Statins and Cardiovascular Primary Prevention in CKD: A Meta-Analysis

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Abstract
Background and objectives Multiple meta-analyses of lipid-lowering therapies for cardiovascular primary prevention in the general population have been performed. Other meta-analyses of lipid-lowering therapies in CKD have also been performed, but not for primary prevention. This meta-analysis assesses lipid-lowering therapies for cardiovascular primary prevention in CKD.

Design, setting, participants, & measurements A systematic review and meta-analysis using a random-effects model was performed. MEDLINE was searched between January 2012 and September 2013 for new studies using predefined search criteria without language restrictions. A number of other sources including previously published meta-analyses were also reviewed. Inclusion criteria were randomized control trials of primary prevention with lipid-lowering therapy in non–end stage CKD.

Results Six trials were identified, five including patients with stage 3 CKD only. These studies included 8834 participants and 32,846 person-years of follow-up. All trials were post hoc subgroup analyses of statins in the general population. Statins reduced the risk of cardiovascular disease (the prespecified primary outcome) by 41% in stages 1–3 CKD compared with placebo (pooled risk ratio, 0.59; 95% confidence interval [95% CI], 0.48 to 0.72). For the secondary outcomes, the risk ratios were 0.66 (95% CI, 0.49 to 0.88) for total mortality, 0.55 (95% CI, 0.42 to 0.72) for coronary heart disease events, and 0.56 (95% CI, 0.28 to 1.13) for stroke. In study participants with stage 3 CKD specifically, the results were similar.

Conclusions This meta-analysis suggests that the use of statins in CKD for primary prevention of cardiovascular disease is effective. These findings are consistent with recent guidance for the use of statins in all patients with CKD.


Introduction
CKD is an independent risk factor for cardiovascular morbidity and mortality (1). Previous research has suggested that 5%–10% of the adult population has CKD (2). The role of statins in cardiovascular primary prevention for the general population is well defined (3,4). However, the most recent Cochrane review of statins and primary prevention of cardiovascular disease (3) made no mention of CKD, possibly because most cardiovascular primary prevention trials of statins were performed more than a decade before a standard CKD definition was agreed. Therefore, limited data exist specifically for cardiovascular primary prevention in CKD.

Meta-analyses (5,6) suggest that lipid lowering, predominantly using statins but also statin/fibrate combinations, produced a relative risk reduction of 0.81 (95% confidence interval, 0.74–0.88) for all-cause mortality and relative risk 0.78 (confidence interval, 0.68–0.89) for cardiovascular mortality in non–end stage renal failure CKD, mostly stage 3 CKD. These data were subsequently used to suggest that low-cost generic statins may be cost-effective for cardiovascular primary prevention in CKD (7). These findings are reflected in guidance from Kidney Disease Improving Global Outcomes (KDIGO) (8). Although the Study of Heart and Renal Protection (SHARP) (9) examined benefits of lipid lowering in patients with CKD in secondary care, most of the participants were at high risk of experiencing renal disease progression or requiring RRT. By contrast, the majority of primary care patients with CKD have a significantly increased risk of cardiovascular disease, but do not require secondary care nephrology referral and will not experience progressive renal impairment.

We aimed to assess the evidence for using lipid-lowering therapy in patients with CKD typically encountered in primary care, who lack both pre-existing cardiovascular disease and risk factors associated with progressive worsening of renal function such as proteinuria and/or well phenotyped primary renal disease.

Materials and Methods
MEDLINE was searched for randomized controlled trials of lipid-lowering therapies including patients with CKD using predefined search criteria (see the
Supplemental Material), without language restrictions. In addition, Cochrane databases (10–12) and the National Institutes of Health’s database of clinical trials (13) were searched. All trials included in recent meta-analyses of lipid-lowering therapy and cardiovascular outcomes in general patients with CKD (5,6) and for general population primary prevention (3,4) were reviewed. Because these were high-quality contemporary studies, we limited our search for new studies from January 2012 to September 2013. Authors who had previously published in a similar area were contacted to ask whether they were aware of any unpublished studies. The review protocol is available on request. All identified abstracts were independently assessed by two of the current authors. Each assessor made a shortlist of potential studies for further consideration. The full text of these articles was then reviewed to identify suitable studies. Randomized controlled trials of cardiovascular primary prevention in adults with CKD were included. Either statins or other lipid-lowering treatments were considered as interventions. Studies were included if they provided cardiovascular events, including mortality, or all-cause mortality. A minimum follow-up of 6 months was preset. Studies were included if they did not report renal-related outcomes, but were excluded if they incorporated RRT patients at study commencement. Furthermore, studies including participants with primary renal pathology or high cardiovascular risk categories such as macroalbuminuria (urine albumin/creatinine ratio [ACR] >300 mg/mmol) were also excluded. No minimum was set for the number of study participants. The final list of studies was then discussed by the reviewers and one further author and was unanimously agreed.

These additional studies were assessed for quality, including bias and how CKD subgroups were identified in the individual trials. Two authors independently assessed nonblinded versions of all studies for risk of bias using a standardized proforma based on the Cochrane Handbook for Systematic Reviews and Interventions (14). Comparisons of assessments were made and any discrepancies were discussed until a consensus was achieved. Study authors were contacted for any available, additional relevant information. Results from the identified studies were extracted and statistical analysis was performed using RevMan 5.2 software (15).

All risk ratios (RRs) were calculated from original studies using the published dichotomous data for each treatment group; where unavailable, the RR was used to back-calculate events. Where no events were reported, a correction factor of 0.5 was used to allow an effect size to be calculated (14). Where an event was not reported in an individual trial, the corresponding author was contacted. Pooled RRs with 95% confidence intervals (95% CIs) and P values were calculated using the Mantel–Haenszel method, both by CKD stage and overall. Because heterogeneity of the results was expected, random-effects models were used. Heterogeneity was assessed using the I² and Q statistics.

We calculated absolute risk reductions per 100 person-years and number needed to treat (NNT) for 5 years to prevent one event. We based our calculations on the risk difference

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![Flow chart showing the number of studies identified and reason for inclusion or exclusion in meta-analysis.](image-url)
Table 1. Summary details of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Proportion of Main Cohort with CKD, %</th>
<th>Statin</th>
<th>LDL Reduction in Treatment Group, %</th>
<th>Mean/Median Follow-Up, mo</th>
<th>Mean/Median (SD) Age of Participants, yr</th>
<th>CKD Definition</th>
<th>eGFR Formula</th>
<th>Mean/Median Subgroup eGFR (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFCAPS</td>
<td>4.8</td>
<td>Lovastatin</td>
<td>27.0</td>
<td>61.2</td>
<td>62 (8)</td>
<td>eGFR &lt;60 (1 excluded due to eGFR &lt;15)</td>
<td>MDRD</td>
<td>53 (6.0)</td>
</tr>
<tr>
<td>CARDS</td>
<td>34.2</td>
<td>Atorvastatin</td>
<td>40.8</td>
<td>46.8</td>
<td>65 (6.7)</td>
<td>eGFR &lt;60 (n=1 for eGFR &lt;30)</td>
<td>MDRD</td>
<td>Placebo 54.1 (5.4), statin 53.5 (5.3)</td>
</tr>
<tr>
<td>JUPITER</td>
<td>18.4</td>
<td>Rosuvastatin</td>
<td>51.4</td>
<td>22.8</td>
<td>70 (IQR 65–75)</td>
<td>eGFR &lt;60 (n=14 for eGFR &lt;30)</td>
<td>MDRD</td>
<td>56 (IQR 51–58)</td>
</tr>
<tr>
<td>MEGA</td>
<td>41.4</td>
<td>Pravastatin</td>
<td>18.9</td>
<td>63.6</td>
<td></td>
<td>eGFR &lt;60 (SCR &gt;1.5 mg/dl excluded from original study, 16 excluded from subanalysis due to eGFR &lt;30)</td>
<td>MDRD equation for Japanese patients</td>
<td>Placebo 52.5 (5.6), statin 52.6 (5.7)</td>
</tr>
<tr>
<td>PREVEND IT</td>
<td>100</td>
<td>Pravastatin</td>
<td>24.4</td>
<td>46.0</td>
<td>51 (12)</td>
<td>Excluded if creatinine clearance &lt;60%, CKD defined by proteinuria</td>
<td>Creatinine clearance</td>
<td>eGFR not given; mean SCR placebo 90 μmol/L (14), statin 91 μmol/L (14)</td>
</tr>
<tr>
<td>WOSCOPS</td>
<td>7.6</td>
<td>Pravastatin</td>
<td>31.5</td>
<td>60.0</td>
<td>65.7 (5.6)†</td>
<td>Defined by both CG-eGFR and MDRD-eGFR 30–99.99, 27 excluded due to CG-eGFR &lt;30</td>
<td>MDRD and CG</td>
<td>MDRD 55.0 (8.2), CG 51.8 (6.3)</td>
</tr>
</tbody>
</table>

AFCAPS, Air Force/Texas Coronary Atherosclerosis Prevention Study; CARDS, Collaborative Atorvastatin Diabetes Study; JUPITER, Justification for the Use of Statins in Prevention-an Intervention Trial Evaluating Rosuvastatin; MEGA, Management of Elevated Cholesterol in the Primary Prevention Group of Adult Japanese; PREVEND IT, Prevention of Renal and Vascular Endstage Disease Intervention Trial; WOSCOPS, West of Scotland Coronary Prevention Study; IQR, interquartile range; SCR, serum creatinine; CG, Cockcroft–Gault; MDRD, Modification of Diet in Renal Disease. (.), the MEGA study did not provide an SD or IQR.

†WOSCOPS mean age value refers to mean age across whole CKD Prospective Pravastatin Pooling Project analysis. Mean age of all WOSCOPS participants, including those with no CKD, was 55.2 years (SD 5.5). No specific published value was available for the WOSCOPS’s CKD cohort’s mean age.
Results

Altogether 603 unique manuscripts were reviewed. Figure 1 depicts the screening process and the studies identified, including reasons for inclusion or exclusion. Explanations of the rationale for inclusion/exclusion are available on request. The search identified six trials (16–21). Table 1 describes their key characteristics. For individual trial definitions of events, see the Supplemental Material. These trials included 8834 participants with stages 1–3 CKD. Median follow-up was 46.4 months (range, 22.8–63.6) and all trial results were published in peer-reviewed journals. Three trials (16–18) were terminated early due to interim analysis showing prespecified termination end points having been met. The risk of bias assessment is available in the Supplemental Material.

Five studies reported eGFR based on the Modification of Diet in Renal Disease (MDRD) equation using a single serum creatinine measurement. One study also reported eGFR using the Cockcroft–Gault formula. MDRD results were used for all calculations in the meta-analysis. One study, the Prevention of Renal and Vascular Endstage Disease Intervention Trial (PREVEND IT) (20), used albuminuria as a study entry criterion. PREVEND IT recorded both spot and 24-hour measurements of urinary albumin and the threshold for study inclusion required both a morning urinary albumin concentration of >10 mg/L and 24-hour albumin excretion of 15–300 mg in at least one of two collections. This study excluded participants with a creatinine clearance <60 ml/min per 1.73 m² (equivalent to stages 3–5 CKD at study onset). None of the trials prespecified a CKD subanalysis, with the exception of PREVEND IT, which was specifically a trial of screening in proteinuria with preserved renal function.

Table 2 presents a summary of the overall results of the random-effects models for the pooled RR. Table 3 shows a summary of absolute risk reductions and NNT over 5 years to prevent one event in stage 3 CKD. The only data not in the original study publications related to total mortality in the PREVEND IT trial (20). Data for this category have been published in other meta-analyses (4,21) and their accuracy was confirmed by the corresponding author for PREVEND IT (20). All six trials reported data relating to major cardiovascular events for stages 1–3 CKD, with 409 events occurring in 8834 participants (4.5%) over a total of 32,846 person-years. Lipid-lowering therapy reduced the risk of major cardiovascular events by 41% (RR, 0.59; 95% CI, 0.48 to 0.72; P<0.001), and there was no statistical heterogeneity (I²=0%; P=0.46). The results for CKD 3 only were similar (RR, 0.56; 95% CI, 0.45 to 0.69; P<0.001; I²=0%; P=0.66 for Q test). Figure 2 shows the forest plot for cardiovascular events.

Five trials reported all-cause mortality data. Overall, 255 events occurred in 8530 participants (3.0%) over a total of 31,588 person-years. Lipid-lowering therapy reduced the risk of mortality by 34% (RR, 0.66; 95% CI, 0.49 to 0.88; P=0.01), and there was a low-level heterogeneity (I²=22%; P=0.54). For stage 3 CKD only, mortality was reduced by 38% (RR, 0.62; 95% CI, 0.47 to 0.82; P<0.001). Heterogeneity was lower than for stages 1–3 CKD (I²=10%; P=0.34 for Q test). Figure 3 shows the forest plot for total mortality. Two trials reported cardiovascular mortality data, five trials reported coronary heart disease event data, and four trials reported stroke data. No unpublished data were available.

Differences in RRs were compared, tested for interaction, and then a RRR (the additional relative risk reduction of statins in CKD compared with the risk reduction in the general population) (22) was calculated. The RRR of a cardiovascular event was not statistically significantly lower (RR, 0.78; 95% CI, 0.61 to 1.01; P=0.06) in stage 3 CKD than in the general population. The RRR for all other outcomes was of a similar size and none were statistically significant (total mortality RRR, 0.75; 95% CI, 0.55 to 1.03; P=0.08; Table 4). Limited or no information was published in relation to adverse events for most trials. Three trials reported biochemical abnormalities, none of which reported excess abnormalities for statins. Two trials reported serious adverse events, neither describing excess events associated with statins (see the Supplemental Material for details). Limited information was available from the identified studies in relation to CKD progression, manifesting either as rising creatinine, proteinuria, or progression to end stage renal failure.

Although our original protocol excluded the SHARP study (9), by virtue of its participants’ characteristics, we repeated the meta-analysis including SHARP. Using

<table>
<thead>
<tr>
<th>Table 2. Summary results of random-effects models</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CKD Stage</strong></td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>1–3</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>3 only</td>
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</table>

RR, risk ratio; 95% CI, 95% confidence interval.
published data, we compared our meta-analysis primary outcome with SHARP’s primary outcome, also major cardiovascular events, for nondialysis participants. There was no significant difference (P value for interaction, \( P=0.46 \)) between our original result (RR, 0.56; 95% CI, 0.45 to 0.69) and the result including the SHARP subgroup (RR, 0.63; 95% CI, 0.50 to 0.79). However, when the SHARP subgroup was directly compared with our original result, heterogeneity was observed (\( P^2=86.6\% ; P=0.01 \)). We also tested for heterogeneity in relation to the type of statin used. Three studies (19–21) used pravastatin and three studies used different statins. Doses of pravastatin varied from trial to trial. Testing for subgroup differences for the primary outcome between pravastatin versus all other statins did not show any heterogeneity (\( P=0\% ; P=0.49 \)).

### Discussion

Previous meta-analyses of lipid lowering in nondialysis CKD (5,6) have shown RR reductions for cardiovascular events. However, there has been little consideration of the heterogeneous pathophysiology, including cardiovascular disease, within this diverse group. The current meta-analysis focuses on individuals with CKD but without known cardiovascular disease. This group, comprising mainly individuals with stage 3 CKD but without well clinically phenotyped primary renal diseases, represents the bulk of patients with CKD seen by general practitioners, in which cardiovascular disease prevention may be a more pertinent issue than progression of renal disease.

The prespecified primary outcome of the present meta-analysis showed a 41% reduction in cardiovascular events for participants with stages 1–3 CKD. All secondary outcomes also showed highly significant reductions in events, including a 34% reduction in total mortality. Current KDIGO guidance recommends a statin or a statin/ezetimibe combination for all individuals aged \( \geq 50 \) years with stages 3–5 CKD, if not receiving dialysis or transplanted (8). For those aged \(<50\) years, KDIGO recommends a statin if another cardiovascular risk factor is present, or if 10-year risk of a coronary heart disease event exceeds 10%. The data presented in this meta-analysis support this guidance. The American Heart Association guidance (23) recommends a statin when the 10-year risk of atherosclerotic cardiovascular disease is \( >7.5\% \). In addition, the guidance introduced a new risk assessment tool. However, this guidance does not refer to CKD and cardiovascular primary prevention. The QRisk2 score (24) does provide a fixed CKD adjustment without consideration of staging. Furthermore, the QRisk2 cohort only contained 0.15% of participants with CKD. The commonly used Framingham Risk Score has poor discrimination in CKD (25).

Previous studies suggest that generic statins may be cost-effective for primary prevention in all patients with CKD (7). This article presents the first CKD primary prevention meta-analysis, and these more refined risk reductions are likely to show improved cost-effectiveness. On the basis of the current findings as well as a recent analysis of the effect of CKD on the English National Health Service (26), it is estimated that universal statin use in CKD could prevent 10,750 myocardial infarctions, 7,300 strokes, and 14,900 deaths over 5 years (see the Supplemental Material). However, cautious interpretation of these figures is warranted.

### Table 3. ARR and NNT over 5 years to prevent one event

<table>
<thead>
<tr>
<th>Outcome Event</th>
<th>Stage 3A CKD</th>
<th>Stage 3 CKD</th>
<th>Non-CKD</th>
<th>Published Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ARR</td>
<td>NNT (95% CI)</td>
<td>ARR</td>
<td>NNT (95% CI)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>0.63</td>
<td>(23 to 50)</td>
<td>0.66</td>
<td>(22 to 47)</td>
</tr>
<tr>
<td>Total mortality</td>
<td>0.31</td>
<td>(62 to 138)</td>
<td>0.34</td>
<td>(62 to 138)</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>0.40</td>
<td>(29 to 185)</td>
<td>0.41</td>
<td>(29 to 185)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.18</td>
<td>(45 to 254)</td>
<td>0.28</td>
<td>(45 to 254)</td>
</tr>
</tbody>
</table>

ARR, absolute risk reduction (decrease in events per 100 person-years); NNT, number need to treat for 5 years to prevent one event; 95% CI, 95% confidence interval.
due to the limits of extrapolating RRs from clinical trials to observational prevalence data, particularly in meta-analyses in which baseline event risk varies between trials. Indeed, the most suitable method for NNT calculation is open to debate (27–29).

Although this study contributes additional information to this area, we acknowledge several limitations. All studies were post hoc analyses of general population studies, a study type that is open to bias, including selection bias. Unsurprisingly, given their post hoc nature, there is limited information on other CKD cardiovascular risk stratifying factors, such as proteinuria. However, data suggest (2) that of individuals with stage 3 CKD, approximately 25% have persistent urine ACR \(>3\) mg/mmol and only 6.5% have ACR \(>30\) mg/mmol.
Because the trials presented here were recruited from mainly primary care populations, and not secondary care nephrology services, it is likely that the proportions of micro- and macroalbuminuria are less than the KDIGO proportions (2). This hypothesis is supported by the only included trial to report detailed quantification of proteinuria (17). Within the CKD subgroup of this diabetic nephropathy trial, <3.5% had nephrotic-range proteinuria. The limited information available in relation to adverse events did not raise any safety concerns. Previous data (5,6) have shown no excess adverse events with statins, or other lipid-lowering medications, compared with placebo in CKD. Furthermore, limited data were available in relation to renal outcomes; therefore, no conclusion can be made regarding statin-mediated changes to CKD progression.

We did not formally consider publication bias because all included studies were post hoc analyses. Not all general population primary prevention studies have published such analyses and therefore publication bias may exist. However, of the 13 trials with total mortality data included in the most recent Cochrane meta-analysis for primary prevention (3), the five largest trials have published CKD-related data and are included in this meta-analysis. eGFR measurement is suboptimal in all included studies. A diagnosis of CKD requires two serum creatinine measurements >3 months apart (2), something that occurred in none of the included studies. Use of the MDRD equation (30), utilized to calculate the eGFR in all included studies, has been challenged by the Chronic Kidney Disease Epidemiology Collaboration equation (31) due to the former’s propensity to overdiagnose stage 3 CKD, particularly stage 3A CKD. No study prespecified a CKD-related sub-analysis, but we reflected this in our analysis of bias. Limited published information exists from the studies in relationship to noncholesterol-lowering effects of statins. Only Justification for the Use of Statins in Prevention—An Intervention Trial Evaluating Rosuvastatin (18) provided information relating to the potential role of inflammation. Hazard ratios were similar between the CKD and non-CKD groups, as were relative reductions in both LDL cholesterol and C-reactive protein from baseline. Thus, it is not possible to attribute the benefit of statins to either lipid-lowering properties or pleiotropic effects in CKD.

The five trials reporting stage 3 CKD outcomes had mean/median eGFRs between 53 and 56 ml/min per 1.73 m² with SDs of 5-6 ml/min per 1.73 m². Two trials specifically excluded participants with an eGFR<30 ml/min per 1.73 m². The remaining trials had a minimal number (<1%) of participants with stage 4 CKD. The results including these trials are therefore only likely to be applicable to individuals with stage 3 CKD.

Our results complement those of the SHARP trial (9), the only CKD-specific lipid-lowering trial. The SHARP trial showed an overall statistically significant 17% reduction in major cardiovascular events, as well as a nonstatistically significant reduction in mortality across a wide range of CKD stages, including dialysis. Our sensitivity analysis shows that inclusion of the SHARP data did not significantly change the overall results and conclusions of this meta-analysis. When the SHARP subgroup was considered individually against our meta-analysis, heterogeneity did exist. However, a number of factors may account for this heterogeneity. First, the participants’ characteristics in the SHARP trial contrast significantly with those in the studies included in our meta-analysis. The majority of SHARP participants had advanced (stage 4–5 CKD) renal disease, and SHARP was not specifically a primary prevention trial. Indeed, during the SHARP trial, approximately three times more participants progressed to end stage renal failure than had a major cardiovascular event. More advanced CKD may attenuate statin efficacy, as evidenced by negative statin trials in dialysis (5,6). Second, the SHARP trial used both simvastatin and ezetimibe, thus making the comparison of its 33.1% reduction in LDL cholesterol more difficult to interpret compared with the statin-only trials including in this meta-analysis. Considered alongside the SHARP results, the current meta-analysis supports an expansion of the range of patients with CKD for whom statins may be beneficial. The SHARP trial answered the question of the efficacy of statins in CKD from a nephrologist’s point of view. By identifying studies of patients with stages 1–3 CKD at low risk of CKD progression, the current meta-analysis answers a related question but from the prospective of primary care. Most patients in this group have nonprogressive stage 3 CKD and do not require nephrology referral, but instead need appropriate cardiovascular risk management.

The tools to assess cardiovascular risk in CKD currently remain undefined. Preexisting cardiovascular tools are of limited value, and even the most recent tool has no CKD adjustment. However, the more pertinent questions in primary prevention may be “What works?” and “In whom?” (32). This meta-analysis specifically answers these questions in relation to CKD and statins. Universal use of statins for

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**Table 4. Cardiovascular disease RRs for participants in identified trials with CKD participants removed (without CKD) and RRRs for stage 1–3 CKD versus non-CKD and stage 3 CKD only versus non-CKD**

<table>
<thead>
<tr>
<th>Outcome Event</th>
<th>RR without CKD (95% CI)</th>
<th>Stage 1–3 CKD</th>
<th>Stage 3 CKD Only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RRRs (95% CI)</td>
<td>P Value for Interaction</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>0.71 (0.62 to 0.83)</td>
<td>0.83 (0.65 to 1.05)</td>
<td>0.12</td>
</tr>
<tr>
<td>Total mortality</td>
<td>0.82 (0.71 to 0.95)</td>
<td>0.81 (0.58 to 1.12)</td>
<td>0.19</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>0.71 (0.62 to 0.81)</td>
<td>0.78 (0.57 to 1.05)</td>
<td>0.10</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.67 (0.40 to 1.14)</td>
<td>0.84 (0.55 to 1.40)</td>
<td>0.69</td>
</tr>
</tbody>
</table>

RR, risk ratio; RRR, ratio of risk ratios; 95% CI, 95% confidence interval.
cardiovascular disease primary prevention in all individuals with CKD, excluding dialysis, should be considered.

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None.

References

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