

Supplementary Online Content

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eMethods. Literature Search Strategies for Primary Literature

eTable 1. Inclusion and Exclusion Criteria

eTable 2. AAA Prevalence, Rupture, and Surgery Data for Rescreening Studies (KQ2)

eTable 3. All-Cause and AAA-Related Mortality Data for Rescreening Studies (KQ2)

eTable 4. AAA Growth Rate, Rupture, and Surgery Data for Pharmacotherapy vs Placebo Trials for Small AAAs (KQ4 and KQ5)

eTable 5. Harms Data in Studies of Treatment for Small AAA (KQ5)—Pharmacotherapy vs Placebo

eReferences

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Literature Search Strategies for Primary Literature

Key:

* = truncation

\$ = truncation

ab = word in abstract

kf = keyword heading [word not phrase indexed]

kw = keyword

pt = publication type

ti = word in title

MEDLINE: Screening

Database: Ovid MEDLINE(R) <1946 to September Week 1 2018>, Ovid MEDLINE(R) Daily Update <September 14, 2018>

-
- 1 Aortic Aneurysm, Abdominal/ (17370)
 - 2 abdominal aortic aneurysm\$.ti,ab. (15021)
 - 3 1 or 2 (20880)
 - 4 Mass screening/ (95905)
 - 5 (screen\$ or rescreen\$ or re screen\$).ti,ab. (555648)
 - 6 4 or 5 (583442)
 - 7 3 and 6 (1298)
 - 8 limit 7 to (english language and yr="2013 -Current") (293)

MEDLINE: Clinical trials

Database: Ovid MEDLINE(R) <1946 to September Week 1 2018>, Ovid MEDLINE(R) Daily Update <September 14, 2018>

-
- 1 Aortic Aneurysm, Abdominal/ (17370)
 - 2 abdominal aortic aneurysm\$.ti,ab. (15021)
 - 3 1 or 2 (20880)
 - 4 clinical trials as topic/ or controlled clinical trials as topic/ or randomized controlled trials as topic/ or meta-analysis as topic/ (318970)
 - 5 (clinical trial or controlled clinical trial or meta analysis or randomized controlled trial).pt. (896853)

- 6 random\$.ti,ab. (853765)
 - 7 control groups/ or double-blind method/ or single-blind method/ (178983)
 - 8 clinical trial\$.ti,ab. (271317)
 - 9 controlled trial\$.ti,ab. (160123)
 - 10 (metaanaly\$ or meta analy\$).ti,ab. (100793)
 - 11 or/4-10 (1645301)
 - 12 3 and 11 (2052)
 - 13 limit 12 to (english language and yr="2013 -Current") (518)
 - 14 remove duplicates from 13 (467)
-

MEDLINE: Treatment cohort studies

Database: Ovid MEDLINE(R) <1946 to September Week 1 2018>, Ovid MEDLINE(R) Daily Update <September 14, 2018>

-
- 1 Aortic Aneurysm, Abdominal/co, dt, mo, pc, px, rh, su, th [Complications, Drug Therapy, Mortality, Prevention & Control, Psychology, Rehabilitation, Surgery, Therapy] (13967)
 - 2 cohort studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/ or retrospective studies/ (1761323)
 - 3 Registries/ (73991)
 - 4 cohort\$.ti,ab. (385596)
 - 5 2 or 3 or 4 (1940167)
 - 6 1 and 5 (4757)
 - 7 limit 6 to (english language and yr="2013 -Current") (1114)
 - 8 remove duplicates from 7 (1020)
-

MEDLINE: All key questions [in-process/non-indexed records]

Database: Ovid MEDLINE(R) Epub Ahead of Print <September 14, 2018>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <September 14, 2018>

- 1 abdominal aortic aneurysm\$.ti,ab,kf. (1526)
- 2 limit 1 to (english language and yr="2013 -Current") (1169)
- 3 remove duplicates from 2 (1168)

Cochrane (Wiley) : All key questions

[Cochrane Database of Systematic Reviews : Issue 9 of 12, September 2018](#)

[Database of Abstracts of Reviews of Effects : Issue 2 of 4, April 2015](#)

[Cochrane Central Register of Controlled Trials : Issue 9 of 12, September 2018](#)

- #1 "abdominal aortic aneurysm":ti,ab,kw
- #2 "abdominal aortic aneurysm*":ti,ab,kw
- #3 #1 or #2 Publication Year from 2013 to 2017, in Cochrane Reviews (Reviews and Protocols)
- #4 #1 or #2 Publication Year from 2013 to 2017, in Other Reviews
- #5 #1 or #2 Publication Year from 2013 to 2017 , in Trials

PubMed: all key questions [publisher-supplied records]

Search	Query
#5	#4 AND ("2013/01/01"[Date - Publication] : "3000"[Date - Publication]) AND English[Language]
#4	#3 AND publisher[sb]

Search	Query
#3	#1 AND #2
#2	screen*[tiab] OR rescreen*[tiab] OR re screen*[tiab]OR trial[tiab] OR trials[tiab] OR random*[tiab] OR cohort*[tiab] OR longitudinal*[tiab] OR "follow up"[tiab] OR "followed up"[tiab] OR followup*[tiab] OR prospective*[tiab] OR retrospective*[tiab] OR meta analy*[tiab] OR metaanaly*[tiab] OR registry[tiab] OR registries[tiab] OR register[tiab] OR registers[tiab]
#1	abdominal aortic aneurysm*[tiab]

eTable 1. Inclusion and Exclusion Criteria

	Included	Excluded
Populations	<p>KQs 1–3: Asymptomatic adult population</p> <p>KQs 4, 5: Asymptomatic adult population with small AAAs (i.e., aortic diameter of 3.0 to 5.4 cm)</p>	<p>KQs 1–3: Patients experiencing symptoms related to AAA</p> <p>KQs 4, 5: Patients experiencing symptoms related to AAA; populations with AAAs with an aortic diameter larger than 5.4 cm or smaller than 3.0 cm</p>
Setting	Studies conducted in primary care or other settings with a comparable population to primary care (e.g., general unselected population for screening [KQs 1, 3])	
Disease/condition	AAA (aortic diameter ≥ 3.0 cm)	
Interventions	<p>KQs 1–3: Screening with ultrasound</p> <p>KQs 4, 5: Treatment with pharmacotherapy (e.g., statins, angiotensin converting enzyme inhibitors, antibiotics) or surgical intervention</p>	KQs 1–3: Screening with physical examination, computed tomography, or magnetic resonance imaging
Comparisons	<p>KQs 1, 3: One-time screening vs. no screening</p> <p>KQs 2, 3: Repeat screening vs. no rescreening</p> <p>KQ 4: Pharmacotherapy vs. placebo, surgery vs surveillance alone</p>	<p>KQ 2: Comparison of surveillance interval</p> <p>KQs 4, 5: Comparative effectiveness of treatments</p>
Outcomes	<p>KQs 1, 2: All-cause mortality, aneurysm-related mortality, cardiovascular disease mortality, aneurysm rupture rate, cardiovascular disease events, and quality of life</p> <p>KQ 3: Anxiety and downstream procedures related to false-positive results</p> <p>KQ 4: AAA annual growth rate, all-cause mortality, aneurysm-related mortality, cardiovascular disease mortality, aneurysm rupture rate, cardiovascular disease events, and quality of life</p> <p>KQ 5: Harms (i.e., serious adverse events from pharmacotherapy or surgery)</p>	

	Included	Excluded
Study Designs	<p>KQs 1, 4: Randomized, controlled trials</p> <p>KQs 2, 3: Randomized, controlled trials; large cohort studies (sample size >1,000)</p> <p>KQ 5: Randomized, controlled trials; large cohort studies (sample size >1,000); vascular surgery registries</p>	<p>KQs 1, 4: Case-control, cross-sectional, and cohort studies; editorials, letters, and opinions; cost studies</p> <p>KQs 2, 3: Case-control and cross-sectional studies; editorials, letters, and opinions; cost studies</p>
Countries	Studies conducted in countries categorized as “Very High” on the 2016 Human Development Index (as defined by the United Nations Development Programme)	Studies conducted in countries that are not categorized as “Very High” on the 2016 Human Development Index
Language	English only	Languages other than English
Quality	Fair- and good-quality studies	Poor-quality studies

eTable 2. AAA Prevalence, Rupture, and Surgery Data for Rescreening Studies (KQ2)

Study, Year USPSTF Quality	Mean Followup, years	N Analyzed	Initial Aorta Size range	Large AAA Incidence, n (%)	AAA Rupture, n (%)	All AAA Procedures, n (%)	Elective Surgery, n (%)	Emergency Surgery, n (%)
D'Audiffret, 2002 ¹ Fair	5.9	223	2.5-2.9 cm	> 5 cm: 3 (1.3)	0 (0)	0 (0)	0 (0)	0 (0)
Deveraj, 2008 ² Fair	5.4	358	2.6-2.9 cm	≥ 5.5 cm: 8 (2.2)	NR	NR	NR	NR
Oliver-Williams, 2018 ^{3,4} Good	7.8	1233	2.6-2.9 cm	≥5.5 cm: 181 (14.7)	13 (2.4) ^a	134 (10.9)	124 (10.1)	10 (0.8)
	7.9 ^a	547	2.6-2.9 cm	> 5.4 cm: 87 (15.9)	13 (2.4)	63 (11.5)	57 (10.4)	6 (1.1)
Lederle, 2000 ⁵ Good	4	2622	≤3.0 cm	> 5 cm: 0	0 (0)	0 (0)	NR	NR
Lindholt, 2000 ⁶ Fair	5	248	2.5-2.9 cm	> 5 cm: 0	NR	0 (0)	NR	NR
Scott, 2001 ⁷ Fair	10	649	< 3.0 cm	>5 cm: 0	NR	NR	NR	NR
Soderberg, 2017 ⁸ Fair	5	33 ^b 25 rescreened	2.5-2.9 cm	>5 cm: 0	0 (0)	1 (4)	1 (4) ^c	0
Svensjo, 2014 ⁹ Fair	5	2652 2041 rescreened	<2.5 cm	NR ^d	0	0	0	0

^a From median follow-up of 7.9 years (2.7 to 11-year range)³

^b One woman was misclassified with a normal (2.1cm) aorta at rescanning and was excluded from further analysis

^c One participant was diagnosed with a 4.5cm AAA at 5yr follow-up and was then electively repaired.

^d Did not report >5cm AAA incidence

Abbreviations: AAA = abdominal aortic aneurysm; cm = centimeter; N = population size; n = sample size; NR = not reported

eTable 3. All-Cause and AAA-Related Mortality Data for Rescreening Studies (KQ2)

Study, Year USPSTF Quality	Mean follow-up, years	N Analyzed	All-cause mortality, n (%)	AAA-related mortality, n (%)	Operative mortality, n (%)
D'Audiffret, 2002 ¹ Fair	5.9	223	8 (3.6)	0 (0)	NR
Deveraj, 2008 ² Fair	5.4	358	NR	NR	NR
Oliver-Williams, 2018 ^{3,4} Good	7.8	1233	379 (30.7)	14 (2.4) ^a	7 (11.1) ^a
Lederle, 2000 ⁵ Good	4	2622	NR	0 (0)	NR
Lindholt, 2000 ⁶ Fair	5	248	NR	NR	NR
Scott, 2001 ⁷ Fair	10	649	NR	NR	NR
Soderberg, 2017 ⁸ Fair	5	33 (2.5-2.9 cm AAA diameter group)	5 (15.2)	0 (0)	0 (0)
Svensjo, 2014 ⁹ Fair	5	2652 (<2.5 AAA diameter group)	136 (5.1)	0 (0)	0 (0)
		40 (2.5-2.9 cm AAA diameter group)	2 (5)	0 (0)	0 (0)

^aAAA-related mortality from median followup of 7.9 years (2.7 to 11-year range)³

Abbreviations: AAA = abdominal aortic aneurysm; cm = centimeter; N = population size; n = sample size; NR = not reported

eTable 4. AAA Growth Rate, Rupture, and Surgery Data for Pharmacotherapy vs Placebo Trials for Small AAAs (KQ4 and KQ5)

Study, Year Quality	Comparison	Mean Follow-up, years	Treatment group	N Analyzed	Mean AAA Growth Rate, mm/year	AAA Rupture, n (%)	All AAA Procedures, n (%)	Elective Surgery, n (%)	Emergency Surgery, n (%)
Bicknell, 2016 ¹⁰ AARDVARK Good	Perindopril (IG1) or amlodipine (IG2) vs. placebo	2	IG1	73	1.77 (0.2) ^a	0 (0)	10 (13.7) ^b	NR	NR
			IG2	72	1.81 (0.2) ^a	0 (0)	11 (15.3) ^b	NR	NR
			CG	79	1.68 (0.2) ^a	0 (0)	11 (13.9) ^b	NR	NR
Hogh 2009 ¹¹ Good	Roxithromycin vs. placebo	5	IG	42	1.16 ^c	NR	29 (34.5) ^d	29 (34.5) ^d	NR
			CG	42	2.52 ^c	NR			NR
Karlsson 2009 ¹² Fair	Azithromycin vs. placebo	1.5	IG	106	2.2 (0.12- 0.36) ^e	1 (0.94)	16 (15.1)	15 (14.1) ^f	1 (0.9) ^f
			CG	105	2.2 (0.09- 0.34) ^e	NR	13 (12.4)	NR	NR
Meijer, 2013 ¹³ Fair	Doxycycline vs. placebo	1.5	IG	144	4.1 (3.6-4.5) ^g	0 (0)	21 (14.6)	21 (14.6)	0 (0)
			CG	142	3.3 (2.8-3.7) ^g	2 (1.4)	24 (16.9)	22 (15.5)	2 (1.4)
Mosorin 2001 ¹⁴ Fair	Doxycycline vs. placebo	1.5	IG	17	1.5 (0.0- 3.0) ^h	1 (5.9)	3 (17.6)	2 (11.8)	1 (5.9)
			CG	15	3.0 (0.3-6.0) ^h	0 (0)	6 (40.0)	6 (40.0)	0 (0)
PAT Investigators, 2002 ¹⁵ PAT Good	Propranolol vs. placebo	2.5	IG	276	2.1 (0.29) ⁱ	1 (0.4)	57 (20.6)	56 (20.3)	1 (0.4)
			CG	272	2.6 (0.30) ⁱ	2 (0.7)	74 (27.2)	72 (26.5)	2 (0.7)
Sillensen, 2015 ¹⁶ AORTA Fair	Pemirolast vs. placebo	1	IG	84	2.71 (2.25- 3.16) ^j	0 (0)	6 (7.1)	NR	NR
			CG	84	2.04 (1.58 - 2.50) ^j	0 (0)	2 (2.4)	NR	NR

^a Mean (SE), difference NS (IG1, p=0.78, IG2, p=0.68)

^b Number of patients reaching 5.5 cm or being referred to/having surgery

^c p=0.055

^d Total referred to surgery because AAA was >5.0 cm (treatment group NR)

^e Median (IQR); p=0.85

^fAssumed

^gMean (95% CI), based on a linear mixed model and adjusted for incomplete data. Mean between group difference (95% CI), mm: 0.8 (0.1 to 1.4); p = 0.016

^hMedian (IQR); p-value was not significant

ⁱWhile patients were taking the study drug assigned; values reported as mean growth rate (SD); p=0.10

^jAdjusted mean change (95% CI); p = 0.189; doses of 10 mg and 25 mg are also reported; there was no significant difference in growth rate found between treatment groups

Abbreviations: AAA = abdominal aortic aneurysm; AARDVARK = Aortic Aneurysmal Regression of Dilation: Balue of ACE-Inhibition on RisK trial; AORTA = the Anti-inflammatory Oral Treatment of AAA; CG = control group; IG = intervention group; N = population size; n = sample size; NR = not reported; PAT = propranolol Aneurysm Trial; vs = versus

eTable 5. Harms Data in Studies of Treatment for Small AAA (KQ5)—Pharmacotherapy vs Placebo

Study	Drug name	Mean Followup, years	Treatment Group	N Analyzed	Readmission in 30 days, n (%)	Trial Withdrawals due to AEs related to study medication, n (%)	Complication, n (%)
Bicknell, 2016 ¹⁰ AARDVARK	Perindopril (IG1); amlodipine (IG2)	2.0	IG1	73	NR	2 (2.7)	Serious AEs ^a 19 (26.0)
			IG2	72	NR	4 (5.6)	Serious AEs ^a 12 (16.7)
			CG	79	NR	0 (0)	Serious AEs ^a 16 (20.2)
Hogh 2009 ¹¹	Roxithromycin	2.0	IG	40	NR	0 (0)	No adverse events were reported
			CG	44	NR	0 (0)	No adverse events were reported
Karlsson 2009 ¹²	Azithromycin	1.5	IG	106	NR	3 stopped taking medication	13 (12.3) ^b
			CG	105	NR	2 stopped taking medication	8 (7.6) ^b
Lindholt, 1999 ¹⁷	Propranolol	2.0	IG	30	NR	18 ^c	Serious cardiac arrhythmia: 1 (3.3) ^d Dyspepsia: 3 (10.0) ^d Headache: 2 (6.7) ^d Dizziness: 3 (10.0) ^d
			CG	24	NR	7 ^c	Serious cardiac arrhythmia: 0 (0) ^d Dyspepsia: 1 (4.2) ^d Headache: 1 (4.2) ^d Dizziness: 0 (0) ^d
Meijer, 2013 ¹³	Doxycycline	1.5	IG	144	NR	11 (7.6)	Abdominal pain, nausea, diarrhea 5 (3.5)
			CG	142	NR	3 (2.1)	Abdominal pain, nausea, diarrhea 11 (7.7)
Mosorin 2001 ¹⁸	Doxycycline	1.5	IG	17	NR	1 (5.9) ^e	No adverse events were reported
			CG	15	NR	1 (6.7) ^e	No adverse events were reported

Study	Drug name	Mean Followup, years	Treatment Group	N Analyzed	Readmission in 30 days, n (%)	Trial Withdrawals due to AEs related to study medication, n (%)	Complication, n (%)
PAT Investigators, 2002 ¹⁵ PAT	Propranolol	2.5	IG	267	NR	104 (37.7) ^f	Patients who stopped their medication before surgery or the end of study: 117 (42.4) Reasons for permanently stopping study drug: ⁹ <i>Fatigue</i> : 24 (8.7) <i>Heart failure</i> : 7 (2.5) <i>Bradycardia/AVB</i> : 11 (4) <i>Claudication/Raynaud's disease</i> : 1 (0.4)
			CG	272	NR		Patients who stopped their medication before surgery or the end of study: 73 (26.8) Reasons for permanently stopping study drug: ⁹ <i>Fatigue</i> : 12 (4.4) <i>Heart failure</i> : 2 (0.7) <i>Bradycardia/AVB</i> : 1 (0.4) <i>Claudication/Raynaud's disease</i> : 3 (1.1)
Sillensen, 2015 ¹⁶ AORTA	Pemirolast	1.0	IG1	84	NR	7 discontinued intervention (not specific); 1 withdrew	<i>Any AE</i> : 67 (79.8) <i>Any SAE</i> : 15 (17.9) <i>Serious cardiac disorder</i> : 4 (4.8)
			CG	84	NR		14 discontinued intervention (not specific); 8 withdrew <i>Any AE</i> : 68 (80.9) <i>Any SAE</i> : 15 (17.9) <i>Serious cardiac disorder</i> : 5 (5.9)

^a None of the recorded SAEs were deemed to be related to the trial medications.

^b All patients in CG had GI symptoms and 2 stopped taking meds. In IG: 3 stopped taking meds (1 due to diarrhea, 1 due to arthralgia, 1 had allergic reaction [found to be to antihypertensive med, not study med])

^c Cumulated drop-outs

^d Withdrew due to complications; subset of complications. Full list of complications listed in Figure 18 of article.

^e Discontinued the medication due to an allergic reaction

^f $p < 0.0001$

^g Complete list available in Table 2 of article

Abbreviations: AAA = abdominal aortic aneurysm; AARDVARK = Aortic Aneurysmal Regression of Dilation: Value of ACE-Inhibition on Risk trial; AORTA = the Anti-inflammatory Oral Treatment of AAA; AVB = atrioventricular block; CG = control group; EVAR = endovascular aneurysm repair; GI = gastrointestinal; IG = intervention group; MI = myocardial infarction; N = population size; n = sample size; NR = not reported; PAT = propranolol Aneurysm Trial; PVD = peripheral vascular disease; SAE = serious adverse events; vs = versus

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