

**Current prevalence of screen-detected abdominal aortic aneurysm in women: a systematic review with meta-analysis.**

**SWAN\* collaborative group**

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**ABSTRACT**

**Background:** Although women represent an increasing proportion of those now presenting with abdominal aortic aneurysm (AAA) rupture, the current prevalence of AAA in women is unknown. The contemporary population prevalence of screen-detected AAA in women by both age and smoking status was investigated.

**Methods:** Systematic review of studies screening for AAA, including >1000 women, aged  $\geq 60$  years, undertaken since the year 2000, searching MEDLINE, EMBASE and CENTRAL databases until 13<sup>th</sup> January 2016. Study quality was assessed using the Newcastle-Ottawa scoring system.

**Results:** Eight studies were identified, including only 3 based on population registers. The largest studies were based on self-purchase of screening. Altogether 1,537,633 women were screened. Overall AAA prevalence rates were very heterogeneous, ranging from 0.37 to 1.53%: pooled prevalence 0.74% [95%CI 0.53, 1.03]. The pooled prevalence increased with both age (>1% for women >70 years) and smoking (>1% for ever smokers and >2% in current smokers).

**Conclusions:** The current population prevalence of screen-detected AAA in older women is subject to wide demographic variation. However, in ever smokers and those over 70 years, the prevalence is >1%.

**Registration:** PROSPERO database of systematic reviews CRD42015020444

## Introduction

Previously abdominal aortic aneurysm (AAA) has been considered as a male-dominated disorder, with 4- to 6-fold more men than women receiving both elective and emergency AAA repair and epidemiological studies showing that the prevalence of AAA was 3- to 6-fold higher in men than women (1-3). Also women tend to develop AAA later in life than men (4, 5). Population screening for AAA in men has been introduced in several countries, to reduce the mortality from ruptured AAA (6). However, today almost one third of the patients presenting to hospital with ruptured AAA are women and their mortality is very high, so that women contribute an increasing proportion of AAA deaths (7, 8). Therefore one might question whether women are being offered appropriate diagnosis and adequate management of their AAA before they suffer from a ruptured AAA (9).

Smoking is the strongest risk factor for AAA, the association being much stronger than between smoking and other forms of cardiovascular disease (10). Historically, women took up smoking in large numbers some 15-20 years after men and several studies suggest that today the prevalence of smoking may be higher in women than men (11-13). There has been a steady decline in the prevalence of smoking over the past 25-30 years, most notably among men, which has been linked to a declining prevalence of screen-detected AAA in men, from 4-5% in the 1990s to about 1-2% today (14, 15). Other factors, including the more widespread use of diagnostic imaging leading to an increasing incidental detection of AAA also could have contributed to the declining prevalence of screen-detected AAA in men. There are far fewer data available for women. Here we have conducted a systematic review of contemporary (2000 or later) AAA screening studies in women, to assess the population prevalence and how this may vary with age and smoking.

## Methods

This systematic review was conducted according to the PRISMA guidelines (16) and registered in May 2015 in the PROSPERO database of prospectively registered systematic reviews <http://www.crd.york.ac.uk/PROSPERO/>: Registration number: CRD42015020444. The review protocol was externally reviewed (Professor F Lederle, Minneapolis, USA). The aim was to systematically review published and unpublished data of the *current* (since 2000) prevalence of AAA in women, detected either by ultrasonography or CT scan, defined as having an aortic diameter of  $\geq 3.0$ cm.

We searched the MEDLINE, EMBASE and CENTRAL databases, using a combination of controlled vocabulary (MeSH or Emtree) terms and free text terms in ProQuest Dialog™ and limiting the search to data published since 2000 to identify relevant articles. We restricted our search to major European languages, and used the following terms for the search: abdominal aortic aneurysm, women/gender/sex/women's health/sex difference, genetic predisposition, prevalence / incidence/occurrence/frequency, screening, population / population-based). The final search date was 13<sup>th</sup> January 2016.

Clinicaltrials.gov (<http://clinicaltrials.gov>), Current Controlled Trials (<http://www.controlled-trials.com/>) and the National Research Register (UK) were also searched for details of ongoing or unpublished trials. We complemented this search by scanning reference lists of relevant articles, and manual searches of Endovascular Today and vascular surgery conference proceedings.

### **Study Selection**

The inclusion and exclusion criteria are shown in Table 1. The initial rejection or inclusion was based on the study title; review articles were retained for examination of their references.

Full text-versions of the selected shortlist of documents were obtained. Two reviewers (PU, JTP) individually assessed them to make sure they adhered to the initial eligibility criteria and then selected studies that met the inclusion criteria. Differences of opinion were resolved by discussion.

## Data Extraction and Quality Scoring

A data extraction form, which identified demographic and technical details, and potential biases, in the selected studies, was designed by the reviewers and approved by the full study team. A summary checklist was completed for each study. For four publications study authors were contacted to request additional information for completion of the checklist. Three authors/studies provided us with the requested data. Quality scoring was undertaken using the Newcastle-Ottawa score for cross-sectional studies (17). (Criteria for quality assessment are detailed in the protocol

[http://www.crd.york.ac.uk/PROSPEROFILES/20444\\_PROTOCOL\\_20150412.pdf](http://www.crd.york.ac.uk/PROSPEROFILES/20444_PROTOCOL_20150412.pdf) ).

The following data were independently extracted by the two reviewers: study design, screening setting (including number of centres) and country, AAA screening start/end dates, screening method, AAA definition, population description of women (including ethnicity, age range, smoking and diabetes status), exclusion criteria (particularly if they excluded non-screen detected/known AAAs or previous AAA repairs), the number of women invited to be screened, the number of women who accepted screening, the number of women with AAA (including AAA detection by age and smoking status), and authors' reported limitations of the study.

## Data synthesis and analysis

An estimate of the prevalence (%) was extracted from each study, calculated as the number of women with AAA divided by the number of women who were successfully screened. A 95% confidence interval for the prevalence in each study was calculated using the score confidence interval (18, 19). Three studies (20-22) had included women younger than 60 years of age in their screening. Since the current review excludes this younger group of women, we only included those aged 60 years and above from these studies. A random-effects meta-analysis was performed on the logit probability scale (with standard errors transformed using the delta method) using the method of DerSimonian and Laird (23). Heterogeneity was assessed using the  $I^2$  statistic (24). Further exploration of between study heterogeneity was investigated using meta-regression. Results are presented as Forest plots.

## Results

The flow diagram for selection of relevant articles is shown in Figure 1. A total of 92 unique articles were identified of which 24 (26%) were considered to be potentially relevant and assessed in detail. Six papers based on six studies met our inclusion criteria (20, 21, 25-28) and a seventh study reported on AAA defined as  $\geq 3.5$  cm diameter but data for women with an aortic diameter of  $\geq 3.0$  cm were obtained from the corresponding author (22). All these studies used ultrasonography for screening. Correspondence with the authors provided further details of several studies (21,25,26) and one author (25) provided an eighth unpublished study using ultrasonography for screening. These eight studies were included in the meta-analysis. One study reported on sub-group of a larger study, and was retained for assessment of prevalence by smoking status only (29). One further medium-size study reported on physician-initiated screening (with both ultrasonography and CT scan) in a population, but without defining either the specific criteria for screening or AAA by a minimum aortic diameter and hence provides only a minimum estimate of prevalence (30). All of the studies excluded persons with known AAA from screening.

Of the seventeen studies that were excluded after reviewing the full text, two did not meet our inclusion criteria as they had screened fewer than 1000 women (31), 795 women and (32), 796 women). Three large studies were excluded, one consisted of a selected population (including 14834 Chinese hypertensive women (33)) and the other two had been carried out in 1992 and between 1992 and 1997, respectively (34, 35). A recent French study provided insufficient information (36).

The characteristics of the included studies are summarised in Table 2. We identified two studies of very large cohorts (about 1.5 million women of  $\geq 60$  years), mainly self-referred for self-purchase Life Line screening, from the USA and Great Britain & Ireland (20, 21). The USA Life Line screening data included a minority of subjects (7%) with at least one cardiovascular risk factor, put forward for sponsored Life Line screening: this minority was reported on separately by Derubertis and colleagues (29). These latter data were used to assess the effect of smoking on AAA prevalence, since this was not reported in the overall USA Life Line cohort (20). Smaller studies offering free screening based on population registers were from Sweden, Norway and Italy: but only two of these were of very high quality and in total this type of study contributed only 11,003 women. There were two further published studies (25,26) and one unpublished study offering, by advertisement, sponsored free screening in the USA. This gave an overall total of 1,537,633 women screened in 8 separate studies, with a pooled prevalence of 0.74% [95%CI 0.53, 1.03] in women  $\geq 60$  years but with considerable heterogeneity (Figure 2).

The lowest prevalence (0.31%) was observed in the large UK & Ireland Lifeline study of self-referrals paying for screening (21). Otherwise the overall prevalence of AAA ranged from 0.37% in Sweden to 1.53% in Norway (both studies being based on population registers). The Life Line screening of predominantly self-referred persons purchasing screening yielded rather similar low AAA prevalence in the USA (0.44%) and in Great Britain & Ireland (0.31%). The study of a large predominantly uninsured and ethnically diverse USA population of  $\geq 65$  years, where almost half the women smoked, reported a minimum prevalence of 1.04% (30), also shown in Table 2 for comparison.

The pooled prevalence of AAA increased rapidly with age: 0.43% at 61-70 years, 1.15% in those 71-80 years and 1.68% in those 81+ years of age (Figure 3). However, there was considerable heterogeneity even for these pooled estimates ( $I^2$  74%-94%), and in every age band the prevalence was lowest in the self-referred cohorts and highest in the Norwegian population-register-based cohort. However, when relative risks were assessed, there was more consistency between studies ( $I^2$  0%-49%) than seen with the absolute risks: compared to the 60-69 year age group, the prevalence was 2.7-fold (95% CI 1.8 to 4.2) higher in the 70-79 year age group and 4.3-fold (4.0 to 4.7) higher in the 80+ year old age group.

Only five studies reported on prevalence by smoking status (Table 2), although the recording of smoking status was not uniform. Hupp (unpublished) recorded those who remembered having smoked  $>100$  cigarettes in their lifetime, which is the same definition used by the US Preventive Services Task Force (37). The pooled prevalence was lower for never smokers (0.28%) versus 1.34% for ever smokers (Figure 4). The Jahangir study (30) provides support for this effect since the association between AAA and former smoking had a hazard ratio of 3.4, rising to 9.2 in current smokers. Three studies reported the prevalence in current smokers, 2.08% (27), 4.63% (22) and 2.82% (26). Two of the smaller studies reported similar prevalence for those with and without diabetes (27, 29).

## Discussion

Data on the population prevalence of AAA in women is sparse and systematic review searching identified only a handful of studies conducted since 2000, with a pooled prevalence of 0.74% [95%CI 0.53, 1.03] in women  $\geq 60$  years. This date limitation was introduced because of the observed two-fold reduction in prevalence of screen-detected AAA in men between 1990 and now (15). Of the identified studies only 3 invited women for free screening based on population registers and the remainder recruited by advertisement, with self-referral screening either being sponsored or paid for by the woman screened. This diversity in design implies that the populations screened were of diverse demographic characteristics, particularly with respect to socio-economic status, which is likely to underlie part of the significant heterogeneity observed between studies. For this reason, the physician-referred screening in a largely uninsured Southern USA population with high ethnic diversity is included as a comparator (30). The contemporary pooled prevalence of AAA in women  $\geq 60$  years, reported here, appears to be lower than that for earlier studies. For instance, in the population-register based Chichester (UK) screening trial, the prevalence in 65-80 year old women in 1988-1990 was 1.3% (but 1.7% in those over 70 years) (2).

This study also reports an increasing prevalence of AAA with age and smoking, particularly for current smokers where the prevalence appears to be over 2%. Of all the cardiovascular disorders, AAA has the strongest association with smoking, particularly current smoking (10), and the decline in current smoking in those aged 65 years has been slower in women than men (8,13). The proportion of current smokers varied in the different studies included in this review but was highest in Norway (19), where the prevalence of AAA was highest. Some of the difference in overall prevalence between the neighbouring countries of Norway (19) and Sweden (14) might be explained by differences in smoking prevalence, 25% and 10% respectively. The high prevalence of AAA in women smokers was a notable feature of the Jahangir study (30) to suggest that smoking may have a greater relative impact on prevalence in women than in men. There was insufficient information in the included studies to assess the impact of other risk factors. Other contributions to heterogeneity might come from the variable used for ultrasound diameter measurements, anterior-posterior or transverse, based on inner-to-inner wall, outer-to-outer wall or leading edge-to leading edge: only one study was specific about the measurement reported (27).

All the data derived for this systematic review are based on the definition of an AAA as having a maximum infrarenal aortic diameter of  $\geq 3$ cm on ultrasonography. This definition has been derived for men, where 3.0 cm represents approximately a 50% increase of normal

infrarenal aortic diameter: in men the median diameter of those  $\geq 65$  years is 2.02 cm (38). In women  $\geq 65$  years the median infrarenal aortic diameter is only 1.75 cm (38). This begs the question of whether, for women, the diameter threshold for definition of an AAA should be lower, perhaps 2.6cm. If this were the case, the screen-detected prevalence of AAA in women would be much higher. For instance, with this lower diameter threshold, the prevalence of AAA in 70-year Swedish women would more than double (27). Whether an aortic diameter between 2.6cm and 2.9cm in women represents a clinically significant disease is unknown and only studies with long-term follow-up of this group will determine if there is any clinical benefit in refining the definition of an AAA for women.

The data for the contemporary prevalence of AAA in women should be considered in the context of the ongoing debate as to whether AAA in women are adequately diagnosed and treated. If AAA screening in 65 year old men is cost-effective down to a prevalence rate as low as 0.35% (39), AAA screening also may be cost-effective in 70 year old women (especially since the AAA rupture rate in women is about 4 times that in men for a given AAA diameter (40)). Indeed a modelling study from Sweden already has suggested that AAA screening for older women would be cost-effective, based on an AAA prevalence of 1.1% in 65 year old women (41).

Present guidelines about AAA screening in women are only that it is not recommended for older women who have never smoked (37). This contemporary review, showing a pooled prevalence of 0.74% in women  $\geq 60$  years, rising to a prevalence of  $>1.0\%$  in ever smokers and those  $\geq 70$  years, might stimulate re-opening the debate about offering targeted AAA screening to older women, although the precise target group of women who may benefit from screening remains unclear.

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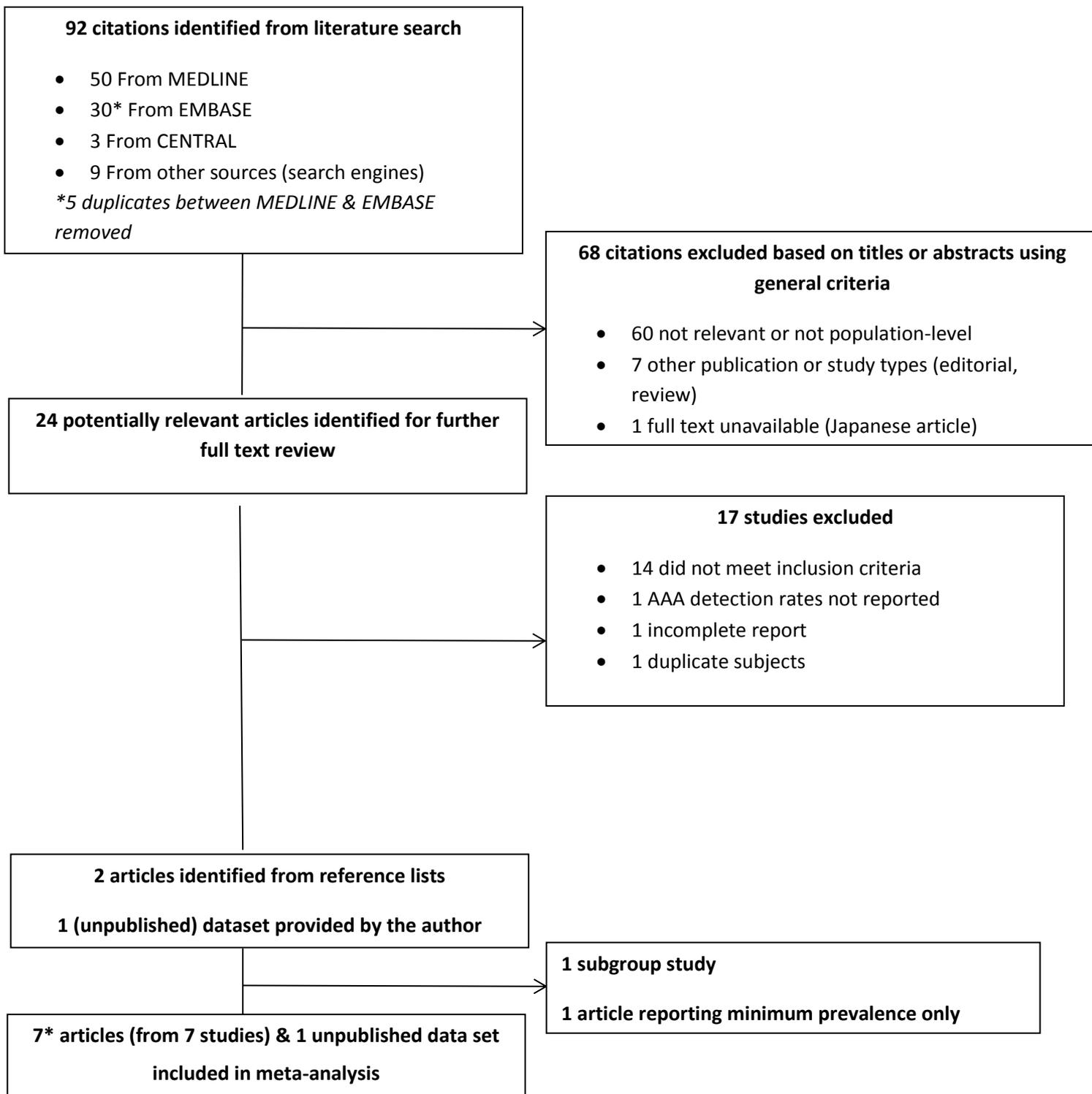
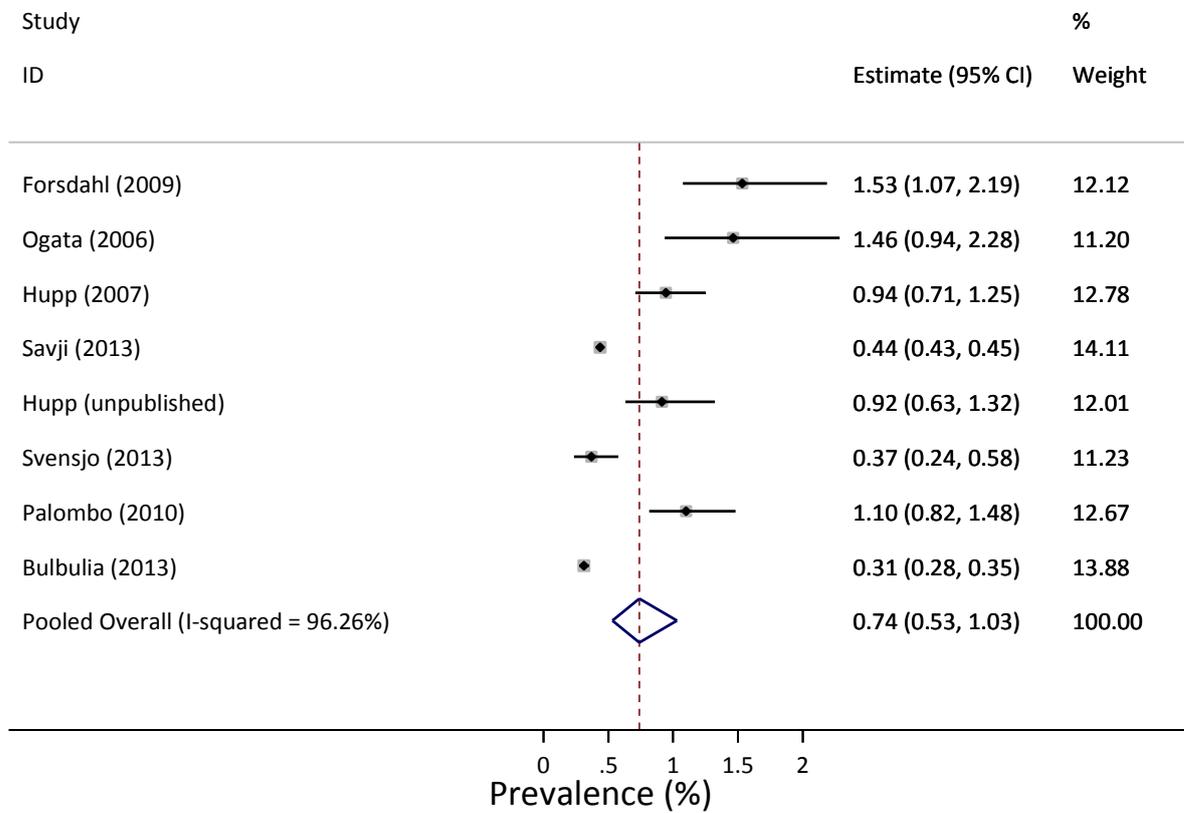


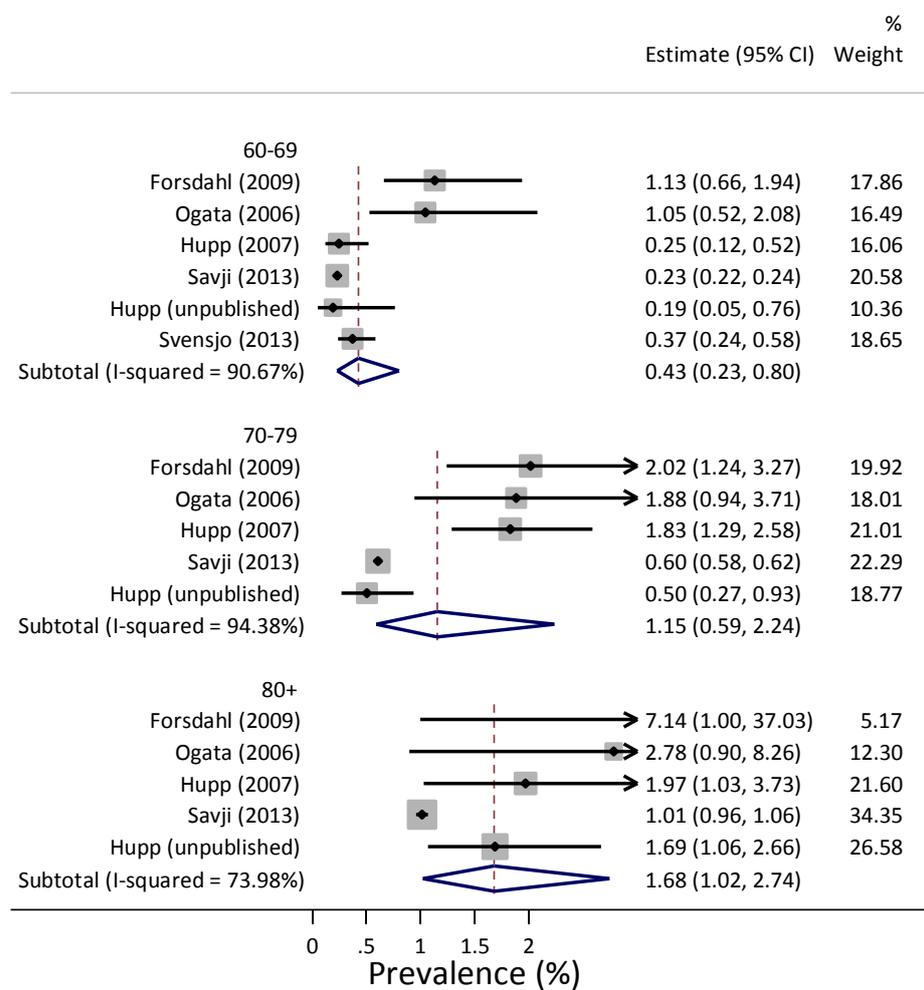
Figure 1 Flow diagram of included studies

**Figure 2 Pooled prevalence of abdominal aortic aneurysm in women  $\geq 60$  years: 8 studies with screening performed between 2001 and 2012**



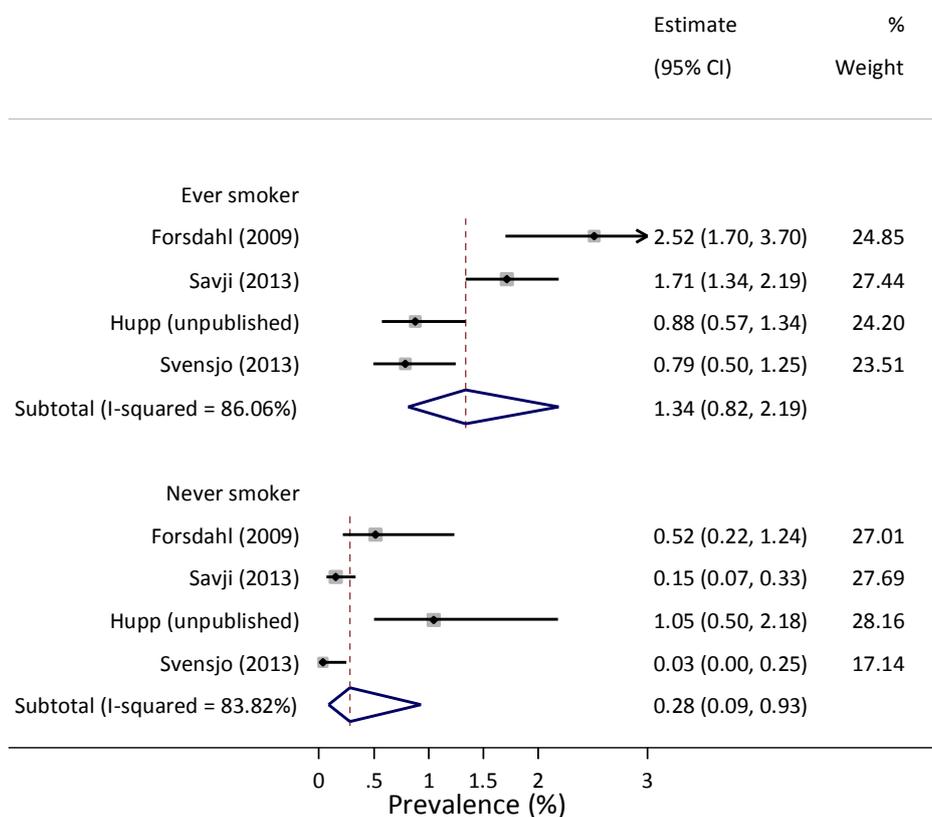
### Figure 3 Prevalence of abdominal aortic aneurysm in women $\geq 60$ years by 10-year age groups

\* Svensjo (2013): all women were aged 70. \*\* Forsdahl (2009) and Savji (2013) presented data for age-groups 60-69, 70-79 and 80-89.



**Figure 4 Prevalence of abdominal aortic aneurysm in women  $\geq 60$  years by smoking status.**

\* Savji (2013) prevalence by smoking obtained from substudy by Derubertis (2007)<sup>29</sup>, which provides data on a subgroup of 10012 women, mean age 69 years, with at least 1 cardiovascular risk factor screened between 2004-2006.



**Table 1 Inclusion and exclusion criteria**

<b>Inclusion criteria</b>	<b>Exclusion criteria</b>
Screening date year 2000 onwards	Review articles
Women $\geq 60$ years of age	Editorials
All ethnic groups	Letters
Population clearly described	Case reports
Studies must include screening of at least 1000 women	Studies of persons with known cardiovascular disease
For studies reporting duplicated data, the most recent or most comprehensive publication will be included.	
Ultrasonography or CT scan for aortic diameter measurement	

**Table 2 Characteristics of included studies, ordered by date of screening.**

The physician-initiated screening study reporting only minimum prevalence (30) is shown in italics in the bottom shaded section.

Study Author Publication year	Selection for screening	Screening dates	Country	Number of women screened (% attendance)	Age range (years)	Never smoked (current smokers) %	†N-O score	Number of AAAs (prevalence %)
<b>Forsdahl 2009</b> <sup>22</sup>	Population-based, free	2001	Norway	1956 (85*)	61-80+	35 (25)	9	30 (1.53)
<b>Ogata 2006</b> <sup>26</sup>	Self-referred, free	2001-2004	USA	1298 (n/a)	60-89	n/a (9.2)	5	19 (1.46)
<b>Hupp 2007</b> <sup>25</sup>	Self-referred, free	2000-2006	USA	4982 (n/a)	60-89	n/a	7	47 (0.94)
<b>Savji 2013</b> <sup>20†</sup>	Mainly self-referred, self-purchased	2003-2008	USA	1428316 (n/a)	61-100	n/a	6	6229 (0.44)
<b>Hupp (unpublished)</b>	Self-referred, free	2006-2008	USA	3060 (n/a)	66-105	22 (n/a)	7	28 (0.92)
<b>Svensjo 2013</b> <sup>27</sup>	Population-based, free	2007-2009	Sweden	5140 (74)	70 only	56 (10)	9	19 (0.37)
<b>Palombo 2010</b> <sup>28</sup>	Population-based, free	2007-2009	Italy	3907 (48)	65+	n/a	7	43 (1.10)
<b>Bulbulia 2013</b> <sup>21</sup>	Self-referred, self-purchased	2008-2012	UK, Ireland	88974 (n/a)	60-80+	n/a	6	278 (0.31)
<i><b>Jahangir 2015</b></i> <sup>30</sup>	<i>Physician-initiated, re-imbursed</i>	<i>2002-2009</i>	<i>USA</i>	<i>11815 (n/a)</i>	<i>65+</i>	<i>42 (21)</i>	<i>5</i>	<i>123 (1.04)</i>

†Does not report aneurysm size & smoking, used for prevalence only due to the very large population of women and supplemented by Derubertis (29), which also uses the same Life Line

screening, but provides data on a subgroup of 10012 women, mean age 69 years, with at least 1 cardiovascular risk factor screened between 2004-2006. \*Similar numbers of men and women screened, overall uptake was 85%. The Jahangir study was not included in data synthesis, but outline details are provided in the table for comparison with a group of lower socio-economic status. \*N-O, Newcastle-Ottawa score, which was used to assess study quality, the highest scores representing the best quality studies ([http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp)). n/a not available

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