Appendixes

Appendix A. Detailed Methods

Appendix B. AAA Screening With Ultrasonography Recommendations

Appendix C. Included Studies

Appendix D. Excluded Studies

Appendix E. Evidence Tables

Appendix F. Subpopulation Evidence Tables

Appendix G. Additional Contextual Question 2 Evidence

Appendix H. Ongoing Studies

Appendix A. Detailed Methods

Literature Search Strategies for Primary Literature

Sources searched: Cochrane Central Register of Controlled Clinical Trials, via Wiley Cochrane Database of Systematic Reviews, via Wiley Database of Abstracts of Reviews of Effects, via Wiley Medline, via Ovid PubMed, publisher-supplied

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 metaanalysis 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>

- 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)

Cochrane Database of Systematic Reviews : Issue 9 of 12, September 2017 Database of Abstracts of Reviews of Effects : Issue 2 of 4, April 2015 Cochrane Central Register of Controlled Trials : Issue 8 of 12, August 2017

- #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, publisher-supplied

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

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)

Existing Systematic Reviews Search

Sources searched (2014-present)	Number of items retrieved
Agency for Healthcare Research and Quality	0
Canadian Agency for Drugs and Technologies in Health	0
Cochrane Database of Systematic Reviews	13 (file attached)
Database of Abstracts of Reviews of Effects	16 (file attached)
Dynamed	1 (links below)
Health Technology Assessment (Centre for Reviews and Dissemination)	8 (file attached)
Institute of Medicine	0
NHS Health Technology Assessment Programme	6 (links below)
National Institute for Health and Clinical Excellence	2 (links below)
PubMed	187 (file attached)

Cochrane (Wiley)

Cochrane Database of Systematic Reviews : Issue 2 of 12, February 2017 Database of Abstracts of Reviews of Effects : Issue 2 of 4, April 2015 Health Technology Assessment Database : Issue 4 of 4, October 2016

- #1 "abdominal aortic aneurysm":ti,ab,kw 642
- #2 "abdominal aortic aneurysms":ti,ab,kw 306
- #3 #1 or #2 Publication Year from 2014 to 2017, in Cochrane Reviews (Reviews and Protocols) 13

16

- #4 #1 or #2 Publication Year from 2014 to 2017, in Other Reviews
- #5 #1 or #2 Publication Year from 2014 to 2017, in Technology Assessments 8

Dynamed

Abdominal aortic aneurysm (last updated 12/19/2016) http://search.ebscohost.com/login.aspx?direct=true&db=dme&AN=114361&site=dynamed-live&scope=site

NHS HTA Programme

HTA - 09/91/39: The development of an algorithm to calculate in individual patients with abdominal aortic aneurysm (AAA) when repair is indicated to improve survival, May 2015 https://www.journalslibrary.nihr.ac.uk/programmes/hta/099139/#/

Calculating when elective abdominal aortic aneurysm repair improves survival for individual patients: development of the Aneurysm Repair Decision Aid and economic evaluation, May 2015 https://www.journalslibrary.nihr.ac.uk/hta/9320/ - DUPLICATE

Screening women for abdominal aortic aneurysm, in progress https://www.journalslibrary.nihr.ac.uk/programmes/hta/1417901/

Endovascular treatment for ruptured abdominal aortic aneurysm, in progress

Appendix A. Detailed Methods

https://www.journalslibrary.nihr.ac.uk/programmes/sr/167205/

Magnetic Resonance Imaging Using Ultrasmall Superparamagnetic Particles of Iron Oxide to Predict Clinical Outcome in Patients Under Surveillance for Abdominal Aortic Aneurysms, in progress https://www.journalslibrary.nihr.ac.uk/programmes/eme/112003/

Surveillance following endovascular aortic aneurysm repair, in progress https://www.journalslibrary.nihr.ac.uk/programmes/hta/157801/

NICE

Endovascular aneurysm sealing for abdominal aortic aneurysm (IPG547), February 2016 <u>https://www.nice.org.uk/guidance/ipg547</u>

Abdominal aortic aneurysm: diagnosis and management, in development https://www.nice.org.uk/guidance/indevelopment/gid-cgwave0769

PubMed

Search	Query	Items found
<u>#5</u>	Search ((#4) AND English[Language]) AND ("2014/01/01"[Date - Publication] : "3000"[Date - Publication])	<u>187</u>
<u>#4</u>	Search #3 AND systematic[sb]	<u>618</u>
<u>#3</u>	Search #1 OR #2	<u>18887</u>
<u>#2</u>	Search abdominal aortic aneurysm*[tiab] AND (publisher[sb] OR inprocess[sb] OR pubmednotmedline[sb])	<u>1424</u>
<u>#1</u>	Search "Aortic Aneurysm, Abdominal"[Mesh] OR abdominal aortic aneurysm*[title]	<u>18334</u>

Category	Included	Excluded
Populations	KQs 1–3: Asymptomatic adult population	KQs 1–3: Patients experiencing symptoms
		related to AAA
	KQs 4, 5: Asymptomatic adult population with small	
	AAAs (i.e., aortic diameter of 3.0 to 5.4 cm)	Kus 4, 5: Patients experiencing symptoms
		related to AAA; populations with AAAS with an
		3.0 cm
Setting	Studies conducted in primary care or other settings	
5	with a comparable population to primary care (e.g.,	
	general unselected population for screening [KQs 1,	
	3])	
Disease/	AAA (aortic diameter ≥3.0 cm)	
Interventions	KOs 1-3: Screening with ultrasound	KOs 1-3: Screening with physical examination
Interventions	Nes 1-5. Screening with ditasound	computed tomography or magnetic resonance
	KQs 4. 5: Treatment with pharmacotherapy (e.g.,	imaging
	statins, angiotensin converting enzyme inhibitors,	
	antibiotics) or surgical intervention	
Comparisons	KQs 1, 3: One-time screening vs. no screening	KQ 2: Comparison of surveillance interval
	KOn 2 2. Depart corresping up, no recorresping	KO2 4 E. Comporative offectiveness of
	Nus 2, 3. Repeat screening vs. no rescreening	treatments
	KQ 4: Pharmacotherapy vs. placebo, surgery vs	
	surveillance alone	
Outcomes	KQs 1, 2: All-cause mortality, aneurysm-related	
	mortality, cardiovascular disease mortality,	
	aneurysm rupture rate, cardiovascular disease	
	events, and quality of life	
	KQ 3: Anxiety and downstream procedures related	
	to false-positive results	
	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	
	KQ 5: Harms (i.e., serious adverse events from	
	pharmacotherapy or surgery)	
Study	KQs 1, 4: Randomized, controlled trials	KQs 1, 4: Case-control, cross-sectional, and
Designs		cohort studies; editorials, letters, and opinions;
	KQs 2, 3: Randomized, controlled trials; large cohort	cost studies
	studies (sample size >1,000)	KOs 2 3: Case-control and cross-sectional
	KQ 5: Randomized, controlled trials: large cohort	studies: editorials letters and opinions: cost
	studies (sample size >1,000); vascular surgerv	studies
	registries	
Countries	Studies conducted in countries categorized as "Very	Studies conducted in countries that are not
	High" on the 2016 Human Development Index (as	categorized as "Very High" on the 2016 Human
	defined by the United Nations Development	Development Index
Languaga		Languages other than English
Quality	Fair- and good-guality studies	Poor-quality studies
addancy		

Appendix A Table 1. Inclusion and Exclusio	n Criteria
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Abbreviations: KQ = Key Question; USPSTF = U.S. Preventive Services Task Force.

Study Design	Adapted Quality Criteria						
Randomized and	Bias arising in the randomization process or due to confounding						
non-randomized	 Valid random assignment/random sequence generation method used 						
controlled trials,	Allocation concealed						
adapted from the	Balance in baseline characteristics						
U.S. Preventive	Bias in selecting participants into the study						
Force methods ¹⁰⁷	CCI only: No evidence of blased selection of sample						
	Fidelity to the intervention protocol						
	Low risk of contamination between groups						
	Participants were analyzed as originally allocated						
	Bias from missing data						
	No. or minimal, post-randomization exclusions						
	Outcome data are reasonably complete and comparable between groups						
	Reasons for missing data are similar across groups						
	Missing data are unlikely to bias results						
	Bias in measurement of outcomes						
	 Blinding of outcome assessors 						
	Outcomes are measured using consistent and appropriate procedures and						
	Instruments across treatment groups						
	No evidence of interential statistics Bias in reporting results selectively						
	No evidence that the measures analyses or subgroup analyses are selectively						
	• No evidence that the measures, analyses, of subgroup analyses are selectively reported						
Cohort studies,	Was there representativeness of the exposed cohort?						
adapted from the	 Was the non-exposed systematic selected? 						
Newcastle-Ottawa	Was the ascertainment of exposure reported?						
Scale	Were eligibility criteria specified?						
	Were groups similar at baseline?						
	Was the reading (interpretation) of the pathology results adequate?						
	Were outcome assessors blinded?						
	Were measurements equal, valid and reliable?						
	 Was followup long enough for outcomes to occur? 						
	Were the statistical methods acceptable?						
	 Was the handling of missing data appropriate? 						
	Was there adjustment for confounders?						
	Was there acceptable followup?						

Appendix A Table 2. Quality Assessment Criteria*

* Good quality studies generally meet all quality criteria. Fair quality studies do not meet all the criteria but do not have critical limitations that could invalidate study findings. Poor quality studies have a single fatal flaw or multiple important limitations that could invalidate study findings. Critical appraisal of studies using *a priori* quality criteria are conducted independently by at least two reviewers. Disagreements in final quality assessment are resolved by consensus, and, if needed, consultation with a third independent reviewer.

Appendix A Figure 1. Literature Flow Diagram



*Studies may appear under more than one Key Question.

Organization (Year)	Population	Surveillance interval
American College of Cardiology and	Men age ≥60 years with a family	<4.0 cm: every 2–3 years
American Heart Association (2013) ⁹⁵	history	4.0–5.4 cm: every 6–12 months
	Men ages 65–75 years who have	
	ever smoked	
	Men & women age >50 years should	
	be asked if they have AAA family	
	history	
American Academy of Family	Refers to USPSTF recommendation	Not stated
Physicians (NR) ⁹⁷	Men ages 65–75 years who have	
	ever smoked	
	Selectively screen men ages 65–75	
	years who have never smoked	
	Recommends against routine	
	screening for women who have	
	never smoked	
American College of Preventive	Men ages 65–75 years who have	Not stated
Medicine (2011) ⁹⁶	ever smoked	
	Recommends against routine	
	screening in women	
Society for Vascular Surgery (2018) ³	All men and women ages 65–75	2.5–3.0 cm: after 10 years
	years with history of tobacco use	3.0–3.9 cm: every 3 years
	Men age ≥55 years with family	4.0–4.9 cm: every 12 months
	nistory	5.0–5.4 cm: every 6 months
	vomen age 265 years if family	
	history/smoker	
Canadian Task Force on Preventive	Men ages 65-80 years	Not stated
Health Care $(2017)^{175}$	Recommends not screening men	
	age >80 or women at any age	
Public Health England (2015) ²⁴⁶	Men ages 65–74 years	3 0–4 4 cm: every 12 months
		4.5–5.4 cm: every 3 months
National Institute for Health and Care	All men age ≥66 years eligible to	3.0–4.4 cm: every 2 years
Excellence (NICE) DRAFT Guideline	self-refer to screening	4.5–5.4 cm: every 3 months
(2018) ¹⁸⁶	Encourage men age ≥66 years with	
	risk factors to be screened	
	Consider screening women age ≥70	
	years with risk factors	
	Risk factors: COPD, family history,	
	history of tobacco use,	
	hyperlipdemia, hypertension,	
	European origin	

Abbreviations: AAA = abdominal aortic aneurysm; COPD = chronic obstructive pulmonary disease.

Below is a list of included studies and their ancillary publications (indented below main results publication):

Key Questions 1 & 3

Chichester

Ashton HA, Gao L, Kim LG, et al. Fifteen-year follow-up of a randomized clinical trial of ultrasonographic screening for abdominal aortic aneurysms. The British journal of surgery. 2007;94(6):696-701. PMID: 17514666. <u>https://doi.org/10.1002/bjs.5780</u>.

Scott RA, Wilson NM, Ashton HA, et al. Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5-year results of a randomized controlled study. The British journal of surgery. 1995;82(8):1066-70. PMID: 7648155.

Scott RA, Bridgewater SG, Ashton HA. Randomized clinical trial of screening for abdominal aortic aneurysm in women. The British journal of surgery. 2002;89(3):283-5. PMID: 11872050. https://doi.org/10.1046/j.0007-1323.2001.02014.x.

Vardulaki KA, Walker NM, Couto E, et al. Late results concerning feasibility and compliance from a randomized trial of ultrasonographic screening for abdominal aortic aneurysm. The British journal of surgery. 2002;89(7):861-4. PMID: 12081734. <u>https://doi.org/10.1046/j.1365-2168.2002.02133.x</u>.

Multicentre Aneurysm Screening Study (MASS)

Thompson SG, Ashton HA, Gao L, et al. Final follow-up of the Multicentre Aneurysm Screening Study (MASS) randomized trial of abdominal aortic aneurysm screening. The British journal of surgery. 2012;99(12):1649-56. PMID: 23034729. <u>https://doi.org/10.1002/bjs.8897</u>.

Ashton HA, Buxton MJ, Day NE, et al. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. Lancet. 2002;360(9345):1531-9. PMID: 12443589.

Kim LG, Ra PS, Ashton HA, et al. A sustained mortality benefit from screening for abdominal aortic aneurysm. Annals of internal medicine. 2007;146(10):699-706. PMID: 17502630.

Kim LG, Scott RAP, Ashton HA, et al. A prolonged mortality benefit from screening for abdominal aortic aneurysm: seven-year follow-up of the MASS trial. SO: The Vascular Society of Great Britain & Ireland Yearbook 2006. 2006:77.

Thompson SG, Ashton HA, Gao L, et al. Screening men for abdominal aortic aneurysm: 10 year mortality and cost effectiveness results from the randomised Multicentre Aneurysm Screening Study. BMJ. 2009;338:b2307. PMID: 19553269.

Viborg

Lindholt JS, Sorensen J, Sogaard R, et al. Long-term benefit and cost-effectiveness analysis of screening for abdominal aortic aneurysms from a randomized controlled trial. The British journal of surgery. 2010;97(6):826-34. PMID: 20473995. <u>https://doi.org/10.1002/bjs.7001</u>.

Lindholt JS, Juul S, Fasting H, et al. Hospital costs and benefits of screening for abdominal aortic aneurysms. Results from a randomised population screening trial. Eur J Vasc Endovasc Surg. 2002;23(1):55-60. PMID: 11748949. https://doi.org/10.1053/ejvs.2001.1534.

Lindholt JS, Juul S, Fasting H, et al. Screening for abdominal aortic aneurysms: single centre randomised controlled trial. BMJ. 2005;330(7494):750. PMID: 15757960. 10.1136/bmj.38369.620162.82

Lindholt JS, Juul S, Henneberg EW. High-risk and low-risk screening for abdominal aortic aneurysm both reduce aneurysm-related mortality. A stratified analysis from a single-centre randomised screening trial. Eur J Vasc Endovasc Surg. 2007;34(1):53-8. PMID: 17331750. https://doi.org/10.1016/j.ejvs.2006.12.031.

Lindholt JS, Juul S, Fasting H, et al. Preliminary ten year results from a randomised single centre mass screening trial for abdominal aortic aneurysm. Eur J Vasc Endovasc Surg. 2006;32(6):608-14. PMID: 16893663. <u>https://doi.org/10.1016/j.ejvs.2006.06.008</u>.

Western Australia

McCaul KA, Lawrence-Brown M, Dickinson JA, et al. Long-term Outcomes of the Western Australian Trial of Screening for Abdominal Aortic Aneurysms: Secondary Analysis of a Randomized Clinical Trial. JAMA Intern Med. 2016;176(12):1761-7. PMID: 27802493. https://doi.org/10.1001/jamainternmed.2016.6633.

Jamrozik K, Norman PE, Spencer CA, et al. Screening for abdominal aortic aneurysm: lessons from a population-based study. Med J Aust. 2000;173(7):345-50. PMID: 11062788.

Norman PE, Jamrozik K, Lawrence-Brown MM, et al. Western Australian randomized controlled trial of screening for abdominal aortic aneurysm. The British journal of surgery. 2003;90(4):492.

Norman PE, Jamrozik K, Lawrence-Brown MM, et al. Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm. BMJ. 2004;329(7477):1259. PMID: 15545293. <u>https://doi.org/10.1136/bmj.38272.478438.55</u>.

Spencer CA, Norman PE, Jamrozik K, et al. Is screening for abdominal aortic aneurysm bad for your health and well-being? ANZ J Surg. 2004;74(12):1069-75. PMID: 15574151. https://doi.org/10.1111/j.1445-1433.2004.03270.x.

Key Question 2

d'Audiffret A, Santilli S, Tretinyak A, et al. Fate of the ectatic infrarenal aorta: expansion rates and outcomes. Annals of vascular surgery. 2002;16(5):534-6.

Devaraj S, Dodds SR. Ultrasound surveillance of ectatic abdominal aortas. Ann R Coll Surg Engl. 2008;90(6):477-82. PMID: 18765027. <u>https://doi.org/10.1308/003588408X301064</u>.

Lederle FA, Johnson GR, Wilson SE, et al. Yield of repeated screening for abdominal aortic aneurysm after a 4-year interval. Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators. Arch Intern Med. 2000;160(8):1117-21. PMID: 10789604.

Oliver-Williams C, Sweeting MJ, Turton G, et al. Lessons learned about prevalence and growth rates of abdominal aortic aneurysms from a 25-year ultrasound population screening programme. Br J Surg. 2018;105(1):68-74. PMID: 29265406. <u>https://doi.org/10.1002/bjs.10715</u>.

Crow P, Shaw E, Earnshaw JJ, et al. A single normal ultrasonographic scan at age 65 years rules out significant aneurysm disease for life in men. The British journal of surgery. 2001;88(7):941-4. PMID: 11442524. <u>https://doi.org/10.1046/j.0007-1323.2001.01822.x</u>.

Darwood R, Earnshaw JJ, Turton G, et al. Twenty-year review of abdominal aortic aneurysm screening in men in the county of Gloucestershire, United Kingdom. Journal of vascular surgery. 2012;56(1):8-13. PMID: 22503187. <u>https://doi.org/10.1016/j.jvs.2011.12.069</u>.

Emerton ME, Shaw E, Poskitt K, et al. Screening for abdominal aortic aneurysm: a single scan is enough. The British journal of surgery. 1994;81(8):1112-3. PMID: 7953333.

McCarthy RJ, Shaw E, Whyman MR, et al. Recommendations for screening intervals for small aortic aneurysms. The British journal of surgery. 2003;90(7):821-6. PMID: 12854107. https://doi.org/10.1002/bjs.4216.

Chichester

Scott RA, Vardulaki KA, Walker NM, et al. The long-term benefits of a single scan for abdominal aortic aneurysm (AAA) at age 65. Eur J Vasc Endovasc Surg. 2001;21(6):535-40. PMID: 11397028. https://doi.org/10.1053/ejvs.2001.1368.

Soderberg P, Wanhainen A, Svensjo S. Five Year Natural History of Screening Detected Sub-Aneurysms and Abdominal Aortic Aneurysms in 70 Year Old Women and Systematic Review of Repair Rate in Women. Eur J Vasc Endovasc Surg. 2017;53(6):802-9. PMID: 28389251. https://dx.doi.org/10.1016/j.ejvs.2017.02.024.

Svensjo S, Bjorck M, Wanhainen A. Editor's choice: five-year outcomes in men screened for abdominal aortic aneurysm at 65 years of age: a population-based cohort study. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2014;47(1):37-44. PMID: 24262320. <u>https://dx.doi.org/10.1016/j.ejvs.2013.10.007</u>.

Additional studies for Key Question 3 (only included for screening harms)

Lesjak M, Boreland F, Lyle D, et al. Screening for abdominal aortic aneurysm: does it affect men's quality of life? Aust J Prim Health. 2012. PMID: 22951209. <u>https://doi.org/10.1071/PY11131</u>.

Viborg Vascular (VIVA)

Lindholt JS, Sogaard R. Population screening and intervention for vascular disease in Danish men (VIVA): a randomised controlled trial. Lancet. 2017. PMID: 28859943. <u>https://dx.doi.org/10.1016/s0140-6736(17)32250-x</u>.

Grondal N, Sogaard R, Lindholt JS. Baseline prevalence of abdominal aortic aneurysm, peripheral arterial disease and hypertension in men aged 65-74 years from a population screening study (VIVA trial). Br J Surg. 2015;102(8):902-6. PMID: 25923784. <u>https://dx.doi.org/10.1002/bjs.9825</u>.

Lucarotti ME, Heather BP, Shaw E, et al. Psychological morbidity associated with abdominal aortic aneurysm screening. Eur J Vasc Endovasc Surg. 1997;14(6):499-501. PMID: 9467527.

Wanhainen A, Rosen C, Rutegard J, et al. Low quality of life prior to screening for abdominal aortic aneurysm: a possible risk factor for negative mental effects. Annals of vascular surgery. 2004;18(3):287-93. PMID: 15354629. <u>https://doi.org/10.1007/s10016-004-0021-x</u>.

Key Questions 4 & 5

<u>Open vs. Surveillance</u>

ADAM

Lederle FA, Wilson SE, Johnson GR, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. N Engl J Med. 2002;346(19):1437-44. PMID: 12000813. https://doi.org/10.1056/NEJMoa012573.

Lederle FA, Wilson SE, Johnson GR, et al. Design of the abdominal aortic Aneurysm Detection and Management Study. ADAM VA Cooperative Study Group. Journal of vascular surgery. 1994;20(2):296-303. PMID: 8040955.

Filardo G, Lederle FA, Ballard DJ, et al. Immediate open repair vs surveillance in patients with small abdominal aortic aneurysms: survival differences by aneurysm size. Mayo Clin Proc. 2013;88(9):910-9. PMID: 24001483. <u>https://dx.doi.org/10.1016/j.mayocp.2013.05.014</u>.

UKSAT

Powell JT, Brown LC, Forbes JF, et al. Final 12-year follow-up of surgery versus surveillance in the UK Small Aneurysm Trial. Br J Surg. 2007;94(6):702-8. PMID: 17514693. <u>https://doi.org/10.1002/bjs.5778</u>.

Brown LC, Powell JT. Risk factors for aneurysm rupture in patients kept under ultrasound surveillance. UK Small Aneurysm Trial Participants. Ann Surg. 1999;230(3):289-96; discussion 96-7. PMID: 10493476.

Brown LC, Thompson SG, Greenhalgh RM, et al. Fit patients with small abdominal aortic aneurysms (AAAs) do not benefit from early intervention. J Vasc Surg. 2008;48(6):1375-81. PMID: 19118733. https://doi.org/10.1016/j.jvs.2008.07.014

Fowkes FG, Greenhalgh RM, Powell JT, et al. Length of hospital stay following elective abdominal aortic aneurysm repair. U.K. Small Aneurysm Trial Participants. Eur J Vasc Endovasc Surg. 1998;16(3):185-91. PMID: 9787298.

Greenhalgh RM, Forbes JF, Fowkes FG, et al. The UK Small Aneurysm Trial: design, methods and progress. Eur J Vasc Endovasc Surg. 1995;9(1):42-8. PMID: 7664011.

Powell JT. Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. N Engl J Med. 2002;346(19):1445-52. PMID: 12000814. https://doi.org/10.1056/NEJMoa013527. Powell JT, Brady AR, Brown LC, et al. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. The UK Small Aneurysm Trial Participants. Lancet. 1998;352(9141):1649-55. PMID: 9853436.

Filardo G, Lederle FA, Ballard DJ, et al. Immediate open repair vs surveillance in patients with small abdominal aortic aneurysms: survival differences by aneurysm size. Mayo Clin Proc. 2013;88(9):910-9. PMID: 24001483. <u>https://dx.doi.org/10.1016/j.mayocp.2013.05.014</u>.

EVAR vs. Surveillance

CAESAR

Cao P, De RP, Verzini F, et al. Comparison of surveillance versus aortic endografting for small aneurysm repair (CAESAR): results from a randomised trial. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2011;41(1):13-25. PMID: 20869890. https://doi.org/10.1016/j.ejvs.2010.08.026

Cao P. Comparison of surveillance vs aortic endografting for small aneurysm repair (CAESAR) trial: study design and progress. Eur J Vasc Endovasc Surg. 2005;30(3):245-51. PMID: 16130206.

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Additional studies for Key Question 5 (only included for treatment harms)

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Reason for Exclusion*
E1. Study Aim
E2. Setting
E2a. Non-HDI country
E2b. Screening and/or intervention is not conducted in, recruited from, or feasible for primary care
E3. Population
E3a. Patients experience symptoms of AAA
E3b. Patients with AAAs with an aortic diameter larger than 5.4 cm or smaller than 3.0 cm
E3c. Patients with known or established CVD
E4. Outcome: No relevant outcomes
E5. Intervention
E5a. Screening with physical examination, CT, or MRI
E5b. Non-relevant treatment for small AAA
E6. Comparator: Not an included comparator (e.g., comparison of surveillance interval [KQ2], active
intervention [KQ4,5])
E7. Study design: Not an included study design, which includes: KQ1,4= Case-control, cross-sectional, and
cohort studies; editorials, letters, and opinions; cost studies; KQ2,3= Case-control and cross-sectional
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E8. Study Quality: Poor
E9. Publication type: Abstract-only, Non-English publication
*Assigned at full-text phase.

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	Author, Year	Study			Mean Length		
Comparison	Trial name	Quality	N Randomized	Country	of FU, y	Intervention	Control
Screening vs.	Ashton, 2007 ¹¹³	Fair	15,382	UK	15.0 (Men	Ultrasound screening; patients with an	Surveillance
no screening	(Men only) & Scott,				only)	aneurysm of 3.0-4.4 cm diameter were	
_	2002 ³⁶ (Women		Men: 6,040			rescanned annually and those with an	
	only)		Women: 9,342		10 (Women	aneurysm of 4.5–5.9 cm diameter were	
					only)	rescanned every 3 months. This was	
	Chichester					continued until February 1994 or until the	
						patient died, underwent surgical	
						intervention, or declined followup.	
	Thompson, 2012 ^{12,}	Good	67,770	UK	13.1	Ultrasound screening; patients with an	Surveillance
	170					aortic diameter of 3.0-4.4 cm were	
						rescanned yearly. Those with an aortic	
	MASS					diameter of 4.5–5.4 cm were rescanned at	
						3-month intervals. Urgent referral to a	
						vascular surgeon was recommended for	
						patients with aortic diameter ≥5.5 cm. QOL	
						was assessed in patients with screen-	
						detected AAA and those with normal scans	
						at 1.5, 3, and 12 months (n=1,956). ¹²	
	Lindholt, 2010 ¹⁴⁷	Good	12,639	Denmark	13	Ultrasound screening; participants with	Surveillance
						aneurysms ≥5 cm were referred to a	
	Viborg					vascular surgeon; those with AAAs 3-4.9	
						cm were offered annual scans to check for	
						expansion. After 5 years those with initial	
						ectatic aorta (diameter 2.5–2.9 cm) were	
						offered rescreening.	
	Lindholt, 2017 ¹⁴⁶	Fair	50,156	Denmark	4.4*	Ultrasound screening; patients with	Surveillance
						aneurysms ≥5 cm were referred to CT	
	VIVA		(Screening			scanning and assessment by a vascular	
			group			surgeon for repair. Participants were invited	
			n=25,078)			to one annual clinical followup, which	
						consisted of ultrasound screening. Person	
						identification numbers were used to search	
						the Danish Vascular Registry for vascular	
						procedures.	
						ABI screening; participants with possible	
						hypertension alone encouraged to consult	
			1			with general practitioner for confirmation of	

Appendix E Table 1. Methodological and Intervention Characteristics of Included One-Time Screening Studies (KQs 1 and 3)

	Author, Year	Study			Mean Length		
Comparison	Trial name	Quality	N Randomized	Country	of FU, y	Intervention	Control
						diagnosis, initiation of prophylactic activities, or both. Blood total cholesterol measurement if diagnosis of AAA or PAD was confirmed with repeated ultrasonography and ABI measurement. If total serum cholesterol concentration exceeded 4.0 mmol/L, participant prescribed statin therapy (40 mg/day simvastatin) and aspirin (75 mg/day). All positive findings and initiated medications communicated to general practitioner to ensure medication continuation and followup.	
	McCaul, 2016 ^{15, 168} Western Australia	Fair	38,480	Australia	12.8*	Ultrasound screening [†] ; QOL (SF-36, EuroQOL EQ-5D) was assessed 12 months after screening (n=365).	Surveillance
Screening harms	Lesjak, 2012 ¹⁴¹	Fair	NR [‡]	Australia	6 mo	At the time of time of screening, self- administered questionnaires were completed including the Medical Outcomes Short Form 36v.2 (MOSF36). Six months after screening, all participants who had an abnormal aortic diameter (≥2.6 cm) were followed up and completed MOSF36 questionnaires (n=53).	A random sample of men with normal scans were followed up 6 months after screening (n=130).
	Lucarotti, 1997 ¹⁵⁰	Fair	NR	UK	1 mo	Men invited to screening filled out the QOL questionnaire (General Health Questionnaire; linear analogue scale) prior to screening. One month after initial screening, the first 61 men with diagnosed AAA (definition NR) were asked to complete the QOL assessment again (n=61).	Men invited to screening filled out the QOL questionnaire (General Health Questionnaire; linear analogue scale) prior to screening. One month after initial screening, the first 100 men with normal scans were asked to complete the QOL assessment again (n=100).

	Author, Year	Study			Mean Length		
Comparison	Trial name	Quality	N Randomized	Country	of FU, y	Intervention	Control
	Wanhainen, 2004 ¹⁷⁴	Fair	NR	Sweden	1.0	Participants were given a QOL assessment questionnaire (SF-36) at baseline and then 12 months after screening. A cohort of participants with screen-detected AAA were followed (n=24).	Participants were given a QOL assessment questionnaire (SF-36) at baseline and 12 months after screening. A cohort of age-/sex-matched controls with normal AAA scans were followed (n=45).

*Median.

[†]After screening, participants were given a letter containing the results of their scan and a copy for their primary care physician. Any followup investigations or referral to a surgeon were arranged by the primary care physician. No attempt was made by investigators to influence clinical management with regards to threshold for intervention or method of repair.

⁺53 men completed the questionnaire (out of 516).

Abbreviations: AA = abdominal a ortic aneurysm; EQ-5D = EuroQOL-5D; MASS = Multicenter Aneurysm Screening Study; QOL = quality of life; SF-36 = Short-form 36-item Health Survey; NR = not reported.

	Author, Year		Mean Age	% Current	% Family	%	% CVD Risk
Comparison	Trial Name	Major Inclusion Criteria	% Female	Smoking	History	Diabetes	Factors
Screening vs. no screening	Ashton, 2007 ¹¹³ (Men only) & Scott, 2002 ³⁶ (Women only) Chichester	Patients ages 65–80 years	72.0* 59.2	NR	NR	NR	NR
	Thompson, 2012 ¹⁷⁰ MASS	Men ages 65–74 years	69.2 0	NR	NR	NR	NR
	Lindholt, 2010 ¹⁴⁷ Viborg	Men ages 64–73 years who lived in Viborg County	67.7 0	NR	NR	NR	NR
	Lindholt, 2017 ¹⁴⁶ VIVA	Men ages 65-74 years living in Central Denmark	69.0* 0	NR	NR	NR	History of, %: Stroke: 3.0 Ml: 2.7 Ischemic heart disease: 6.6 Peripheral occlusive arterial disease: 1.1
	McCaul, 2016 ¹⁵ Western Australia	Men ages 64–83 years living in Perth and surrounding towns	72.6 0	NR	NR	NR	NR
Screening harms	Lesjak, 2012 ¹⁴¹	Rural men ages 65-74 years who attended a community- based screening for AAA	NR 0	NR	NR	NR	NR
	Lucarotti, 1997 ¹⁵⁰	Men born between 1925 and 1928 living in Gloucestershire and participating in the AAA screening program	NR 0	NR	NR	NR	NR
	Wanhainen, 2004 ¹⁷⁴	Men and women ages $65-75$ years with screen-detected AAA (\geq 3.0 cm) along with a group of adults with a normal scan to act as controls	71.0 19.4	NR	NR	NR	NR

Appendix E Table 2. Patient Characteristics of Included One-Time Screening Studies (KQs 1 and 3)

*Median.

Abbreviations: AAA = abdominal aortic aneurysm; MASS = Multicenter Aneurysm Screening Study; NR = not reported.

Author, Year		Total AAA				
Trial Name	Total Scanned	(Prevalence), n (%)	≥5.5 cm, n (%)	5.0 to 5.9 cm, n (%)	4.5 to 5.4 cm, n (%)	3.0 to 4.4 cm, n (%)
Scott, 1995 ¹³	5,394 (men and women)*	218 (4.0)	19 (0.4) [†]	20 (0.4) [†]	NR	179 (3.3) ^{†,‡}
Chichester						
Thompson, 2012 ^{12,} 170	27,147 (men)	1,334 (4.9)	166 (0.6)	NR	223 (0.8)	944 (3.5)
MASS						
Lindholt, 2010 ^{14, 143,} 147	4,860 (men)	191 (3.9) [§]	24 (0.5)	NR	NR	NR
Viborg						
Lindholt, 2017 ¹⁴⁶	25,078 (men)	619 (3.3)	61 (0.3)	NR	NR	558 (3.0)
VIVA						
McCaul, 2016 ^{15, 155}	12,203 (men)	879 (7.2)	61 (0.5)	NR	115 (0.9) [¶]	699 (5.7) [¶]
Western Australia						

Appendix E Table 3. Percent of Screened Population With AAA of the Specified Size

* From 5-year followup (Scott, 1995).¹³

† Estimated.

[‡]AAA of 3.0 to 4.0 cm.

[§] N analyzed for prevalence: 4,816.

AAA of 3.0 to 4.9 cm.

¶ From 3.6-year followup (Norman, 2004).¹⁵⁵

Abbreviations: AAA = abdominal aortic aneurysm; MASS = Multicenter Aneurysm Screening Study; NR = not reported.

Study, Year					Mean length of	Measurement	Rescreening intervals; number
Quality	Trial	Ν	N Analyzed	Country	follow up (yrs)	technique	of times rescreened
D'Audiffret,	Patients from	223	223	US	5.9	Aortic measurements	Rescreening annually after aortic
2002121	the ADAM trial				Range: NR	were made in both the	diameters of 2.5–2.9 cm were
Fair						anteriorposterior and	identified
						transverse planes and the	
						greatest diameter was	5 repeat scans
Doverni 2009123	Dotionto from	000	250		5 4	Accessed	Pasarooning of obnormal cortag
Deveraj, 2000	the Good Hope	999	330	UK	Dango: 1 14 years	Assessed	(2.6, 2.0 cm) appually
					Range. 1-14 years	antenopostenor diameter	
	Scrooping						ND
	Brogram						NK
Oliver-Williams	Patients from the	80 150	1 222		7.8	Maximum anteroposterior	Men with small AAA (2.4–4.4 cm
2018 ¹⁵⁶	Gloucestershire	00,100	1,200	UIX	Range: 2 7–11	diameter assessed by	had annual ultrasound followup
Good	Aneurysm				vearst	measurement from the	
	Screening Study				youro	inner wall to the inner	6 (3–11) [‡] repeat scans
	Corooning Olday					wall of the aorta	
Lederle 2000 ¹³⁸	Patients from	15 098	2 622	US	4	Assessed infrarenal and	Rescreening in those found to
Good	the ADAM trial	,	_,=		Range: NR	suprarenal aortic	have no AAA 4 years after initial
						diameter	screening
							3
							1 repeat scan
Lindholt, 2000 ¹⁴⁸	Case/control	6,339	248 for 2.5-	Denmark	5	Infrarenal aorta was first	Those with aortas 2.5–2.9 cm
Fair	study of the		2.9 group		Range: 3–5 yrs	visualized	were offered rescreening 3 to 5
	Viborg Trial					anteroposteriorly in its	years after initial screen; control
			275 Control			entire length. Its	group were those with no AAA
			group			anteroposteriorly and	
						transversely diameters	
						were measured and	
						recorded at their maximal	
						sizes.	
Scott, 2001 ¹⁶⁵	Cohort of 65-	1,011	649	UK	10	Both anteroposterior and	Individuals with normal-sized
Fair	year-old men				Range: NR	transverse measurements	aortas at initial scan were
	found to have					of aortic diameter were	rescreened every 2 years.
	normal aorta					taken and the maximum of	(These patients were NOT
						the two measurements	Chichester trial participants.)
						was used as the defining	
						diameter.	5 repeat scans

Appendix E Table 4. Methodolog	ical and Intervention Characteristic	cs of Included Rescreenir	a Studies ((KQ 2)

Study, Year					Mean length of	Measurement	Rescreening intervals; number
Quality	Trial	Ν	N Analyzed	Country	follow up (yrs)	technique	of times rescreened
Soderberg, 2017 ¹⁶⁷ Fair	Population- based cohort of 70-year-old women	5,140	2.5–2.9 cm group: 33; 26 rescanned	Sweden	5 Range: NR	The maximum anteroposterior diameter was registered according to the leading edge to leading edge principle	All women with screen-detected subaneurysms with a diameter of 2.5–2.9 cm were rescanned at 5 years.
			group: 19			leading edge principle.	1 repeat scan
Svensjo, 2014 ¹⁶⁹ Fair	Population- based cohort of 65-year-old men	3,270	<2.5 cm group: 2,652 2.5–2.9 cm group: 40 ≥3.0 cm group: 44	Sweden	5 Range: 5 yrs	The maximum anteroposterior diameter of the infrarenal aorta was recorded using the leading edge to leading edge principle.	Individuals with an infrarenal aortic diameter of 2.5–2.9 cm were rescanned after 5 years. 1 repeat scan

*Median.

[†] Duration of followup was calculated for each man as the time from the initial scan to death, or to most recent scan if the individual had not died.

‡ Median (IQR) within.

Abbreviations: AAA = abdominal aortic aneurysm; ADAM = Abdominal Aortic Aneurysm Detection and Management Study; IQR = interquartile range; NR = not reported.

Author, Year Quality	Major Inclusion Criteria	Mean AAA Size	Mean Age % Female	% Current Smoking	% Family History	% Diabetes	% CVD Risk Factors
D'Audiffret, 2002 ¹²¹ Fair	Those with aortic diameters of 2.5–2.9 cm	2.7 cm	68.4 NR	81.6*	13.9	11.2	PAD: 12.5 HTN: 49.8 Hypercholesterolemia: 17.5
Deveraj, 2008 ¹²³ Fair	Men found to have ectatic aortas (2.6– 2.9 cm in diameter) at first scan with a minimum of 1-year followup	2.8 cm	NR 0	NR	NR	NR	NR
Oliver-Williams, 2018 ¹⁵⁶ Good	Men ages 65–66 years at the time of original study who had aortic diameters <2.6 cm	 1.7 cm (initial screening in years 2010–2015) 2.1 cm (initial screening in early 1990s) 	65.3 [†] 0	NR	NR	NR	NR
Lederle, 2000 ¹³⁸ Good	VA patients ages 50–79 years without AAA (aortic diameters of ≤3.0 cm) who were part of the ADAM trial	2.0 cm	66.0 2.4	14.6	6.0	17.6	HTN: 55.2 High cholesterol: 38.9 CAD: 36.6 Any atherosclerosis: 42.3
Lindholt, 2000 ¹⁴⁸ Fair	Men ages 65–73 years with either identified small AAA (2.5–2.9 cm) or those with a normal initial scan (along with 380 controls)	NR	65.6 0	NR	NR	NR	NR
Scott, 2001 ¹⁶⁵ Fair	Male patients with a normal aorta on their initial scan at age 65 years	NR	65 0	NR	NR	NR	NR

Appendix E Table 5. Baseline Characteristics of Included Rescreening Studies for Small AAA (KQ 2)

Author, Year	Major Inclusion		Mean Age	% Current	% Family		
Quality	Criteria	Mean AAA Size	% Female	Smoking	History	% Diabetes	% CVD Risk Factors
Soderberg, 2017 ¹⁶⁷	All 70-year-old	2.64 for 2.5-2.9	70	36	21 [‡]	NR	Coronary disease: 12
Foir	women identified	cm group	100				HTN: 39
Fair	through the National						Hyperlipidemia: 36
	Population Registry,						Claudication: 9
	in two neighboring						
	counties in Sweden.						
	Women diagnosed	3.52 cm for ≥3.0	70	63	5 [‡]	NR	Coronary disease: 16
	with subaneurysmal	cm group	100				HTN: 68
	aortas (2.5–2.9 cm)						Hyperlipidemia: 47
	were followed.						Claudication: 11
Svensjo, 2014 ¹⁶⁹	2006–2007	1.85	70	NR	NR	NR	NR
Fair	All men age 65		0				
1 dii	years identified in						
	the National						
	Population Registry						
	in Uppsala County.						
	Deserves d 0014						
	Rescanned 2011–						
	2012. Men with a						
	nistory of AAA repair						
	were excluded from						
	invitation.						

* Defined as smoking history.

† Median.

‡ Family history defined as first-degree relative.

Abbreviations: AAA = abdominal a ortic aneurysm; CAD = coronary artery disease; CVD = cardiovascular disease; HTN = hypertension; NR = not reported; PAD = peripheral artery disease; VA = Department of Veterans Affairs.

Comparison	Author, Year Trial Name	Study Quality	N Randomized	Country	Mean Length of FU, vears	Instrument	Group	Quality of Life Data
Screening vs. no screening	Ashton, 2007 ¹¹³ (Men only) & Scott, 2002 ³⁶ (Women only) Chichester	Fair	15,382 Men: 6,040 Women: 9,342	UK	15.0 (Men only) 10 (Women only)			
	Thompson, 2012 ^{12, 170} MASS	Good	67,770	UK	13.1	SF-36, HADS, EQ-5D	Surgery	3 months Physical Health, mean: 50.0 [‡] Mental Health, mean: 48.4 [∥] Depression, mean: 3.0 [‡] Anxiety, mean: 29.1 [‡] Weighted Health Index, mean: 0.85 [‡] 12 months Physical Health. mean: 51.1 [‡] Mental Health, mean: 50.6 [‡] Depression, mean: 3.1 [‡] Anxiety, mean: 28.6 [‡] Weighted Health Index, mean: 0.85 [‡] 2 months
	Lindholt 2010 ¹⁴⁷	Cood	12.620	Donmark	12		Surveinance	Physical Health, mean: 51.0 [‡] Mental Health, mean: 51.7 [↓] Depression, mean: 3.0 [‡] Anxiety, mean: 28.9 [‡] Weighted Health Index, mean: 0.83 [‡] 12 months Physical Health, mean: 49.8 [‡] Mental Health, mean: 50.1 [‡] Depression, mean: 3.2 [‡] Anxiety, mean: 29.6 [‡] Weighted Health Index, mean: 0.83 [‡]
	Lindholt, 2010 ¹⁴⁷	G000	12,639	Denmark	13			
	Viborg							

Appendix E Table 6. Quality of Life Results of Included One-Time Screening Studies (KQs 1 and 3)

	Author, Year	Study			Mean Length			
Comparison	Trial Name	Quality	N Randomized	Country	of FU, years	Instrument	Group	Quality of Life Data
	Lindholt, 2017 ¹⁴⁶	Fair	50,156	Denmark	4.4*			
	VIVA		n=25,078)					
	McCaul, 2016 ^{15, 168} Western Australia	Fair	38,480	Australia	12.8*	MOS SF-36; HADS, EQ-5D	AAA Group	12 months Physical Functioning, mean (SD): 62.9 (27.4) [∥] Mental Health, mean (SD): 81.3 (15.9) Anxiety/Depression, mean (SD): 3.6 (3.0) Health States Score, mean (SD): 0.83 (0.18)
							CG	12 months Physical Functioning, mean (SD): 68.9 (25.8) [∥] Mental Health, mean (SD): 78.3 (17.7) Anxiety/Depression, mean (SD): 3.6 (3.2) Health States Score, mean (SD): 0.80 (0.21)
Screening harms	Lesjak, 2012 ¹⁴¹	Fair	NR [‡]	Australia	6 month	MOS SF-36, HADS	AAA Group	Physical FunctioningPrescreening score, mean (SD):40.4 (10.7)Postscreening score, mean (SD):41.1 (11.7)Mental HealthPrescreening score, mean (SD):49.6 (11.1)Postscreening score, mean (SD):49.8 (11.9)DepressionPrescreening score, mean (SD):5.1 (4.1)Postscreening score, mean (SD):5.5 (4.6)

	Author, Year	Study			Mean Length			
Comparison	Trial Name	Quality	N Randomized	Country	of FU, years	Instrument	Group	Quality of Life Data
							CG	AnxietyPrescreening score, mean (SD):5.1 (3.9)Postscreening score, mean (SD):5.9 (4.9)Physical FunctioningPrescreening score, mean (SD):41.3 (11.7)Postscreening score, mean (SD):44.3 (10.2)Mental HealthPrescreening score, mean (SD):51.6 (10.5)Postscreening score, mean (SD):51.8 (10.7)DepressionPrescreening score, mean (SD):4.2 (3.3)Postscreening score, mean (SD):4.1 (3.6)AnxietyPrescreening score, mean (SD):5.3 (3.8)Postscreening score, mean (SD):5.3 (3.8)Postscreening score, mean (SD):
	Lucarotti, 1997 ¹⁵⁰	Fair	NR	UK	1 month	GHQ	AAA Group	4.8 (3.7) Prescreening score, mean (SD): 15.71 (9.13)‡ Postscreening score, mean (SD): 14.25 (7.68)≢
							CG	Prescreening score, mean (SD): 15.51 (9.17)‡ Postscreening score, mean (SD): 14.36 (7.28)‡
	Wanhainen, 2004 ¹⁷⁴	Fair	NR	Sweden	1.0	SF-36	AAA Group	Physical Health Cluster Mean score before screening: 43 [‡] Mean score after screening: 43 [‡]

	Author, Year	Study			Mean Length			
Comparison	Trial Name	Quality	N Randomized	Country	of FU, years	Instrument	Group	Quality of Life Data
								Mental Health Cluster
								Mean score before screening: 52
								Mean score after screening: 49
							CG	Physical Health Cluster
								Mean score before screening: 46 [‡]
								Mean score after screening: 44 [‡]
								Mental Health Cluster
								Mean score before screening: 51 [‡]
								Moon score offer screening: 52 [‡]
								wear score alter screening. 52

* Median.

 $^{\dagger}\,53$ men completed the questionnaire (out of 516).

 \ddagger Between group: p = NS.

§ Within group: p = NS.

∥p<0.05.

Abbreviations: AAA = abdominal a ortic aneurysm; CG = Control group; EQ-5D = European Quality of Life; GHQ = General Health Questionnaire; HADS = Hospital Anxiety & Depression Scale; MASS = Multicenter Aneurysm Screening Study; MOS SF-36 = Medical Outcomes Short Form-36; NR = not reported; SD = standard deviation; SF-36 = Short Form-36; UK = United Kingdom.

Appendix E. Evidence Tables

			N		Mean followup,		
Intervention	Study, Year	Quality	randomized	Country	years	Intervention	Control
Open surgery vs. surveillance	Lederle, 2002 ¹⁴⁰ ADAM	Good	1,136	United States	4.9	Elective open surgery within 6 weeks of AAA identification	Surveillance until AAA reached 5.5 cm, enlarged by at least 0.7 cm in 6 months/1.0 cm in 1 year, or symptoms developed
	Powell, 2007 ¹⁶¹⁻¹⁶³ UKSAT	Good	1,090	United Kingdom	12	Elective open surgery within 3 months of AAA identification	Surveillance until AAA reached 5.5 cm, rapidly increased in diameter (>1 cm/year) or developed symptoms
EVAR vs. surveillance	Cao, 2011 ¹¹⁸ CAESAR	Fair	360	20 European/Western Asian hospitals	2.6‡	Patients received surgery via EVAR as soon as possible	Surveillance until AAA reached 5.5 cm in diameter, a rapid increase of >1 cm/year was found, or the aneurysm became symptomatic
	Ouriel, 2010 ¹⁵⁸ PIVOTAL	Fair	728	United States	1.7	Patients underwent EVAR ≤30 days of randomization	Surveillance until AAA reached 5.5 cm or enlarged ≥0.5 cm between any two 6- month assessments
Pharmacotherapy vs. placebo	Bicknell, 2016 ¹¹⁴ AARDVARK	Good	227	United Kingdom	2	10 mg perindopril (IG1) or 5 mg amlodipine (IG2) daily for 2 years	Placebo
	Hogh 2009 ¹³²	Good	92	Denmark	5	300 mg oral roxithromycin once daily for 28 days	Placebo
	Karlsson, 2009 ¹³³	Fair	247	Sweden	1.5	600 mg azithromycin once daily for 3 days, followed by 600 mg once a week for 15 weeks	Placebo
	Lindholt, 1999 ¹⁴²	Fair	54	Denmark	2	40 mg propranolol twice a day for 2 years	Placebo
	Meijer, 2013 ¹⁵²	Fair	286	The Netherlands	1.5	100 mg doxycycline daily for 18 months	Placebo

Appendix E Table 7. Methodological and Intervention Characteristics of Included Treatment Studies (KQs 4 and	on Characteristics of Included Treatment Studies (KQs 4 and 5)
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			N		Mean followup,		
Intervention	Study, Year	Quality	randomized	Country	years	Intervention	Control
	Mosorin, 2001 ¹⁵³	Fair	32	Finland	1.5	150 mg doxycycline	Placebo
						daily for 3 months	
	PAT Investigators,	Good	552	Canada	2.5	20 mg propranolol twice a	Placebo
	2002 ¹⁶⁴					day; increased to 40 mg	
						after 1 week, 80 mg after	
	PAT					2 weeks, and 120 mg at 4	
						weeks. Target dose was	
						80–120 mg twice a day.	
						Patients observed for	
				-		mean of 2.5 years	
	Sillensen, 2015 ¹⁶⁶	Fair	168	Multisite	1	40 mg pemirolast twice	Placebo
						a day [#] for 52 weeks	
	AORTA						

* No AAA-related death was found in both groups.

† This study also reported 5-year followup data on growth rate.

‡ Median.

§ Due to a large loss to followup, efficacy data were not usable. However, these losses were due to adverse events so the harms data are included.

This study is included for KQ5 (harms) only.

[¶]15 sites participated from Sweden, Denmark, and the United Kingdom.

[#]Study also reports 10 mg twice a day and 25 mg twice a day.

Abbreviations: AAA = abdominal aortic aneurysm; ADAM = Abdominal Aortic Aneurysm Detection and Management Study; AORTA: the Anti-inflammatory Oral Treatment of AAA; CAESAR = Comparison of Surveillance vs. Aortic Endografting for Small Aneurysm Repair; N = sample size; NA = not applicable; EUROSTAR = European Collaborators on Stent-Graft Techniques for aAbdominal Aortic Aneurysm Repair; PAT = Propanolol Aneurysm Trial; PIVOTAL = Positive Impact of Endovascular Options for Treating Aneurysms Early; UKSAT = UK Small Aneurysm Trial.

			Mean Age	AAA Diameter	% Current	% Family	
Intervention	Study, Year	Major Inclusion Criteria	% Female	at Baseline, cm	Smoking	History	% CVD Risk Factors
Open surgery vs. surveillance	Lederle, 2002 ¹⁴⁰ ADAM	Patients ages 50–79 years with AAA 4.0– 5.4 cm identified via CT within the previous 12 weeks	68.1 0.8	4.7	39.2	12.9	Coronary disease: 41.9 Cerebrovascular disease: 12.4 Hypertension: 56.4
	Powell, 2007 ¹⁶¹⁻¹⁶³ UKSAT	Patients ages 60–76 years with asymptomatic, small AAA (4.0–5.5 cm)	69.3 17.5	4.6	37.1	NR	Hypertension: 39 Probable ischemic heart disease: 14
EVAR vs. surveillance	Cao, 2011 ¹¹⁸ CAESAR	Patients ages 50–79 years; nonsymptomatic AAA 4.1–5.4 cm in diameter measured by CT within the previous 3 months	68.9 4.2	4.7	55.3	NR	Coronary disease: 39.2 Hypertension: 75.3
	Ouriel, 2010 ¹⁵⁸ PIVOTAL	Patients ages 40–90 years with AAA between 4.0 and 5.0 cm found by CT performed ≤3 months prior; eligible for EVAR	70.5 13.4	4.4	91.0	23.5	MI: 31.3 CHF: 6.2 CAD: 55.4 PVD: 28.2 Hypertension: 77.8
Pharmacotherapy vs. surveillance	Hogh 2009 ¹³²	AAA ≥3.0 cm detected by ultrasound the day of study entry; exclusively men	72.5 0	3.8	59.5	NR	NR
	Karlsson, 2009 ¹³³	Patents aged ≤80 years with AAA 3.5–4.9 cm	71 [†] 18.5	NR	40	14	MI: 31.0 Stroke: 14.1 Hypertension: 62.5
	Lindholt, 1999 ¹⁴²	Men with AAA 3.0–4.9 cm	69.2 0	3.4	NR	NR	NR
	Meijer, 2013 ¹⁵²	Aneurysm diameter 3.5– 5.0 cm, or a larger aneurysm unfit for repair, or declined repair	70.0 18.2	4.3	35.0	25.2	History of CVD: 52.1
	Mosorin, 2001 ¹⁵³	Aneurysm diameter perpendicular to the aortic axis of ≥3.0 cm in size or a ratio of	68.4 9.4	3.3	35.4	NR	Hypertension: 40.2

Appendix E Table 8. Patient	Characteristics of Included	Treatment Studies	(KQs 4 and 5)
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			Mean Age	AAA Diameter	% Current	% Family	
Intervention	Study, Year	Major Inclusion Criteria	% Female	at Baseline, cm	Smoking	History	% CVD Risk Factors
		infrarenal to suprarenal aortic diameter of ≥1.2 and a diameter <5.5 cm; followup of at least 6 months with two or more ultrasound examinations					
	PAT Investigators, 2002 ¹⁶⁴ PAT	Asymptomatic small AAA (3.0–5.0 cm; some centers only, 3.0–4.5 cm) measured by ultrasound; no contraindications to study drug	68.9 16	3.8	34.7	NR	Angina: 14.8 Heart failure: 2.0 Claudication: 19.2 Hyperlipidemia: 33.6 Hypertension: 35.8 Ml: 16.9 Stroke: 6.3
	Bicknell, 2016 ¹¹⁴ AARDVARK	Men or women age ≥55 years, with AAA 3.0–5.4 cm, and an SBP <150 mm Hg	71.3 5.8	4.0	25.0	NR	Hypertension: 0
	Sillensen, 2015 ¹⁶⁶ AORTA	Patients age ≥50 years with AAA 3.9–4.9 cm	70.9 8.9	4.4	41.1	NR	History of cardiac disorders: IG: 38.0 CG: 42.0

*Defined as angina, MI, arrhythmia, or heart failure.

†Median.

‡Mean.

Abbreviations: AAA = abdominal aortic aneurysm; ADAM = Abdominal Aortic Aneurysm Detection and Management Study; AORTA: the Anti-inflammatory Oral Treatment of AAA; CAD = coronary artery disease; CAESAR = Comparison of Surveillance Versus Aortic Endografting for Small Aneurysm Repair; CHF = congestive heart failure; CT = computed tomography; CVD = cardiovascular disease; EUROSTAR = European Collaborators on Stent-Graft Techniques for Abdominal Aortic Aneurysm Repair; EVAR = endovascular aneurysm repair; MI = myocardial infarction; NR = not reported; PAT = Propranolol Aneurysm Trial; PIVOTAL = Positive Impact of Endovascular Options for Treating Aneurysms Early; PVD = peripheral vascular disease; UKSAT = UK Small Aneurysm Trial.

Appendix E. Evidence Tables

Author Yoor				Mean	Surgical	Population Characteristics in	N (%) of	Definition
Quality	Registry	Country	Recruitment	years	Included	AAA	Small AAA	AAA
Budtz-Lilly, 2017 ¹¹⁶ Fair	Vascunet	International*	Data on primary intact AAA repairs were collected from vascular registries for the time period of 2005–2013. Data on small AAA <5.5 cm available for <u>2010–</u> <u>2013</u> time period. It was estimated that coverage of participating registries was >90% for the majority, 80% in Norway, and 62% in Australia.	NR	EVAR, open	Mean age (range): NR % Female: NR % Smokers: NR	12,610 (25.6)	<5.5 cm
Golledge, 2007 ¹²⁹ Fair	ASERNIP-S	Australia	Surgeries performed from <u>November 1999</u> to <u>May 2001</u> were recorded in the registry. Participation by vascular surgeons was initially enforced. An audit cross checking Health Insurance Commission data found >90% of procedures were included.	3.2 (Median)	EVAR	Mean age (range): 75 (NR) % Female: 15.9 % Current smokers: 11.0	478 (49.7)	≤5.5 cm

Appendix E Table 9. Methodological Characteristics of Included Registry	/ Studies ((KQ5)
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Appendix E. Evidence Tables

				Mean	Surgical	Population Characteristics in		Definition
Author, Year				Followup,	Technique(s)	Patients With Small	N (%) of	of Small
Quality	Registry	Country	Recruitment	years	Included	AAA	Small AAA	AAA
Lo, 2013 ¹⁴⁹	VSGNE	US	Voluntary	1.0	EVAR, open	Mean age (range): 71	1,336 (37.1)	<5.5 cm
Foir			collaboration among			(NR)		
Fall			vascular surgeons,			% Female: 26.2		
			cardiologists, and			% Smokers (past or		
			radiologists from 30			current): 88.5		
			community hospitals in					
			New England The					
			data are validated					
			periodically to ensure					
			that all procedures are					
			included in the					
			registry. This					
			publication analyzed					
			<u>2003–2011</u> data.					
Overbey,	ACS NSQIP	US	A nationally	NR	EVAR, open	Mean age (range):	5,126 (51.1)	Smallest
2017139			validated, risk-			72.3 (NR)		quartile:
Fair			adjusted dataset			% Female: 21.9		3.5–5 cm
1 dii			comprising major			% Current smokers:		Second
			surgical procedures			33.0		quartile:
			outcomes. Data are					5.01–5.5 cm
			collected from					CIII
			medical charts by a					
			trained Surgical					
			Clinical Reviewer.					
			This article is					
			analysis of 2011–					
			2015 data.					

Author, Year Quality	Registry	Country	Recruitment	Mean Followup, years	Surgical Technique(s) Included	Population Characteristics in Patients With Small AAA	N (%) of Small AAA	Definition of Small AAA
Peppelenbosch,	EUROSTAR	International [†]	110 European	1.7	EVAR	Mean age (range):	1,962 (44.7)	4.0–5.4
2004 ¹⁶⁰			institutions participate			69.7 (43–94)		cm
			in the registry. Patient			% Female: 7.0		
Fair			data are recorded on			% Smokers: NR		
			case record forms and					
			submitted. Only					
			elective treatments are					
			tracked. This article is					
			an analysis of <u>1997–</u>					
			2002 data.					

* Eleven countries: Australia, Denmark, Hungary, Iceland, New Zealand, Norway, Sweden, Switzerland, United Kingdom, Finland (Helsinki region only), and Germany. [†]Austria, Belgium, Denmark, United Kingdom, France, Germany, Greece, Israel, Italy, Luxembourg, Monaco, the Netherlands, Norway, Poland, Spain, Sweden, and Switzerland.

Abbreviations: AAA = abdominal aortic aneurysm; CAD = coronary artery disease; CT = computed tomography; CVD = cardiovascular disease; EUROSTAR = European Collaborators on Stent-Graft Techniques for Abdominal Aortic Aneurysm Repair; EVAR = endovascular aneurysm repair; MI = myocardial infarction; NR = not reported; PAT = Propranolol Aneurysm Trial; PIVOTAL = Positive Impact of Endovascular Options for Treating Aneurysms Early; PVD = peripheral vascular disease; US = United States.

Appendix E. Evidence Tables

		QOL		Treatment	N		Mean Difference (95%
Intervention	Study	Screening	Time Period	Group	Analyzed	QOL Scores, Mean (SD)¶	CI), P-Value
Open surgery vs.	Forbes 1998 ¹²⁷	MOS	Baseline	IG	480	Physical function: 64.2 (30.7)	Physical function: -2.3
Surveillance	LIKSAT	subscale		<u> </u>	510	$\frac{1}{2}$	Mental health: 0.7 (-1.5
	0110/11			00	512	Mental health: $79.5(17.0)$	to 2.8): NR
			12 months	IG	429	Physical function: 62 1 (29 9)	Physical function: 1.7
			nost-		120	Mental health: 81 7 (17 9)	(-2.3 to 5.7)
			randomization			Mean difference from BL:	Mental health: 2.1 (-0.4
			Tandomization			Physical function: -3.5 (-6.1 to -0.8)	to 4 5)
						Mental health: 0 (-1.5 to 1.5)	
				CG	436	Physical function: 60.3 (30.2)	
						Mental health: 79.6 (18.6)	
						Mean difference from BL:	
						Physical function: -6.2 (-8.8 to -3.7)	
						Mental health: 0 (1.7 to 1.8)	
EVAR vs.	De Rango	SF-36*	Baseline	IG	173	Mean difference (95% CI) from BL:	IG vs. CG
surveillance	2011 ¹²²		through 6			Overall QOL: 4.6 (2.3 to 7)	Overall QOL: 5.4 (2.1 to
			months post-			Physical functioning: -0.6 (-3.7 to 2.4)	8.8); p=0.002
			randomization			Mental health: 5.2 (2.8 to 7.5)	Physical function: 3.8
	CAESAR			CG	166	Mean difference (95% CI) from BL:	$(0.5 \ 10 \ 7.2), \mu = 0.02$
						Overall QOL: -0.8 (-3.2 to 1.6)	to 0.2 ; $n=0.0005$
							to 9.3), p=0.0005
						Mental health: -0.8 (-3.2 to 1.5)	
			Baseline	IG	173	Mean difference (95% CI) from BI :	IG VS CG
			through end of	10		Overall QOL: $4.6(2.3 \text{ to } 7)$	Overall QOL: 2.4 (-1.7
			followup§			Physical functioning: -0.6 (-3.7 to 2.4)	to 6.6); p=0.25
			lonotrup			Mental health: 5.2 (2.8 to 7.5)	Physical function: 1.5
				CG	166	Mean difference (95% CI) from BL:	(-2.6 to 5.5); p=0.48
						Overall QOL: -6.3 (-9.3 to -3.4) [∥]	Mental health: 2.0 (-2.4
						Physical functioning: -8.2 (-12.0 to	to 6.4); p=0.38
						-4.4)	
						Mental health: 4.8 (-7.9 to -1.7)	
	Eisenstein,	EQ-5D [#]	Baseline	IG	351	Utility score: 0.805 (0.1)**	NR
	2013124				0.50	Visual analog scale: 77.8 (14)	
				CG	350	Utility score: 0.783 (0.2)	
	FIVUTAL		24 months		205	Visual analog scale. $76.2 (15)$	
			24 MUNUS	0	205	Visual analog scale: 76.2 (17)	
			host-naselline	CG	197	$Utility score: 0.817 (0.2)^{**}$	
						Visual analog scale: 76.5 (18)	

Appendix E Table 10. Quality of Life Results in Studies of Treatment for Small AAA (KQs 4 and 5)

		QOL		Treatment	Ν		Mean Difference (95%
Intervention	Study	Screening	Time Period	Group	Analyzed	QOL Scores, Mean (SD)¶	CI), P-Value
Pharmacotherapy	Lindholt 1999 ¹⁴²	ScreenQL*†	Baseline	IG	30	NR	Overall QOL: -5.83 (6.2) [‡] ;
vs. surveillance			through 2 y				p=0.05
							Emotional domain: -0.35
							(2.1) [‡] ; p=0.59
							Health perception: -1.39
							(2.98) [‡] ; p=0.13
				CG	24	NR	Overall QOL: -1.70 (5.5) [‡] ;
							p=0.07
							Emotional domain: 0.00
							(2.0) [‡] ; p=0.69
							Health perception: -0.38
							(2.10) [‡] ; p=0.30
	PAT Investigators,	SF-36*	Baseline	IG	276	Physical function: 70.8 (23.9)	Physical function: p=0.11
	2002 ¹⁶⁴					Mental health: 78.9 (17.3)	Mental health: p=0.45
				CG	272	Physical function: 74.1 (24.0)	
	PAT					Mental health: 77.8 (17.9)	
			1 month post-	IG	276	Physical function: 68.9 (18.9)	Physical function:
			randomization			Mental health: 78.9 (17.6)	p=0.006
				CG	272	Physical function: 74.4 (23.8) Mental health: 78.3 (17.5)	Mental health: p=0.58

*Lower score denotes poorer status.

†A validated generic and global QOL questionnaire with 24 items evaluating six categories: general QOL, emotional health, physical health, psychosomatic distress, social and family functions, and marriage.

‡Mean (SD); change from baseline in each group, not IG vs. CG.

§Mean, 3 years from baseline (SD, 1.2 years).

p<0.01.

⁹Only summary scores reported here. For complete subscales please see full text.

Utility score uses responses to the five dimensions (Mobility, Self-care, Usual activity, Pain/discomfort, Anxious/depressed) to compute a value on a scale of -0.54 to 1.00; higher utility score indicates a better quality of life and a negative value indicates a health state worse than death that can be used to quality-adjust study patient survival time. The final EQ-5D element, visual analog score (VAS), provides a one-question assessment of an individual's quality of life and ranges from 0 to 100, with a higher score indicating a better quality of life.

**Utility score N analyzed by group and followup: Baseline IG n = 348, CG n = 349; 24-month postbaseline IG n = 203, CG n = 191.

Abbreviations: BL = baseline; CAESAR = Comparison of Surveillance Versus Aortic Endografting for Small Aneurysm Repair; <math>CG = control group; EVAR = endovascular aneurysm repair; IG = intervention group; MOS = Medical Outcomes Study; NR = not reported; PAT = Propanolol Aneurysm Trial; QOL = quality of life; SF-36 = Short-Form 36-Item Health Survey; UKSAT = UK Small Aneurysm Trial.

Author, Year Trial Name Quality	Mean Followup, years	Age Description	Group	N Analyzed	All- Cause Mortality, n (%)*	HR (95% CI)	AAA- Related Mortality, n (%)*	HR (95% CI)	30-Day Mortality, n (%)*	30-Day Mortality for Elective Repairs, n (%)*	30-Day Mortality For Emergency Repairs, n (%)*
Lindholt,	13	≤65 years	IG	2,742	NR	NA	6 (0.2)	0.36 (0.14–	NR	NR	NR
2010147			CG	2,687	NR		16 (0.6)	0.93)	NR	NR	NR
. <i>a</i> i		66–73 years	IG	3,591	NR	NA	13 (0.4)	0.33 (0.18–	NR	NR	NR
Viborg			CG	3,619	NR		39 (1.1)	0.62)	NR	NR	NR
		64–73 years	IG	-	-	-	19 (0.3)	0.34 (0.20-	-	-	-
Good		Main trial results (see Table 2)	CG	-	-	-	55 (0.9)	0.57)	-	-	-
McCaul, 2016 ¹⁵	12.8	65–74 years	IG	13,266	5,456 (41.1)	NR [†]	48 (0.4)	0.92 (0.62– 1.36) [†]	14 (3.7) [‡]	6 (1.6)§	8 (57.1)
Western			CG	13,239	5,501 (41.6)		52 (0.4)		21 (6.9) [‡]	11 (4.0) [§]	10 (37.0)
Australia		64-83 years Main trial	IG	19,249	9,739 (50.6)	NR†	90 (0.46)	0.91 (0.68– 1.21) [†]	34 (6.0)#	18 (3.4)**	16 (61.5)††
Fair		results (see Table 2)	CG	19,231	9, <mark>832</mark> (51.1)		98 (0.51)		36 (7.9)#	17 (4.1)**	19 (43.2)††

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* P value for interaction NR.

[†]Rate ratio (95% CI). Rate ratios reported as AAA-related and non-AAA deaths, not available for all-cause mortality.

‡ N analyzed, IG: 382, CG: 303.

§ N analyzed for IG: 368, CG: 276.

N analyzed for IG: 14, CG: 27.

N analyzed for IG: 562, CG: 458.

** N Analyzed for IG: 536, CG: 414.

^{††} N Analyzed for IG: 26, CG: 44.

Abbreviations: AAA = abdominal a ortic aneurysm; CG = control group; CI = confidence intervals; HR = hazard ratio; IG = intervention group; N = population size; n = sample size; NA = not applicable; NR = not reported.

Author, Year Trial Name Quality	Age	Outcome	Never Smoked, n (%)	Ever Smoked, n (%)	OR (95% CI)	P-Value for Interaction
McCaul, 2016 ¹⁵	64–83 years	AAA Mortality	4 (0.11)	28 (0.3)	2.95 (1.04-8.43)	NR
	(screened)	All-cause	1,310 (36.2)	4,072 (47.4)	1.59 (1.47–1.72)	
Western Australia		Mortality				
	65–74 years	AAA Mortality	1 (0.04)	15 (0.2)	6.31 (0.83–47.81)	
Fair	(screened)	All-cause	707 (26.7)	2,502 (39.7)	1.81 (1.63–2.00)	
		Mortality				

* These outcomes reflect rates in the screened group; there was no outcome reporting by smoking status in the unscreened group for comparison. This subgroup analysis does not address whether screening has a differential benefit in smokers.

Abbreviations: AAA = abdominal a ortic aneurysm; CG = control group; CI = confidence intervals; IG = intervention group; N = population size; n = sample size; NA = not applicable; NR = not reported; OR = odds ratio.

Author, Year Trial Name	Mean Followup			N	AAA Prevalence.	AAA Rupture.	HR (95% CI) for AAA	All AAA Procedures	Elective Surgery	Emergency Surgery, n	P-Value for	HR (95% CI) for Emergency
Quality	years	Description	Group	Analyzed	n (%)	n (%)	Rupture	n (%)	n (%)	(%)	Interaction	Surgery
McCaul, 2016 ¹⁵	12.8	Age 65– 74 years	IG	13,266	785.6 (6.6)	NR	NR	382 (2.9)	368 (2.77)	14 (0.11)*	NR	NR
Western Australia			CG	13,239	NR	NR		303 (2.3)	276 (2.08)	27 (0.20)*		
Fair												
		Age 64– 83 years Main trial	IG	19,249	879 (7.2)†	72‡	NR	562 (2.9)	536 (2.78) [§]	26 (0.14)*	NR	NR
		(see Table 1)	CG	19,231	NR	99		458 (2.4)	414 (2.15)	44 (0.23)*	NR	

Appendix F Table 3. AAA Prevalence, Rupture, and Surgery Data for Age Subpopulations in One-Time Screening Trials (KQ3a)

* Total surgery for rupture.

† N analyzed for prevalence: 12,203.

‡ p=0.04.

§ p<0.001.

Abbreviations: AAA = abdominal a ortic aneurysm; CG = control group; CI = confidence intervals; HR = hazard ratio; IG = intervention group; N = population size; n = sample size; NA = not applicable; NR = not reported.

Appendix F. Subpopulation Evidence Tables

Author, Year Trial name Quality	Age	Outcome	Never Smoked, n (%)	Ever Smoked, n (%)	OR (95% CI)	P-Value for Interaction
McCaul, 2016 ¹⁵	64–83 years	AAA Diameter ≥3.0 cm	117 (3.24)	758 (8.83)	2.90 (2.37 to 3.53)	NR
2010		AAA Elective operations	2 (0.06)	16 (0.19)	3.37 (0.78 to 14.68)	
Western	65–74 years	AAA Diameter ≥3.0 cm	55 (2.08)	496 (7.87)	4.03 (3.04 to 5.34)	
Australia		AAA Elective operations	26 (0.98)	253 (4.01)	4.22 (2.81 to 6.33)	
Fair		AAA Ruptures	1 (0.04)	11 (0.17)	4.63 (0.60 to 35.85)	

Appendix F Table 4, AAA diameter, re	upture, and surgery data for smoking	subpopulations in one-time screening	g trials (KQ3a)

Abbreviations: AAA = abdominal a ortic aneurysm; CG = control group; CI = confidence intervals; IG = intervention group; N = population size; n = sample size; NA = not applicable; NR = not reported; OR = odds ratio.

Study, Year Quality	Mean Followup, years	Description	Treatment Group	N Subgroup	All-Cause Mortality, n (%)	HR (95% CI)	P-Value for Interaction	AAA- Related Mortality, n (%)	HR (95% CI)
Lederle,	4.9	50–59 years	IG	47	8 (17.0)	1.02 (0.38–2.73)*	NR	NR	NR
2002140			CG	51	8 (15.7)			NR	
		60–69 years	IG	251	61 (24.3)	1.34 (0.93–1.93)*		-	-
ADAM			CG	279	55 (19.7)			NR	NR
		70–79 years	IG	271	74 (27.3)	1.10 (0.78–1.55)*		NR	NR
Good			CG	237	59 (24.9)			NR	NR
Powell,	12	60–66 years	IG	176	89 (50.6)	0.73 (0.55–0.99)	0.152	NR	NA
2007 ¹⁶¹⁻		-	CG	171	102 (59.6)			NR	
163		67–71 years	IG	191	120 (62.8)	0.86 (0.66–1.11)		NR	NA
		-	CG	190	125 (65.8)			NR	
UKSAT		72–76 years	IG	196	153 (78.1)	1.08 (0.79–1.38)†		NR	NA
Good			CG	166	125 (75.3)			NR	

Appendix F Table 5. All-Cause and AAA Mortality Data for Age Subpopulations in Open vs. Surveillance Trials (KQ4a)

* Relative risk.

[†] Primary adjustments made for age, sex, initial AAA diameter, smoking status, mean of left and right ankle-brachial pressure indexes, forced expiratory volume in 1 sec, and aspirin use.

Abbreviations: AAA = abdominal a ortic aneurysm; ADAM = Abdominal a ortic aneurysm Detection and Management study; CG = control group; CI = confidence interval; HR = hazard ratio; IG = intervention group; N = population size; n = sample size; NR = not reported; RR = relative risk; UKSAT = the UK Small Aneurysm Trial.

Appendix F. Subpopulation Evidence Tables

Study, Year Quality	Mean Followup, years	Description	Treatment Group	N Subgroup	All-Cause Mortality, n (%)	HR (95% CI)	P-Value for Interaction	AAA- Related Mortality, n (%)	HR (95% CI)
Powell,	12	Men	IG	468	299 (63.8)	0.90 (0.76-1.06)*	0.756	NR	NR
2007 ¹⁶¹⁻¹⁶³			CG	434	284 (65.4)			NR	
		Women	IG	95	63 (66.3)	0.89 (0.62–1.28)		NR	NR
UKSAT			CG	93	68 (73.1)			NR	
Good									

Appendix F Table 6. All-Cause and AAA Mortality Data for Sex Subpopulations in Open vs. Surveillance Trials (KQ	≀4a)
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* Primary adjustments made for age, sex, initial AAA diameter, smoking status, mean of left and right ankle-brachial pressure indexes, forced expiratory volume in 1 sec, and aspirin use.

Abbreviations: AAA = abdominal a ortic aneurysm; CG = control group; CI = confidence interval; HR = hazard ratio; IG = intervention group; N = population size; n = sample size; NR = not reported; RR = relative risk; UKSAT = the UK Small Aneurysm Trial.

Study, Year Quality	Mean Followup, years	Description	N Subgroup	All-Cause Mortality, n (%)	HR (95% CI) ^{†, ‡}	P-Value for Interaction
Powell, 2007 ¹⁶¹⁻¹⁶³	10*	Current Smoker (at baseline)	404	204 (50.5)	1.25 (1.03–1.53)	NR
		Former Smoker	620	259 (41.8)	1.00	
UKSAT		Never Smoker	64	32 (50.0)	1.30 (0.88–1.92)	
Good						

Appendix F Table 7. All-Cause Mortality Data for Smoking	g Subpopulations in Open vs. Surveillance Trials (KQ4a)
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*Data are from Powell 2002.¹⁶¹

[†] HRs and P-values determined by Cox proportional hazards regression analysis and adjusted for baseline age, sex, smoking status, aneurysm diameter, average of left and right ankle-brachial pressure indexes, forced expiratory volume in 1 sec, and use or nonuse of aspirin.

⁺This subgroup analysis reports all-cause mortality HRs by smoking status in the entire study population. It does not provide outcomes by IG and CG in smokers and nonsmokers so does not provide comparisons to determine if there is a differential treatment effect of early surgery by smoking status.

Abbreviations: AA = abdominal a ortic aneurysm; CG = control group; CI = confidence interval; HR = hazard ratio; IG = intervention group; N = population size; n = sample size; NR = not reported; RR = relative risk; UKSAT = the UK Small Aneurysm Trial.

Appendix G Box 1. Overall Summary (Contextual Question 2)

- Major risk factors confirmed to be: older age, male sex, smoking, family history.
- Older adults have higher prevalence and risk of rupture but also higher surgical mortality and competing causes of mortality compared to younger adults. Screening is only rational for surgical candidates. Validated surgical prognostic models are available for decision-making although some issues around predictive accuracy have been raised.
- Women have lower prevalence, higher rupture risk at same diameter but at older age than men. Women have higher surgical morbidity and mortality compared to men. While women female smokers have prevalence approaching that of men in the trials, their surgical morbidity and mortality remain higher than men. A 2018 DA estimated NNIS for 65-70 year old women 1800-3900 (compared to 700 for men).
- With declining prevalence of AAA, male smokers and those with family history have AAA prevalence that approach that of men in the landmark screening trials. There is no available evidence to suggest that smokers or those with family history have different surgical outcomes.

Overall Risk by Demographic Characteristics and Smoking Status: Large Cohort Studies and Contemporary Trial

These cohorts and one contemporary screening trial confirm that older age, male sex, smoking and family history are the strongest risk factors for AAA development.

Lifetime AAA prevalence from contemporary US cohort for age, sex, smoking, race³⁰

ARIC Cohort: This cohort reported women have half to one-third the prevalence of AAA as men. Female current smokers have a similar risk as male former smokers. This study is a prospective, community cohort of 15,792 individuals recruited in the U.S. between 1987-1989 and followed through 2013. It reported an overall lifetime risk of developing a clinically significant AAA was 5.6% (95% CI 4.8-6.1). Risk was higher for men (8.2%), whites (6.5%), current smokers (10.5%) and those in the top 2 tertiles of smoking pack-years (9.0% and 11.1%). There was a gradient effect identified for the length of smoking years.

AAA prevalence risk from US self-referred, self-pay screening cohort^{29, 179}

Life Line Screening Cohort: A self-referred, retrospective cohort of 3.1 million participants was analyzed to assess risk factors for developing AAA (US, 2003-2008). This population was fairly young (20% <50 yrs), 65% female, and predominantly white (87%). This analysis confirmed that male, smoking, increasing age, family history, and cardiovascular disease are factors that increase risk for developing AAAs. Protective factors were frequent exercise and consumption of nuts, fruits and vegetables. Smoking cessation also reduced risk. This pattern of risk factors mirrors the analysis done on this same dataset examining predictors of large AAA (size \geq 5.0cm)

Risk factors in contemporary Danish screening population²²

VIVA trial: The VIVA trial is a contemporary RCT in Denmark which randomizes male participants aged 65-74 yrs to screening for AAA, PAD, and hypertension or to usual practice of no systematic screening. 18,749 men attended screening and AAA was identified in 619 men (3.3%). Current smoking and family history were strong risk factors for identification of AAA. Current smoker n=258/619 OR 3.25 (2.76 - 3.84). First-degree relative with AAA n=41/619 OR 2.45 (1.76 - 3.41).

Prevalence

Women

The best available evidence estimating AAA prevalence in women is derived from a new meta-analysis by the SWANN collaborative. There is an additional large UK Lifeline cohort that was published subsequent to the meta-analysis.

AAA prevalence in women from meta-analysis of screening cohorts²³

Overall pooled prevalence of AAA > 3.0 cm estimated to be 0.74% (95% CI 0.53, 1.03) with a higher prevalence in ever-smokers 1.34% (95% CI 0.82, 2.19) and a lower prevalence in never smoking women of 0.28% (95% CI 0.09, 0.93). These estimates are far lower than reported prevalence in men. This is a systematic review and meta-analysis of eight cohort studies (population-based, self-referral, and physician-initiated screening) of AAA screening of 1.5 million women age 60 years and older in Ireland, Italy, Norway, Sweden, UK, US. The range of prevalence reported in these studies was 0.31 to 1.46%.

AAA prevalence in UK self-referred, self-pay screening cohort²⁴⁷

Life Line Screening Cohort: The first 50,000 women self-referring and self-paying to attend the Life Line Screening program in the UK and Ireland (2012-2013) were included. The prevalence of AAA in women 66 to 85 yrs was 0.29% (72/25,170). The prevalence in nonsmoking women was 0.26%. In women younger than 66 years of age, the prevalence was 0.02%. In women 66-85 years with a 40-pack year history of smoking, prevalence was 2.14% but there were few women in this category (3/140) so this estimate lacks precision.

Smokers

With declining overall prevalence of AAA over the past 2 decades, one VA study suggests that contemporary male smokers have similar AAA prevalence to those of participants in the 4 landmark screening trials.

AAA prevalence male smokers in a contemporary cohort²¹²

This study shows that the prevalence of male ever smokers reaches the prevalence seen in the major screening trials even though overall prevalence is decreasing. A regional VA health care network identified male smokers 65 to 75 yrs of age who had smoked at least 100 cigarettes in their lifetime and screened them for AAA between 2007 and 2011 (n=8,751). The prevalence of for any aneurysm \geq 3.0 cm was 7.2% with 77.9% of the aneurysms identified measuring between 3.0 – 4.4 cm.

Family history

New evidence from a contemporary Danish screening trial reports that men with a family history of AAA have prevalence similar to those of participants in the 4 landmark screening trials.

AAA prevalence in those with a family history

Reported estimates of prevalence of AAA in those with a family history vary widely and are obtained using a variety of methodology.

The prevalence of AAA in 65 to 74 year old men with at least one first-degree relative with AAA was 6.7%.²¹⁷ This is double the prevalence of those without a family history reported in VIVA (3.0%) and having a female relative with the disease had a higher association with AAA risk (OR

4.32 if female first degree relative; OR 1.61 if male relative). The screened arm of the Danish VIVA trial is the only analysis we identified estimating the prevalence of familial AAA based on population-based screening (N=18,614 screened; 569 with a positive family history based on a questionnaire).

The prevalence of AAA in women with a positive family history in the Life Line Screening cohort (self-referred, self-pay US), was reported to be 1%.¹¹ This is still much lower than the prevalence of men in the screening trials.

AAA Rupture Risk for Subgroups

An IPDMA and large UK population cohort demonstrate that older adults, women, current smokers and those with high MAP have higher risk of rupture when controlled for other risk factors.

Small AAA rupture risk from meta-analysis of international studies⁶⁹

Women and current smokers have the highest risk of rupture when controlling for the diameter of the AAA. Individuals under surveillance for small AAAs (n=15,475; k=18; Australia, Canada, Denmark, Norway, Spain, UK, US) were monitored for AAA growth and rupture. The influence of risk factors on rupture was evaluated in an individual patient meta-analysis. Authors found higher rupture rates for women (HR 3.76 [95% CI 2.58, 5.47]), current smokers (HR 2.02 [95% CI 1.33, 3.06]), and those with higher mean arterial blood pressure HR 1.32 [95% CI 1.11, 1.56]).

Large UK population cohort AAA rupture risk³⁸

The Oxford Vascular Study was a prospective, population-based cohort in the UK (n=92,728, 2002-2014) that looked at the effect of patient characteristics on acute AAA events (AAA rupture or the symptomatic AAA). Men accounted for 72.8% of the acute events and incidence per 100,000 population per year greatly increased with age although current smokers incurred events at younger ages than ex-smokers or never-smokers. Wide confidence intervals make comparing rates in current female smokers and past male smokers difficult.

Operative Mortality and Complications

Women

A new meta-analysis reports consistent evidence showing that women have higher post-operative complication rates following EVAR and open repair.

A systematic review (k= 8, n=19,247)²⁰² found women had higher 30-day mortality compared to men in both EVAR and open repairs. Women had higher 30-day mortality (2.31%) than men (1.37%) after EVAR procedures OR 1.67 (95% CI 1.38, 2.04) and open repair (5.37% vs 2.82%) OR 1.76 (95% CI 1.35, 2.30).

Age

A new meta-analysis reports consistent evidence showing that octagenarians have higher post-operative complication rates following EVAR compared to younger adults.

Meta-analysis comparing surgical outcomes in ≥80 yr olds to <80 yr olds¹⁸⁰

A systematic review and meta-analysis (k=9, n=25,723) of surgical outcomes in EVAR procedures

in patients \geq 80 yrs compared to younger patients. Octogenarians had a higher 30-day mortality (3.7% vs 1.7%; OR 2.372 [1.992, 2.825]) and a higher rate of 30-day endoleak (25.83% vs 21.31%; OR 1.281 [1.183, 1.388]). Although, octogenarians had higher harms, the authors state that the absolute rates are acceptable.

Family History

A retrospective review of a large US surgical registry did not indicate that individuals with a family history have worse surgical outcomes than individuals without a family history.

Vascular Quality Initiative registry comparing surgical outcomes for those with and without a family history of AAA. ²⁴⁸

Surgical outcomes were compared for patients with or without a family history of AAA in the VQI registry from 2003-2017. 1997 individuals were identified to have a family history and 18,815 were without a family history. Procedures included open repair and EVAR. No differences were identified in postoperative complications (p=0.510), 30-day mortality (p=0.177), or long-term mortality (p=0.259).

Current Clinical Practice: Surgical Threshold

New data from national registries demonstrate that AAA repair thresholds are lower in clinical practice for both men and women in the US compared to the UK; the US has lower AAA related deaths compared to the UK.

UK v US comparative data of contemporary surgical practice comparing surgical approaches and threshold for intervention in men and women¹⁰⁴

It is much more common for men and women in the US to undergo repair prior to reaching the indicated surgical thresholds of 5.5 cm for men (39.21% vs 8.82%) and 5.0 cm for women (17.19% vs. 4.72%) compared to the UK. A review of registry data in England and US was undertaken to identify the frequency of AAA repair along with the aortic diameter at the time of repair (2005-2012; n=29,300 in England; n=278,921 in US). Repairs in the US were undertaken at a smaller diameter (5.83 cm vs 6.37 cm, p<0.001) although AAA-related death and hospitalization due to AAA rupture were more common in England.

Outcomes Table for Screening Women

A new decision-analysis with CEA reports that screening women is not cost effective and estimates NNIS of 3,900 to prevent 1 AAA death in women.

Decision-analysis of screening women (outcomes table)²¹⁰

A decision analysis assessing AAA screening in women. If women were screened at age 65 years, 3,900 women would need to be invited to be screened to prevent one AAA-related death with an overdiagnosis rate of 33%. A second strategy of screening women at age 70 years would require 1,800 invitations to screen to prevent one AAA-death with an overdiagnosis rate of 55%. Uncertainty around the AAA prevalence in women makes it difficult to accurately estimate the effects of screening.

Appendix G Table 1. Odds ratios of risk factors associated with developing AAA	s (based on
adjusted multivariate analyses)	

Factors Associated With AAA	Any AAA ≥3 cm ²⁹	Any AAA ≥5 cm ¹⁷⁹
Male sex (vs. female sex)	5.71	7.70
Female sex (vs. male sex)	NR	NR
Age (vs. <55 years)		
55–59	2.76	3.20
60–64	5.35	8.10
65–69	9.41	13.20
70–74	14.46	20.70
75–79	20.43	32.0
≥80	28.37	53.10
Hispanic/black/Asian (vs. white)	0.69 to 0.72	0.70
Family history of AAA	3.80	3.20
Smoking: years (<10 years, 10 to 35 years, or >35 years) + PPD	2.61 to 12.13	2.60 to 14.50
(≤0.5, 0.5 to 1, >1)		
Smoking cessation (5 to 10 years, >10 years)	0.42 to 0.87	0.50 to 0.80
Diabetes	0.75	0.70
CVD morbidities	1.1 to 1.7	1.10 to 1.70

Abbreviations: AAA = abdominal aortic aneurysm; CVD = cardiovascular disease; NR = Not reported; PPD = packs per day.

Participants						
Trial Identifier	Study Name	Location	N	Intervention	Outcome Measures	Status Aug 2018
NCT01756833	Non-Invasive Treatment of Abdominal Aortic Aneurysm Clinical Trial (N-TA^3CT) Michael Terrin	US	Men and women age 55 years and older N=261	Doxycycline 100 mg po bid for 2 years vs. placebo	AAA growth	Active, expected completion 2019. <u>Protocol</u> published 2016
NCT01683084	Study of the Effectiveness of Telmisartan in Slowing the Progression of Abdominal Aortic Aneurysms (TEDY) (Ronald L Dalman)	US	Adults ages 50 to 85 years N=22	Telmisartan 40 mg daily for 24 mo vs. placebo	Rate of AAA growth, AAA diameter, AAA biomarkers, QoL	Completed 2016. No result publication found. Protocol published 2015
NCT02717481	Using US to Evaluate Aortic Aneurysm Size Based on 3D Co- registration to Previous CT Scan (Diana Gaitini)	Israel	Men and women age 18 years and older diagnosed with AAA or following invasive repair N=120	Ultrasound	Primary: Exact and reliable evaluation of the aneurysm size Secondary: The size difference between systolic and diastolic aneurysm; aneurysm neck size and changes following an invasive procedure to repair it (EVAR); evaluation of the pressure on the aneurysmal wall	Not yet recruiting, expected completion 2018
NCT01205945	The Effect of Abdominal Aortic Aneurysm Screening on Mortality in Asian Population (Jin Hyun Joh)	South Korea	Men and women ages 50 to 85 years with CVD risk factors, family history of AAA N=12,000	Ultrasound	Benefits of screening older population	Ongoing, estimated completion 2017. No publications found.
NCT02345590	Eplerenone in the Management of Abdominal Aortic Aneurysms (Leah Isles)	Australia	Men and women ages 60 to 90 years with AAA 30 to 49 mm N=172	Eplerenone 25mg/day vs. placebo	AAA maximum orthogonal diameter	Ongoing, estimated completion 2019.
NCT02229006	Sodium Fluoride Imaging of Abdominal Aortic Aneurysms (SoFIA3) (Rachael O Forsythe)	UK	Men and women age 50 years and older in MA3RS study with AAA >40 mm N=100	Radiation: 18F-NaF PET-CT	Primary: Change in AAA anteroposterior diameter at 6 and 12 months measured with CTA Secondary: Co-localization of 18F-NaF with USPIO uptake on MRI scanning	Completed 2017. No publications found.

Participants						
Trial Identifier	Study Name	Location	N	Intervention	Outcome Measures	Status Aug 2018
NCT02604303	A Prospective Analysis on the Expansion Rates of Abdominal Aortic Aneurysms (Eugene S. Lee)	US	Veteran men and women age 21 years and older screened for AAA by VA N=200	Observational using screening	Primary: aortic expansion rate measured with ultrasound Secondary: RhoA levels	Ongoing, expected completion Nov 2018.
NCT02070653	The Efficacy of Ticagrelor on Abdominal Aortic Aneurysm (AAA) Expansion (TicAAA) (Anders Wanhainen)	Sweden	Men and women ages 50 to 85 years with AAA 35 to 49 mm N=145	Ticagrelor 180 mg/day vs. placebo	Primary: AAA volume growth measured with MRI Secondary: AAA diameter growth measured with ultrasound and MRI; need for surgery; rupture	Completed 2018. No publications found.
NCT02548546	Estimation of Biomechanical Aortic Wall Properties in Healthy and Aneurysmal Aortas Using Novel Imaging Techniques (Houssam Farres)	US	Men and women age 21 years and older with AAA ≥1.5x normal diameter N=30	Surveillance vs. open repair vs. EVAR	Primary: ECHO imaging Secondary: ECG-gated MRA imaging	Ongoing (recruiting), expected completion Aug 2018.
NCT02225756	Cyclosporine A in Patients With Small Diameter Abdominal Aortic Aneurysms (ACA4) (Eric Allaire)	France	Men with AAA 30 to 49 mm, women with AAA 25 to 44 mm, 50 to 85 years N=360	Cyclosporine vs. placebo	Primary: AAA diameter evolution on CT-scanner 12 months after treatment interruption Secondary: AAA diameter evolution on duplex-scanner 12 months after treatment interruption; all-cause CV mortality/morbidity	Ongoing (recruiting), expected completion Sep 2018.
NCT02022436	Evaluation of Predictors of Aortic Aneurysm Growth and Rupture (Rabih Chaer)	US	Men and women age 21 years and older diagnosed with AAA N=148	Contrast ultrasound	Primary: time to growth and/or rupture of abdominal aortic aneurysm Secondary: AAA biomarkers	Ongoing (recruiting), expected completion Jul 2020.
NCT02179801	Screening Cardiovascular Patients for Aortic aNeurysms (SCAN) (Hans-Henning Eckstein, Karl-Ludwig Laugwitz)	Germany	Men any age with 1 or more risk factors for AAA and coronary artery intervention N=1,000	Ultrasound screening	Primary: prevalence of AAA Secondary: prevalence of AAA in the cohort requiring treatment; correlation of risk factors for AAA with risk factors for CAD; distribution of risk factors	Ongoing (recruiting), expected completion Apr 2018. No publications found.

Appendix G. Additional Contextual Question 2 Evidence

			Participants			
Trial Identifier	Study Name	Location	N	Intervention	Outcome Measures	Status Aug 2018
NCT02846883	Safety and Efficacy of Allogeneic MSCs in Promoting T-regulatory Cells in Patients With Small Abdominal Aortic Aneurysms (VIVAAA) (Michael Patrick Murphy, Richard L. Roudebush)	US	Men and women ages 40 to 80 years diagnosed with AAA 35 to 45 mm	Intravenous infusion of 1 or 3 million allogeneic MSCs/kg vs. placebo	Primary: incidence of treatment-related adverse events at 12 months Secondary: changes in inflammatory AAA biomarkers; change in aortic inflammation measured by 18-FDG PET/CT	Ongoing (recruiting), expected completion 2021.
ISRCTN10945166	Abdominal Aortic Aneurysm Screening by Ultrasonography in Primary Care (Ana Claveria)	Spain	Men ages 65 to 74 years N=3,348	Screening	Primary: impact of early diagnosis on overall/CV mortality with incidental AAA Secondary: CV mortality; surgery for AAA; type of hospital discharge	Ongoing, expected completion 2021.
NCT01420991	Brain and Abdominal Aneurysm Study (BAAS) (James Meschia)	US	Men and women age 18 years and older diagnosed with intracranial aneurysm N=81	Opportunistic screening	Primary: prevalence of AAA Secondary: functional outcomes at 30 days	Ongoing, expected completion 2024.
NCT00662480	Randomized Preventive Vascular Screening Trial of 65-74 Year Old Men in the Central Region of Denmark (VIVA)	Denmark	40,000	Screening for hypertension, lower limb atherosclerosis, and abdominal aortic aneurysm	All-cause mortality, cardiovascular events	Active, expected completion Dec 2023. Median (4.4 year) results published in 2017. ¹⁴⁶
ISRCTN12157806	The Danish Cardiovascular Screening Trial (DANCAVAS) (Jes Lindholt)	Denmark	45,000	Large population- based, randomized, clinical multicenter trial testing combination cardiovascular screening in men ages 65 to 74 years	All-cause mortality, costs, and cost-effectiveness after 3, 5, and 10 years to assess possible health and/or societal benefits of the screening; nationwide registry-based information on health care consumption	Ongoing, expected completion Jan 2026. <u>Protocol</u> published 2015.