

Appendix

Section I. Method Inputs and Assumptions.

Model Inputs

Parameter estimates in **Tables 1 and 2** were derived from sources that either represented best available evidence (e.g., trial data or meta-analyses if available) or population-specific data (e.g., Canada- or Ontario-specific sources of data). Specifically, prevalence rates and size distributions were obtained from the Multicentre Aneurysm Screening Study and a published systematic review and meta-analysis. Surgical outcomes represented recent Ontario province-wide estimates for both emergency and scheduled open surgery and EVAR. Life expectancy was obtained from the Canadian Vital Statistics by Statistics Canada (Canadian federal government) for 2021. Similarly, utilities were informed by the most recent health-related quality of life weights by Statistics Canada, determined through the 2015 Canadian Community Health Survey, whereas disutilities have not been empirically quantified and, therefore, informed through the expert opinion of the author group. Cost data were informed by Ontario-specific reimbursement data by the Ontario Case Costing Initiative from Ontario Health (Ontario provincial government) for 2021. Remaining data were obtained from other published decision analyses. The 2008 model from Canada was used to inform screening uptake in order to have a more representative estimate of the AAA screening acceptance and attitude of the Canadian population. For estimates that were not expected to be substantially different, such as rupture risks at different AAA sizes, more recent studies from other countries were used instead of the older Canadian study.

Assumptions

The probability of growth and/or rupture varied by size: growth rates of AAAs were assumed to be linear at 0.1 cm per year for small AAAs and 0.4 cm per year for medium AAAs.(1–3) Large AAAs in the screened arm would be scheduled for surgery within the same three-month cycle period, whereas those in the unscreened arm would have a set rupture rate. Based on expert opinion, growth was assumed to occur at the same average rate for all individuals within a given size category. For each size category, we assumed that AAAs were at the midpoint of their size category and would reach the next size category after reaching the specific size threshold (e.g., small AAAs in men (3.0–4.4cm) started at 3.7cm and would reach a medium size after 32 cycles at a growth rate of 0.1cm per year, unless the patient dies before reaching that cycle. The probability of rupture was assumed to be twice as high among women compared to men.(4–6) The probability of undergoing a specific type of surgery and death from rupture before emergency repair (i.e., 50% die before reaching the hospital) was assumed to be similar among men and women; however, the probability of death after repair was higher among women compared to men based on Ontario-specific population-based operative outcome estimates.(7,8) Life expectancy was determined based on age- and sex-specific mortality rates using Canadian life tables for the general population obtained from Statistics Canada.(9) Normal age- and sex-specific utilities were derived from the Canadian Health Utilities Index.(10) Disutility after aneurysm repair was assumed to be similar among men and women. As is common in economic modeling, utility estimates are a necessary simplification of reality based on best available evidence and expert opinion. While a small subset of the patient population receiving surgery may have a long-term disutility associated with more severe complications, we assumed that the patients following AAA repair returned to their baseline quality of life. As such, the disutility was applied only once after

surgery (i.e., only during one 3-month cycle following surgery). The disutility value is reflective of a decrement in health related quality of life from usual post-operative recovery and impact of potential surgical complications. For the base-case analysis, screening ultrasonography was assumed to be 100% sensitive and specific as, in reality, sensitivity (94%-100%) and specificity (98%-100%) are known to be high.(11) Participation following an invitation to screen was considered at 73%(12); however, we assumed that individuals who accept the initial invitation for screening would remain compliant with follow-up AAA surveillance. This is consistent with low drop-out rates for follow-up after initial screening observed in existing population-based screening programs.(13) Costs for ultrasound, preoperative assessment, interventions (open repair and EVAR; scheduled and emergency; including procedure-related costs and hospital stay), and follow-up were obtained from the Ontario Case Costing Initiative.(14,15) All costs were adjusted to 2022CA\$ using the Consumer Price Index.(16)

Section II. Comparison of Screening Programs.

Condition Screened	Number Needed to Screen
Abdominal aortic aneurysms (our model) <ul style="list-style-type: none">• Male subjects aged 65 years• Female subjects aged 65 years• Male subjects aged 75 years• Female subjects aged 75 years	222 588 370 714
Breast cancer(17)	1,724 (1,176-3,704)
Colorectal cancer(18) <ul style="list-style-type: none">• Fecal occult blood test• Flexible sigmoidoscopy	377 (249-887) 864 (672-1,266)
Prostate cancer(19)	1,410 (1,142-1,721)

Section III. Base Case and Alternative Scenarios.

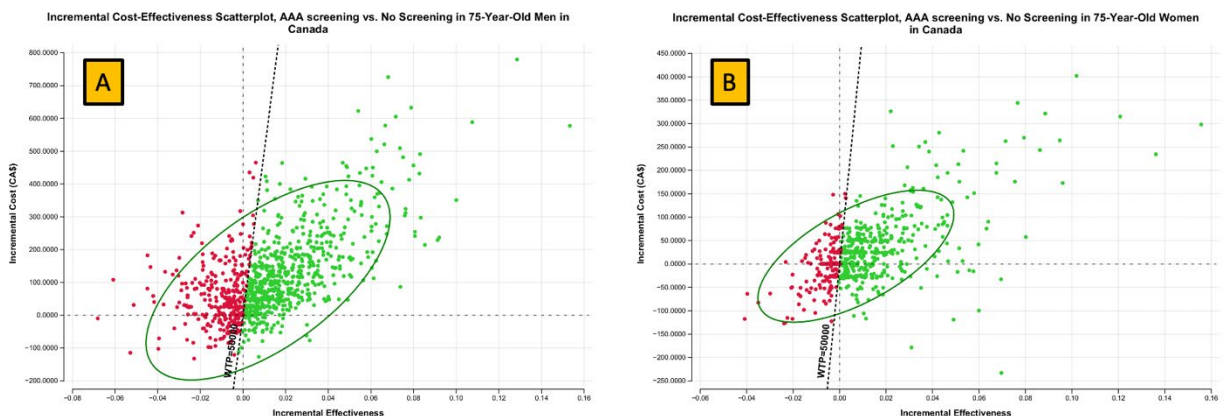
Base Case Analysis

Cost-effectiveness scatterplots and curves display the likelihood that an intervention in a decision analytic model is cost-effective within the constraints of the model's input parameters when placed against willingness-to-pay thresholds. These thresholds represent the sum individuals are willing to pay to gain 1 quality-adjusted life-year (QALY), or 1 year of life lived in full health. For example, the common willingness-to-pay threshold of CA\$50,000/QALY indicates that people would be willing to pay up to CA\$50,000 to gain 1 QALY. If an intervention falls below this threshold, favorable cost-effectiveness is accepted; if it falls above the threshold, no cost-effectiveness is accepted in purely economic terms. Graphically, incremental cost-effectiveness scatterplots display the incremental costs (y-axis) and effectiveness (x-axis) between an intervention and a comparator on a graph, whereby positive values represent either increased costs or effectiveness for the intervention relative to the comparator. As such, the northeast quadrant displays increased costs and effectiveness, the southeast quadrant decreased costs and increased effectiveness, the southwest quadrant decreased costs and effectiveness, and the northwest quadrant increased costs and decreased effectiveness. Drawing a linear willingness-to-pay threshold (e.g., CA\$50,000/QALY) can then show all values falling under or right from the threshold and, thus, display cost-effectiveness. In turn, the cost-effectiveness acceptability curves display how many of the model iterations are likely cost-effective at different willingness-to-pay thresholds, allowing for an assessment of "extent" of cost-effectiveness (e.g., determining whether marginal changes in an intervention may result in a substantially greater or lesser likelihood of being cost-effective at given thresholds).

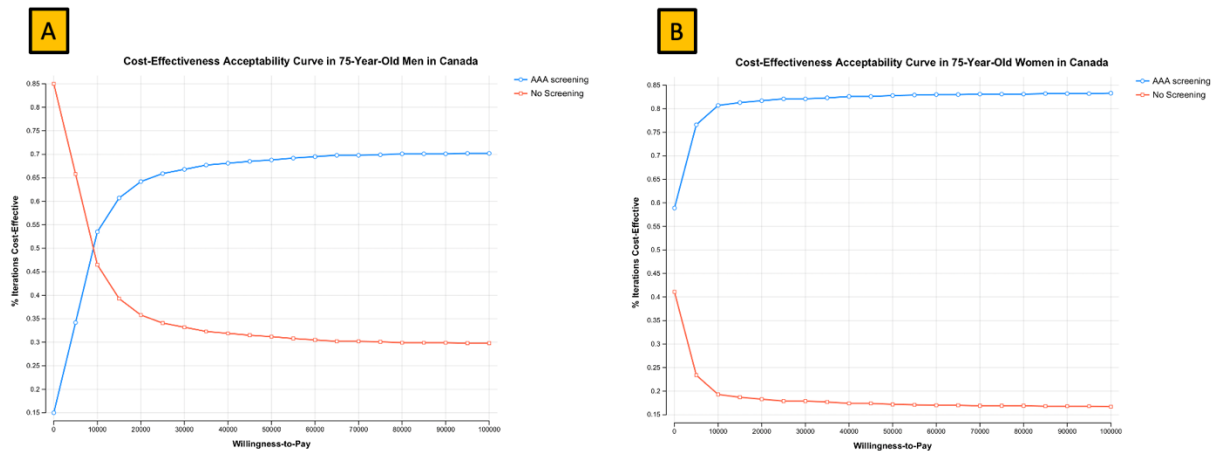
In people aged 65 years in Canada, screening is likely cost-effective. In the main manuscript, **Figure 2** shows that the majority of model iterations (i.e., outputs of the model when run multiple times) fall under the threshold of CA\$50,000/QALY, as illustrated by the green dots in the northeast and southeast quadrants. **Figure 3** illustrates that, at the threshold of CA\$50,000/QALY, there is nearly 90% likelihood of cost-effectiveness. Only at very low willingness-to-pay thresholds, which do not exist in high-income countries, do curves cross and is it more likely for a screening program to not be cost-effective than be cost-effective.

Alternative Scenarios

In male and female subjects aged 75 years in Canada, screening remains likely cost-effective, albeit less so compared to 65-year-old male and female subjects. **Supplemental Figure 1** suggests that a majority of model iterations still fall in the northeast and southeast quadrants (green dots), albeit fewer than those for the base case analysis in **Figure 2**. **Supplemental Figure 2** illustrates that the model remains likely cost-effective at most thresholds, albeit less likely than in the base case analysis (**Figure 3**).



Supplemental Figure 1. Incremental cost-effectiveness scatter plot for abdominal aortic aneurysm (AAA) screening versus no screening in male subjects aged 75 years (left) and female subjects aged 75 years in Canada (right). *WTP* = *Willingness-to-pay*.



Supplemental Figure 2. Cost-effectiveness acceptability curve for abdominal aortic aneurysm (AAA) screening versus no screening in male subjects aged 75 years (left) and female subjects aged 75 years in Canada (right).

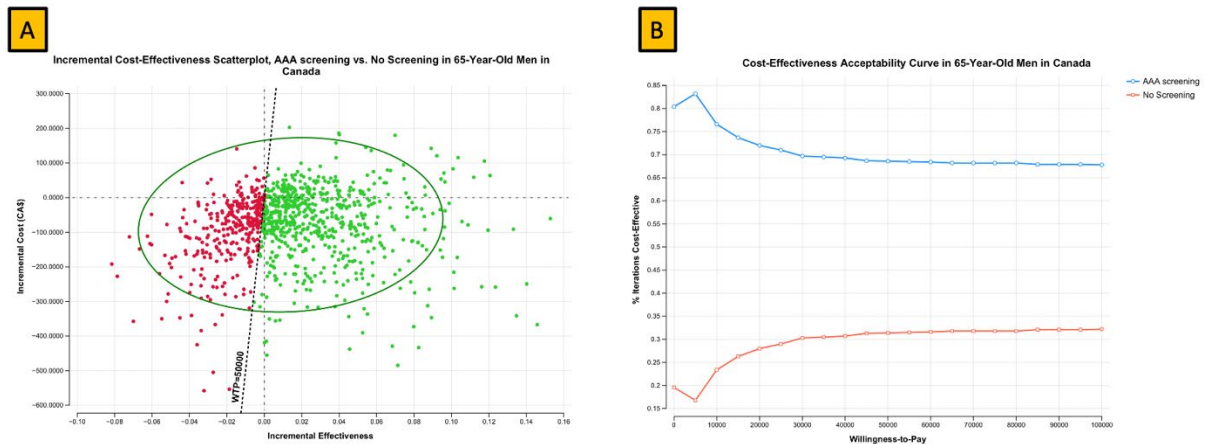
Section IV. Sensitivity Analyses.

Several sensitivity analyses were performed to evaluate the robustness of findings in our base-case analysis (i.e., 65-year-old male and female subjects in Canada).

Pre-Hospital Death

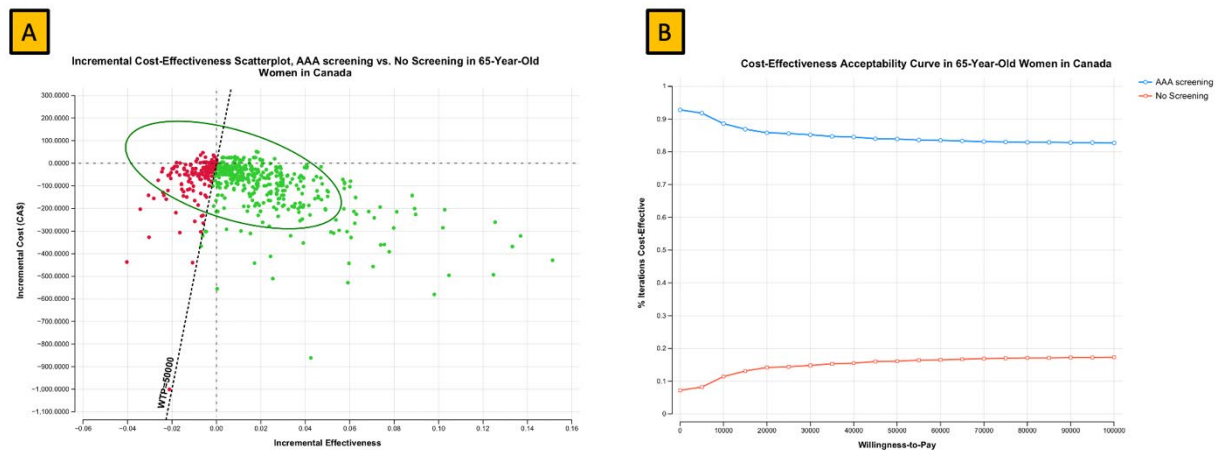
Decreasing out-of-hospital (i.e., pre-hospital) death from 50% to 0% resulted in persistent net benefits and ICERs in favour of screening as a result of more people with ruptures reaching the hospital in time for emergency surgery in the no-screening arm.

In 65-year-old male subjects, QALY gains reduced but remained in favour of screening versus no screening (14.95 vs. 14.94). Costs were lower for screening compared to no screening, resulting in a negative cost-utility of -CA\$5,622/QALY. Screening remained most likely cost-effective in 68.6% of model iterations. **Supplemental Figure 3** shows the incremental cost-effectiveness scatterplot and cost-effectiveness acceptability curves.



Supplemental Figure 3. Incremental cost-effectiveness scatter plot (left) and cost-effectiveness acceptability curve (right) for abdominal aortic aneurysm (AAA) screening versus no screening in male subjects aged 65 years in Canada with no pre-hospital death from rupture.

In 65-year-old female subjects, QALY gains reduced (16.20 vs. 16.19) with a negative cost-utility of -CA\$6,472/QALY. The negative cost-utility was the result of lower costs in the screening vs. no screening group. Screening remained most likely cost-effective in 83.9% of model iterations. **Supplemental Figure 4** shows the incremental cost-effectiveness scatterplot and cost-effectiveness acceptability curves.



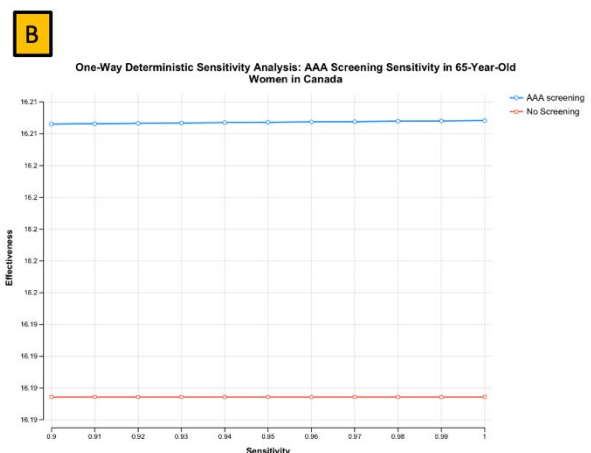
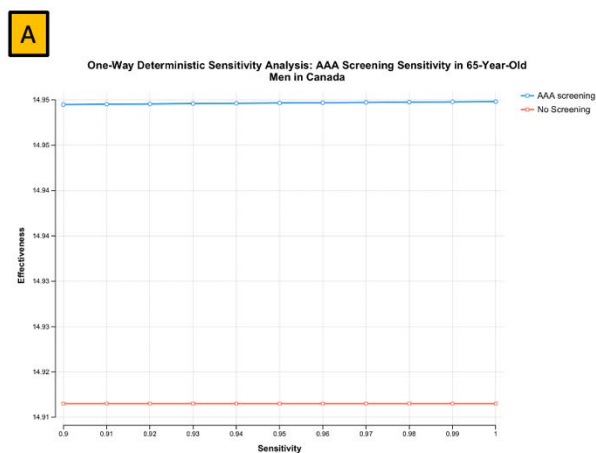
Supplemental Figure 4. Incremental cost-effectiveness scatter plot (left) and cost-effectiveness acceptability curve (right) for abdominal aortic aneurysm (AAA) screening versus no screening in female subjects aged 65 years in Canada with no pre-hospital death from rupture.

Screening Uptake

Reducing the screening uptake from 73.3% to 50.0% resulted in comparable outcomes. In 65-year-old male subjects, screening had marginally smaller QALY gains (14.94 vs. 14.91) compared to no screening with a cost-utility of CA\$2,290/QALY. Screening remained most likely cost-effective in 83.7% of model iterations. In 65-year-old female subjects, screening had marginally comparable QALY gains (16.20 vs. 16.19) compared to no screening with a cost-utility of CA\$683/QALY. Screening remained most likely cost-effective in 88.0% of model iterations. The more favourable cost-utility with lower screening adherence is likely the result of lower screening costs.

Sensitivity

One-way deterministic sensitivity analyses were performed for the sensitivity of ultrasound screening for values between 90-100% sensitivity. As costs remained stable and changes in effectiveness were marginal (**Supplemental Figure 5**), the cost-utility did not substantially change for both male and female subjects.



Supplemental Figure 5. One-way deterministic sensitivity analysis for sensitivity of ultrasound for abdominal aortic aneurysm (AAA) screening in male subjects (left) and female subjects (right) aged 65 years in Canada.

Specificity

One-way deterministic sensitivity analyses were performed for the specificity of ultrasound screening for values between 90-100% specificity. At lower specificity, costs for the screening program increased due to increased scheduled surgical procedures, whereas changes in effectiveness were marginal due to low rates of surgery (only for false positive large AAAs) and favorable outcomes of scheduled surgery. At a specificity of 96% and below, the net monetary benefit of AAA screening was lower than that of no screening.

Follow-Up Compliance

One-way deterministic sensitivity analyses were performed for follow-up compliance after initial ultrasound screening for values between 90-100% compliance. These values were chosen as drop-out rates from follow-up after initial positive screening are known to be low.⁽¹³⁾ Costs and effectiveness did not substantially change for both male and female subjects resulting in sustained clinical utility, albeit at higher ICERs.

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