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Do the quality of the trials and the year of publication affect the efficacy of intervention to improve seasonal influenza vaccination among healthcare workers?

Results of a systematic review

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Introduction: Despite longstanding recommendations by public-health authorities vaccination coverage in health care workers worldwide are poor. The aim of this study is to conduct a systematic review of the trials conducted to increase seasonal influenza vaccination rates among health care workers.

Results: 10 articles met the pre-determined criteria. For all article the score calculation was performed.

Discussion: The combination of an educational and a promotional element appared the most effective in augmenting the influenza vaccination coverage among health care workers. But some cases, the intervention did not contribute to increasing the vaccination rates among health care workers. In any case, the quality of controlled trials plays an important role in the results obtained by carrying out a specific intervention and contributed to obtaining this debatable results.

Materials and Methods: Research was conducted using Scopus and PubMed database. We selected all clinical trials to perform the meta-analyses.

Introduction

The most efficient means of preventing a significant number of influenza infections, and the resulting morbidity and mortality, is an annual pre-exposure vaccination. Simply staying home from work when manifestly ill is not effective as a strategy to prevent transmission.[1] (Poland et al., 2005) as the virus may be shed for at least 1 d prior to symptomatic illness (Bridges et al., 2003, Mc Lennan et al., 2010).[2,3]

Studies have shown that immunization of health care workers (HCW) protects their patients (Wilde et al., 1999, Hayward et al., 2006, Ito et al., 2006),[4-6] from influenza infection. In addition, vaccinating HCW can also reduce influenza-related absenteeism, ensuring the capacity of the healthcare system to meet society needs (Sartor et al., 2002).[7]

Despite longstanding recommendations by public-health authorities vaccination coverage in health care workers worldwide are very poor, with only about 4–40% coverage rates being achieved (Mc Lennan et al., 2010).[3] In Europe rarely exceeds 30% (Blank et al., 2009).[8] Rates are particularly low in nursing staff, the HCWs in closest contact with patients (Toronto et al., 2010, La Torre et al., 2011).[9,10]

As alternative to mandatory approach, that poses many questions on HCW autonomy, several public health organizations and hospitals have embarked in the endeavor entailing the increase of seasonal influenza vaccination rate among HCW by setting up interventions. Previous studies have reported the effectiveness of various campaigns in medical setting. Most were before-after studies, and fewer were randomly controlled (Abramson et al., 2010).[11]

The interventions have included educating HCWs about the benefits of influenza vaccination, making the vaccine free and easy to obtain for all HCWs, providing feedback of vaccination rates, obtaining a signed declination from HCWs who refuse vaccination, and others (Polgreen et al., 2008).[12]

The only attempt to assess the effectiveness of interventions had previously been performed by a systematic review of Lam and coworkers (2010).[13] They evaluated studies published in 2008 at the latest. However, in their study Lam et al., did not focus the attention on quality evaluation of the studies, in order to assess if quality can affects the results of interventions.

The aim of this study is to conduct a systematic review of the trials conducted to increase seasonal influenza vaccination rates among HCW, to evaluate their effectiveness and the influence of the quality and the year of publication of the studies on the outcomes. This study focuses solely on interventions aimed to increase the seasonal influenza vaccination rate or studies that reported rate before and after an intervention and excludes studies presenting results on pandemic influenza.

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Results

Identification of relevant research. In total 1,504 articles were identified in both PubMed and Scopus. Of these, 1,263 were removed because not relevant (lack of intervention, intervention concerning pandemic influenza instead of seasonal influenza, or focus diverging from health care workers). The remaining 259 articles were subjected to a screening of both the title and the abstract in the two search engines separately, and to the removal of duplicates in each database. Subsequently, 70 articles were found in the search engine PubMed and 74 were found in Scopus. The number of articles that were present in both search engines was 38, leaving 106 articles having to be assessed for eligibility. Of these 106 results, 96 were further eliminated because of an unwanted or faulty study design, because no our outcomes or because data was self-reported or missing, or because the full-text was unavailable to the university. Finally, 11 articles met the pre-determined criteria described above. A the end just one was excluded because a letter to editor and although it described the interventions aimed to increase the seasonal influenza vaccination rate including all data, there were many limit in insufficiently reported, being published as a letter.

We included in the review the trial performed by Hayward et al., 2006 although the specific context where the trial took place was different from the others.

Quality Assessment. JADAD scale was used in order to assess the quality of the 10 controlled trials.

Of the 10 articles, two investigators independently found that 6 were of good quality, while the remaining 4 were of bad quality. More specifically, 6 articles scored ≥ 3 2006,[5] Dey et al., 2001,[14] Kimura et al., 2007,[15] Abramson et al., 2010,[16] Looijmans-van den Akker et al., 2010,[17] Lemaitre 2009,[18] while the studies by Ohrt et al. (1992),[19] Doratotaj et al. (2008),[20] Rothan-Tondeur et al. 2010,[21] Tannenbaum et al. 1993,[22] were scored < 3. Please refer to **Table 1** for an overview of the selected literature.

When a study was given a score below 3, it was often because the randomization was not adequately described. Thus, potential bias could arise from such studies, specifically in the case in which randomization was not conducted properly.

Types of interventions. It is of primary importance to increase the rate of influenza vaccination among health care workers. Attempts to succeed in such an endeavor are numerous and of different nature. During the literature search, various types of interventions were encountered, ranging from educational interventions to vaccination campaigns or to more drastic measures such as the obligatory use of masks to all health care workers that were not vaccinated, or the use of mandatory declination forms when refusing vaccination. Of the 10 articles found for this systematic review, 5 made use solely of educational interventions. More specifically, the article by Rothan-Tondeur and coworkers (2010)[21] promoted influenza vaccination through a slide-show and leaflets, the study by Hayward et al. (2006)[5] made use of nurses promoting vaccination and educational leaflets, the intervention performed in the work by Abramson[16] was composed by a lecture session and by e-mails giving a brief overview of the relevant literature, Ohrt et al. (1992)[19] used an educational memorandum, and Tannenbaum et al. (1993)[22] made use of information sessions and posters. The remaining articles made use not only of educational methods, but also of alternative methods in the attempt of increasing vaccination rates among health care workers. As a matter of fact, the controlled trial performed by Looijmans-van den Akker et al. (2010)[17] entailed a multi-faceted intervention composed by posters and leaflets informing health care workers of influenza vaccination, by a plenary one-hour information meeting and by an appointment with a physician promoting vaccination.

In the studies conducted by Kimura et al. (2007)[15] and Dey et al. (2001),[14] free vaccination was offered to all health care workers, who were informed of this initiative through e-mails and posters. Finally, the studies by Kimura et al. (2007)[15] and Doratotaj et al. (2008)[20] were composed of three intervention groups. In the former study, in addition to an educational intervention entailing a 10 min video, leaflets, posters and flyers, a vaccination day was set up in which health care workers were given the opportunity to get vaccinated free of charge against influenza. Thus, one intervention group received the educational intervention, the second one was subject to the vaccination day, and the third group had both the educational intervention and the vaccination day. In the latter study, the first group was given an educational letter, the second group had the opportunity to win a 3,000 dollar Caribbean trip for two and the last group received both the letter and the ticket offer.

During the literature search, articles were selected if participants were exclusively health care workers or part of the health care personnel. In most articles, no distinction was made between different health care workers, e.g., physicians and nurses. In contrast, in the study by Dey et al. (2001),[14] participants were separated in two groups: those that worked in Primary Health Care Teams (PHCT) and those that worked in Nursing Homes (NH). Also, in the study conducted by Looijmans-van den Akker (2010),[17] health care workers were divided into three groups: physicians, nurses and nursing assistants.

Pooleed analysis and Sensitivity analyses. Data extracted from the articles were analyzed with StatsDirect.

Both data from the control group and the intervention group prior to, and following, the intervention were introduced into the program.

The Relative Risk (RR) and 95% Confidence Interval (CI), with its lower and upper limit (LL and UL) were calculated for each article. In our case a higher relative risk means that interventions contribute to increase the vaccination rates among health care workers.

When considering all studies, the vaccination rate almost doubled in the intervention group compared with the control group, the random effect model gave a RR = 2.03 (95% CI: 1.45–2.85) (I^2 = 98.1%; Cochran Q = 50,224 (df = 10) $p < 0.0001$) (Egger bias = 5,768,842 (95% CI = -5,383–16,920) p = 0.272) (see **Fig. 2**).

Then we repeated the pooled analysis of the trials without Hayward et al., 2006 because the results of this trial are clearly "out of range" and are highly dependent on the specific context

Table 1. Characteristics of the selected studies (clinical trials)

Bibliography rank	Authors and (Citation number)	Year of publi-cation	Study design	Total experimen-tal n.	Vaccinated pre (exp) n. (%)	Vaccinated post (exp) n. (%)	Total con-trol n.	Vaccinated pre n. (%)	Vaccinated post n. (%)	JADAD score 1 (1–5)	JADAD score 2 (1–5)	JADAD score 3 (1–5) definitive
1	Rothan-Tondeur et al.[21]	2010	cluster-RCT	1,201	336 (28%)	408 (34%)	1144	286 (25%)	366 (32%)	-1	-1	-1
2	Hayward et al.**[5]	2006	cluster-RCT (2003–2004)	1,610		570 (35.4%)	1674		84 (5%)	4	3	4 (resolving)
2	Hayward et al.**[5]	2006	cluster-RCT (2004–2005)	1,726		527 (30.5%)	1766		67 (3.8%)			4 (resolving)
3	Dey et al.[14]	2001	cluster-RCT	PHCT*: 457		100 (21.9%)	PHCT*: 395		83 (21%)	4	3	4 (resolving)
				NH*: 768		78 (10.2%)	NH*: 1364		77 (5.6%)			
4	Kimura et al.[15]	2007	cluster-RCT	Ed*: 821	240 (29%)	298 (34%)	1517	467 (31%)	450 (28%)	4	4	4
				(vacc.day) 832	292 (35%)	410 (46%)						
				(ed + vacc. Day) 754	295 (39%)	439 (53%)						
5	Abramson et al.[16]	2010	cluster-RCT	163	44 (27%)	86 (52.8%)	181	36 (19.9%)	48 (26.5%)	3	4	4 (resolving)
6	Ohrt et al.[19]	1992	cluster-RCT	180	50	103	175	48	85	2	2	2
7	Lemaitre et al.[18]	2009	cluster- RT	989	198	678	1015	200		4	4	4
8	Tannenbaum et al.[22]	1993	cluster-CT	135	23	35	133	22	13	-1	-1	-1
9	Looijmans I et al.[17]	2009	cluster-RT	Tot. 3,086 (20%)			Tot. 3,550 (21%)			4	4	4
				(1) All HCWs Vaccinated		774/3085 (25.1%)			582/3,550 (16.4%)			
				(2) Physician Vaccinated		43/70 (61.4%)			37/75 (49.3%)			
				(3) Nurses Vaccinated		94/179 (52.5%)			79/287 (27.5%)			
				(4) Nursing assistants Vaccinated		429/2095 (20.5%)			296/2,138 (13.8%)			
10	Doratotaj et al.[20]	2008	cluster-RT	200		tot. 78 (39%)	200		tot. 76 (38%)	1	1	1
				200		tot. 84 (42%)	200					
				200		tot. 89 (44.5%)	200					

*PHCT, Pshycians; NH, Nurse; Ed, Educational; **Hayward et al. (2006) The study delineated a pair matched cluster randomized controlled trial during the winters of 2003–4 and 2004–5. We considered the study as two in one and the study have a different and specific context in comparison to the others. ***RCT, randomized controlled trial; CT, controlled trial; RT, randomized trial.

where the trial took place. So, the random effect model gave a RR = 1.48 (95% CI: 1.22–1.81) (I^2 = 93.3%; Cochran Q = 11,883 (df = 8) p < 0.0001) (Egger bias = -0.262048 (95% CI = -8,188–7,664) p = 0.9399) (see **Fig. 3**).

When only taking into consideration studies that scored 3 or higher on the JADAD scale[5,14,15,16,17,18] the relative risk increased (RR = 2.55; 95%CI: 1.64–4.95) [I^2 = 98.4%; Cochran Q = 375.63 (df = 6) p < 0.0001] [Egger bias = 10.93 (92.5% CI = -6.18–28.04) p = 0,1615] (see **Fig. 4**) meaning that interventions have positive results.

In this case too we performed the analysis without Hayward et al., 2006 for the same reasons as previous and results were (RR = 1.66; 95% CI: 1.32–2.08) [I^2 = 92.9%; Cochran Q = 56 (df = 4) p < 0.0001] [Egger bias = -1,412,413 (92.5% CI = -15,12944 to 12,304,614) p = 0.8004] (see **Fig. 5**).

This suggests that the inherent quality of controlled trials has an influence in the results obtained by carrying out an intervention and a specific context where the trial took place too.

Considering the median age of publication that resulted 2007, the analysis for studies published after 2007 Rothan-Tondeur et al., 2010, Lemaitre et al., 2009,[18] Abramson 2010,[16] and Looijmans-van den Akker et al., 2010 [17] and Doratotaj et al., 2008[20] resulted: pooled RR = 1.50 (95% CI: 1.12–2.01) [I^2 = 95.9%; Cochran Q = 97,554 (df = 4) p < 0.0001] [Egger bias = -2,328,521 (95% CI = -25,434,346 to 20,777,304) p = 0.7695] (see **Fig. 6**).

In addition, considering only high quality studies published after 2007 2009,[18] Abramson 2010[16] and Looijmans-van den Akker et al., 2010[17]—so excluding from the previous analysis Rothan-Tondeur et al., 2010 and Doratotaj et al., 2008[20]—a pooled RR = 1.86 (95% CI: 1.43–2.43) [I^2 = 91.8%; Cochran Q = 24,380 (df = 2) p < 0.0001] (see **Fig. 7**), suggesting in this case too that the inherent quality of controlled trials has an influence in the results obtained by carrying out an intervention although is in a little difference.

For studies published before 2007—without Hayward et al., 2006: pooled RR = 1.42 (95% CI: 1.14–1.76) [I^2 = 75.9%; Cochran Q = 12,446 (df = 3) p = 0.006] [Egger bias = 3,492,152 (92.5% CI = -3,193,986 to 1,017,829) p = 0.214].

Considering on the base of study design the only cluster-RCT—without Hayward et al., 2006[5]—resulted: a pooled RR = 1.48 (95% CI: 1.12– 1.95) [I^2 = 95.3%; Cochran Q = 106,300 (df = 5) p < 0.0001] [Egger bias = 0.990986 (95% CI = -18,651–16,669) p = 0.8837] (**Fig. 8**) and stratified for only high quality ones (> 3 Jadad's score) we obtained: a pooled RR = 1.70 (95% CI: 1.23–2.34) [I^2 = 94.3%; Cochran Q = 12.80 (df = 3) p < 0.0001] [Egger bias = -1,010,601 (95% CI = -31,393,718 to 29,372,516) p = 0.8993] (**Fig. 9**).

Discussion

In this systematic review, we retrieved 10 controlled trials which addressed interventions designed to increase the influenza vaccination coverage among health care workers. The vast majority of the studies used an educational campaign or at least an educational component in the intervention, in the attempt to increase the influenza vaccination rates among health care workers. On the one hand, it emerged that the combination of an educational and a promotional element, such as the vaccination day in the study by Kimura et al. (2007),[15] were the most effective in augmenting the influenza vaccination coverage among health care workers. On the other hand, in some cases it appeared that the intervention did not contribute to increasing the vaccination rates among health care workers as reported by Dey et al.[14]

In any case, this systematic review asserted that the quality of controlled trials plays a role in the results obtained by carrying out a specific intervention. As a matter of fact, when only including studies that scored 3 or higher in the JADAD scale, the relative risk was equal to 2.55 (1.64–4.95), while it was 2.03 (1.45–2.85) when including all studies. But it's true that the context were the intervention is made is important too as for Haward in which the study was performed in a large private chain of UK care homes and the outcome of the study was not the effectiveness of interventions (they adopted a policy for influenza vaccination of staff in randomly selected intervention homes while maintaining their usual policy of not actively promoting staff vaccination in control homes) but the effect of vaccinating care home staff against influenza on mortality, health service use, and influenza like illness among residents. In fact when we excluded Hayward et al., 2006,[5] the RR (the efficacy of intervention in prevalence of post vaccination compared with pre vaccination) was from 1.54 (1.25–1.90) for all other studies included in the review to a little higher value of 1.66 (1.32–2.05) for studies that scored 3 or higher in the JADAD scale.

The limitations of this study include that a risk of bias might have risen through the combination of different interventions, e.g., free vaccination and educational interventions. Also, the insertion of studies that were reviewed as being of bad quality might introduce a form of bias as it is probable that the randomization in these studies had not been performed properly. However, we hope that this risk of bias was limited, as we conducted two analyses: one including these articles and the other one which only considered articles of good quality.

The strength of this systematic review is that the current scientific literature was extensively searched through two databases with seven combinations of keywords. Moreover, PRISMA criteria were applied in every section of the article, thus providing the reader with a transparent reporting of the data.

The influenza vaccination of health care workers can be considered as a new challenge for public health professionals, as inadequate influenza vaccination coverage leads to increased morbidity and mortality in patients, and health care workers and their families.

Our hope is that this study will be a helpful tool for hospitals and other health care facilities that are trying to achieve higher influenza vaccination coverage among their personnel. This systematic review provides facilities that are undertaking such an attempt with an overview of the data that is available today and with an indication of the effectiveness of some measures compared with others.

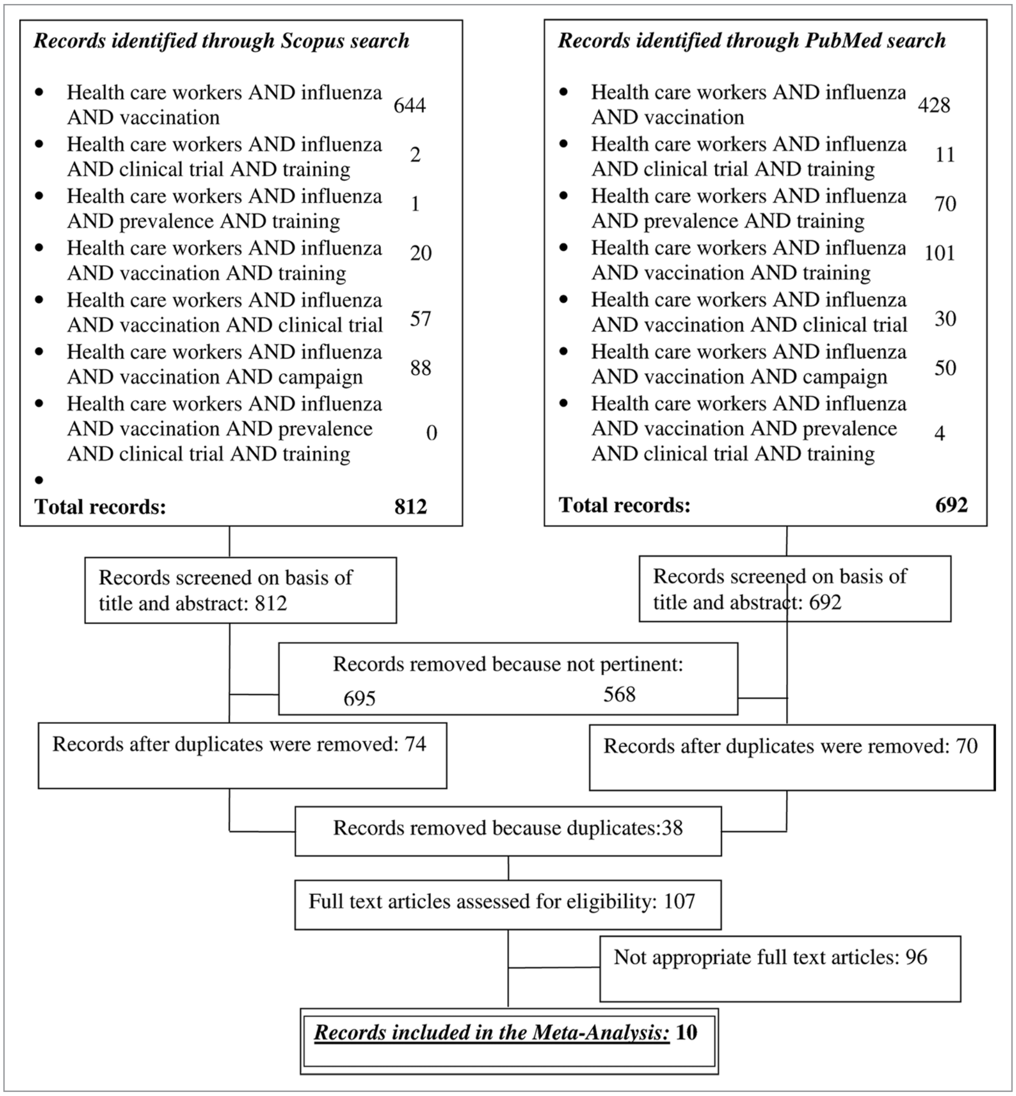

Figure 1. Flow-chart of search criteria of the systematic review.

Materials and Methods

Identification of relevant studies. Literature review was conducted using two medical databases: Scopus and PubMed. The keywords used were: "health care workers," "influenza," "vaccination," "prevalence," "clinical trial," "campaign" and "training."

We performed searches for: "Health care workers AND influenza AND vaccination;" "Health care workers AND influenza AND clinical trial AND training;" "Health care workers AND influenza AND prevalence AND training;" "Health care workers AND influenza AND vaccination AND training;" "Health care workers AND influenza AND vaccination AND clinical trial;" "Health care workers AND influenza AND vaccination AND campaign;" "Health care workers AND influenza AND vaccination AND prevalence AND clinical trial AND training." Search criteria are summarized in **Figure 1**.

The selection was limited to articles published in English, Italian and French and we did not apply any date restrictions. We selected for our analysis all studies evaluating influenza vaccination campaigns for health care personnel. We defined such campaigns as organized efforts to promote greater vaccination coverage among staff members.

After, only trials studies were included and the selection was performed according to the PRISMA criteria (**Fig. 1**).[23]

Articles were examined and were excluded if:[1] they researched pandemic instead of seasonal influenza;[2] studies were not pertaining seasonal influenza interventions and[3] if the full text was not available.

We included only trials focused on interventions aimed to increase the seasonal influenza vaccination rates among HCW. In the specific case of trials with before-after research designs, article was excluded if it did not report influenza vaccination rates prior to the year of intervention. This led to a strict selection of the results.

When Medline outcomes overlapped, therefore all duplicate articles were removed. Then the eligible papers were obtained the full text. This literature review was completed in June 2012.

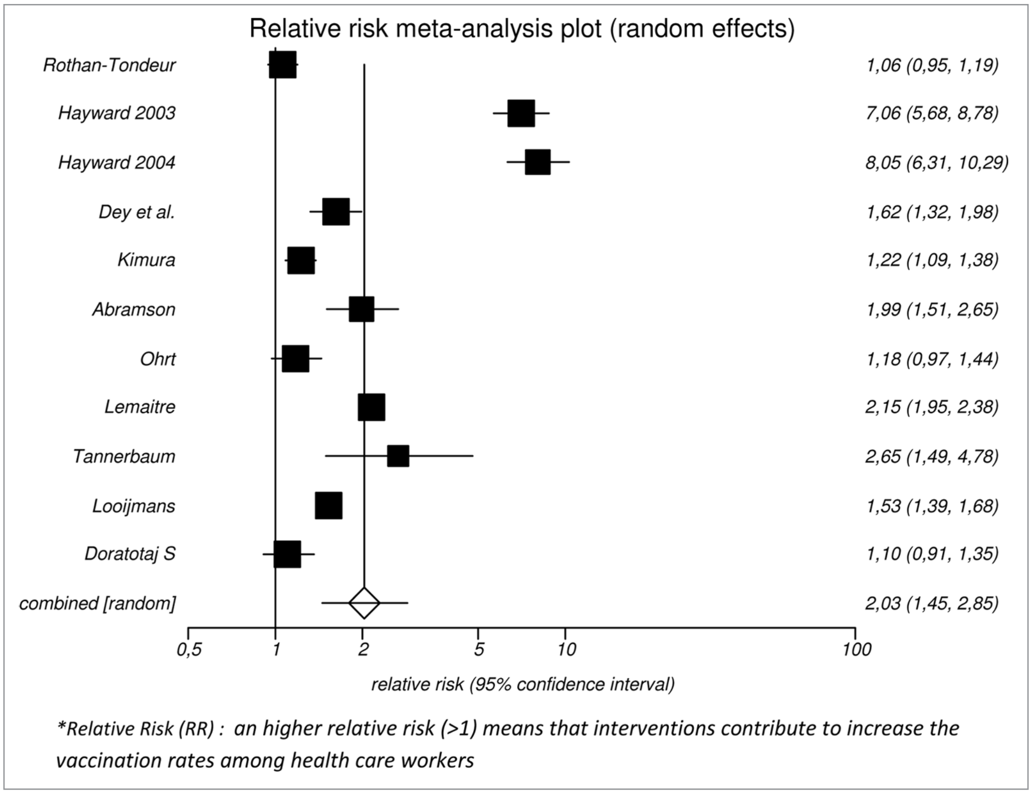

Figure 2. Forrest plot of the analysis concerning all the included studies. *Relative Risk (RR): a higher relative risk (> 1) means that interventions contribute to increase the vaccination rates among health care workers.

Quality assessment and data extraction. The methodological quality of randomized controlled trials (RCTs) is commonly evaluated in order to assess the risk of bias. JADAD scale was used in order to assess the quality of the controlled trials. The Jadad system consists of three topics (description of randomization, of blinding, of withdrawals and drop outs) that are directly related to reducing bias. The possible answers to all the three questions are yes/no. There are five possible points for its quality score: three single points for yes responses and two additional points for appropriate methods of randomization and ensuring blindness of allocation. The maximal score given in this scale being 5, a study is declared of good quality when the score assigned to it is equal or greater than 3 and of bad quality when the score is below 3.

The studies were reviewed independently by two different researchers to assess their quality, (**Table 1**) according to the JADAD scale, ranging from 0 (poor) to 5 (rigorous).[24] Discrepancies about quality were recorded and solved by a third researcher (**Table 1**).

To perform the meta-analysis we extracted data. The same two reviewers used a data collection form to independently abstract data from the studies. The information extracted were: author, year, study design, population types involved in the study (HCW) and responders, prevalence, intervention assessed designed to increase the uptake of seasonal influenza vaccines among health care workers, vaccinated pre and post intervention (when data was available) and control group.

The reviewers discussed any discrepancies in their results to reach agreement. The characteristics of each study are shown in **Table 1** and **Table 2**.

Statistical Analysis. We synthesized the data abstracted from all studies and then stratified them by quality (**Table 1**). For randomized controlled trials with before-and-after studies with a control group, we used the post-intervention vaccination rates to calculate risk ratios (RR) and 95% confidence intervals (95%CI). We summarized the results in a forest plot (**Fig. 2**). The statistical analysis was conducted using StatsDirect 2.7.8 statistical software version.

Pooled analysis. The pooled incidence of influenza vaccination following to intervention among HCW was calculated considering all studies included in the review and after stratifying by high quality ones (score ≥ 3).

The pooled incidences were calculated as the back-transformation of the weighted mean of the transformed incidences,[25] using inverse arcsine variance weights for the fixed effects model and DerSimonian-Laird weights for the random effects model.[26] Together the pooled RR with relative 95% CI and forest plots were realized. We computed the Cochran chi-square (Cochran Q) test[27] to evaluate studies heterogeneity, thus using the random effect model when the test highlighted differences between studies and the fixed effect model when no significant differences were shown.

Funnel plots were used in order to control for the presence of publication bias.[28,29] Sensitivity analyses were performed to

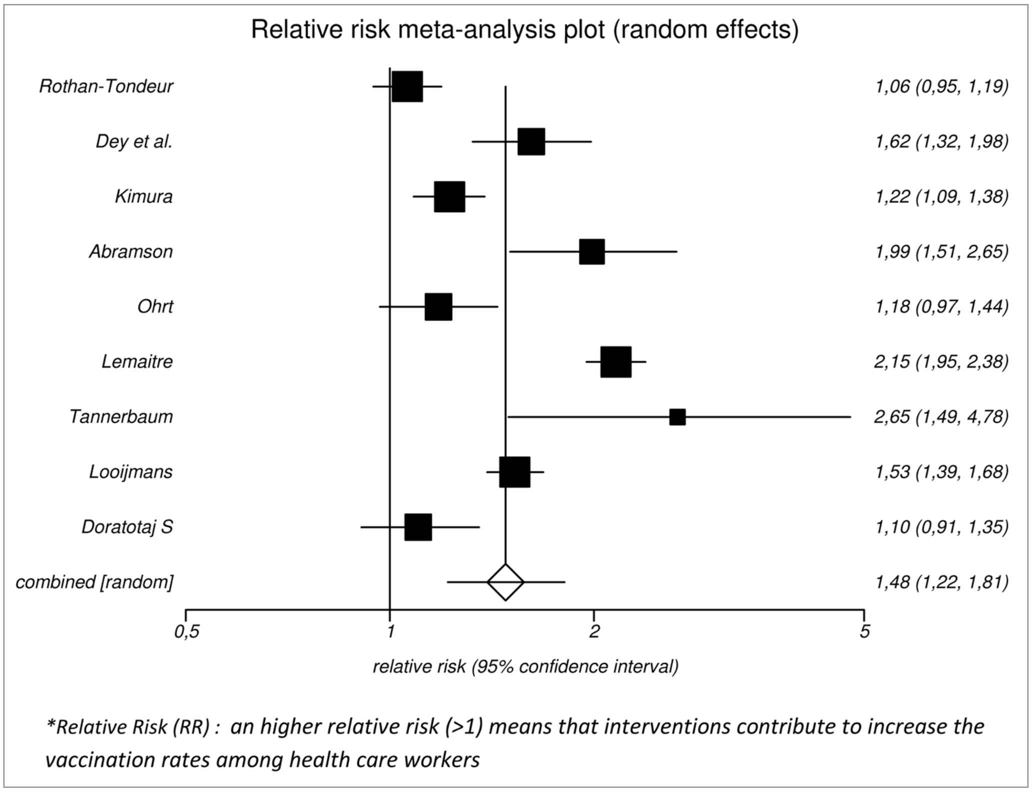

Figure 3. Forrest plot of the analysis concerning all the included studies without Hayward et al., 2006. *Relative Risk (RR): a higher relative risk (> 1) means that interventions contribute to increase the vaccination rates among health care workers.

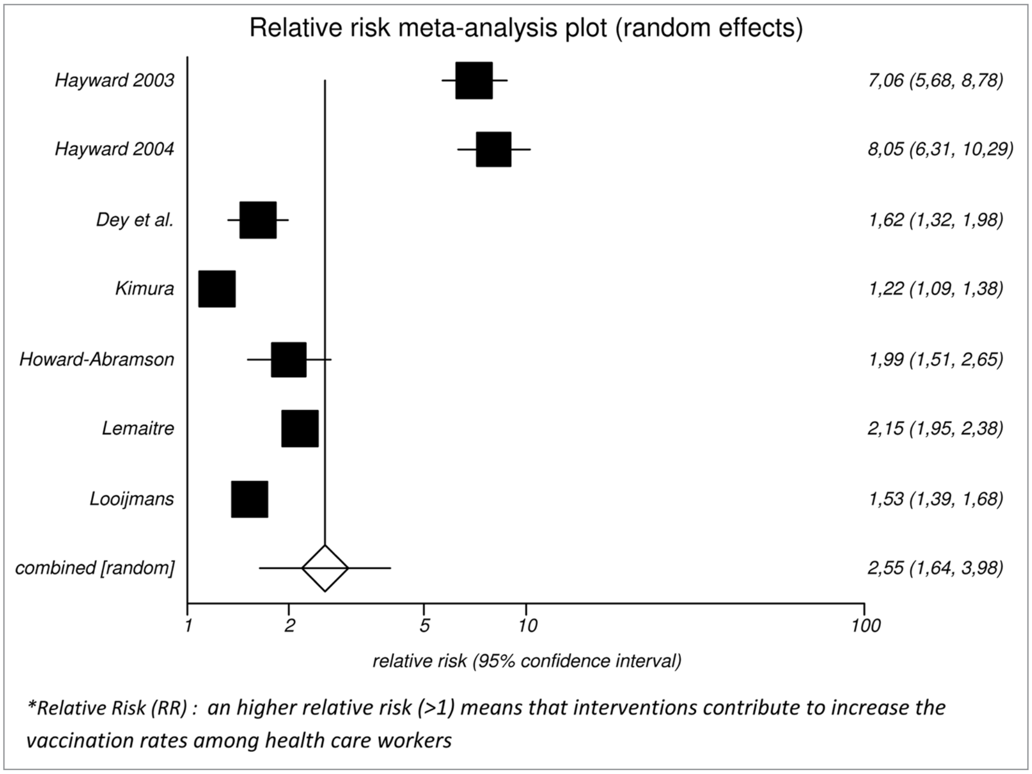

Figure 4. Forrest plot of the analysis concerning only high quality studies for Jadad's scale (score > 3). *Relative Risk (RR): an higher relative risk (> 1) means that interventions contribute to increase the vaccination rates among health care workers.

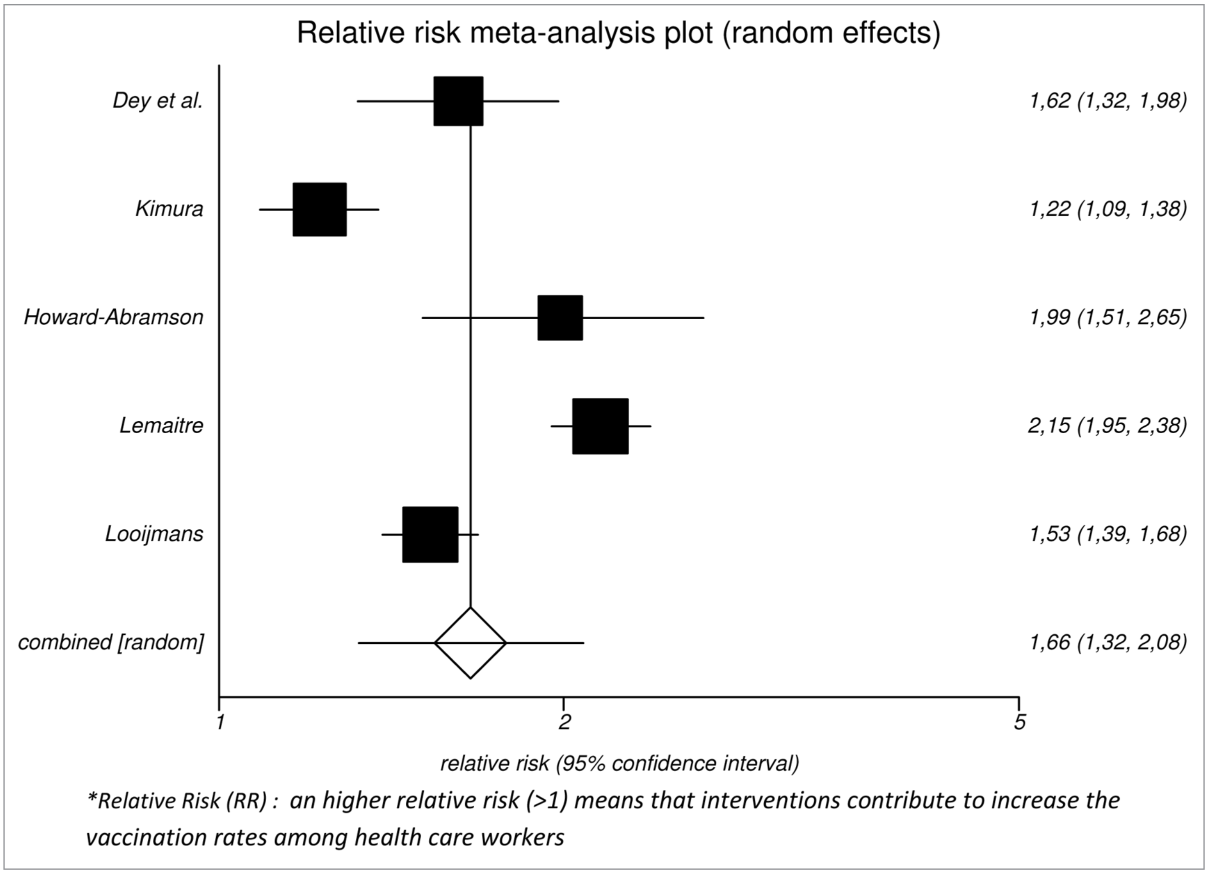

Figure 5. Forrest plot of the analysis concerning only high quality studies for Jadad's scale (score > 3) without Hayward et al., 2006. *Relative Risk (RR): a higher relative risk (> 1) means that interventions contribute to increase the vaccination rates among health care workers.

assess bias, for example publication year, study design, specific context where the trial took place, high quality studies resulting with Jadad scale.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

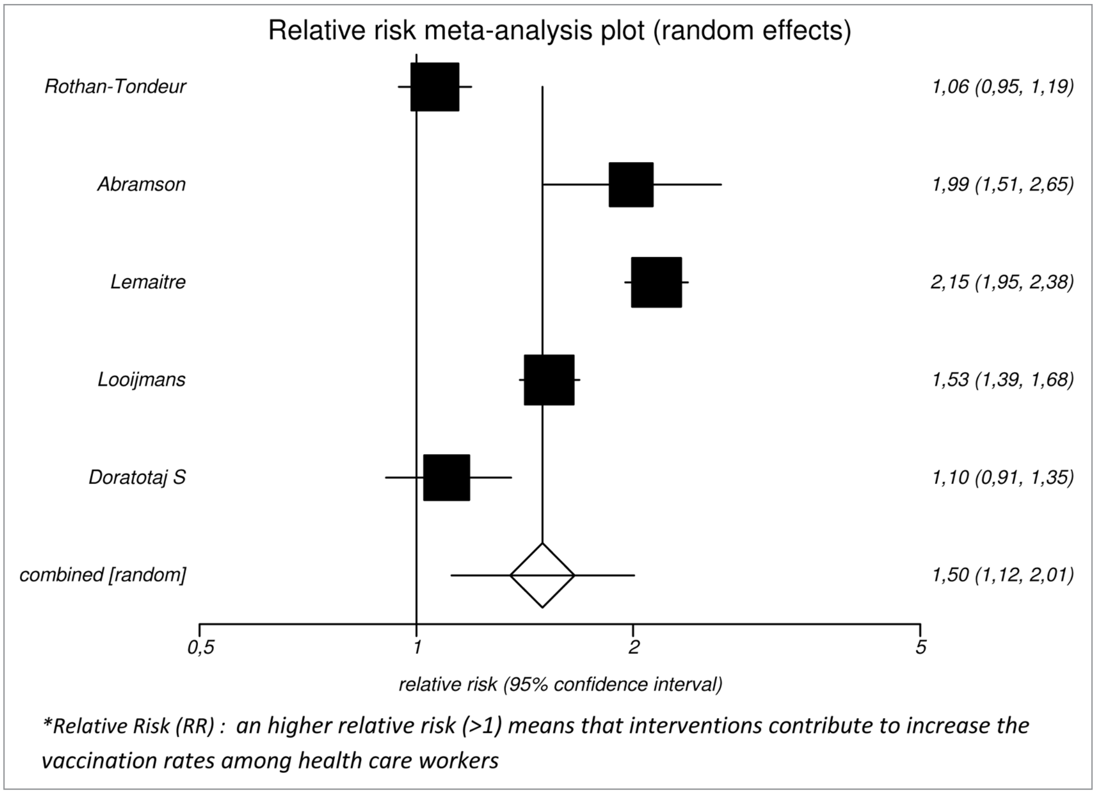

Figure 6. Forrest plot of the analysis concerning only studies published after 2007. *Relative Risk (RR): a higher relative risk (> 1) means that interventions contribute to increase the vaccination rates among health care workers.

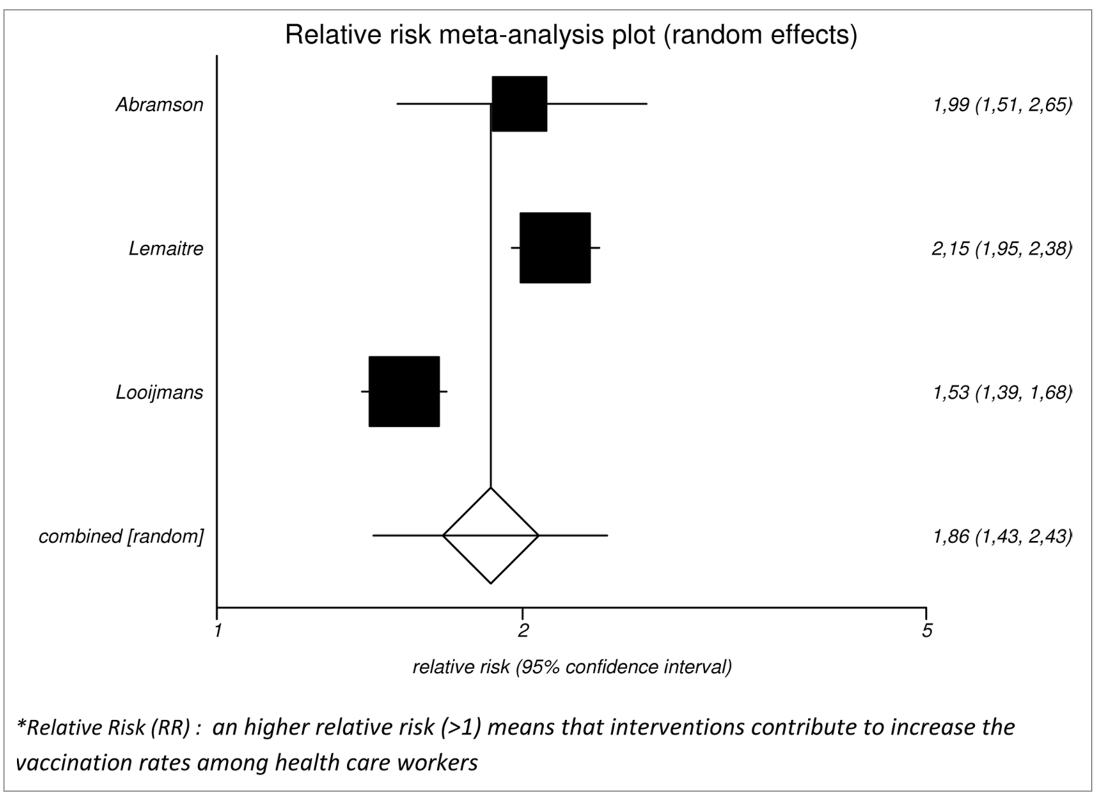

Figure 7. Forrest plot of the analysis concerning only studies published after 2007 and with high quality score to Jadad's scale (> 3 score). *Relative Risk (RR): an higher relative risk (> 1) means that interventions contribute to increase the vaccination rates among health care workers.

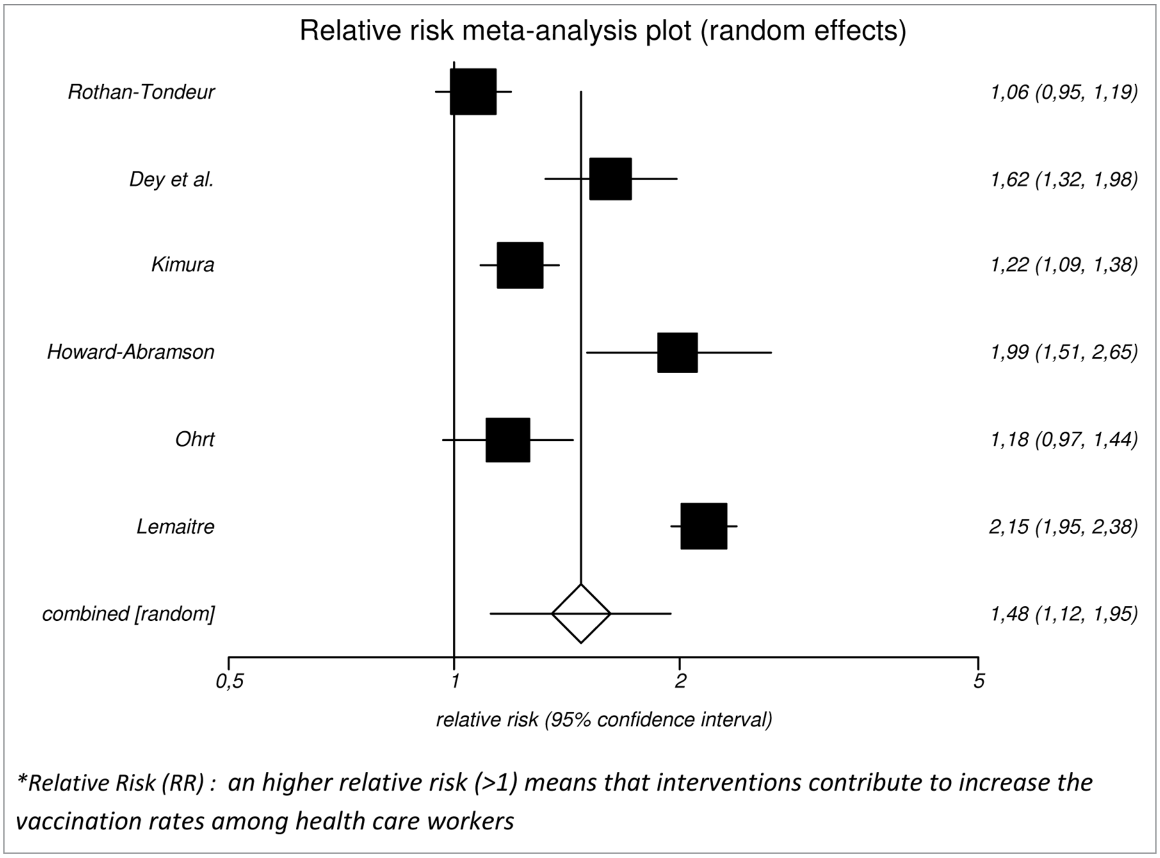

Figure 8. Forrest plot of the analysis concerning only Cluster-RCT studies—without Hayward et al., 2006—and with high quality score to Jadad's scale (> 3 score). *Relative Risk (RR): a higher relative risk (> 1) means that interventions contribute to increase the vaccination rates among health care workers.

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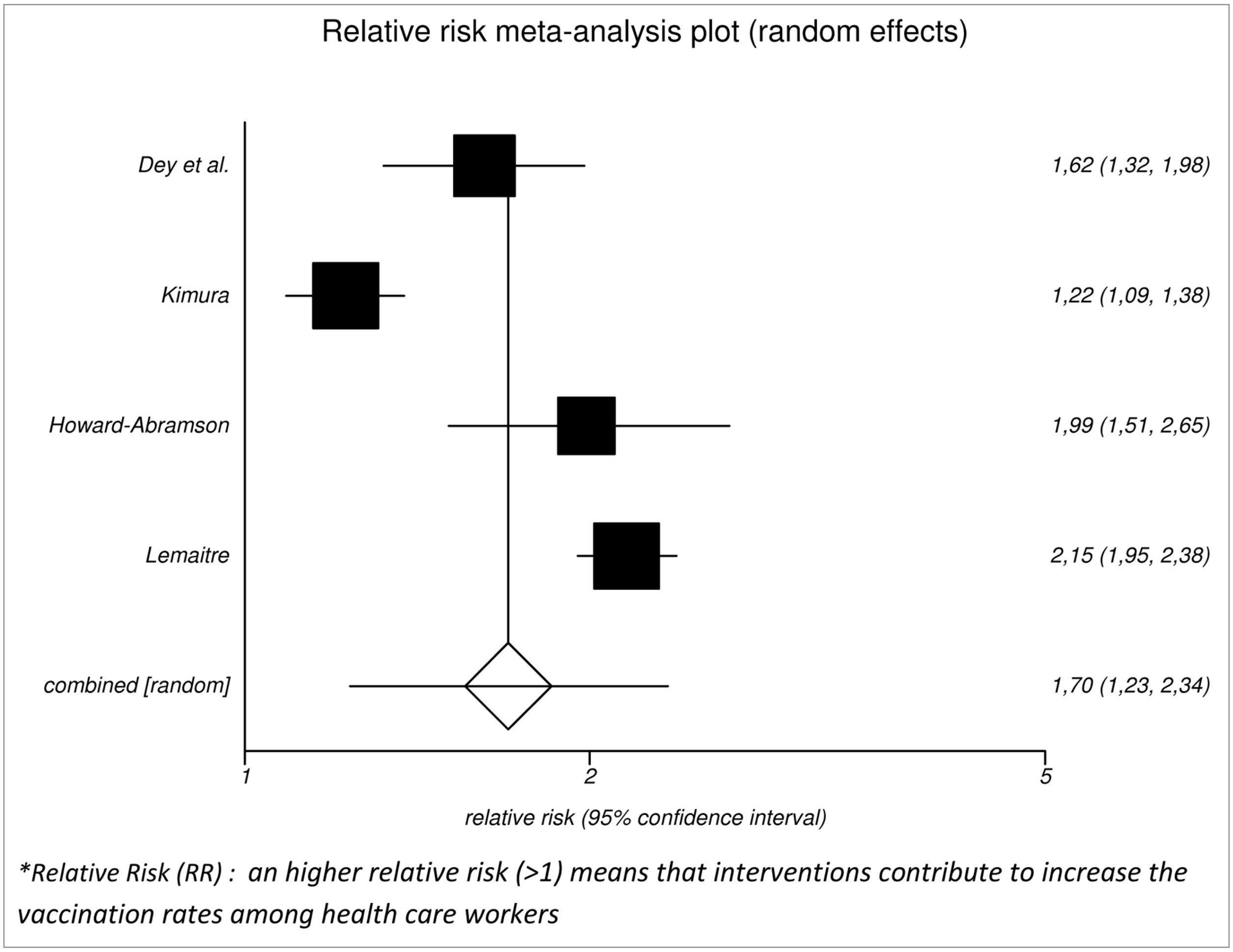

Figure 9. Forrest plot of the analysis concerning only Cluster-RCT studies—without Hayward et al., 2006—and with high quality score to Jadad's scale (> 3 score). *Relative Risk (RR): a higher relative risk (> 1) means that interventions contribute to increase the vaccination rates among health care workers.

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Table 2. Characteristics of Interventions of the included studies

Bibliography rank	Authors and (Citation number)	Study design	Total experimental n.	Intervention
1	Rothan-Tondeur et al. [21] 2010	cluster-RCT	1,201	PARTICIPANTS:geriatric wards were randomly assigned to two clusters. INTERVENTION: The program cluster (24 wards; 1,918 HCWs) received the active program whereas no action was taken in the control cluster (19 wards; 1,728 HCWs). The program was educational; its objective was to convince HCWs to be vaccinated by giving them top-down scientific information and developing a sense of altruism. Data from HCWs from the program cluster and HCWs from the control cluster were collected. Educational: Give information about flu through slideshow, leaflets and a guide.
2	Hayward et al.** [5] 2006	cluster-RCT(2003–2004)	1,610	PARTICIPANTS:Nursing home staff) and residents care homes intervention homes and matched control homes). INTERVENTION: Vaccination offered to staff in intervention homes but not in control homes. Educational: Nurse promoting and leaflets.
2	Hayward et al.,**[5] 2006	cluster-RCT (2004–2005)	1,726	PARTICIPANTS:Nursing home staff) and residents care homes intervention homes and matched control homes). INTERVENTION: Free vaccination communicated by letter in which benefits were elencated and posters.
3	Dey et al.[14]	cluster-RCT	PHCT*: 457	PARTICIPANTS:All HCW in primary health care teams(PHCT) and nursing home (NH) in Bury and Rochdale Health Authority were offered free vaccination from their general practitioner. INTERVENTION: Free- vaccination communicated by letter in which benefits were elencated and posters
			NH*: 768	INTERVENTION: Free vaccination communicated by letter in which benefits were elencated and posters
4	Kimura et al.[15] 2007	cluster-RCT	Ed*: 821	PARTICIPANTS: Health care workers at LTCFs were surveyed regarding their knowledge and attitudes about influenza and the influenza vaccine. Results were used to develop 2 interventions, an educational campaign and Vaccine Day (a well-publicized day for free influenza vaccination of all employees at the worksite). Seventy facilities were recruited to participate in an intervention trial and randomly assigned to 4 study groups. INTERVENTION: Educational:10 min video, brochures, flyers and posters.
			(vacc.day) 832	INTERVENTION: Vaccine day:a well-publicized day in which free vaccination is offered.
			(ed + vacc. Day) 754	INTERVENTION: Educational 10 min video, brochures, flyers, posters and Vaccine day (a well-publicized day in which free vaccination is offered).
5	Abramson et al.[16] 2010	cluster-RCT	163	PARTICIPANTS: Primary care clinics with direct patient contact (physicians, nurses, pharmacists, and administrative and ancillary staff). Thirteen clinics were randomly selected for an intervention that consisted of a lecture session given by a family physician, e-mail-distributed literature and reminders, and a key figure from the local staff who personally approached each staff member. INTERVENTION: Educational:lecture session, e-mail distributed literature and reminders
6	Ohrt et al.[19] 1992	cluster-RCT	180	PARTICIPANTS: Four hundred 42 internal medicine, obstetricsgynecology, and general surgery residents and junior medical students. INTERVENTION: The four interventions employed were[1] an educational memorandum outlining vaccine indications sent to all study group members,[2] a personal letter mailed to a random sample of half of the remaining unimmunized persons,[3] a telephone call to half of the unimmunized letter recipients, and[4] vaccine offered directly to the remaining unimmunized persons in clinics and conferences. In addition, a questionnaire was administered to all persons requesting or offered vaccine - Educational memorandum +letter + telephone call + vaccine offered

Table 2. Characteristics of Interventions of the included studies (continued)

Bibliography rank	Authors and (Citation number)	Study design	Total experimental n.	Intervention
7	Lemaitre et al.[18] 2009	Cluster-RT	989	PARTICIPANTS: All persons aged 60 and older residing in the nursing homes. INTERVENTION: A cluster-randomized controlled trial was conducted in which 40 nursing homes matched in pairs were randomly allocated to a vaccination (intervention) arm or a no-intervention control arm. Influenza vaccine was administered to volunteer staff after a face-to-face interview. No intervention took place in control nursing homes. Randomization was centralized and based on a simple computerized random number generator. In the intervention arm, a promotional campaign based on posters, leaflets, and an information meeting with the study team between September 15 and October 31, 2006, first sensitized staff to the benefits of influenza vaccination. The campaign described the potential benefits of influenza vaccination for one's own protection and that of the residents. Influenza vaccination was further recommended during face-to-face interviews with each member of staff present in the nursing homes between November 6 and December 15, 2006. The study team individually met all administrative staff, technicians, and caregivers to invite them to participate, and volunteers were vaccinated at the end of the interview. During the interview, prior vaccination status and, if appropriate, the reason for nonvaccination were also collected. Promotional campaign based on posters, leaflets, and an information meeting
8	Tannenbaum et al.[22] 1993	Cluster- CT	135	PARTICIPANTS:The intervention was performed in a 135-bed nursing home in Montreal INTERVENTION: The intervention program consisted of information session for all staff given by phycians on five different occasion over a one-week-oeriod. Following these sessios, memos providing similar information were distribuited to the staff and posters were placed on each floor in the nursing home. Vaccination clinics were held on three different occasions over the subsequent two weeks; vaccine eas also available on request - Information sessions and posters+informational memos
9	Looijmans I et al.[17] 2009	cluster-RT	Tot. 3,086 (20%) 1) all HCWs vaccinated 2) physicians vaccinated 3) nurses vaccinated 4) nursing assistants vaccinated	PARTICIPANTS:all Dutch nursing homes were sent an invitation letter to participate in this study. Only nursing homes that did not intend to offer routine influenza vaccination to their HCWs were ineligible for the trial. So nursing homes were included into the trial and were randomly allocated to an intervention and a control group by computer, each group consisting of 18 homes. Allocation was balanced on three variables; number of beds (a measure for size), influenza vaccine uptake among HCWs in 2005 and geographical region (northern, eastern, southern or western Netherlands). All intervention homes were visited between September 28th and October 12th to prepare for the trial. We pragmatically defined HCWs as all the nursing home personnel with direct patient contact for more than 1 h a week. INTERVENTION: Multifaceted implementation programs 3 components: [1]Educational (posters and leaflets);[2] Plenary one-hour information meeting;[3] Appointment with physician promoting vaccination
10	Doratotaj et al.[20] 2008	cluster-RT	200+200+200	PARTICIPANTS: Eligible study participants consisted of 6723 physicians and nurses with predominantly direct patient contact at an urban tertiary care hospital. INTERVENTION: The study investigated a novel approach for improving influenza vaccination rates among HCW. Eight hundred employees we selected, 200 each from the following 4 categories: professional staff, resident physicians, registered nurses, and li censed practical nurses. Subjects were randomly assigned to receive[1] no intervention,[2] a letter explaining the importance of influenza vaccine for HCW,[3] a ticket activated with influenza vaccine administration for a raffle of a free Caribbean vacation for 2, or [4] both the educational letter and the raffle ticket. We compared the proportion of employees receiving vaccination and participating in the raffle across groups. Educational letter/raffle ticket (win vacation)/Educational letter and raffle ticket/