Adherence to drugs that prevent cardiovascular disease: meta-analysis on 376,162 patients

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CRD summary
The authors concluded that around one third of patients with previous myocardial infarction and around half without a myocardial infarction did not adhere to drugs prescribed for coronary heart disease event prevention. Review methodological flaws, and limitations of the evidence and methods to measure adherence suggest that the findings may not be accurate and therefore may not be reliable.

Authors' objectives
To estimate adherence to drugs for primary or secondary prevention of cardiovascular disease.

Searching
PubMed was searched but search dates were not reported. Search terms were reported. Reference lists of relevant studies and reviews were manually searched.

Study selection
Eligible for inclusion were studies that measured adherence to drugs for the prevention of coronary heart disease in patients with and without a diagnosis of coronary heart disease. Drug classes included aspirin, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, calcium channel blockers, thiazide diuretics, and statins. Studies had to measure adherence using pharmacy prescription refill data and report the number of patients obtaining drugs for at least 75% of days over a defined period of time. Studies were also required to report the method of payment for medication (self-payment, state payment, or assisted payment).

Included studies were conducted in the USA, Canada, Australia, and Europe from 1998 up to 2010. The mean age of included patients was 65 years; 49% were male. Approximately half of the studies were of patients without a history of coronary heart disease (patients being treated for hypertension or high cholesterol) who received drugs for the primary prevention of coronary heart disease. The remaining studies were of patients with a diagnosis of coronary heart disease (patients with a history of myocardial infarction, ischaemic heart disease, angina, percutaneous coronary intervention, or coronary artery bypass grafting) who received drugs for the secondary prevention of recurrent events.

The method of payment in 17 studies was assisted payment; in two studies it was state payment, and in one study it was self-payment.

The authors did not state how many reviewers screened studies for inclusion.

Assessment of study quality
The authors did not state that they assessed study quality.

Data extraction
Two reviewers independently extracted mean adherence to each drug class, weighted by the number of patients taking each drug, to estimate mean adherence (%) for each study, along with 95% confidence intervals. Where methods of payment were not reported, study authors were contacted.

Methods of synthesis
A random-effects model was used to combine mean percentage adherence, with 95% confidence intervals (CIs). Levels of statistical heterogeneity were reported (p values).

Subgroup analyses were performed to determine adherence in primary and secondary prevention, for drug classes, and for payment methods. Meta-regression was used to explore heterogeneity using the variables of age, gender, method of payment, and duration of treatment.

Results of the review
Twenty studies (376,162 patients) were included in the review. Follow-up ranged from 12 to 120 months.

The overall level of adherence was 57% (95% CI 50 to 64) over a median period of 24 months. Subgroup analyses indicated adherence levels of 50% (95% CI 45 to 56) for primary prevention studies (11 studies) and 66% (95% CI 56 to 75) for secondary prevention studies (nine studies); the difference was statistically significant (p=0.012). There was evidence of statistical heterogeneity across studies (p<0.001).

Subgroup analyses by drug class indicated a statistically significant lower adherence for thiazides compared with angiotensin receptor blockers in primary prevention (p=0.02). There were no other significant differences for primary or secondary prevention.

Meta-regression showed a 0.15% decrease in adherence per month of follow-up (p=0.07). No other effects were found.

**Authors' conclusions**

Approximately one third of patients with a history of myocardial infarction and approximately half of patients who had not had a myocardial infarction did not adhere to drugs for the prevention of coronary heart disease events. Adherence did not greatly depend on class of drug.

**CRD commentary**

The review question and supporting inclusion criteria were broadly defined. The literature search was minimal and no search dates were reported, which meant that potentially relevant data may have been missed. Data extraction was undertaken in duplicate, but it was unclear whether this was true for study screening, so there was potential for reviewer error and bias. Study quality was not assessed, which meant that it was not possible to determine the robustness of the findings.

A large number of patients were included in the review, but study details were minimal. There was evidence of statistical heterogeneity; the reasons for this could not be identified through statistical exploration. The authors highlighted the limitations in measuring adherence by prescription refills as this was not necessarily evidence that the drug had been taken; eligible studies were restricted to those that measured adherence using pharmacy prescription refill data. This meant that the findings may overestimate adherence.

The review had some methodological flaws and the limitations of the evidence and methods to measure adherence suggest that the findings may not be accurate and therefore may not be reliable.

**Implications of the review for practice and research**

Practice: The authors stated that adherence was not greatly dependent on the class of drug prescribed, suggesting that interventions to improve adherence need to be broadly applied.

Research: The authors stated that there was a need for a simple and effective method that can be combined with each new drug prescription to improve adherence to cardiovascular drugs.

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