Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The pharmacologic treatment of peripheral arterial disease (PAD) was investigated. The treatments considered were aspirin, pentoxifylline, papaverine and dipyridamole.

Type of intervention

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised all US DOD health-care beneficiaries with a minimum of 90 days' exposure to a PAD-related treatment, and at least an 80% prescription fill rate. Further inclusion criteria were a recorded diagnosis of PAD and at least one inpatient admission for ICD-9-CM (International Classification of Diseases, 9th Rev., Clinical Modification) codes corresponding to other specified peripheral vascular diseases (443.8) unspecified peripheral vascular disease (443.9), and atherosclerosis of native arteries of extremities with (440.21) and without (440.20) intermittent claudication. Inpatient admissions were deemed to be PAD-related if the primary diagnosis matched the ICD-9-CM codes mentioned above, or if the secondary diagnosis matched those ICD-9CM codes and a PAD-related procedure was performed. PAD-related procedures included balloon angioplasty, femoropopliteal bypass, bypass graft-vein, bypass graft other than vein, lower extremity amputation, revision of vascular procedures of the lower extremities, thromboendarterectomy, and skin grafts of the lower extremities. Patients with admissions for ICD-9-CM codes pertaining to human immunodeficiency virus infection were excluded from the analysis.

Setting
The setting can be presumed to be primary and secondary care in the USA, as reimbursed by the US DOD. No information was given on whether the procedures recorded were primary admissions or the result of a referral.

Dates to which data relate
The dates to which the effectiveness and cost data related were 1 October 1992 to 1 July 1997. The price year was 1996.

Source of effectiveness data
The effectiveness data were extracted, retrospectively, from the Uniformed Services Prescription Database Project and the Patient Administration Systems and Biostatistics Activity databases maintained by the DOD.

Link between effectiveness and cost data
The effectiveness data were derived from the same patient sample as the cost data.

**Study sample**
The study sought to include all patients who met the inclusion criteria, limited to the available dates of prescription data. Papaverine was dropped from the analysis due to a low sample size (n<10). The final sample consisted of 339 patients. Of these, 222 were exposed to aspirin alone, 60 to pentoxifylline and 57 to dipyridamole. Twenty-four patients in the pentoxifylline group and 31 in the dipyridamole group were cross-exposed to aspirin. The mean age of the patients included in the study was 67.6 years, 72.6% were male and 77.9% were white. There were no statistically significant differences, (p=0.05), between the treatment groups in terms of their age, ethnicity, sex, co-morbid disease (defined as myocardial infarction, angina, hypertension or diabetes), total number of days' supply of drugs or total number of days under study.

**Study design**
This was a retrospective cohort study. The data were collected from one database covering 49 Uniformed Services facilities sites in the USA, and a second database covering army hospitals and clinics in the USA. The mean number of days under study was 1,589.6 days overall (95% confidence interval, CI: 1,574.4 - 1,604.8)

**Analysis of effectiveness**
All the patients included in the study were accounted for in the analysis. The differences between the treatment groups were investigated using general linear models. The number of PAD-related hospitalisations prior to the study period was used as a covariate to adjust for disease severity. The outcome measures in the analysis were the number of PAD-related examination procedures (EXM), the number of PAD-related invasive procedures (INV), the number of PAD-related hospitalisation days (HDAY), and the cost of PAD-related procedures (COST). The study also reported the number of days' supply of the drugs under consideration.

**Effectiveness results**
The adjusted least-squares mean INV was 0.018 for patients receiving aspirin alone, 0.117 for patients receiving pentoxifylline (including those cross-exposed to aspirin), and 0.070 for patients receiving dipyridamole (including those cross-exposed to aspirin).

The adjusted least-squares mean EXM was 0.093 for patients receiving aspirin alone, 0.081 for patients receiving pentoxifylline (including those cross-exposed to aspirin), and 0.043 for patients receiving dipyridamole (including those cross-exposed to aspirin).

The adjusted least-squares mean HDAY was 0.840 for patients receiving aspirin alone, 1.317 for patients receiving pentoxifylline (including those cross-exposed to aspirin), and 1.951 for patients receiving dipyridamole (including those cross-exposed to aspirin).

**Clinical conclusions**
In separate models for each of the outcome measures, a significant treatment effect was found only in the model where INV was a dependent variable. Patients treated with aspirin had the lowest number of INV, followed by patients treated with dipyridamole, and then patients treated with pentoxifylline.

**Measure of benefits used in the economic analysis**
There was no summary measure of benefit. A cost-consequences analysis was therefore conducted.

**Direct costs**
The direct costs of the health service were used in the analysis. PAD-related invasive and examination procedures were
included. The mean number of INV, EXM and HDAY were reported in the effectiveness results. The cost data were obtained from a national database of submitted charges. Discounting was relevant, as the costs were incurred over more than one year, but was not carried out. The study reported the average PAD-related procedure costs for the time under study. The costs were reported in 1996 prices, and were inflated using the consumer price index for physician services.

**Statistical analysis of costs**
The costs were treated in a deterministic manner.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analyses were undertaken.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The adjusted least-squares mean COST was $103.890 for patients receiving aspirin alone, $373.870 for patients receiving pentoxifylline (including those cross-exposed to aspirin), and $206.182 for patients receiving dipyridamole (including those cross-exposed to aspirin). When the analysis was reconducted with those patients cross-exposed to aspirin in separate groups, a significant treatment group effect was found in the separate model for COST.

**Synthesis of costs and benefits**
Not applicable.

**Authors' conclusions**
Treatment with aspirin may prevent the need for surgery to lessen the patients' symptoms of peripheral arterial disease (PAD).

**CRD COMMENTARY - Selection of comparators**
The comparators were selected on the basis of current practice. You must decide whether aspirin, pentoxifylline and dipyridamole are widely used health technologies for the treatment of PAD in your own setting.

**Validity of estimate of measure of effectiveness**
The study attempted to measure all PAD-related procedures to see if treatment resulted in a reduction in the number of procedures. This was appropriate since the recorded procedures could be identified, according to a strict definition, with relative ease given the retrospective design. The patient groups were not necessarily comparable at analysis, so there may well have been selection bias. A relatively small number of covariates was used to adjust for potential confounding.
Validity of estimate of measure of benefit
There was no summary measure of benefit. A cost-consequences analysis was conducted.

Validity of estimate of costs
The costs used were specific to the study population. All of the categories of cost relevant to this perspective were included, but the lack of detail reduces the generalisability of these to other perspectives. The accuracy of the cost data relies on the assumption that US DOD health-care beneficiaries would not have sought health care outside of the DOD system. The price year was given and appropriately adjusted for inflation. However, discounting was not performed.

Other issues
The results of this analysis are specific to the USA. The study used observational data and, as such, there is the potential for bias or confounding by unknown covariates. The authors highlighted the potential for the results to be confounded by the prescribing habits of physicians, if physicians prescribe each treatment to a different set of patients. The authors acknowledged that the study provides information for designing future research, rather than answering the question of which of the treatments is most cost-effective. The authors made appropriate comparisons of their findings with those from other studies. The issue of generalisability to other settings was not addressed.

Implications of the study
The authors recommended that further research be conducted to test the validity of the assumptions used in this analysis. They recommended more research into the long-term effects of pharmacological treatment of PAD, to support the use of such treatments.

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Other publications of related interest

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