# Association of cardiovascular health screening with mortality, clinical outcomes, and health care cost: A nationwide cohort study 

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## A R T I C L E I N F O

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#### Abstract

Objective. To determine whether a cardiovascular disease (CVD) health screening program is associated with CVD-related health conditions, incidence of cardiovascular events, mortality, healthcare utilization, and costs.

Methods. Cohort study of a 3\% random sample of all Korea National Health Insurance members 40 years of age or older and free of CVD or CVD-related health conditions was conducted. A total 443,337 study participants were followed-up from January 1, 2005 through December 31, 2010.

Results. In primary analysis, the hazard ratios for CVD mortality, all-cause mortality, incident composite CVD events, myocardial infarction, cerebral infarction, and cerebral hemorrhage comparing participants who attended a screening exam during 2003-2004 compared to those who did not were 0.58 ( $95 \% \mathrm{Cl}$ : 0.53-0.63), 0.62 ( $95 \%$ CI: $0.60-0.64$ ), 0.82 ( $95 \%$ CI: $0.78-0.85$ ), 0.84 ( $95 \% \mathrm{CI}: 0.75-0.93$ ), 0.84 ( $95 \% \mathrm{CI}: 0.79-0.89$ ), and 0.73 ( $95 \% \mathrm{CI}$ : 0.67-0.80), respectively. Screening attenders had higher rates of newly diagnosed hypertension, diabetes mellitus, and dyslipidemia, lower inpatient days of stay and cost, and lower outpatient cost compared to nonattenders.

Conclusions. Participation in CVD health screening was associated with lower rates of CVD, all-cause mortality, and CVD events, higher detection of CVD-related health conditions, and lower healthcare utilization and costs.


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## Introduction

Cardiovascular disease (CVD) is the most common cause of morbidity and mortality in the world (Celermajer et al., 2012; Minino et al., 2011). Since several CVD risk factors are modifiable, prevention programs routinely screen for hypertension, diabetes, and dyslipidemia (Dalton and Soljak, 2012; Nakanishi et al., 1996; Perk et al., 2012; Thomsen et al., 2006; Will and Loo, 2008) expecting that early detection and treatment

[^0]of CVD-related health conditions (hypertension, diabetes, dyslipidemia) will decrease the burden of CVD (U.S. Preventive Services Task Force, 2001, 2007, 2008). The effectiveness of screening programs for CVD-related health conditions on health outcomes and healthcare utilization, however, is unclear. Some (Bernacki et al., 1988; Kaczorowski et al., 2011; Nakanishi et al., 1996), but not all (Thomsen et al., 2006; Thomsen et al., 2005), studies have reported higher outpatient treatment rates of CVD-related health conditions and lower hospitalization among participants in screening programs. These studies have been limited by the use of relatively small samples from a limited area (Ren et al., 1994; Thomsen et al., 2006; Thomsen et al., 2005), short followup periods (Nakanishi et al., 1996; OXCHECKStudygroup, 1995), or high attrition rates (South-East London Screening Study Group, 2001). Moreover, there is no study that directly links screening to lower CVD events and mortality in the general population (Ebrahim et al., 2011; Krogsboll et al., 2012).

We hypothesized that screening would be associated with higher detection and outpatient care of CVD-related health conditions and lower incidence of CVD events and mortality. We thus conducted a population-based cohort study to determine whether a nationwide CVD health screening program is associated with CVD incidence, mortality, healthcare utilization, and costs.

## Methods

## Screening program in Korea

In South Korea, a country with universal healthcare coverage, the Korean National Health Insurance (KNHI) Corporation provides a biennial CVD health screening program to all national health insurance members over 40 years of age free of charge. KNHI is a mandatory social insurance that covers virtually all Koreans except for Medicaid beneficiaries in the lowest income bracket (approximately $3 \%$ of the population). The prevention programs aim to detect and treat CVD-related health conditions including hypertension, diabetes, and dyslipidemia early to reduce the burden of CVD and offers subsequent educational counseling or treatment referral for participants with identified health problems. KNHI sends invitation letters to all national health insurance members over 40 years of age. Eligible members can get the screening examination at medical institutions including private clinics and hospitals, and public health centers engaged voluntarily for the national screening program. After the screening, all medical institutions are obligated to report the screening results and send appropriate documented feedback to screening attenders to get reimbursed by the KNHI. People who have abnormal values detected are recommended to seek confirmation of the diagnosis and relevant medical services from nearby medical facilities, and medical services are then provided mainly by private healthcare providers on a fee-for-service basis which is then again reimbursed by the KNHI.

## Study population and design

We randomly selected a $3 \%$ sample $(\mathrm{n}=621350)$ of all KNHI members 40 years of age or older as of December 31, 2002 and made a retrospective cohort. We excluded participants with cancer, diabetes, hypertension, dyslipidemia, or any related CVD including stroke and myocardial infarction ( $\mathrm{n}=170490$ ). As screening was provided biennially, we used two-year windows (e.g., 2003-2004 or 2005-2006) to define participation in screening programs. As a consequence, we further excluded participants who died $(\mathrm{n}=6404)$ or were lost to followup ( $\mathrm{n}=1119$ ) before January 1,2005 , which is the end of the first two-year period. The final sample size was 443,337 participants. The study was approved by the institutional review board of the Seoul National University Hospital.

## Data collection

KNHI collects information necessary for reimbursement of each medical service including age, sex, monthly insurance premium (a proxy for economic status), disability status, disease codes, and costs incurred. Past medical history was based on the diagnoses in KNHI medical service claims data during 2002, coded using the International Classification of Diseases, 10th revision (ICD-10) (Wilchesky et al., 2004). Comorbidities were summarized using the Charlson comorbidity index, a weighted measure of comorbidity. Index is composed of 19 conditions including previous CVD, heart failure, lung diseases, renal diseases, hematologic disorders, liver diseases, neurologic abnormalities, cancers, and AIDS (Klabunde et al., 2007; Klabunde et al., 2000; Nuttall et al., 2006; Sundararajan et al., 2004). In Korea, insurance premium is imposed according to income levels. We used monthly insurance premium as a proxy for their economic status while it might not fully capture the socioeconomic status of a subject, especially if they are retired because it was the only available information representing people's economic status. People with disabilities were identified using the National Disability Registry which contained information about types (15 groups: e.g. auditory, visual, mental, etc.) and severity of disability (Grades 1 to 6 : very severe to mild) (Park et al., 2008). As people with any disabilities comprised only $2 \%$ of the study sample, we classified the subjects into people without disability and with any disability regardless of type and severity.

We obtained screening participation data from the KNHI screening database. Health questionnaires included information on smoking (non-smoker, ex-smoker, current smoker) and alcohol intake (drinker, non-drinker). Physical exams included measurements of weight, height, and blood pressure. Body mass index (BMI) was calculated as weight in kilograms divided by height in
squared meters. Laboratory tests included total cholesterol and fasting blood glucose.

## Study outcomes

The primary outcome of the study was CVD mortality. Secondary outcomes were incidence of CVD events, all-cause mortality, detection of CVD-related health conditions, healthcare utilization, and costs. Vital status was ascertained routinely by KNHI by matching with the National Death Registry. Koreans who died abroad were also registered and under-ascertainment of deaths because of out-migration was negligible. CVD deaths were defined as deaths with underlying ICD-10 codes I00-I99 as registered in the National Death Registry data.

Incidence of CVD events, including myocardial infarction (ICD-10 codes I21-I22), ischemic stroke (I63), and hemorrhagic stroke (I60-I62) were defined as inpatient hospitalizations from KNHI claims records. Detection of CVDrelated health conditions was defined as the presence of claims for hypertension (I10, I15), diabetes (E10, E118, E119, E13, E149), or hypercholesterolemia (E78) within one year after the screening period. According to instructions from the KNHI, reimbursement for hypertension can be made when blood pressure is $\geq 140 / 90 \mathrm{~mm} \mathrm{Hg}$ at two or more separate visits. According to the American Diabetic Association's guideline, diabetes is defined when fasting blood glucose is $\geq 126 \mathrm{mg} / \mathrm{dL}$ at two or more separate visits, $\mathrm{HbA1c} \geq 6.5 \%$ two or more separate visits, 2-h plasma glucose $\geq 200 \mathrm{mg} / \mathrm{dL}$, or classic symptoms of hyperglycemia with a random plasma glucose $\geq 200 \mathrm{mg} / \mathrm{dL}$ are present. Hypercholesterolemia is defined when total cholesterol is $>240 \mathrm{mg} /$ dL at two or more separate visits at least 3 months apart. Healthcare utilization and healthcare expenditures incurred included number of inpatient and outpatient days and expenses for diagnosis, monitoring, and treatment of CVD, hypertension, diabetes, dyslipidemia, or related conditions during 2005-2010 from KNHI claims records.

## Statistical analysis

We conduct two sets of analyses to test the robustness of the results (Fig. 1). For the primary analysis, we performed multivariate analyses according to attending a health screening visit during 2003-2004 with adjustment for baseline age, sex, economic status, disability, and comorbidity index.

We conducted secondary analysis to control for hidden confounding factors associated with screening attendance. Therefore, for the secondary analysis, we restricted the analysis to 160,607 participants who had attended a health screening visit in 2003-2004. Each of above multivariate analyses were repeated in secondary analysis with adjustment for same covariates considered in the primary analysis plus information on smoking, drinking, body mass index, hypertension, diabetes, and hypercholesterolemia obtained in the 2003-2004 screening visit. Thus, the secondary analysis compares participants who already attended a prior screening visit and who had similar demographic factors, comorbidities, life-style, and CVD-related health conditions. The secondary analysis resulted in 155,620 participants.

In both the primary and the secondary analyses, association between participation in health screening and mortality (CVD and all-cause) and the risk of CVD events (myocardial infarction, cerebral infarction and cerebral hemorrhage, and composite events) was estimated by using Cox proportional-hazards regression models. In the primary analysis, follow-up started on January 1, 2005, while in the secondary analysis, follow-up started on January 1, 2007. Follow-up extended until the development of a CVD endpoint, death, or December 31, 2010, whichever came first. Incidence per 1000 person-years and hazard ratios were reported for each analysis.

In our cohort, the status of screening participation may change over time. For this reason, we also conducted a sensitivity analysis using time-dependent Cox models (Dekker et al., 2008). To investigate the effect of age at screening on the potential difference, we conducted stratified analysis with age $<60$ and age $\geq 60$. Additionally, we repeated the primary and secondary analyses after propensity score matching.

We performed a chi-square test to compare the detection of cardiovascular disease related health conditions within one year after attendance in a cardiovascular health screening program. The differences in healthcare utilization and healthcare expenditures between attenders and non-attenders were analyzed using analysis of covariance (ANCOVA). Statistical analyses were performed in STATA 12.0 (STATA Corp./SE). Statistical significance was defined as two-tailed p-values of $<0.05$.


Fig. 1. Flowchart of study participants: Flowchart showing eligible participants for primary and secondary analysis in our retrospective cohort study.

## Results

Among 443,337 study participants, 160,607 (36.2\%) underwent screening in 2003-2004, and 110,278 underwent subsequent screening in 2005-2006 (Fig. 1). Characteristics of the attenders and nonattenders are described in Table 1.

In the primary analysis, participants who attended a health screening visit during 2003-2004 had significantly lower risks of all-cause mortality and cardiovascular events during 2005-2010 compared to those who did not attend a health screening visit. Incidence per 1000 person-years for cardiovascular and all-cause mortality were 2.00 ( $95 \% \mathrm{Cl}: 1.93-2.07$ ) and 10.53 ( $95 \% \mathrm{Cl}$ : 10.37-10.68) for non-attenders, and 0.77 ( $95 \% \mathrm{CI}: 0.72-0.83$ ) and 4.86 ( $95 \% \mathrm{CI}: 4.72-5.01$ ) for attenders, respectively. The hazard ratios ( $95 \%$ confidence interval [CI]) for cardiovascular mortality, all-cause mortality, incident composite CVD events, myocardial infarction, cerebral infarction, and cerebral hemorrhage were 0.58 ( $95 \%$ CI: $0.53-0.63$ ), 0.62 ( $95 \%$ CI: $0.60-0.64$ ), 0.82 ( $95 \% \mathrm{CI}$ :
$0.78-0.85$ ), 0.84 ( $95 \%$ CI: $0.75-0.93$ ), 0.84 ( $95 \%$ CI: $0.79-0.89$ ), and 0.73 ( $95 \% \mathrm{CI}: 0.67-0.80$ ), respectively (Table 2 and Fig. 2).

In the secondary analysis, restricted to participants who attended a screening exam in 2003-2004 and further adjusted for life style and CVD-related health conditions, participants who attended a further screening visit during 2005-2006 also had significantly lower CVD and all-cause mortality during 2007-2010 compared to those who had not attended a further screening visit. The hazard ratios for CVD and all-cause mortality were 0.73 ( $95 \% \mathrm{CI}$ : $0.60-0.88$ ) and 0.67 ( $95 \%$ CI: $0.62-0.72$ ), respectively (Table 2). In the secondary analysis, the rate of incident composite CVD events, myocardial infarction, cerebral infarction, and cerebral hemorrhage were similar in participants who attended a further screening exam compared to those who did not, but the number of cases was small and the $95 \% \mathrm{Cl}$ was relatively wide. The hazard ratios for incident composite cardiovascular events, myocardial infarction, cerebral infarction, and cerebral hemorrhage were 0.98 ( $95 \%$ CI: 0.89-1.09), 1.01 ( $95 \%$ CI: 0.81-1.27), 0.97 ( $95 \%$ CI: 0.86-1.10), and

Table 1
Characteristics of study participants by attendance in a cardiovascular health screening program.

| Variable | By attendance in 2003-2004 screening ${ }^{\text {a }}(\mathrm{n}=443,337$ ) |  | p | By attendance in 2005-2006 screening among attenders in 2003-2004 screening $^{\mathrm{b}}$ ( $\mathrm{n}=155,620$ ) |  | p |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Non-attenders | Attenders |  | Non-attenders | Attenders |  |
|  | ( $\mathrm{n}=282,730$ ) | ( $\mathrm{n}=160,607$ ) |  | ( $\mathrm{n}=45,342$ ) | ( $\mathrm{n}=110,278$ ) |  |
| Age, years, mean (SD) | 51.61 (11.1) | 50.30 (9.3) | <0.001 | 51.07 (10.0) | 49.79 (8.8) | <0.001 |
| Female gender, n (\%) | 148,242 (52.4) | 69,377 (43.2) | <0.001 | 21,874 (48.2) | 45,010 (40.8) | <0.001 |
| Economic status ${ }^{\text {c }}$, n (\%) |  |  | <0.001 |  |  | <0.001 |
| 1st quartile (low) | 47,855 (16.9) | 29,848 (18.6) |  | 9139 (20.2) | 19,701 (17.9) |  |
| 2nd quartile | 59,045 (20.9) | 28,549 (17.8) |  | 8867 (19.6) | 18,779 (17.0) |  |
| 3rd quartile | 75,938 (26.9) | 37,531 (23.4) |  | 10,704 (23.6) | 25,693 (23.3) |  |
| 4th quartile (high) | 99,892 (35.3) | 64,679 (40.3) |  | 16,632 (36.7) | 46,105 (41.8) |  |
| Disability ${ }^{\text {d }}$, n (\%) | 6392 (2.3) | 2671 (1.7) | <0.001 | 967 (2.1) | 1597 (1.5) | <0.001 |
| Charlson comorbidity index, Mean (SD) | 0.35 (0.72) | 0.44 (0.79) | <0.001 | 0.43 (0.79) | 0.44 (0.78) | 0.012 |
| BMI, n (\%) |  |  |  |  |  | <0.001 |
| Mean (SD) |  | 23.7 (2.9) |  | 23.8 (3.00) | 23.7 (2.83) |  |
| $<18.5 \mathrm{~kg} / \mathrm{m}^{2}$ |  | 4168 (2.6) |  | 1331 (3.0) | 2593 (2.4) |  |
| $18.5-23 \mathrm{~kg} / \mathrm{m}^{2}$ |  | 62,194 (38.7) |  | 17,249 (38.0) | 42,873 (38.9) |  |
| $23-25 \mathrm{~kg} / \mathrm{m}^{2}$ |  | 44,256 (27.6) |  | 12,210 (26.9) | 30,843 (28.0) |  |
| $25-30 \mathrm{~kg} / \mathrm{m}^{2}$ |  | 46,469 (28.9) |  | 13391 (29.5) | 31808 (28.8) |  |
| $>30 \mathrm{~kg} / \mathrm{m}^{2}$ |  | 3419 (2.1) |  | 1161 (2.6) | 2161 (2.0) |  |
| Smoking, n (\%) |  |  |  |  |  | $<0.001$ |
| None |  | 101,537 (63.2) |  | 29,818 (65.8) | 70,632 (64.1) |  |
| Past |  | 15842 (9.9) |  | 3804 (8.4) | 11,734 (10.6) |  |
| Current |  | 40,237 (25.1) |  | 11,720 (25.9) | 27,912 (25.3) |  |
| Drinking, n (\%) |  |  |  |  |  | <0.001 |
| None-drinker |  | 85,845 (53.5) |  | 25,874 (57.1) | 58,445 (53.0) |  |
| Drinker |  | 72,495 (45.1) |  | 19,468 (42.9) | 51,833 (47.0) |  |
| Systolic blood pressure, n (\%) |  |  |  |  |  | $<0.001$ |
| Mean (SD) |  | 125.0 (17.7) |  | 125.6 (18.4) | 124.7 (17.0) |  |
| $<140 \mathrm{~mm} \mathrm{Hg}$ |  | 125,629 (78.2) |  | 34,758 (76.7) | 87,120 (79.0) |  |
| $\geq 140 \mathrm{~mm} \mathrm{Hg}$ |  | 34,978 (21.8) |  | 10,584 (23.3) | 23,158 (21.0) |  |
| Diastolic blood pressure, n (\%) |  |  |  |  |  | <0.001 |
| Mean (SD) |  | 78.5 (11.5) |  | 78.6 (11.7) | 78.5 (11.2) |  |
| $<90 \mathrm{~mm} \mathrm{Hg}$ |  | 124,927 (77.8) |  | 35,056 (77.3) | 85,994 (78.0) |  |
| $\geq 90 \mathrm{~mm} \mathrm{Hg}$ |  | 35,680 (22.2) |  | 10,286 (22.7) | 24,284 (22.0) |  |
| Fasting glucose level, n (\%) |  |  |  |  |  | $<0.001$ |
| Mean (SD) |  | 95.5 (28.2) |  | 96.7 (30.2) | 95.0 (26.9) |  |
| $<126 \mathrm{mg} / \mathrm{dL}$ |  | 151,970 (94.6) |  | 42,513 (93.8) | 104,805 (95.0) |  |
| $\geq 126 \mathrm{mg} / \mathrm{dL}$ |  | 8637 (5.4) |  | 2829 (6.2) | 5473 (5.0) |  |
| Total cholesterol, n (\%) |  |  |  |  |  | $<0.001$ |
| Mean (SD) |  | 198.0 (38.6) |  | 198.8 (39.5) | 198.0 (37.6) |  |
| $<240 \mathrm{mg} / \mathrm{dL}$ |  | 140,329 (87.4) |  | 39,324 (86.7) | 96,631 (87.6) |  |
| $\geq 240 \mathrm{mg} / \mathrm{dL}$ |  | 20,278 (12.6) |  | 6018 (13.3) | 13,647 (12.4) |  |

Numbers for each variable may not add up to $100 \%$ due to missing values.
${ }^{\text {a }}$ Primary analysis: by attendance in a cardiovascular health screening program 2003-2004.
${ }^{\text {b }}$ Secondary analysis: by attendance in a cardiovascular health screening program 2005-2006 among attenders in 2003-2004 screening.
${ }^{\text {c }}$ Economic status: monthly insurance premium was used as a proxy for economic status.
${ }^{\text {d }}$ Disability: subjects were classified into people without disability and with any disability.
0.84 ( $95 \%$ CI: $0.68-1.03$ ), respectively (Table 2). In sensitivity analyses using participation in a health exam as a time-dependent variable, the results were consistent with our primary and secondary analyses, although the associations were stronger in time-dependent models and also significant in secondary analysis (Supplementary Table 2). The results were consistent in age stratified analyses (Supplementary Table 3).

With respect to detection of CVD-related health conditions, the proportion of participants with newly diagnosed hypertension ( $5.21 \%$ vs. $4.97 \%, \mathrm{p}=0.001$ ), diabetes mellitus ( $1.32 \%$ vs. $1.23 \%, \mathrm{p}=0.01$ ), and dyslipidemia ( $3.37 \%$ vs. $2.83 \%$, $\mathrm{p}<0.001$ ) during 2005 was higher in participants who attended screening during 2003-2004 compared to those who did not (Table 3). The differences in identifying CVDrelated health conditions one year after the 2005-2006 screening period, however, were largely attenuated and no longer statistically significant in our secondary analysis restricted to participants who had already been screened in 2003-2004 except dyslipidemia ( $4.02 \%$ vs. $3.70 \%, p=0.01$ ).

When we evaluated healthcare utilization and costs in our primary analysis, participants who attended a screening exam in 2003-2004 had lower inpatient days of stay, inpatient cost and outpatient cost
and higher outpatient visits during 2005-2010 compared to those who did not attend a screening exam (Table 4). When we restricted the analyses to participants who had attended a screening exam in 2003-2004, those who attended a further screening visit in 2005-2006 had lower inpatient days of stay and cost and higher outpatient days during 2007-2010, but similar inpatient costs and outpatient costs with participants who had not attended a further screening visit. In analyses with propensity score matching, the results were also consistent (Supplementary Figs. 1, 2, Supplementary Tables 1, 4, 5, 6).

## Discussion

In this large cohort study of CVD health screening, we found that screening practices were associated with lower rates of CVD and allcause mortality and CVD events, increased detection of CVD-related health conditions, and lower healthcare utilization and costs. These findings were evident even with participants who participated in prior screening after adjusting CVD-related health conditions, smoking status, alcohol intake, comorbidities, hypertension, diabetes, and hypercholesterolemia, reducing the likelihood that the observed differences are due

Table 2
Hazard ratios for mortality and cardiovascular events by attendance in a cardiovascular health screening program.

|  | Person-years |  | No. of events |  | Incidence per 1000 person-years |  | HR (95\% CI) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Non-attenders | Attenders | Non-attenders | Attenders | Non-attenders | Attenders |  |
| By attendance in 2003-2004 screening ( $n=443,337)^{\text {a }}$ |  |  |  |  |  |  |  |
|  |  |  | $\mathrm{n}=282,730$ | $\mathrm{n}=160,607$ |  |  |  |
| Cardiovascular mortality | 1,639,385.6 | 950,646.6 | 3272 | 731 | 2.00 (1.93-2.07) | 0.77 (0.72-0.83) | 0.58 (0.53-0.63) |
| All-cause mortality | 1,639,385.6 | 950,646.6 | 17,256 | 4624 | 10.53 (10.37-10.68) | 4.86 (4.72-5.01) | 0.62 (0.60-0.64) |
| Composite cardiovascular events ${ }^{\text {b }}$ | 1,605,107.4 | 934,758.5 | 7338 | 3108 | 4.57 (4.47-4.68) | 3.32 (3.21-3.44) | 0.82 (0.78-0.85) |
| Myocardial infarction | 1,633,254.5 | 947,112.3 | 1343 | 645 | 0.82 (0.78-0.87) | 0.68 (0.63-0.74) | 0.84 (0.75-0.93) |
| Cerebral infarction | 1,617,032.2 | 940,623.6 | 4642 | 1926 | 2.87 (2.79-2.95) | 2.05 (1.96-2.14) | 0.84 (0.79-0.89) |
| Cerebral hemorrhage | 1,631,787.5 | 947,661.3 | 1918 | 734 | 1.18 (1.12-1.23) | 0.77 (0.72-0.83) | 0.73 (0.67-0.80) |
| By attendance in 2005-2006 screening among attenders in 2003-2004 screening ( $n=155,620$ ) ${ }^{\text {c }}$ |  |  |  |  |  |  |  |
|  |  |  | $\mathrm{n}=45,342$ | $\mathrm{n}=110,278$ |  |  |  |
| Cardiovascular mortality | 178,395.65 | 437,890.98 | 230 | 267 | 1.29 (1.13-1.47) | 0.61 (0.54-0.69) | 0.73 (0.60-0.88) |
| All-cause mortality | 178,395.65 | 437,890.98 | 1450 | 1824 | 8.13 (7.72-8.56) | 4.17 (3.98-4.36) | 0.67 (0.62-0.72) |
| Composite cardiovascular events ${ }^{\text {b }}$ | 262,898.43 | 647,915.95 | 668 | 1356 | 2.54 (2.36-2.74) | 2.09 (1.98-2.21) | 0.98 (0.89-1.09) |
| Myocardial infarction | 267,690.79 | 655,743.34 | 126 | 285 | 0.47 (0.40-0.56) | 0.43 (0.39-0.49) | 1.01 (0.81-1.27) |
| Cerebral infarction | 265,026.53 | 651,879.22 | 447 | 842 | 1.69 (1.54-1.85) | 1.29 (1.21-1.38) | 0.97 (0.86-1.10) |
| Cerebral hemorrhage | 267,734.72 | 656,266.48 | 164 | 305 | 0.61 (0.53-0.71) | 0.46 (0.42-0.52) | 0.84 (0.68-1.03) |

${ }^{\text {a }}$ Primary analysis: by attendance in a cardiovascular health screening program 2003-2004, adjusted for age, sex, disability, economic status and Charlson comorbidity index.
${ }^{\text {b }}$ Composite cardiovascular events: sum of myocardial infarction, cerebral infarction, and cerebral hemorrhage.
${ }^{\text {c }}$ Secondary analysis: by attendance in a cardiovascular health screening program 2005-2006 among attenders in 2003-2004 screening, additional adjustment for secondary analysis included smoking status, alcohol intake, body mass index (BMI), hypertension, diabetes, and hypercholesterolemia.
to self-selection of healthier participants in screening programs. Although there is still a possibility of unmeasured confounders, we think that our secondary analysis, which was adjusted for the risk factor levels and for previous screening behavior extensively, is suggestive of a possible true effect of cardiovascular screening on the outcomes.

The effect of screening programs for CVD-related health conditions is controversial. While some trials showed increased treatment and reduced admission (Kaczorowski et al., 2011), others showed no differences in health care utilization and in mortality (Krogsboll et al., 2012). Indeed, a recent meta-analysis reported a lack of survival benefit of screening programs, but most studies included in this meta-analyses were conducted before 1990 (Krogsboll et al., 2012), when the cut-off for initiating treatment of CVD-related health conditions was higher than it is today (2013; Moser, 1997; Shuman and Spratt, 1981) and highly effective CVD drugs including statins (LaRosa et al., 1999), angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers (Savarese et al., 2013) were either not commonly used or not available. Our findings thus suggest that CVD screening in modern practice settings is potentially effective.

In our study, participants who attended a screening visit were more likely to have subsequent claims for hypertension, diabetes and dyslipidemia in the following year, confirming that increased detection of CVD-related health conditions lead to subsequent care (James et al., 2014; Lackland et al., 2014). Similar results have been found in a cohort study in Taiwan (Lin et al., 2011). As we reviewed the claims data, new claims involved not only early detection of CVD-related health conditions but also early interventions to deal with the CVD-related health conditions. These associations were not evident in our secondary analysis, however, possibly because a two-year screening interval might be too short to detect additional new cases of CVD-related health conditions (Glasziou et al., 2008; Mancia et al., 2007; Takahashi et al., 2012; Williams et al., 2004).

We also found that screening participation was associated with lower inpatient use and cost and with lower outpatient cost. In screening programs, participants with suspected hypertension, diabetes, or dyslipidemia are recommended to follow up with an external physician or to return to the clinic for treatment. Screening attenders thus increases their number of outpatient visits, but they generally do not need expensive tests and complex treatment. Conversely, non-attenders may visit outpatient clinics when symptoms or complications become evident, resulting in more expensive testing. Also, there was a possibility that
non-attenders tended to have worse lifestyles compared with attenders, which we could not control in the primary analysis, which may lead to poor compliance, higher complications, and higher per-visit costs. Non-attenders also have a higher rate of CVD, resulting in higher rate of hospitalizations and inpatient costs. More formal economic analyses, however, are needed to establish the cost-effectiveness of CVD screening programs.

Our study is not a randomized controlled trial, thus caution is needed in the interpretation of our study results. First, effects of non-response on mortality are considerable (Jousilahti et al., 2005), and it is not possible to separate the effect of the screening activities per se from the effect of non-response bias with this kind of study design. Although we tried to minimize this problem with various sensitivity analyses, the fundamental problem of self-selection remains. In addition, although consideration of participation in previous screening visits and further adjustment for CVD-related health conditions, health behaviors, and comorbidities did not significantly alter the conclusions, we could not fully adjust potential confounding factors including physical activity and family history of CVD. Additional randomized control trials are needed to prove the effect of CVD screening programs.

The comprehensive evaluation of a multiple CVD health screening program, with simultaneous assessment of CVD-related health condition management, CVD mortality and events, and healthcare utilization and costs is one of the strengths. The use of a large, nationwide sample of target population for the screening may be another strength. Since joining the KNHI is mandatory for all Koreans except for Medicaid beneficiaries (about $3 \%$ of the total population), losses to follow-up or censoring were minimal.

## Conclusions

In this large nationwide study we found that participation in CVD health screening was associated with lower rates of CVD and all-cause mortality and CVD events, increased detection of CVD-related health conditions, and lower healthcare utilization and costs. Our findings are consistent with the hypothesis that participation in CVD health screening in the context of appropriate follow-up care may result in substantial health benefits and may effectively foster population health promotion. In the absence of large randomized controlled trials, our findings are suggestive of the effectiveness of participation in CVD screening programs.


Fig. 2. Kaplan-Meier survival estimates for cardiovascular and all-cause mortality: the survival curves are compared by attendance in a screening program in $2003-2004$.

Table 3
Detection of cardiovascular disease related health conditions within one year after attendance in a cardiovascular health screening program.

|  | Non-attenders | Attenders | $\mathrm{p}^{\mathrm{a}}$ |
| :--- | :---: | :---: | :---: |
| By attendance in 2003-2004 screening $(n=443,337)^{\mathrm{b}}$ |  |  |  |
|  | $\mathrm{n}=282,730$ | $\mathrm{n}=160,607$ |  |
| Hypertension, $\mathrm{n}(\%)$ | $12,696(4.97)$ | $7479(5.21)$ | 0.001 |
| Diabetes mellitus, $\mathrm{n}(\%)$ | $3411(1.23)$ | $2071(1.32)$ | 0.01 |
| Dyslipidemia, $\mathrm{n}(\%)$ | $7366(2.72)$ | $5253(3.46)$ | $<0.001$ |
| By attendance in 2005-2006 screening among attenders in 2003-2004 screening |  |  |  |
| $(n=155,620)^{\mathrm{c}}$ |  |  |  |
|  | $\mathrm{n}=45,342$ | $\mathrm{n}=110,278$ |  |
| Hypertension, $\mathrm{n}(\%)$ | $1718(4.71)$ | $4092(4.58)$ | 0.32 |
| Diabetes mellitus, $\mathrm{n}(\%)$ | $1305(3.04)$ | $3278(3.12)$ | 0.40 |
| Dyslipidemia, $\mathrm{n}(\%)$ | $1483(3.70)$ | $3893(4.02)$ | 0.01 |

[^1]Supplementary data to this article can be found online at http://dx. doi.org/10.1016/j.ypmed.2014.11.007.

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## Conflict of interest

The authors declare that there are no conflicts of interests.

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## Table 4

Healthcare utilization and cost by attendance in a cardiovascular health screening program.

|  | Mean (95\% CI) |  | $\mathrm{p}^{\text {a }}$ |
| :---: | :---: | :---: | :---: |
|  | Non-attenders | Attenders |  |
| By attendance in 2003-2004 screening ( $n=443,337)^{\text {b }}$ |  |  |  |
|  | $\mathrm{n}=282,730$ | $\mathrm{n}=160,607$ |  |
| In-patient days per person | 3.92 (3.79-4.06) | 2.67 (2.49-2.86) | <0.001 |
| In-patient cost per person ${ }^{\text {c }}$ | 480 (468-491) | 375 (360-392) | <0.001 |
| Out-patient days per person | 5.50 (5.45-5.56) | 5.83 (5.75-5.91) | <0.001 |
| Out-patient cost per person ${ }^{\text {c }}$ | 135 (131-139) | 125 (120-130) | 0.002 |
| By attendance in 2005-2006 screening among attenders in 2003-2004 screening$(n=155,620)^{\mathrm{d}}$ |  |  |  |
|  | $\mathrm{n}=45,342$ | $\mathrm{n}=110,278$ |  |
| In-patient days per person | 2.50 (2.27-2.73) | 1.70 (1.55-1.85) | <0.001 |
| In-patient cost per person ${ }^{\text {c }}$ | 307 (285-330) | 278 (264-293) | 0.03 |
| Out-patient days per person | 4.06 (3.96-4.16) | 4.47 (4.41-4.54) | <0.001 |
| Out-patient cost per person ${ }^{\text {c }}$ | 97 (92-101) | 98 (95-101) | 0.68 |

${ }^{\text {a }} \mathrm{p}$-Values derived using analysis of covariance.
${ }^{\mathrm{b}}$ Primary analysis: by attendance in a cardiovascular health screening program 2003-2004, adjusted for age, sex, disability, economic status and Charlson comorbidity index. Health care utilization and cost were aggregated from 2005 to 2010.
${ }^{c}$ Unit -1 US dollar ( $=\sim 1000$ Korean won).
${ }^{\text {d }}$ Secondary analysis: by attendance in a cardiovascular health screening program 2005-2006 among attenders in 2003-2004 screening, additional adjustment for secondary analysis included smoking status, alcohol intake, body mass index (BMI), hypertension, diabetes, and hypercholesterolemia. Health care utilization and cost were aggregated from 2007 to 2010.

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[^1]:    ${ }^{\text {a }}$ p-Values derived using a Chi-square test.
    b Primary analysis: by attendance in a cardiovascular health screening program 2003-2004.
    c Secondary analysis: by attendance in a cardiovascular health screening program 2005-2006 among attenders in 2003-2004 screening.

