

**Efficacy of In-Hospital Multidimensional Interventions of
Secondary Prevention after Acute Coronary Syndrome:
A Systematic Review and Meta-Analysis**

THESE

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et présentée a la Faculté de biologie et de médecine de l'Université de Lausanne

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*Efficity of in-hospital multidimensional interventions of
secondary prevention after acute coronary syndrome. A
systematic review and meta-analysis*

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Rapport de synthèse

Contexte

Les programmes de prévention cardiovasculaire secondaire après un événement coronarien aigu ont pu démontrer leur efficacité dans le contexte des soins ambulatoires. L'hospitalisation pour une maladie aiguë peut être considérée comme un « instant charnière », particulièrement adapté à un changement de comportement de santé et où des interventions de prévention secondaire, telle l'éducation du patient, pourraient être particulièrement efficaces. De plus, la prescription de médicaments de prévention cardiovasculaire durant l'hospitalisation semble augmenter la proportion des patients traités selon les recommandations sur le long terme. Récemment, plusieurs études ont évalué l'efficacité de programmes de prévention ayant pour but l'éducation des patients et/ou une augmentation du taux de prescription de médicaments prouvés efficaces par les médecins en charge. L'article faisant l'objet du travail de thèse synthétise la littérature existante concernant l'efficacité en termes de mortalité des interventions multidimensionnelles de prévention cardiovasculaire après un syndrome coronarien aigu, débutées à l'hôpital, centrées sur le patient et ciblant plusieurs facteurs de risque cardiovasculaire.

Méthode et Résultats

En utilisant une stratégie de recherche définie à l'avance, nous avons inclus des essais cliniques avec groupe contrôle et des études avant-après, débutées à l'hôpital et qui incluaient des résultats cliniques de suivi en terme de mortalité, de taux de réadmission et/ou de récurrence de syndrome coronarien aigu. Nous avons catégorisé les études selon qu'elles ciblaient les patients (par exemple une intervention d'éducation aux patients par des infirmières), les soignants (par exemple des cours destinés aux médecins-assistants pour leur enseigner comment prodiguer des interventions éducatives) ou le système de soins (par exemple la mise en place d'itinéraires cliniques au niveau de l'institution).


Globalement, les interventions rapportées dans les 14 études répondant aux critères montraient une réduction du risque relatif (RR) de mortalité après un an (RR= 0.79; 95% intervalle de confiance (IC), 0.69-0.92; n=37'585). Cependant, le bénéfice semblait dépendre du type d'étude et du niveau d'intervention. Les études avant-après suggéraient une réduction du risque de mortalité (RR, 0.77; 95% IC, 0.66-0.90; n=3680 décès), tandis que le RR était de 0.96 (95% IC, 0.64-1.44; n=99 décès) pour les études cliniques contrôlées. Seules les études avant-après et les études ciblant les soignants et le système, en plus de cibler les patients, semblaient montrer un bénéfice en termes de mortalité à une année.

Conclusions et perspectives

Les preuves d'efficacité des interventions de prévention secondaires débutées à l'hôpital, ciblant le patient, sont prometteuses, mais pas définitives. En effet, seules les études avant-après montrent un bénéfice en termes de mortalité. Les recherches futures dans ce domaine devraient tester formellement quels éléments des interventions amènent le plus de bénéfices pour les patients.

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Efficacy of In-Hospital Multidimensional Interventions of Secondary Prevention After Acute Coronary Syndrome A Systematic Review and Meta-Analysis

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Background—Secondary prevention programs for patients experiencing an acute coronary syndrome have been shown to be effective in the outpatient setting. The efficacy of in-hospital prevention interventions administered soon after acute cardiac events is unclear. We performed a systematic review and meta-analysis to determine whether in-hospital, patient-level interventions targeting multiple cardiovascular risk factors reduce all-cause mortality after an acute coronary syndrome.

Methods and Results—Using a prespecified search strategy, we included controlled clinical trials and before-after studies of secondary prevention interventions with at least a patient-level component (ie, education, counseling, or patient-specific order sets) initiated in hospital with outcomes of mortality, readmission, or reinfarction rates in acute coronary syndrome patients. We classified the interventions as patient-level interventions with or without associated healthcare provider-level interventions and/or system-level interventions. Twenty-six studies met our inclusion criteria. The summary estimate of 14 studies revealed a relative risk of all-cause mortality of 0.79 (95% CI, 0.69 to 0.92; $n=37\,585$) at 1 year. However, the apparent benefit depended on study design and level of intervention. The before-after studies suggested reduced mortality (relative risk [RR], 0.77; 95% CI, 0.66 to 0.90; $n=3680$ deaths), whereas the RR was 0.96 (95% CI, 0.64 to 1.44; $n=99$ deaths) among the controlled clinical trials. Only interventions including a provider- or system-level intervention suggested reduced mortality compared with patient-level-only interventions.

Conclusions—The evidence for in-hospital, patient-level interventions for secondary prevention is promising but not definitive because only before-after studies suggest a significant reduction in mortality. Future research should formally test which components of interventions provide the greatest benefit. (*Circulation*. 2008;117:3109-3117.)

Key Words: coronary disease ■ counseling ■ mortality ■ patients ■ risk factors

Guidelines developed by the American Heart Association/American College of Cardiology recommend pharmacological and lifestyle interventions to reduce recurrent events in patients with ST-segment myocardial infarction and non-ST-segment elevation myocardial infarction.^{1,2} A variety of outpatient secondary prevention programs have demonstrated their efficacy in prior systematic reviews of randomized controlled trials.^{3,4} Beginning secondary prevention while the patient is in hospital might further improve outcomes.

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Inpatient education after myocardial infarction might have an impact on cardiovascular risk factor (CVRF) management, as suggested by a review of inpatient education interventions.⁵ In-hospital smoking cessation counseling interventions

during the hospital stay appear effective in a systematic review of randomized controlled trials, although they have not been specifically reviewed systematically for patients with recent myocardial infarction.⁶ Interest in the inpatient setting for secondary prevention is heightened by the recognized potential of hospitalization after an acute illness as a “teachable moment” for behavioral change that may increase the benefit of counseling interventions delivered to hospitalized patients.⁷

Early, in-hospital initiation of preventive therapies might increase the likelihood of being adequately treated.⁸ In recent years, multiple studies have assessed pragmatic interventions targeting an increase in prescription rates by physicians and/or long-term medication adherence by patients.^{9,10} However, these interventions have not yet been systematically reviewed or meta-analyzed. Furthermore, the interventions

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have not been formally stratified according to levels of intervention, as proposed for the categorization of interventions targeting long-term adherence.¹¹ Recognizing this, we conducted a systematic review to determine whether in-hospital secondary prevention interventions improve outcomes of patients who have suffered an acute coronary syndrome.

Methods

Categorizing the Intervention

In conducting our review, we categorized secondary prevention programs described in the literature on the basis of a conceptual model that considers the levels of intervention.¹¹ The first tier, patient-level interventions, targets patients directly through counseling, education, or patient-specific order sets. To be included in our systematic review, interventions had to involve at least the patient level. Second, healthcare provider-level interventions included those that tried to change the attitudes or knowledge of healthcare providers (eg, improving physician's skills and effectiveness in counseling through an educational program or education/reminders on benefits of specific therapies).¹² Third, system-level interventions involved a global change in the organization of care (eg, critical pathways or facility outcome reporting).¹³ Our systematic review thus includes at least patient-level interventions, with some operating additionally at the provider and/or system levels.

Study Selection

To be selected in our review, studies had to fulfill 6 inclusion criteria. First, the studied population had to be patients hospitalized for an acute coronary syndrome, defined as unstable angina, non-ST-segment myocardial infarction, or ST-segment myocardial infarction. Second, the intervention had to be a patient-level intervention (ie, at least a part of the intervention had to target the patient directly through education, counseling, or patient-specific order sets). Third, the intervention had to target multiple CVRFs (at least 2 among smoking cessation, blood pressure, blood lipids, diet, weight, and physical activity) or an increase in >1 efficacious secondary prevention drug therapy (antiplatelet agents, β -blockers, angiotensin-converting enzyme inhibitors, blood lipid-lowering drug). Fourth, intervention had to be initiated during the hospital stay. Fifth, the study had to report follow-up clinical outcomes after the hospital stay like mortality, readmission rates, reinfarction rates, or CVRF control (smoking cessation, blood lipids control, diet change, weight reduction, and physical activity improvement). And sixth, studies had to describe a comparison between patients receiving an intervention and patients not receiving the intervention (ie, a control group).

The exclusion criteria were studies assessing only the impact of invasive procedures (ie, angiography, coronary artery bypass graft surgery) or early revascularization interventions (eg, thrombolysis). We also excluded interventions aimed only at changing professional behavior or the healthcare system and thus not directly involving the patient.

Outcomes

The primary outcome of interest was all-cause mortality at follow-up. Secondary outcomes were differences in readmission rates or reinfarction rates, CVRF control at follow-up, and the percent of patients leaving the hospital with proven beneficial medications.

Search Strategy

We structured our search to identify clinical trials and before-after studies of secondary prevention interventions initiated in hospital that provided follow-up outcomes of mortality, readmission rates, or CVRF control in patients with acute coronary syndrome using both electronic and manual search strategies. All languages were considered eligible.

We searched MEDLINE (1966 through March 2007), EMBASE (1980 through March 2007), CINAHL (1982 through March 2007), PsycINFO (1967 through March 2007) database, and the Cochrane Controlled Clinical Trial register (1996 through March 2007) using a recommended approach for systematic reviews of randomized trials.¹⁴ For MEDLINE, we derived 4 comprehensive search themes that were combined with the Boolean operator "and." We created the first theme representing our patient population of interest by using an exploded MeSH heading for the term "Myocardial Ischemia/nu, pc, dh, dt, th" (nursing, prevention and control, diet therapy, drug therapy, therapy). We created the second theme for the interventions of interest by using the Boolean search term "or" to search for the following terms appearing as exploded MeSH headings: "health services administration" or "health promotion" or "caregivers/ed" (education) or "rehabilitation" or "health behavior" or "risk reduction behavior" or "tobacco use cessation" or the terms appearing as text words: "brief.mp" (mp is title, original title, abstract, name of substance word, subject heading word) or "multip\$.mp." The third theme for the intervention setting of interest was created by using the exploded MeSH headings "hospitals" or "inpatients" or the unexploded MeSH headings "hospitalization" or "patient discharge" or the term appearing as the text word "hospital setting\$.mp." The fourth theme for study design used a highly sensitive study filter for interventional studies (both controlled clinical trials and before-after studies).^{14,15} For EMBASE, CINAHL, and PsycINFO, we adapted the MeSH terms to the MeSH terms of the searched database. For the Cochrane Controlled Clinical Trial register, we used a similar search strategy by text words only in which the comprehensive search themes "patient population" and "intervention" were combined using the Boolean term "and."

Data Extraction and Quality Assessment

In a 2-step selection process, 2 investigators (R.A. and J.G.) independently reviewed the titles and abstracts of all citations to identify studies meeting inclusion criteria. In addition, 1 investigator (R.A.) screened the reference list of identified studies for other potentially relevant studies. The same 2 investigators reviewed the relevant reports in full text for eligibility and independently extracted data from all studies fulfilling eligibility criteria. Data extracted included characteristics of the intervention, type of study, baseline clinical characteristics of the participants, and relevant outcomes. Authors of the studies were contacted for additional information when applicable. Because data on cause-specific mortality (eg, cardiovascular mortality) were rarely reported as such, we abstracted the data for all-cause mortality only. We decided not to abstract the secondary outcomes on CVRF control of blood pressure control, physical activity, diet change, and weight control initially targeted for our systematic review because they were rarely and/or variably reported among the selected studies.

We categorized the studies according to their design into clinical trials (involving allocation of individual patients to intervention and control groups) and before-after studies. We considered study design as the primary study quality measure. For the clinical trials, we also reported on study quality with the Jadad et al¹⁶ quality score, adapting it to the present situation. We did not include blinding of study participants to intervention because it is difficult to achieve in the study of lifestyle interventions. Items to assess study quality were methods of randomization (2 points) and reporting of losses to follow-up (1 point), thus leading to a maximum score of 3 points for study quality.¹⁷

Statistical Analysis

Data from all the selected studies were combined to estimate the pooled relative risk (RR) with 95% CIs using a random-effects model. The presence of heterogeneity across trials was evaluated with the Q and I² statistics, with an I² value >50% indicating at least moderate statistical heterogeneity.¹⁸ Indicative RRs were provided when appropriate. Pooling was performed for mortality and for the secondary outcomes of readmission, reinfarction, and smoking cessation. Recognizing the clinical heterogeneity between clinical controlled trials and before-after studies, we also analyzed data

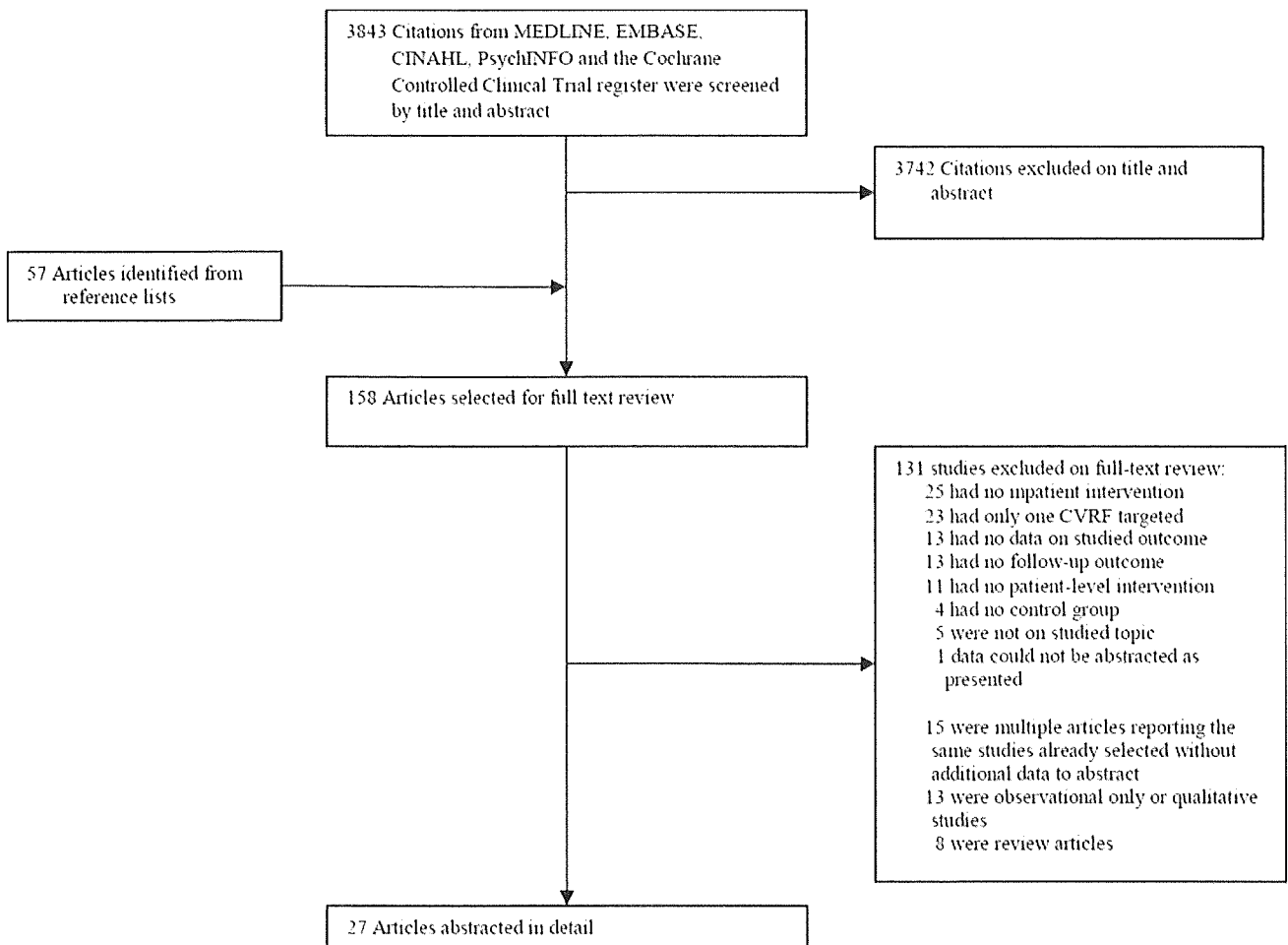


Figure 1. Flow diagram of the study selection process.

separately. In the forest plots, we present data from controlled clinical trials on top, before-after studies on the bottom, and summary statistics for each study type, as well as an overall summary statistic that combines both study types. We do not report the overall RR of the prescription rates of proven efficacious therapies because of the statistical heterogeneity of $>95\%$ for the I^2 statistic observed after pooling. We performed meta-regression to analyze clinical and study quality factors on treatment effects, but recognizing the generally limited statistical power of meta-regression, we conducted (and present) a stratified analysis to explore the potential influence of study design and various intervention factors on RR for mortality. The possibility of publication bias was assessed through use of Begg's test and with visual assessment of a funnel plot.¹⁹ All statistical analyses were performed with Stata version 9.1 (Stata Corp, College Station, Tex).

The authors had full access to and take responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

We identified a total of 3843 unique citations through our search strategy. After a 2-step screening process, 27 articles reporting 26 studies were identified and fulfilled our inclusion criteria.^{9,10,20–44} Figure 1 shows details of study selection. Two articles reporting on the same study but providing different outcomes were abstracted for this analysis.^{42,43} There were 7 disagreements among the reviewers about

eligibility of the studies, leading to a κ value of 0.76. All disagreements were resolved by consensus.

A total of 2467 patients were examined in 16 clinical controlled trials and 38 581 patients in 10 before-after studies. Fourteen clinical controlled trials were described as randomized. The study characteristics, study population, study quality and design, type of intervention, and main findings are presented in Table I of the online Data Supplement. Seven studies included not only a patient-level intervention but also a healthcare provider-level and/or a system-level intervention.^{9,10,39–44} Fourteen studies also included an outpatient component lasting 3 to 24 months.^{9,20,22,26–31,33–36,42}

Meta-Analysis of All-Cause Mortality

Of the 26 studies, 19 provided data on all-cause mortality, with an outcome assessment time varying from 1 to 24 months. Among these, 14 provided follow-up data on mortality at 1 year (see supplementary Table II and Figure 2). Among clinical trials, only 1 study reported a statistically significant difference in all-cause mortality between intervention and control patients at 1 year,²³ whereas 4 before-after studies did so.^{9,10,39,44} The overall pooled RR for all-cause mortality was 0.78 (95% CI, 0.71 to 0.86; P for heterogeneity = 0.28; $I^2 = 14\%$) using a random-effect model. The pooled RR for 1-year all-cause mortality was 0.79 (95% CI, 0.69 to

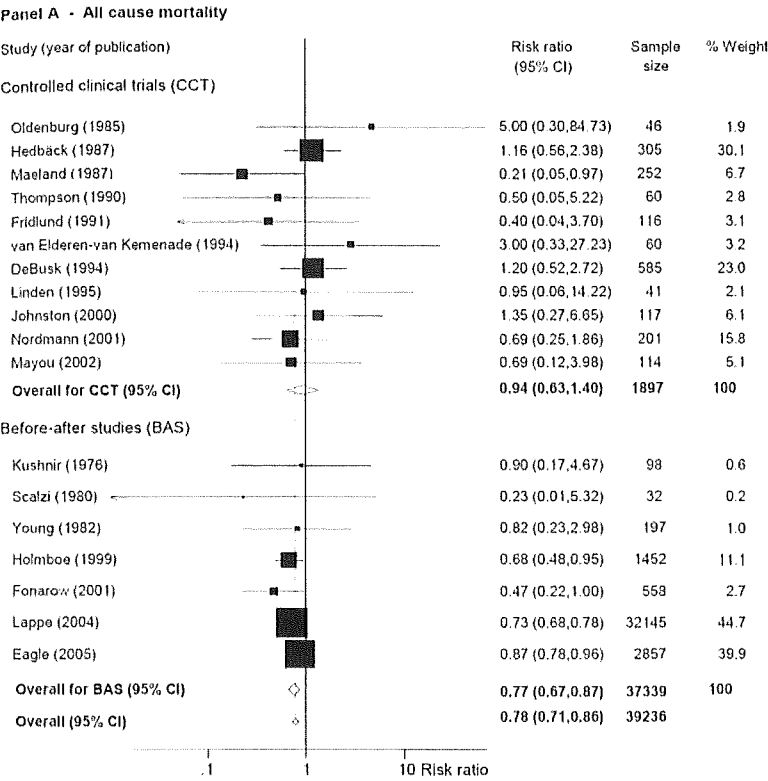
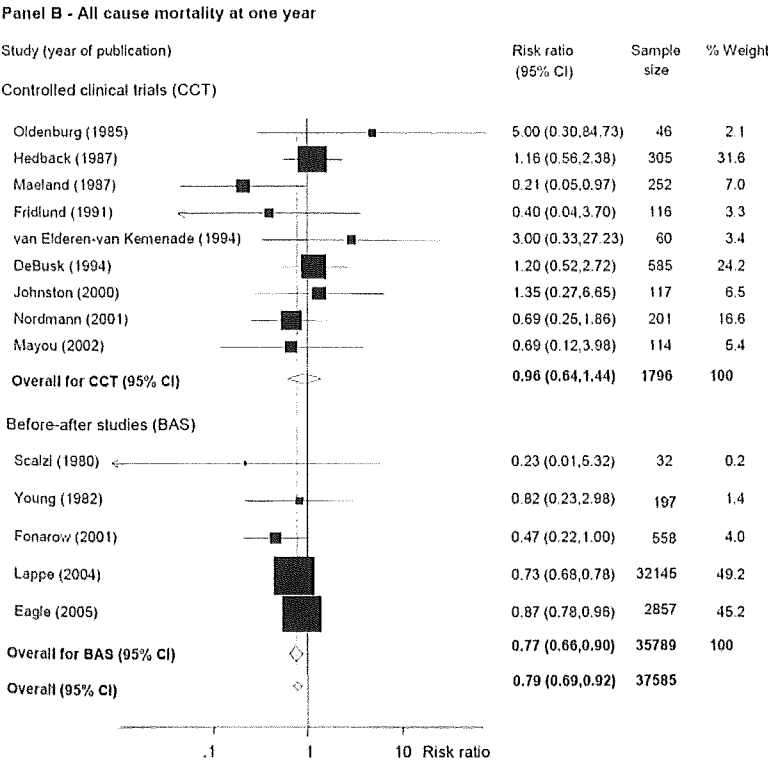


Figure 2. A, Impact of interventions on all-cause mortality (A; n=18 studies) and all-cause mortality at 1 year (B; n=14 studies).



0.92), with a value for statistical heterogeneity of $P=0.12$ and an I^2 of 32%.

The Table presents meta-analysis results for all-cause mortality at 1 year stratified by a number of important clinical factors and study design factors. First, the study design seemed to have an effect on the results. For clinical trials, the RR was 0.96 (95% CI, 0.64 to 1.44) based on analysis of 99

deaths versus 0.77 (95% CI, 0.66 to 0.90) for before-after studies that examined 3680 deaths. Second, if the intervention involved only patients through counseling and education, the RR was 0.93 (95% CI, 0.63 to 1.36), whereas it was 0.77 (95% CI, 0.65 to 0.92) if the intervention also included a provider-level or system-level intervention. Third, among the studied interventions, the continued outpatient component did

Table. Stratified Analysis of All-Cause Mortality for In-Hospital Interventions

Variable	Studies, n	RR	95% CI
Mortality after discharge (from 2 mo to 1 y), all studies	18	0.78	0.71–0.86
Mortality at 1 y only	14	0.79	0.69–0.92
Design of study			
Controlled clinical trials	9	0.96	0.64–1.44
Before-after studies	5	0.77	0.66–0.90
Level of intervention			
Patient-level only	11	0.93	0.63–1.36
Patient-level + healthcare provider-/system-level intervention	3	0.77	0.65–0.92
Continuing intervention in the outpatient setting			
Yes	9	0.84	0.58–1.22
No	5	0.78	0.65–0.94
Targets an increase in prescription rates of proven efficacious medication			
Yes	6	0.80	0.68–0.93
No	8	0.75	0.39–1.46

not seem to change the apparent benefit of interventions notably (for interventions with a continuing outpatient component: RR, 0.84; 95% CI, 0.58 to 1.22; for interventions without a continuing outpatient component: RR, 0.78; 95% CI, 0.65 to 0.94). Fourth, interventions targeting an increase in use of proven efficacious medications were associated with a statistically significant beneficial effect (RR, 0.80; 95% CI, 0.68 to 0.93) that was not observed among the interventions not targeting an increase in these medications (RR, 0.75; 95% CI, 0.39 to 1.46), although with similar effect sizes.

There was no evidence of asymmetry in the funnel plot analysis for mortality at 1 year in both overall and separate analyses by study design (data not shown), and Begg's test was correspondingly not significant ($P > 0.60$ for all associations), findings that make significant publication bias unlikely. However, because our analyses are based on a limited number of studies, publication bias is still not definitively excluded.¹⁹

Meta-Analysis of Secondary Outcomes

Figure 3 and supplementary Table II present information on readmission rates, reinfarction rates, and smoking cessation rates. Eleven of the 26 included studies provided information on readmission rates or reinfarction rates.^{9,21–23,26,32,38,40,41,43,44} The definition of readmission and reinfarction varied across studies (see supplementary Table II), and time of readmission or reinfarction assessment ranged from 1 to 12 months. For 1 study,⁴⁰ we considered the combined outcome of death or readmission as the readmission rate because separate data were not available. The pooled RR for readmission between the intervention and control groups was 0.84 (95% CI, 0.73 to 0.98; P for heterogeneity=0.16; $I^2=32\%$; Figure 3). In stratified analyses by study design, we found a pattern for readmission rate similar to that for all-cause mortality. For clinical trials, the RR was 0.96 (95% CI, 0.79 to 1.17) based

on analysis of 274 readmissions versus 0.71 (95% CI, 0.54 to 0.94) for before-after studies that examined 6586 readmissions. For reinfarction, the RR was 0.59 (95% CI, 0.32 to 1.07), but pooled results should be considered with caution because of significant statistical heterogeneity ($P=0.04$, $I^2=90\%$). For clinical trials, the RR was 0.51 (95% CI, 0.23 to 1.13) based on analysis of 87 reinfarctions versus 0.81 (95% CI, 0.20 to 3.31) for before-after studies that examined 41 reinfarctions. This stratified analysis also should be interpreted with caution because of the small number of studied outcomes.

Thirteen studies reported the smoking cessation rates at various time points ranging from 6 weeks to 18 months.^{20,22–24,26–29,31–33,38,42} For 1 study, data could not be abstracted for statistical analysis because it did not provide the number of smokers at the beginning of the study.³⁸ In-hospital interventions showed increased smoking cessation rates (RR, 1.29; 95% CI, 1.02 to 1.63), but there was evidence of heterogeneity (P for heterogeneity=0.001; $I^2=66\%$; Figure 3).

Figure 4 and supplementary Table II present information on the 7 studies that targeted an increase in use of proven efficacious therapies at discharge.^{9,10,26,39,40,43,44} Most studies showed a significant increase in prescription of each of these treatments. However, it should be noted that 1 study, the before-after study by Fonarow and colleagues,⁹ showed particularly positive results. Because of its combined large size and strongly positive results, this study introduced significant statistical heterogeneity of findings across studies, a finding that led us to avoid pooling of RRs for use of efficacious therapies.

Discussion

The evidence summarized in this review suggests benefit from in-hospital interventions for multiple outcomes, including mortality. However, the evidence is not definitive; a number of caveats and questions emerge from our results. First, the possible mortality benefit is statistically significant only in before-after studies. Second, those before-after studies are the studies in which the interventions were multilevel interventions that also targeted an increase in prescription rates of proven efficacious therapies. Third, there was both clinical and statistical heterogeneity for some of the end points assessed.

A prior nonsystematic review from 1992 on the benefits from in-hospital education after myocardial infarction that considered only isolated patient-level interventions found no significant reduction in mortality despite improved CVRF control.⁵ We found similar results by looking only at the clinical trials included in our meta-analysis. The studies reviewed were mainly isolated patient-level interventions, with inpatient education and counseling as the major interventions; collectively, such studies suggest an improved smoking cessation rate associated with the interventions. Yet, despite such benefits, the overall effect on mortality of isolated patient-level interventions appears to be modest. It needs to be noted, however, that low statistical power and event rates in these clinical trials (ie, a total of 104 deaths studied) might be contributing to their equivocal findings.

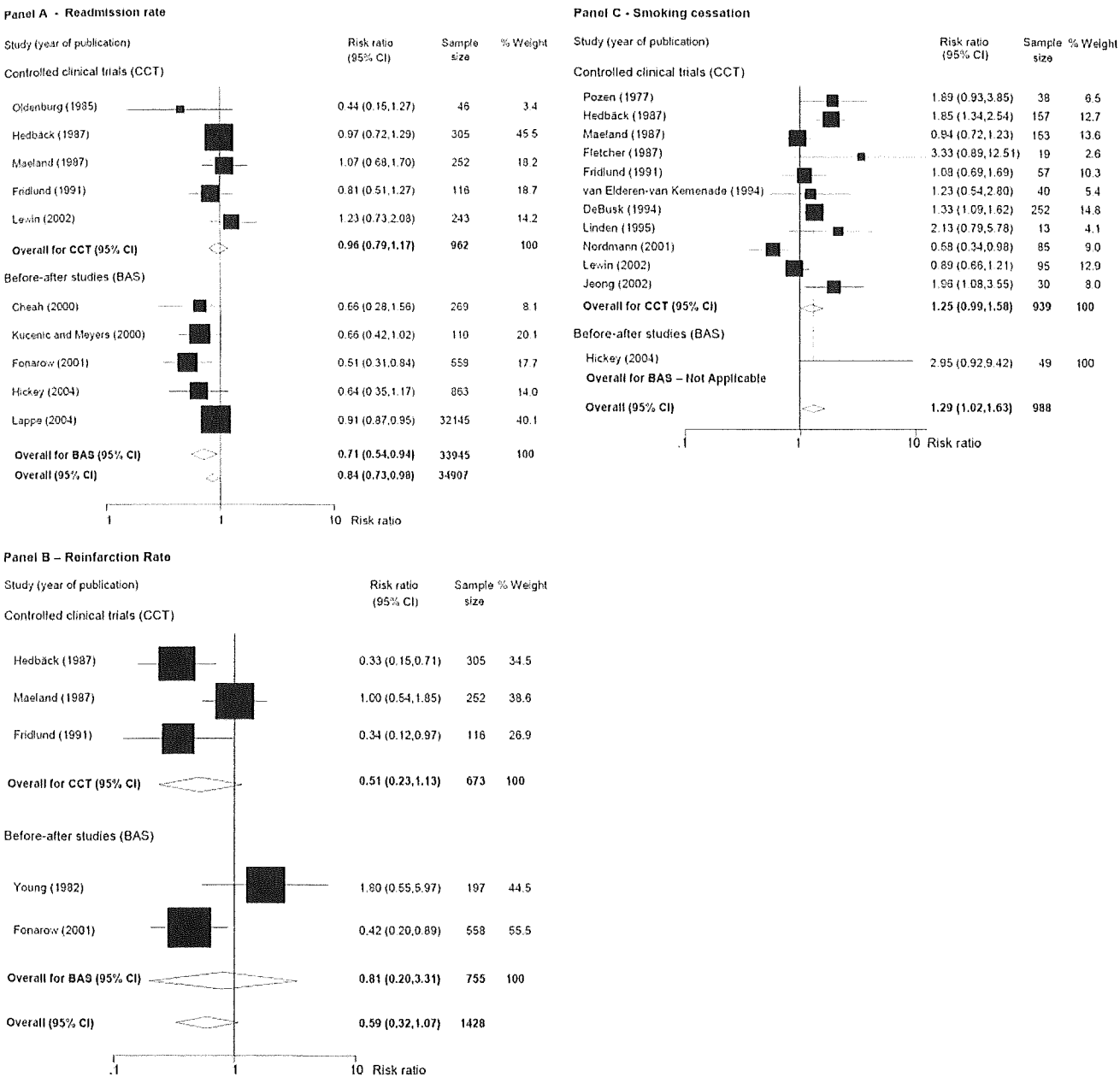


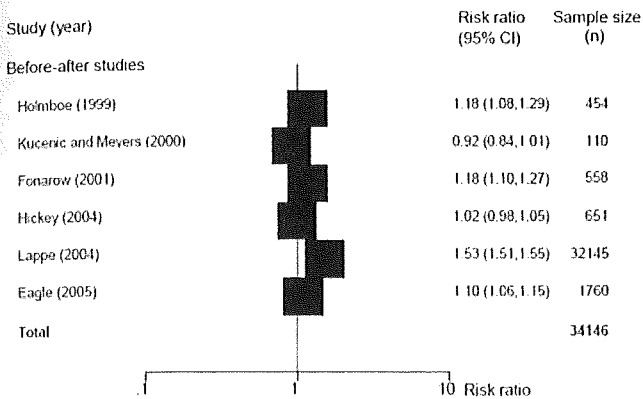
Figure 3. Impact of interventions on readmission rates (A; n=10 studies), reinfarction rates (B; n=5 studies), and smoking cessation (C; n=12 studies).

Individual studies in heart failure patients have shown that a major effect on mortality can be expected by increasing the prescription rate of proven efficacious therapies.⁴⁵ In-hospital initiation of evidence-based cardiovascular therapies and patient education seem to improve long-term patient compliance and clinical outcomes.^{8,46} This might be the mechanistic clue to the observed benefit in mortality outcomes because these factors were the target of the interventions assessed in most of the identified before-after studies.

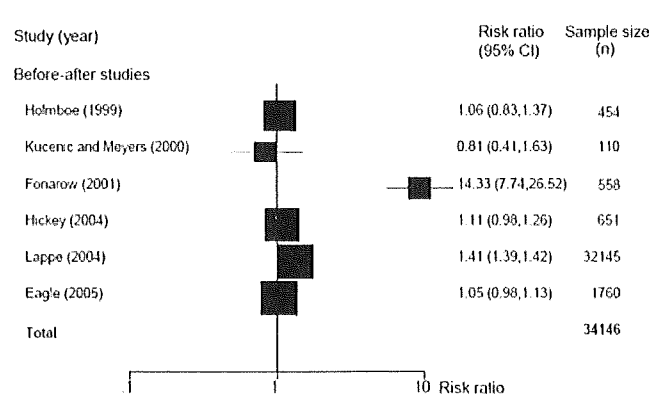
We have asserted that the evidence of mortality benefit from such interventions is promising but not definitive because the significant mortality benefit is seen only in before-after studies. A large-cluster randomized controlled trial could test the efficacy of multilevel, in-hospital prevention more definitively. Accordingly, one possible proposal for

the needed “next research step” would be to call for a large-cluster randomized controlled trial comparing a major secondary prevention intervention with usual care. However, some may already accept the benefit of multilevel interventions based on existing evidence and instead propose that future studies should move beyond comparisons with usual care to instead assess the specific elements of interventions that are most effective. For example, a relevant study question would be whether interventions need to be continued longitudinally in the outpatient setting versus simply administered during hospitalization. Our study did not suggest a significant difference in efficacy on this factor, but a randomized comparison would be more definitive. Similarly, future studies could formally assess whether interventions should rely only on system-level components without patient-level

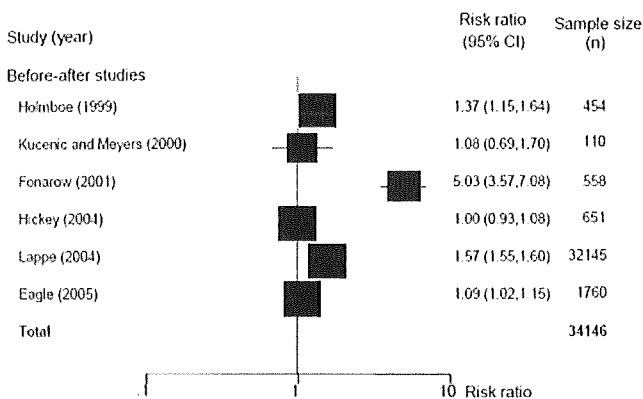
Panel A – Use of anti-platelet agents



Panel C - Use of angiotensin converting enzyme inhibitors



Panel B - Use of beta-blockers



Panel D – Use of lipid lowering drugs

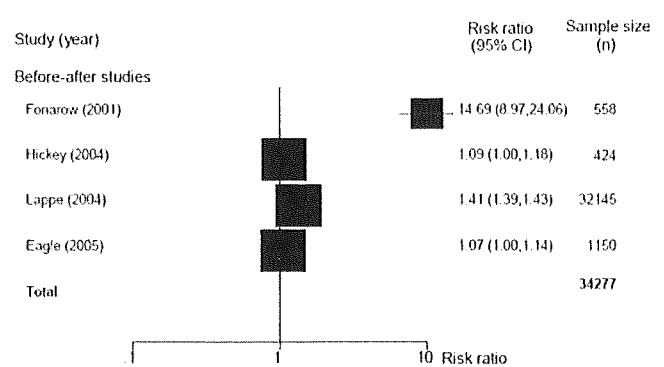


Figure 4. Impact of interventions on prescription rates of antiplatelet agents (A; n=6 studies), β -blockers (B; n=6 studies), angiotensin-converting enzyme inhibitors (C; n=6 studies), and lipid-lowering drugs at discharge (D; n=4 studies).

intervention versus other combinations of levels of intervention. Our conceptual categorization of secondary prevention programs by levels of intervention should facilitate future evaluations of such interventions.

The major limitation of our systematic review (inherent to the studies that we have systematically reviewed) is that the reported mortality results rely mainly on data from before-after studies. Because of ongoing trends of both increased use of proven efficacious therapies and decreased cardiovascular mortality,^{47,48} the outcome benefits seen in this study could relate to weakness of study design rather than the interventions. The Guidelines Applied to Practice (GAP) project tried to control this factor through a rapid cycle quality improvement strategy, thereby reducing the time for outcome measurement, and showed a reduction in mortality at 1 year.¹⁰ Furthermore, the same group compared process outcomes of 11 control hospitals that wanted to participate in GAP but were not selected relative to 10 GAP intervention hospitals and demonstrated that “wanting to improve” did not achieve the degree of change in process outcomes observed in participating hospitals.⁴⁹ Also of note, Lappe and colleagues⁴⁴ provided data on mortality trends in a study region of interest and found that a secondary prevention intervention program was probably contributing to improved outcomes over and above the trends in their study region.

There are other limitations in this body of literature. First, for most of the studies identified, mortality was not a primary

outcome, and as a result, the monitoring of this outcome may not have been optimal in all studies. Second, there was major clinical heterogeneity in the interventions studied, and our interpretation of interventions also was challenged by heterogeneity in the reporting of some outcomes. Smoking cessation rates were abstracted, but only 1 study provided a confirmation of smoking cessation by cotinine level measurement.²⁸ The definitions of readmission rates also were numerous, with some studies considering same-cause readmissions and others all-cause readmissions. For the studies reporting data on reinfarction rate, there was no definition of reinfarction in the methods section for most of them. The meta-analysis of secondary outcomes such as reinfarction and smoking cessation led to RRs with significant statistical heterogeneity, and these pooled data should be interpreted with caution. Finally, we caution that although we carefully reviewed the full text of rehabilitation interventions and screened the reference lists of former systematic reviews on outpatient rehabilitation,^{3,4} it is possible that our search strategy might have missed some studies on secondary prevention interventions in the outpatient setting that also had a component beginning during the hospital stay.

Conclusions

The evidence on the efficacy of in-hospital, patient-level interventions for secondary prevention after acute coronary disease is promising but not definitive. Because a significant

reduction in mortality has been shown only in the before-after studies performed to date, larger randomized controlled trials with sufficient statistical power may be needed to confirm these promising findings. However, there may no longer be sufficient equipoise to study multilevel inpatient interventions on secondary prevention versus merely usual care. Future studies may be more relevant to providers and participants if they move toward randomized studies assessing the components of interventions that contribute the most to improved outcomes. Our findings suggest that interventions may be more effective when they target not only the patient but also the providers and the healthcare system.

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CLINICAL PERSPECTIVE

Secondary prevention programs for patients experiencing an acute coronary syndrome have been shown to be effective in the outpatient setting. Interest in the inpatient setting for secondary prevention is heightened by the recognized potential of hospitalization after an acute disease as a “teachable moment” for behavioral change that may increase the benefit of counseling interventions delivered to hospitalized patients. Early in-hospital initiation of medications also might increase the likelihood of being adequately treated. In recent years, multiple studies have assessed pragmatic interventions targeting patient education and/or an increase in prescription rates by physicians. The present work pools the results of the existing studies to determine whether in-hospital, patient-level interventions targeting multiple cardiovascular risk factors reduce all-cause mortality after an acute coronary syndrome. We included controlled clinical trials and before-after studies and classified the interventions as patient-level interventions (ie, education or counseling interventions) with or without associated healthcare provider-level interventions (eg, improving physician skills and effectiveness in counseling through an educational program) and/or system-level interventions (eg, facility outcome reporting). Overall, the studied interventions seemed to reduce the risk of all-cause mortality at 1 year. However, the apparent benefit depended on study design and the level of intervention. Only interventions including a provider- or system-level intervention suggested reduced mortality compared with patient-level-only interventions. Because only before-after studies suggest a significant reduction in mortality, the evidence for in-hospital, patient-level interventions for secondary prevention is promising but not definitive. Future research should formally test which components of interventions provide the greatest benefit.