense) + Reinforcement	Phase I: None (with AHR) Phase II: WHO5	Direct observation by infection control and nursing supervisors	WHO "Five Moments of Hand Hygiene"	Hand hygiene compliance AHR consumption	Spain
Koff (2011)	ITS	Total: 36 months Baseline: 12 month Intervention: 12 months Post-Intervention: 12 months December 2006 to November 2009	A medical-surgical ICU (number of beds not reported)	Ward	HCWs (nursing staff, physicians, and respiratory therapists)	EDU+FED	None (with AHR)	Direct observation by infection control	Upon entering the patient care environment and after leaving	Hand hygiene compliance Hand hygiene decontamination event Ventilator associated pneumonia (VAP) rate Catheter-related bloodstream infection (CRBSI) rate	USA

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Doron (2011)	ITS	Total: 18 months Baseline: 6 months Intervention: 12 months September 2007 to February 2009	A 425-bed hospital, an academic medical center	Hospital	HCWs	WHO-5	SYS+EDU+FED+REM (with AHR)	Direct observation by trained staff	Before touching the patient or an object in the patient's room and before or after the encounter with the patient	Hand hygiene compliance	USA
Marra (2010, 2011)	ITS	Total: 21 months, East Step-down Unit (SDU) Baseline: 3 months Intervention: 19 months West Step-down Unit (SDU) Baseline: 6 months Intervention: 15 months April 2008 to November 2009	Two 20-bed SDUs from a private tertiary care hospital (all had single bed rooms)	Ward	HCWs	WHO-5	None (with AHR)	n/a	Dispenser count	Hand hygiene event Alcohol gel consumption Incidence of healthcare associated infections	Brazil
Yngstrom (2011)	ITS	Total: 10 months Baseline: 3 months Intervention: 6 months September 2004 to June 2005	A 110-bed multidisciplinary district hospital	Hospital	HCWs	SYS+EDU+FED+GOAL	None (with AHR)	Direct observation by trained nurse at each ward	Use of short-sleeved uniforms, protective clothing, aprons and gloves, hand disinfection with AHR, and wearing rings and wristwatches	Basic hygiene compliance Incidence of healthcare associated infection in ventilated patients (healthcare-associated infections with regard to ventilator associated pneumonia, intubation-related infections in blood vessels and healthcare-associated urinary infections).	Sweden
Helms (2010)	ITS	Total: 12 months Baseline: 3 months Intervention: 9 months August 2007 to July 2008	A 116-bed hospital	Hospital	HCWs	WHO-5	None (with AHR)	Direct observation by selected staff members and volunteers	WHO "Five Moments of Hand Hygiene" *(Information from author contact)	Hand hygiene compliance Incidence of HAIs; urinary tract infection, ventilator associated pneumonia and central line infections	USA
Chou (2010)	ITS	Total: 57 months (4 years 9 months) Baseline: 21 months Intervention: 36 months April 2005 to December 2009	A hospital, part of a 9-hospital healthcare system	Hospital	HCWs	WHO-5+INC+GOAL	None (with AHR)	Direct observation by a staff liaison from each department	Based on opportunities	Hand hygiene compliance	USA

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Vernaz (2008)	ITS	Total: 72 months (6 years) Baseline: 22 months (1 year and 10 months) Intervention: 50 months (4 years and 2 months) February 2000 to September 2006	A 2,200 bed tertiary university hospital	Hospital	HCWs	WHO-5 (Swiss national campaign)	SYS (with AHR at point of care)	n/a	Procurement	AHR consumption Antibiotics use Incidence of MRSA and <i>C. difficile</i> (number of clinical isolates per 100 patient-days)	Switzerland
Whitby (2008)	ITS	Total: 2 years Baseline: 4 to 5 months Intervention: 18 months 2004 to 2006	5 wards from a 800-bed hospital with 3 intervention groups 1) Washington campaign (1 ward) 2) Geneva campaign (2 wards) 3) AHR substitution (2 wards)	Ward	HCWs	Group I: WHO-5 Group II: SYS+EDU+REM+SAF Group III: SYS	None (with AHR)	n/a	Dispenser (liquid soap) count	Hand hygiene events per occupied bed-day	Australia
Mayer (2011)	CCT/ITS	Total: 16 months CCT step-down Baseline: 2 months Intervention phase I: varied between 2 to 7 months August 2000 to November 2001 ITS (less than 3 time points baseline); 2 years 9 months April 2003 to December 2006	3 units (6 wards) from a 450-bed hospital Intervention 2 units (4 wards) Control 1 unit (2 wards) Step-down phase 1 and 2	Ward	HCWs	Phase I: SYS+EDU+FED Phase II: WHO-5+INC	None (unclear AHR use)	Direct observation by trained part-time staff	Before, after, or before and after contact patient or patient's environment.	Hand hygiene compliance	USA
Barner-Brutner (2011)	CCT	Total: 7 months Baseline: 1 month Intervention: 6 months April to October 2005	3 medical-surgical units from an urban healthcare system Intervention: 2 wards with different interventions Control: 1 ward	Ward	Nurses and patient care assistants	Phase I: EDU+REM Phase II: EDU+INC+GOAL	EDU (with AHR use)	Direct observation by trained staff	Before or after, or before and after patient contact.	Hand hygiene compliance	USA
Benning (2011)	CBA	Total: 20 months (as a second phase of a national improving the quality of healthcare program) March 2007 to September 2008	Total 18 hospitals Intervention: 9 hospitals Control: 9 matched hospitals by size and geographic area	Hospital	HCWs	SYS+REM+SAF	None (with AHR)	n/a	Procurement	Soap and AHR consumption	England and Wales
Gould (1997)	CBA	Total: 3 months intervention period Data on date is not available	Total 4 surgical wards from a teaching hospital Intervention: 2 surgical wards Control: 2 surgical wards	Ward/Individual	Nurses	EDU	None (unclear AHR use)	Direct observation by researchers	Frequency, appropriateness and duration of hand decontamination compliance and the use of gloves	Hand decontamination compliance	UK

*SYS: system change, EDU: education, FED: feedback, REM: reminders, SAF: institutional safety climate, INC: incentives, GOAL: goal-setting, ACC: accountability, WHO-5: a combined intervention strategies including SYS, EDU, FED, REM, and SAF, AHR: alcohol based hand rub, HHC: hand hygiene compliance, HCW: healthcare worker, n/a: information is not available.

Table 4: Resource use extracted data

No	Author (year), Study design	Intervention	Comparison	Settings	Resource use (Material)	Resource use (Time)	Sources	Total cost (\$US)	No of bed	Intervention period (day)	Cost per 1,000 bed-day (\$US)	Base year
1	Huis (2013), CRCT	WHO-5 + goal-setting	WHO5 (except institutional safety climate)	Netherlands	State of art strategies Alcohol hand rub Material including website, leaflets, posters, newsletters, article in hospital magazines	State of art strategies Hand hygiene direct observation Extra time for performing hand hygiene	Separate paper ^[63]	320,278 ^T (€ 246,368)	993	365	883.7	2009
					Team and leader directed strategies Same as above	Team and leader directed strategies Same as SAS above Coach salary Staffing costs for managers, role models and nurses in coaching session and preparation		474,068 ^Y (€ 364,668)	1225	365	1,060.5	
2	Higgins (2013), ITS	WHO-5 + incentive	None (with AHR)	Ireland	A mobile interactive stand-alone computer using gaming technology and annual license Swab and ATP machine	Research Assistant for audit and training 1.79 full-time equivalent (287 hours) assuming salary as £2,500 per month	Author contact	42,358 ^Y (£ 26,474)	170	450	553.7	2010
3	Armellino (2012), ITS	Feedback + goal-setting	None (unclear AHR use)	USA	21 Video cameras	n/a	Paper	50,000	17	630	4,668.5	2008
4	Morgan (2012), ITS	System change + education + feedback + reminders	None (with AHR)	USA	60 alcohol dispensers system in two wards 12 posters in total	1.46 FTE (234 hours) of research assistant (10-20 hours a week for trouble shooting, refilling, and collecting data from the devices, and 2 hours a month to design and present posters)	Author contact	6,960	27	105	2,455.0	2010

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5	Mestre (2012), ITS	Phase I: WHO-5 Phase II: WHO-5 (intense) + Reinforcement	Phase I: None (with AHR) Phase II: WHO-5	Spain	Alcohol handrub solution Material for campaign including posters, pens, and candy	Hand hygiene direct observation Data analysis and interpretation	Separate Paper ^[64]	19,259	n/a	365	385.2	2011
6	Doron (2011), ITS	WHO-5	System change + education + feedback + reminders (with AHR)	USA	Cost for marketing consultancy	n/a	Author contact	35,000 - 50,000	425	365	225.6-322.3	2008-9
7	Mayer (2011), CCT	Phase I: System change + education + feedback Phase II: WHO-5 + incentive	None (unclear AHR use)	USA	Prizes as candy, chocolate bars, pizza and others	2.25 FTE (yearly) of Infection preventionists 0.6 FTE of Manager 0.35 FTE of Clark	Paper	165,600	450	365	1,008.2	2003-6
8	Harne-Britner (2011), ITS	Phase I: Education + reminders Phase II: Education + incentive + goal-setting	Education (with AHR use)	USA	Printing, supply for education program	Staff time for preparation of education program Attendance at education programs including data collection training, in services, review material. Investigator monitoring for study. Validation of data collection tool and analysis	Author contact	4,835	n/a	180	n/a	2005

^y Assumed exchange rates: € 1 Euro = \$US 1.3 and £1 British pound = \$US 1.6
^{*} HHC: hand hygiene compliance, HCW: healthcare worker, POS: point of care service, AHR: alcohol based hand rub, CRCT: cluster randomized controlled trial, RCT: randomized controlled trial, ITS: Interrupted time series study, CCT: controlled clinical trial, CBA: controlled before and after study, WHO-5: a combined intervention including system change, education, feedback, reminders, and institution safety climate, n/a: information is not available.

Table 5: Results of the re-analysis of studies using interrupted time series.

Study	Comparison	Baseline Level (intercept)		Baseline trend	Change in trend	Change in level	^d Hand Hygiene change (%HHC)		
		%HHC	Coefficient (SE)	Coefficient (SE)	Coefficient (SE)	Coefficient (SE)	Mean	95% Confidence interval	
Lee, Hosp 4	T1 vs T7	44.6	-0.215 (0.30)	-0.081 (0.10)	0.130 (0.10)	0.606 (0.26)	29.9	3.5	56.4
Lee, Hosp 7	T7 vs T7	53.8	0.154 (0.29)	0.281 (0.07)	-0.151 (0.08)	-1.042 (0.25)	-11.5	-13.5	-9.5
Lee, Hosp 8	T2 vs T7	44.6	-0.215 (0.26)	0.059 (0.06)	0.014 (0.06)	0.563 (0.19)	13.3	-9.2	35.8
Lee, Hosp 9	T7 vs T7	62.3	0.503 (0.33)	0.088 (0.13)	-0.094 (0.13)	-0.007 (0.51)	-9.7	-63.6	44.3
Derde	T4 vs T5	52.8	0.112 (0.04)	-0.015 (0.01)	0.133 (0.02)	0.346 (0.05)	16.3	13.6	19.1
Higgins	T1 vs T9	37.2	-0.428 (0.17)	-0.009 (0.25)	-0.030 (0.03)	2.448 (0.25)	48.8	45.4	52.3
Doron	T6 vs T7	70.7	0.204 (0.12)	0.187 (0.10)	-0.040 (0.03)	0.586 (0.01)	4.7	2.3	7.1
^a Chou	T1 vs T11	54.9	0.198 (0.03)	-0.039 (0.00)	0.151 (0.01)	0.453 (0.17)	56.4	53.1	59.8
Marra	T1 vs T7	45.7	-0.173 (0.07)	0.020 (0.06)	0.063 (0.03)	0.218 (0.06)	11.5	3.4	19.6
Helms	T1 vs T7	91.3	2.350 (0.42)	-0.297 (0.18)	0.354 (0.19)	0.706 (0.33)	35.9	-5.8	77.7
Kirkland	T1 vs T7	51.3	0.052 (0.14)	-0.097 (0.04)	0.111 (0.04)	4.443 (1.03)	83.3	77.0	89.6
Al-Tawfiq	T1 vs T10	41.3	-0.350 (0.09)	-0.014 (0.02)	0.081 (0.07)	2.328 (0.21)	49.9	42.8	57.0
Crews	T3 vs T8	50.7	0.028 (0.12)	-0.070 (0.02)	0.103 (0.02)	3.679 (0.22)	38.2	35.5	40.9
^a Talbot (Phase I)	T3 vs T11	56.7	0.271 (0.20)	-0.006 (0.02)	0.109 (0.02)	0.363 (0.41)	18.5	-1.4	38.4
Talbot (Phase II)	T11 vs T12	81.1	1.455 (0.45)	-0.020 (0.01)	0.060 (0.01)	0.464 (0.05)	15.0	10.6	19.5
^b Jaggi	^c Unclear intervention details	19.5	-1.420 (0.26)	0.080 (0.02)	-0.006 (0.03)	-0.586 (0.34)	-14.8	-33.1	3.6
^{a, b} Armellino (2012)	T1 vs Feedback+Goal-setting	7.6	-2.493 (0.15)	-0.088 (0.133)	0.849 (0.235)	3.046 (0.68)	45.4	38.5	52.3
^{a, b} Armellino (2013)	T1 vs Feedback+Goal-setting	29.0	-0.895 (0.04)	0.122 (0.10)	-0.109 (0.08)	2.267 (0.14)	74.9	65.5	84.4
^b Salmon	T1 vs T3	42.7	-0.295 (0.17)	0.003 (0.02)	0.021 (0.02)	0.485 (0.22)	17.9	-0.3	36.2

^a Evidence of auto correlation; Newey-West standard errors are reported.

^b Studies excluded in the network meta-analysis (see Appendix 6 for exclusion criteria).

^c Details of intervention were not clear.

^d The mean change in hand hygiene compliance during the post-intervention period attributed to the intervention accounting for baseline trends (see Appendix 3 for details)

Supplementary
Appendix 1: Electronic search strategy

Databases	Adapted from Gould et al.	Adapted from Huis et al.
MEDLINE	1 Handwashing/ 2 (hand antisepsis or handwash\$ or hand wash\$ or hand disinfection or hand hygiene or surgical scrub\$.tw. 3 1 or 2 4 exp Hand/ 5 exp Sterilization/ 6 4 and 5 7 3 or 6 8 randomized controlled trial.pt. 9 controlled clinical trial.pt. 10 intervention studies/ 11 experiment\$.tw. 12 (time adj series).tw. 13 (pre test or pretest or (posttest or post test)).tw. 14 random allocation/ 15 impact.tw. 16 intervention?.tw. 17 chang\$.tw. 18 evaluation studies/ 19 evaluat\$.tw. 20 effect?.tw. 21 comparative study/ 22 animal/ 23 human/ 24 22 not 23 25 or/8-21 26 25 not 24 27 7 and 26 28 limit 27 to yr="2009 -Current" 29 exp hospitals/ 30 hospital\$.tw. 31 exp inpatients/ 32 inpatient\$.tw. 33 exp health care/ 34 health care\$.tw. 35 healthcare\$.tw. 36 infirmaries\$.tw. 37 nosocomial\$.tw. 38 intensive care unit\$.tw. 39 ward\$.tw. 40 OR/29-39 41 28 and 40	1 Randomized controlled trial/ 2 random\$.tw. 3 experiment\$.tw. 4 (time adj series).tw. 5 (pre test or pretest or post test or posttest).tw. 6 impact.tw. 7 intervention\$.tw. 8 chang\$.tw. 9 evaluat\$.tw. 10 effect?.tw. 11 compar\$.tw. 12 control\$.tw. 13 or/1-12 14 limit 13 to humans 15 (hand washing or handwashing or hand hygiene) 16 14 and 15 17 limit 16 to yr="2009 - Current" 18 exp hospitals/ 19 hospital\$.tw. 20 exp inpatients/ 21 inpatient\$.tw. 22 exp health care/ 23 health care\$.tw. 24 healthcare\$.tw. 25 infirmaries\$.tw. 26 nosocomial\$.tw. 27 intensive care unit\$.tw. 28 ward\$.tw. 29 OR/18-28 30 17 and 29 *EPOC Methodological filter Randomized Controlled Trial [publication type] OR Controlled Clinical Trial [publication type] OR Comparative Study OR Evaluation Studies OR 'comparative study' OR 'effects' OR 'effect' OR 'evaluations' OR 'evaluating' OR 'evaluation' OR 'evaluates' OR 'changing' OR 'changes' OR 'change' OR 'interventions' OR 'intervention' OR 'impact' OR 'random allocation' OR 'post test' OR 'posttest' OR 'pre test' OR 'pretest' OR 'time series' OR 'experimental' OR 'experiments' OR 'experiment' OR 'intervention studies' OR 'intervention study' OR 'controlled clinical trial' OR 'randomised controlled trial' OR 'randomized controlled trial'
EMBASE	1 Handwashing/ 2 (hand antisepsis or handwash\$ or hand wash\$ or hand disinfection or hand hygiene or surgical scrub\$.tw. 3 1 or 2 4 exp Hand/ 5 exp Sterilization/ 6 4 and 5 7 3 or 6 8 randomized controlled trial/ 9 randomi\$.tw. 10 exp controlled clinical trial/ 11 controlled clinical trial\$.tw.	1 Randomized controlled trial/ 2 random\$.tw. 3 experiment\$.tw. 4 (time adj series).tw. 5 (pre test or pretest or post test or posttest).tw. 6 impact.tw. 7 intervention\$.tw. 8 chang\$.tw. 9 evaluat\$.tw. 10 effect?.tw. 11 compar\$.tw. 12 control\$.tw.

	<p>12 intervention studies/ 13 experiment\$.tw. 14 (time adj series).tw. 15 (pre test or pretest or (posttest or post test)).tw. 16 random allocation/ 17 impact.tw. 18 intervention?.tw. 19 chang\$.tw. 20 evaluation studies/ 21 evaluat\$.tw. 22 effect?.tw. 23 comparative study/ 24 animal/ 25 human/ 26 24 not 25 27 or/8-23 28 27 not 26 29 7 and 28 30 limit 29 to yr="2009 -Current" 31 exp hospitals/ 32 hospital\$.tw. 33 exp hospital patient/ 34 inpatient\$.tw. 35 exp health care/ 36 health care\$.tw. 37 healthcare\$.tw. 38 infirmary\$.tw. 39 nosocomial\$.tw. 40 intensive care unit\$.tw. 41 ward\$.tw. 42 or/31-41 43 30 and 42</p>	<p>13 or/1-12 14 limit 13 to humans 15 (hand washing or handwashing or hand hygiene). 16 14 and 15 17 limit 16 to yr="2009 - Current" 18 exp hospital/ 19 hospital\$.tw. 20 exp hospital patient/ 21 inpatient\$.tw. 22 exp health care/ 23 health care\$.tw. 24 healthcare\$.tw. 25 infirmary\$.tw. 26 nosocomial\$.tw. 27 intensive care unit\$.tw. 28. ward\$.tw. 29 or/18-28 30 17 and 29</p>
CINAHL	<p>1 (MH "Handwashing+") 2 (hand antiseptis OR handwash* OR hand wash* OR hand disinfection OR hand hygiene OR surgical scrub*) 3 1 OR 2 4 Hand* 5 Sterilization* 6 4 AND 5 7 3 OR 6 8 (MH "Clinical Trials+") 9 clinical trial* 10 randomi* 11 controlled clinical trial* 12 intervention studies* 13 experiment* 14 "time series" 15 (MH "Pretest-Posttest Design+") 16 random allocation* 17 impact* 18. intervention? 19. chang* 20. (MH "Evaluation Research+") 21. evaluat* 22. effect? 23. comparative study* 24.(MH "Animals+") 25.(MH "Human+") 26. 24 NOT 25 27. OR/8-23 28. 27 NOT 26 29. 7 and 28 30. limit 29 to yr="2009 -Current"</p>	<p>1(MH "Clinical Trials+") 2 clinical trial* 3 "comparative studies" 4 "experimental studies" 5 "time series" 6 impact* 7 evaluat* 8 effect* 9 (MH "Pretest-Posttest Design+") 10 (MH "Quasi-Experimental Studies+") 11 or/1-10 12 (MH "Handwashing+") 13 (handwashing OR hand hygiene) 14 or/12-13 15 11 and 14 16 limit 15 to yr="2009 - Current" 17 (MH "Hospitals+") 18 (MH "Hospital Units+") 19 Intensive Care Units 20 (MH "Inpatients") 21 (MH "Child, Hospitalized") 22 (MH "Adolescent, Hospitalized") 23 (MH "Aged, Hospitalized") 24 (hospitalized OR hospitalised) 25 (health care OR healthcare) 24 healthcare\$.tw. 25 infirmary\$.tw. 26 nosocomial\$.tw. 27 intensive care unit\$.tw. 28. ward\$.tw. 26 or/17-25 27 16 AND 26</p>

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	31 (MH "Hospitals+") 32 (MH "Hospital Units+") 33 hospital* 34 Intensive Care Units 35 (MH "Inpatients") 36 (MH "Child, Hospitalized") 37 (MH "Adolescent, Hospitalized") 38 (MH "Aged, Hospitalized") 39 (hospitalized OR hospitalised) 40 (health care OR healthcare) 24 healthcare\$.tw. 25 infirmary\$.tw. 26 nosocomial\$.tw. 27 intensive care unit\$.tw. 28. ward\$.tw. 41 or/31-40 42 30 AND 41	
17 18 19 20 21 22 23 24 25 26 27 28 29	BNI 1 handwash* (137) 2 hand wash* (170) 3 hand antisept* (22) 4 hand disinfection (39) 5 hand hygiene (369) 6 hand decontamination (43) 7 hand cleansing (29) 8 hand cleaning (27) 9 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 (599) 10 hand (1438) 11 strilization (106) 12 9 OR 11 (702) 13 limit 12 to "2009 to Current"	n/a
30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60	CRD Database n/a	1 MeSH DESCRIPTOR Clinical Trial EXPLODE ALL TREES 2 Clinical Trial* 3 control* 4 random* 5 comparative stud* 6 experimental stud* 7 time series* 8 impact* 9 intervention* 10 evaluat* 11 effect* 12 Chang* 13 Compar* 14 Experiment* 15 (pretest OR pre test OR posttest OR post test) 16 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 17 MeSH DESCRIPTOR Handwashing EXPLODE ALL TREES 18 (hand washing OR handwashing OR hand hygiene) 19 #17 OR #18 20 #15 AND #19 21 (#20) FROM 2009 TO 2013 22 MeSH DESCRIPTOR Hospitals EXPLODE ALL TREES (MH 23 MeSH DESCRIPTOR Hospital Units EXPLODE ALL TREES (MH 24 hospital* 25 Intensive Care Unit* 26 MeSH DESCRIPTOR Inpatients EXPLODE ALL TREES

		<p>27 MeSH DESCRIPTOR Adolescent, Hospitalized EXPLODE ALL TREES 28 MeSH DESCRIPTOR Adolescent, Institutionalized EXPLODE ALL TREES 29 MeSH DESCRIPTOR Child, Hospitalized EXPLODE ALL TREES 30 MeSH DESCRIPTOR Child, Institutionalized EXPLODE ALL TREES 31 (hospitalised OR hospitalized OR healthcare OR health care) 32 #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 33 #21 AND #32</p>
Cochrane Library	<p>1 MeSH descriptor: [Hand hygiene] explode all trees 2 (hand antiseptis OR handwash* OR hand wash* OR hand disinfection OR hand hygiene OR surgical scrub*) 3 1 OR 2 4 Hand* 5 Sterilization* 6 4 AND 5 7 3 OR 6 8 MeSH descriptor: [Clinical Trial] explode all trees 9 clinical trial* 10 randomi* 11 controlled clinical trial* 12 intervention studies* 13 experiment* 14 time series* 15 (pretest OR pre test OR posttest OR post test) 16 random allocation* 17 impact* 18 intervention? 19 chang* 20 evaluat* 21 effect* 22 comparative study* 23 OR/8-22 24 7 and 23 25 limit 24 to yr="2009 -Current" 26. MeSH descriptor: [Hospitals] explode all trees 27 MeSH descriptor: [Hospital Units] explode all trees 28 hospital* 29 Intensive Care Unit* 30 MeSH descriptor: [Inpatients] explode all trees 31 MeSH descriptor: [Adolescent, Hospitalized] explode all trees 32 MeSH descriptor: [Adolescent, Institutionalized] explode all trees 33 MeSH descriptor: [Child, Hospitalized] explode all trees 34 MeSH descriptor: [Child, Institutionalized] explode all trees 35 (hospitalised OR hospitalized OR healthcare OR health care) 36 #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 37 #25 AND #36</p>	<p>1 MeSH descriptor: [Clinical Trial] explode all trees 2 Clinical Trial* 3 control* 4 random* 5 comparative stud* 6 experimental stud* 7 time series* 8 impact* 9 intervention* 10 evaluat* 11 effect* 12 Chang* 13 Compar* 14 Experiment* 15 (pretest OR pre test OR posttest OR post test) 16 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 17 MeSH descriptor: [Hand hygiene] explode all trees 18 (hand washing OR handwashing OR hand hygiene) 19 #17 OR #18 20 #16 AND #19 21 (#20) FROM 2009 TO 2013 22 MeSH descriptor: [Hospitals] explode all trees 23 MeSH descriptor: [Hospital Units] explode all trees 24 hospital* 25 Intensive Care Unit* 26 MeSH descriptor: [Inpatients] explode all trees 27 MeSH descriptor: [Adolescent, Hospitalized] explode all trees 28 MeSH descriptor: [Adolescent, Institutionalized] explode all trees 29 MeSH descriptor: [Child, Hospitalized] explode all trees 30 MeSH descriptor: [Child, Institutionalized] explode all trees 31 (hospitalised OR hospitalized OR healthcare OR health care) 32 #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 32 #21 AND #32</p>

1 2 3 4 5 6	Current Clinical Control Trial	n/a	("hand hygiene" OR "hand washing" OR "handwashing" OR "hand sanitizer" OR "hand rubbing" OR "hand rubs") AND ("hospital" OR "healthcare" OR "inpatients" OR "intensive care unit" OR "hospitalised" OR "hospitalized" OR "nosocomial")
7 8 9 10 11	ACP journal	("hand hygiene" OR "hand washing" OR "handwashing" OR "hand sanitizer" OR "hand rubbing" OR "hand rubs") AND ("hospital" OR "healthcare" OR "inpatients" OR "intensive care unit" OR "hospitalised" OR "hospitalized" OR "nosocomial")	n/a
12 13 14 15 16 17 18 19 20 21 22 23 24 25 26	Evidence- Based Medicine Reviews	1 handwashing.sh. 2 handwash\$.tx. 3 hand wash\$.tx. 4 hand disinfection.tx. 5 hand hygiene.tx. 6 surgical scrub\$.tx. 7 hand decontamination.mp. [mp=ti, to, ab, tx, kw, ct, sh, hw] 8 hand cleansing.mp. [mp=ti, to, ab, tx, kw, ct, sh, hw] 9 hand cleaning.mp. [mp=ti, to, ab, tx, kw, ct, sh, hw] 10 1or2or3or4or5or6or7or8or9 11 from 10 keep 1-249 12 10 13 limit 12 to yr="2005 Current"	n/a

Appendix 2: Classification for level of information on resources use

Level of information on resources use for interventions

High: Stated clearly what the interventions were and how they were implemented and described clearly what materials were used and how much time for each person was spent as well as the duration of the implementation period.

Moderate: Stated what the interventions were and how they were implemented but lacking a clear description of materials used and person-time involved as well as time spent for each intervention.

Low: Stated only what the interventions were and how they were implemented. Largely lacking any details on materials used, person involved as well as the time spent.

Appendix 3: Analysis of interrupted time series data

Data from interrupted time series were re-analysed when data on the number of opportunities and hand hygiene compliance at different time points could be obtained.

If $n(t)$ represents the number of hand hygiene opportunities in a study at time t and $y(t)$ represents the number of occasions where compliance was observed, then we used the following generalized linear model to evaluate the effect of the intervention:

$$y(t) \sim \text{binomial}(\pi(t), n(t)) \quad [1]$$

$$\ln(\pi(t)/(1-\pi(t))) = a + b \times t + c \times \mathbf{1}_{t \geq t.int} + d \times \mathbf{1}_{t \geq t.int} \times (t - t.int) \quad [2]$$

where $\pi(t)$ is the probability of hand hygiene at time t , $t.int$ is the time of the intervention, $\mathbf{1}_{t \geq t.int}$ is a function of t taking the value 1 if $t \geq t.int$ and zero otherwise. In this expression the parameter a measures baseline compliance, b the initial pre-intervention trend, c the step (level) change associated with the intervention, and d corresponds to the change in trend associated with the intervention. These parameters were estimated for each study that was re-analysed. In this model an intervention can increase hand hygiene either through a step increase in compliance at the time of the intervention ($c > 0$) or through a trend for increased compliance ($d > 0$).

It is also useful to obtain a statistic that summarizes the effectiveness of the intervention, accounting for both changes in trend and level. There are several possibilities and we consider two: the mean percentage change in hand hygiene compliance in the post-intervention period attributed to the intervention (an absolute measure of change in compliance) and the mean log odds ratio of hand hygiene associated with the intervention (a relative measure).

The first statistic, the mean percentage change in hand hygiene compliance, is given by 100 times the mean difference between the value of $\pi(t)$ predicted by equation [2] and the value of $\pi(t)$ that would be expected if the terms c and d were set to zero (i.e. the expected compliance probability if the intervention had not occurred), where the mean is taken over the post-intervention interval $[t.int, t.end]$, where $t.end$ is the time of the end of post-intervention period. This is equivalent to $100/(t.end - t.int)$ multiplied by the area between the following two curves (representing the hand hygiene compliance probability given the intervention and the hand hygiene compliance probability that would be expected without the intervention, respectively) for $t.int \leq t \leq t.end$:

$$\pi_1(t) = \frac{\exp(a+bt+c\mathbf{1}_{t \geq t.int}+d\mathbf{1}_{t \geq t.int}(t-t.int))}{1+\exp(a+bt+c\mathbf{1}_{t \geq t.int}+d\mathbf{1}_{t \geq t.int}(t-t.int))} \quad [3]$$

$$\pi_0(t) = \frac{\exp(a+bt)}{1+\exp(a+bt)} \quad [4]$$

This is given by $100 \times \frac{A_1 - A_0}{t.end - t.int}$ where the areas A_1 and A_0 are found by integrating [3] and [4] over this range:

$$A_1 = \int_{t.int}^{t.end} \pi_1(t) dt \quad A_0 = \int_{t.int}^{t.end} \pi_0(t) dt$$

which gives

$$A_1 = \frac{\ln(1 + \exp(a + b \times t.end + c + d \times (t.end - t.int)))}{(b + d)(1 + \exp(a + b \times t.int + c))}$$

$$A_0 = \frac{\ln(1 + \exp(a + b \times t.end))}{b(1 + \exp(a + b \times t.int))}.$$

An associated standard error was obtained using the delta method making use of the covariance matrix obtained by fitting the full generalized linear model described by equations [1] and [2].

The relative measure of hand hygiene change associated with the intervention is the mean log odds ratio for hand hygiene. This is defined as the mean value of the logarithm of ratio of the odds of hand hygiene compliance in the post-intervention period given by equation [2] to the odds of hand hygiene given by equation [2] but setting term c and d to zero. This is given by

$$c + d \times (t.end - t.int)/2$$

and the associated variance is given by

$$\text{var}(c) + \text{var}(d) \times ((t.end - t.int)/2)^2 + 2 \times \text{cov}(c, d) \times (t.end - t.int)/2.$$

Appendix 4: WINBUGS code for network meta-analysis

a) Base case analysis

```

1
2
3
4
5 # Trial-level data given as treatment differences
6 # Random effects model
7
8 model{
9     for(i in 1:ns) {
10        y[i] ~ dnorm(delta[i],prec[i]) # normal likelihood for trials
11        var[i] <- pow(se[i],2) # calculate variances
12        prec[i] <- 1/var[i] # set precisions
13        #Trial-specific mean diff distributions
14        delta[i] ~ dnorm(md[i],bytau.sq[c[i]])
15        #Mean of random effects distributions
16        md[i] <- d[t[i,2]] - d[t[i,1]]
17        #Deviance contribution
18        dev[i] <- (y[i]-delta[i])*(y[i]-delta[i])*prec[i]
19        #summed residual deviance contribution for this trial
20        resdev[i] <- sum(dev[i])
21    }
22    totresdev <- sum(resdev[]) #Total Residual Deviance
23    d[1]<-0 #Treatment effect is zero for reference treatment
24
25    for (k in 2:nt){d[k] ~ dnorm(0,.0001)
26    }
27    for ( i in 1:nc){
28        tau.sq[i]<-max(0.01,t.s[i])
29        t.s[i]~dnorm(2,10)
30        bytau.sq[i]<- 1/tau.sq[i]
31    }
32    #Ranking
33    for (k in 1:10) {
34        rk[k] <- 11-rank(d[],k)
35        best[k] <- equals(rk[k],1)}
36
37 } # *** PROGRAM ENDS
38
39 # ns= number of studies;
40 # nt=number of treatments;
41
42 #Data
43 list(ns=14, nt=10, nc=10)
44 c[] t[,1] t[,2] y[] se[]
45 1 1 5 0.4711 0.1647
46 2 1 8 2.4499 0.1691
47 3 3 6 5.8455 0.5953
48 4 3 9 0.7974 0.4078
49 5 9 10 1.0656 0.1131
50 6 1 7 2.2700 0.3041
51 1 1 5 5.4996 1.4148
52 8 4 5 0.3847 0.1541
53 1 1 5 1.9448 0.8245
54 9 1 9 2.8740 0.1402
55 1 1 5 1.3230 0.8183
56 10 5 5 -1.8738 0.6183
57 7 2 5 0.6408 0.4910
58 10 5 5 -0.5222 1.2273
59
60 END
61
62 Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes
63
64 test 0.000 0.000 -0.000 0.000
65 y 13.817 1.222 12.595 26.412
66 total 13.817 1.222 12.595 26.412

```

b) Sensitivity analysis

Code and results for sensitivity analysis exclude the multiple time implementation studies including Helms et al., Kirkland et al., Al-Tawfiq et al., and Crews et al.

```

# Trial-level data given as treatment differences
# Random effects model
model{
  for(i in 1:ns) {
    y[i] ~ dnorm(delta[i],prec[i]) # normal likelihood for trials
    var[i] <- pow(se[i],2) # calculate variances
    prec[i] <- 1/var[i] # set precisions
    # trial-specific mean diff distributions
    delta[i] ~ dnorm(md[i],bytau.sq[c[i]])
    # mean of random effects distributions, with multi-arm
    trial correction
    md[i] <- d[t[i,2]] - d[t[i,1]]

    #Deviance contribution
    dev[i] <- (y[i]-delta[i])*(y[i]-delta[i])*prec[i]
    #summed residual deviance contribution for this trial
    resdev[i] <- sum(dev[i])
  }
  totresdev <- sum(resdev[]) #Total Residual Deviance
  d[1]<-0 #treatment effect is zero for reference treatment
  for (k in 2:nt){ d[k] ~ dnorm(0,.0001)
}
for ( i in 1:nc){
  tau.sq[i]<-max(0.01,t.s[i])
  t.s[i]~dnorm(2,10)
  bytau.sq[i]<- 1/tau.sq[i]
}
#Ranking
for (k in 1:8) {
  rk[k] <- 9-rank(d[,k])
  best[k] <- equals(rk[k],1)}
} # *** PROGRAM ENDS

# ns= number of studies;
# nt=number of treatments;

#Sensitivity anlysis: exclude Crews, Kirkland, Helms and Al-Tawfiq.
list(ns=10, nt=8, nc=8)
c[] t[,1] t[,2] y[] se[]
1 1 5 0.4711 0.1647
2 3 7 0.7974 0.4078
3 7 8 1.0656 0.1131
4 1 6 2.2700 0.3041
5 4 5 0.3847 0.1541
6 1 7 2.8740 0.1402
1 1 5 1.3230 0.8183
7 5 5 -1.8738 0.6183
8 2 5 0.6408 0.4910
7 5 5 -0.5222 1.2273
END

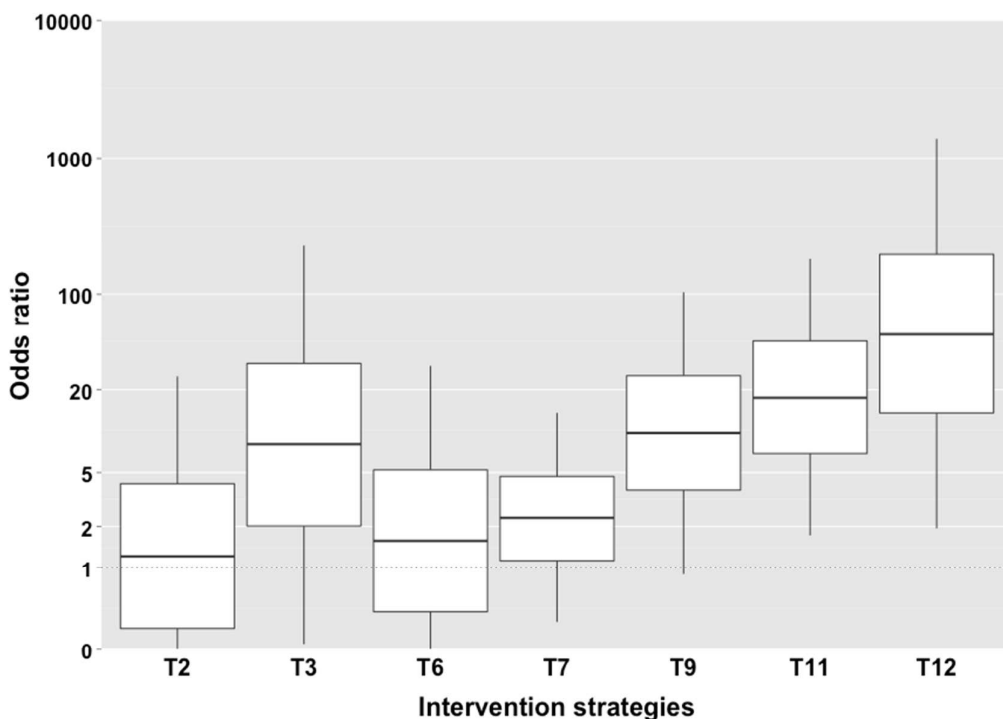
```

Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes

	Dbar	Dhat	pD	DIC
test	0.000	0.000	-0.000	0.000
y	13.817	1.222	12.595	26.412
total	13.817	1.222	12.595	26.412

Results

Box-and-whiskers plot showing relative efficacy of different hand hygiene intervention strategies compared with standard of care without the multiple time implementation studies estimated by network meta-analysis from interrupted time series studies. Lower and upper edges represent 25th and 75th percentiles from the posterior distribution; the central line represents the median. Whiskers extend to the 5th and 95th percentiles. Intervention strategies were as follows: T2-System change; T3-Education; T6-System change+Education+Feedback+Reminders; T7-WHO-5; T9-WHO-5+Incentives; T11-Incentives+Goal-setting; T12-WHO-5+Incentives+Goal-setting+Accountability.



Appendix 5: Excluded studies with reason by EPOC criteria.

No.	Authors	Year	Meet inclusion criteria	Meet EPOC criteria	Reason for exclusion ^a
1	Abela	2012	Y	N	UBA with no control
2	Aboumatar	2012	Y	N	ITS with inadequate data collection points
3	Alemagno	2010	Y	N	UBA with no control
4	Allegranzi	2010	Y	N	UBA with no control
5	Allegranzi	2013	Y	N	UBA with no control
6	Ananda-Rajah	2010	Y	N	ITS with inadequate data collection points
7	Apisarnthanarak	2010	Y	N	UBA with no control
8	Apisarnthanarak	2010	Y	N	CBA with uncomparable control
9	Ardizzone	2013	Y	N	UBA with no control
10	Barahona-Guzman	2014	Y	N	ITS with inadequate data collection points
11	Barbut	2013	Y	N	UBA for AHR use/ ITS for HAI rate
12	Barrera	2011	Y	N	ITS with inadequate data collection points
13	Bessesen	2013	Y	N	UBA with no control
14	Bingham	2010	Y	N	UBA with no control
15	Biswal	2013	Y	N	UBA with no control
16	Boog	2013	Y	N	ITS with inadequate data collection points
17	Borges	2012	Y	N	UBA with no control
18	Bouadma	2010	Y	N	UBA with no control
19	Buffet-Bataillon	2010	Y	N	UBA with no control
20	Bukhari	2011	Y	N	UBA, no baseline data
21	Caniza	2009	Y	N	UBA with no control
22	Chen	2011	Y	N	UBA with no control
23	Cheng	2010	Y	N	UBA for AHR use/ ITS for HAI rate
24	Costers	2012	Y	N	UBA with no control
25	Cumbler	2013	Y	N	ITS with inadequate data collection points
26	Davis	2010	Y	N	UBA with no control
27	de Macedo	2012	Y	N	UBA with no control
28	di Martino	2011	Y	N	UBA with no control
29	DiDiodato	2013	Y	N	UBA with no control
30	Dierssen-Sotos	2010	Y	N	UBA with no control
31	Dierssen-Sotos	2010	Y	N	UBA with no control
32	Dilek	2012	Y	N	UBA with no control
33	Dos Santos	2013	Y	N	ITS with inadequate data collection points
34	El-Kafrawy	2013	Y	N	UBA with no control
35	Eveillard	2011	Y	N	UBA with no control
36	Fakhry	2012	Y	N	UBA with no control
37	Fitzpatrick	2011	Y	N	UBA with no control

1	38	Forrester	2010	Y	N	UBA with no control
2	39	Garcia-Rodriguez	2013	Y	N	UBA with no control
3	40	Garcia-Vazquez	2011	Y	N	UBA with no control
4	41	Gill	2009	Y	N	CBA with only 1 control
5	42	Graf	2013	Y	N	UBA with no control
6	43	Grant	2011	Y	N	UBA with no control
7	44	Grayson	2011	Y	N	ITS with inadequate data collection points
8	45	Helder	2010	Y	N	UBA with no control
9	46	Helder	2012	Y	N	UBA, no baseline data
10	47	Henderson	2012	Y	N	UBA with no control
11	48	Homa	2011	Y	N	ITS with inadequate data collection points
12	49	Jaggi	2013	Y	N	UBA with no control
13	50	Jamal	2012	Y	N	ITS with inadequate data collection points
14	51	Jeong	2013	Y	N	UBA with no control
15	52	Kanj	2013	Y	N	UBA with no control
16	53	KelcÃkova	2012	Y	N	UBA, no baseline data
17	54	Kim	2013	Y	N	UBA with no control
18	55	Kindness	2010	Y	N	UBA, no baseline data
19	56	Kowitt	2013	Y	N	ITS with inadequate data collection points
20	57	Langston	2011	Y	N	UBA with no control
21	58	Leblebicioglu	2013	Y	N	UBA with no control
22	59	Leblebicioglu	2013	Y	N	UBA with no control
23	60	Levchenko	2011	Y	N	UBA with no control
24	61	Linam	2011	Y	N	UBA with no control
25	62	Ling	2012	Y	N	UBA with no control
26	63	Lobo	2010	Y	N	UBA with no control
27	64	Marra	2013	Y	N	UBA, no baseline data
28	65	Mathai	2011	Y	N	UBA with no control
29	66	Mazi	2013	Y	N	ITS with inadequate data collection points
30	67	Molina-Cabrillana	2010	Y	N	UBA with no control
31	68	Monistrol	2012	Y	N	UBA with no control
32	69	Monistrol	2013	Y	N	UBA with no control
33	70	Mukerji	2013	Y	N	UBA with no control
34	71	Pontivivo	2012	Y	N	ITS with inadequate data collection points
35	72	Prospero	2010	Y	N	UBA with no control
36	73	Rahim	2009	Y	N	UBA with no control
37	74	Rees	2013	Y	N	ITS with inadequate data collection points
38	75	Reichardt	2014	Y	N	UBA with no control
39	76	Rello	2013	Y	N	UBA with no control
40	77	Roberts	2012	Y	N	ITS with inadequate data collection points
41	78	Rogers	2010	Y	N	UBA with no control
42	79	Rosenthal	2010	Y	N	UBA with no control
43	80	Rosenthal	2013	Y	N	UBA with no control
44	81	Rosenthal	2012	Y	N	UBA with no control
45	82	Rosenthal	2012	Y	N	UBA with no control
46	83	Rosenthal	2012	Y	N	UBA with no control

1	84	Rosenthal	2012	Y	N	UBA with no control
2	85	Sahud	2012	Y	N	ITS with inadequate data
3						collection points
4	86	Saint	2009	Y	N	UBA with no control
5	87	Salama	2013	Y	N	UBA with no control
6	88	Santos	2013	Y	N	UBA with no control
7	89	Saramma	2011	Y	N	UBA with no control
8	90	Scheithauer	2012	Y	N	UBA, no baseline data
9	91	Scheithauer	2013	Y	N	UBA with no control
10	92	Scheithauer	2013	Y	N	UBA with no control
11	93	Scheithauer	2013	Y	N	UBA with no control
12	94	Seirafian	2013	Y	N	UBA with no control
13	95	Seto	2013	Y	N	ITS with inadequate data
14						collection points
15	96	Simmons	2013	Y	N	UBA with no control
16	97	Son	2011	Y	N	UBA with no control
17	98	Song	2013	Y	N	ITS with inadequate data
18						collection points
19	99	Tromp	2012	Y	N	UBA with no control
20	100	van den Hoogen	2011	Y	N	UBA with no control

^aUBA; uncontrolled before and after study, CBA; controlled before and after study, ITS; interrupted time series study, AHR; alcohol based hand rub, and HAI; healthcare associated infection.

Appendix 6: Details of extracted intervention components and level of information on resource use.

Author (year)	Study design	1.System Change	2.Education & Training	3.Feedback	4.Reminders	5.Institutional safety climate	6.Others including Goal-setting, Incentives, and Accountability	Control/Baseline intervention	Level of information on resources use
Fuller (2012)	CRCT	Not done but available as part of the national campaign	Not done but available as part of the national campaign	Observation and feedback by "Ward Coordinator" performed one repeating 4-week cycle. The tasks were hand hygiene observation of an individual health care worker, and immediate feedback as well as preparing an action plan to feed back at a ward meeting. Training program for observers is required (Total 62 training visits, 1 to 1.5 hour)	Not done but available as part of the national campaign	Not done but available as part of the national campaign	Goal-setting: Ward coordinators were asked to fill out a form to record, observations, feedback, goals and action plans.	National "Cleanyourhands" campaign as routine practice (similar to WHO-5)	M
Huis (2013)	CRCT	Adequate product and facilities	Education for improving relevant knowledge and skills. Distribution of educational material/written information about hand hygiene Website	Feedback Bar charts of hand hygiene rates	Reminders Distribution of posters replace every 12 weeks Interviews and messages in newsletters or hospital magazines General reminders by opinion leaders/ward management	Gaining active commitment and initiative of ward manager. Modelling by informal leaders at the ward; demonstrating good hand hygiene behavior, instructing and stimulating their colleagues	Goal-setting: Setting norms and targets within the team Three interactive team sessions (1–1.5 hour each) Analysis of barriers and facilitators to determine how nurses could best adapt their behaviour in order to reach their goal Nurses address each other in case of undesirable hand hygiene behavior All managers received a 4-hr training before the start of the intervention	State of the art strategy (SAS) implemented intervention 1 to 4	H
Mertz (2010)	CRCT	Sink and AHR dispensers were available	Small group teaching seminars	Meeting of clinical manager and staff on the intervention units and the later meeting provide the specific performance feedback (biweekly meeting for 6 months)	Posters and pamphlets	Not done	Not done	System change was done Sink and AHR dispensers were available before the intervention period in both control and intervention arm	M
Huang (2002)	CRCT	Not done	Educational intervention (Universal precaution training) provided by 3 trained investigator: including a) a 2-hr lecture, b) a 1-hr demonstration, and c) 30 min discussion	Not done	Not done	Not done	Not done	No intervention but received training after the study finished	M
Fisher (2013)	RCT	AHR dispensers and basins were available at point of care	Not done	Quantified individual feedback by receiving confidential and weekly written feedback reports of hand hygiene compliance	Real-time reminders (audible beeps) using a wireless hand hygiene monitoring system	Not done	Not done	AHR dispensers and basins were available at point of care	M

1	Salamati (2013)	RCT	AHR dispensers and basin were available at point of care	Hand hygiene education was performed by an infection control nurse via a 2 hours lecture; the lecture session was repeated a few times in such a way as to cover all the personnel working in different shifts.	Motivational Interview; five sessions of interviewing with maximum of 15 participants for 90 minutes.	Not done	Not done	Not done	AHR dispensers were available at point of care Hand hygiene education	M
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7	Derde (2014)	ITS	Not done	Education sessions	Direct feedback after observation and Monthly feedback of local compliance rates is provided to wards to guide the content of each local hand hygiene program.	Visual reminders (no details)	Not done	Not done	Reminder as posters	L
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11	Lee (2013)	ITS	AHR at point of care	Training and education of healthcare worker	Observation and feedback of hand hygiene practices	Reminders in the workplace (e.g. posters)	Improving the safety climate in the institution with management support for the initiative	Not done	One unit was no intervention and another unit was system change changing AHR formulation. The other two were WHO-5.	L
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15	Marra (2013)	ITS	Positive deviance (PD)* group incorporated in changing the position of AHR dispensers, recommending a change in the pressure of the tap water and added the dispensers in the corridors. *PDs were defined as those HCWs who wanted to change, to think, to develop new ideas for improving HH and who stimulated other HCWs.	Positive Deviants (PD) meeting with all HCWs twice monthly The hospital PD coordinators provided PD training for all HCWs including nurses, physicians, physical therapists, speech pathologists, and nutritionists who used the dispensers and provided the opportunities to express feelings about hand hygiene.	PDs showed the HHC% and discussed their performance in every meeting.	Some ideas and strategies were related to the reminders such as preparing badges for doctors who perform HH and noting them as examples and preparing a short theater presentation discussing "My 5 Moments for Hand Hygiene" with their peers.	PD initiated engaging people to involve by inviting another PD in the next meeting	Not done	No intervention (but the AHR was available)	M
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29	Al-Tawfiq (2013)	ITS	Increase availability of hand sanitizers (AHR)	Education Formation of hand hygiene compliance team Educational presentations	Feedback Posting data on intranet Compliance criteria shared with health care professionals Inclusion in dashboard with goal-setting Devotion of activity to low performing units Face-to-face feedback during weekly tracer rounds Frequent audit and feedback and discussed the feedback findings with each unit supervisor and fostering ways to improve	Promotion Flashing pins "Wash your hands stay healthy" Ask me "have you washed your hands" pins Hand hygiene banners throughout the organization Magnetic door posters promoting hand hygiene	Leadership commitment Senior leadership engagement included monthly tracking of the compliance rates and communicating to management and hospital staff during monthly meeting and through the dashboard	Goal-setting: Setting compliance goals Increased the stated goal to 75% Increased the goal to 85%	No intervention (but the AHR was available)	M
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1	Armellino (2013)	ITS	Not done	Not done	Feedback metrics tabulated by a central server database delivered back to the HCWs through electronic light emitting diode boards, electronic mail summaries, and weekly performance reports.	Not done	Not done	24 video cameras and motion sensors at handwashing sinks and sanitizer dispensers to record hand hygiene opportunities Goal-setting: Setting the targeted compliance as >=95%	Video cameras were installed during baseline period as well but without feedback.	M
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6	Armellino (2012)	ITS	Not done	Not done	Feedback metrics tabulated by a central server database delivered back to the HCWs through electronic light emitting diode boards, electronic mail summaries, and weekly performance reports.	Not done	Not done	24 video cameras and motion sensors at hand washing sinks and sanitizer dispensers to record hand hygiene opportunities Goal-setting: Setting the targeted compliance as >=95%	Video cameras were installed during baseline period as well but without feedback.	M
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11	Chan (2013)	ITS	38 AHR dispensers were installed and changed the location	Not done	Not done	Not done	Not done	Not done	No intervention (but the AHR was available)	M
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15	Crews (2013)	ITS	More than 900 wall dispensers were installed and substituted with new alcohol-based hand rubs.	Annual educational training for clinical staff including physician and hospital staff	Routine feedback to HCWs	Marketing committee launched a campaign that emphasized branding hand hygiene with a positive image. Slogan and child-friendly posters and signs with the message were displayed at strategic locations. Additional items containing the message, including pens, buttons, calendars, and coloring books, were widely distributed.	Not done	Goal-setting: Hand hygiene goal added to employee Three goals related to quality or patient safety Reward incentives: If the goals are achieved, every employee receives a financial reward.	Multiple unit-based educational initiatives and use of a gel-based alcohol hand rub	M
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24	Salmon (2013)	ITS	Not done	Hand hygiene auditor training program based on the WHO "My 5 moments for hand hygiene" in the orientation program for final year nursing students, 1- hour session including lecture and practical auditing using WHO video tools and 398 nursing students from 3 nursing schools involved.	Not done	Not done	Not done	Not done	No intervention/routine practice	M
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33	Talbot (2013)	ITS; Phase I	As part of the bundle of readiness assessment and planning program	Expanded HH direct observation program Observation program was expanded to include all inpatient and outpatient locations. The observers attended required training on a standardized observation methodology	Readiness assessment and planning The project bundle focused planners on addressing the following: defining the problem, ensuring project alignment with the organization's mission, securing financial support, defining performance and measurement objectives, and establishing leadership commitment.	System-wide marketing campaign Poster messaging and targeted talks aimed to increase HH awareness and its importance in preventing HAIs.	Leadership goal-setting Improved HH adherence was adopted as an institutional quality improvement goal and the performance related to the goal immediately became a factor in annual performance evaluations and incentive compensation for medical center leaders.	Goal-setting: Modest HH adherence goals were set in the first year of the program (adherence of 65% as a threshold goal, 75% as a target goal, and 85% as a reach goal) with the intent of increasing performance requirements each year. Reward incentive: Financial incentives via a self-insurance trust allocation rebate program. The component of the allocation rebate was worth up to 25% of the total rebate	Phase I: Hand hygiene annual faculty and staff training	M
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							dollars (2.5% of yearly premiums). For example, for a physician whose yearly premium was \$10,000.00, the rebate amounted to \$250.00.		
	Phase II	Same as Phase I above	Same as Phase I above	Same as Phase I above	Same as Phase I above	Hand Hygiene executive committee The committee consisted of key physician and nursing leaders was established to review location performance monthly and direct interventions.	Goal-setting and Reward incentive Same as Phase II above, a follow-up campaign Location-specific accountability interventions Units with low adherence were identified for interventions on the basis of a system-wide hand hygiene intervention pyramid. Structured individual accountability interventions Observers provided direct feedback when a hand hygiene opportunity was missed. System leadership monitored event reporting and acted as necessary, consistent with organizational policies concerning behaviors that undermine a culture of safety.	Phase II: Intervention Implemented in Phase I.	
Higgins (2013)	ITS	Increased supplies of hand AHR, dispenser at bedside.	Adenosine triphosphate (ATP) monitoring system, a mobile stand-alone computer system, was purchased and used in the clinical area during spot audits and also at regular intervals outside the staff canteen to measure handwashing technique. HCWs were selected at random and asked to wash their hands with soap and water. Once the hands were completely dry, the swab was rubbed against the tips of each finger, in between each finger and then in an S-shape along the palm of one hand.	Monthly hand hygiene audit and verbal feedback provided directly to staff during the audits.	Posters displaying hand hygiene technique and information of "WHO 5 moments" placed at the key area of the hospital. Advertising campaign was carried out in the hospital through e-mails and general hospital mail. An information leaflet was designed and copies were left in the canteen, at nurses' stations, in staff meeting rooms etc.	Commitment from management, hand hygiene audit results were provided to the hospital executive team and board.	Reward incentive: Fob watches were provided as spot prizes	No intervention (but the AHR was available)	M

1	Helder (2012)	ITS	Not done	Not done	Not done	Screen servers for 6 computer screens, 2 per unit, were involved to emphasize the need for improved adherence to hand hygiene protocols and were designed according to theoretical principles of message framing. The messages on the screen servers were replaced by a newly designed 2-screen series every 2 weeks.	Not done	Not done	AHR dispensers were available at point of care. However, five months before the study present, a multidisciplinary infection prevention education program was organized.	M
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10	Kirkland (2012)	ITS	Optimised availability of hand sanitiser	Education and training Developed electronic learning module and training video that provided hand hygiene education for all staff. It was accessible through the hospital intranet. A 'certification' program was also available by which staff demonstrated HH competency.	Measurement and feedback Routine HH audits Monthly unit specific data published on an intranet site available to all staff, and reported to executive leadership, clinical leaders and board members	Marketing and communication Marketing staff created a series of posters and screen savers, stories in medical center publications and local news outlets, and direct communication with staff about expectations and progress towards goals.	Leadership and accountability Leadership publicly emphasised the importance of hand hygiene	Not done	No intervention (but the AHR was available)	M
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18	Morgan (2012)	ITS	Installed multiple automated, networked, touch free AHR and soap dispensing units at the entrance to each room and the sink in each room	Infection control and research staff monthly visited each unit to present the poster, remind staff about the importance of hand hygiene, and answer any questions about the study. The WHO 5 Moments for Hand Hygiene were discussed in training.	Feedback compliance was provided for entry and exit based on human observation.	Two posters in each unit to display unit-specific monthly and quarterly hand hygiene compliance rate also included infection control reminders to link hand hygiene with infection prevention (e.g. unit infection rates, photos of unit staff performing hand hygiene, general HAI education)	Not done	Not done	No intervention (but the AHR was available)	M
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26	Stone (2012)	ITS	Alcohol hand rub at bedside	Not done	Regular audit and feedback of compliance	Posters reminding HCWs to clean their hands	Empowering patients to remind HCWs	Not done	No intervention/routine practice	L
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28	Jaggi (2012)	ITS	Not clear	Not clear	Not clear	Not clear	Not clear	Identify key area of improvement	No intervention/routine practice	L
29								Training for a bundle of prevention		
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34	Lee (2012)	ITS	Dispenser installation and Pocket-sized containers provided	All HCWs received continuing education and pre-service education on hand hygiene issues by experienced infection control nurses (ICN)	Monitoring and feedback of hand hygiene compliance monthly by infection control nurses	Posters	Not done	HCWs were encouraged to educate their patients and families about proper hand hygiene.	No intervention/routine practice	L
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1	Mestre (2012)	ITS	AHRs were placed at all bedsides on high risk areas (ER, ICUs)	Theoretical and practical workshop to all HCWs and practical sessions	Audit by a hand hygiene monitor team 8 HCWs direct observation with 2 evaluation periods and 25 days of monitoring Feedback through informal interactive session on every ward at the end of evaluation periods (2 sessions)	Posters and handout, replaced monthly	Commitment by administrative and nursing director	Not done	Phase I: No intervention/routine practice Promotion of hand hygiene such as staff education, reminders, and six months hand hygiene audit was performed during baseline period but it was neither structured nor sustained on time.	H
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10			AHRs were placed at all bedsides in conventional wards while maintaining those at corridors.	Maintain as above	Audit by a hand hygiene monitor team 8 HCWs carried out direct observation with 17 evaluation periods and 51 days of monitoring. 3 randomized days every 3 weeks ("3/3 strategy") Feedback using control charts on every ward at institutional and individual level.	Maintain as above	Maintain as above Corrective actions: Modification of incorrect HH habits, clarification of doubts and positive reinforcement were conducted	Not done	Phase II: Intervention Implemented in Phase I.	H
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18	Koff (2011)	ITS	Not done	A personalized hand hygiene device was worn by HCWs used for recording the frequency of hand disinfection event.	Feedback was provided to both individuals and the entire group.	Not done	Not done	Not done	Wall-mounted dispensers were installed	M
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23	Doron (2011)	ITS	Hand-sanitizer dispensers provided in all public non-patient care areas	Educational program; online teaching, grand rounds lectures and nurses	Close observation with feedback	Promoting campaign by email to introduce the campaign to employees Posters; large size to introduce to patients and families, small size for the walls in various places) Handout for new patients Stickers and pins with positive and humorous messages A private advertising firm was contracted to develop a professional marketing campaign for the hospital.	Leadership commitment Chief medical officer and CEO spoke about HH at every given opportunity Heads of department and ICU directors were asked to make hand hygiene an educational priority and to personally carry out hand hygiene observation	Not done	During 2007 to July 2008 (baseline period), intervention component 1 to 4, including placement of hand sanitizers, reminder signs, education, and feedback with observed compliance, was implemented but reinforced with a new strategy together with component 5 during the intervention period.	M
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Marra (2010, 2011)	ITS	Changing the position of alcohol gel dispensers in the patient rooms and to put more in the corridors.	Positive deviants (PD) meeting with all SDU HCWs twice monthly, 1.5 hour each, attendance about 35-40 to discuss and provide training for all HCWs including nurses, physicians, physical therapists, speech pathologists, and nutritionists who used the dispensers and provide the opportunities to express feelings about hand hygiene.	PD showed the hand hygiene compliance and discussed their performance in every meeting.	Incorporated laminated sheets on "My Five Moments for Hand Hygiene" as the first page in all of SDU patient medical records.	PD initiated engaging people to involve by inviting another PD in the next meeting	Not done	No intervention (but the AHR was available)	M
Yngstrom (2011)	ITS	Alcohol hand disinfection at every bed together with pictures and posters, and instruction.	Meeting monthly (reporting, evaluation, feedback and discussion) and continuous education program (Department level)	Feedback of hand hygiene performance during the meeting	Not done	Not done	Goal-setting: The goal was a 40% reduction in healthcare associated infections in ventilated patients. Process objective The process objective was 100% of staff to implement basic hygiene routines.	No intervention (but the AHR was available)	L
Helms (2010)	ITS	Alcohol foam dispenser installed both inside and outside patients room. Pocket-sized container for all staff Hand sanitizing station in the main lobby, emergency lobby and waiting rooms	Aggressive education program Implementation of "You bugged me" program, staff member presenting another employee with a card if they witnessed them not washing their hand properly. The infection control coordinator attended all the staff meeting in all departments and provided educations on proper hand hygiene technique. One part of the program is the use of the fluorescent lotion to see effects of handwashing	Direct feedback when staffs forget to perform hand hygiene via "You bugged me" program.	Signs to remind the staff to wash their hands. Flyers to educate patients' visitors The patients were educated on admission to remind the staff to wash their hands.	Chief executive Officer (CEO) and Chief Nurse Officer (CNO) involved in activity for the penalty of non compliance	Not done	No intervention (but the AHR was available)	M
Chou (2010)	ITS	Adding AHR dispensers in each patient room installed in all public area including outpatient clinics	Enhanced educational material includes added interactive demonstration "fluorescent germs" and bacterial cultures of hands before and after hand hygiene to hospital-wide educational programs to impress the important of hand hygiene and posters contest	Hand hygiene liaison (at least one staff each department) responsible for review in HH policy, ensuring availability of HH product, observing HH at least 20 opp. each month) Feedback in hand hygiene compliance	Posters from the contest displayed in the key areas.	Hospital wide support; the bundle of this intervention was introduced to hospital administration for their support and approval and presented to multiple leadership committees consisting of physicians, nursing directors and managers and other leaders A violation letter was sent to managerial personnel of noncompliant individuals to take corrective action with violators.	Goal-setting and Reward incentive: Nursing units were rewarded with pizza parties if they achieved and sustained the targeted hand hygiene compliance.	No intervention (but the AHR was available)	M

1 2 3 4 5 6 7 8 9 10 11 12	Vernaz (2008)	ITS	Pocket-sized containers using AHR were available during baseline and intervention)	Not clear	Not clear	Not clear	Not clear	Spring 2003: Applying social marketing theory to promote standard precautions and isolation precautions mentioned hand hygiene as an element of standard precautions (did not target the promotion of AHR in particular) Autumn 2005: Swiss national hand hygiene promotion campaign and the global patient safety challenge entitled 'Clean your hand is safer care' with an exclusive focus on the frequent and proper of AHR.	Pocket-sized bottles for AHR were provided.	L
13 14 15 16 17 18 19 20 21 22	Whitby (2008)	ITS 1) Washing ton campaign	AHR placed at the end of each bed, chart trolleys and in medication preparation areas. Liquid soap provided at handwashing basin. (Pre intervention: 1 month)	Pre intervention: 4 months A series of meetings led by seniors and attended by all clinical and non-clinical staff Intervention phase 1: 2 months Informal lectures by the project nurses	Intervention phase 1: 2 months Staff developed talking-wall promotional cartoons with prizes awarded and the additional cartoons developed by an external artist.	Intervention phase 1: 2 months Information in accordance with CDC's guidelines was provided via pay slips	Intervention phase 2: 3 months "Walk-arounds" by executive medical and nursing members and photograph of senior staff with speech balloons at each ward in the last month	Large photographs of the hospital executive were positioned throughout the wards	No intervention (but the AHR was available)	M
23 24 25 26 27 28 29 30 31		2) Geneva campaign	AHR placed at the end of each bed, chart trolleys and in medication preparation areas. Liquid soap provided at handwashing basin. (Pre intervention: 1 month)	Pre intervention: 5 months Clinician-led meetings, semi-structured format all clinical and non-clinical staff	Not done	Intervention phase 1: 2 months Posters and Screen savers	Intervention phase 2: 5 months "Walk-arounds" by executive medical and nursing members AND Photograph of senior staff with speech balloons at each ward in the last month	Not done	No intervention (but the AHR was available)	
32 33 34 35 36 37 38 39 40		3) AHR substitution	AHR placed at the end of each bed, chart trolleys and in medication preparation areas. Liquid soap provided at handwashing basin. (Pre intervention: 1 month) (Pre intervention: 4-5 months)	Not done	Not done	Not done	Not done	Not done	No intervention (but the AHR was available)	

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Mayer (2011)	CCT	Positioning dispensers of alcohol sanitizer in convenient locations	Education program providing standardized unit in-service presentations prepared by infection preventionist, the hospital epidemiologist, physician groups, and infection control personnel and clinical staff.	Ongoing audit with monthly feedback by infection preventionist	Not done	Not done	Not done	No intervention/routine practice	H
	ITS	Introduce AHR and positioning the dispensers	Education program providing standardized unit in-service presentations prepared by infection preventionist, the hospital epidemiologist, physician groups, and infection control personnel and clinical staff.	Ongoing audit with monthly feedback by infection preventionist	Posters with catchy phrases were placed throughout the hospital.	Monthly meeting of a hand hygiene committee comprising infection preventionists, nurse managers, service directors and hospital epidemiologist to encourage staff involvement and to provide unit specific feedback.	Reward incentive: through "Positive reinforcement" The hand hygiene committee generated new motivational campaign themes to maintain interest. An example of a group motivator theme was the "War on Germs" to encourage unit teamwork. Publicizing that the unit with the best hand hygiene compliance would win a pizza party Individual incentives theme, in which individuals who were caught in the act of performing hand hygiene were entered into monthly drawings to win prizes.	No intervention/routine practice	
Harne-Britner (2011)	CCT	Not done	Hand washing self-study module and additional education sessions about microorganisms	Not done	Posters (bugs and agar plates) placed and rotated the location	Not done	Not done	Hand washing self-study module	M
		Not done	Hand washing self-study module	Not done	Not done	Not done	Goal-setting and Reward incentive: hand hygiene adherence goal and reward with pizza party. Unit-based recognition by peers on a sticker poster and rewarding some incentives, e.g. movie ticket, gift card, unit recognition and pizza party.	Hand washing self-study module	
Benning (2011)	CBA	Make AHR available at the bedside	Not done	Not done	Posters on wards updated monthly	Encouraged patients to ask staff to clean their hands	Not done	Control: no intervention but "cleanyourhands" campaign implemented during 2004-2005 (in both groups)	L
Gould and Chamberlain (1997)	CBA	Not done	Educational program by experienced nurse teachers with specific expertise (5 different sessions, 30 min each)	Not done	Not done	Not done	Not done	No intervention/routine practice	M

* AHR: alcohol based hand rub, CRCT: cluster randomised controlled trial, RCT: randomised controlled trial, ITS: Interrupted time series study, CCT: controlled clinical trial, CBA: controlled before and after study.

Appendix 7: Reasons for exclusion from network meta-analysis.

4 studies were excluded from the network meta-analysis. The reasons were:

- i.) Conducted in only nursing students (Salmon 2013)
- ii.) Hand hygiene intervention and control period unclear (Jaggi 2012)
- iii.) Reporting compliance only at entry and exit from the patients room (Armellino 2012, 2013)

Salmon S, Wang XB, Seetoh T, Lee SY, Fisher DA. A novel approach to improve hand hygiene compliance of student nurses. *Antimicrob Resist Infect Control* 2013;2:16.

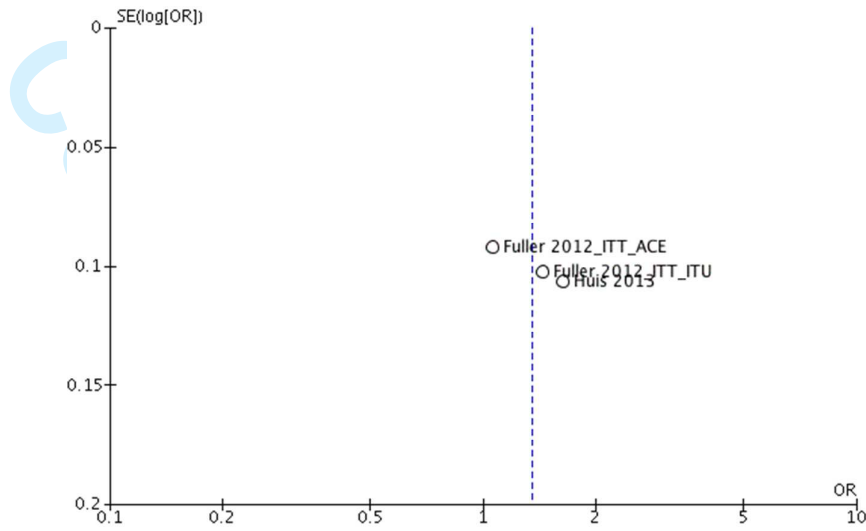
Jaggi N, Sissodia P. Multimodal supervision programme to reduce catheter associated urinary tract infections and its analysis to enable focus on labour and cost effective infection control measures in a tertiary care hospital in India. *J Clin Diagn Res* 2012;6:1372-76.

Armellino D, Trivedi M, Law I, Singh N, Schilling M, Hussain E, et al. Replicating changes in hand hygiene in a surgical intensive care unit with remote video auditing and feedback. *Am J of Inf Control* 2013;41:925-27.

Armellino D, Hussian E, Schilling ME, Senicola W, Eichorn A, Dlugacz Y, et al. Using high-technology to enforce low-technology safety measures: the use of third-party remote video auditing and real-time feedback in healthcare. *Clin Infect Dis* 2012;54:1-7.

Appendix 8: Funnel plots

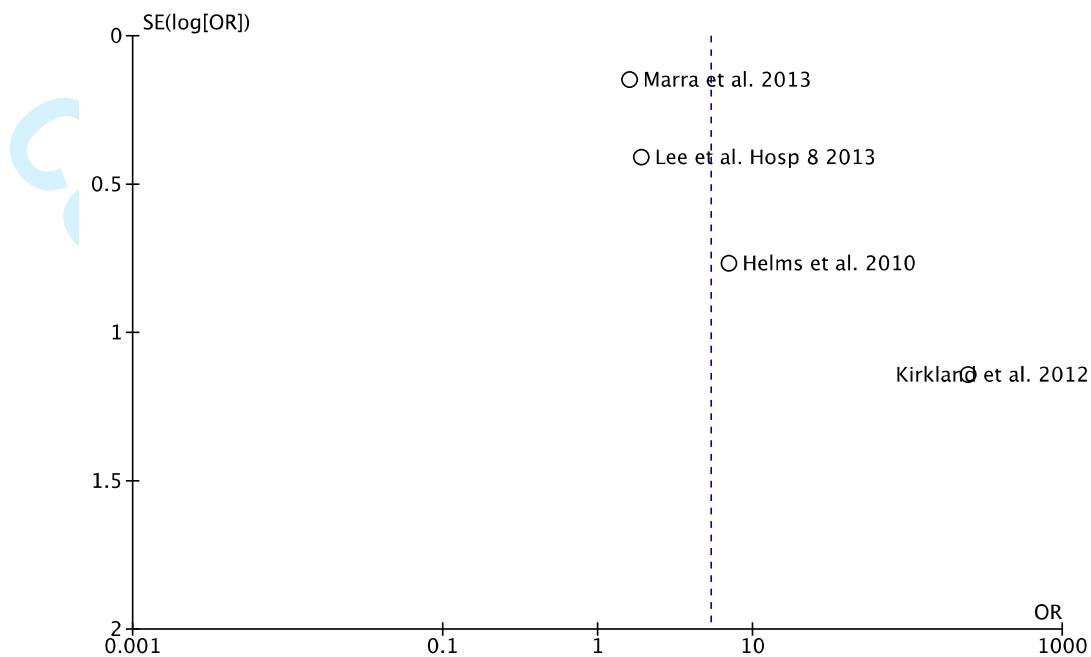
Funnel plots of RCT studies, WHO5 VS WHO5+GOAL
Random effects model



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Funnel plot of ITS studies, no intervention compared to WHO5
Random effects model



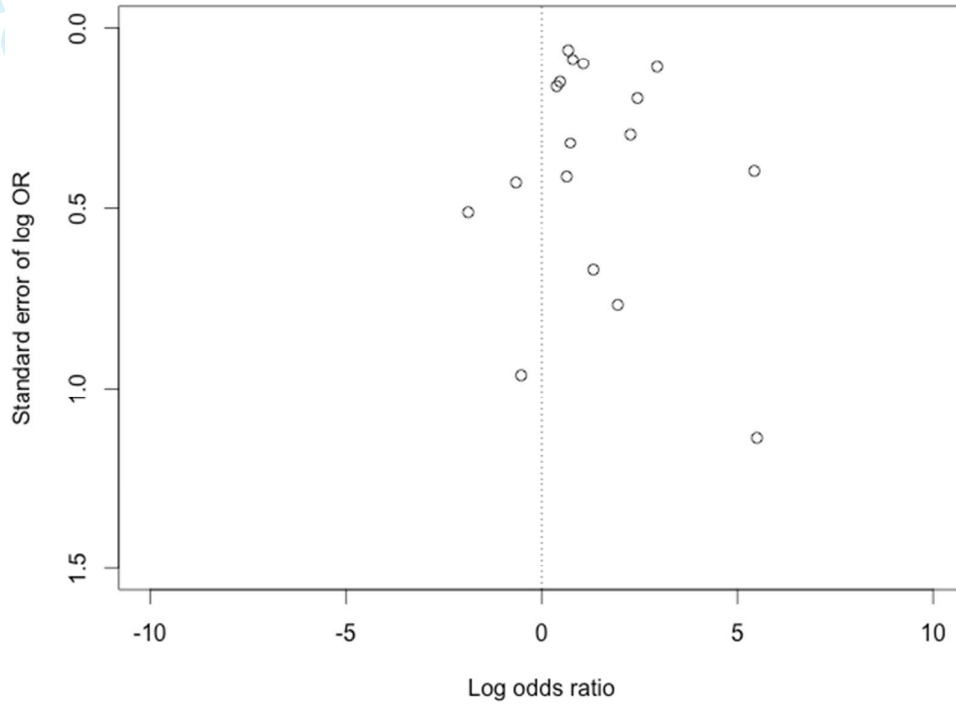
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Funnel plot of all ITS studies

Random effects model



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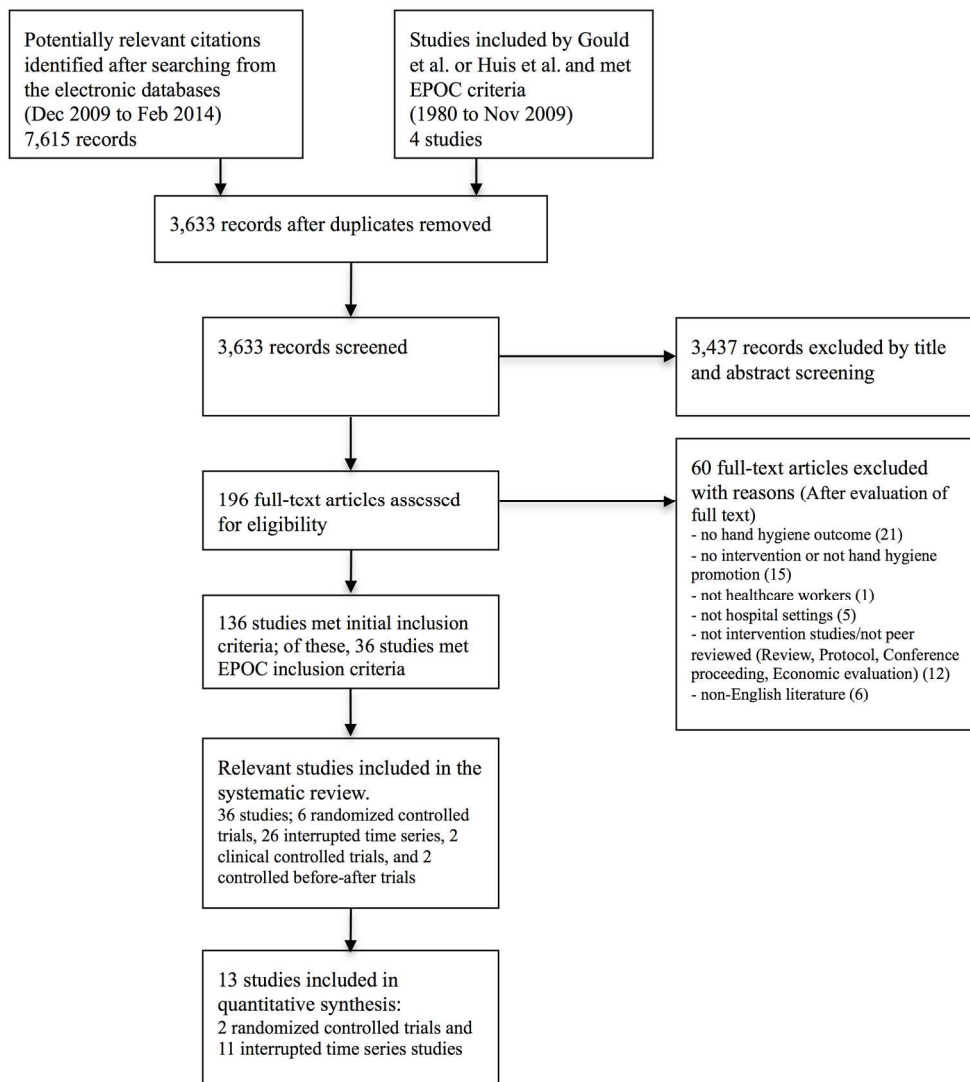


Figure 1: Systematic review flow chart
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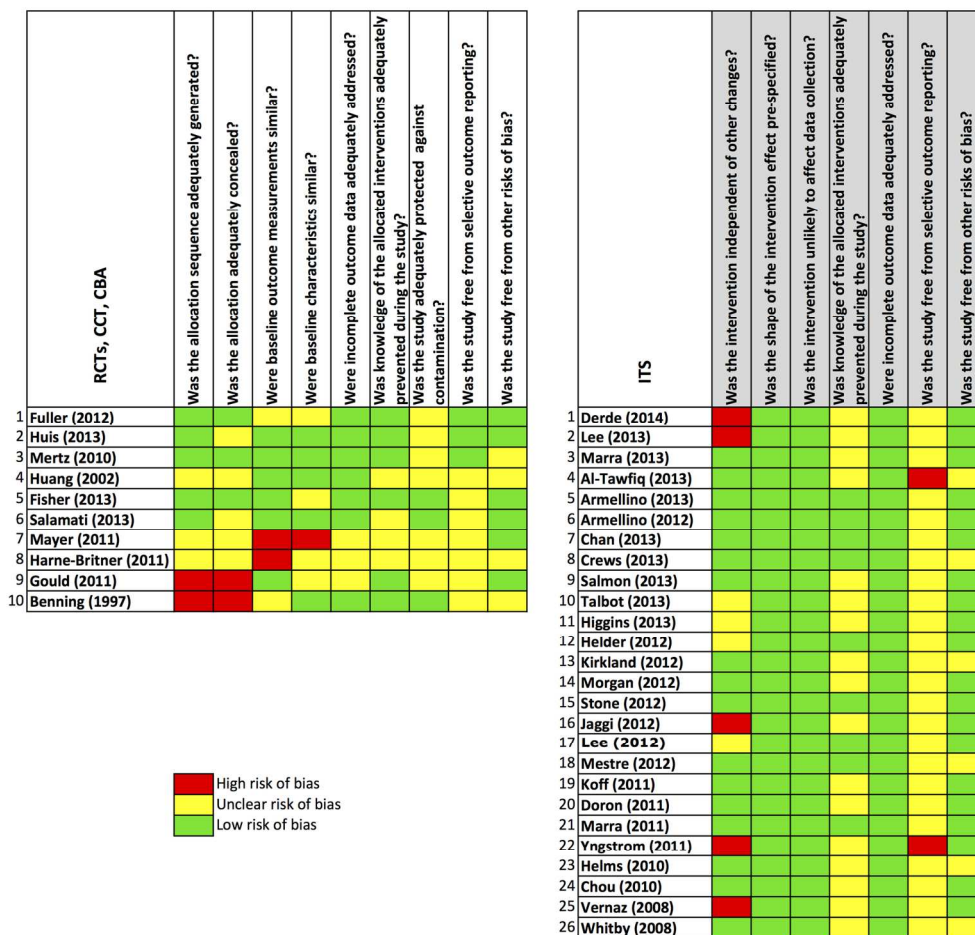


Figure 2: Assessment of risk of bias in all included studies.
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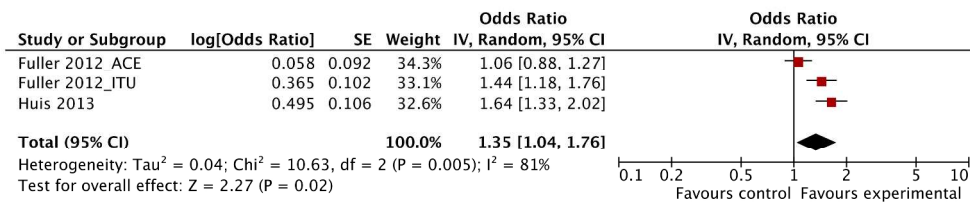


Figure 3: Forest plot of the associations between WHO-5 and goal-setting compared with WHO-5 alone and hand hygiene compliance from RCTs

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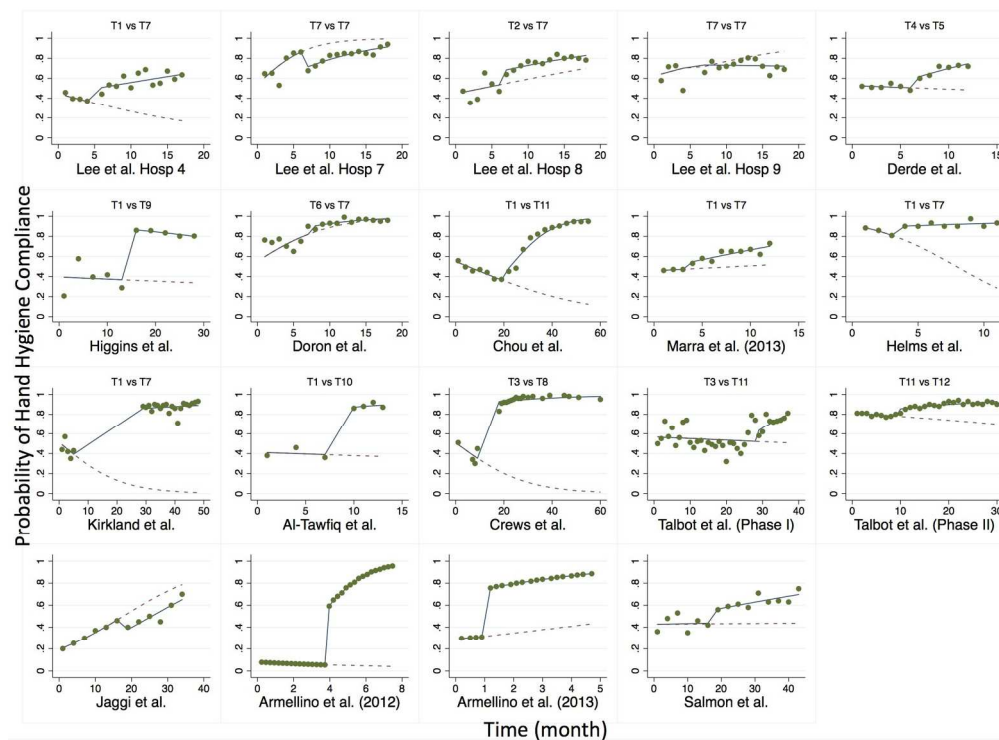


Figure 4: Re-analysis of studies involving interrupted time series where the outcome was hand hygiene compliance. Points represent observations, solid lines show expected values from fitted segmented regression models, and broken lines represent extrapolated pre-intervention trends.

*The last four studies (Jaggi et al., Armellino et al. (2012), Armellino et al. (2013), and Salmon et al.) were not eligible for the network meta-analysis.

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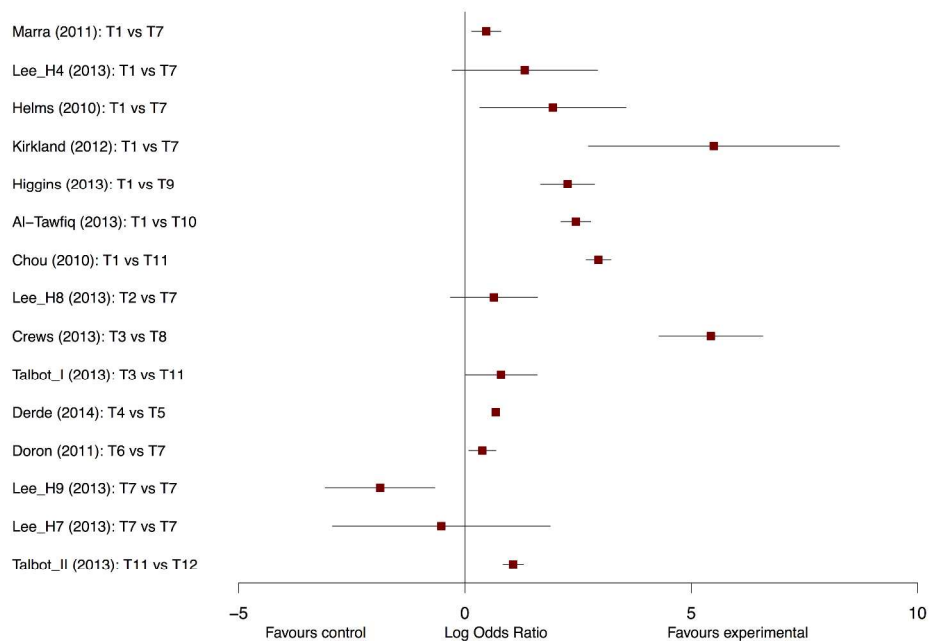


Figure 5: Forest plot showing the effect size as mean log odds ratios for hand hygiene compliance for all direct pair-wise comparisons from interrupted time series studies. Note that Lee H4, Lee H7, Lee H8, and Lee H9 all come from a multi-centre study. In two of the hospitals (H7 and H9) the baseline strategy was already equivalent to WHO-5

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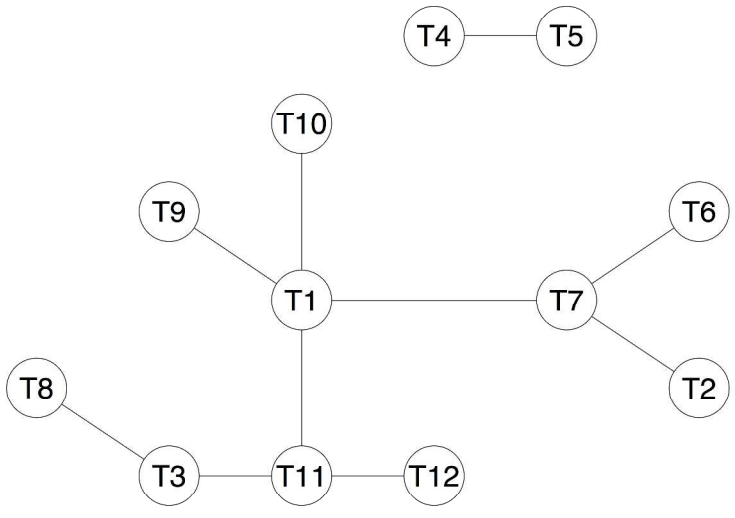


Figure 6: Network structure of indirect treatment comparison of 12 different hand hygiene intervention strategies from interrupted time series studies.
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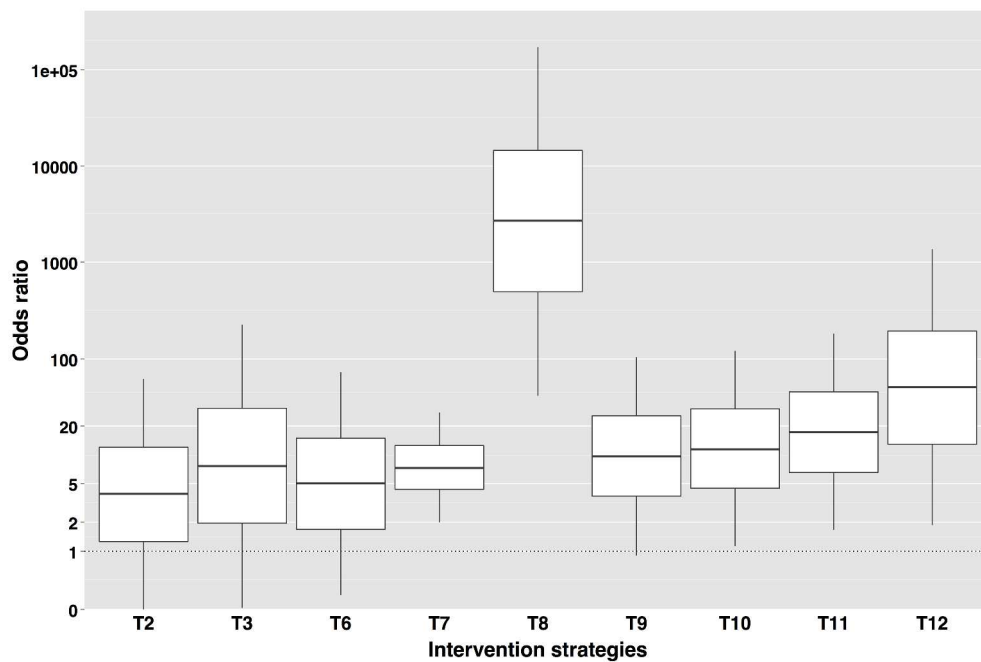


Figure 7: Box-and-whiskers plot showing relative efficacy of different hand hygiene intervention strategies compared with standard of care estimated by network meta-analysis from interrupted time series studies. Lower and upper edges represent 25th and 75th percentiles from the posterior distribution; the central line represents the median. Whiskers extend to the 5th and 95th percentiles. Intervention strategies were as follows: T2-System change; T3-Education; T6-System change+Education+Feedback+Reminders; T7-WHO-5; T8-System change+Education+Feedback+Incentives+Goal-setting; T9-WHO-5+Incentives; T10-WHO-5+Goal-setting; T11-Incentives+Goal-setting; T12-WHO-5+Incentives+Goal-setting+Accountability.
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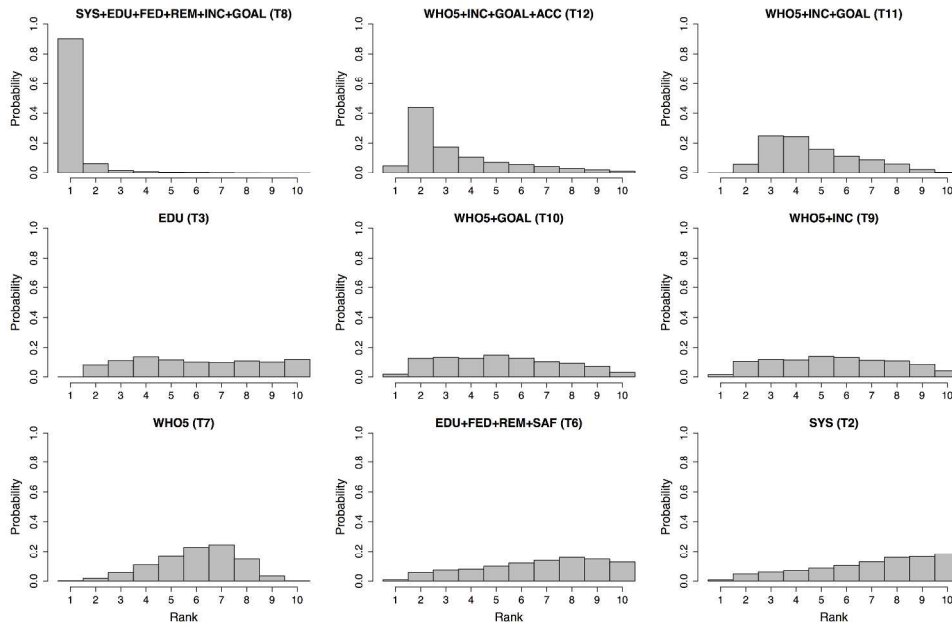


Figure 8: Rankograms showing the probabilities of possible rankings for each intervention strategy (rank 1=best, rank 10=worst).
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