Supplement I - Model details

This supplement describes several details about the structure and development of the microsimulation model for neonatal hearing screening. The model is stochastic: Each parameter value has a specific distribution (e.g, normal, exponential or Weibull distribution) and events (hearing impairment, screening, treatment) are allocated randomly in the population. Therefore, each run generates a slightly different population and events, which results in slightly different outcomes. This process reflects the variation as found in real life. Also the model is a continuous time model, which means that events may occur at any moment in time, instead of at fixed time slots (for example annual).

Natural history

Input from multiple large cohort studies was used to calibrate the model on prevalence of hearing impairment at birth by level of severity (Berninger et al. 2011; Cone-Wesson et al. 2000; H. Fortnum et al. 1997; Watkin et al. 2011).

The best fit micro-simulation model estimated 22.7 per 10,000 neonates with hearing impairment >25dB, of which 16.8 per 10,000 children were born with hearing impairment greater than 40 dB (6.4 unilateral, 10.4 bilateral).

Test sensitivity

The program sensitivity reported by Kennedy et al. (2005) for the OAE-aABR two-stage approach was 92% for detecting hearing impairment > 40 dB. This is the only large controlled trial study. We obtained estimates of the single stage test sensitivities from this two-stage protocol using the equation: test sensitivity OAE* test sensitivity aABR = program sensitivity.

Table A provides some possible combinations in this case where the program sensitivity of OAE-aABR is 92%.

Table A. Single test sensitivities resulting in a program sensitivity of 92%

Test sensitivity OAE	Test sensitivity aABR	Program sensitivity OAE-aABR
97%	95%	92%
96%	96%	92%
95%	97%	92%
94%	98%	92%
93%	99%	92%
92%	100%	92%

The test sensitivity of aABR is probably higher compared to the test sensitivity of OAE because aABR can detect auditory neuropathy. Since the test sensitivity isprobably lower than 100%, we choose to use 95% for OAE and 97% for aABR as single-test sensitivities in the microsimulation-model for detecting hearing impairment > 40 dB. Using these as a starting-point, we modelled several hypothetical test protocols, many of which not currently found in empirical studies. For example, the three-stage protocol OAE-OAE-aABR program sensitivity was calculated 95% * 95% * 97% = 88%. We assumed the test sensitivity for detecting hearing impairment between 26 and 40 dB is quartered.

Supplement II: Sensitivity analyses

One-way sensitivity analyses were performed for input parameters on the distribution of severity categories of hearing loss; the age of clinical detection; screening attendance rates; costs of diagnosis and quality of life. These alternative cost-effectiveness projections are presented with a 3% discount rate for both costs and effects.

Transition probabilities related to the prevalence of severity categories of hearing loss were varied between a minimum and a maximum value (Table A). Figures A1 and A2 show that the cost-effectiveness ratio of all programs changed if the distribution of severity changed. If assuming a higher prevalence of mild hearing impairment in the population, the OAE-aABR is the preferred program with an average cost of € 12,159 per QALY gained. This exceeds the willingness-to-pay threshold for Albania slightly. If assuming a higher prevalence of severe hearing impairment in the population, the OAE-aABR (maternity) ICER is € 2,025.

Input values on the age of clinical detection were increased according to the findings of Watkin, Baldwin[1], who assessed the age of identification of hearing impairment in London districts with no or minimal audiology facilities (Table B). We used the findings from their earliest observations (1973-1977), which might reflect certain circumstances in Albania. Figure B shows that longer duration times for clinical detection predicted an increase in QALYs gained and therefore an ICER of € 2,371 for the OAE-aABR (maternity) protocol.

Next, we analyzed the model predictions for decreased attendance rates for screening rounds 2 and 3. If performed on in-patients, the attendance rate decreases from 95% to 80%. If performed on out-patients, the attendance rate decreases from 70% to 50%. This affects the overall program sensitivity and the PPV (Table C1). Using the lower attendance rates for the second and third round resulted in less referrals for audiological follow-up and in less cases detected. The effect of lower attendance did not change the order of the protocols, but the cost-effectiveness ratio increased due to increased costs and less QALYs gained (Figure C1). The OAE-aABR (maternity) protocol was estimated € 6,071 per QALY gained. All other protocols exceeded the Albanian willingness-to-pay threshold.

Following, a hypothetical higher attendance rate in rounds 2 and 3 is tested. We assumed 100% attendance rate for in-patient s and a 95% rate for out-patients (Table C2). Again, this affects both the overall program sensitivity and the PPV. Figure C2 shows this alternation of the model does not affect the preference for protocol OAE-aABR (maternity), being most cost-effective at € 3,759 per QALY gained.

Additionally, higher quality of life estimates were used as reported by Carroll and Downs[2] (Table D). They assessed parents' preferences in the general population for several disease states. This adjustment in our model calculations resulted in all programs exceeding the willingness-to-pay threshold, with the cheapest program (OAE-aABR maternity) costing € 24,895 per QALY gained (Figure D).

Finally, we increased costs per diagnosis from € 60 to € 200. Imposing this maximum value did increase the costs of all screening protocols, but still showed the OAE aABR (maternity) protocol to be the most cost-effective of all programs (Figure E). With an average cost-effectiveness ratio of €7,399, this program is still below the willingness-to-pay threshold for Albania.

Table A. Transition probabilities related to the prevalence of severity categories of hearing loss.

Category	Transition probabilities Baseline	Transition probabilities Minimum	Transition probabilities Maximum
Unilateral 26 – 40 dB	0.148	0.2	0.05
Unilateral 41 – 80 dB	0.134	0.25	0.10
Unilateral > 80 dB	0.142	0.15	0.15
Bilateral 26 – 40 dB	0.113	0.20	0.10
Bilateral 41 – 80 dB	0.304	0.10	0.35
Bilateral > 80 dB	0.158	0.10	0.25

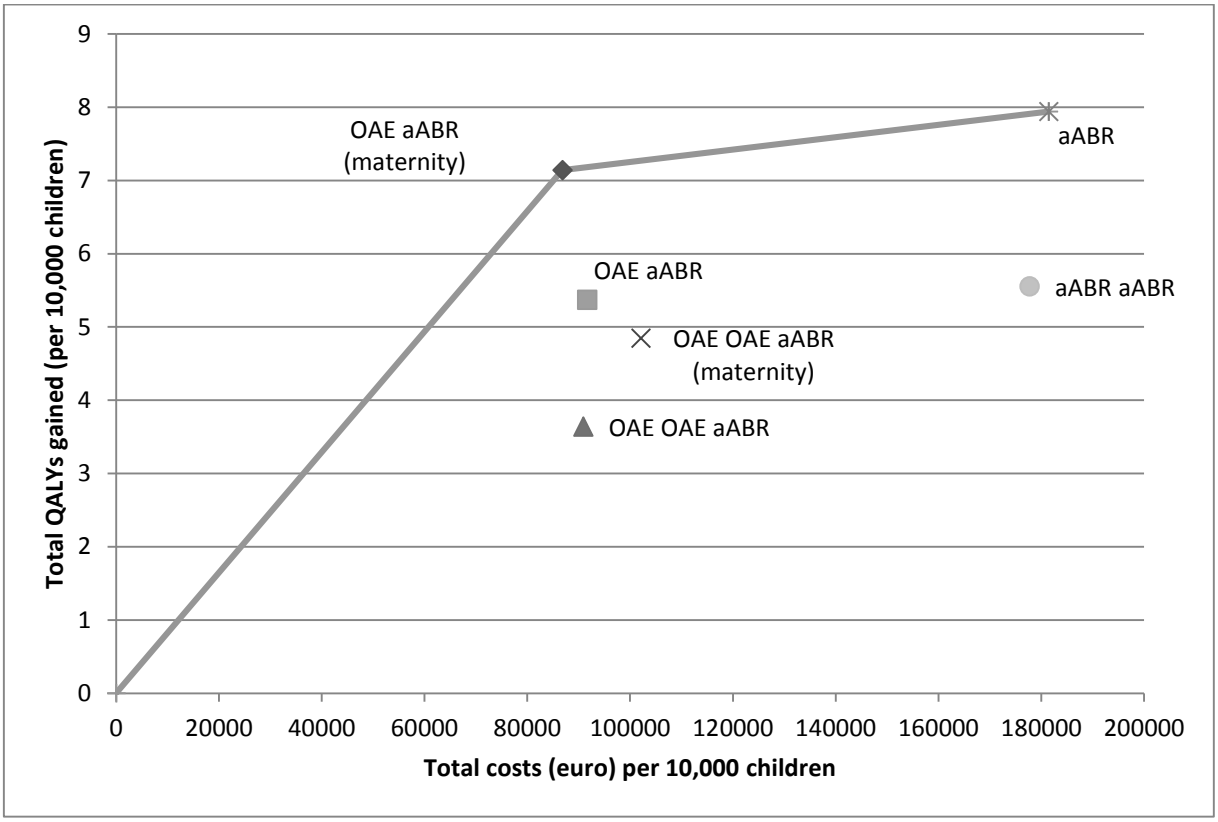

Figure A1. The total costs and total QALYs gained for each protocol using minimum values of prevalence distributions.

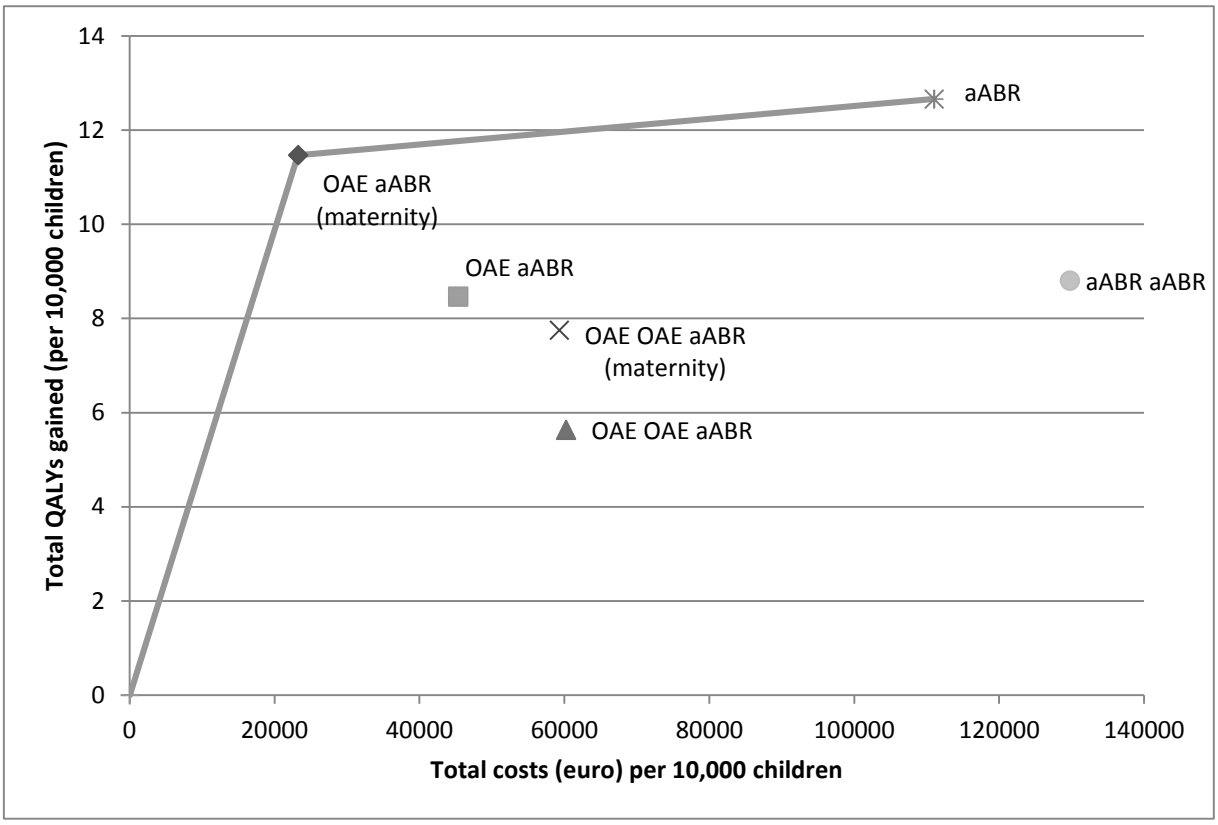

Figure A2. The total costs and total QALYs gained for each protocol using maximum values of prevalence distributions.

Table B. Age of clinical detection

Category	**MISCAN** Baseline value Mean (s.d.)	**Watkin (1991)** Period 1973-1977 Mean (s.d.)
Unilateral	4 years (1)	6.3 years (2.6)
Bilateral, 26-40 dB	3 years (1)	7.3 years (2.7)
Bilateral, 41-80 dB	2 years (1)	5.5 years (1.5)
Bilateral, >80 dB	1 year (0.5)	2.6 years (1.4)

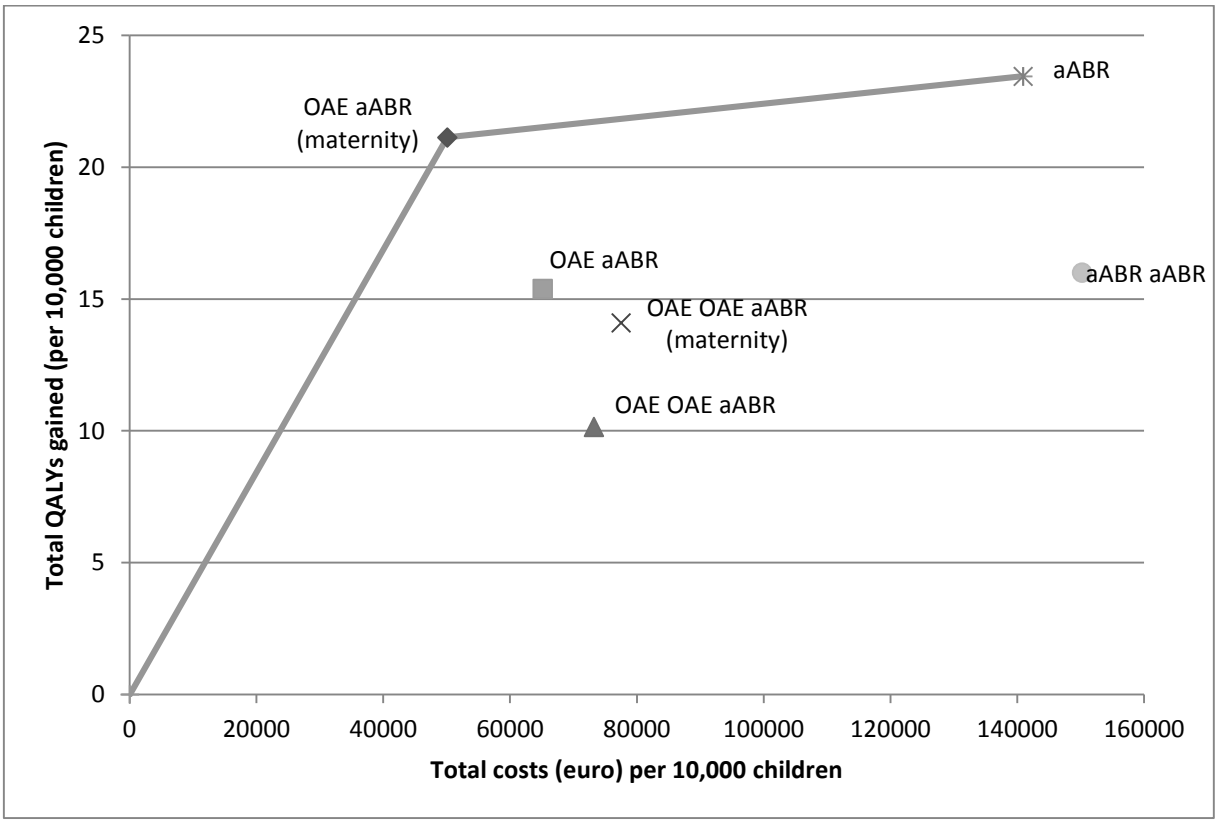

Figure B. The total costs and total QALYs gained for each protocol using longer duration times for clinical detection.

Table C1. Lower attendance rates for sensitivity analyses.

Screening protocol	Round 1 attendance	Round 2 attendance	Round 3 attendance	Overall attendance	Program sensitivity (adjusted for attendance)	Overall PPV
OAE OAE aABR	95%	50%	50%	24%	21%	17.8%
OAE OAE aABR (maternity)	95%	80%	50%	38%	33%	8.7%
OAE aABR	95%	50%	X	48%	44%	5.6%
OAE aABR (materniy)	95%	80%	X	76%	70%	5.6%
aABR aABR	95%	50%	X	48%	45%	8.2%
aABR	95%	X	X	95%	92%	2.5%

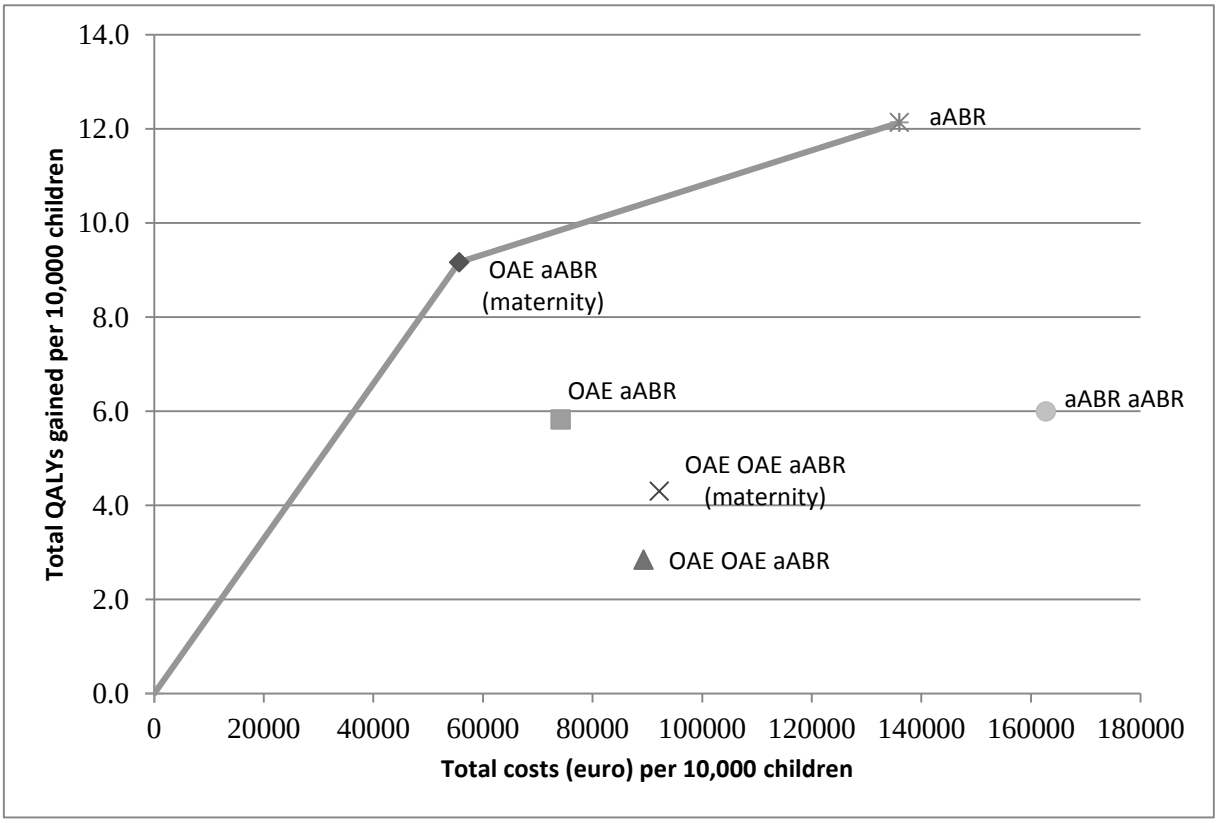

Figure C1. The total costs and total QALYs gained for each protocol using a lower attendance.

Table C2. Higher attendance rates for sensitivity analyses.

Screening protocol	Round 1 attendance	Round 2 attendance	Round 3 attendance	Overall attendance	Program sensitivity (adjusted for attendance)	Overall PPV
OAE OAE aABR	95%	95%	95%	86%	75%	4.9%
OAE OAE aABR (maternity)	95%	100%	95%	90%	79%	3.7%
OAE aABR	95%	95%	X	90%	83%	2.9%
OAE aABR (maternity)	95%	100%	X	95%	87%	4.5%
aABR aABR	95%	95%	X	90%	85%	4.3%
aABR	95%	X	X	95%	92%	2.5%

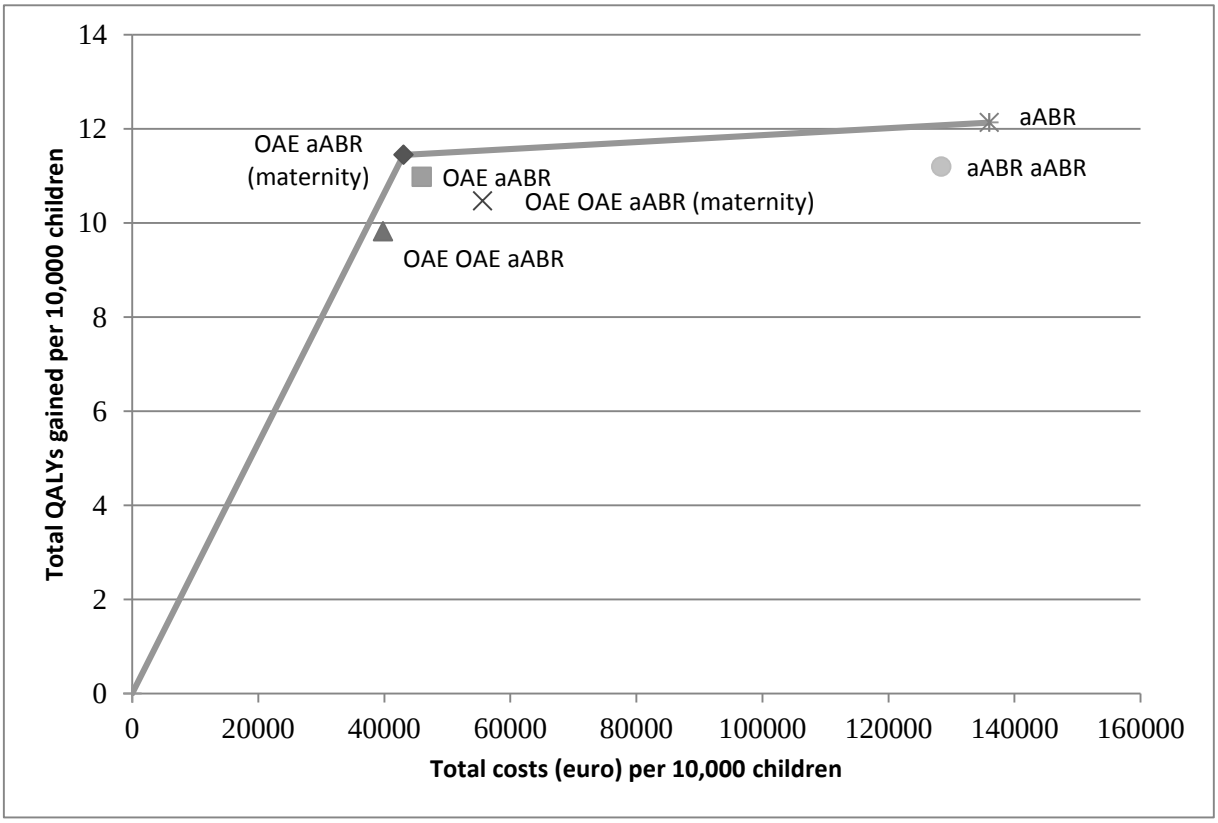

Figure C2. The total costs and total QALYs gained for each protocol using a lower attendance.

Table D. One-way sensitivity analyses assuming higher utilities.

Hearing impairment category	Baseline utility of hearing loss	Higher utility estimates (Standard Gamble method) [2]
Minimal (26-40 dB)	0.85	0.92
Moderate (41-80 dB)	0.661	0.91
Profound (>81 dB)	0.467	0.86

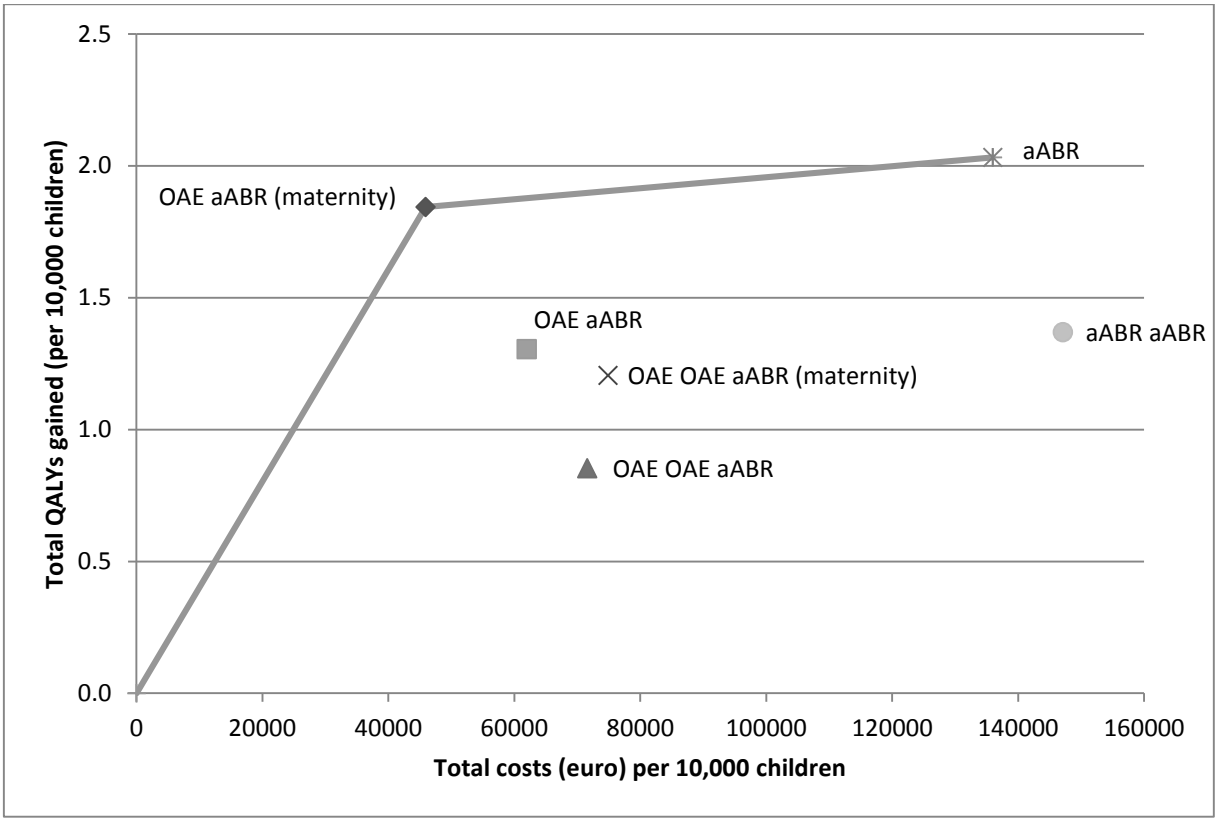

Figure D. The total costs and total QALYs gained for each protocol using higher utilities for hearing loss.

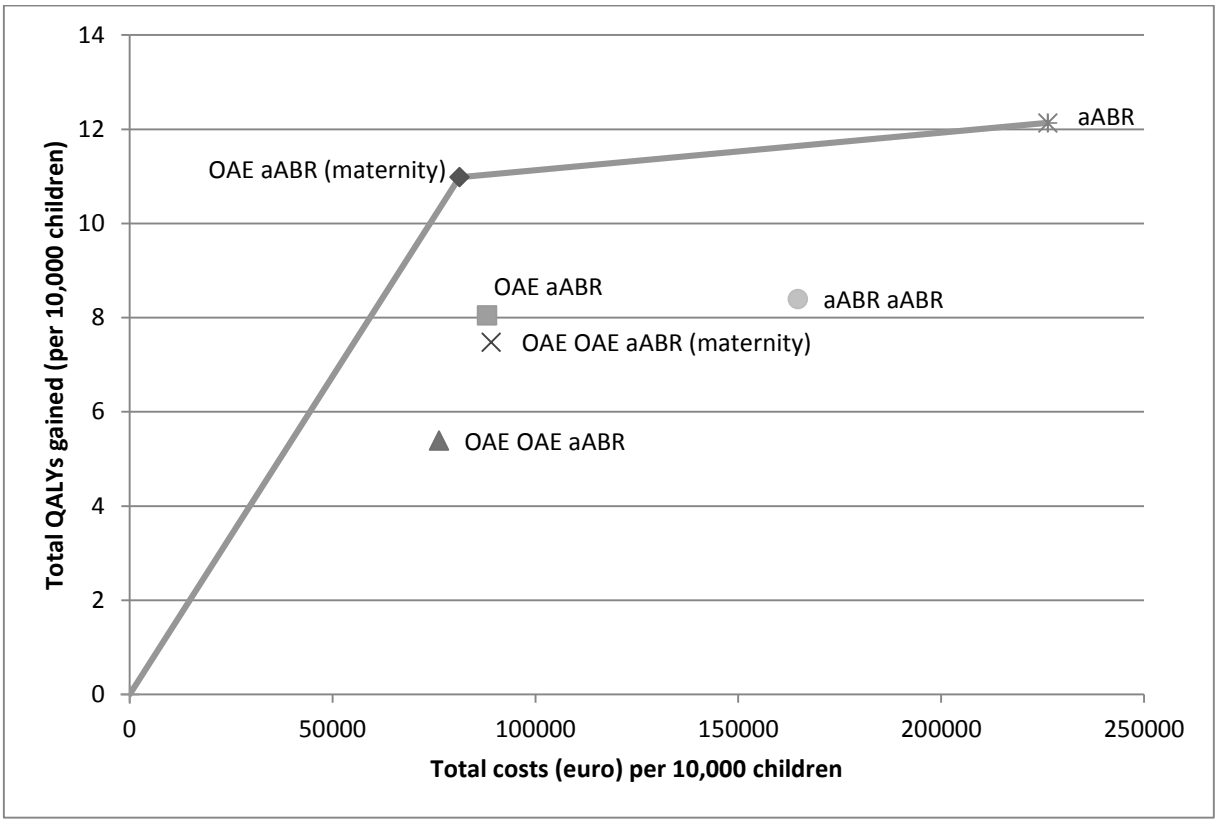

Figure E. The total costs and total QALYs gained for each protocol using € 200 per diagnostic consultation.

References

1. Watkin PM, Baldwin M, McEnery G. Neonatal at risk screening and the identification of deafness. *Arch Dis Child* 1991; **66**(10 Spec No): 1130-5.
2. Carroll AE, Downs SM. Improving Decision Analyses: Parent Preferences (Utility Values) for Pediatric Health Outcomes. *The Journal of Pediatrics* 2009; **155**(1): 21-5.e5.