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Optimizing Surveillance and Re-intervention Strategy Following Elective Endovascular Repair of Abdominal Aortic Aneurysms

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Background: EVAR for abdominal aortic aneurysm has an initial survival advantage over OR, but more frequent complications increase costs and long-term aneurysm-related mortality. Randomized controlled trials of EVAR versus OR have shown EVAR is not cost-effective over a patient's lifetime. However, in the EVAR-1 trial, postoperative surveillance may have been sub-optimal, as the importance of sac growth as a predictor of graft failure was overlooked.

Methods: Real-world data informed a discrete event simulation model of postoperative outcomes following EVAR. Outcomes observed EVAR-1 were compared with those from 5 alternative postoperative surveillance and re-intervention strategies. Key events, quality-adjusted life years and costs were predicted. The impact of using complication and rupture rates from more recent devices, imaging and re-intervention methods was also explored.

Results: Compared with observed EVAR-1 outcomes, modeling full adherence to the EVAR-1 scan protocol reduced abdominal aortic aneurysm (AAA) deaths by 3% and increased elective re-interventions by 44%. European Society re-intervention guidelines provided the most clinically effective strategy, with an 8% reduction in AAA deaths, but a 52% increase in elective re-interventions. The cheapest and most cost-effective strategy used lifetime annual ultrasound in primary care with confirmatory computed tomography if necessary, and reduced AAA-related deaths by 5%. Using contemporary rates for complications and rupture did not alter these conclusions.

Conclusions: All alternative strategies improved clinical benefits compared with the EVAR-1 trial. Further work is needed regarding the cost and accuracy of primary care ultrasound, and the potential impact of these strategies in the comparison with OR.

Keywords: abdominal aortic aneurysms, discrete event simulation, economic evaluation, endovascular aneurysm repair, surveillance

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The endovascular aneurysm repair (EVAR) stent-graft has become the treatment of choice for elective repair of abdominal aortic aneurysm. Numerous studies have demonstrated an initial survival advantage over open repair (OR), less time in operating theatre, less use of intensive care and lower overall length of stay in hospital.[1–6] Nevertheless, EVAR is also associated in these trials with increased late aneurysm-related mortality.[6] Complications may lead to aneurysm sac pressurization, growth and eventually rupture.[7] Hence EVAR requires more vigilant surveillance and more late re-interventions than OR.[8] As a result, EVAR has not been shown to be cost-effective over the patient's lifetime at conventional thresholds used in the UK.[9,6]

Health economic assessment of EVAR in the UK has largely been based on long-term follow-up data from the EVAR-1 trial.[6,10,11] However, it has been hypothesized that postoperative surveillance in this trial was sub-optimal, and that a more modern surveillance schedule might have produced a more favorable result.[6] Clearly, as the trial cannot be re-run, this theory is impossible to confirm or refute definitively. Nevertheless, earlier detection of complications, via a computed tomography (CT) or ultrasound (US) scan, and appropriate corrective surgery may have prevented some ruptures. The recommended surveillance protocol for the EVAR-1 trial was contrast-enhanced CT at 1, 6, and 12 and yearly thereafter.[12] However, this protocol was not rigorously followed,[6] in part reflecting the diversity of clinical practice at the time.[13,14] The way such complications are monitored and treated has since changed radically. It is possible some patients may have been overtreated, whereas others who should have received re-intervention were left untreated, with associated possible adverse consequences. Various proposals have been made for risk-stratified surveillance strategies based on presence of early endoleak or poor component overlap.[15–17] European Society guidelines for post-EVAR follow-up have also recommended duplex US in low-risk patients, which may lessen the cumulative radiation dose and overall costs.[16] A study in the USA revealed that a third of the total costs of EVAR during the first 5-years was from radiologic studies.[8] However, the impact of these recommendations on the cost-effectiveness of EVAR has not been formally assessed. Furthermore, the rate of sac growth is an important predictor of graft failure and rupture[18] and is likely to have a proximal cause in an underlying endoleak complication.[7] Grootes et al[18] found that at 2 years post-repair, positive aneurysm growth rate (>0 mm/yr) preceded 85% of subsequent ruptures or rupture-preventing re-interventions in the next 2 years, and 44% of patients without rupture or rupture-preventing re-interventions had no preceding sac growth.

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The objective of this work was to evaluate the effectiveness and cost-effectiveness of different surveillance and re-intervention strategies using data from both the EVAR-1 and EVAR-2 trials and a contemporary cohort from Helsinki University Hospital (HUH) in Finland. A model was constructed to investigate the clinical and cost implications of different protocols under different generations of EVAR devices, without having to conduct another costly and long-term randomized trial.

METHODS

A discrete event simulation model was developed in R to contrast different potential post-EVAR surveillance strategies in terms of key events, life-years and costs. The reference case assessed the long-term cost-effectiveness of the postoperative surveillance and re-intervention strategy observed in the EVAR-1[1] trial, since this most closely approximates real-life practice. We additionally assessed 5 further strategies, including the official protocol of the EVAR-1 trial.

Model Structure

Key events included in the model were abdominal aortic aneurysm (AAA)-related complications, ruptures, re-interventions, and deaths. Complications were divided into: (1) a composite outcome comprising any of: kinking, migration, endoleak type I, endoleak type III (hereafter referred to as "restricted cluster" complications), (2) endoleak type II, (3) preoperative sac growth: ≥10 mm change in sac diameter from preoperative diameter, (4) large sac growth: ≥5 mm per annum pro rata expansion based on scans ≥6 months apart, and (5) small sac growth: ≥0 mm and <5 mm per annum pro rata expansion, based on scans ≥6 months apart. These categories reflect complications that are important predictors of postoperative events (including other complication types) and/or are of interest as indicators of future surveillance or re-intervention strategies. The use of the "restricted cluster" of complications enables endoleak type II to be tracked separately from sac growth, and so differs from the "cluster" previously described[6] [which comprises (1) together with (2) and (4) in combination]. This is important here because some policies of interest seek to make management decisions based on sac growth alone (ie, without reference to endoleak type II). Furthermore, because endoleak type II alone may not be considered severe enough to warrant intervention, we did not include it in the restricted cluster definition. This, therefore, enables modeling of sac growth in conjunction with endoleak type II and sac growth alone.

Fig. 1 shows the model structure. Decision events relate to scans (timing and modality, CT/US) and elective re-interventions. Stochastic events were complications, rupture, emergency re-intervention, AAA-related death, or other causes of death. Modeling of complications was restricted to ≥30 days postintervention to exclude in-hospital complications in same admission as the index intervention. In the model, complications that occur were only detected at the next scan, with a given sensitivity. However, patients become at risk

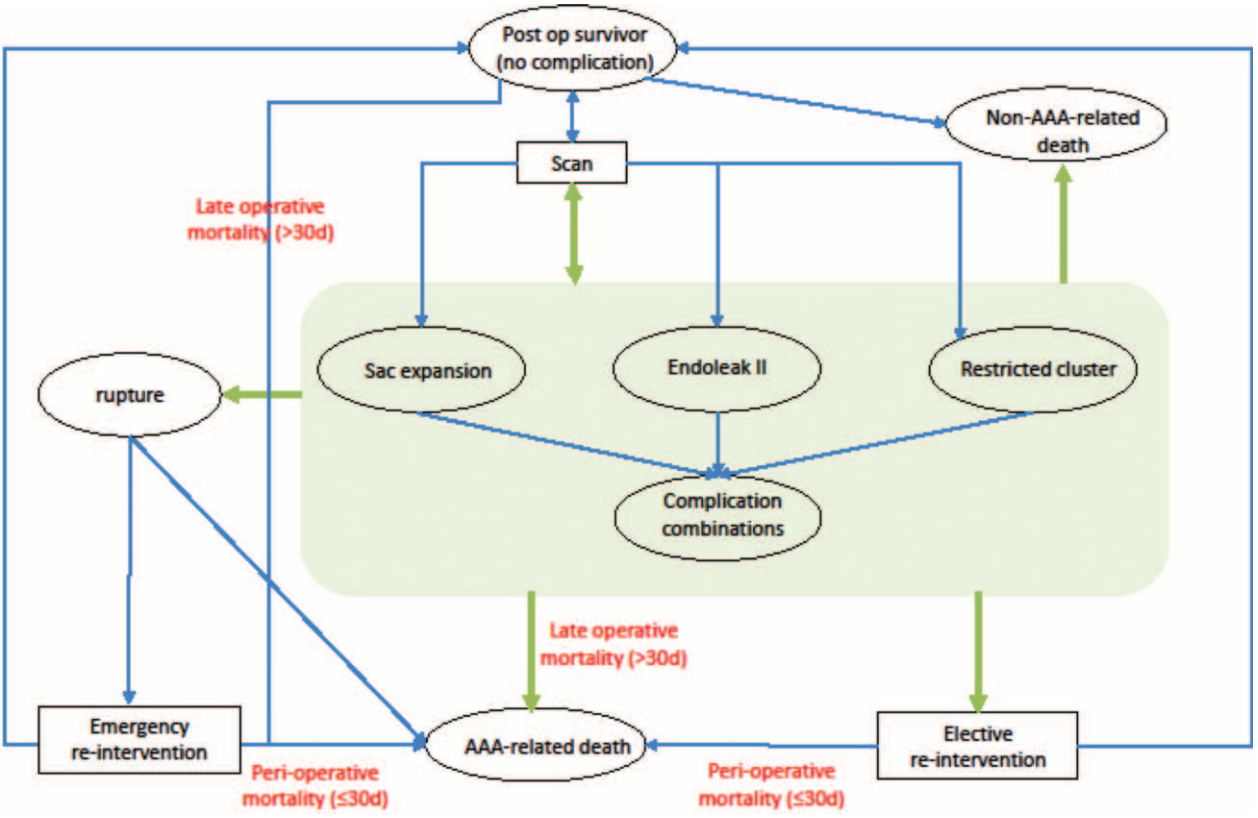

FIGURE 1. Structure of the discrete event simulation model. Circles = uncosted events; rectangles = costed events. Green arrows indicate transitions from any of the complication states contained in the green box. Late operative mortality (>30 d) represents deaths coded as AAA-procedure-related mortality occurring >30 d after last re-intervention, without rupture.

TABLE 1. Total Numbers of Events at 15 yr, for a Cohort of N = 848 (EVAR-1 and EVAR-2 Patients) Observed in the Trial Data and Predicted by Strategy A (Internal Validation)

Event	EVAR Observed*	Strategy A	% Change from Observed
Modeled Scan Policy	**NA**	**Empirical**	
Modeled Re-intervention Policy	**NA**	**Empirical**	
CT scans	4274	4732	11%
US scans	NA	NA	NA
Restricted cluster complications	201	186	−7%
Type II endoleaks	195	194	−1%
Small sac growth	339	368	9%
Large sac growth	205	209	2%
Preoperative sac growth	120	121	1%
Elective re-interventions	185	184	−1%
Emergency re-interventions	11	12	9%
Ruptures	44	44	0%
AAA deaths	70	72	3%
Non-AAA deaths	609	666	9%
Mean costs	£3283†	£3517	7%
Mean life-years	7.476‡	7.398	−1%

*Censoring-inflated for: elective re-interventions, complications and non-AAA deaths. Excludes events occurring post-(re)-intervention in those with 30 d postoperative mortality. Excludes complications occurring within 30 d of an (re)intervention.

†Calculated directly from observed numbers of events and costs used as model inputs.

‡Kaplan-Meier restricted mean life-years (based on all-cause mortality, accounting for censoring) at 15-yr.

CT indicates computed tomography; EVAR, elective endovascular aneurysm repair; NA, not applicable; US, ultrasound.

of rupture from the time the complication occurs. Therefore, long surveillance intervals increase the risk that an undetected complication will lead to rupture.

Alternative Policies

Six surveillance/re-intervention protocols were modeled. Strategy A models the EVAR Trials under imperfect adherence to surveillance and re-intervention protocols. This strategy serves as a reference for comparison with alternative strategies. In this model, the empirical distribution of time to next CT scan, stratified by number of previous scans, was used to generate scan times. Similarly, the time to re-intervention of a detected complication was modeled using observed times in the EVAR trials.[6] This reflects the lack of formal re-intervention policy in the trials, meaning this decision varied according to clinician discretion and local practice. Numbers and timings of key events predicted from Strategy A were compared to those observed in the trials (internal validation).

Strategy B models surveillance according to the EVAR trials stated protocol (CT scan at 1 m, 6 m, 12 m and annually thereafter)[19] but still with no formal re-intervention policy. Strategy C uses the trial scan protocol together with the European Society for Vascular Surgery 2011 re-intervention guidelines[16] (elective re-intervention if ''restricted cluster'' or preoperative sac). Strategy D uses the European Society for Vascular Surgery scan protocol (6-month scan omitted in patients without a previous complication/re-intervention; US in low-risk patients after 12 months) and re-intervention protocol.[16] Strategy E has no long-term follow-up: annual US surveillance to 5 years (with immediate CT confirmation for cluster and preoperative sac growth detected by US) and no further scans thereafter. This is based on the premise that most post-EVAR complications occur early, with much lower risk of rupture thereafter. Strategy F considers a novel scan protocol using a 3-month (rather than 1-month) CT scan. There is subsequently a 2-stage surveillance process, with (1) surveillance scans at 12 months and annually using portable US in a primary care setting and (2) immediate CT to look for restricted cluster complications where the US scan finds positive sac growth (>0 mm/yr pro-rata). All subsequent scans for these individuals are then via CT until re-intervention. Re-intervention is undertaken if type II endoleak with large sac growth (>5 mm/annum) or any restricted cluster complication is found at any CT scan.

Rate Estimation

Model transition rates and probabilities (Fig. 1) were estimated using individual patient data from (i) the EVAR-1[1,10] and EVAR-2[2,20] trials combined, accounting for case-mix (''base-case'') and (ii) a contemporary cohort of patients recruited from 2000 to 2015 in HUH, Finland[18] (sensitivity analysis).

For the base-case, we included all patients who had an elective EVAR operation (in either trial arm), excluding those who converted to OR during the primary operation. The HUH cohort was used only to update the rates of complications (including rupture), receipt of intervention after rupture and postoperative mortality, to reflect how the proposed strategies might perform in the same EVAR-1 patient cohort if they were treated with later generation endovascular devices, improved imaging, and re-intervention techniques. Time to each complication type, rupture, and non-AAA death was modeled, with adjustment for age, sex, and previous complications when these effects were statistically significant ($P < 0.05$). In the estimation of empirical time to re-intervention (Strategies A and B only), number of previous re-interventions were adjusted for as an a priori factor for face validity.

In the EVAR trials, complications occurred at a high rate in the 3 months after intervention (28 restricted cluster complications and 32 type II endoleaks per 100 person-years). After 6 months rates for both reduced to 3 events per 100 person-years. In HUH, rates in the first 3 months were 30 and 60 per 100 person-years for restricted cluster complications and type II endoleaks, respectively, and 3–5 events per 100 person-years after 6 months. In the EVAR trials, rates for small and large sac expansion in the first year were around 5 per 100 person-years, but the rate of small sac expansion increased in subsequent years to 11 per 100 person-years- (Supplement Table 8, http://links.lww.com/SLA/B798). Rates of large and small sac expansion were generally lower in HUH, with around 4 per 100 person-years after 2 years. Hazard ratios for factors affecting these rates (including prior occurrence of other complications) are given in

TABLE 2. Total Numbers of Events at Lifetime, for a Cohort of N = 10,000 EVAR-1-type Patients Undergoing an Initial EVAR Procedure: Using Rates Estimated from EVAR Trials

Event	Strategy A	Strategy B		Strategy C		Strategy D		Strategy E		Strategy F	
	Events	Events	% Change†	Events	% Change†	Events	% Change†	Events	% Change†	Events	% Change†
Scan policy	**Empirical**	**EVAR Policy**		**EVAR Policy**		**ESVS**		**Follow-up Until 5-yr**		**Primary Care US**	
Re-intervention policy	**Empirical**	**Empirical**		**ESVS**		**ESVS**		**ESVS**		**High Risk***	
CT scans	61,375	102,326	67%	102,867	68%	49,322	−20%	15,002	−76%	49,075	−20%
US scans	NA	NA	NA	NA	NA	51,510	NA	51,784	NA	53,094	NA
Restricted cluster complications	2503	2600	4%	2695	8%	2676	7%	2535	1%	2496	0%
Type II endoleaks	2446	2567	5%	2472	1%	2475	1%	2361	−3%	2371	−3%
Small sac growth	4948	5095	3%	4919	−1%	4918	−1%	4774	−4%	5111	3%
Large sac growth	2715	2832	4%	2785	3%	2786	3%	2682	−1%	2714	0%
Preoperative sac growth	1514	1554	3%	1687	11%	1692	12%	1611	6%	1448	−4%
Elective re-interventions	2608	3764	44%	3955	52%	3883	49%	2625	1%	2175	−17%
Emergency re-interventions	169	153	−10%	132	−22%	135	−20%	160	−5%	155	−8%
Ruptures	617	553	−10%	487	−21%	497	−19%	579	−6%	565	−8%
AAA deaths	963	930	−3%	889	−8%	897	−7%	935	−3%	915	−5%
Non-AAA deaths	9037	9070	0%	9111	1%	9103	1%	9065	0%	9085	1%
NNT to prevent 1 AAA death†	NA	304		134		150		350		205	
Mean costs, discounted‡ (% change with 95% CI)	£3440	£4966	44% (41% to 48%)	£5263	53% (41% to 66%)	£4933	44% (32% to 55%)	£3617	5% (−4% to 15%)	£2991	−13% (−19% to −7%)
Mean quality-adjusted life-years (QALYs), discounted‡ (% change with 95% CI)	5.460	5.467	0.1% (−0.2% to 0.5%)	5.484	0.4% (0% to 0.9%)	5.481	0.4% (−0.1% to 0.8%)	5.473	0.3% (0% to 0.5%)	5.477	0.3% (0.1% to 0.6%)
Incremental net benefit†,‡,§ (95% CI)	NA	−£1375 (−£1738, −£1010)		−£1333 (−£1952, −£805)		−£1072 (−£1689, −£564)		£99 (−£347, £535)		£804 (−£489, £1201)	

Figures in Strategies B-F are numbers of underlying complications (rather than detected complications).

*Restricted cluster complication or type II endoleak plus large sac growth.

†Compared to Strategy A.

‡Means with uncertainty intervals derived from 1000 probabilistic sensitivity analysis iterations.

§Calculated at a willingness to pay of £20,000 per QALY.

CI indicates confidence interval; CT, computed tomography; EVAR, elective endovascular aneurysm repair; NNT, number needed to treat; US, ultrasound.

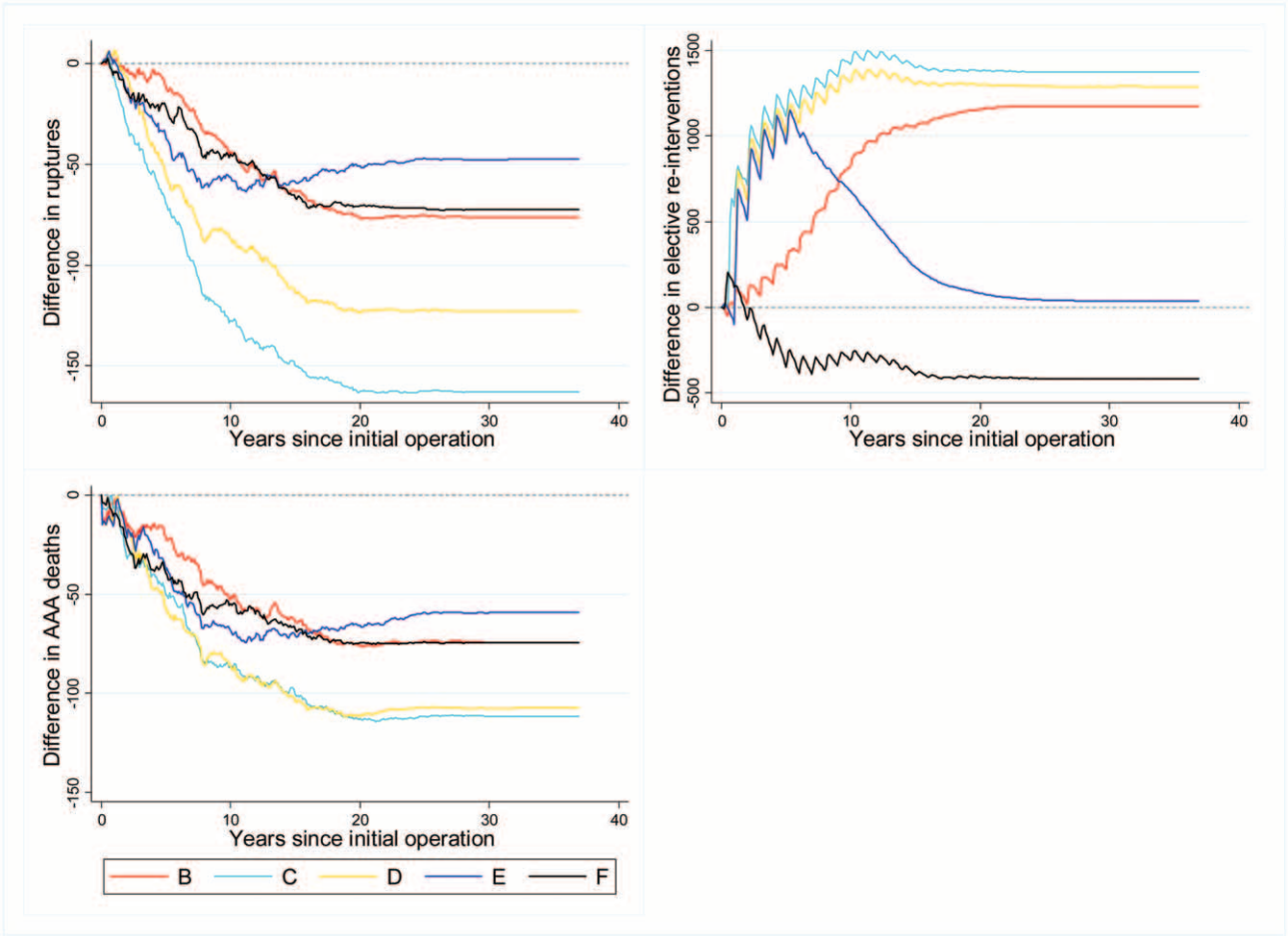

FIGURE 2. Differences in numbers of key events for Strategies B-F compared to Strategy A, for 10,000 individuals (lifetime models based on rates estimated from EVAR trials). EVAR indicates elective endovascular aneurysm repair.

Supplement Tables 3, http://links.lww.com/SLA/B798 and 4, http://links.lww.com/SLA/B798. The occurrence of small or large sac expansion increased the restricted cluster complication (ie, migration, kinking, type I or III endoleak) rate by approximately 60% in the EVAR trials. In the EVAR trials, 28% of those rupturing had an emergency re-intervention; 30-day postoperative mortality (AAA-related) was 2.6% after the initial EVAR operation, 1.7% after elective re-intervention, and 27% after emergency re-intervention (Supplement Table 4, http://links.lww.com/SLA/B798). In HUH, 30-day postoperative mortality was much lower at 0.3% after the initial operation and 0.9% after elective re-intervention.

Costs and Health-related Quality of Life (HRQOL)

The perspective is that of the UK National Health Service, the price year is 2015/2016, and the discount rate is 3.5% per year.[21] Costs were ascribed to scans, emergency, and elective re-interventions.[22] The cost of the initial aneurysm repair was not included as the study is concerned only with postintervention follow-up. Mean life-years were calculated as the meantime to all-cause mortality. Quality-adjusted life-years (QALYs) accounted for reduced HRQOL after elective and emergency re-interventions. Costs, HRQOL weights (utilities) and scan sensitivity to detect complications are given in the Supplement, http://links.lww.com/SLA/B798.

Model Implementation and Validation

The model was run for 500,000 iterations (see Supplement, http://links.lww.com/SLA/B798), where each iteration represents a hypothetical individual drawn randomly from the required population. For the Strategy A validation, draws are made from a population with the same age and sex distributions as the EVAR-1 and EVAR-2 trials, and run for up to 15 years to match trial follow-up. Subsequently, for strategies A-F, draws were made from a population with EVAR-1-like age and sex characteristics and run until death to give a lifetime time-horizon. Event numbers for the initial validation were scaled to the cohort size (N = 848) for comparison with observed data. For the strategy comparisons, event numbers are scaled to a cohort of 10,000 patients.

A probabilistic sensitivity analysis was undertaken to quantify uncertainty in the outcomes. One thousand Monte Carlo simulations, each with 100,000 hypothetical individuals, were performed with regression parameters for each transition sampled jointly from their asymptotic multivariate distributions (see Supplement, http://links.lww.com/SLA/B798). The overall mean cost, QALYs and incremental net benefit compared to Strategy A were calculated and uncertainty summarized using the 2.5th and 97.5th percentiles.

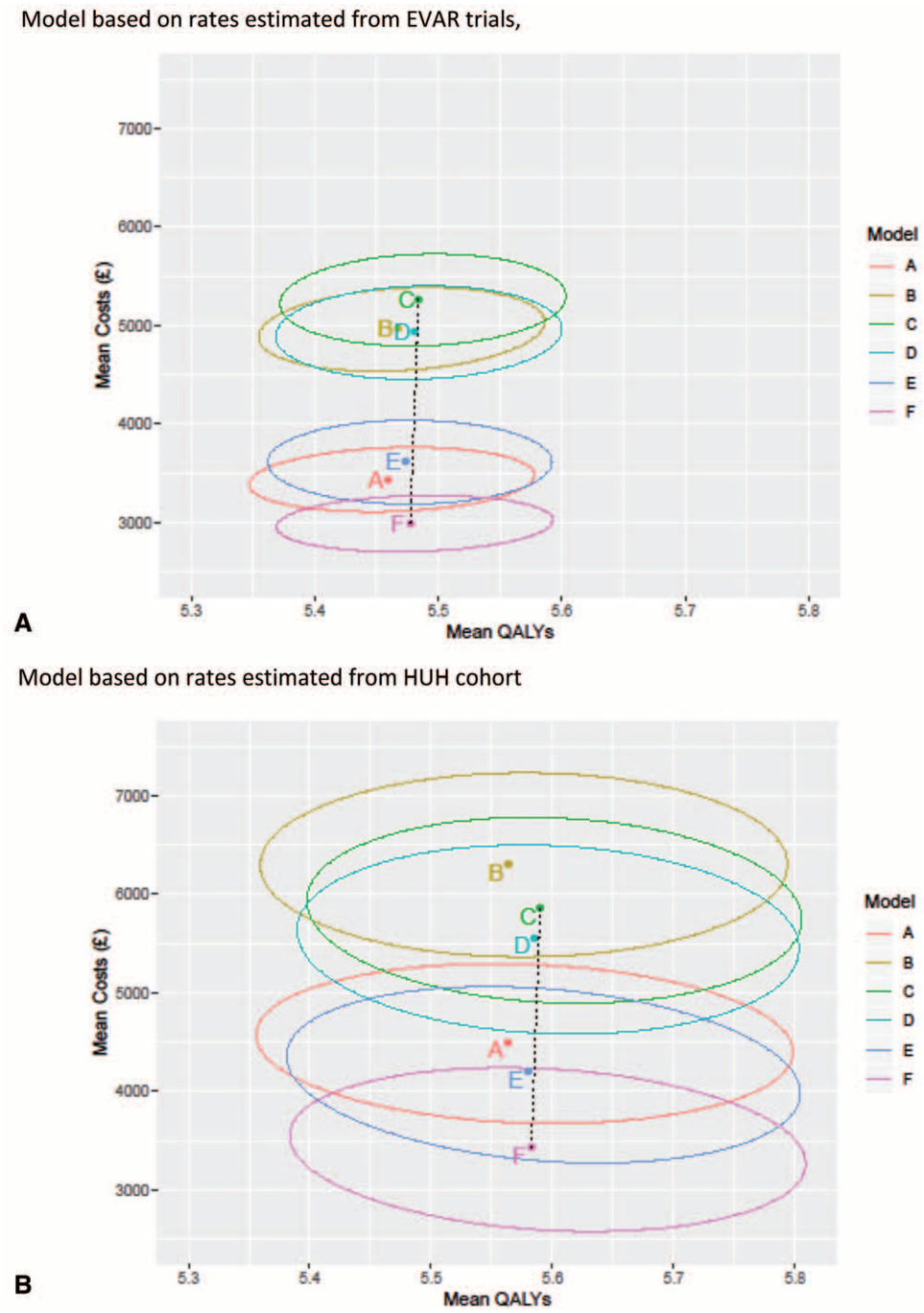

FIGURE 3. Contour plots (ellipses) with efficiency frontier (dotted line) for lifetime results from Strategies A-F, using (A) Model based on rates estimated from EVAR trials, (B) Model based on rates estimated from HUH cohort. EVAR indicates elective endovascular aneurysm repair; HUH, Helsinki University Hospital.

Sensitivity Analyses

Sensitivity analysis is used to investigate how robust model outputs are (mean total cost and mean QALYs) to variation in model inputs. The cost and sensitivity of US in primary care to detect sac growth (Strategy F) is uncertain, as this technology has not been implemented. The base-case assumes US detects all sac growth events with the cost of a primary care US taken from NHS reference costs for an in-hospital US scan (minus any outpatient costs). In sensitivity analysis I, the base-case cost for a US scan (£58) was doubled in a one-way sensitivity analysis. In sensitivity analysis II, it was assumed that 40% of sac growth events go undetected via this method. Sensitivity analysis III is a multi-way sensitivity analysis using rates of complications and operative mortality estimated from HUH data, and re-evaluating all 6 strategies based on these rates.

RESULTS

Model Validation

Strategy A simulates the surveillance and re-intervention rates as seen in the EVAR 1 and 2 trials and is used to validate the discrete

TABLE 3. Sensitivity Analysis I and II Results: Total Numbers of Events at Lifetime, for a Cohort of N = 10,000 EVAR-1-type Patients Undergoing an Initial EVAR Procedure: Using Rates Estimated from EVAR Trials

Event	Strategy A	Strategy F		Strategy F: Sensitivity Analysis I		Strategy F: Sensitivity Analysis II	
	Events	Events	% Change†	Events	% Change†	Events	% Change†
Scan Policy	**Empirical**	**Primary Care US**		**As F With Primary Care US Cost ×2**		**As F With Primary Care US Sensitivity = 0.6**	
Re-intervention Policy	**Empirical**	**High Risk***		**High Risk***		**High Risk***	
CT scans	61,375	49,075	−20%	As strategy F		45,434	−26%
US scans	NA	53,094	NA			56,176	NA
Restricted cluster complications	2503	2496	0%			2481	−1%
Type II endoleaks	2446	2371	−3%			2368	−3%
Small sac growth	4948	5111	3%			5078	3%
Large sac growth	2715	2714	0%			2702	0%
Preoperative sac growth	1514	1448	−4%			1450	−4%
Elective re-interventions	2608	2175	−17%			2081	−20%
Emergency re-interventions	169	155	−8%			162	−4%
Ruptures	617	565	−8%			583	−6%
AAA deaths	963	915	−5%			923	−4%
Non-AAA deaths	9037	9085	1%			9077	0%
NNT to prevent 1 AAA death†	NA	205		As strategy F		246	
Mean costs, discounted‡	£3391	£2964	−13%	£3223	−5%	£2839	−16%
Mean quality-adjusted life-years (QALYs), discounted‡	5.491	5.507	0.3%	5.507	0.3%	5.505	0.3%
Incremental net benefit†,‡,§	NA	£738		£478		£832	

Figures in Strategies F are numbers of underlying complications (rather than detected complications).
*Restricted cluster complication or type II endoleak plus large sac growth.
†Compared to Strategy A.
‡Calculated deterministically.
§Calculated at a willingness to pay of £20,000 per QALY.
CT indicates computed tomography; EVAR, elective endovascular aneurysm repair; NNT, number needed to treat; US, ultrasound.

event simulation (see Supplement, http://links.lww.com/SLA/B798). Predicted numbers of events at 15 years were generally well-calibrated (within ±10%) with the observed events in the trials (Table 1).

Model Outputs

All strategies showed a reduction in ruptures compared to Strategy A with the largest reductions in Strategies C and D (Table 2). Strategies B, C, and D also showed large increases in elective re-interventions; in the case of Strategies B and C because there were more CT scans, and in the case of Strategies C and D because these models also assumed adherence to a strict re-intervention policy. Fig. 2 shows the differences in events over time for each lifetime model compared to Strategy A.

Because Strategy F only sends patients with US-detected sac growth (and not those with restricted cluster events alone) for CT and possible re-intervention, this policy has considerably fewer elective re-interventions than other strategies. There are fewer ruptures than Strategy A, though ruptures are higher than the more intense surveillance strategies (Strategies C and D). Strategies C and D are the most clinically effective strategies giving a 7%–8% reduction in AAA deaths compared with Strategy A. Nevertheless, as these patients are elderly, this does not translate to substantially increased life-years. Strategy F shows a 13% reduction in costs, which arises because US scans in primary care are substantially cheaper than in hospital and because there are considerably fewer elective re-interventions. Overall, compared to Model A, the number needed to treat to prevent 1 AAA death is lowest in Strategies C and D, highlighting the clinical effectiveness of these strategies (Table 2).

In the base case model, Strategies A, B, and E would not be cost-effective at any willingness to pay for a QALY, because they are more expensive and less effective than other options. (Fig. 3A). Strategy C offers a slightly greater QALY gain than F, but at considerably greater cost, giving an incremental cost-effectiveness ratio (ICER) for C versus F of over £325,000/QALY. Strategy D would not be considered cost-effective because it has an even higher ICER compared to Strategy F, but fewer QALYs than C. At a willingness to pay of £20,000/QALY, after accounting for parameter uncertainty, the likelihood that Strategy F is the most cost-effective option is over 90%.

Sensitivity Analyses

Sensitivity analysis I examined the impact of doubling the cost of US scan in primary care, from £58 to £116. The mean total cost per patient increased by 9% compared to a model using £58, but strategy F was still the most cost-effective. Sensitivity analysis II investigated the impact of a reduction in accuracy of US in primary care to detect sac growth from 100% to 60%. This reduced the clinical effectiveness by 8%, but also reduced CT scans, elective re-interventions, and costs; strategy F was still the most cost-effective (Table 3).

Modeling based on HUH event rates (sensitivity analysis III) shows a similar pattern of results (Table 4), though the absolute numbers of ruptures are higher (due to a higher observed rupture rate in HUH) whilst AAA deaths are lower, due to substantially improved postoperative mortality after elective (re)-interventions. Similarly to the base case model, Strategies A, B, and E would not be cost-effective at any willingness to pay for a QALY (Fig. 3B). The ICER for C versus F using the HUH data is over £346,000/QALY; D versus F has an even higher ICER compared to F, but fewer QALYs than C. At a willingness to pay of £20,000/QALY, the probability that Strategy F is the most cost-effective option remains over 90%.

TABLE 4. Sensitivity Analysis III Results: Total Numbers of Events at Lifetime, for a Cohort of N = 10,000 EVAR-1-type Patients Undergoing an Initial EVAR Procedure: Using Rates Estimated from HUH Cohort

Event	Strategy A	Strategy B		Strategy C		Strategy D		Strategy E		Strategy F	
	Events	Events	% Change†	Events	% Change†	Events	% Change†	Events	% Change†	Events	% Change†
Scan Policy	**Empirical**	**EVAR Policy**		**EVAR Policy**		**EJVES**		**Follow-up Until 5-yr**		**Primary Care US**	
Re-intervention Policy	**Empirical**	**Empirical**		**EJVES**		**EJVES**		**EJVES**		**High Risk***	
CT scans	62,892	104,436	66%	105,940	68%	61,620	−2%	15,453	−75%	33,750	−46%
US scans	NA	NA	NA	NA	NA	41,282	NA	53,962	NA	69,481	NA
Restricted cluster complications	2796	2928	5%	2970	6%	2950	6%	2798	0%	2651	−5%
Type II endoleaks	5525	5954	8%	5435	−2%	5434	−2%	5098	−8%	5209	−6%
Small sac growth	2712	2753	2%	2662	−2%	2674	−1%	2642	−3%	2833	−5%
Large sac growth	2787	2861	3%	2853	2%	2846	2%	2761	−1%	2906	4%
Preoperative sac growth	1474	1543	5%	1602	9%	1593	8%	1528	4%	1356	−8%
Elective re-interventions	3390	4953	46%	4033	19%	3944	16%	2658	−22%	2409	−29%
Emergency re-interventions	455	434	−5%	397	−13%	399	−12%	432	−5%	416	−9%
Ruptures	897	866	−3%	794	−11%	802	−11%	861	−4%	839	−6%
AAA deaths	694	688	−1%	624	−10%	634	−9%	663	−4%	648	−7%
Non-AAA deaths	9306	9312	0.1%	9376	0.8%	9366	0.6%	9337	0.3%	9352	0.5%
NNT to prevent 1 AAA death†	NA	1667		143		167		323		217	
Mean costs, discounted‡ (% change with 95% CI)	£4499	£6302	40% (33% to 47%)	£5854	30% (17% to 45%)	£5557	24% (11% to 38%)	£4192	−7% (−17% to 3%)	£3429	−24% (−32% to −14%)
Mean quality-adjusted life-years (QALYs), discounted‡ (% change with 95% CI)	5.563	5.564	0% (−0.4% to 0.4%)	5.590	0.5% (0% to 1.4%)	5.585	0.4% (−0.1% to 1.2%)	5.580	0.3% (0% to 0.7%)	5.583	0.3% (0% to 0.8%)
Incremental net benefit†,‡,§ (95% CI)	NA	−£1793 (−£2319, −£1199)		−£825 (−£1676, £136)		−£628 (−£1480, £305)		£635 (£68, £1221)		£1456 (£885, £2061)	

Figures in Strategies B-F are numbers of underlying complications (rather than detected complications).
*Restricted cluster complication or type II endoleak plus large sac growth.
†Compared to Strategy A.
‡Means and uncertainty intervals derived from 1000 probabilistic sensitivity analysis iterations.
§Calculated at a willingness to pay of £20,000 per QALY.
CI indicates confidence interval; CT, computed tomography; EVAR, elective endovascular aneurysm repair; NNT, number needed to treat; US, ultrasound.

DISCUSSION

Follow-up surveillance in the EVAR trials did not closely follow protocol and may have been sub-optimal. Deviations from protocol arose as postoperative care decisions were made in the absence of evidence to inform best practice. Modeling of full protocol adherence confirmed that this approach would have reduced ruptures and AAA deaths; however, the results also suggest that there would have been an associated large increase in elective re-interventions, which come at a considerable extra cost. Furthermore, all the other strategies we considered increased mean life-years compared to the observed data.

Among the 5 alternative postoperative surveillance strategies evaluated, European Society guidelines offer the largest clinical benefit, but the difference between strategies in terms of QALYs is very small. A primary care US strategy provides substantial cost savings, and therefore results in the most cost-effective approach to post-EVAR care.

Adopting a strategy of primary care US scanning that only measures sac growth has a number of implications. In the EVAR trials, 62% of new restricted cluster complications (ie, kinking, migration, endoleak type I and III) are not preceded by recorded sac growth. Such individuals would not receive elective re-intervention under this strategy until sac growth causes them to be sent for a CT scan, where the cluster complication can be identified. Therefore this primary care strategy may delay elective re-intervention in these patients if sac growth is not evident. However, this also means that elective re-intervention is restricted only to those most at risk of future rupture, thus considerably reducing overall costs. This strategy also reduces CT scans, further reducing costs, and is likely to be preferred by patients, who are able to remain at or near home and to avoid annual hospital visits.

Our modeling uses real-world data from ground-breaking clinical trials. The data from the EVAR-1 and EVAR-2 trials covers up to 15 years follow-up, hence life-time extrapolation for these patients, whose average age is 75, can be considered reasonably robust. Internal validation of the model against the observed data performed well, giving confidence that the model provides a good representation of the underlying system. Additionally, modeling using contemporary data from Helsinki suggests that conclusions regarding the optimal surveillance strategy are unchanged in patients with current-generation endovascular devices.

Nevertheless, the study employs some assumptions, which may be limitations. To provide the most robust estimates possible of event rates, data from patients in both the EVAR-1 and EVAR-2 trials were pooled (averaged), though there may be some additional frailty for scan recall and events in the EVAR-2 patients not accounted for by factors included in our rate modeling. A common strategy is employed across all patients in each of the strategies; a larger dataset may enable exploration of the possibility that a stratified approach may further maximize clinical benefits. The study considers that handheld portable US carried out quickly and cheaply in primary care (without a hospital outpatient visit) can accurately identify those most at risk of future rupture by using an indicator of any sac growth over 0 mm/annum.[23] However, US-measured sac diameters may be subject to significant inter-observer variability,[24] leading to less accurate detection of true sac growth. Uncertainty regarding the cost and accuracy of primary care-based US to detect sac growth was assessed in sensitivity analyses, and did not materially affect the results. The study also does not assume that primary care-based US could confirm cluster complications, which would still require hospital CT. However, these results should be treated with caution, as such an approach requires full testing and validation of feasibility, sensitivity, and specificity in primary care before recommendation.

This work has not included an OR policy arm. Nevertheless, these findings have important implications relevant to the ongoing debate regarding the cost-effectiveness of EVAR versus OR. A previous analysis using long-term follow-up data from the EVAR-1 trial showed small QALY gains for EVAR but significantly higher mean lifetime costs of over £3500, with an ICER of over £200,000.[6] This analysis assumed a postoperative surveillance policy similar to Strategy A. We have shown that alternative surveillance and re-intervention policies may increase QALYs gained. Furthermore, a new policy using primary care US additionally reduces costs considerably and can be expected to substantially improve cost-effectiveness of EVAR in comparison to OR. Comprehensive comparison of EVAR versus OR using latest devices, imaging, endovascular re-intervention techniques and local anesthetic for shorter hospital stays is, therefore, needed.

Box 1 Summary of Results (Base-case)

- Strategy B. Had the EVAR trials followed scan protocol, we estimate a reduction of AAA deaths of 3% compared to what was observed, but an increase of elective re-interventions of 44%, making this a costly strategy.
- Strategies C (ESVS guidelines for re-intervention) and D (full ESVS guidelines) would be clinically the most effective strategies, with a 20% reduction in ruptures and 7%–8% reduction in AAA-related deaths. However, elective re-interventions increase by ~50%.
- Strategy E (annual follow-up with CT, terminated at 5-yr) reduces AAA-deaths by 3%, though this strategy is neither the most clinically effective or cheapest option.
- Strategy F (annual primary care US) is not the most clinically effective strategy but is the cheapest, and could still reduce ruptures by 8% and AAA-related deaths by 5%. It is the most cost-effective option, although the cost and sensitivity/precision of a hand-held primary care ultrasound scan is currently uncertain so results should be treated with a degree of caution.

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