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# Economic implications of screening strategies in arteriovenous fistulae

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Practice guidelines recommend performing angiography in arteriovenous fistulae (AVF) when access blood flow (Qa) is <500 ml/min, but a Qa threshold of <750 ml/min is more sensitive for stenosis. No economic evaluation has evaluated the optimal Qa threshold for angiography in AVF, or determined whether screening AVF is more economically efficient than intervening only when AVF is thrombosed. We compared two screening strategies using Qa thresholds of <750 and <500 ml/min, respectively, with no access screening. Expected per-patient access-related costs (in 2002 Canadian dollars) were \$3910, \$5130, and \$5250 in the no screening, Q<sub>A</sub>500, and Q<sub>A</sub>750 arms, respectively over 5 years. Notably, screening strategies did not reduce expected access-related costs under any clinically plausible scenario. The cost to prevent one episode of AVF failure appeared to be approximately \$8000–\$10 000 over 5 years for both screening strategies, compared with no screening. Although the incremental cost effectiveness of screening (compared to no screening) was similar in the base case for the Q<sub>A</sub>500 and Q<sub>A</sub>750 strategies, the relative economic attractiveness of the Q<sub>A</sub>750 strategy was adversely affected under several plausible scenarios. Also, the Q<sub>A</sub>750 strategy would require many additional angiograms to prevent an additional episode of AVF failure, compared with the Q<sub>A</sub>500 strategy. Screening of AVF resulted in a modest increase in net costs, and seems to require a net expenditure of ~\$9000 to prevent one episode of AVF failure. If screening is adopted, our findings suggest that angiography should be performed when Qa is <500 rather than <750 ml/min, especially when access to angiography is limited.

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Measurement of access blood flow (Qa) identifies stenosis in native vessel arteriovenous fistulae (AVF),<sup>1</sup> and correction of stenosis improves access patency.<sup>2</sup> Canadian clinical practice guidelines recommend performing angiography in AVF when Qa <500 ml/min,<sup>3</sup> which is associated with a positive predictive value for stenosis of approximately 70%. Recent data suggest that performing angiography when Qa is <750 ml/min has a higher sensitivity for stenosis without unduly reducing specificity compared with the <500 ml/min threshold,<sup>2</sup> although this is controversial.<sup>1</sup> In addition to the potential clinical benefits of access flow measurements, a retrospective study suggests that access blood flow measurements reduce resource use.<sup>4</sup>

In theory, a higher Qa threshold such as <750 ml/min might improve patency rates by detecting more AVF with significant stenoses – allowing them to be preemptively treated with angioplasty. On the other hand, Qa of 500–750 ml/min are commonly observed in AVF with no clinical evidence of dysfunction.<sup>5</sup> As thrombosis is relatively infrequent in AVF, and rarely occurs when Qa is >350 ml/min,<sup>2</sup> a higher Qa threshold might lead to increased resource use (i.e. angiograms and angioplasties) without improving access patency. However, a formal economic evaluation has not been performed to test this hypothesis, or to determine whether screening AVF for subclinical stenosis is a better use of scarce resources than reserving intervention for AVF which have thrombosed.

To assess the economic efficiency of access flow monitoring in AVF, and in an attempt to define the optimal threshold values for angiography in patients with AVF, we performed an economic evaluation to examine the costs and consequences of different Qa thresholds for angiography in patients with native vessel AVF. We compared three strategies: Qa thresholds for angiography of <750 and <500 ml/min, respectively, and a comparator arm which involved no access screening.

## RESULTS

### Model predictions and face validity

Table 1 shows the outcomes and costs associated with each strategy over 5 years in the base case scenario. The model predicted that the proportion of patients who would

**Table 1 | Outcomes and costs associated with each strategy over 5 years: base case**

Outcome variables	No screen	Q <sub>A</sub> 500	Q <sub>A</sub> 750
Proportion of patients who develop AVF thrombosis (%)	45.2	19.6	17.1
Proportion of patients who develop complete AVF failure owing to thrombosis (requiring temporary catheter) (%)	23.4	9.8	8.4
Mean number of months for which original AVF is used for dialysis	34.8	37.0	37.2
Proportion of patients dead by 5 years (%)	41.0	41.0	41.1
Proportion of patients transplanted by 5 years (%)	9.9	10.1	10.0
Proportion of patients who had an angiogram performed (%)	40.2	66.9	83.0
Mean number of angiograms per patient	0.40	1.27	1.55
Proportion of patients who had an angioplasty performed to treatment stenosis (%)	40.2	64.6	74.0
Mean number of angioplasties per patient	0.40	1.23	1.38
Mean number of catheter placements per patient over 5 years	0.679	0.251	0.229
Proportion of patients who ended up dialyzing with a permanent catheter (%)	14.5	5.3	4.9
Proportion of patients who end up dialyzing with an AVF created at a different location (%)	6.6	2.8	2.4
Proportion of patients who end dialyzing with a graft (%)	4.5	1.9	1.7
Access-related costs over 5 years (discounted at 5% in base case)	\$3910	\$5130	\$5250
Number needed to screen to prevent one AVF failure		7.4 <sup>a</sup>	71 <sup>b</sup>
Incremental cost to prevent one AVF failure		\$9030	\$8520
Cost of screening	\$0	\$1180	\$1200
Cost of maintaining access patency i.e. angiograms, angioplasties, and declotting, temporary catheters	\$3300	\$3770	\$3880
Cost of new access surgeries	\$610	\$180	\$170

AVF, arteriovenous fistulae.

<sup>a</sup>Q<sub>A</sub>500 compared to No screen strategy.

<sup>b</sup>Q<sub>A</sub>750 compared to Q<sub>A</sub>500 strategy.

experience an episode of access thrombosis would range from 45.2% in the no screening arm, to 19.6 and 17.1% in the Q<sub>A</sub>500 and Q<sub>A</sub>750 strategies, respectively. The proportion of patients predicted to experience fistula loss under each scenario was 23.4, 9.8, and 8.4%, respectively. By design, mortality and transplantation rates did not vary between screening strategies. The model predicted that 81.9% of patients with untreated stenosis who did not die or receive a transplant would experience AVF failure over a 5-year period. The similarity of this prediction to the estimates from the control arm of a recent randomized trial of patients with AVF stenosis<sup>6</sup> suggests that the model had reasonable validity.

### Base case scenario

The expected proportion of patients requiring angiograms and angioplasties, and the total predicted number of such procedures were substantially higher under the Q<sub>A</sub>750 and Q<sub>A</sub>500 strategies, compared with no screening (Table 1). In addition, the expected proportion of patients who would require a dialysis catheter, placement of a new AVF, or placement of a graft were all approximately three times higher when access screening was not performed compared with either of the screening arms. Expected per-patient access-related costs were \$3910, \$5130, and \$5250 in the no screening, Q<sub>A</sub>500, and Q<sub>A</sub>750 arms, respectively. Notably, access-screening strategies did not reduce expected access-related costs under any clinically plausible scenario.

In the base case scenario, the Q<sub>A</sub>500 and Q<sub>A</sub>750 strategies were associated with superior clinical outcomes and higher costs compared with the NS strategy. In the base case analysis, the relative gain in efficacy of the Q<sub>A</sub>750 strategy per additional dollar spent (compared with the Q<sub>A</sub>500 strategy) was similar to the relative gain in efficacy of the Q<sub>A</sub>500 strategy (compared with the NS strategy). Thus, in the base

case, the relative economic attractiveness of the two screening strategies was very similar, although the Q<sub>A</sub>750 strategy was associated with a higher use of radiological resources.

To offer a more concrete example, consider a hypothetical dialysis unit which currently treats 100 patients with AVF but does not perform access screening. Our model predicts that if such a facility were to adopt the Q<sub>A</sub>500 strategy, additional costs of \$122 000 would result over 5 years. The expected number needed to screen to prevent one episode of access failure was 7.4, meaning that the hypothetical dialysis unit would be expected to observe 13.5 fewer episodes of fistula loss under the Q<sub>A</sub>500 strategy (vs no screening), and avert the placement of 43 hemodialysis catheters over 5 years.

In comparison, for a hypothetical dialysis unit of 100 patients, which was performing screening using the Q<sub>A</sub>500 strategy, the model predicted that adopting the Q<sub>A</sub>750 strategy instead would result in 28 additional angiograms, avert the placement of two hemodialysis catheters, and result in 1.4 fewer episodes of fistula loss – while increasing net costs by approximately \$12 000 over 5 years.

### Sensitivity analyses

In most of the sensitivity analyses, the Q<sub>A</sub>500 strategy appeared slightly more attractive than the Q<sub>A</sub>750 strategy. In some scenarios, the Q<sub>A</sub>500 strategy was eliminated by extended dominance (see Materials and Methods section). In all such cases, the absolute difference between the Q<sub>A</sub>500 and Q<sub>A</sub>700 strategies was very small, suggesting that either strategy might be appropriate. However, there were several scenarios in which the Q<sub>A</sub>500 strategy was substantially more attractive than the Q<sub>A</sub>750 strategy. For example, a scenario in which screening was less sensitive and specific for stenosis (i.e. consistent with the only other prospective study that subjected all patients undergoing access flow monitoring to

angiography<sup>7</sup>) resulted in costs per fistula loss averted of \$10 150 and \$25 530 for the  $Q_A500$  (vs no screening) and  $Q_A750$  (vs  $Q_A500$ ) strategies, respectively (Table 2).

#### **Sensitivity analyses: likelihood of stenosis and AVF thrombosis**

Increasing the prevalence of stenosis or the risk of AVF thrombosis improved the predicted cost effectiveness of both screening strategies, compared with the base case (Table 2). On the other hand, reducing the prevalence of stenosis or the risk of thrombosis substantially decreased the economic attractiveness of the  $Q_A750$  strategy (compared with the  $Q_A500$  strategy) (Table 2).

#### **Sensitivity analyses: availability and effectiveness of angioplasty and declothing**

The assumption that underlies the use of screening strategies in AVF is that preemptive correction of stenosis with angioplasty improves outcomes compared with an expectant approach of declothing AVF after thrombosis. Therefore, both screening strategies appeared more favorable in scenarios in which angioplasty was more effective for preventing thrombosis in stenotic but functioning AVE, when AVF declothing was less effective than in the base case, or when facilities for AVF declothing were unavailable (Table 2). In the base case analysis, AVF that had undergone successful declothing were no longer screened and their subsequent survival was based on the available literature (Table 3).<sup>13–17</sup> We reanalyzed the model assuming that screening (and angioplasty, if required) was continued after successful declothing, which did not substantially alter our results (data not shown). Conversely, reducing the efficacy of angioplasty for correction of stenosis, as might be observed in clinical practice, reduced the economic attractiveness of both screening strategies.

#### **Sensitivity analyses: costs of screening procedure and health care**

Results were sensitive to the cost of the screening procedure. As expected, increasing the cost of access screening by 50% reduced the economic attractiveness of access screening. The results of our analysis were not sensitive to plausible changes in the estimates used for the cost of health care.

#### **Sensitivity analyses: failure rate in AVF with stenosis but $Q_a > 500$ ml/min**

The base case analysis used data from a recent randomized trial to estimate the risk of failure in AVF with  $Q_a > 500$  ml/min, despite untreated subclinical stenosis (11.3% per year).<sup>6</sup> However, another recent publication indicates that the risk of AVF loss in this situation is markedly lower.<sup>1</sup> When this latter scenario was modeled in sensitivity analysis, the economic attractiveness of the  $Q_A500$  strategy (compared with no screening) remained unchanged, but the  $Q_A750$  strategy became considerably less attractive. Results were similar in an intermediate scenario in which the risk of AVF loss in AVF with untreated subclinical stenosis and  $Q_a > 500$  ml/min was

5.7% per year. Thus, our findings were sensitive to the prognosis of AVF with  $Q_a$  between 500 and 750 ml/min.

#### **Summary of findings from sensitivity analysis**

In sensitivity analysis, the predicted net increase in costs from screening 100 patients over 5 years ranged from as low as \$55 000 to as high as \$180 300 for the  $Q_A500$  strategy, and from \$69 000 to \$192 500 for the  $Q_A750$  strategy (each compared with no screening). The results of the model were not sensitive to plausible variations in the cost of health care, rate of transplantation, overall risk of death, or discounting rate. More detailed results of the sensitivity analyses appear in the Supplementary Appendix.

#### **Cost implications of AVF screening**

There are approximately 280 000 hemodialysis patients in the United States, of whom approximately 27–30% have AVE. Our base case analysis suggests that the placement of approximately 34 500 dialysis catheters could be averted, and 11 400 cases of AVF failure prevented over 5 years if all dialysis providers adopted the  $Q_A500$  strategy, compared with a scenario in which no screening was performed. However, these clinical benefits would apparently require an additional net outlay of approximately \$100 million, representing an average of \$20 million annually.

#### **DISCUSSION**

This economic analysis used the best available data to project the costs and consequences of two strategies for the screening of AVF for stenosis, compared with no screening. The model suggested that screening is associated with a modest net increase in access-related costs, regardless of the  $Q_a$  threshold for angiography that is selected. In the base case scenario, the mean increase in per-patient access-related costs associated with screening was \$1220 and \$1340 over 5 years for the  $Q_A500$  and  $Q_A750$  strategies, respectively. Thus, a hypothetical dialysis unit with 100 patients with AVF that did not perform screening could expect to spend an additional \$122 000 over 5 years to adopt the  $Q_A500$  strategy, or \$134 000 to adopt the  $Q_A750$  strategy.

We expressed the benefit associated with access screening in terms of reductions in fistula loss and exposure to central venous catheters. In the base case analysis, the model predicted that 13.6 and 15% fewer patients would experience fistula loss over 5 years in the  $Q_A500$  and  $Q_A750$  strategies, and that 9.2 and 9.6% fewer patients would require a permanent dialysis catheter over 5 years in the  $Q_A500$  and  $Q_A750$  strategies. Although the monetary value of preventing these outcomes is difficult to quantify, the absolute increases in cost associated with screening were relatively modest, suggesting that screening may represent good value for money.

We performed a variety of sensitivity analyses to determine which characteristics were likely to influence the cost effectiveness of screening AVF for subclinical stenosis. Both screening strategies appeared most economically

**Table 2 | Sensitivity analysis**

Outcome variables	No screening	QA500	QA750
<i>Base case analysis</i>			
Access-related costs over 5 years	\$3910	\$5130	\$5250
Number needed to screen to prevent one AVF failure		7.4	71
Incremental cost to prevent one AVF failure		\$9030 <sup>a</sup>	\$8520
<i>Screening strategies less sensitive and specific for stenosis<sup>7</sup></i>			
Access-related costs over 5 years	\$3910	\$5360	\$5590
Number needed to screen to prevent one AVF failure		7	111
Incremental cost to prevent one AVF failure		\$10 150	\$25 530
<i>Prevalence of stenosis reduced to 0.3</i>			
Access-related costs over 5 years	\$3610	\$4900	\$5060
Number needed to screen to prevent one AVF failure		7.8	143
Incremental cost to prevent one AVF failure		\$10 080	\$22 860
<i>Prevalence of stenosis increased to 0.6</i>			
Access-related costs over 5 years	\$4190	\$5330	\$5430
Number needed to screen to prevent one AVF failure		6.3	52.6
Incremental cost to prevent one AVF failure		\$7170 <sup>a</sup>	\$5260
<i>Effectiveness of angioplasty at reducing AVF failure reduced by 50%</i>			
Access-related costs over 5 years	\$3910	\$5276	\$5424
Number needed to screen to prevent one AVF failure		8.9	111
Incremental cost to prevent one AVF failure		\$12 090	\$16 440
<i>Effectiveness of angioplasty at reducing AVF failure improved by 50%</i>			
Access-related costs over 5 years	\$3910	\$4890	\$5000
Number needed to screen to prevent one AVF failure		5.9	59
Incremental cost to prevent one AVF failure		\$5760	\$6470
<i>Risk of AVF failure reduced by 50% in all groups</i>			
Access-related costs over 5 years	\$3100	\$4820	\$4960
Number needed to screen to prevent one AVF failure		10.9	125
Incremental cost to prevent one AVF failure		\$18 700	\$17 500
<i>Risk of AVF failure increased by 50% in all groups</i>			
Access-related costs over 5 years	\$4390	\$5350	\$5470
Number needed to screen to prevent one AVF failure		6.4	55.6
Incremental cost to prevent one AVF failure		\$6110	\$6670
<i>AVF declotting not performed in any patients</i>			
Access-related costs over 5 years	\$4360	\$5210	\$5290
Number needed to screen to prevent one AVF failure		3.9	40
Incremental cost to prevent one AVF failure		\$3350 <sup>a</sup>	\$3200
<i>Probability of AVF declotting reduced to 0.5 (from 1.0) and efficacy of declotting reduced to 0.5 (from 0.89)</i>			
Access-related costs over 5 years	\$4310	\$5,270	\$5,370
Number needed to screen to prevent one AVF failure		4.6	4.3
Incremental cost to prevent one AVF failure		\$4420	\$4560
<i>AVF failure rate in patients with untreated stenosis with Qb &gt; 500 ml/min from observational data<sup>1</sup></i>			
Access-related costs over 5 years	\$3860	\$4950	\$5120
Number needed to screen to prevent one AVF failure		6.6	250
Incremental cost to prevent one AVF failure		\$7220	\$42 500
<i>Mortality risks assumed different for patients with AVF, graft, line</i>			
Access-related costs over 5 years	\$3860	\$5070	\$5160
Number needed to screen to prevent one AVF failure		7.1	66.7
Incremental cost to prevent one AVF failure		\$8580 <sup>a</sup>	\$6000
<i>Cost of screening procedure increased by 50%</i>			
Access-related costs over 5 years	\$3910	\$5713	\$5835
Number needed to screen to prevent one AVF failure		7.4	71
Incremental cost to prevent one AVF failure		\$13 340 <sup>a</sup>	\$8660

Table 2 | Continued

Outcome variables	No screening	Q <sub>A</sub> 500	Q <sub>A</sub> 750
<i>Cost of screening procedure decreased by 50%</i>			
Access-related costs over 5 years	\$3910	\$4460	\$4600
Number needed to screen to prevent one AVF failure		7.4	71
Incremental cost to prevent one AVF failure		\$4070	\$9940

AVF, arteriovenous fistulae.

The Q<sub>A</sub>500 strategy is compared with no screening, and the Q<sub>A</sub>750 strategy is compared with the Q<sub>A</sub>500 strategy.

<sup>a</sup>Although the Q<sub>A</sub>500 strategy was more effective than the no screening strategy, it was associated with a higher incremental cost to prevent one AVF failure than the Q<sub>A</sub>750 strategy (compared with the Q<sub>A</sub>500 strategy), and as such, the Q<sub>A</sub>500 is ruled out by extended dominance. In these cases, selection of the Q<sub>A</sub>750 strategy provides more clinical benefit per dollar spent, although more resources would be required per patient for the Q<sub>A</sub>750 strategy, and in each instance, the absolute difference between the Q<sub>A</sub>500 and Q<sub>A</sub>750 strategies is small.

Table 3 | Transition probabilities

Variable	Strategy			Sources
	No screen	Q <sub>A</sub> 500	Q <sub>A</sub> 750	
Prevalence of AVF stenosis	45%	45%	45%	Tessitore <i>et al.</i> <sup>2</sup>
Sensitivity of transonic to detect stenosis	NA	0.555	0.890	Tessitore <i>et al.</i> <sup>2</sup>
Specificity of transonic to detect stenosis	NA	0.707	0.878	Schwarz <i>et al.</i> <sup>7</sup>
		0.984	0.9	Tessitore <i>et al.</i> <sup>2</sup>
Likelihood of declot success <sup>a</sup>	First declot	0.778	0.444	Schwarz <i>et al.</i> <sup>7</sup>
	Second and subsequent declot		0.89	Haage <i>et al.</i> <sup>8</sup>
Risk of AVF failure after successful declot	3 mo: 0.25			Haage <i>et al.</i> <sup>8</sup>
	6 mo: 0.35			
	12 mo: 0.5			
<i>After failure of initial AVF</i>				Manns <i>et al.</i> <sup>9</sup>
Probability of inserting perm. Catheter	0.336			
Probability of creating second AVF	0.486			
Probability of creating graft	0.178			
<i>After failure of second AVF</i>				
Probability of inserting perm. Catheter	0.562			
Probability of creating second AVF	0.250			
Probability of creating graft	0.188			
Risk of primary access failure	After creation of next AVF	0.47		Manns <i>et al.</i> <sup>9</sup>
	After creation of graft	0.152		
Annual risk of complete graft failure	0.30			Mehta <i>et al.</i> <sup>10</sup>
Yearly risk of death in patients with an AVF	0.105			Pasten <i>et al.</i> <sup>11</sup>
Yearly risk of transplant	0.027			Canadian Organ Replacement Register <sup>12</sup>

AVF, arteriovenous fistulae; mo, months.

<sup>a</sup>Only one declot was attempted per AVF.

attractive in scenarios where angioplasty of stenotic AVF was assumed to be particularly effective for preventing thrombosis, where stenosis was relatively frequent, or where declotting of thrombosed AVF was unavailable or relatively ineffective. As patency rates after AVF declotting appear to vary widely between institutions,<sup>8,18</sup> examination of local outcomes following intervention in clotted AVF may aid dialysis directors in deciding whether AVF screening would be relatively advantageous for their facility.

In theory, dialysis units might perform access screening to reduce costs, improve patient outcomes, or both. Previous work found that vascular access screening reduces access-related costs by decreasing the need for radiological procedures and hospitalization.<sup>4</sup> However, the majority of subjects in this latter study had polytetrafluoroethylene

grafts, which thrombose and fail more frequently than AVF. Our model captured all access-related costs (including hospitalization for vascular procedures and sepsis) and found no evidence that access screening reduced net costs under any clinically plausible scenario. The slightly higher net access-related costs associated with both screening strategies in AVF suggest that Q<sub>A</sub> monitoring is worthwhile if reduced exposure to central venous catheters translates into a morbidity or mortality benefit – a hypothesis which (although unproven) seems likely.<sup>11,19–21</sup>

Under the base case scenario, the incremental cost to prevent an episode of AVF failure was similar for the Q<sub>A</sub>500 and Q<sub>A</sub>750 strategies, suggesting that if cost effectiveness were the only consideration, an individual dialysis unit might choose to adopt the Q<sub>A</sub>750 strategy and prevent as many

episodes of AVF failure as possible. However, this conclusion was sensitive to several assumptions, including the prevalence of stenosis and the efficacy of angioplasty for preventing thrombosis in stenotic AVF. Most importantly, if fistulae with undetected stenosis but  $Q_a > 500$  ml/min are unlikely to fail,<sup>1</sup> the  $Q_{A750}$  strategy does not represent an efficient use of resources compared with the  $Q_{A500}$  strategy. In the base case, we derived the probability of AVF failure in this setting from a study in which follow-up  $Q_a$  measurements did not trigger angiography, even if  $Q_a$  declined further over time.<sup>6</sup> Although an AVF with stenosis and an initial  $Q_a$  of 600 ml/min would not initially undergo angiography under the  $Q_{A500}$  strategy, the available data suggest that in most such cases,  $Q_a$  will decline to  $< 500$  ml/min on follow-up measurements – allowing the lesion to be detected and treated before thrombosis occurs. Thus, the base case probably underestimates the cost to prevent an episode of AVF loss associated with the  $Q_{A750}$  strategy, especially when follow-up  $Q_a$  measurements are regularly performed. Finally, the number of angiograms required under the  $Q_{A750}$  strategy was approximately 22% higher than in the  $Q_{A500}$  strategy, which may be an additional consideration in settings where access to angiography is limited.

Our analysis took a single-payer perspective, which appears appropriate for the United States as well as Canada, as Medicare in the United States reimburses both access screening (via the composite rate for outpatient dialysis) and hospitals for providing angiograms and access surgery. However, there appears to be little financial incentive for dialysis providers to screen AVF for subclinical stenosis, as reimbursement for dialysis does not appear to be contingent on the performance of access screening. At present, there is no consensus as to whether \$9,000 represents a reasonable expenditure to prevent one episode of AVF failure. If such consensus is reached, linking reimbursement to the actual provision of access screening in AVF could be considered.

Our study has several limitations that should be considered. First, there was considerable uncertainty in some of the model parameters. We attempted to deal with this through extensive use of sensitivity analysis and found that screening AVF for subclinical stenosis was not cost saving under any plausible scenario. Although it is possible that the  $Q_{A750}$  strategy is marginally more cost effective than the  $Q_{A500}$  strategy, the incremental cost for the two strategies varied from similar (under most scenarios) to substantially higher for the  $Q_{A750}$  strategy. We did not find the  $Q_{A750}$  strategy to be substantially more cost effective than the  $Q_{A500}$  strategy under any scenario. Second, although costs were predominantly based on Canadian data, using data that reflected higher health-care costs (as in the US) did not qualitatively alter our conclusions. In addition, clinical data were derived from Canadian, Italian, and German studies. As such, our results are likely applicable to other health-care settings. However, the use of multiple different studies to estimate the causes and consequences of screening may have introduced additional uncertainty which was not captured by

our model. Third, as many centers do not perform declotting of native AVF, screening may be more beneficial than our base case analysis suggests. Fourth, we did not consider other potential screening strategies such as regular physical examination, less frequent  $Q_a$  measurements, or lower  $Q_A$  thresholds. Although potentially less expensive than the screening strategies we evaluated, the effectiveness of these strategies is unclear. Fifth, we did not have data on health-related quality of life, which might well be affected by access failure and also by strategies aimed at preventing it. Sixth, we assumed that nurses (rather than dialysis technicians) would perform access screening, which reflects clinical practice in Canada. Using less costly personnel to perform  $Q_a$  measurements would be expected to improve the cost effectiveness of both screening strategies, although, as noted within our sensitivity analysis, it did not make screening cost saving. Finally, decision models may not sufficiently capture complexities of clinical decision making. However, as suggested by modeling guidelines,<sup>22</sup> we have attempted to create a model which is as simple as possible while capturing the essentials of health states and interventions. It is reassuring that the incidence of AVF failure, as predicted by the model, was similar to that observed in the control arm of a prospective clinical trial.<sup>6</sup> Our conclusions may require modification as new evidence emerges, as the number of patients with AVF failure in the available clinical trials was low. In addition, a more precise estimate of the risk and consequences of AVF failure would have been useful for our analysis. Finally, future studies should confirm the prognosis of apparently well-functioning AVF with  $Q_a > 500$  ml/min, as this variable was of critical importance for our analysis.

In conclusion, screening AVF for subclinical stenosis does not appear to reduce access-related costs, although the modest predicted cost of \$8000–\$10 000 to prevent one episode of AVF failure may represent good value for money. The incremental cost effectiveness of screening was similar in the base case for the  $Q_{A500}$  and  $Q_{A750}$  strategies. However, adopting the  $Q_{A750}$  strategy would require a relatively large number of additional angiograms to prevent an episode of AVF failure, and the relative economic attractiveness of this strategy (compared with the  $Q_{A500}$  strategy) was adversely affected under several plausible scenarios. These data suggest that dialysis providers which perform access screening in AVF should use the  $Q_{A500}$  strategy, especially in settings where access to angiography is limited.

## MATERIALS AND METHODS

### Population

In the baseline analysis, we evaluated a simulated cohort of prevalent hemodialysis patients whose characteristics were representative of typical North American dialysis patients with AVF in terms of age (38% were over 60 years of age), sex (68% male), and comorbidity (23% with diabetes).<sup>11</sup> To be consistent with the best quality study on this topic,<sup>2</sup> in the base case analysis, we assumed the prevalence of stenosis in functioning AVF to be 45%.<sup>2</sup> We considered the impact of higher<sup>7</sup> and lower estimates in sensitivity analyses.

## Screening strategies

We assumed that screening studies would be performed bimonthly using indicator dilution technology, where the ultrasound velocity through blood is the indicator, and dilution is provided by a bolus of normal.<sup>7,23</sup> For purposes of resource use, we assumed that patients would have Qa measured twice in succession during the same dialysis treatment, and that a Transonic HD02 device (Transonic Systems Inc., Ithaca, NY, USA) would be used for screening. In all scenarios, we assumed that AVF with clinical evidence of dysfunction or abnormalities on physical examination would undergo angiography.

## Model

We used decision analysis to model the costs and consequences of different Qa thresholds for angiography in patients with native vessel AVF over a 5-year period. The perspective of the economic evaluation was that of the health-care purchaser as only direct health service costs were analyzed. A Markov process<sup>24</sup> was used to model transitions, over recurring 2-month cycles, between the different clinical states that were considered (see Figure 1 and Supplementary Appendix). As the impact of AVF failure on patients' survival and health-related quality of life is unknown, expressing the results as a cost per quality-adjusted life year would be inappropriate. Therefore, the potential clinical benefit of screening was expressed as the expected number of months that each patient could be dialyzed with an AVF (rather than a dialysis catheter or graft), the occurrence of AVF failure (abandonment of the AVF for use in dialysis), and the number of dialysis catheter insertions and other access-related procedures that would be required per patient.

## Diagnostic properties of access flow monitoring and efficacy of treatment for stenosis

Two prospective studies in AVF have performed both Qa monitoring and angiography in all subjects (regardless of Qa).<sup>2,7</sup> These data were

used to construct receiver operating characteristic curves for the diagnostic efficiency of different Qa thresholds to detect hemodynamically significant stenosis. In the base case analysis, we used the data from Tessitore *et al.*;<sup>2</sup> sensitivity analyses considered results from the study by Schwarz *et al.*<sup>7</sup> The efficacy of angioplasty for correcting stenosis was estimated as specified in the Supplementary Appendix.<sup>6,28</sup> We obtained the other necessary clinical parameters from a literature review (Table 3).

## Resource use

All costs are measured in 2002 Canadian dollars (1 CAN\$ = 0.69US\$) (Table 3). Screening costs were estimated from a Canadian prospective study of hospital-based outpatient hemodialysis clinics, and were based on the annual number of access-screening procedures, the useful life of the screening device (7 years), and the nursing time required for monitoring.<sup>9</sup> This included nursing time for arranging angiograms that were ordered because of screening, and organizing any subsequent management (angioplasty and surgery). The cost of other access-related healthcare included costs from all access-related procedures, hospitalization for access-related indications, and treatment of outpatient access-related infections<sup>9</sup> (Table 4). The cost of caring for patients who did not receive screening included these latter access-related costs, but not costs due to screening. We did not consider health-care costs that were unrelated to vascular access as they are not known to be influenced by access screening.

## Sensitivity analysis

As any model involves assumptions and uncertainties, extensive sensitivity analyses were carried out. These analyses assessed the effect of varying baseline estimates within clinically plausible ranges on access-related costs and clinical outcomes including the probability of AVF failure, and the number of angiograms and line placements required (Supplementary Appendix).

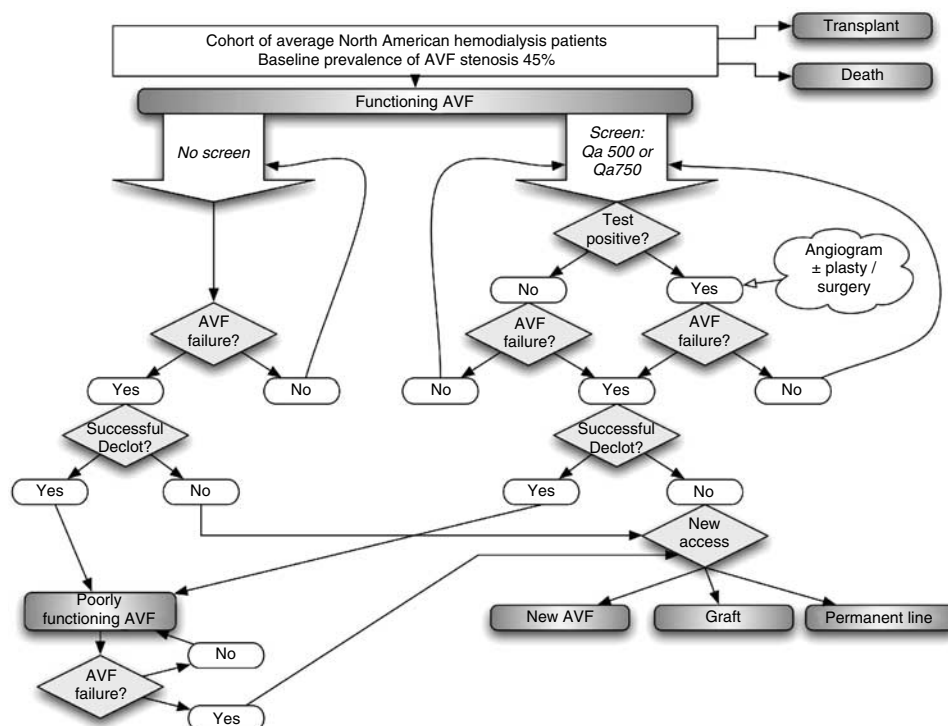


Figure 1 | Flow diagram for decision tree.

**Table 4 | Cost of vascular access screening and procedures**

Variable	Base case	Range	Sources
Cost of ultrasound screening per session	\$58		Manns <i>et al.</i> <sup>9</sup>
Cost of fistulogram without angioplasty	\$484		Manns <i>et al.</i> <sup>9</sup>
Cost of fistulogram and angioplasty	\$1172		Manns <i>et al.</i> <sup>9</sup>
Cost of AVF declot	\$1203		Manns <i>et al.</i> <sup>9</sup>
Cost of surgery to create a new AVF	\$1558		Manns <i>et al.</i> <sup>9</sup>
Cost of surgery to create a new graft	\$1780		Manns <i>et al.</i> <sup>9</sup>
Cost of inserting a temporary dialysis line	\$601		Manns <i>et al.</i> <sup>9</sup>
Cost of inserting a permanent dialysis line	\$925		Manns <i>et al.</i> <sup>9</sup>
Mean cost of maintaining a functioning AVF per year <sup>a</sup>	\$586	\$0–732 (interquartile range)	Lee <i>et al.</i> <sup>25</sup>
Mean cost of maintaining a graft per year <sup>b</sup>	\$4850	\$590–6725 (interquartile range)	Lee <i>et al.</i> <sup>25</sup>
Mean cost of maintaining a permanent dialysis catheter per year <sup>c</sup>	\$3238	\$0–3156 (interquartile range)	Lee <i>et al.</i> <sup>25</sup>
Discount rate (costs and effects)	5% per annum		Canadian Coordinating Office for Health Technology Assessment <sup>26</sup>

AVF, arteriovenous fistulae.

<sup>a</sup>Includes cost of maintaining AVF per year (including cost of fistulograms done for clinical indications and not related to ultrasound screening technique).

<sup>b</sup>Cost of maintaining a graft per year (including cost of fistulograms, angioplasties and cost of new access surgeries required).

<sup>c</sup>Cost of maintaining a permanent dialysis catheter (including cost of new catheters required for malfunction, costs of TPA, and cost of treating infections (including hospitalization)).

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## SUPPLEMENTARY MATERIAL

### Appendix.

## REFERENCES

1. Tonelli M, Jhangri GS, Hirsch DJ *et al.* Best threshold for diagnosis of stenosis or thrombosis within six months of access flow measurement in arteriovenous fistulae. *J Am Soc Nephrol* 2003; **14**: 3264–3269.
2. Tessitore N, Bedogna V, Gammara L *et al.* Diagnostic accuracy of ultrasound dilution access blood flow measurement in detecting stenosis and predicting thrombosis in native forearm arteriovenous fistulae for hemodialysis. *Am J Kidney Dis* 2003; **42**: 331–341.
3. Jindal KK, Ethier J, Lindsay RM *et al.* Clinical practice guidelines for vascular access. Canadian Society of Nephrology. *J Am Soc Nephrol* 1999; **10**: S287–S321.
4. McCarley P, Wingard RL, Shyr Y *et al.* Vascular access blood flow monitoring reduces access morbidity and costs. *Kidney Int* 2001; **60**: 1164–1172.
5. Tonelli M, Jindal K, Hirsch D *et al.* Screening for subclinical stenosis in native vessel arteriovenous fistulae. *J Am Soc Nephrol* 2001; **12**: 1729–1733.
6. Tessitore N, Lipari G, Poli A *et al.* Can blood flow surveillance and pre-emptive repair of subclinical stenosis prolong the useful life of arteriovenous fistulae? A randomized controlled study. *Nephrol Dial Transplant* 2004; **19**: 2325–2333.
7. Schwarz C, Mitterbauer C, Boczula M *et al.* Flow monitoring: performance characteristics of ultrasound dilution versus color Doppler ultrasound compared with fistulography. *Am J Kidney Dis* 2003; **42**: 539–545.
8. Haage P, Vorwerk D, Wildberger JE *et al.* Percutaneous treatment of thrombosed primary arteriovenous hemodialysis access fistulae. *Kidney Int* 2000; **57**: 1169–1175.
9. Manns B, Tonelli M, Yilmaz S *et al.* Establishment and maintenance of vascular access in incident hemodialysis patients: a prospective cost analysis. *J Am Soc Nephrol* 2005; **16**: 201–209.
10. Mehta S. Statistical summary of clinical results of vascular access procedures for haemodialysis. In: Sommer BG, HM WL (eds). *Vascular Access for Hemodialysis*. Gore & Associates, 1991, pp 145–157.
11. Pastan S, Soucie JM, McClellan WM. Vascular access and increased risk of death among hemodialysis patients. *Kidney Int* 2002; **62**: 620–626.
12. 2001 Report, Volume 1: Dialysis and Renal Transplantation, Canadian Organ Replacement Register. 2001.
13. Clark TW, Hirsch DA, Jindal KJ *et al.* Outcome and prognostic factors of restenosis after percutaneous treatment of native hemodialysis fistulas. *J Vasc Interv Radiol* 2002; **13**: 51–59.
14. Palder SB, Kirkman RL, Whittemore AD *et al.* Vascular access for hemodialysis. Patency rates and results of revision. *Ann Surg* 1985; **202**: 235–239.
15. Cohen MA, Kumpe DA, Durham JD *et al.* Improved treatment of thrombosed hemodialysis access sites with thrombolysis and angioplasty. *Kidney Int* 1994; **46**: 1375–1380.
16. Beathard GA. Percutaneous transvenous angioplasty in the treatment of vascular access stenosis. *Kidney Int* 1992; **42**: 1390–1397.
17. Guerra A, Raynaud A, Beyssen B *et al.* Arterial percutaneous angioplasty in upper limbs with vascular access devices for haemodialysis. *Nephrol Dial Transplant* 2002; **17**: 843–851.
18. Turmel-Rodrigues L, Pengloan J, Rodrigue H *et al.* Treatment of failed native arteriovenous fistulae for hemodialysis by interventional radiology. *Kidney Int* 2000; **57**: 1124–1140.
19. Xue JL, Dahl D, Ebben JP *et al.* The association of initial hemodialysis access type with mortality outcomes in elderly Medicare ESRD patients. *Am J Kidney Dis* 2003; **42**: 1013–1019.
20. Dhingra R. Type of vascular access and mortality in U.S. hemodialysis patients. *Kidney Int* 2001; **60**: 1443–1451.
21. Polkinghorne KR, McDonald SP, Atkins RC *et al.* Vascular access and all-cause mortality: a propensity score analysis. *J Am Soc Nephrol* 2004; **15**: 477–486.
22. Weinstein MC, O'Brien B, Hornberger J *et al.* Principles of good practice for decision analytic modeling in health-care evaluation: report of the ISPOR Task Force on Good Research Practices – Modeling Studies. *Value Health* 2003; **6**: 9–17.
23. Depner TA, Krivitski NM. Clinical measurement of blood flow in hemodialysis access fistulae and grafts by ultrasound dilution. *ASAIO J* 1995; **41**: M745–M749.
24. Sonnenberg F, Beck J. Markov models in medical decision making: A practical guide. *Med Decision Making* 1993; **13**: 322–338.
25. Lee H, Manns BJ, Taub K *et al.* Cost analysis of ongoing care of patients with end-stage renal disease: the impact of dialysis modality and dialysis access. *Am J Kidney Dis* 2002; **40**: 611–622.
26. Canadian Coordinating Office for Health Technology Assessment Guidelines for economic evaluation of pharmaceuticals: Canada. Canadian Coordinating Office for Health Technology Assessment: Ottawa, 1997.
27. Drummond M, O'Brien B, Stoddart G, Torrance G. *Methods for the Economic Evaluation of Health Care Programmes*. 2nd edn. Oxford University Press: Oxford, 1997.
28. Tessitore N, Mansucto G, Bedogna V *et al.* A prospective controlled trial on effect of percutaneous transluminal angioplasty on functioning arteriovenous fistulae survival. *J Am Soc Nephrol* 2003; **14**: 1623–1627.