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Original Article

Simulations of the effects of scheduled abdominal aortic aneurysm repair on survival

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Summary

I simulated survival with and without scheduled repair of abdominal aortic aneurysms with different diameters in different populations. The results imply that scheduled repair should be determined by the combination of a patient's monthly mortality hazard and aneurysm diameter. The median survival of some patients will be extended by the scheduled repair of aneurysms smaller than 55 mm, whereas the median survival of other patients will be curtailed by repair of any aneurysm. The results also suggest that, on average, surveillance is futile: the effect of scheduled aneurysm repair on an individual's median survival did not change but the cohort effect diminished as patients died during surveillance. The results of the UK Small Aneurysm Study were reproduced in simulation and are compatible with the repair of aneurysms smaller than 55 mm diameter. Epidemiological simulations suggest that past randomised controlled trials underestimate the effect of aneurysm repair today.

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Introduction

This paper simulates survival in patients with abdominal aortic aneurysms. The simulations address the following questions:

- 'How might a patient's general risk of dying – due to age, health and fitness – affect his/her survival trajectories with and without scheduled aneurysm repair?'
- 'How might the aneurysm diameter affect survival trajectories with and without scheduled repair?'
- 'How much does endovascular repair prolong survival compared with open repair?'
- 'When is the optimum time and what is the optimum aneurysm diameter to schedule repair and how are they affected by a patient's general risk of dying?'
- 'How applicable today are the results of randomised controlled trials of scheduled aneurysm repair conducted 20 years ago?'
- 'How might we quantify the net effect of scheduled aneurysm repair on survival – can we reasonably expect to distinguish between those whose lives would be shortened by surgery and those whose lives would be extended?'

Although ruptured aneurysms can kill, scheduled aneurysm repair can also kill. Patients with aneurysms can die from a myocardial infarction, pneumonia, colon cancer, a road traffic accident and by many mechanisms other than aneurysm rupture. A patient might reasonably anticipate that they would be counselled on the net survival effect of scheduled abdominal aortic aneurysm repair, as an individual, not as an

elusive 'average' patient. Earlier repair of some aneurysms less than 55 mm diameter compared with later repair of some aneurysms, often less than 55 mm diameter, 22 years ago [1], had little effect on median survival, which has resulted in the crude conclusion that surgeons should avoid repair on male aneurysms less than 55 mm diameter. An even cruder conclusion is that in males, surgeons should repair aneurysms 55 mm diameter or larger, made in the absence of randomised controlled trials, supported by the weak logic that larger aneurysms are more likely to rupture and kill. The conclusion that a diameter of 55 mm divides injudicious surgery from injudicious surveillance ignores the massive variation in patients' life expectancies, their probabilities of dying before an aneurysm ruptures and their probabilities of dying as a result of having surgery.

The indiscriminate institution of a 55 mm aneurysm diameter to define acceptable clinical practice is contrasted by the widespread rejection of the ineffectiveness of endovascular repair in 'unfit' patients with aneurysms of a mean (SD) diameter of 68 (10) mm [2], again 20 years ago. The transient relative safety of endovascular compared with open repair [3], coupled with 'advances in technology', might explain the futile practice of operating on patients unlikely to benefit. Survival at one postoperative month as a measure of success typifies a thoughtless approach to the wisdom of surgery.

For the past 6 years, I and my colleagues have attempted to estimate and graph survival trajectories with and without scheduled abdominal aortic aneurysm repair for individual patients. Patients consider the estimated net effect of surgery, as well as their reduced survival probability immediately after surgery and their later increased survival probability. Patients with higher monthly mortality hazards have higher postoperative mortalities, less life to gain and a greater proportion of life to loose from scheduled aneurysm repair. Patients with otherwise long life expectancies may benefit from scheduled repair of aneurysms smaller than 55 mm diameter, whereas patients with short life expectancies will not benefit from repair of a large aneurysm even if rupture of the aneurysm is the most likely cause of death. For some patients, scheduled surgery will not increase survival and may result in a net reduction in survival. When I see such a patient who presents to our pre-operative assessment clinic after screening, I wonder whether they might have been better counselled before participating in the screening programme.

Patients should be the arbiters of their own fate and it is with them in mind that I have developed a survival calculator. This paper uses the calculator validated in the companion paper of postoperative survival in nearly 1000 patients after scheduled repair of abdominal aortic aneurysms [4].

Methods

I generated three survival curves for individuals or cohorts with abdominal aortic aneurysm: one without surgical repair; one after scheduled open repair; and one after scheduled endovascular repair. The survival curve with surgery accommodated the mortality hazard associated with surgery. The survival curve without surgery accommodated the mortality hazard of rupture from an expanding aneurysm. Both curves are based upon a common underlying survival curve to which the hazards of surgery or aneurysmal rupture are added. The common underlying survival curve starts with a monthly mortality hazard. In an accompanying paper, I have described in detail how variables are entered into a calculator to generate a monthly mortality hazard and subsequent survival curve for an individual without an abdominal aortic aneurysm [4]. In summary, the calculator uses: year; sex; age; height; weight; blood creatinine concentration and estimated glomerular filtration rate; myocardial infarction; stroke; peripheral arterial disease; angina; transient cerebral ischaemia; peak oxygen consumption and ventilatory equivalent for carbon dioxide (at the anaerobic threshold), both from a cardiopulmonary exercise test. I also described how the temporary increase in mortality resulting from scheduled open and endovascular aneurysm repair is incorporated into the calculation.

For the simulations in this paper, I entered values into the calculator that generated initial monthly mortality hazards of 0.5–2%. I chose these mortality hazards to illustrate problems faced by patients likely to present for ultrasound screening and scheduled repair of abdominal aortic aneurysm. Many different combinations of different values can result in the same

mortality hazard. The calculator uses the monthly mortality to then generate a survival curve, which I have assumed was insensitive to the particular combination of values that generated the initial mortality hazard. For instance, a monthly mortality of 0.5% can be generated by the combination: the year 2000, male, 76 years old, 76 kg, 175 cm, no cardiovascular event (as detailed above), creatinine 113 $\mu mol.l^{-1}$, peak oxygen consumption 1431 $ml.min^{-1}$, ventilatory equivalent 30. The same monthly mortality can be generated by: the year 1996, female, 72 years old, 65 kg, 171 cm, myocardial infarct, creatinine 82 $\mu mol.l^{-1}$, peak oxygen consumption 950 $ml.min^{-1}$, ventilatory equivalent 36. The calculator would predict the same survival trajectory for these two patients.

I simplified the temporary increase in the mortality hazard caused by surgery as lasting one postoperative month, after which survival paralleled the pre-operative common underlying survival curve. I assumed that in the first postoperative month, the mortality rate increased compared with the pre-operative rate; ten times after open repair and four times after endovascular repair [1, 3]. I assumed the annual expansion of aneurysm diameter [5] to be:

$$(0.0014 \times \text{mm} \times \text{mm}) - (0.065 \times \text{mm}) + 0.15.$$

I assumed the annual rate of fatal rupture to be:

$$(0.0001 \times \text{mm} \times \text{mm}) - (0.0068 \times \text{mm}) + 0.1215,$$

where 'mm' is the aneurysm diameter in millimetres at the beginning of the year. I calculated the difference in median survival with and without surgery.

Results

In simulations, the higher a patient's mortality hazard, the larger the aneurysm had to be for scheduled surgery to prolong survival, with endovascular repair prolonging survival by 2–6 more months than open repair. Figure 1 illustrates simulated survival with and without surgery for aneurysms 45–85 mm diameter and patients with initial monthly mortalities of 1%, 1.3% or 2%. Scheduled aneurysm repair increases median survival most for patients with the lowest mortality and the largest aneurysms. The differential effect on median survival of endovascular compared with open repair was greatest for patients with the highest monthly mortalities.

Figure 2 illustrates the continuous relationship between the effect of scheduled repair on median life expectancy and aneurysm diameter, for patients with monthly mortality hazards of 0.5%, 1% or 2%. This graph shows that the survival of some patients would be increased by scheduled surgery on aneurysms smaller than 55 mm diameter. Table 1 presents survival in 1000 patients with aneurysms 45 mm diameter and initial monthly mortality hazards of 0.5%, 1% or 2%. Survival was simulated for three scenarios: no surgery; immediate open repair of 45 mm aneurysms; and open repair when aneurysms were 55 mm diameter, expected after 6 years' surveillance. Immediate open aneurysm repair prolonged median survival by 3 years in patients with a monthly mortality hazard of 0.5%, but had no effect for patients with a hazard of 1% and decreased survival in patients with a 2% hazard. Delayed aneurysm repair at 55 mm did not alter the median survival in any cohort, i.e. if screening identified a 45 mm diameter aneurysm in a patient with a monthly mortality hazard of 0.5% he (or she) should be offered immediate surgery. Surgery at 55 mm would prolong individual median survival by the same amount, 3 years (see below), but the median survival of the cohort would not be extended by planned delay because 37% of the cohort would have died in the intervening 5 years, more than a third of them from aneurysm rupture.

Figure 3 shows the effect of surgery on the median survival of cohorts versus the effect of surgery on the median survival of individuals. There were six cohorts, three with an initial monthly mortality hazard of 1% and three with an initial monthly mortality hazard of 0.5% (similar to the hazard estimated for the cohort in the Multicentre Aneurysm Screening Study [6, 7]). Observation started with aneurysm diameters of 40 mm, 45 mm or 50 mm. Median survival was increased most by scheduled repair of aneurysms that were largest (50 mm diameter in this example) when observation began. Median survival was increased most for patients with the lowest initial monthly mortality hazard, 0.5% in this example. The effect of scheduled aneurysm repair on the median survival of total cohorts (black lines) decreased the longer surgery was delayed. However, the effect of scheduled repair on the median survival of surviving individuals (red lines)

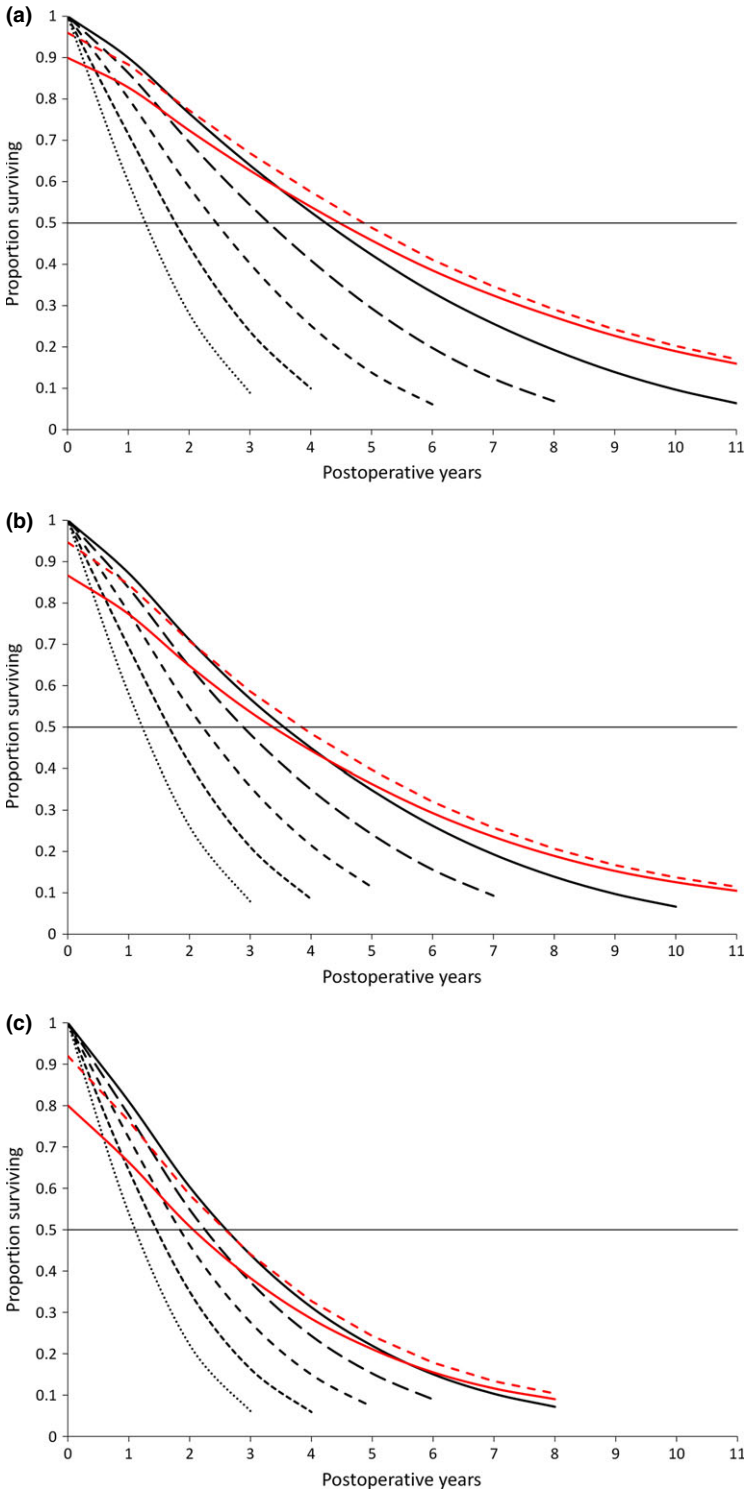

Figure 1 Simulated survival curves for patients with initial monthly mortality hazards of a) 1%, b) 1.3% and c) 2%, following scheduled open (—) or endovascular (– –) abdominal aortic aneurysm repair. Survival for these patients without surgery is illustrated for five different aneurysm diameters: 45 mm (—); 55 mm (– –); 65 mm (- - -); 75 mm (----); and 85 mm (·····). Surgery increases median survival most for patients with the lowest mortality hazards, but surgery shortens survival in patients with 2% initial mortality (c) when aneurysms were smaller than 60 mm (open repair) or 47 mm (endovascular repair). Open repair compared with endovascular repair shortens median survival by: (a) 3 months; (b) 5 months; (c) 6 months.

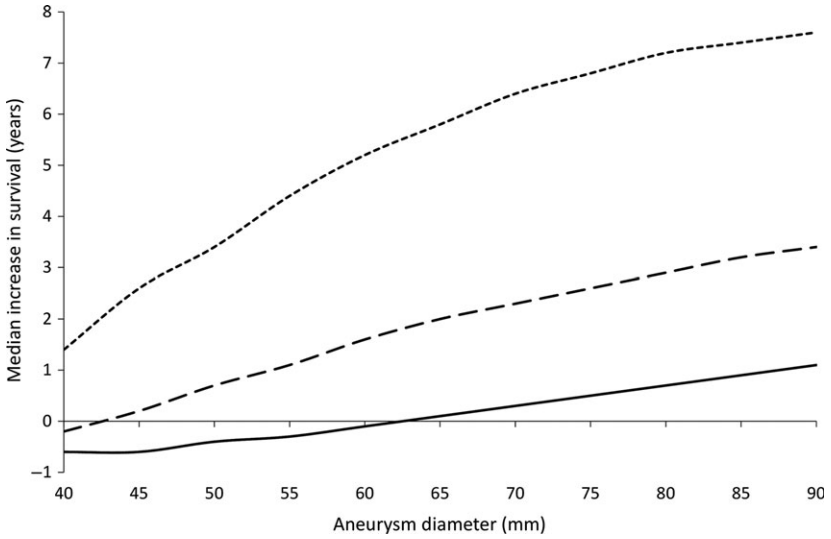

Figure 2 The surgical effect on median survival is continuously related to aneurysm size, illustrated for patients with initial mortality hazards of 0.5% (·····), 1% (- - -) and 2% (——).

remained fairly constant: decreasing general survival, which would reduce the effect of surgery, was counterbalanced by increasing mortality associated with an expanding aneurysm.

I estimated monthly mortalities for cohorts at the start of the UK Small Aneurysm Trial (UK SAT) and the US Aneurysm Detection and Management (ADAM) trial as 1/249 (0.40%) and 1/317 (0.32%), respectively, for which the mean aneurysm diameter was 46 mm (ultrasound) and 47 mm (CT scan), respectively [8, 9]. These diameters are similar to the 45 mm aneurysm group simulated in Table 1, for which immediate repair extended median survival by 3 years compared with delayed repair at 55 mm in a cohort with an initial mortality hazard of 0.5%. So why did UK SAT and ADAM conclude that earlier surgery did not prolong survival? Table 2 simulates results for UK SAT as if all the 'surgery group' had immediate aneurysm repair and it took 5 years for aneurysm expansion to reach 55 mm in the surveillance group, at which point they all immediately had surgery. The results are similar to the group in Table 1 that had an initial aneurysm diameter of 45 mm and monthly mortality hazard of 0.5%, i.e. immediate surgery extended survival by 3 years compared with aneurysm surveillance with surgery at 55 mm. Table 2 also simulates how the implementation of the UK SAT resulted in less polarised cohorts, due to delayed and incomplete repair in the 'surgery group', coupled with repair of aneurysms smaller than 55 mm in the surveillance group. The simulated results in Table 2 almost exactly match the reported survival, both illustrated by Fig. 4 that also shows that the simulation generated the observed crossover in survival curves 2–3 years after recruitment. In contrast, the results of ADAM are incompletely explained by simulation (Fig. 5). Simulation replicated the overall trajectories of the 'surgery' and 'surveillance' ADAM cohorts. However, the simulated crossing of survival curves at 1.5 years – simulated and observed at 2.5 years in the UK SAT – was not observed in ADAM.

The magnitude and direction of the effect of surveillance and scheduled surgery on the survival of patients with abdominal aortic aneurysms depends upon their baseline mortality rate and the initial aneurysm diameter. General population mortality rates have fallen year on year for more than five decades. The results of a published trial, conducted in the past would, therefore, be wrong if applied unadjusted to the current population. I simulated the recruitment of the UK SAT cohort today, 'UK SAT 2015'. The initial monthly mortalities of these new cohorts, 22 years later, would be half the original, i.e. 0.20% (Table 3). Median survival would be extended 4–5 years by early surgery if UK SAT were repeated today. I have replicated the results of seven other randomised, controlled

Table 1 Simulated survival over 11 years in cohorts of 1000 patients with initial monthly mortality rates of: (a) 0.5%, (b) 1% and (c) 2%. All patients had abdominal aortic aneurysms (AAAs) 45 mm diameter that: were not repaired; had immediate open repair; had open repair when 55 mm diameter, 6 years later. The boxes bracket the median life expectancies (500 survivors). Immediate open repair: (a) prolonged median survival; (b) did not affect median survival; (c) shortened median survival.

Year	0	1	2	3	4	5		6	7	8	9	10	11		
AAA diameter; mm	45	46	48	50	51	53	Subtotal	55	57	60	62	65	68	Subtotal	Total
a)															
No surgery	1000	946	871	793	712	629		545	462	381	302	228	160		
Deaths; year^{-1}	0	54	75	78	81	83	371	84	83	82	79	74	68	469	840
Deaths; year^{-1}%	0	5	8	9	10	12		13	15	18	21	25	30		
AAA deaths; year^{-1}	0	23	26	28	30	32	139	32	33	33	30	25	21	173	312
AAA/all deaths; %	0	42	34	36	37	39		38	40	40	38	34	31		
Open repair at 45 mm	955	924	875	825	774	723		671	621	572	523	474	427		
Deaths; year^{-1}	45	31	49	50	51	51	232	52	50	49	49	49	47	296	573
Deaths; year^{-1}%	5	3	6	6	7	7		7	7	8	9	9	10		
Deaths delayed; year^{-1}	−45	23	26	28	30	32	94	32	33	33	30	25	21	173	267
Open repair at 55 mm	1000	946	871	793	712	629		508	481	443	405	367	329		
Deaths; year^{-1}	0	54	75	78	81	83	371	102	46	38	38	38	38	300	671
Deaths; year^{-1}%	0	5	8	9	0	12		16	9	8	9	9	10		
Deaths delayed; year^{-1}	0	0	0	0	0	0		−18	37	43	40	36	30	169	169
b)															
No surgery	1000	906	782	662	550	450		358	278	211	155	109	72		
Deaths; year^{-1}	0	94	124	120	112	100	550	92	80	67	56	46	37	378	928
Deaths; year^{-1}%	0	9	14	15	17	18		20	22	24	27	30	34		
AAA deaths; year^{-1}	0	28	30	29	27	23	137	21	16	14	10	6	4	71	208
AAA/all deaths; %	0	30	24	24	24	23		23	20	21	18	13	11		
Open repair at 45 mm	900	834	740	649	564	487		416	352	299	253	213	180		
Deaths; year^{-1}	100	66	94	91	85	77	413	71	64	53	46	40	33	307	820
Deaths; year^{-1}%	10	7	11	12	13	14		15	15	15	15	16	15		
Deaths delayed; year^{-1}	−100	28	30	29	27	23	37	21	16	14	10	6	4	71	108
Open repair at 55 mm	1000	906	782	662	550	450		302	263	213	171	135	106		
Deaths; year^{-1}	0	94	124	120	112	100	550	120	67	49	42	36	29	344	894
Deaths; year^{-1}%	0	10	16	18	20	22		40	26	23	25	27	27		
Deaths delayed; year^{-1}	0	0	0	0	0	0		−28	13	18	14	10	8	34	34
c)															
No surgery	1000	810	604	439	313	219		150	99	63	39	24	14		
Deaths; year^{-1}	0	190	206	165	126	94	781	69	51	36	24	15	10	205	986
Deaths; year^{-1}%	0	19	25	27	29	30		32	34	36	38	38	42		
AAA deaths; year^{-1}	0	53	51	40	28	20	137	13	12	10	2	0	0	71	208
AAA/all deaths; %	0	28	25	24	22	21		19	24	28	8	0	0		
Open repair at 45 mm	800	663	508	383	285	211		155	116	90	68	51	38		
Deaths; year^{-1}	200	137	155	125	98	74	789	56	39	26	22	17	13	173	962
Deaths; year^{-1}%	20	17	23	25	26	26		27	25	22	24	25	25		
Deaths delayed; yr^{-1}	−200	53	51	40	28	20	−8	13	12	10	2	−2	−3	32	24
Open repair at 55 mm	1000	810	604	439	313	219		110	78	53	36	23	15		
Deaths; year^{-1}	0	190	206	165	126	94	781	89	52	25	17	13	8	204	985
Deaths; year^{-1}%	0	19	25	27	29	30		41	40	32	32	33	33		
Deaths delayed; year^{-1}	0	0	0	0	0	0		−20	1	11	7	3	2	4	4

trials of abdominal aortic aneurysm repair, which can be accessed online (Appendix S1).

The pre-operative aneurysm diameters were recorded for the Torbay cohort of 302 patients whose postoperative survival has been reported [4]. The effects of surgery on survival could, therefore, be simulated for individuals: scheduled surgery increased the median survival of the cohort by a median of 5 years 4 months after open repair and 5 years 7 months after endovascular repair. However, surgery increased survival by more than 18 years in the subgroup in the lowest mortality

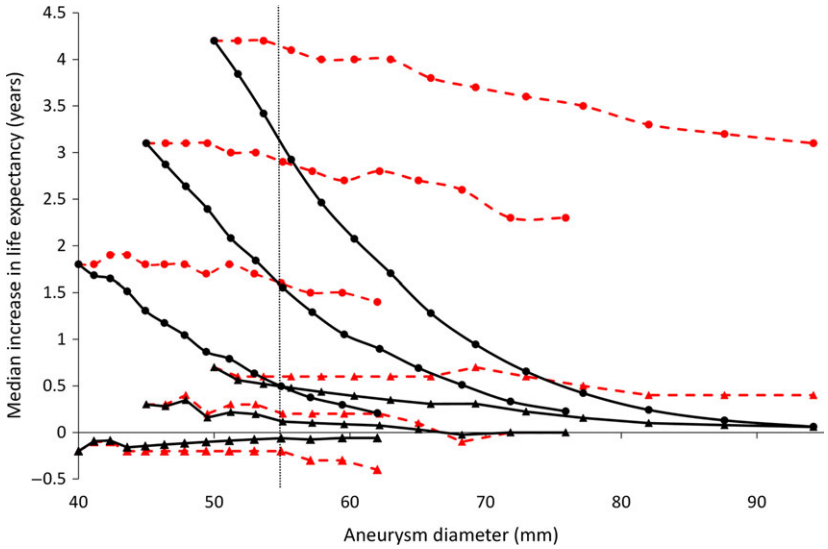

Figure 3 The effect of surgery on the median survival of cohorts (black) versus the effect of surgery on the median survival of individuals still alive (red) during 13 years of surveillance (markers). There were six cohorts, three with an initial monthly mortality hazard of 0.5% (•--• and •--•) and three with an initial monthly mortality hazard of 1% (▲--▲ and ▲--▲). Surveillance started with aneurysm diameters of 40 mm, 45 mm or 50 mm. Median survival was increased most by scheduled repair of aneurysms that were largest (50 mm diameter in this example) when observation began. Median survival was increased most for patients with the lowest initial monthly mortality hazard, 0.5% in this example. The effect of scheduled aneurysm repair on the median survival of total cohorts (black) decreased the longer surgery was delayed but remained fairly constant for individuals (red).

hazard decile, but decreased survival in the subgroup in the highest mortality hazard decile (Fig. 6). Figure 7 illustrates the simulated relationship between monthly mortality hazard, aneurysm diameter and the extension of median survival with open (black) or endovascular (red) repair by (from top to bottom) 1 year, 2 years, 4 years or 6 years. Scheduled aneurysm repair would be indicated for combinations of mortality hazard and aneurysm diameter that intersected below whichever line is chosen as the minimum worthwhile increase in survival, whereas scheduled repair would be contraindicated for intersections above the line of indication. Median survival might be extended by 4–6 years following scheduled repair of 30 mm diameter aneurysms in patients with particularly low monthly mortality hazards. The r^2 value for each polynomial trend line exceeds 0.995.

Discussion

The simulations in this paper suggest a number of conclusions.

1 It is a patient's characteristics, not aneurysm diameter, that predominantly determine the benefit or harm caused by scheduled aneurysm repair.
2 Scheduled repair of abdominal aortic aneurysms as small as 40 mm diameter can prolong survival in some patients, therefore a threshold of 55 mm for intervention will fail to prevent avoidable deaths.
3 Scheduled repair of abdominal aortic aneurysms larger than 55 mm, or 65 mm, or 75 mm, can shorten survival in some patients, therefore an intervention threshold of 55 mm will cause avoidable deaths.
4 Surveillance is predominantly futile – the absolute increase in median survival caused (in appropriate patients) by scheduled aneurysm repair is not increased by waiting: the increased probability of a larger aneurysm's rupturing is counterbalanced by the patient's diminished survival from other causes. In addition, the absolute benefit that might be realised from operating on a cohort early is partly lost by waiting (see point 2).

Table 2 Simulated survival for the UK Small Aneurysm Trial (UK SAT) participants: (a) as the study was conducted (see Fig. 4); (b) as if participants allocated 'surgery' had open repair immediately and participants allocated 'surveillance' had open repair after abdominal aortic aneurysms (AAAs) had expanded to 55 mm. The median survival for surgery triggered by aneurysm expansion to 55 mm was 7–8 years, which was prolonged to 10–11 years by immediate repair at 46 mm (b). The difference in median survival of 3 years was reduced to about 1 year in UK SAT because of premature surgery in the 'surveillance' cohort (median survival 8–9 years) and incomplete and delayed repair in the 'surgery' cohort (median survival 9–10 years). The initial monthly mortality was 0.40%. All the numbers are simulated, except for group sizes, the initial aneurysm size, and '*Reported survival*'. The boxes bracket the median life expectancies in the 'Earlier surgery' cohort (282 survivors) and the 'Later surgery' cohort (264 survivors).

Year	**0**	**1**	**2**	**3**	**4**	**5**		**6**	**7**	**8**	**9**	**10**	**11**	**12**		
AAA diameter; mm	**46**	**48**	**49**	**51**	**53**	**55**	**Subtotal**	**57**	**59**	**62**	**65**	**68**	**72**	**76**	**Subtotal**	**Total**
a)																
Earlier surgery (n = 563)																
No surgery	563	529	488	444	398	351		303	254	206	160	117	79	48		
Deaths; year^{-1}	0	34	41	44	46	47	202	48	49	48	46	43	38	31	303	505
Deaths; year^{-1}%	0	6	8	9	10	12		14	16	19	22	27	32	39		
Scheduled repairs; year^{-1}	248	242	11	8	2	2		1	1	0	0	0	0	0		
Survival by treatment	553	512	485	457	429	403		377	351	325	300	275	251	228		
Reported survival			488		428			375		318		255		118*		
Deaths; year^{-1}	10	41	27	28	28	26	160	26	26	26	25	25	24	23	175	335
Deaths; year^{-1}%	2	7	5	6	6	6		6	7	7	8	8	9	9		
Deaths delayed; year^{-1}	−10	−7	14	16	18	21	42	22	23	22	21	18	14	8	128	170
Later surgery (n = 527)																
No surgery	527	495	456	415	373	328		283	238	193	150	110	74	44		
Deaths; year^{-1}	0	32	39	41	42	45	199	45	45	45	43	40	36	30	284	483
Deaths; year^{-1} %	0	6	8	9	10	12		14	16	19	22	27	33	41		
Scheduled repairs; year^{-1}	96	88	61	36	25	14		6	1	0	0	0	0	0		
Survival by treatment	523	490	455	421	389	357		330	298	266	237	209	184	160		
Reported survival			466		393			329		261		215		69*		
Deaths; year^{-1}	4	33	45	34	32	32	180	27	32	32	29	28	25	24	197	377
Deaths; year^{-1} %	1	6	9	7	8	8		8	10	11	11	12	12	13		
Deaths delayed; year^{-1}	−4	−1	−6	7	10	13	19	18	13	13	14	12	11	6	87	106
b)																
Immediate repair (n = 563)																
No surgery	563	529	488	444	398	351		303	254	206	160	117	79	48		
Deaths; year^{-1}	0	34	41	44	46	47	202	48	49	48	46	43	38	31	303	505
Deaths; year^{-1} %	0	6	8	9	10	12		14	16	19	22	27	32	39		
Open repair at 46 mm	540	521	496	471	445	418		391	364	337	311	286	261	237		
Deaths; year^{-1}	23	19	25	25	26	27	145	27	27	27	26	25	25	24	181	326
Deaths; year^{-1} %	2	7	5	6	6	6		6	7	7	8	8	9	9		
Deaths delayed; year^{-1}	−23	15	16	19	20	20	67	21	22	21	20	18	13	7	122	189
Delayed repair (n = 527)																
No surgery	527	495	456	415	373	328		283	238	193	150	110	.74	44		
Deaths; year^{-1}	0	32	39	41	42	45	199	45	45	45	43	40	36	30	284	483
Deaths; year^{-1} %	0	6	8	9	10	12		14	16	19	22	27	33	41		
Open repair at 55 mm	527	495	456	415	373	308		293	272	251	230	208	188	168		
Deaths; year^{-1}	0	32	39	41	42	65	219	15	21	21	21	22	20	20	140	359
Deaths; year^{-1} %	0	6	8	9	10	17		5	7	8	8	10	10	11		
Deaths delayed; year^{-1}	0	0	0	0	0	−20	−20	30	24	24	22	18	16	10	144	124

*Incomplete follow-up at 12 years: less than 12 years had elapsed since recruitment for half of each cohort.

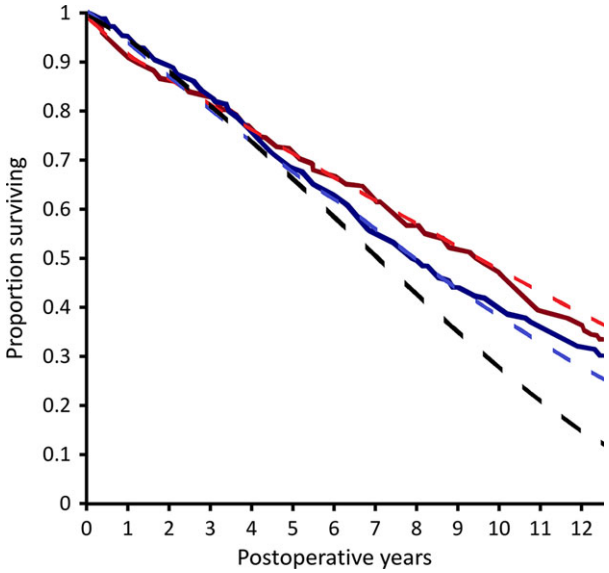

Figure 4 Reported and simulated results of the UK Small Aneurysm Trial [7] that allocated participants with a mean abdominal aortic diameter of 46 mm to early surgery (reported —, simulated - - -) or surveillance up to a diameter of 55 mm (reported —, simulated - - -). The mean follow-up was 12 years, when the mean diameter of aneurysms without surgery would have been about 80 mm. The trial as conducted was limited to detecting a difference in median survival of 6–12 months if follow-up was complete at 10 years (Table 2): early surgery was not immediate and was incomplete (94%), whereas more than a third of the 76% of repairs in the surveillance cohort were on aneurysms smaller than 55 mm. The black dashed line is survival without surgery at any time.

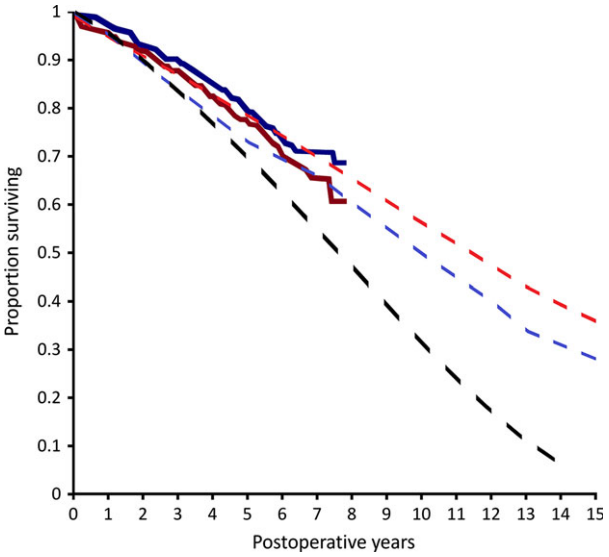

Figure 5 Reported and simulated results of the US Aneurysm Detection and Management trial [9] that allocated participants with a mean abdominal aortic diameter of 47 mm to early surgery (reported —, simulated - - -) or surveillance up to a diameter of 55 mm (reported —, simulated - - -). The mean follow-up was five years, when the mean diameter of aneurysms without surgery would have been about 57 mm. The trial was limited to detecting a difference in median survival of less than 1 year if follow-up was complete at 11 years: early surgery was not immediate and was incomplete (93%), whereas many repairs in the 62% of the surveillance cohort were on aneurysms smaller than 55 mm. The black dashed line is survival without surgery at any time.

5 The results of the UK Small Aneurysm Trial and, to a lesser extent, the US Aneurysm Detection and Management trial can be reproduced in simulation. Simulation suggests that their results have been misinterpreted. Scheduled repair at 46 mm and 47 mm, respectively, would have prolonged median survival by about 3 years compared with repair at 55 mm. Repairs of aneurysms smaller than 55 mm in the surveillance group, coupled with incomplete and delayed repair in the early surgery group, reduced the power of both trials to detect a difference in survival.

6 The results, reported or simulated, of the UK SAT and US ADAM trial cannot be used today without adjustment. The UK SAT would have the power to determine a difference in median survival if it were conducted in exactly the same way today (2015), as early surgery would extend median survival by about 4.5 years, or by six years with 100% adherence to the protocol. Historical results become more inaccurate with time: the value of 4.5 years will underestimate the effect of early surgery in the future if the year-on-year reduction in general population mortality continues.

7 Endovascular repair extends median survival by 2–3 months for most patients, if one ignores the annual 1% fatalities due to rupture after endovascular repair, which might negate the small extension to survival afforded by EVAR. Survival is dominated by patients' variables and whether an aneurysm is repaired or not; it is hardly affected by how the aneurysm is repaired.

Table 3 The UK Small Aneurysm Trial, median recruitment year 1993 (Table 2), updated to 2015 as the median recruitment year: (a) as the study was conducted; (b) as if participants allocated 'surgery' had open repair immediately and participants allocated 'surveillance' had open repair after abdominal aortic aneurysms (AAAs) had expanded to 55 mm. The initial monthly mortality for a cohort with the same age and co-morbidity has fallen during 22 years from 0.40% to 0.20%. The rates of aneurysm repair reported for UK SAT would result in a median survival of 11–12 years in the surveillance group and 16 years in the 'surgery' group (the table has not been extended to 16 years). Immediate repair would extend median survival to 18–19 years, whereas repair at 55 mm would increase the median survival by 1 year from that calculated with the rates of repair in the surveillance cohort. The boxes bracket the median life expectancies in the 'Earlier surgery' cohort (282 survivors) and the 'Later surgery' cohort (264 survivors).

Year	0	1	2	3	4	5		6	7	8	9	10	11	12		
AAA diameter; mm	46	48	49	51	53	55	Subtotal	57	59	62	65	68	72	76	Subtotal	Total
a)																
Earlier surgery (n = 563)																
No surgery	563	540	510	478	442	403		360	314	265	215	164	116	73		
Deaths; year^{-1}	0	23	30	32	36	39	160	43	46	49	50	51	48	43	330	490
Deaths; year^{-1} %	0	4	6	6	8	9		11	13	16	19	24	29	37		
Scheduled repair; year^{-1}	248	242	11	8	2	2		1	1	0	0	0	0	0		
Survival by treatment	558	534	519	502	486	469		454	438	422	405	387	369	350	16 yr	
Deaths; year^{-1}	5	24	15	17	16	17	94	15	16	16	17	18	18	19	119	213
Deaths; year^{-1} %	1	4	3	3	3	3		3	4	4	4	4	5	5		
Deaths delayed; year^{-1}	−5	−1	15	15	20	22	66	28	30	33	33	33	30	24	211	277
Later surgery (n = 527)																
No surgery	527	505	478	448	414	377		337	294	248	201	154	109	68		
Deaths; year^{-1}	0	22	27	30	34	37	150	40	43	46	47	47	45	41	309	459
Deaths; year^{-1} %	0	4	5	6	8	9		11	13	16	19	23	29	38		
Scheduled repair; year^{-1}	96	88	61	36	25	14		6	1	0	0	0	0	0		
Survival by treatment	525	504	481	460	439	418		400	376	351	327	302	279	256		
Deaths; year^{-1}	2	21	23	21	21	21	109	18	24	25	24	25	23	23	162	271
Deaths; year^{-1} %	0	4	5	4	5	5		4	6	7	7	8	8	8		
Deaths delayed; year^{-1}	−2	1	4	9	13	16	41	22	19	21	23	22	22	18	147	188
b)																
Immediate repair (n = 563)																
No surgery	563	540	510	478	442	403		360	314	265	215	164	116	73		
Deaths; year^{-1}	0	23	30	32	36	39	160	43	46	49	50	51	48	43	330	490
Deaths; year^{-1} %	0	4	6	6	8	9		11	13	16	19	24	29	37		
Open repair at 46 mm	552	543	531	518	505	491		476	461	445	428	410	390	370	18–19 yr	
Deaths; year^{-1}	23	19	25	25	26	27	145	27	27	27	26	25	25	24	181	326
Deaths; year^{-1} %	2	7	5	6	6	6		6	7	7	8	8	9	9		
Deaths delayed; year^{-1}	−23	15	16	19	20	20	67	21	22	21	20	18	13	7	122	189
Delayed repair (n = 527)																
No surgery	527	505	478	448	414	377		337	294	248	201	154	109	68		
Deaths; year^{-1}	0	22	27	30	34	37	150	40	43	46	47	47	45	41	309	459
Deaths; year^{-1} %	0	4	5	6	8	9		11	13	16	19	23	29	38		
Open repair at 55 mm	527	505	478	448	414	367		358	346	333	319	305	289	273	12–13 yr	
Deaths; year^{-1}	0	22	27	30	34	47	160	9	12	13	14	14	16	16	91	251
Deaths; year^{-1} %	0	4	5	6	8	11		2	3	4	4	4	5	6		
Deaths delayed; year^{-1}	0	0	0	0	0	−10	−10	31	31	33	33	33	29	25	215	205

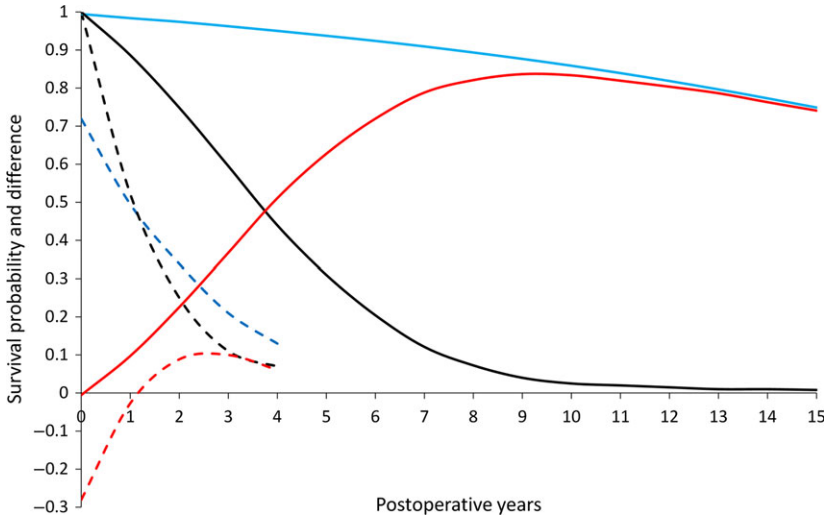

Figure 6 Simulated effect on survival of scheduled abdominal aortic aneurysm repair for the Torbay patient decile (34/302, solid lines) with the lowest monthly mortality hazard and the decile (29/302, dashed lines) with the highest monthly mortality hazard [4]. The lines indicate survival with (— and - - -) and without surgery (— and - - -). The difference between these two survivals is the red lines. Simulation suggested that surgery extended median survival in the lowest mortality hazard decile by about 18 years, but that surgery curtailed survival by about 1 month in the highest mortality hazard decile.

8 Screening should be based upon an individual's calculated monthly mortality coupled with the probability that he/she has an aneurysm sufficiently large that treatment would prolong survival by a meaningful period. A more effective screening programme might be to identify and treat aneurysms 40 to 55 mm diameter in people with low mortality hazards, which would involve repairing many more abdominal aortic aneurysms than currently undertaken. The harm or benefit caused by screening is dependent upon treating the right people and also screening the right people, which cannot be determined by age and sex alone.

The discrimination and the calibration of the calculator that I used in these simulations have been tested against independent survival data in nearly 1000 patients [4]. Inaccuracies in simulated survival would be insufficient to discount the listed conclusions. The most likely inaccuracies in these simulations are the rates of aneurysm growth and aneurysm rupture: the epidemiology of both is heterogeneous [5]. Some of the heterogeneity might be explained by patients' variables, which could only be determined with individual patient data from the studies that have reported these rates, so the uncertainty around the values of aneurysm growth and rupture are likely to remain as these data are probably unavailable. For instance, the rupture rate is higher in women for a given aneurysm diameter, so the simulations in this paper are more applicable to men than women. The inaccuracies introduced into the simulations explored in this paper are universal: they apply as much to the logic underlying current treatment and screening practices. The variation in the survival of individuals is dominated by known patient variables, rather than the unknown accuracy of estimated aneurysm growth and rupture rates. This paper uses those known variables, whereas current screening and treatment do not use known variables.

The results of these simulations challenge the basis on which abdominal aortic aneurysms are screened, observed and repaired. There are implications for patients, clinicians and those who commission and run screening programmes. The screening programme should reconsider how it selects an appropriate population, incorporating differences between people and also changes in the prevalence and behaviour of

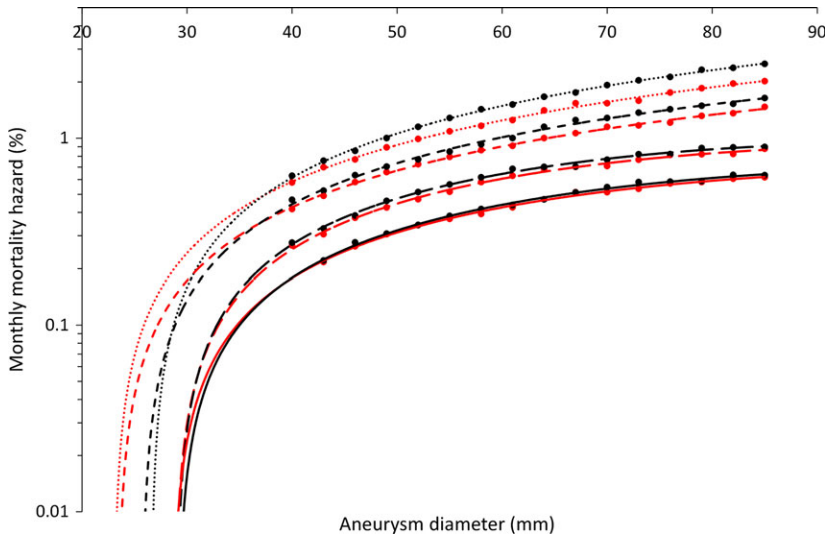

Figure 7 Isosurvival curves of median life extension after open (black) and endovascular (red) abdominal aortic aneurysm repair by: 1 year (····· and ·····); 2 years (---- and ----); 4 years (– – and – –); or 6 years (—— and ——). For example, a patient with a monthly mortality hazard of 0.5% would expect surgery to extend their survival by: 2 years (aneurysm 41 mm); 4 years (aneurysm 52 mm); or 6 years (aneurysm 66 mm). Combinations of aneurysm size (horizontal axis) and patient monthly mortality hazard (vertical logarithmic scale) that intersect below the lines indicate larger increases in median survival, intersections above the line indicate smaller increases in median survival. The fitted polynomial trend lines ($r^2 > 0.995$ for all) relate monthly mortality hazard (%) to aneurysm diameter ('mm') with the following equations (top to bottom lines), starting with 1-year extension for open repair (black) and finishing with 6-year extension for endovascular repair (red). Monthly mortality hazard = $(-0.00006 \times mm \times mm + 0.0499 \times mm - 1.2824)$, $(-0.00004 \times mm \times mm + 0.0369 \times mm - 0.8297)$, $(-0.00008 \times mm \times mm + 0.036 \times mm - 0.8754)$, $(-0.00005 \times mm \times mm + 0.0291 \times mm - 0.6529)$, $(-0.0002 \times mm \times mm + 0.037 \times mm - 0.9173)$, $(-0.0002 \times mm \times mm + 0.0337 \times mm - 0.8357)$, $(-0.0001 \times mm \times mm + 0.0241 \times mm - 0.6075)$, $(-0.0001 \times mm \times mm + 0.0226 \times mm - 0.5618)$.

aneurysms [10]. I had anticipated that some patients might be too frail to benefit from the repair of any aneurysm but I had not anticipated that the repair of small aneurysms might be beneficial. I was surprised that waiting for an aneurysm to grow is unlikely to increase the absolute surgical effect on median life expectancy for an individual, although the relative change in survival would increase. For instance, surgery might increase median survival by 3 years for an individual now or in 5 years' time (should they survive), but with a decreasing life expectancy 3 years represents an increasing proportion of survival available to an individual. This example stimulates a question, "What is the metric by which the value of aneurysm repair is gauged and is it the same for everyone?" Figure 7 could be used to determine whom to screen and it could help patients decide whether their aneurysms should be repaired. Not only does one have to consider the absolute and relative effect of surgery on survival, but one also has to consider the morbidity associated with operating or not operating, coupled with whether to continue or discontinue surveillance when surgery is contraindicated or declined.

Competing interests

No external funding and no competing interests declared. JC is an Editor of *Anaesthesia* and this manuscript has undergone additional external review as a result.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Supplementary material.

Table S1.. Data used to simulate six randomised controlled trials of scheduled abdominal aortic aneurysm repair: CAESAR; PIVOTAL; EVAR 2; OVER; EVAR 1; DREAM.

Figure S1. CAESAR simulation.

Figure S2. PIVOTAL simulation.

Figure S3. EVAR 2 simulation.

Figure S4. OVER simulation.

Figure S5. EVAR 1 simulation.

Figure S6. DREAM simulation.

