# SYSTEMATIC REVIEW PROTOCOL for consideration by PROSPERO

Prof Janet Powell (JTP), Dr Pinar Ulug (PU), Imperial College London

Prof Simon Thompson (ST), University of Cambridge

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## Title: Current prevalence of abdominal aortic aneurysm in women.

### 1.1. Introduction

In spring 2009, the National Abdominal Aortic Aneurysm Screening Programme (NAAASP) was launched, with complete coverage across the UK by 2014 [1]. This screening programme is for men only (at the age of 65 years using ultrasonography), since screening trials have shown the benefit of screening in men [2]. Men who are identified with small AAA (from 3.0 to <5.5cm in diameter) are kept under regular surveillance, whilst those with larger AAA are referred for elective aneurysm repair. Even though the prevalence of abdominal aortic aneurysm (AAA) in men appears to be declining, screening remains cost-effective, since the costs and mortality associated with repair of ruptured AAA are both very high [3,4]. Screening programmes for men also are in place in Sweden and several other European countries [5]. In the USA, screening is recommended for men who have ever smoked [6]. The apparent reduction in the prevalence of AAA in men with time has been attributed to changes in population smoking and increased use of cardioprotective medications, as for other cardiovascular diseases such as myocardial infarction.

Historically the prevalence and incidence of abdominal aortic aneurysm (AAA) has been much lower in men than women [7-9] and screening for women has not been recommended. In England, the proportion of women amongst cases of AAA rupture is increasing steadily [10] and a recent screening study from Sweden has suggested that screening women for AAA might be cost-effective [11]. This Swedish study screened women at the age of 70 years (in contrast to 65 years for men), since there is some evidence that AAA develop at an older age in women [12]. Smoking remains the dominant risk factor for AAA in women. Ultrasonography is the main measurement method for aortic diameter in screening studies, but some hospital-based or cohort studies may use computed tomography (CT scan).

In older women the normal diameter of the abdominal aorta is smaller than in men [13]. Therefore the conventional diameter threshold for an AAA might need revising downwards compared to the

threshold of 3cm used in men. The growth rate of AAA is similar in men and women; however for any given aortic diameter, the risk of small AAA rupture is 4-fold higher in women than men [14]. The aortic diameter is measured differently in different studies; for example the difference between inner-to-inner and outer-to-outer wall diameters may vary by as much as 0.7cm. Therefore, there are several unknowns concerning the current prevalence of AAA in women.

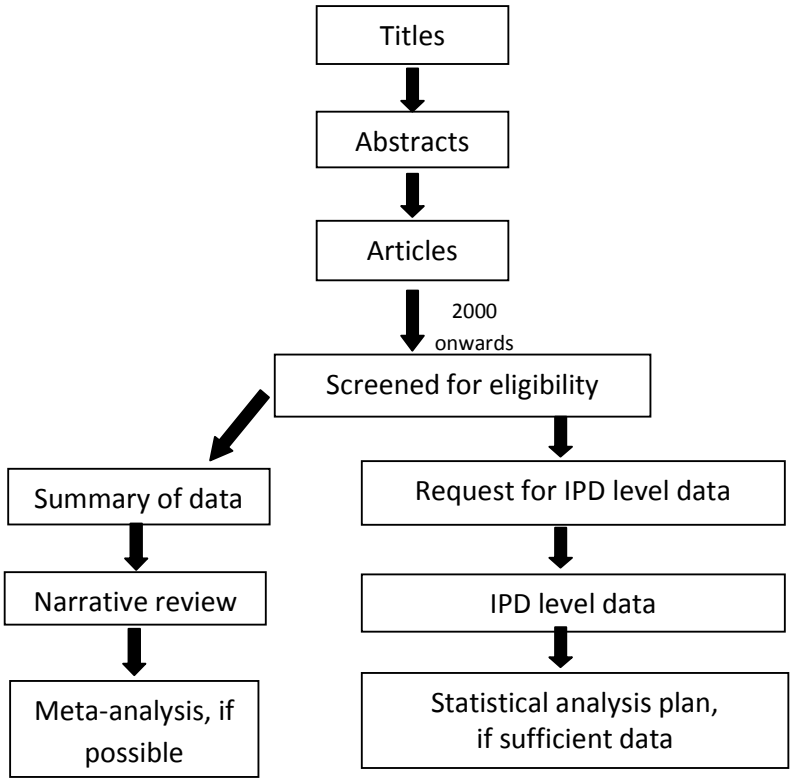
Using the threshold diameter of 3cm to diagnose an AAA in women, the table below highlights some of the published data.

Table 1. Indicative prevalence of AAA of ≥3cm diameter in women in last 10 years

| **Author** | **Aortic diameter measured** | **Prevalence** | **Additional info** |
|---|---|---|---|
| Svensjo *et al*., 2012 [12] | Anterior-posterior (AP), Leading edge to leading edge | 19/5140 (0.4%) | 70 year women, 74.2% acceptance rate for screening<br>Prevalence increased to 11/518 (2.1%) in current smokers |
| Kent *et al*., 2010 [9] | Larger of AP or transverse | 4727/1978422 (0.2%) | <85 years self-referred for Lifeline screening |
| Derubertis *et al*., 2007 [8] | "largest AP", probably outer-to-outer | 74/10012 (0.7%) | >50 years, mean 70 years |

This systematic review will be made up of three elements: literature searching, summary of data, and meta-analysis if sufficient data are available (see Figure below) and will be conducted according to the PRISMA guidelines and PRISMA guidelines for systematic reviews and meta-analyses of individual participant data [15]. Studies will also be identified which may hold individual person level data for maximum aortic diameter in women of specific ages and by smoking habit.

## Strategy: Systematic Reviews




1.2. Specific Aims

The aims of this study are to systematically review published and unpublished data of the current prevalence of AAA in women, measured either by ultrasonography or CT scan.

We will focus on the following question:

- What is the population prevalence of AAA in women?

We are also interested in three related questions:

- How does prevalence vary at ages between 65 and 80 years?
- How does prevalence vary by smoking habit?
- How does prevalence vary if the threshold diameter for AAA is reduced to 2.5cm?

## 1.3. Methods

*Narrative review*

This protocol will be sent for external review (Professor F Lederle, Minneapolis, USA) and approved by the project team in order to answer the above questions. The protocol will be followed rigorously by the systematic reviewers (PU, JS, JTP). A systematic search of the literature will be performed, limiting the search to data published within since 2000. Search strategies will be designed for MEDLINE, EMBASE and CENTRAL using a combination of controlled vocabulary (MeSH or EMTREE) terms and free text terms. Clinicaltrials.gov (http://clinicaltrials.gov), Current Controlled Trials (http://www.controlled-trials.com/) and the National Research Register (UK) will also be searched for details of ongoing or unpublished trials. All articles between 2000 (MEDLINE or EMBASE) and up until 2014/5, which match the inclusion and exclusion criteria (see below), will be selected for the systematic review.

Other sources of information will also be searched:

- Reference lists of published key articles
- Conference abstracts and notes
- Key authors will be contacted to identify additional sources of publications/data

The restriction on language of publications applies to English and the other major European languages.

## 1.4. Study Selection

The exclusion criteria (see below) will be applied to all the accumulated sources of information, such as peer-reviewed articles, conference notes, books, and unpublished data. The initial rejection or inclusion will be based on the study title. However, if the study title is obscure, the abstract will be reviewed. In cases where abstracts are unavailable or inconclusive, the full article will be acquired and reviewed.

Exclusion criteria:

- Review articles
- Editorials

- Letters
- Case reports
- Studies where data have been duplicated
- Less than 1000 women screened

Full text-versions of the selected shortlist of documents will be obtained. The two reviewers (PU, JTP) will individually assess them to make sure that they adhere to the initial eligibility criteria. The two reviewers will then individually select studies that meet the inclusion criteria (see below). If an agreement cannot be reached, a third author (JS) will cast the deciding vote.

The inclusion criteria will be as follows:

- women ≥60 years of age
- All ethnic groups
- Population clearly described
- Studies must include screening of at least 1000 women
- For studies reporting duplicated data, the most recent or most comprehensive publication will be included.
- Ultrasonography or CT scan for aortic diameter measurement

1.5. Data Extraction and Quality Scoring

A data extraction form, which identifies technical details, person characteristics and potential biases etc., in the selected documents, will be designed independently by the reviewers. The results of the checklist will be summarised for each study and any study publication that fails to provide sufficient details will be either rejected or the study authors will be contacted for completion of the checklist. The demographic details (age, ethnicity, cigarette smoking status) will also be described. Any study in which authors who does not respond to the reviewer's repeated correspondence for essential information will be withdrawn from the selected shortlist of documents.

Quality scoring will be undertaken using the Newcastle-Ottowa score [16]. Criteria for quality assessment will include:

- Description of screened population
- Response rates to invitation to screening
- Description of outcomes how aortic diameter was ascertained and its repeatability.
- Reporting methods: graphic, descriptive, tables, statistical uncertainty
- Heterogeneity (chronological time; country)

1.6 Data synthesis and analysis

*Narrative review*

The data synthesis will summarise the extracted data of the included and eligible studies. All the relevant information (e.g. intervention, population, outcomes) will be tabulated. The ineligible studies will also be tabulated (giving reasons for exclusion).

If feasible, an estimate of the average prevalence (%) together with its standard error will be extracted from each study. Where 95% confidence intervals are quoted in place of standard errors, these will be converted by assuming normality and using the formula se= (ucl – lcl)/3.92, where ucl and lcl are the upper and lower limits of the 95% confidence interval [17].

If a sample standard deviation and the number of subjects is quoted then this will be converted to a standard error of the mean using the formula se=sd/sqrt(n). If a 95% reference range is quoted, then this will first be converted to an approximate standard deviation using the formula sd = (urr-lrr)/3.92, where urr and lrr are the upper and lower limits of the 95% reference range, and then to a standard error of the mean as above.

*Meta-analysis*

A random-effects meta-analysis will be conducted on the logit probabililty scale (with standard errors transformed using the delta method) using the method of DerSimonian and Laird [18]. Heterogeneity will be assessed using the $I^2$ statistic. Further exploration of between study heterogeneity will be investigated using meta-regression, for example using the mean baseline diameter as a study level covariate. Results will be presented with Forest plots, and small study/ publication bias investigated using funnel plots.

*IPD meta-analysis*

For studies that provide individual person data an analysis of prevalence according to varying diameter thresholds will be undertaken. Variables (e.g. age, smoking) that may affect prevalence rates will be investigated under the statistical supervision of ST.

## 1.7. References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