

# Supplementary appendices with univariate sensitivity analyses

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## Appendix A

### **Univariate sensitivity analysis: Baseline = Fully parameterized effectiveness against non-invasive CAP for both vaccines**

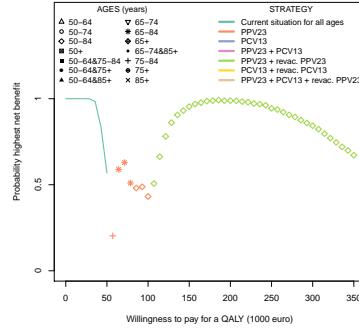
In this supplementary file, we present a visual overview of the effectiveness and cost-effectiveness of the different strategies in the different age groups, assuming fully parameterized baseline effectiveness of PPV23 and PCV13 against non-invasive CAP, unless explicitly mentioned otherwise, and show the univariate (or one way) sensitivity of these outcomes.

This supplement shows Cost-Effectiveness Acceptability Frontiers (CEAFs) and cost-effectiveness planes (CE planes) by age group targeted, on each page for a different scenario. Each page or scenario is defined by the change in a single variable or assumption versus the baseline.

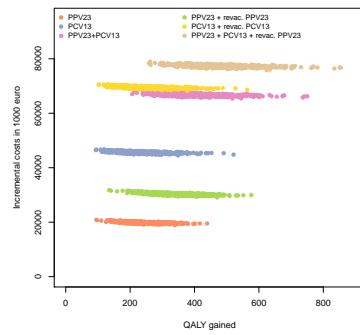
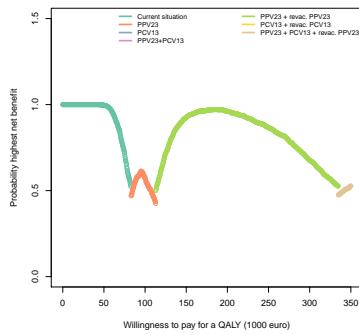
CEAFs have the attractive feature of summarizing parameter uncertainties in the ICERs in relation to a range of willingness to pay values. We use CEAFs showing for each willingness to pay (WTP) level over a wide range, the probability that the strategy depicted at that WTP level is the one strategy (amongst all strategies being compared) that results in the highest net benefit (when a QALY is valued at the WTP level shown). In the CE planes the realizations of 1000 simulations in terms of costs and effects (QALYs), results in clouds of 1000 points - one cloud for each incremental strategy - plotted versus the origin, where the origin of the plane represents the current situation. The further to the right, the more effective, the higher, the more costly a particular strategy is versus the current situation. Note that the same 1000 simulations per strategy are used to produce all the results we present under uncertainty.

For a stated “one way” deviation from the baseline above, each page shows at the top the CEAF over all age groups and strategies combined. Below this summary CEAF, we show more specific CEAFs by one of three age groups (on the left), along with their corresponding CE plane (on the right).

**Baseline: Fully parameterised effectiveness against non-invasive CAP for both PPV23 and PCV13**

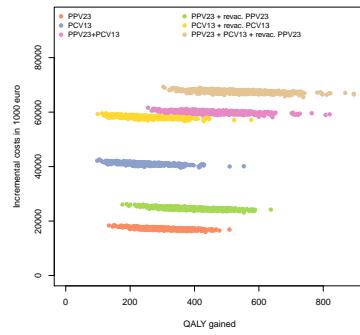
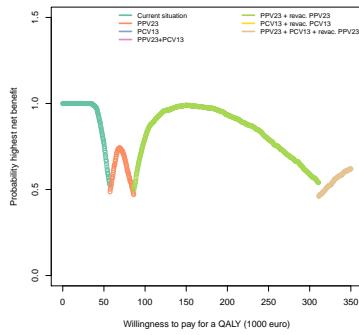


CEAFs: all age groups and strategies



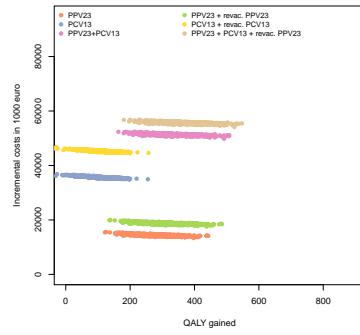
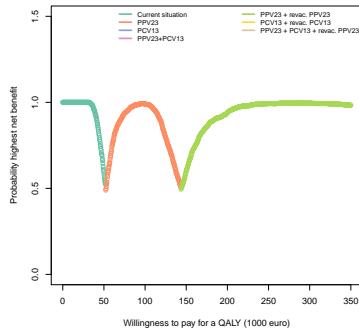
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

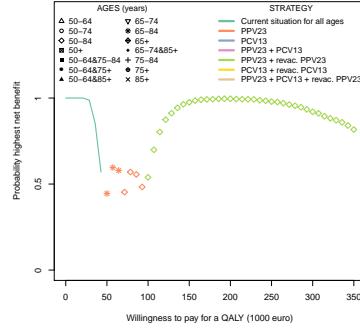
CE plane: age 65y - 74y



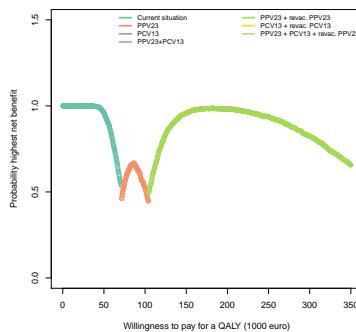
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

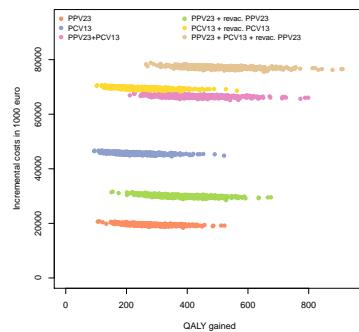
**Higher PPV23 protection against non-invasive CAP, by assuming ratio vaccine effectiveness non-IPD/IPD = 0.77, instead of baseline 0.55**



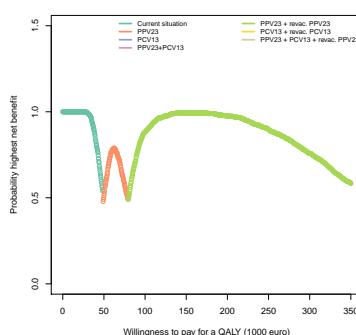
CEAFs: all age groups and strategies



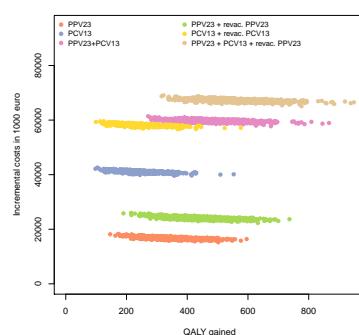
CEAFs: age 50y - 64y



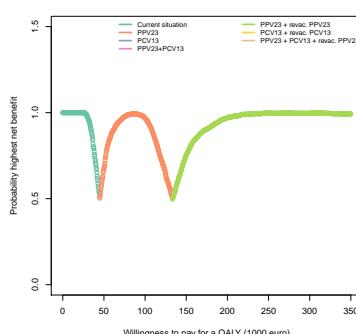
CE plane: age 50y - 64y



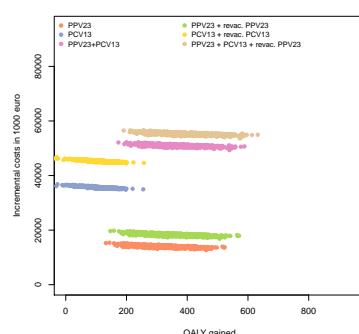
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

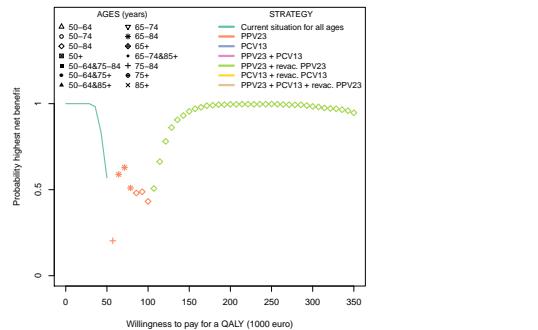


CEAFs: age 75y - 84y

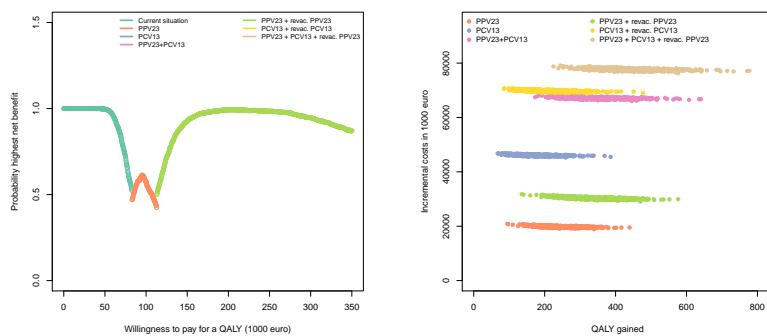


CE plane: age 75y - 84y

## 5 years of PCV13 protection followed by no protection, and baseline PPV23 protection

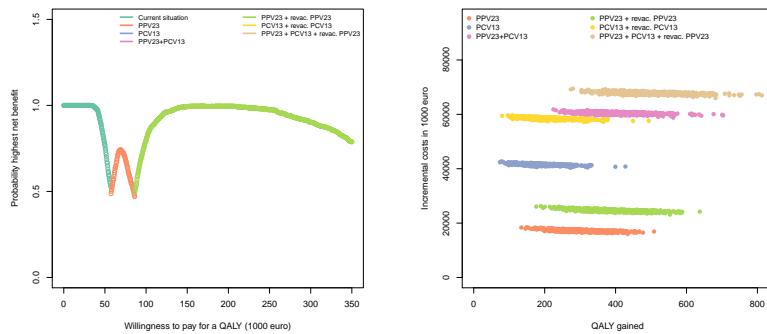


CEAFs: all age groups and strategies



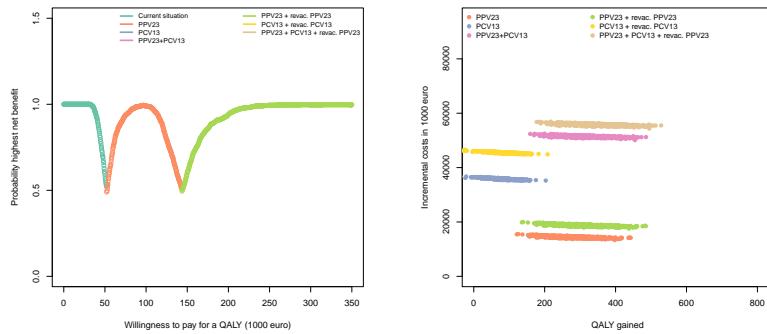
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



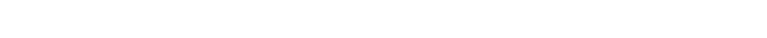
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

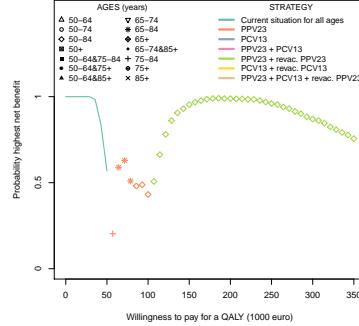
CE plane: age 65y - 74y



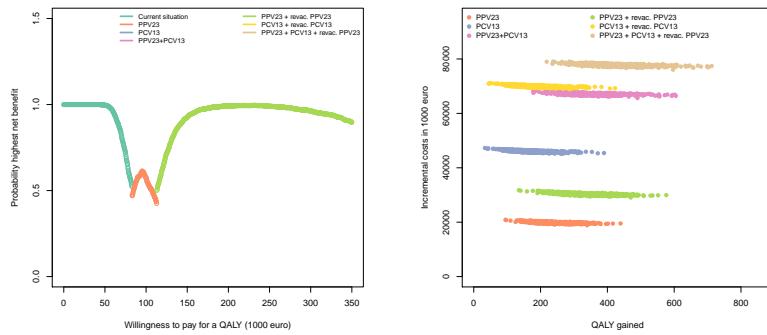
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## Age independent VE for PCV13 from age 50 to 84y

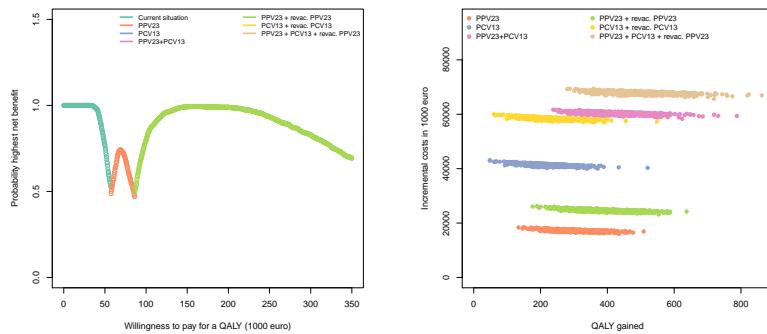


CEAFs: all age groups and strategies



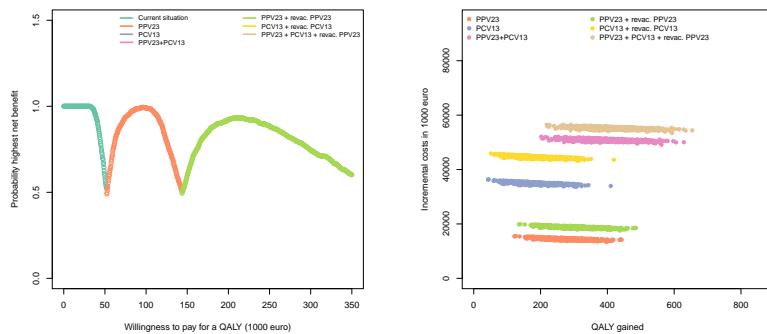
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

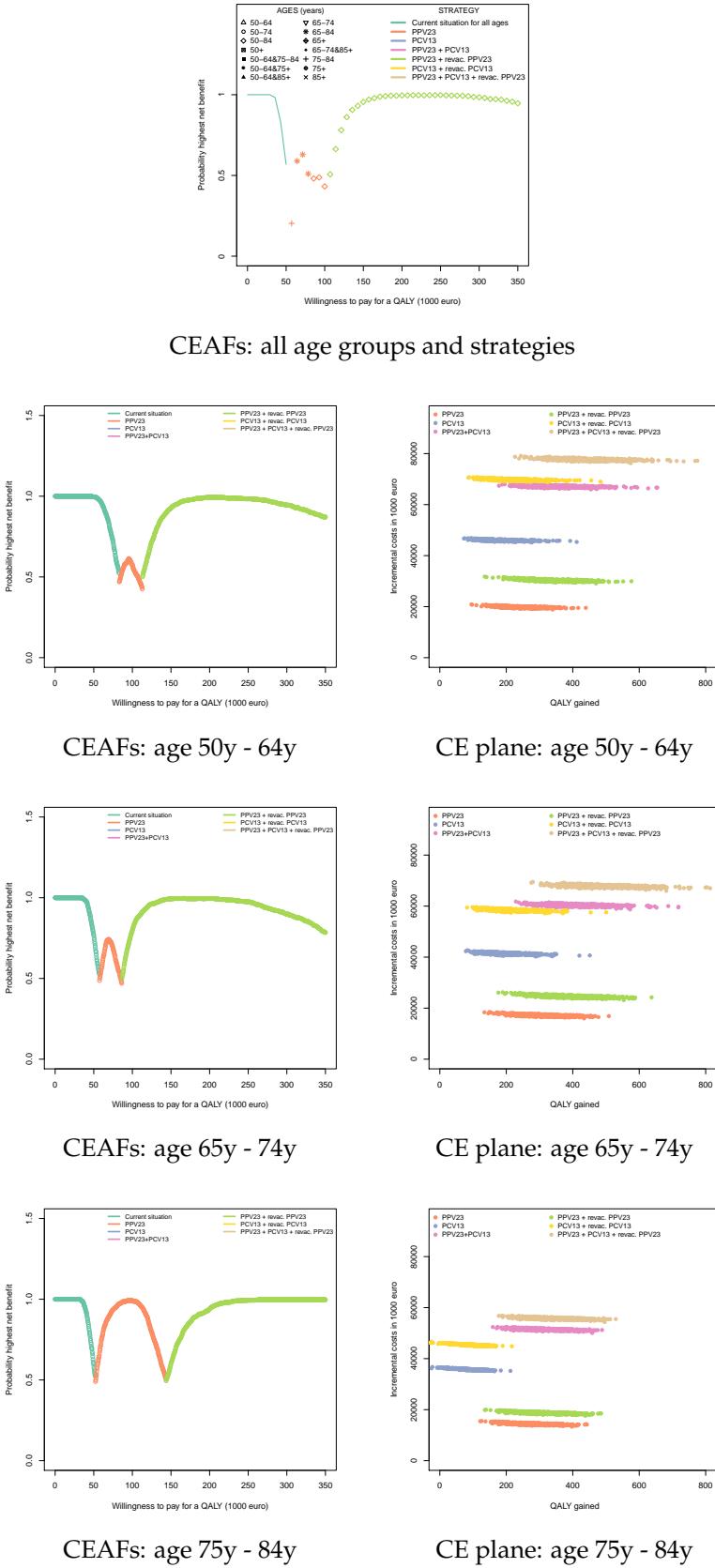
CE plane: age 65y - 74y



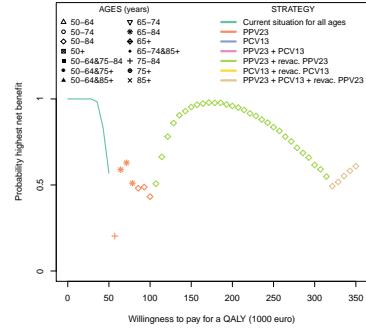
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

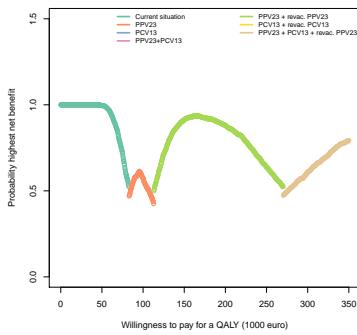
**Minimum duration of PCV13 protection (4 years fixed protection followed by rapid waning to no protection at 10 years), and baseline PPV23 protection**



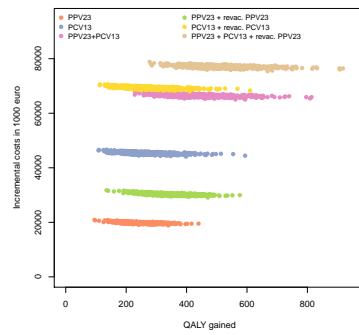
**Maximum duration of PCV13 protection (9 years fixed protection followed by slow waning to no protection at 20 years), and baseline PPV23 protection**



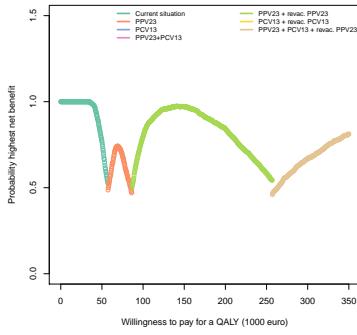
CEAFs: all age groups and strategies



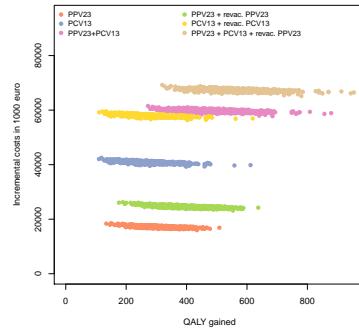
CEAFs: age 50y - 64y



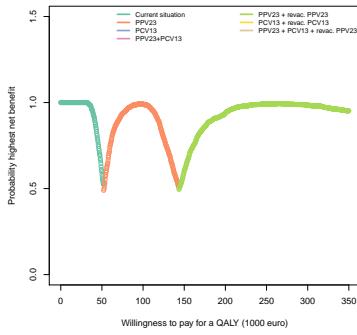
CE plane: age 50y - 64y



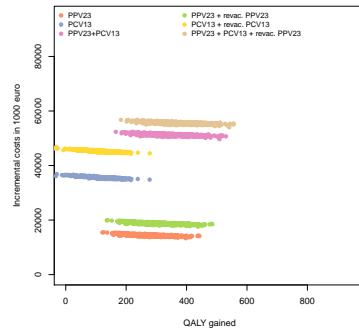
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

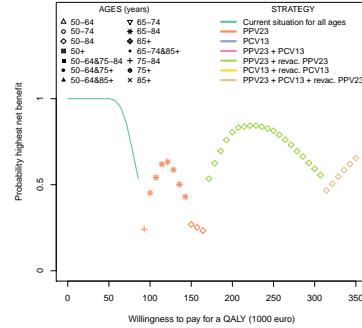


CEAFs: age 75y - 84y

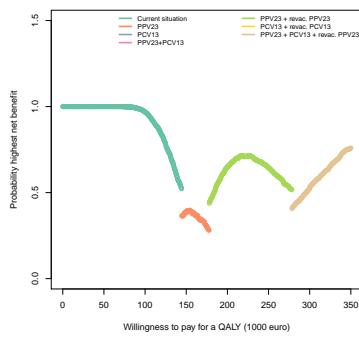


CE plane: age 75y - 84y

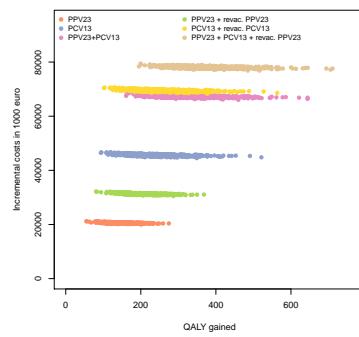
**2 years of complete (without waning) PPV23 protection followed by no protection, and baseline PCV13 vaccine protection**



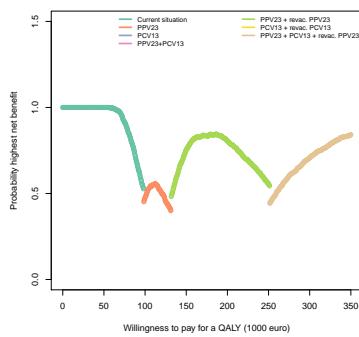
CEAFs: all age groups and strategies



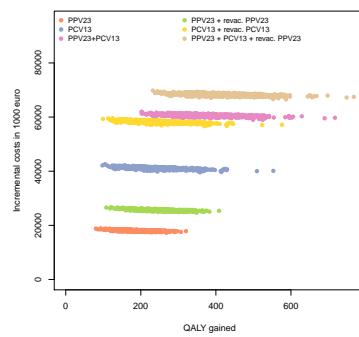
CEAFs: age 50y - 64y



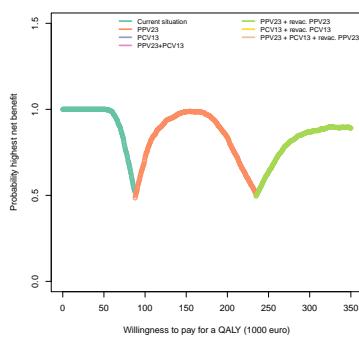
CE plane: age 50y - 64y



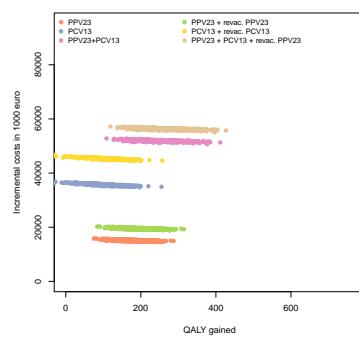
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

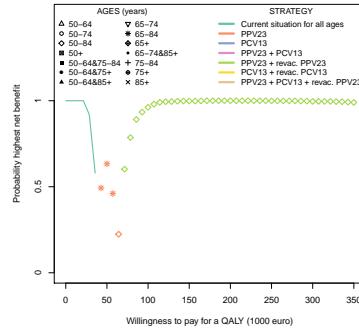


CEAFs: age 75y - 84y

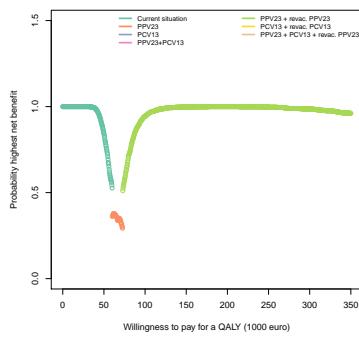


CE plane: age 75y - 84y

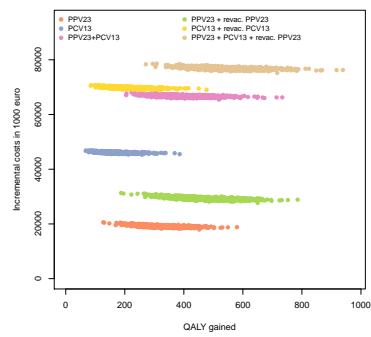
**5 years of complete (without waning) protection followed by no protection for both PCV13 and PPV23**



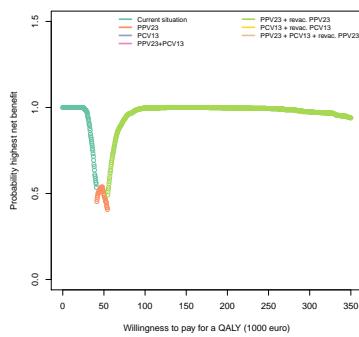
CEAFs: all age groups and strategies



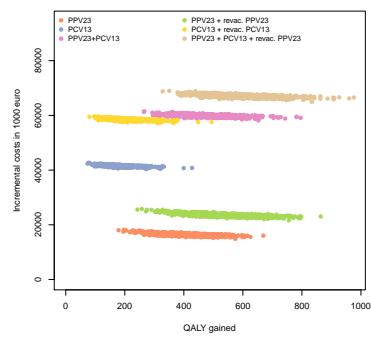
CEAFs: age 50y - 64y



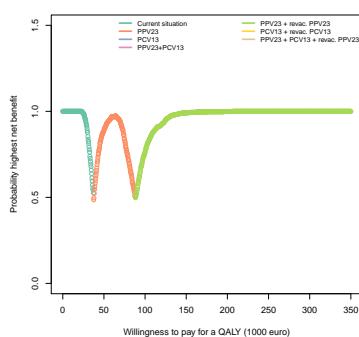
CE plane: age 50y - 64y



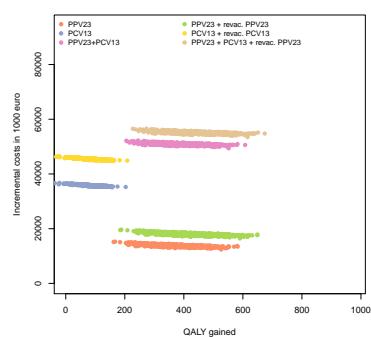
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

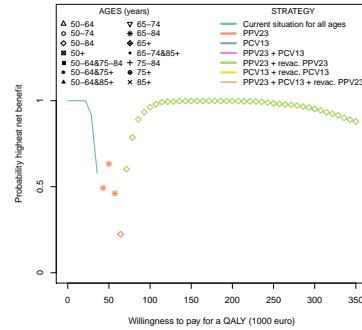


CEAFs: age 75y - 84y

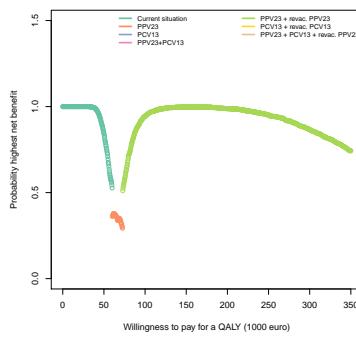


CE plane: age 75y - 84y

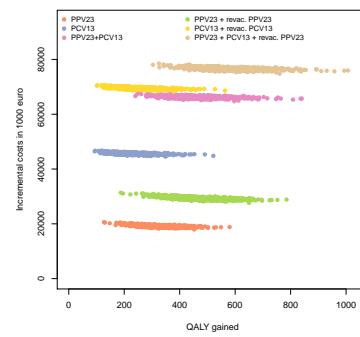
**5 years of complete (without waning) PPV23 protection followed by no protection, and baseline PCV13 vaccine protection**



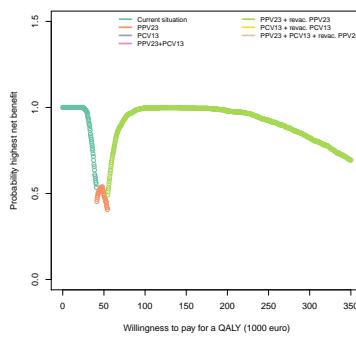
CEAFs: all age groups and strategies



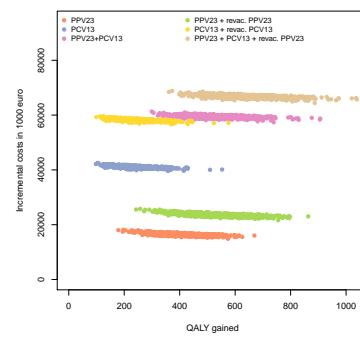
CEAFs: age 50y - 64y



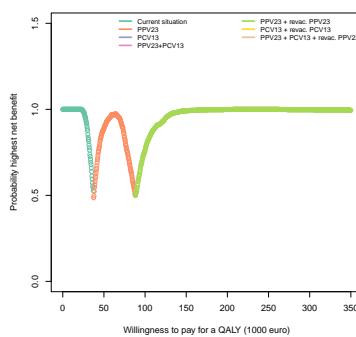
CE plane: age 50y - 64y



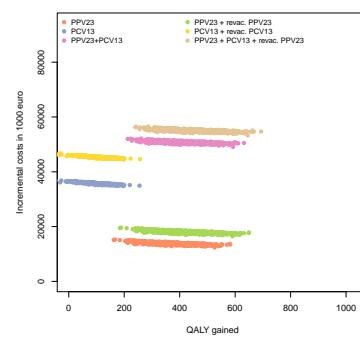
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

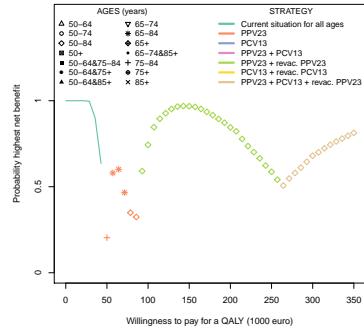


CEAFs: age 75y - 84y

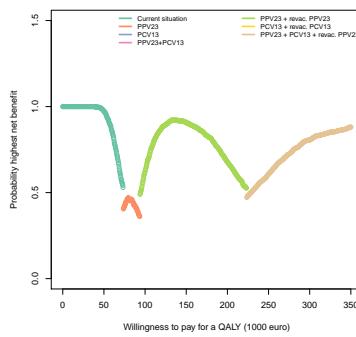


CE plane: age 75y - 84y

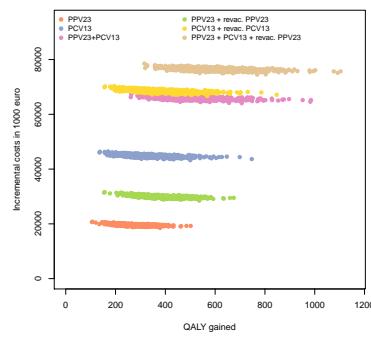
**Minimum PCV13 incidence decline (PCV13 serotype incidence -10% per year, baseline (76%) replacement)**



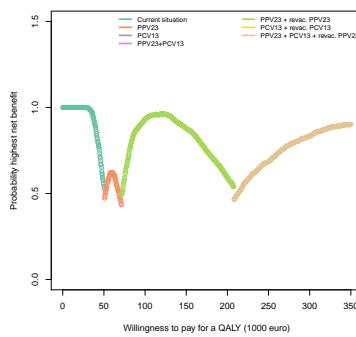
CEAFs: all age groups and strategies



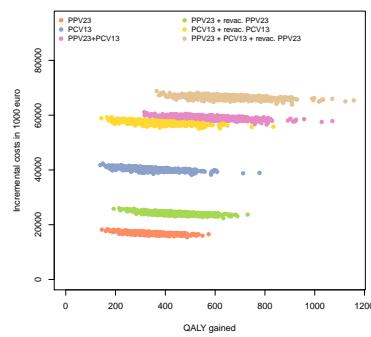
CEAFs: age 50y - 64y



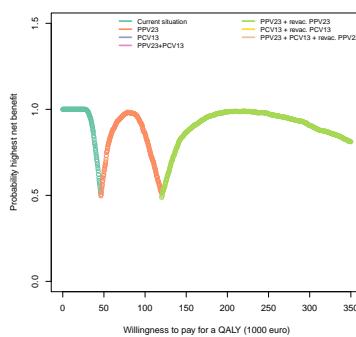
CE plane: age 50y - 64y



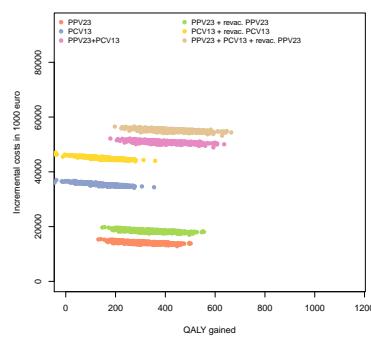
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

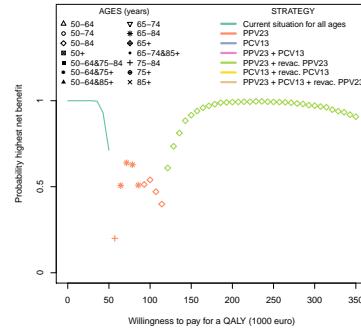


CEAFs: age 75y - 84y

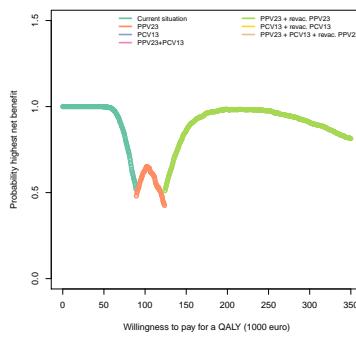


CE plane: age 75y - 84y

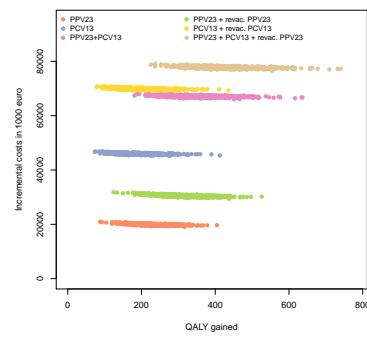
**Maximum PCV13 incidence decline (PCV13 serotype incidence -20% per year, baseline (76%) replacement)**



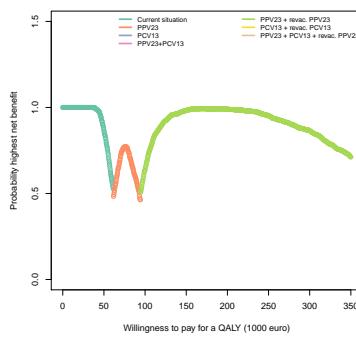
CEAFs: all age groups and strategies



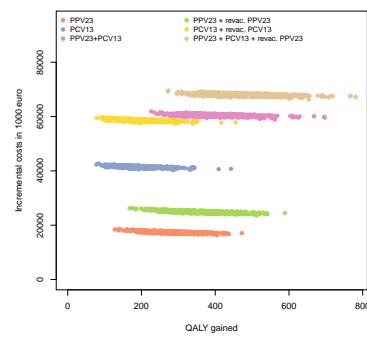
CEAFs: age 50y - 64y



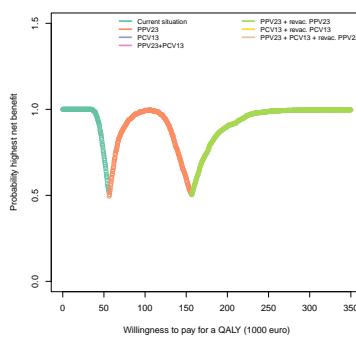
CE plane: age 50y - 64y



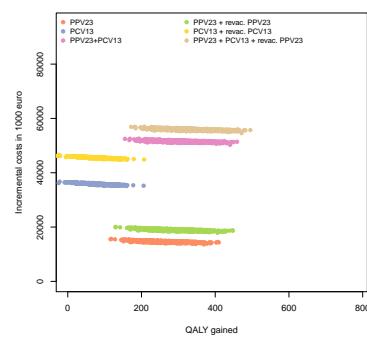
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

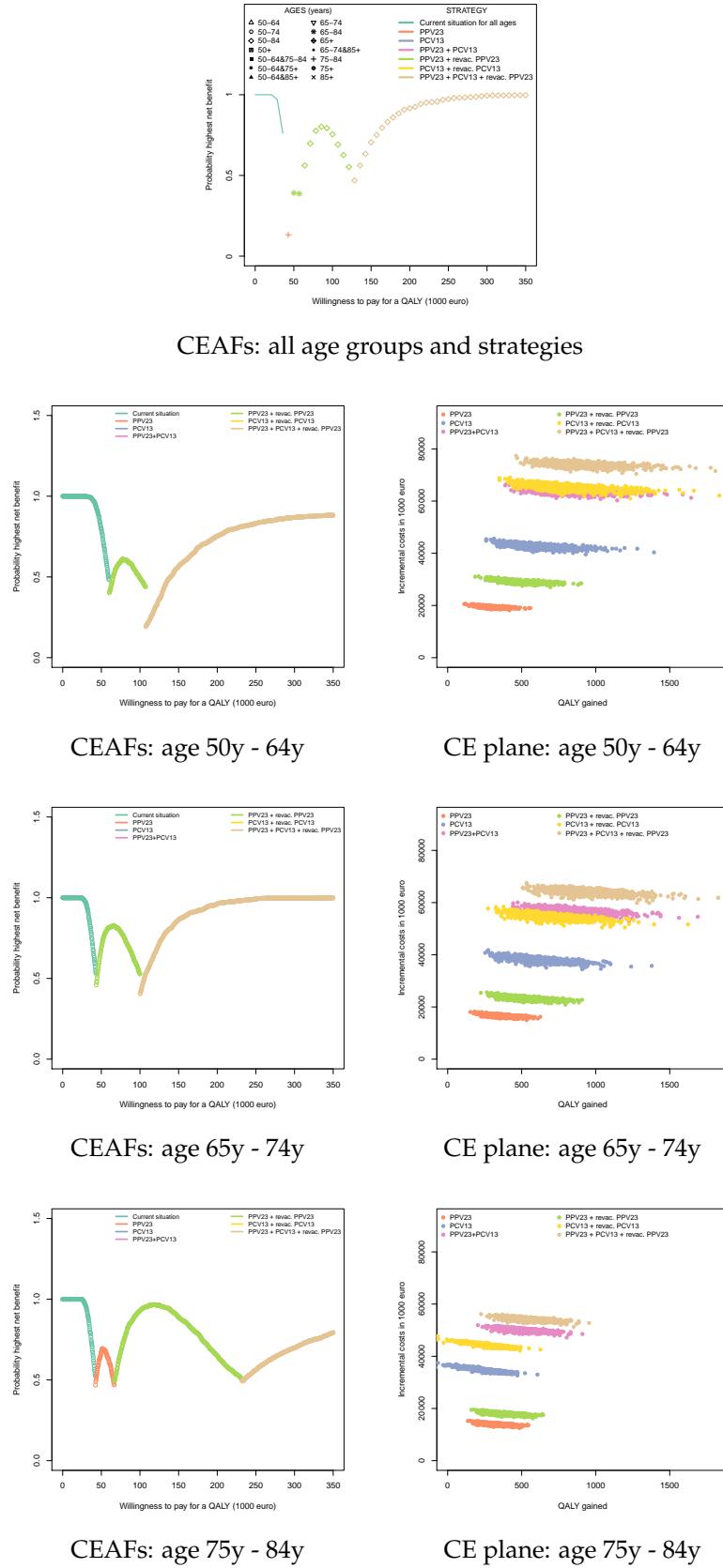


CEAFs: age 75y - 84y

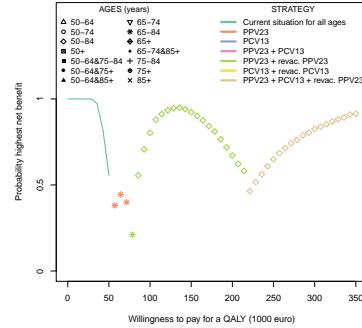


CE plane: age 75y - 84y

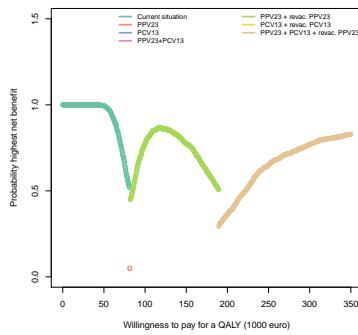
**Quick PCV13 serotype relapse: PCV13 incidence returns to 2015 value within 7 years  
(0% replacement of PCV13 incidence decline by non-PCV13 types)**



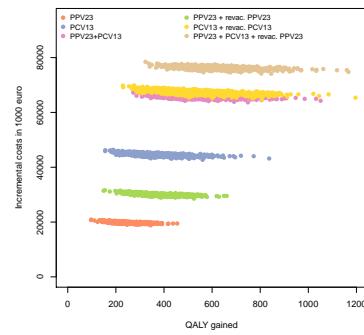
**Slow PCV13 serotype relapse: PCV13 incidence returns to 2015 value within 15 years  
(0% replacement of PCV13 incidence decline by non-PCV13 types)**



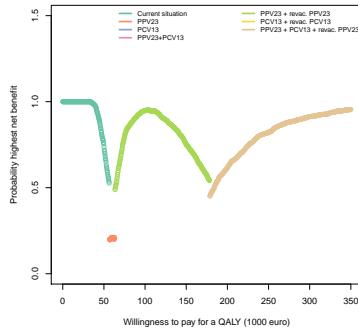
CEAFs: all age groups and strategies



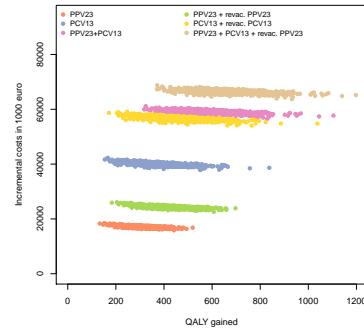
CEAFs: age 50y - 64y



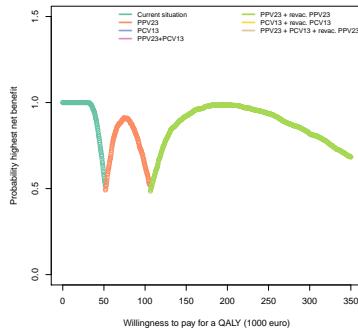
CE plane: age 50y - 64y



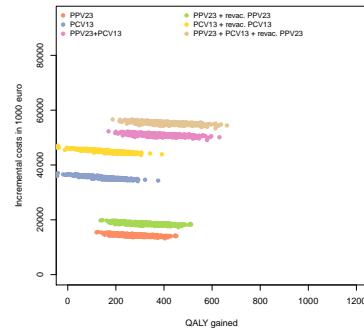
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

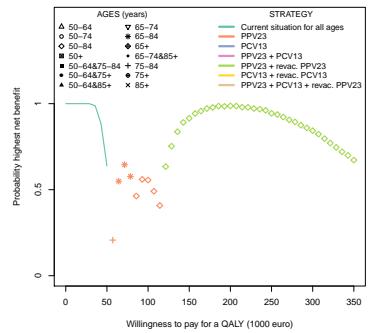


CEAFs: age 75y - 84y

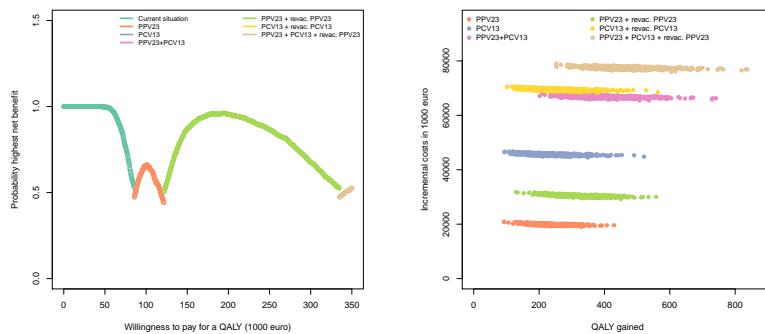


CE plane: age 75y - 84y

## Serotype replacement: 34% (2013 serocoverage data) instead of 76% (2015 baseline)

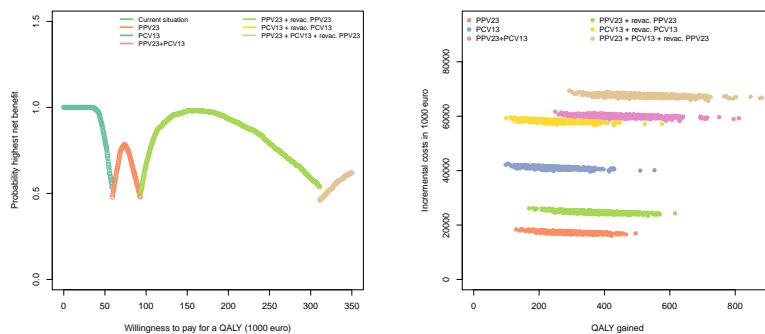


CEAFs: all age groups and strategies



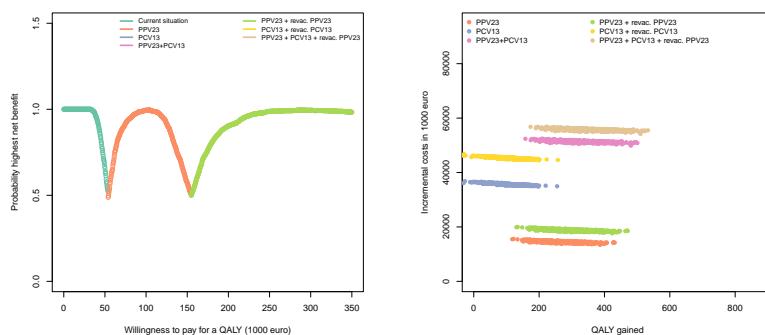
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

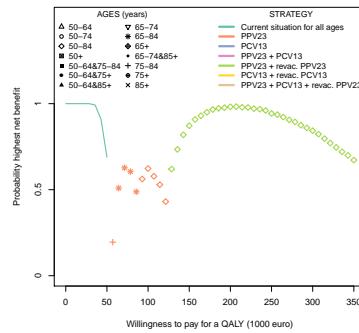
CE plane: age 65y - 74y



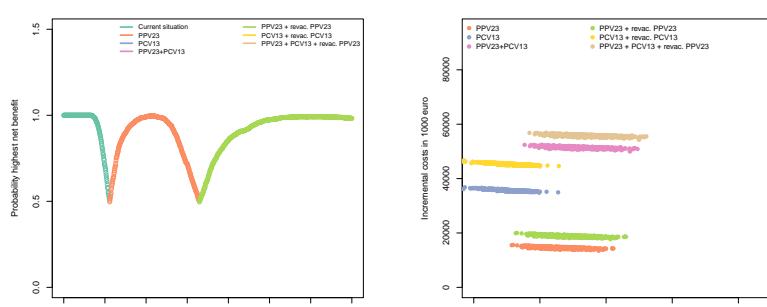
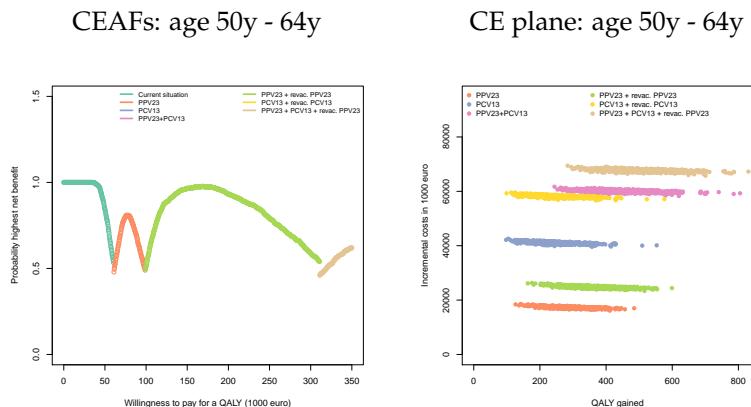
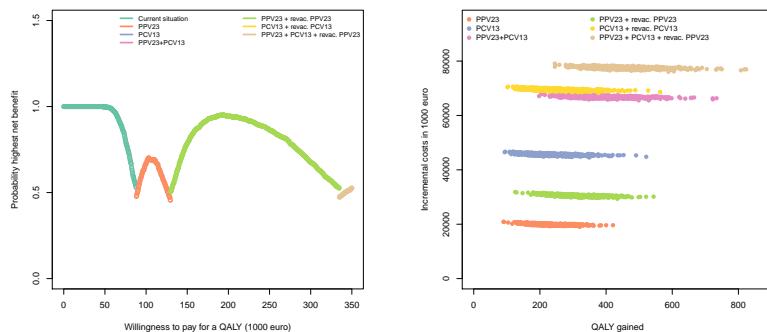
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## Serotype replacement extreme low: 0% instead of 76% (2015 baseline)

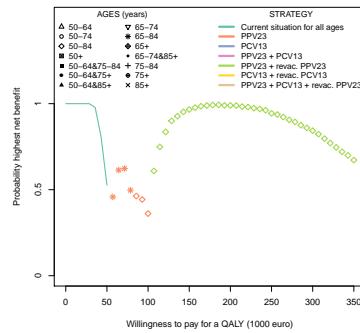


CEAFs: all age groups and strategies

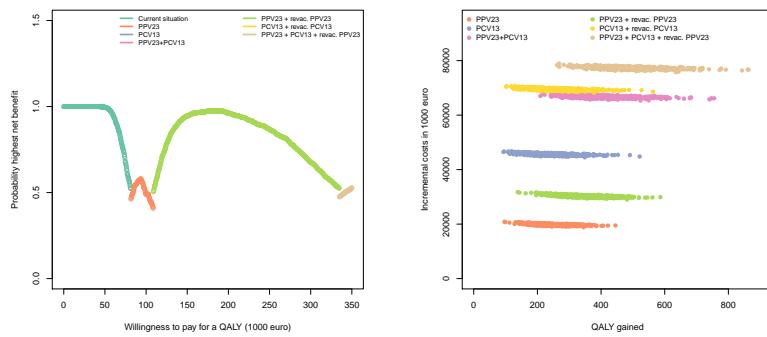


CEAFs: age 75y - 84y      CE plane: age 75y - 84y

## Serotype replacement extreme high: 100% instead of 76% (2015 baseline)

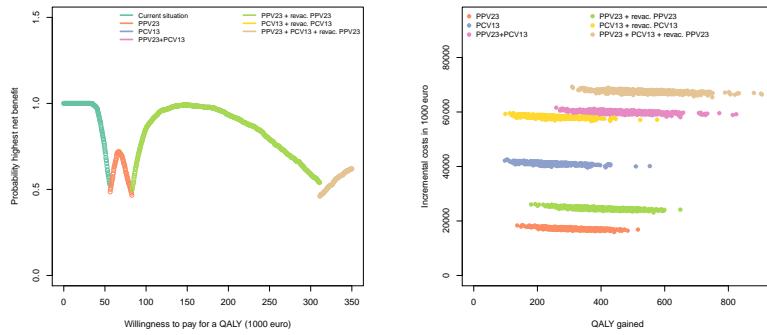


CEAFs: all age groups and strategies



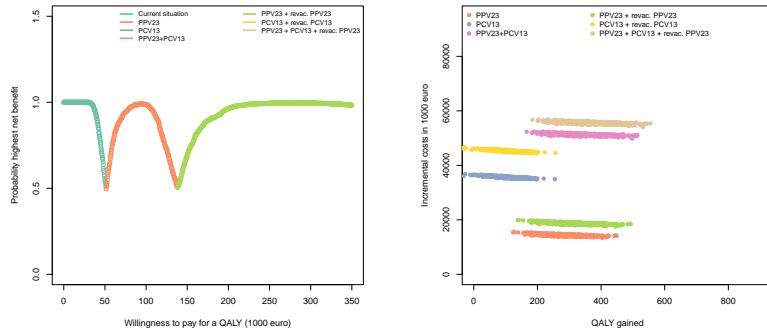
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

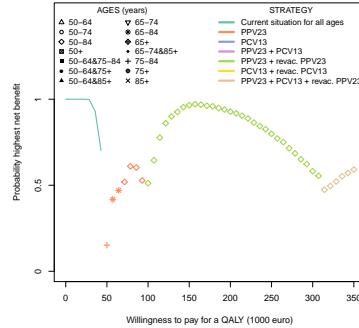
CE plane: age 65y - 74y



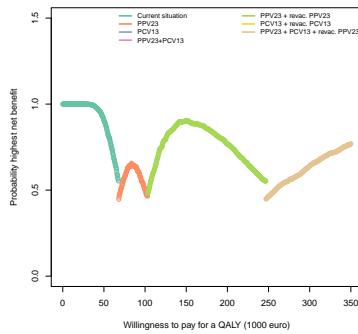
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

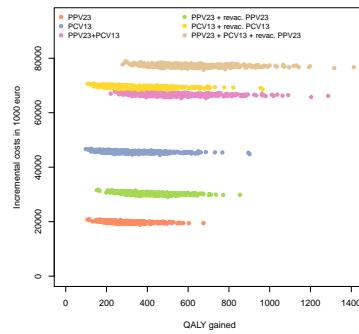
**Higher percentage of pneumococcal pneumonia in outpatient CAP (27% (Said 2013) instead of 10.5%)**



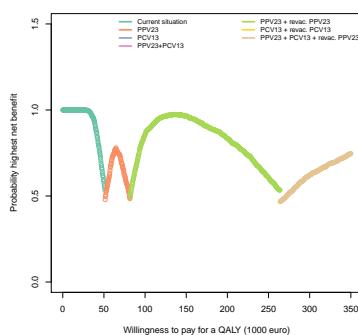
CEAFs: all age groups and strategies



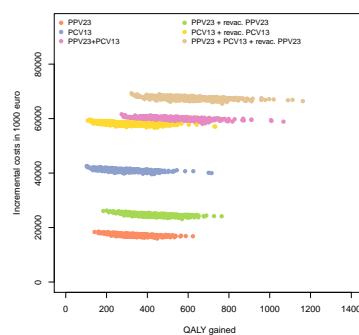
CEAFs: age 50y - 64y



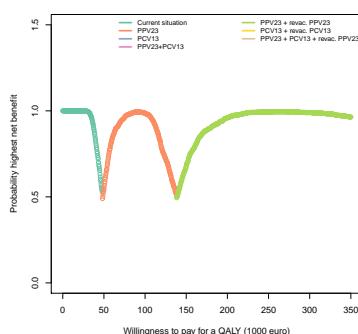
CE plane: age 50y - 64y



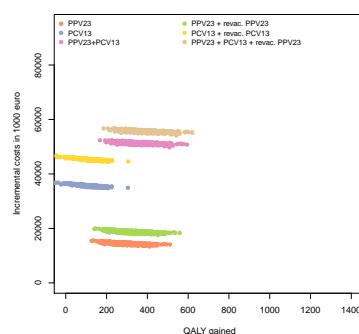
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

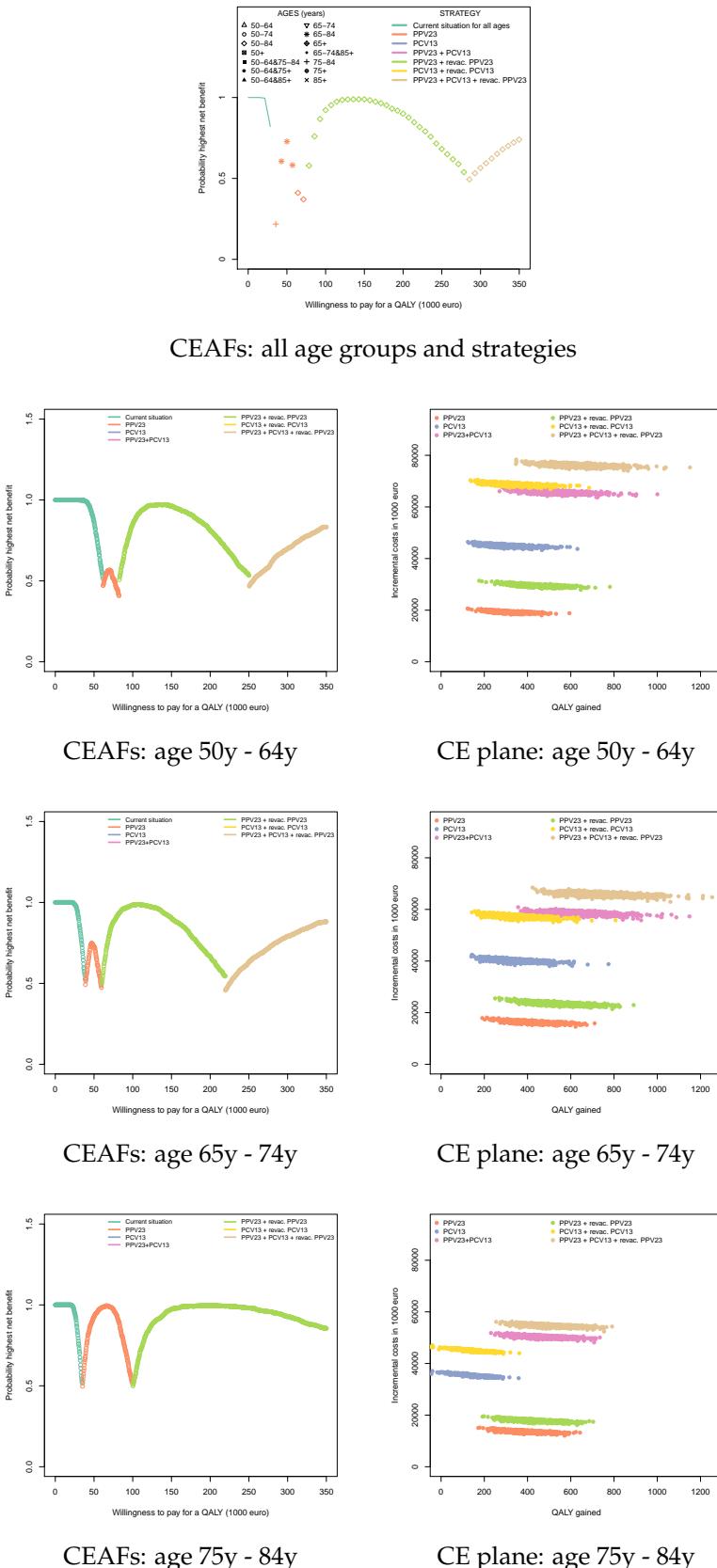


CEAFs: age 75y - 84y

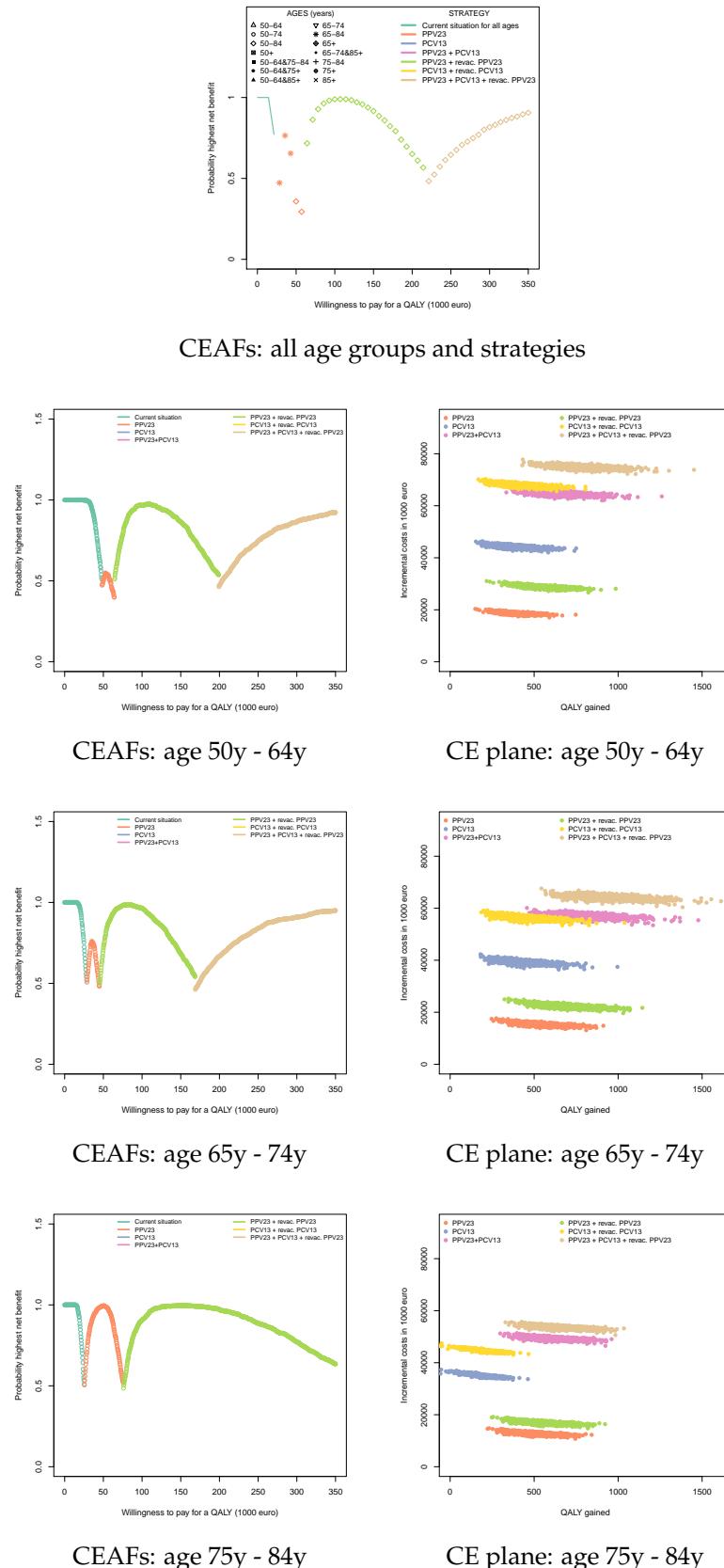


CE plane: age 75y - 84y

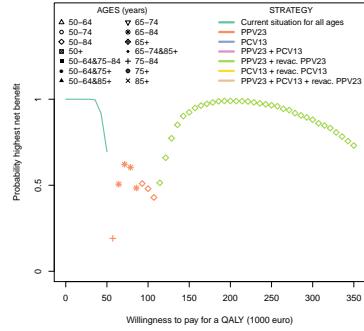
## Higher hospitalised pneumococcal pneumonia incidence: 1.5 x baseline



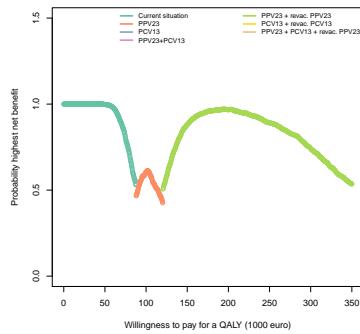
## Higher hospitalised pneumococcal pneumonia incidence: 2 x baseline



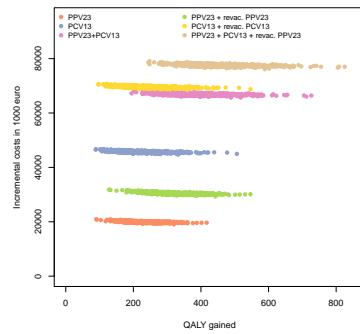
**Lower incidence of hospitalisations (94% of baseline, assuming no underreporting in NRC)**



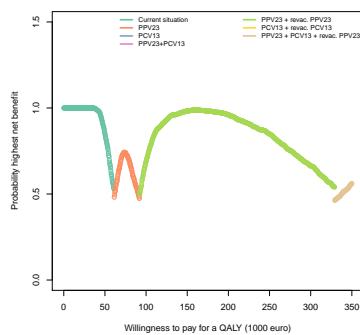
CEAFs: all age groups and strategies



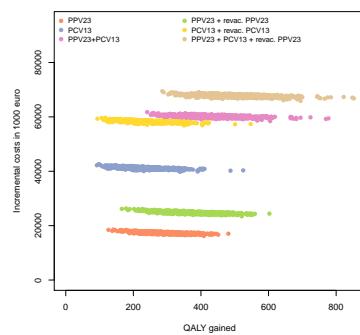
CEAFs: age 50y - 64y



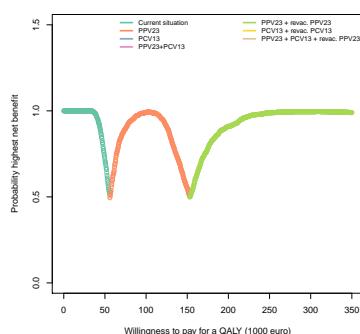
CE plane: age 50y - 64y



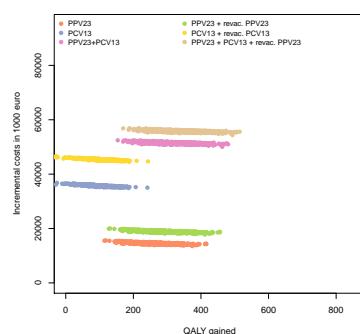
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

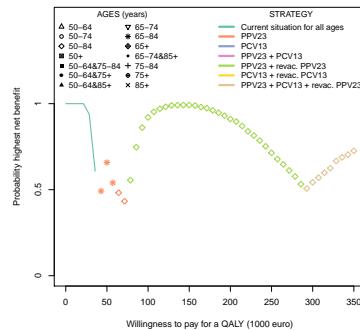


CEAFs: age 75y - 84y

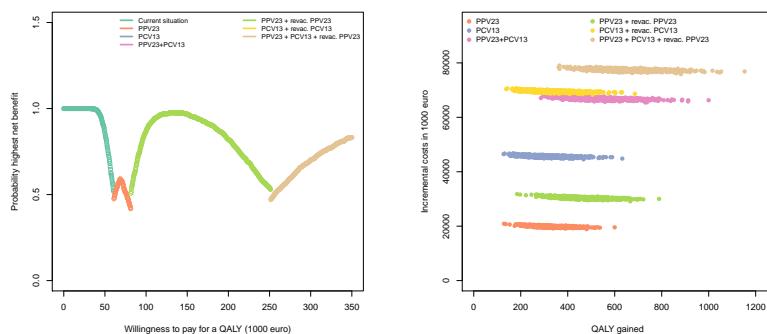


CE plane: age 75y - 84y

## High mortality: Death rate of hospitalised cases: 150% of base

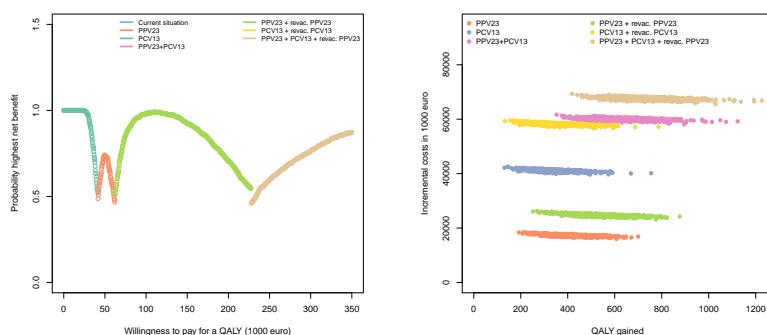


CEAFs: all age groups and strategies



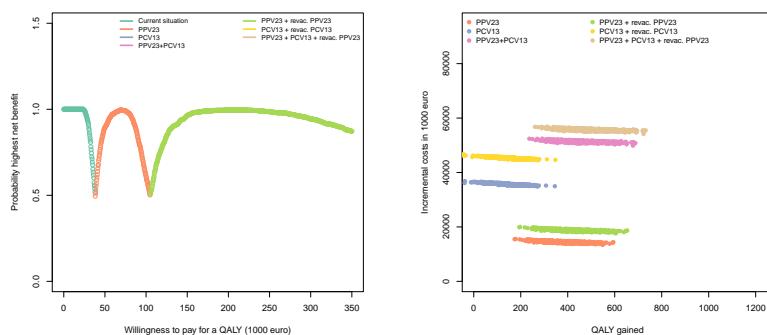
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

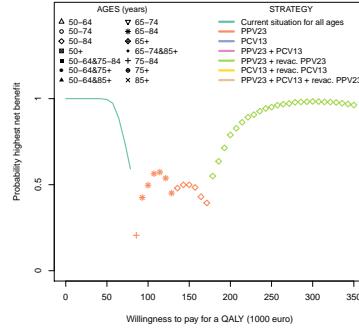
CE plane: age 65y - 74y



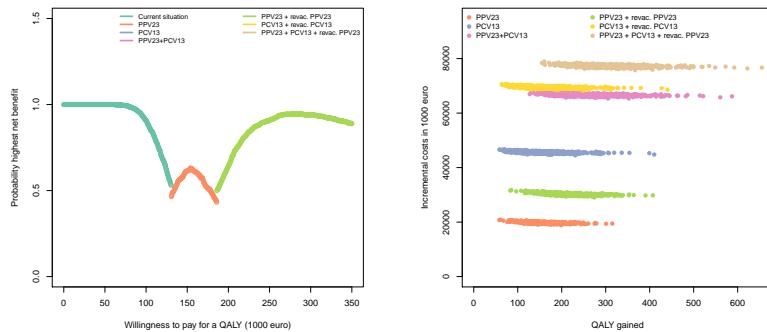
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## Low mortality: Death rate of hospitalised cases: 50% of baseline

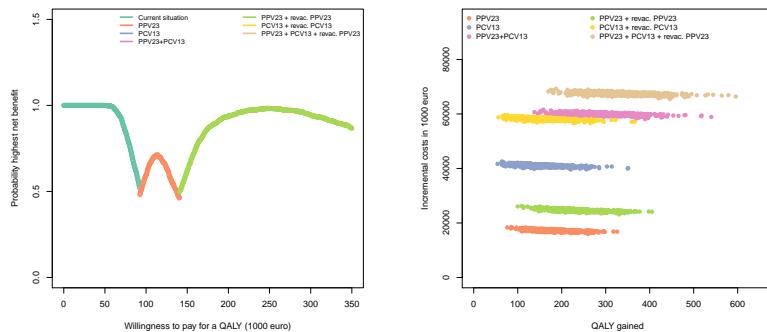


CEAFs: all age groups and strategies



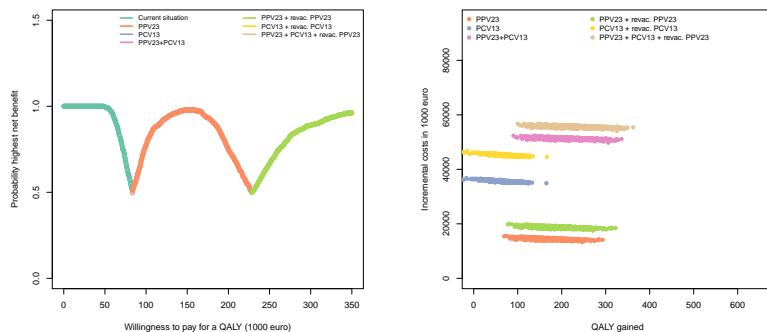
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

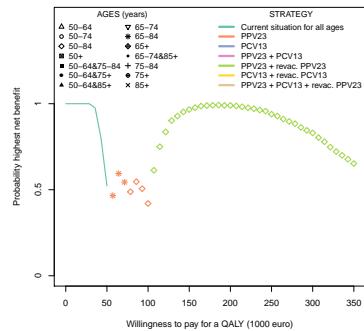
CE plane: age 65y - 74y



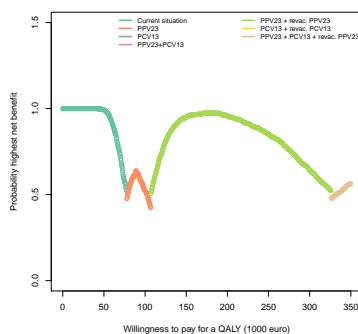
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

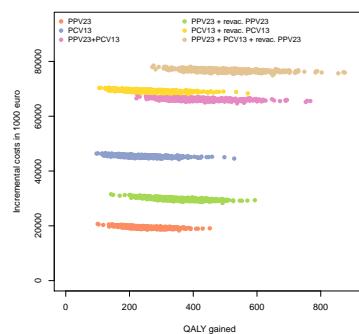
## More meningitis sequelae (probabilities of 20% for hearing loss and 22% for neurological sequelae)



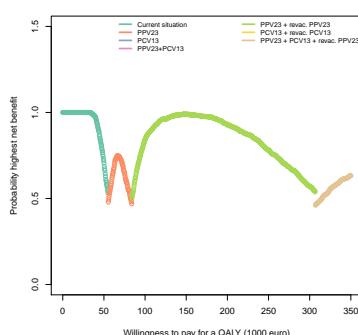
CEAFs: all age groups and strategies



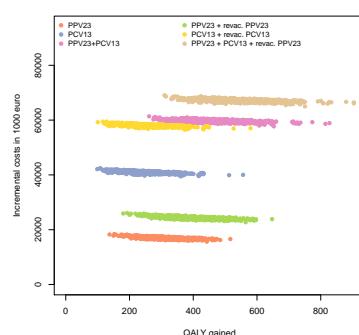
CEAFs: age 50y - 64y



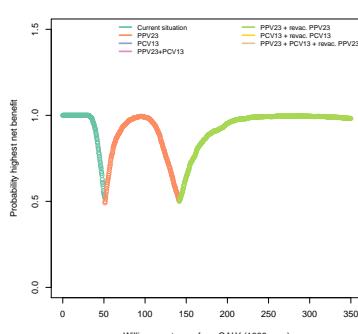
CE plane: age 50y - 64y



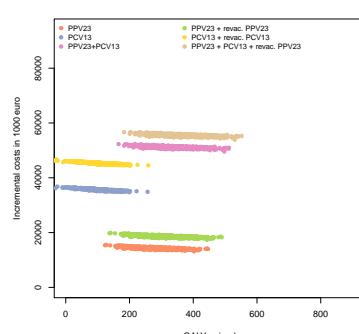
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

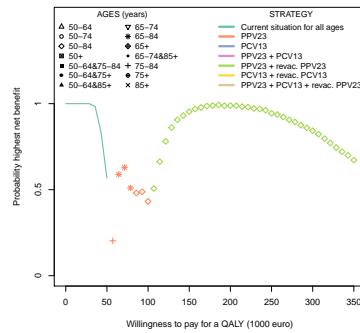


CEAFs: age 75y - 84y

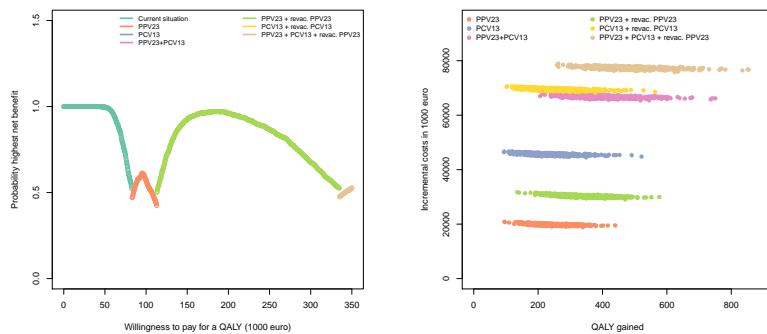


CE plane: age 75y - 84y

## Higher costs CAP for outpatients (1 extra GP consult per case)

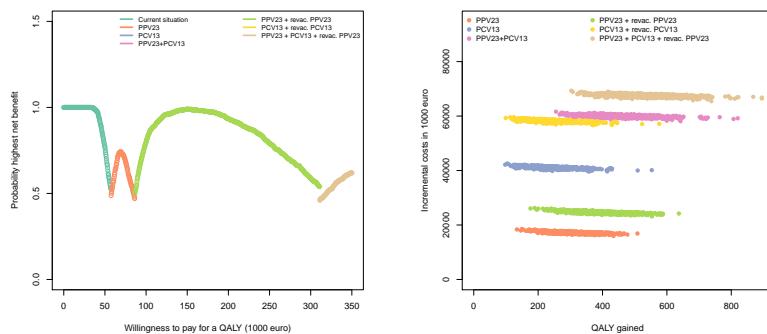


CEAFs: all age groups and strategies



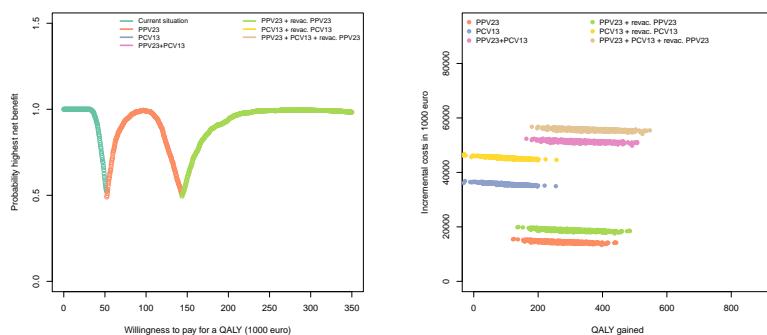
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

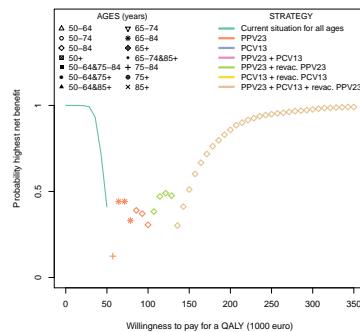
CE plane: age 65y - 74y



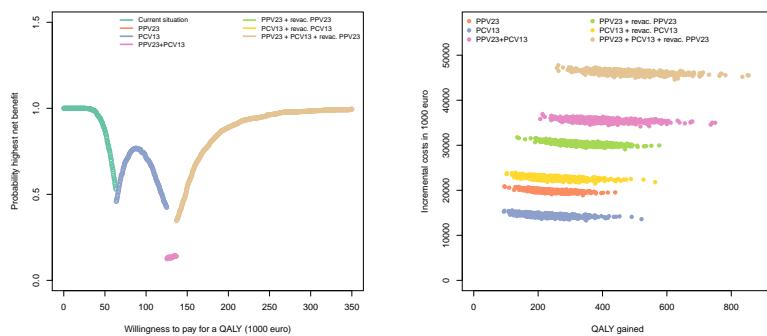
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## 75% reduction of the baseline PCV13 price, baseline PPV23 price

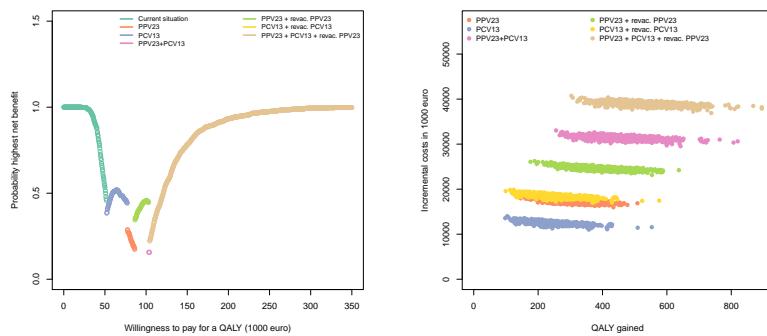


CEAFs: all age groups and strategies



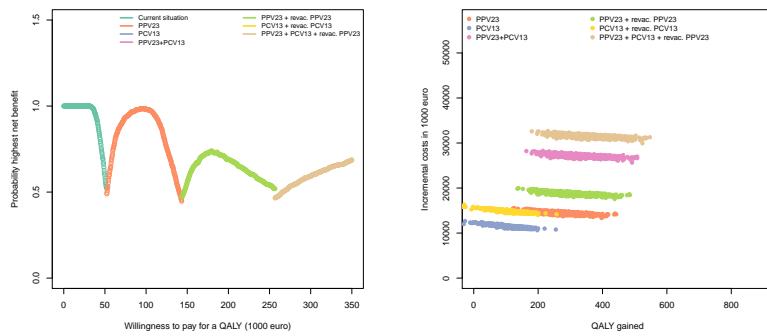
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

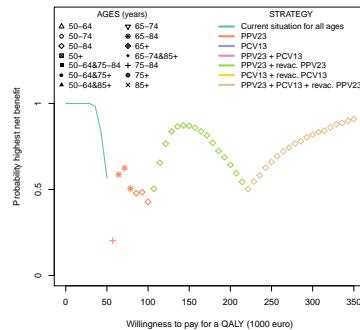
CE plane: age 65y - 74y



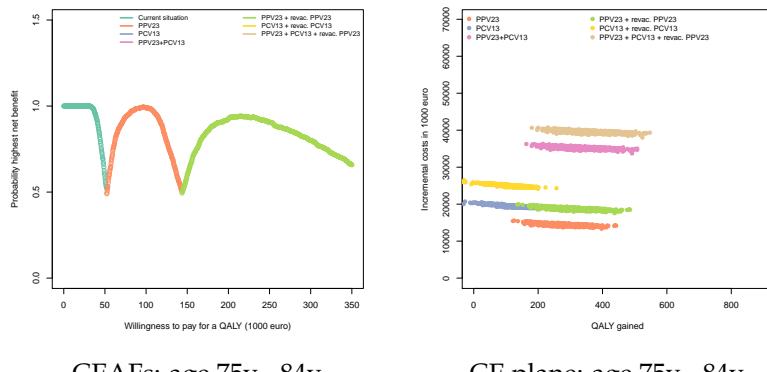
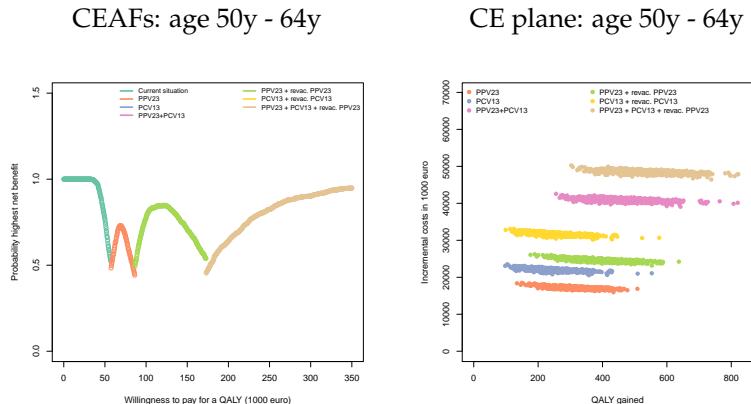
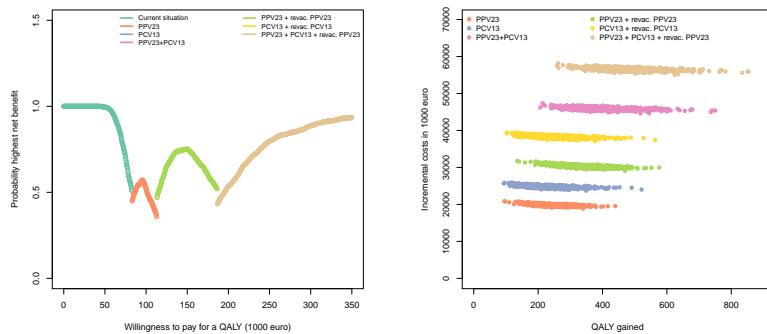
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

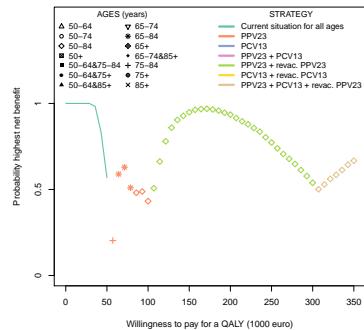
## 50% reduction of the baseline PCV13 price, baseline PPV23 price



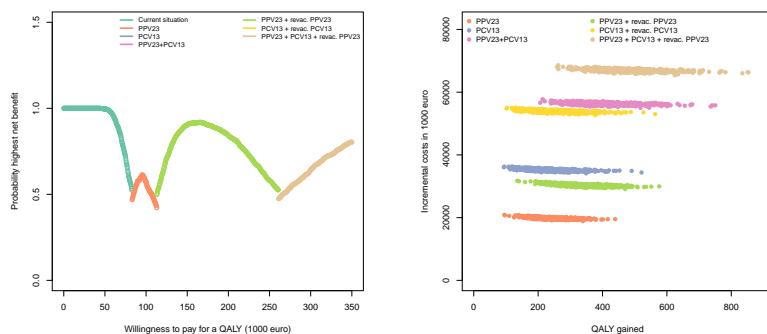
CEAFs: all age groups and strategies



## 25% reduction of the baseline PCV13 price, baseline PPV23 price

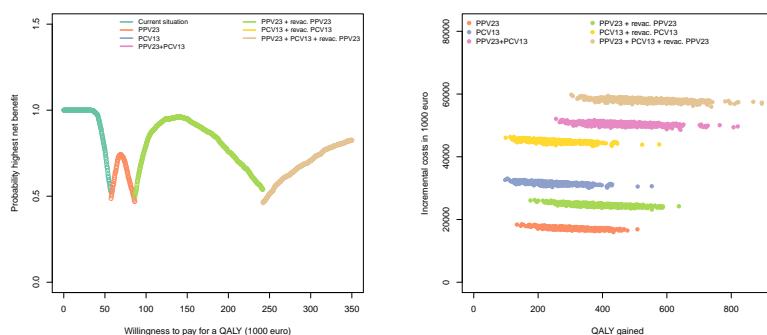


CEAFs: all age groups and strategies



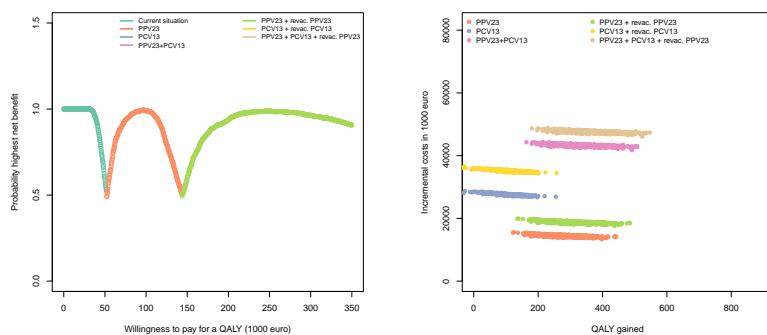
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



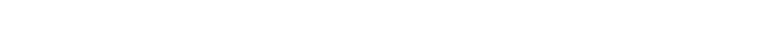
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

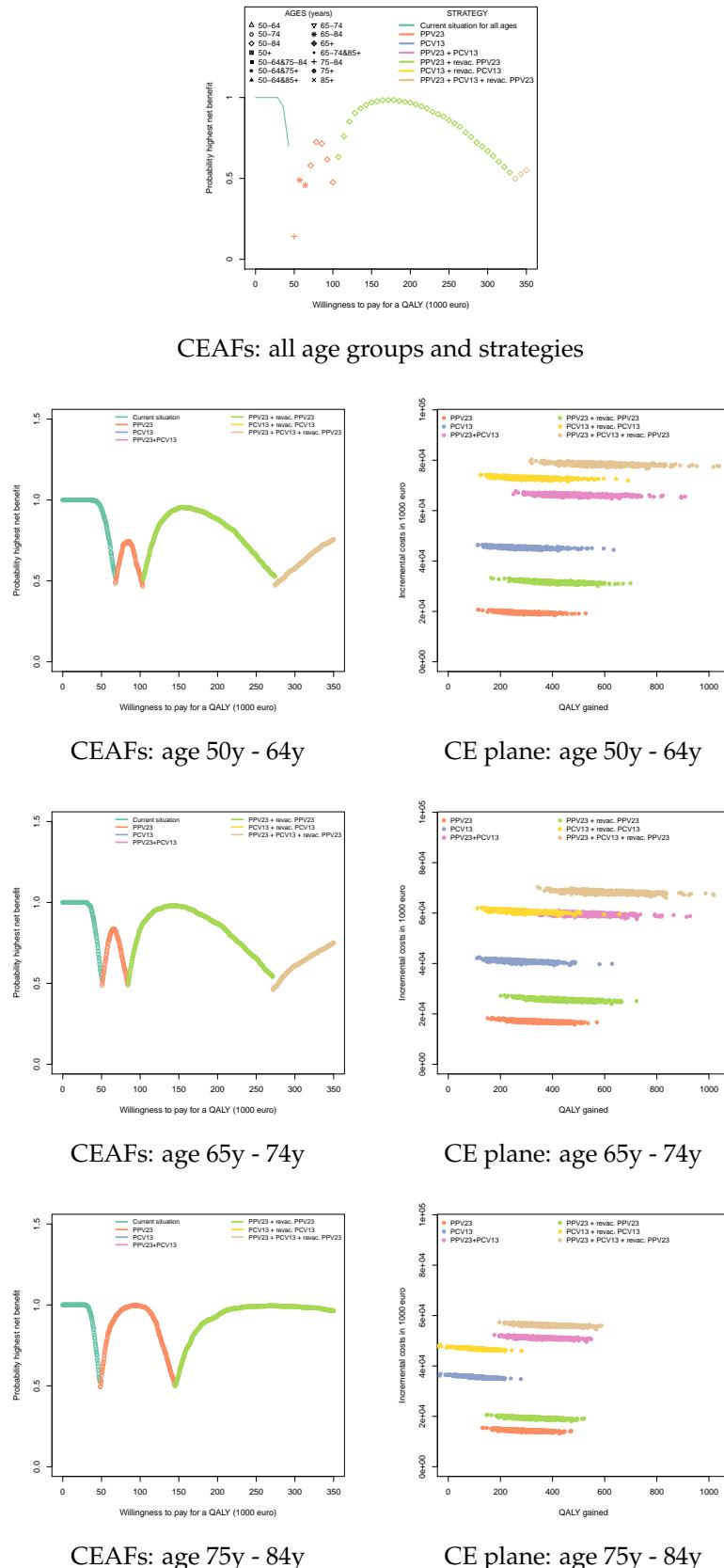
CE plane: age 65y - 74y



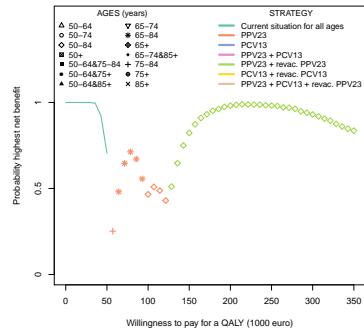
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

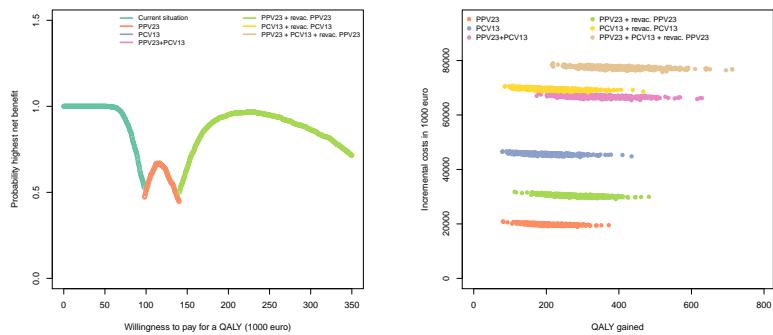
## No discounting: discount rate costs and effects: 0%



## Discount rate for costs and effects: 3%

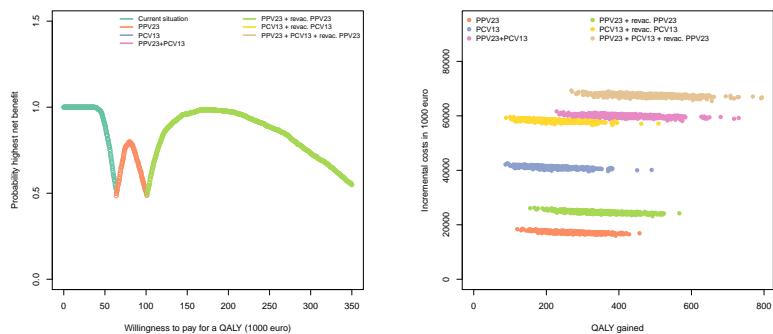


CEAFs: all age groups and strategies



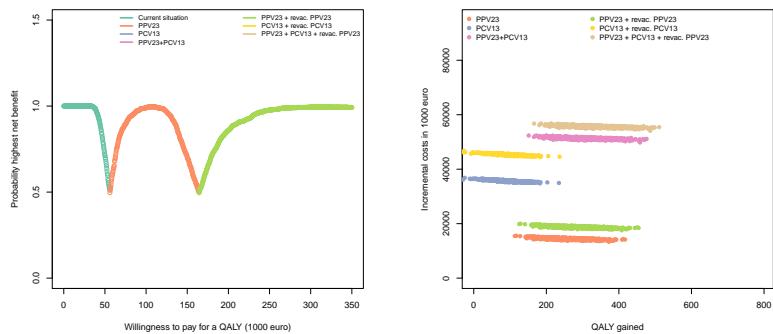
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

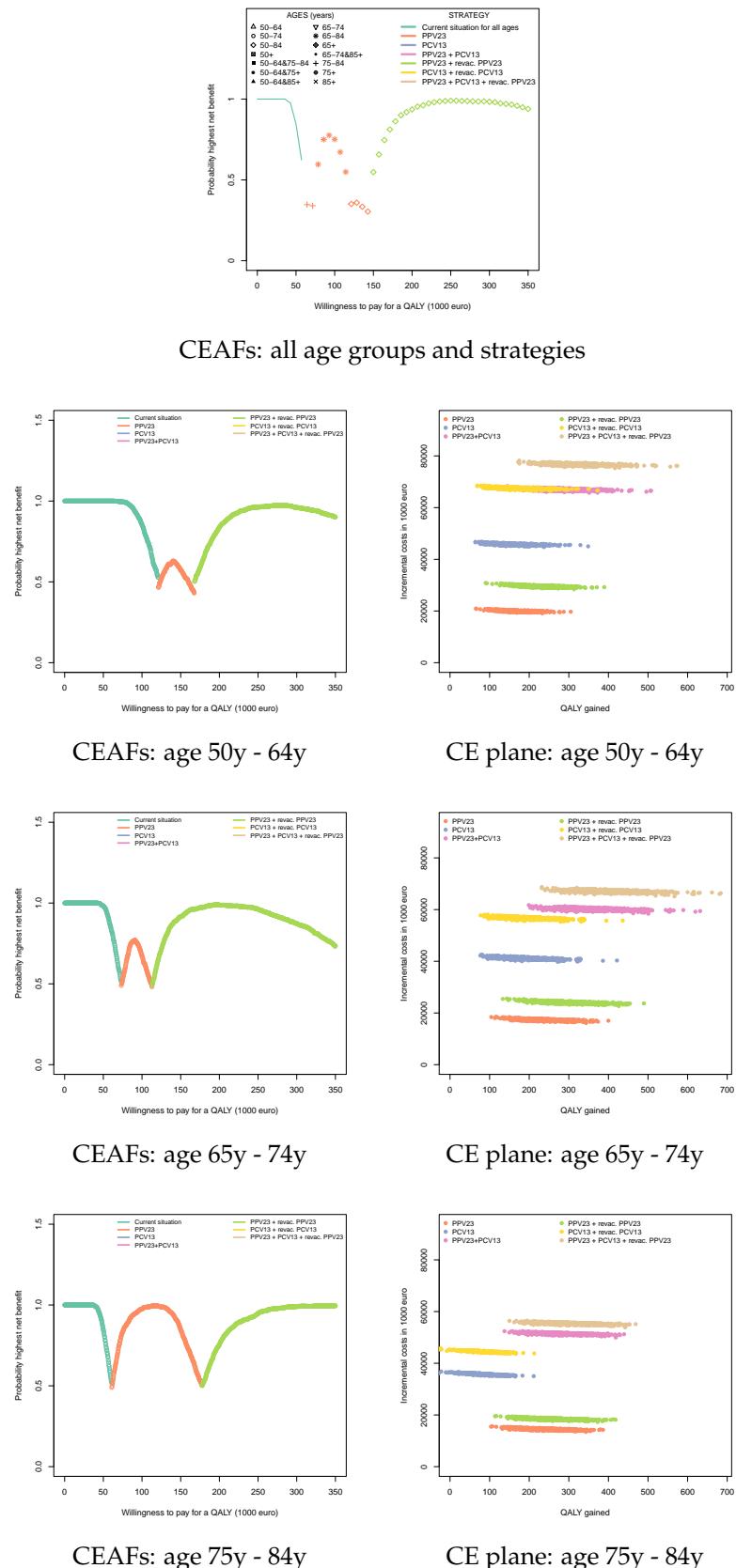
CE plane: age 65y - 74y



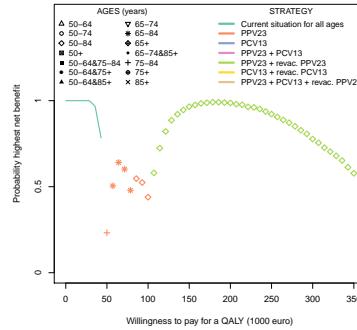
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

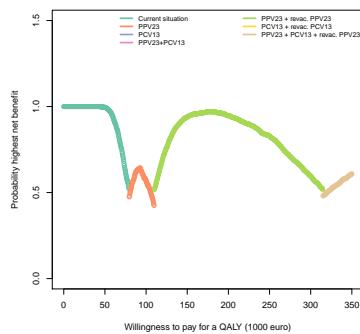
## Discount rate for costs and effects: 5%



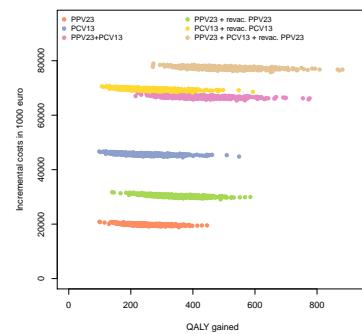
## Using QALY loss averaged over all risk groups (baseline: low risk group only)



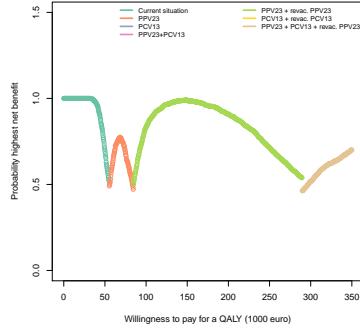
CEAFs: all age groups and strategies



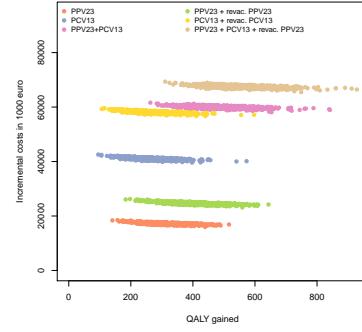
CEAFs: all age groups and strategies



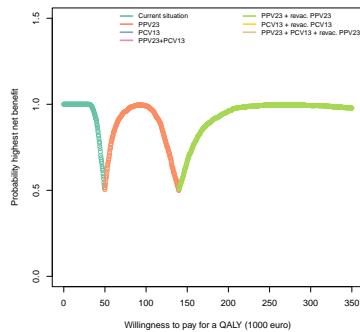
CE plane: all age groups and strategies



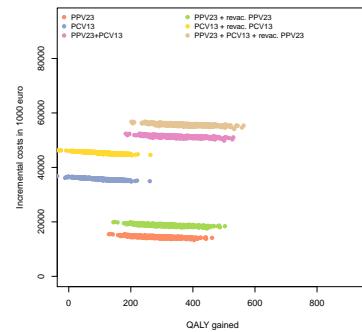
CEAFs: age 50y - 64y



CE plane: age 50y - 64y



CEAFs: age 65y - 74y



CE plane: age 65y - 74y

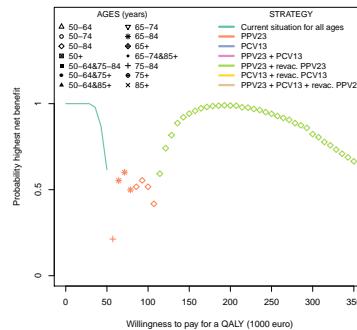


CEAFs: age 75y - 84y

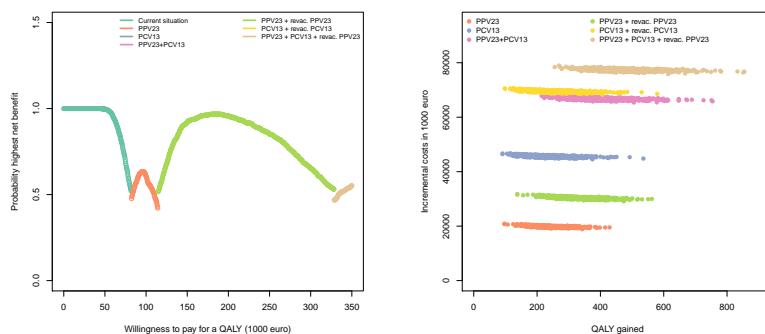


CE plane: age 75y - 84y

## Using QALY loss of the medium risk group only (baseline: low risk group only)

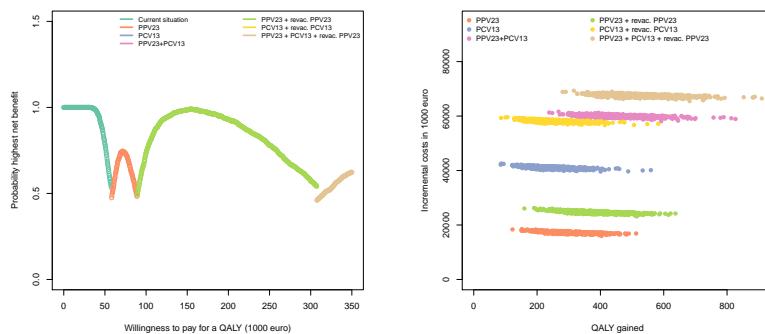


CEAFs: all age groups and strategies



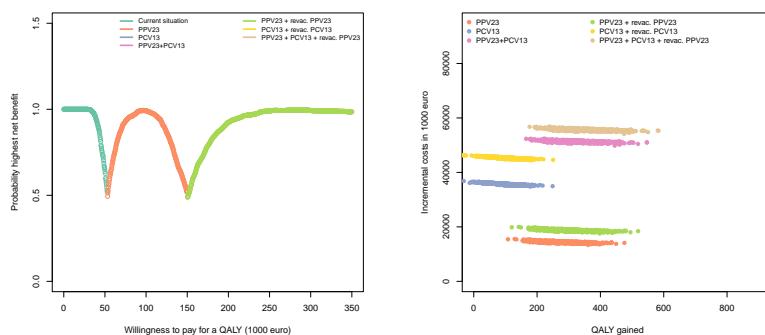
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

CE plane: age 65y - 74y



CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## Appendix B

### **Univariate sensitivity analysis: Baseline = Fully parameterised baseline PCV13 effectiveness and 0% PPV23 effectiveness against non-invasive CAP**

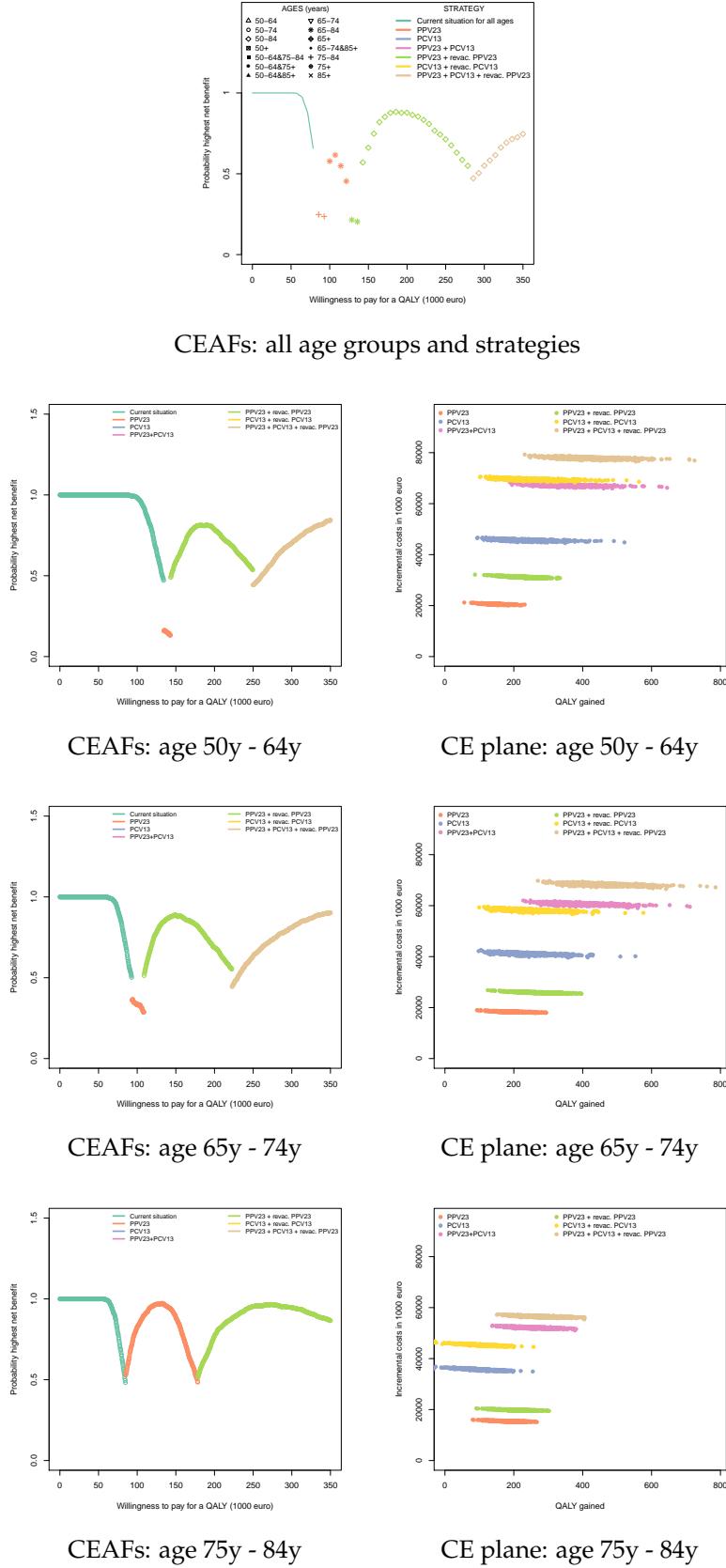
In this supplementary file, we present a visual overview of the effectiveness and cost-effectiveness of the different strategies in the different age groups, assuming fully parameterised baseline PCV13 effectiveness and 0% PPV23 effectiveness against non-invasive CAP, unless explicitly mentioned otherwise, and show the univariate (or one way) sensitivity of these outcomes.

This supplement shows Cost-Effectiveness Acceptability Frontiers (CEAFs) and cost-effectiveness planes (CE planes) by age group targeted, on each page for a different scenario. Each page or scenario is defined by the change in a single variable or assumption versus the baseline.

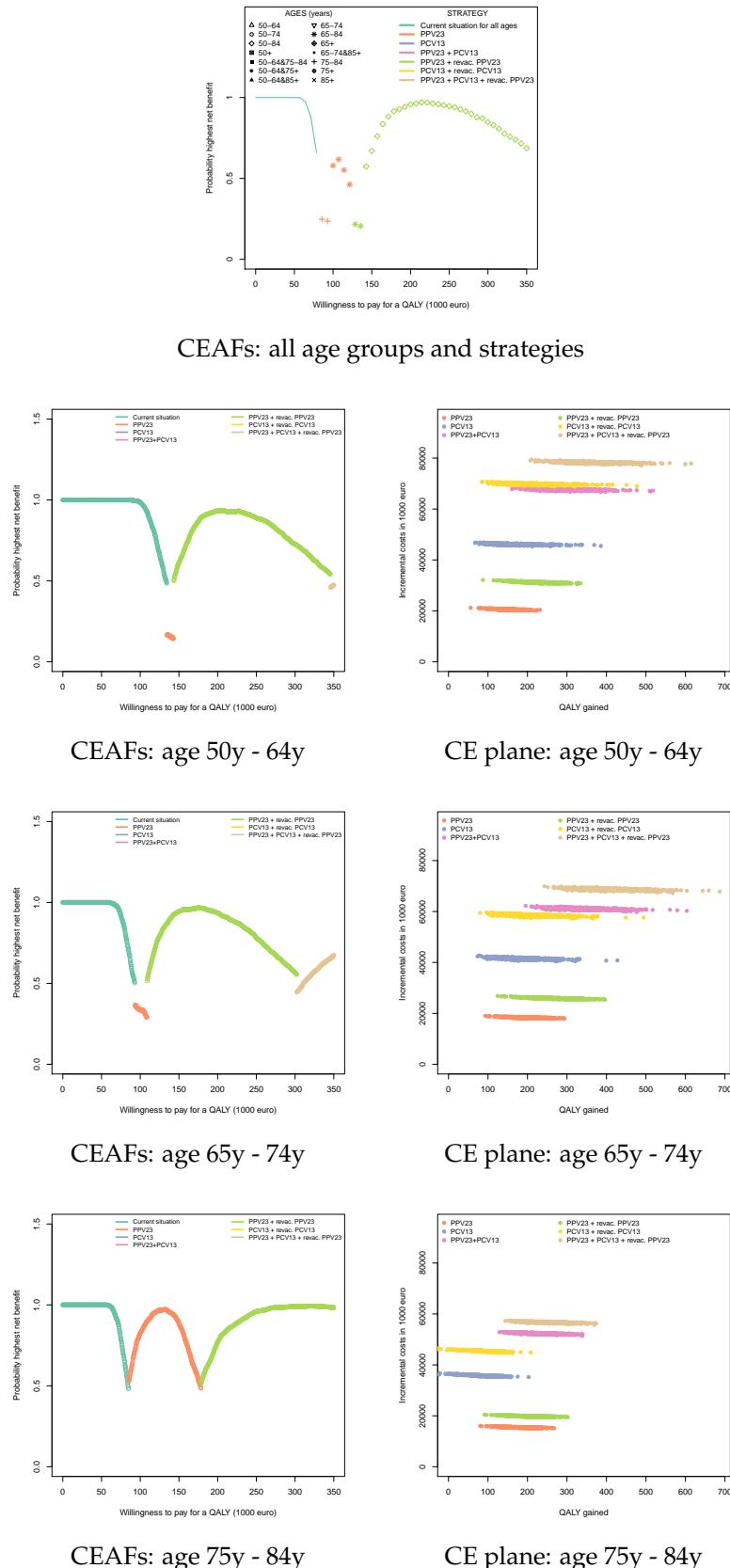
CEAFs have the attractive feature of summarizing parameter uncertainties in the ICERs in relation to a range of willingness to pay values. We use CEAFs showing for each willingness to pay (WTP) level over a wide range, the probability that the strategy depicted at that WTP level is the one strategy (amongst all strategies being compared) that results in the highest net benefit (when a QALY is valued at the WTP level shown). In the CE planes the realizations of 1000 simulations in terms of costs and effects (QALYs), results in clouds of 1000 points - one cloud for each incremental strategy - plotted versus the origin, where the origin of the plane represents the current situation. The further to the right, the more effective, the higher, the more costly a particular strategy is versus the current situation. Note that the same 1000 simulations per strategy are used to produce all the results we present under uncertainty.

For a stated “one way” deviation from the baseline above, each page shows at the top the CEAF over all age groups and strategies combined. Below this summary CEAF, we show more specific CEAFs by one of three age groups (on the left), along with their corresponding CE plane (on the right).

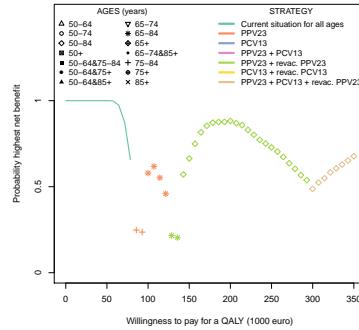
**Baseline: PPV23 0% effectiveness against non-invasive CAP + PCV13 with baseline fully parameterised effectiveness**



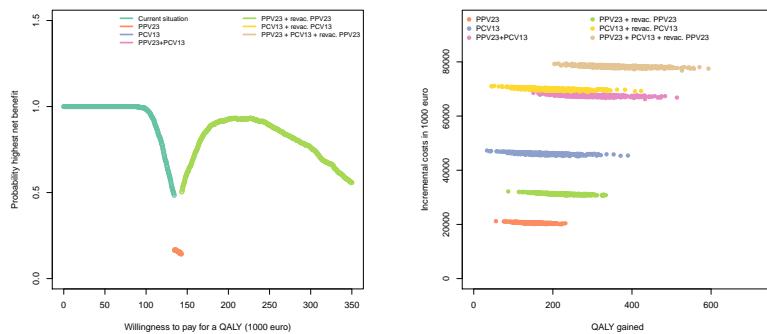
## 5 years of PCV13 protection followed by no protection, and baseline PPV23 protection



## Age independent VE for PCV13 from age 50 to 84y

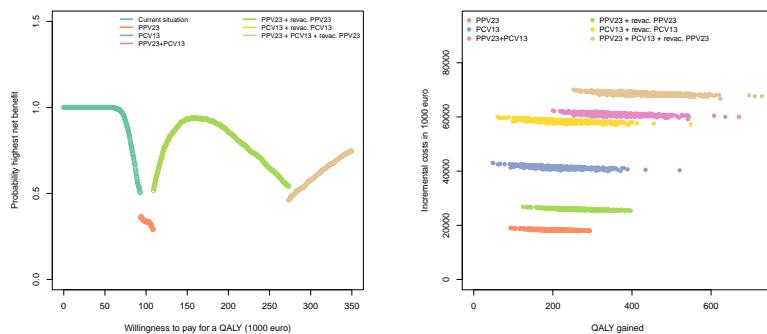


CEAFs: all age groups and strategies



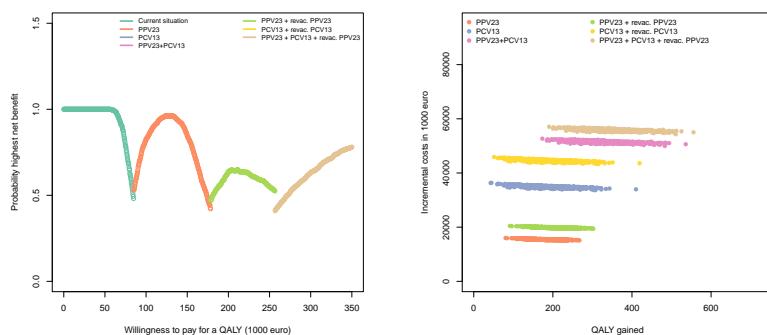
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

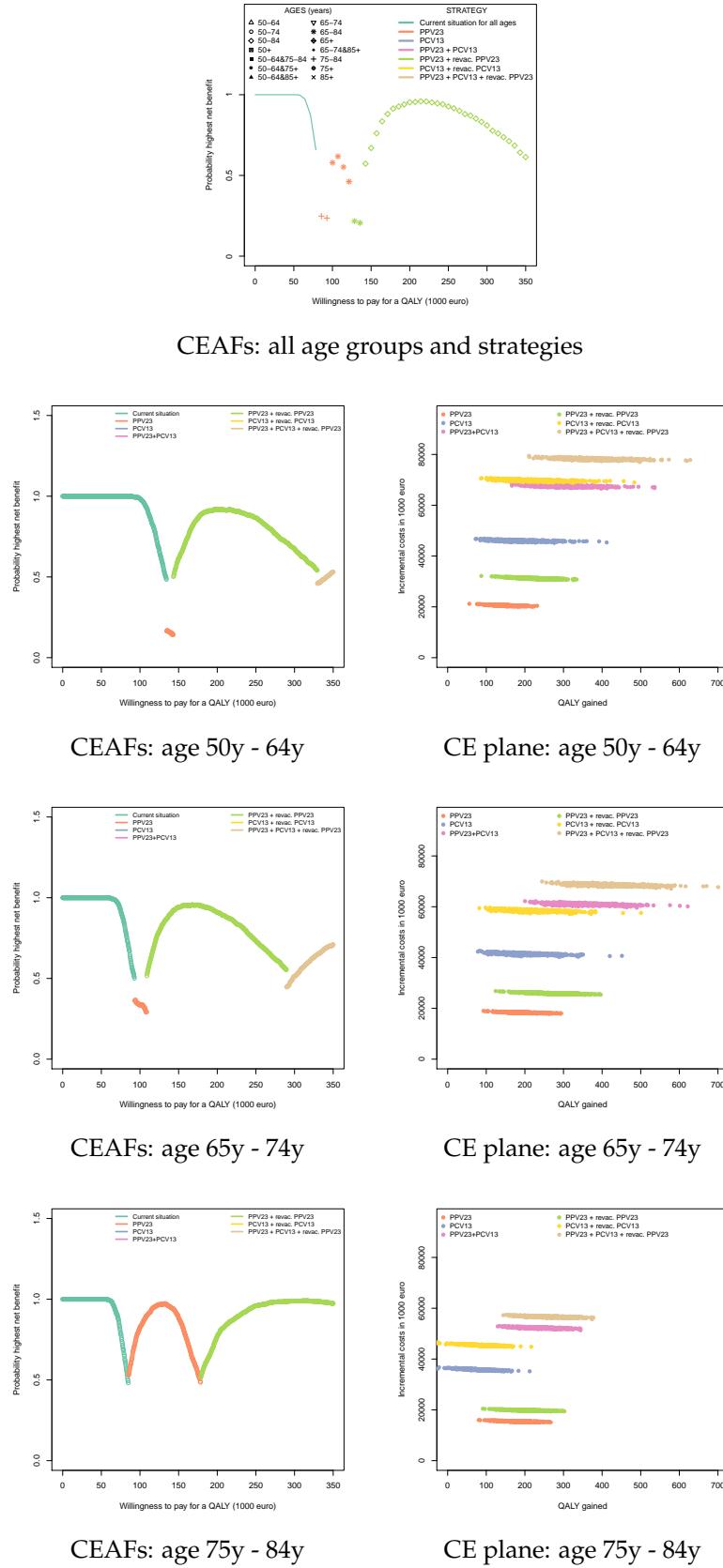
CE plane: age 65y - 74y



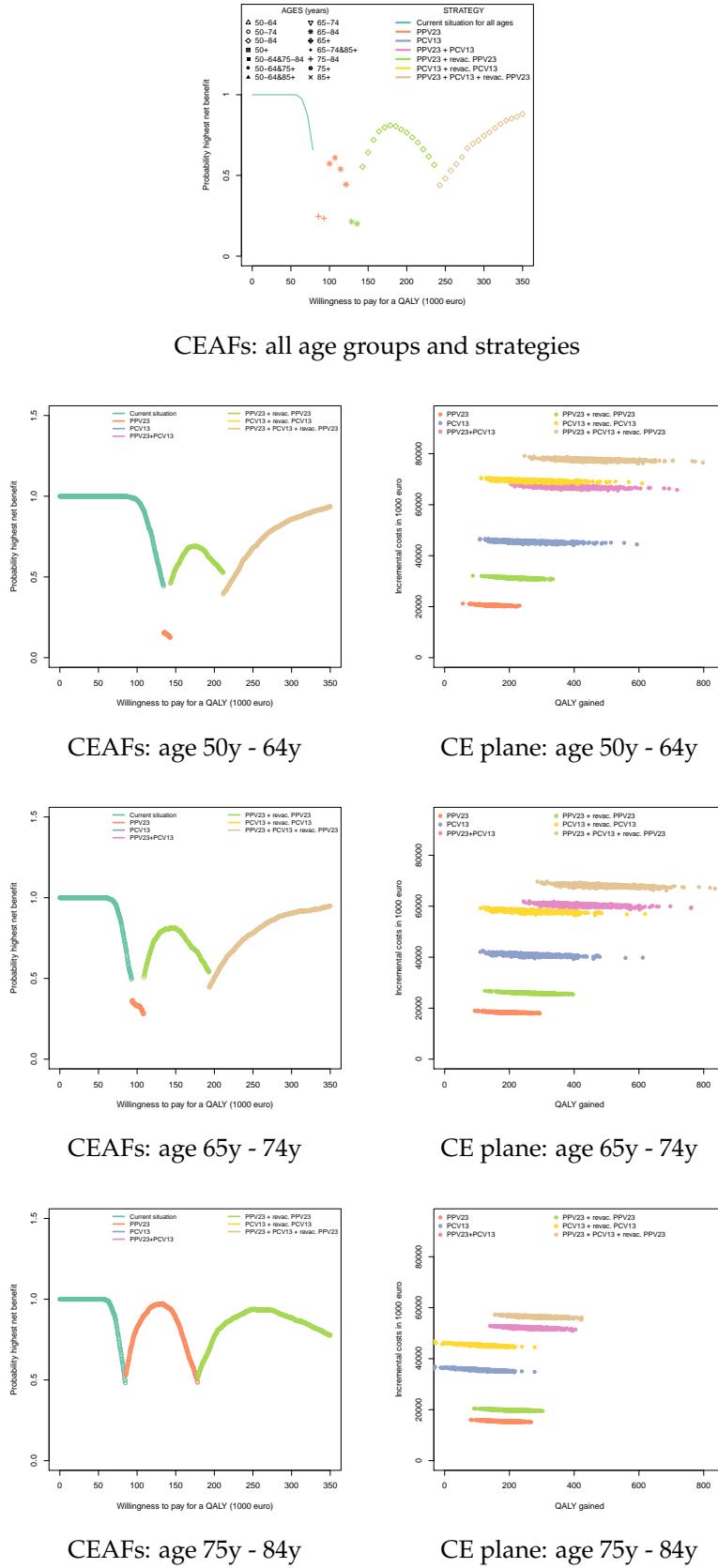
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

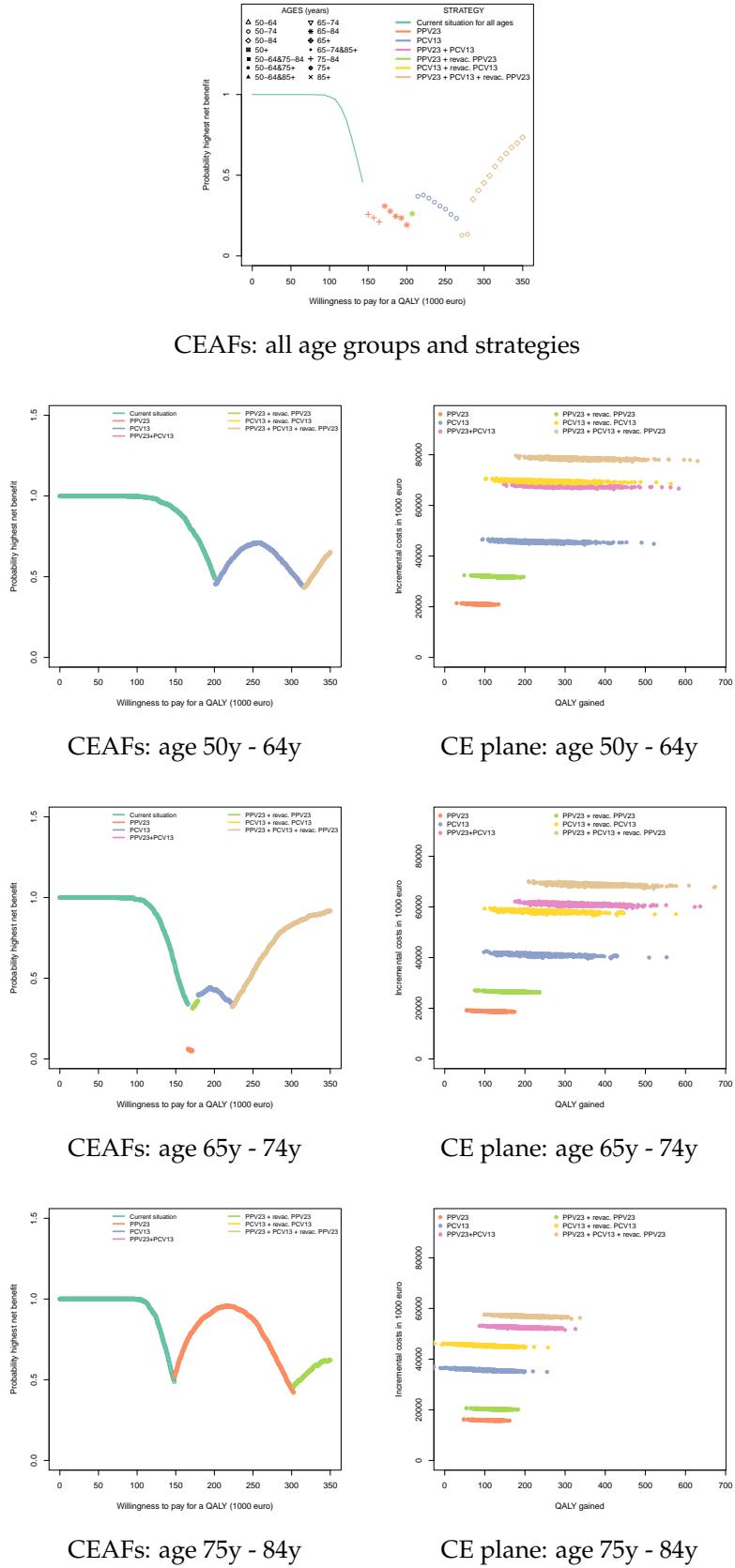
**Minimum duration of PCV13 protection (4 years fixed protection followed by rapid waning to no protection at 10 years), and baseline PPV23 protection**



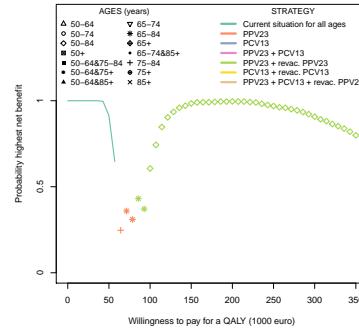
**Maximum duration of PCV13 protection ((9 years fixed protection followed by slow waning to no protection at 20 years), and baseline PPV23 protection**



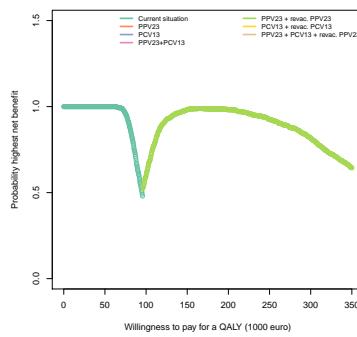
**2 years of complete (without waning) PPV23 protection followed by no protection, and baseline PCV13 vaccine protection**



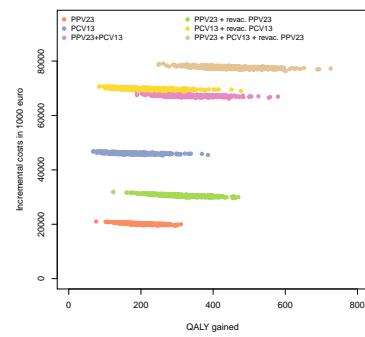
**5 years of complete (without waning) protection followed by no protection for both PCV13 and PPV23**



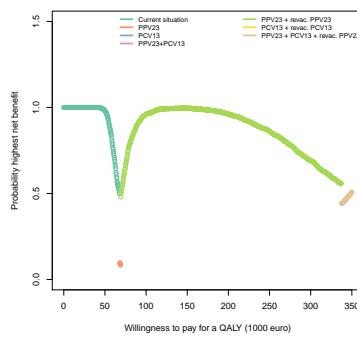
CEAFs: all age groups and strategies



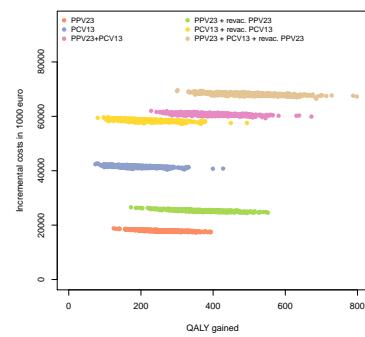
CEAFs: age 50y - 64y



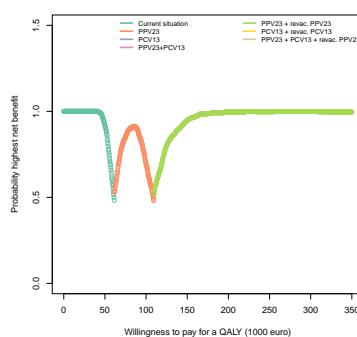
CE plane: age 50y - 64y



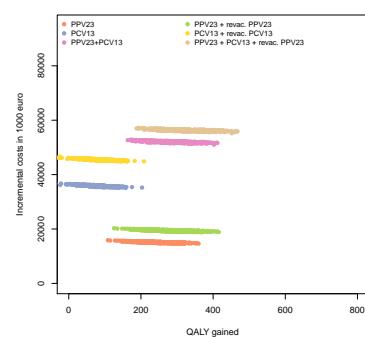
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

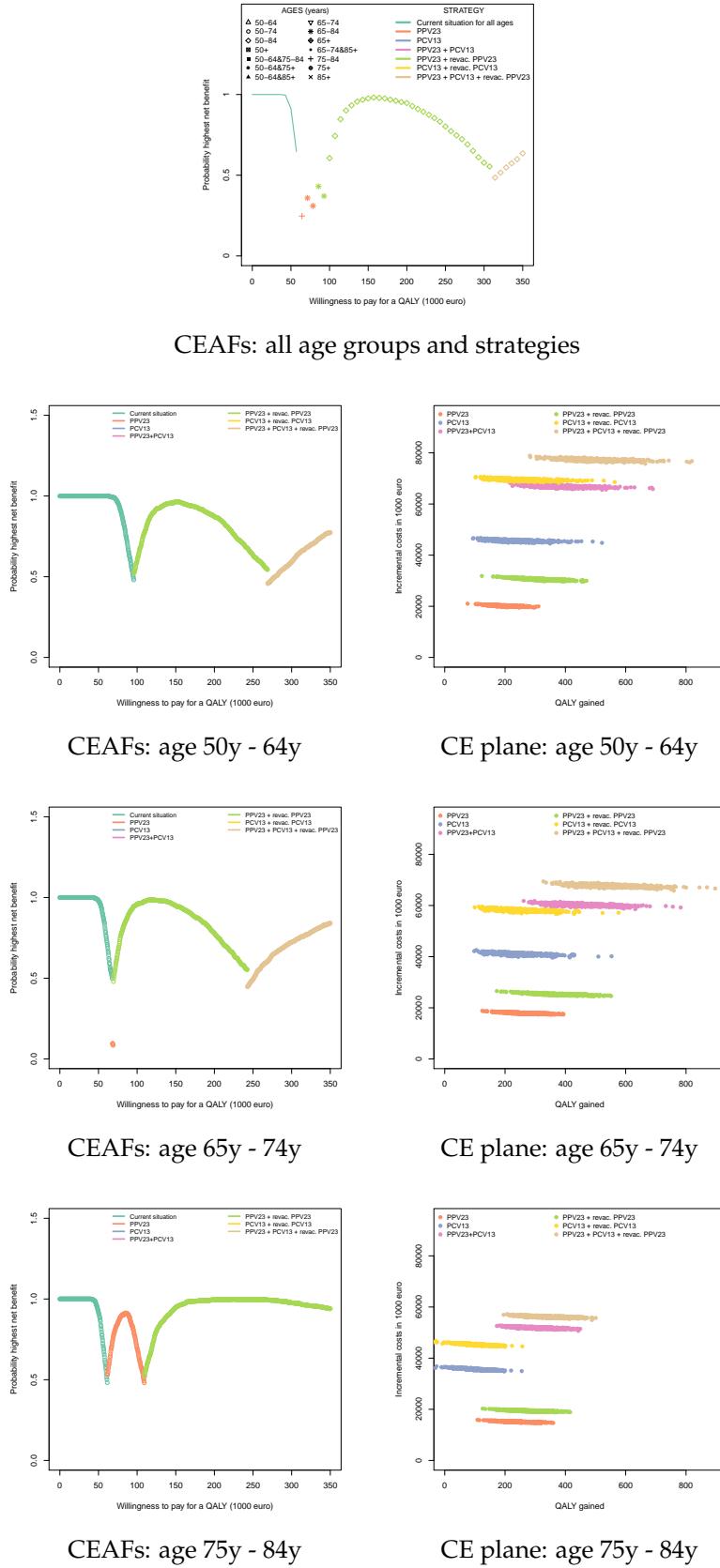


CEAFs: age 75y - 84y

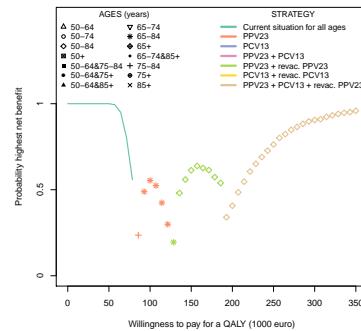


CE plane: age 75y - 84y

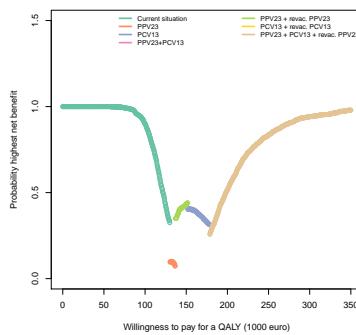
**5 years of complete (without waning) PPV23 protection followed by no protection, and baseline PCV13 vaccine protection**



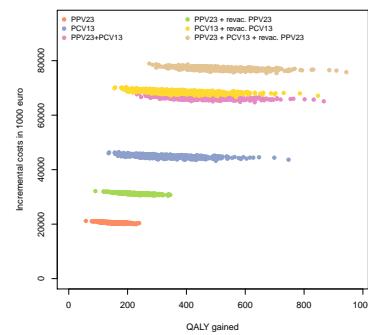
**Minimum PCV13 incidence decline (PCV13 serotype incidence -10% per year, baseline (76%) replacement)**



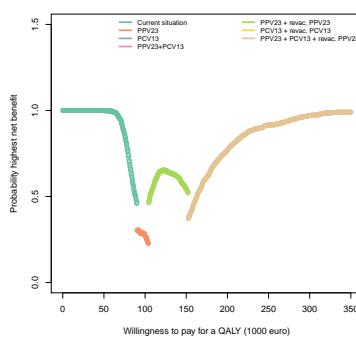
CEAFs: all age groups and strategies



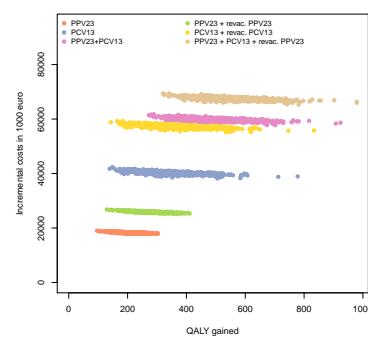
CEAFs: age 50y - 64y



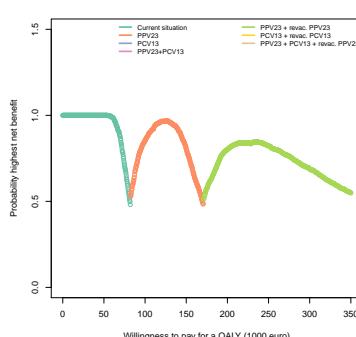
CE plane: age 50y - 64y



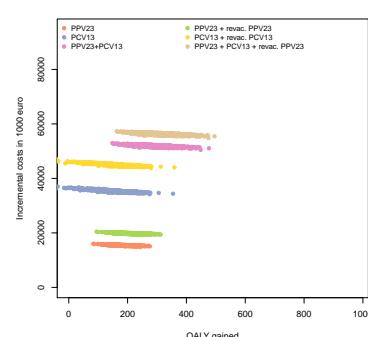
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

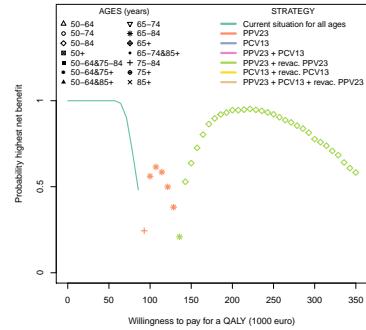


CEAFs: age 75y - 84y

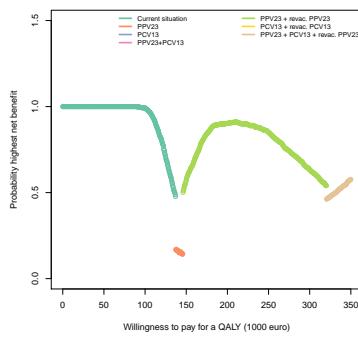


CE plane: age 75y - 84y

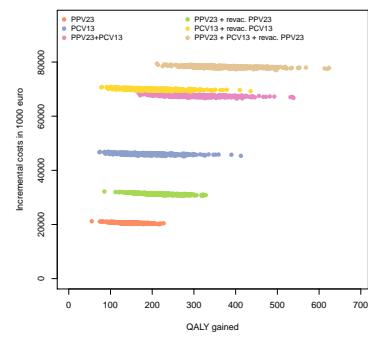
**Maximum PCV13 incidence decline (PCV13 serotype incidence -20% per year, baseline (76%) replacement)**



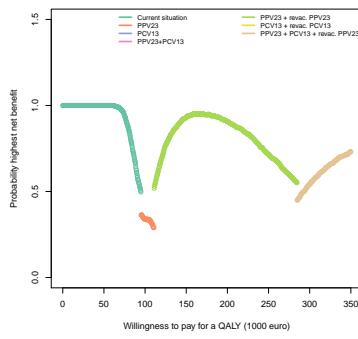
CEAFs: all age groups and strategies



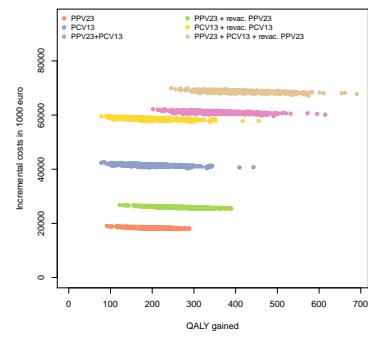
CEAFs: age 50y - 64y



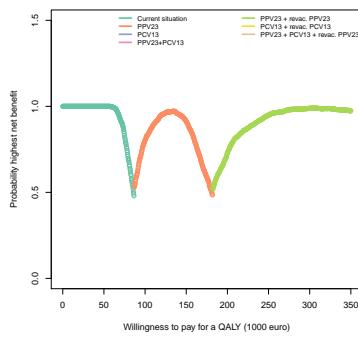
CE plane: age 50y - 64y



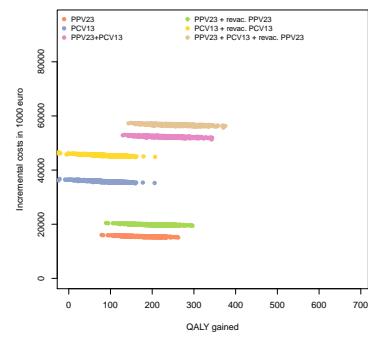
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

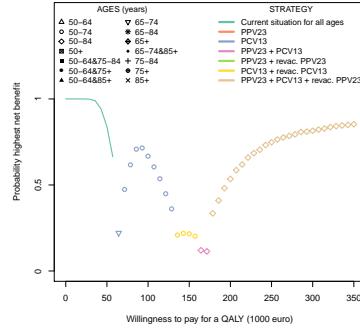


CEAFs: age 75y - 84y

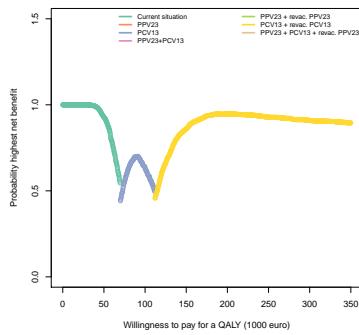


CE plane: age 75y - 84y

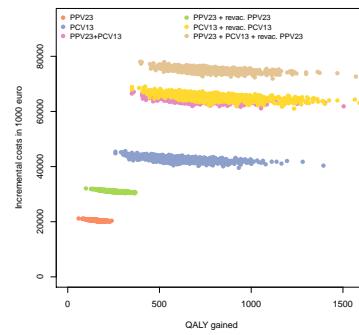
**Quick PCV13 serotype relapse: PCV13 incidence returns to 2015 value within 7 years  
(0% replacement of PCV13 incidence decline by non-PCV13 types)**



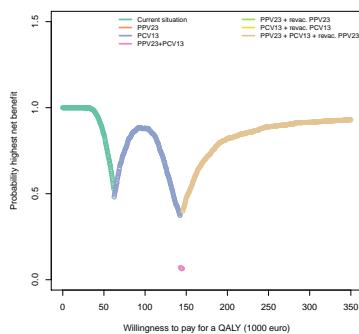
CEAFs: all age groups and strategies



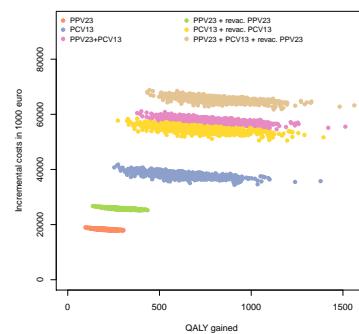
CEAFs: age 50y - 64y



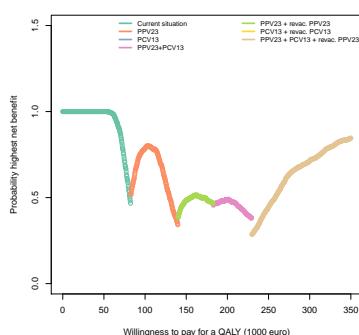
CE plane: age 50y - 64y



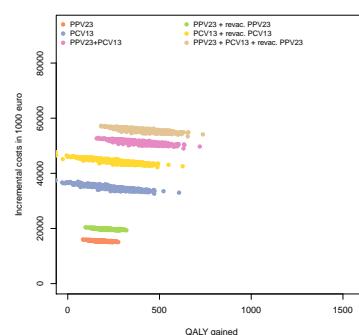
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

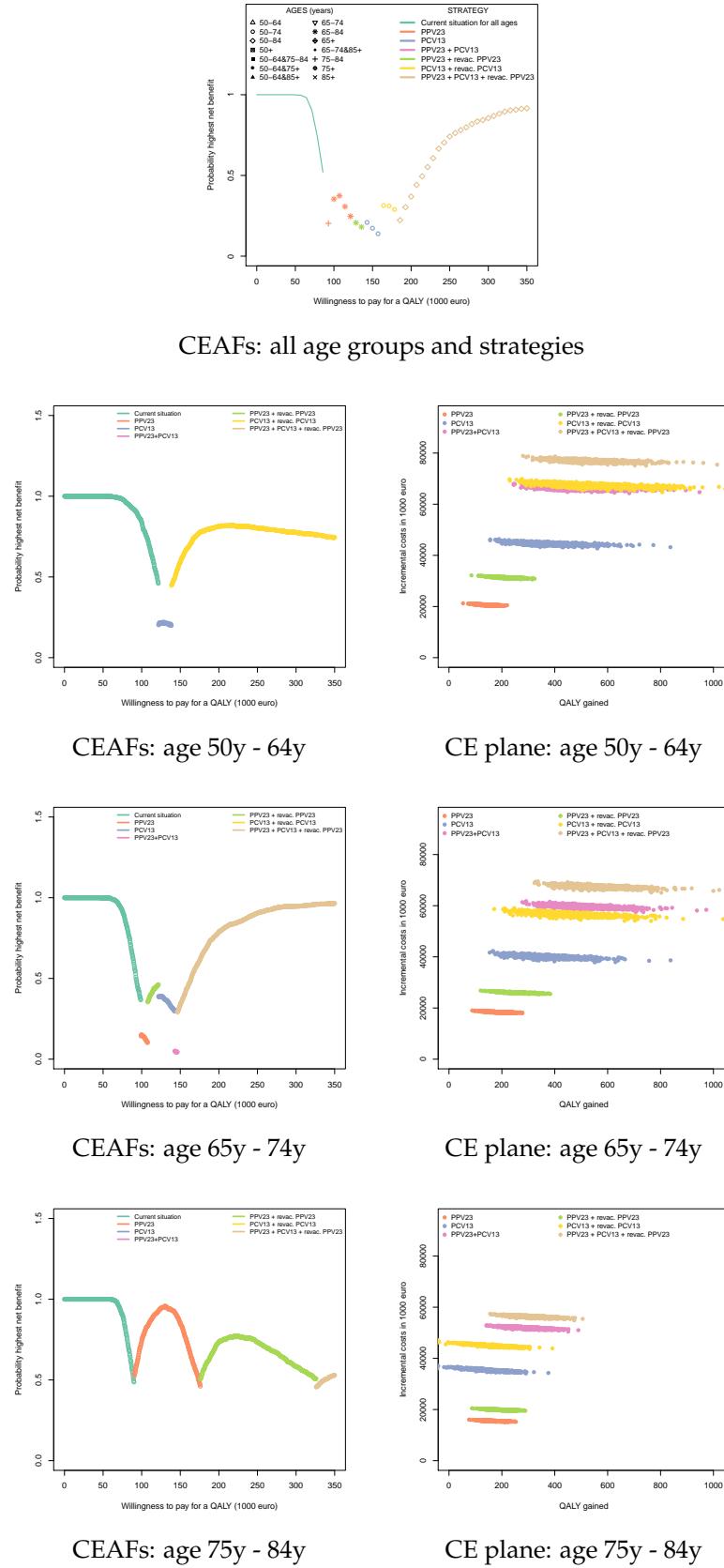


CEAFs: age 75y - 84y

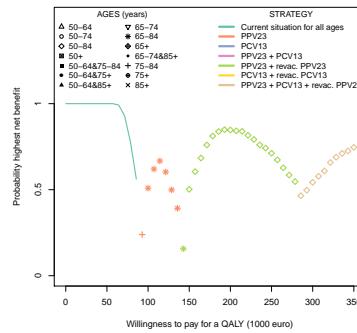


CE plane: age 75y - 84y

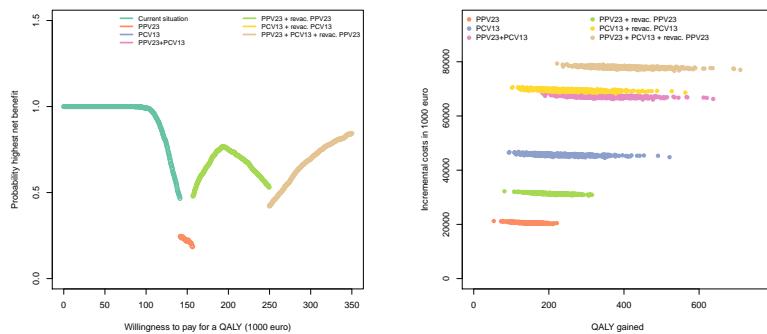
**Slow PCV13 serotype relapse: PCV13 incidence returns to 2015 value within 15 years  
(0% replacement of PCV13 incidence decline by non-PCV13 types)**



## Serotype replacement: 34% (2013 serocoverage data) instead of 76% (2015 baseline)

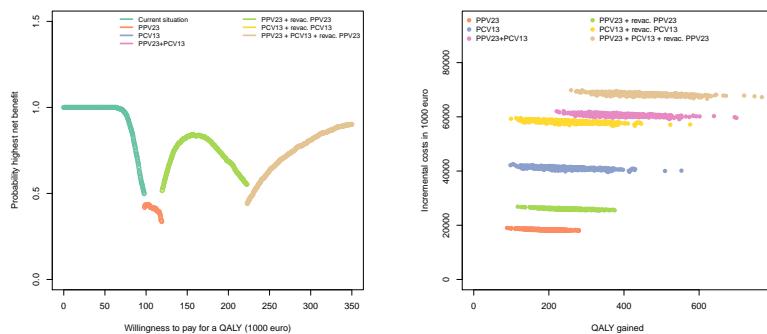


CEAFs: all age groups and strategies



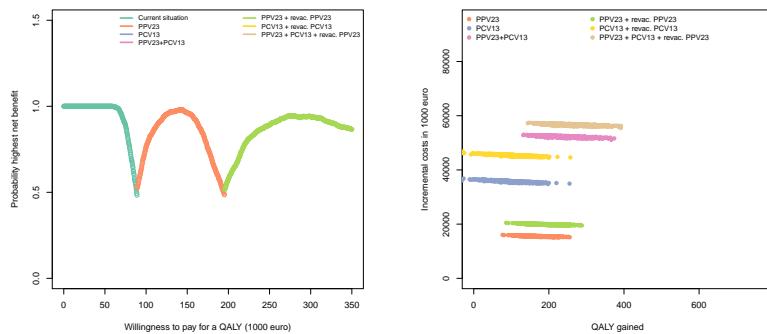
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

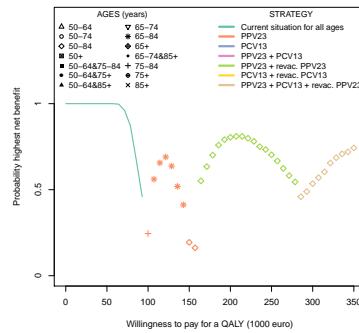
CE plane: age 65y - 74y



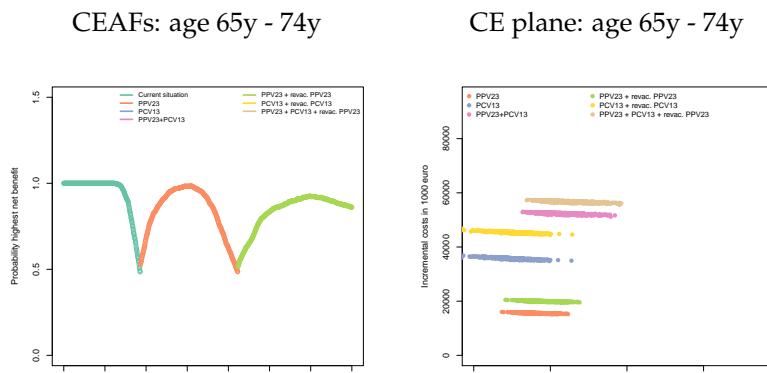
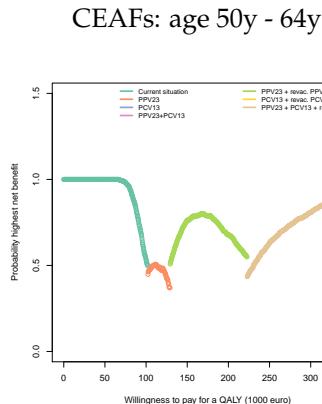
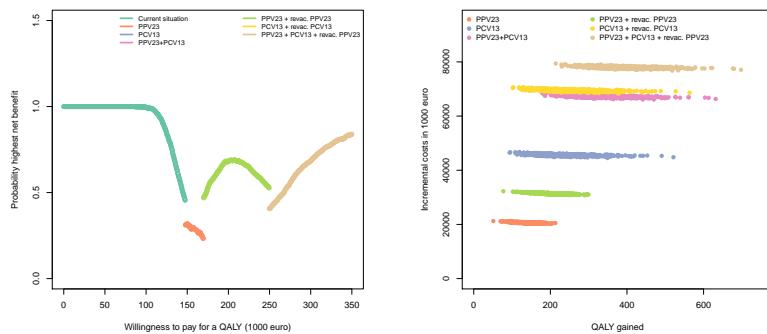
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## Serotype replacement extreme low: 0% instead of 76% (2015 baseline)



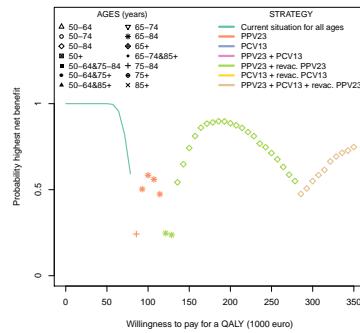
CEAFs: all age groups and strategies



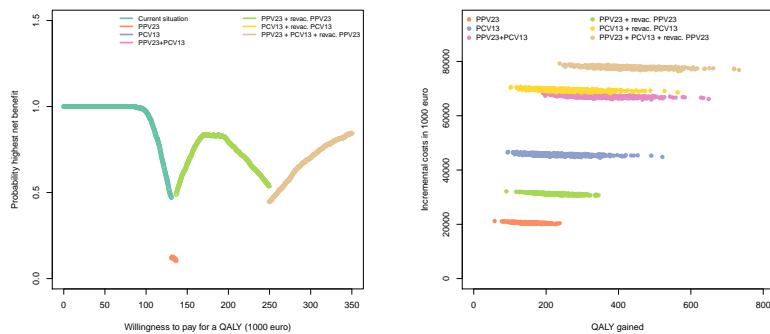
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## Serotype replacement extreme high: 100% instead of 76% (2015 baseline)

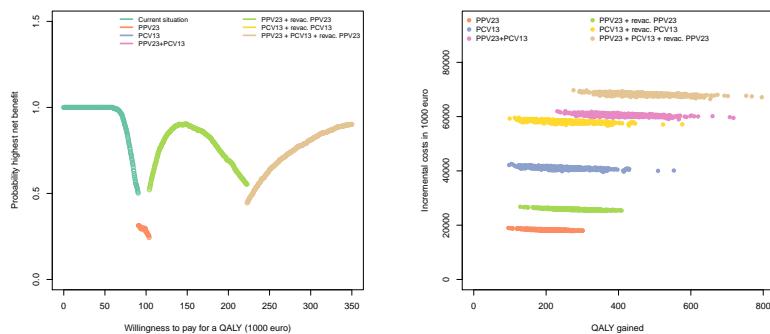


CEAFs: all age groups and strategies



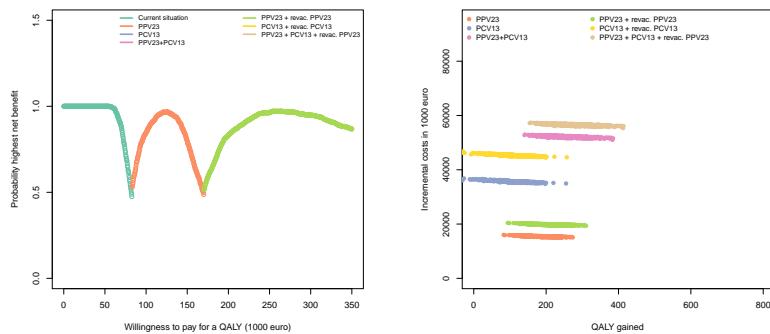
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

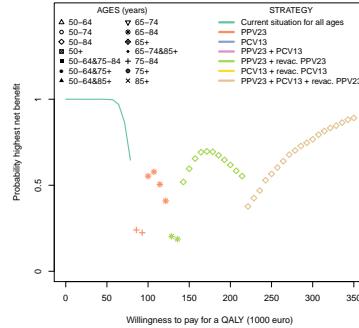
CE plane: age 65y - 74y



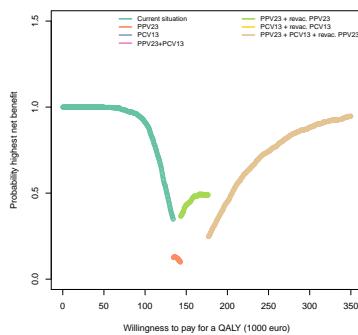
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

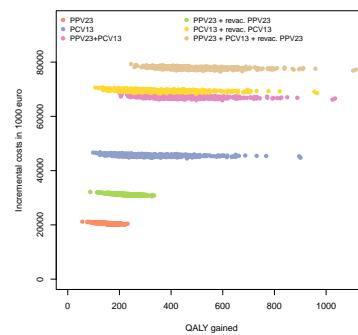
## Higher percentage of pneumococcal pneumonia in outpatient CAP (27% (Said 2013) instead of 10.5%)



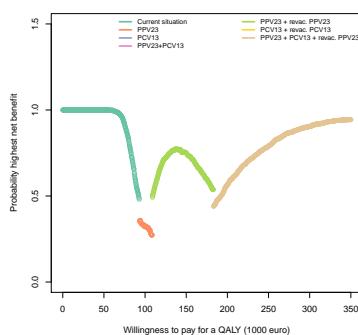
CEAFs: all age groups and strategies



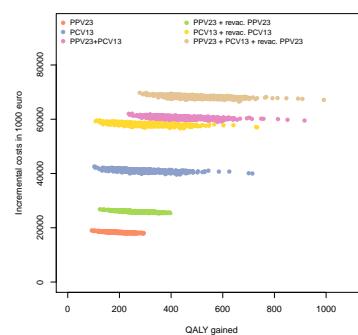
CEAFs: age 50y - 64y



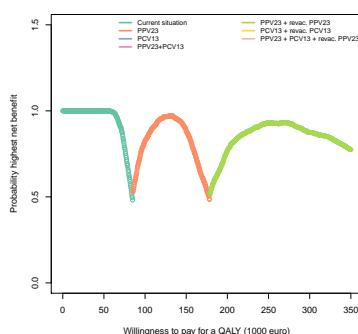
CE plane: age 50y - 64y



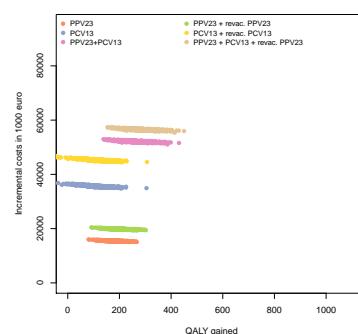
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

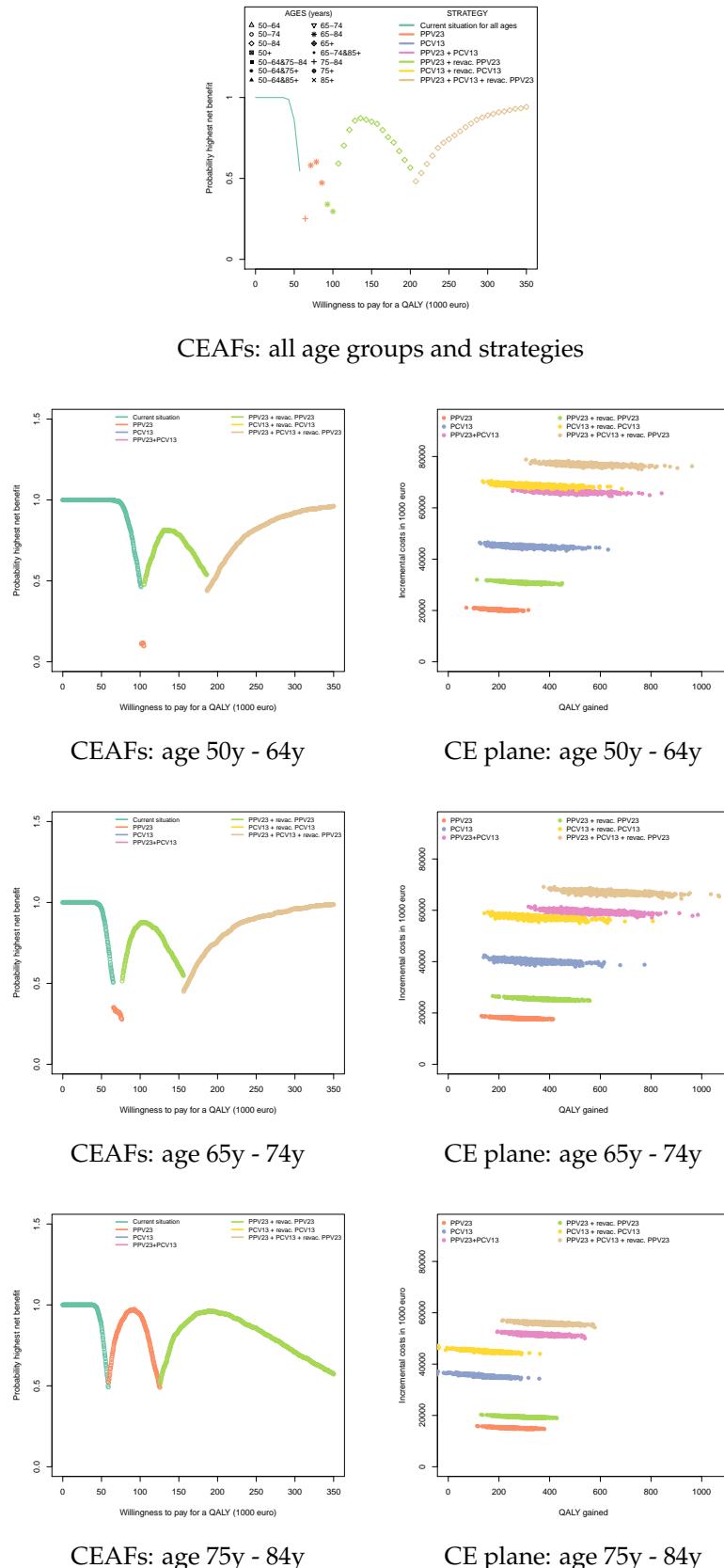


CEAFs: age 75y - 84y

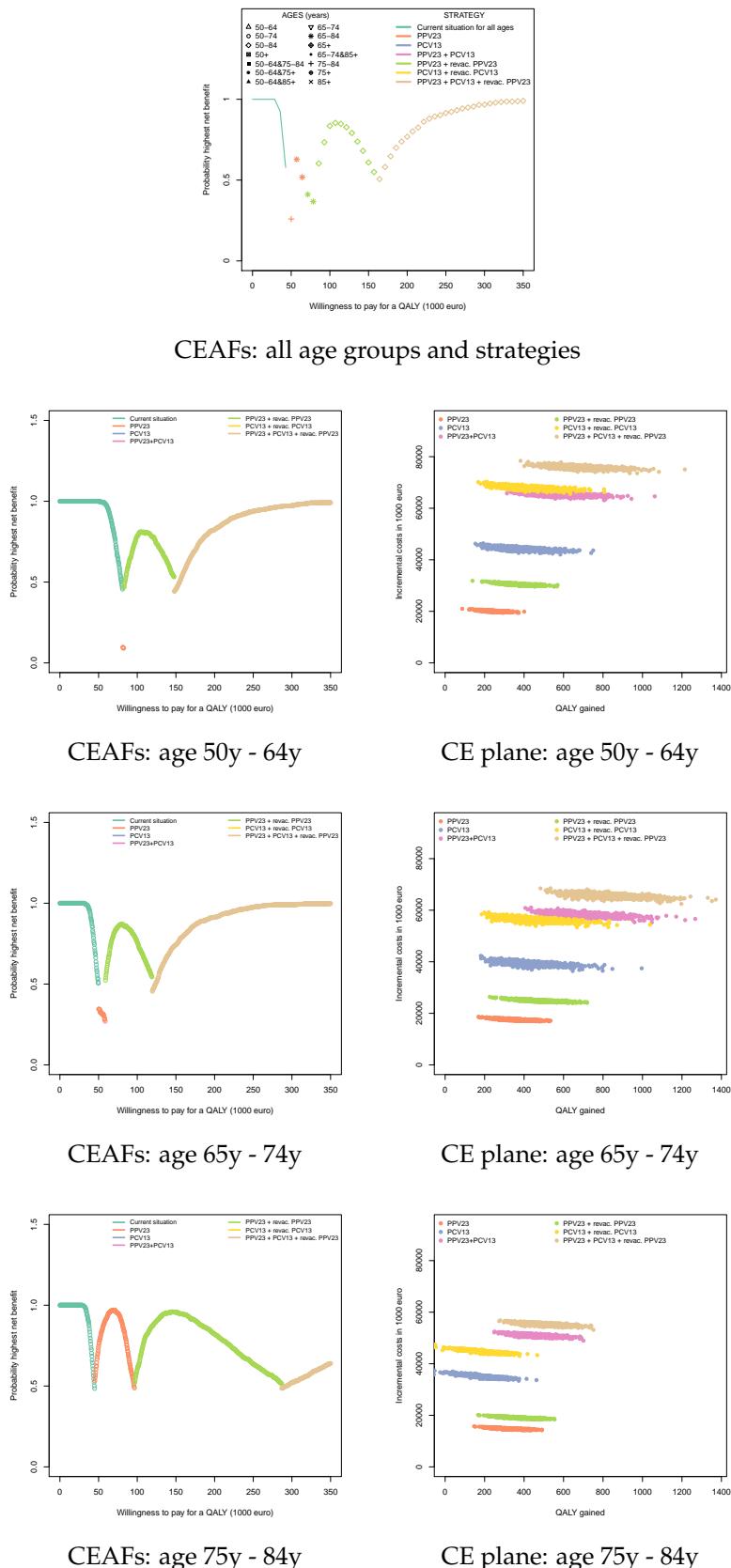


CE plane: age 75y - 84y

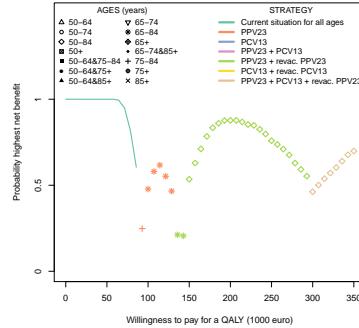
## Higher hospitalised pneumococcal pneumonia incidence: 1.5 x baseline



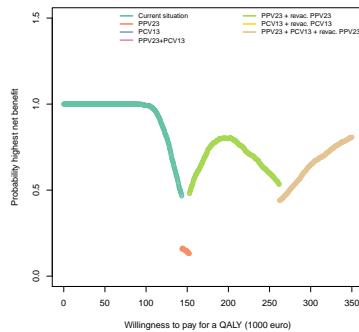
## Higher hospitalised pneumococcal pneumonia incidence: 2 x baseline



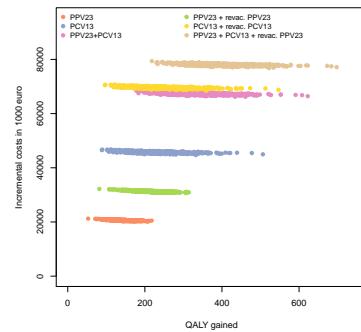
**Lower incidence of hospitalisations (94% of baseline, assuming no underreporting in NRC)**



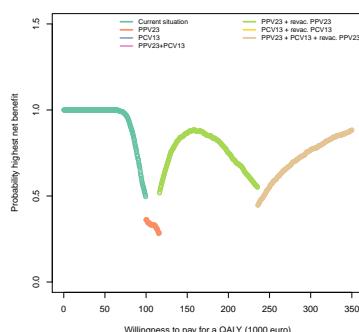
CEAFs: all age groups and strategies



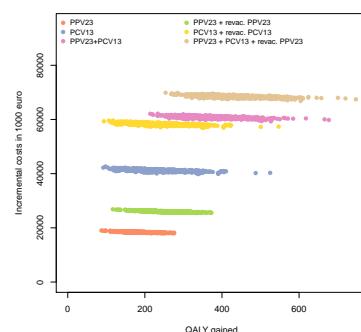
CEAFs: age 50y - 64y



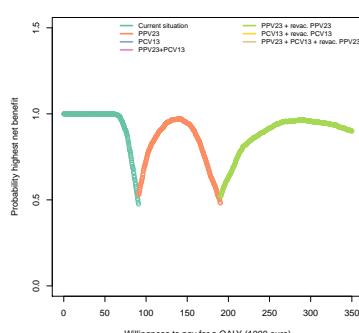
CE plane: age 50y - 64y



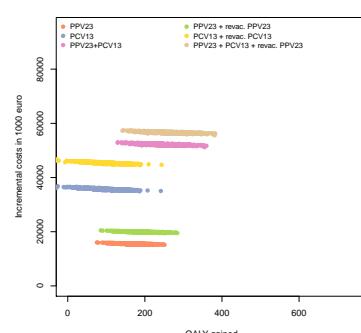
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

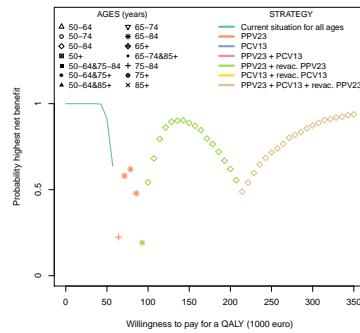


CEAFs: age 75y - 84y

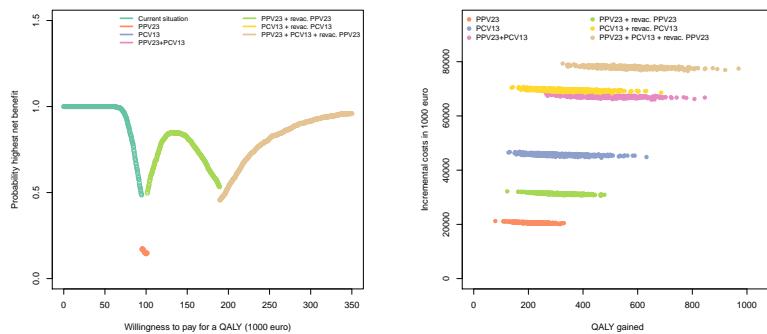


CE plane: age 75y - 84y

## Low mortality: Death rate of hospitalised cases: 50% of baseline

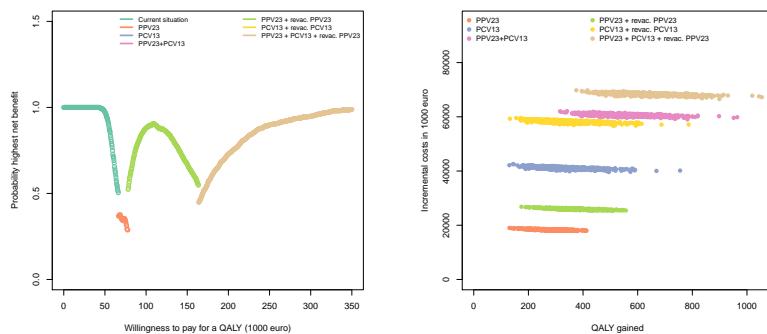


CEAFs: all age groups and strategies



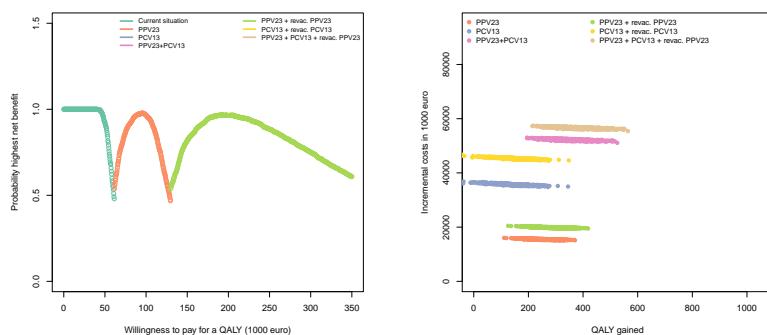
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

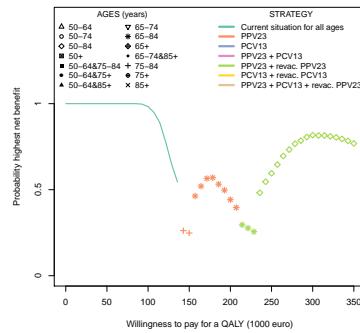
CE plane: age 65y - 74y



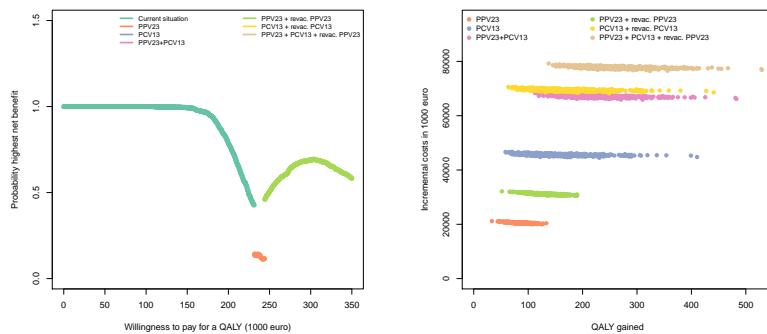
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## High mortality: Death rate of hospitalised cases: 150% of base

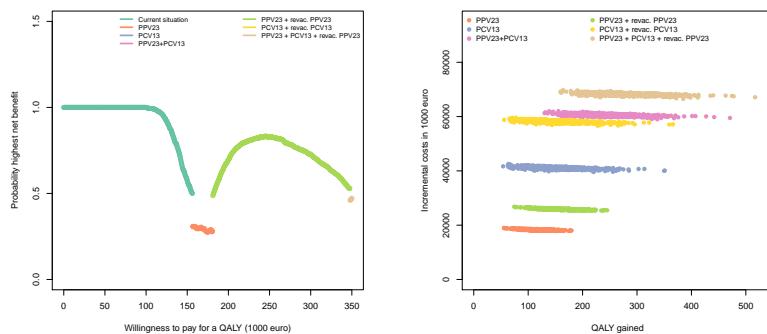


CEAFs: all age groups and strategies



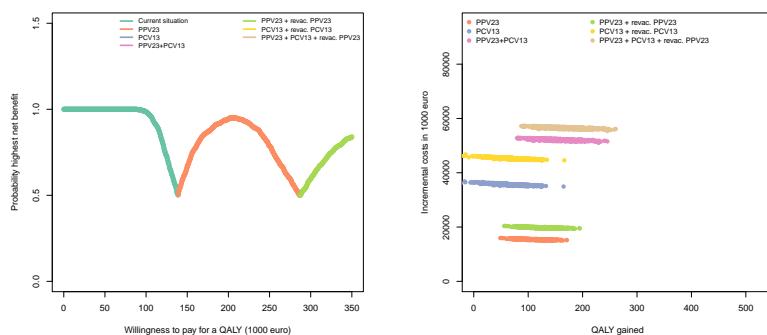
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

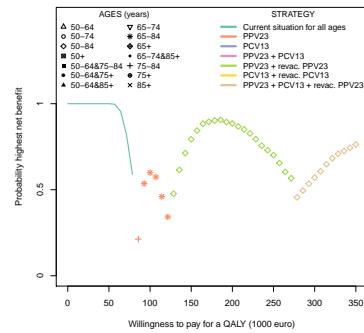
CE plane: age 65y - 74y



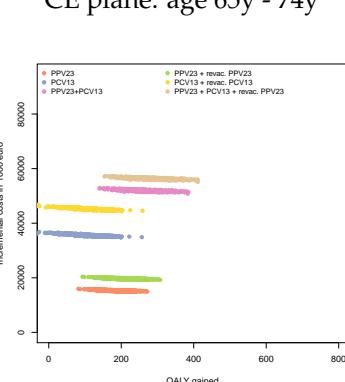
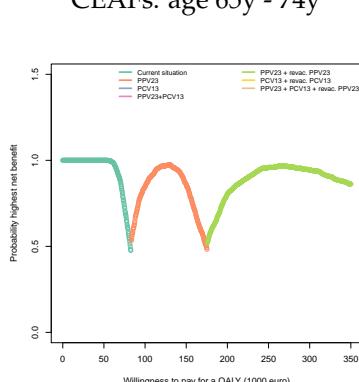
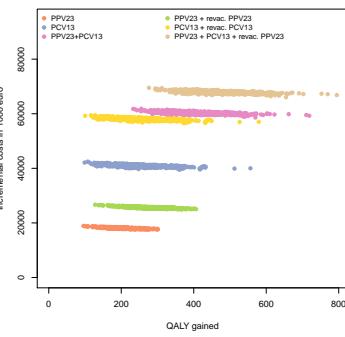
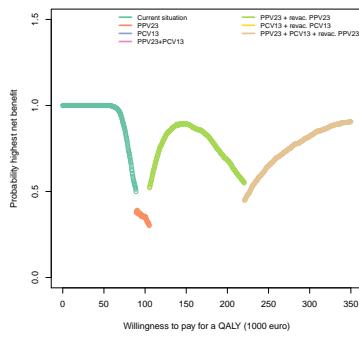
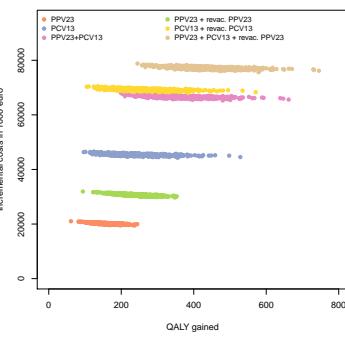
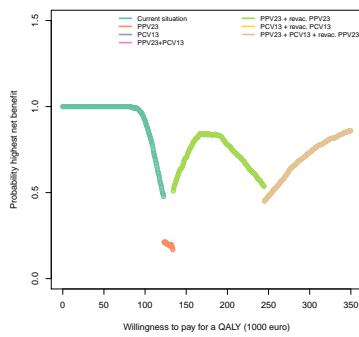
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

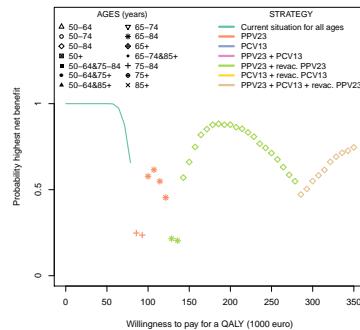
## More meningitis sequelae (probabilities of 20% for hearing loss and 22% for neurological sequelae)



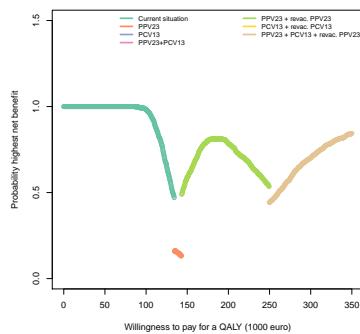
CEAFs: all age groups and strategies



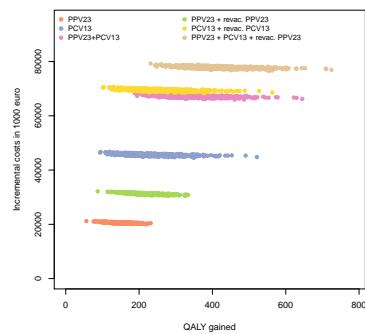
## Higher costs CAP for outpatients (1 extra GP consult per case)



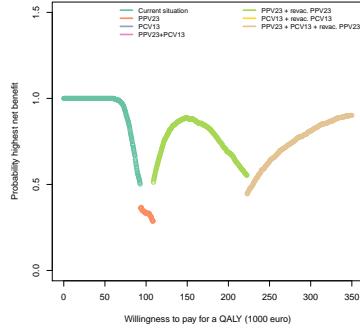
CEAFs: all age groups and strategies



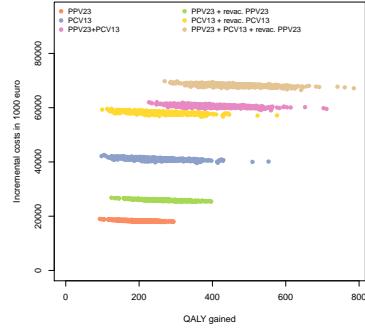
CEAFs: all age groups and strategies



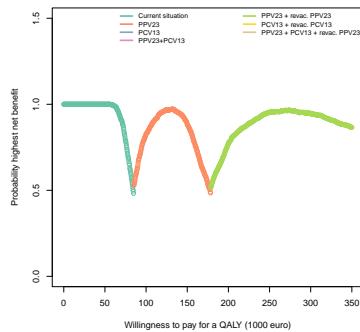
CE plane: all age groups and strategies



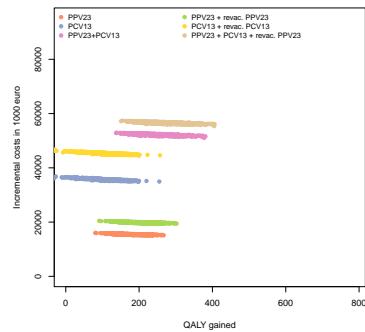
CEAFs: age 50y - 64y



CE plane: age 50y - 64y



CEAFs: age 65y - 74y



CE plane: age 65y - 74y

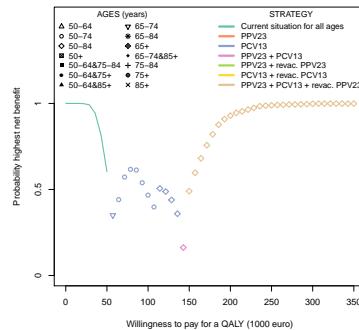


CEAFs: age 75y - 84y

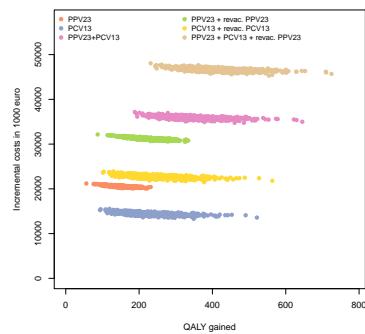
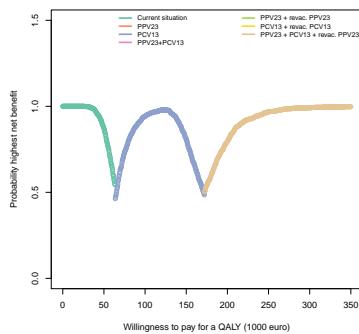


CE plane: age 75y - 84y

## 75% reduction of the baseline PCV13 price, baseline PPV23 price

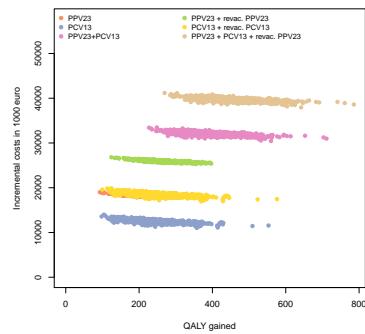
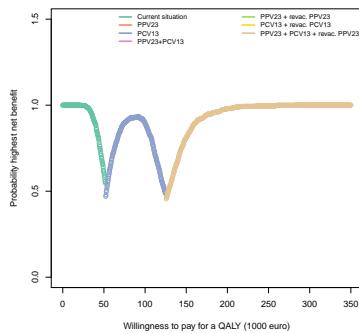


CEAFs: all age groups and strategies



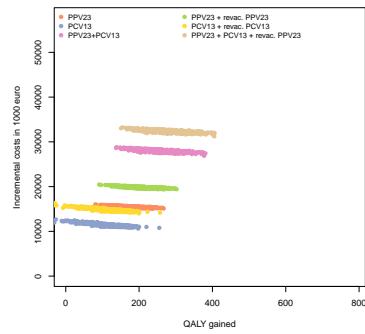
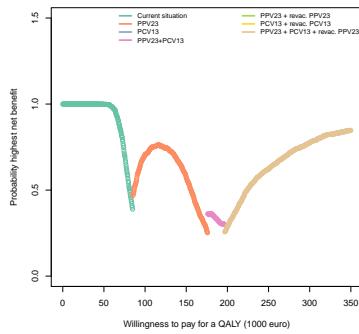
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

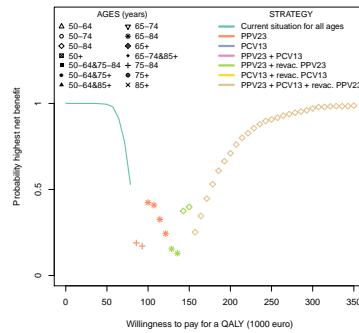
CE plane: age 65y - 74y



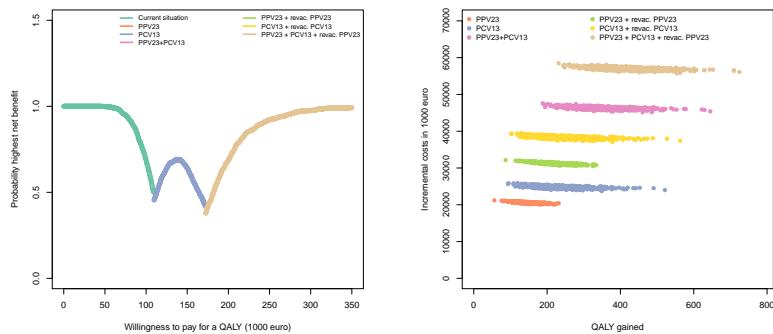
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## 50% reduction of the baseline PCV13 price, baseline PPV23 price

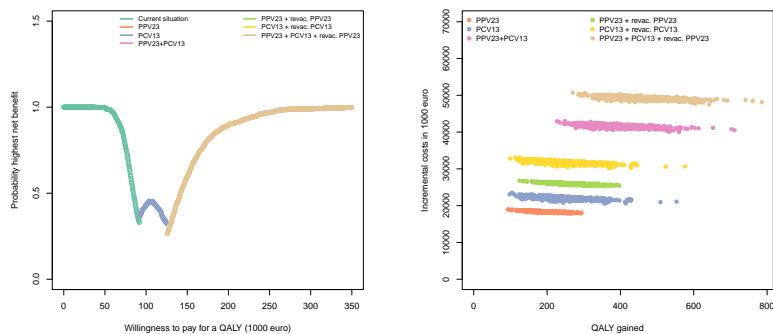


CEAFs: all age groups and strategies



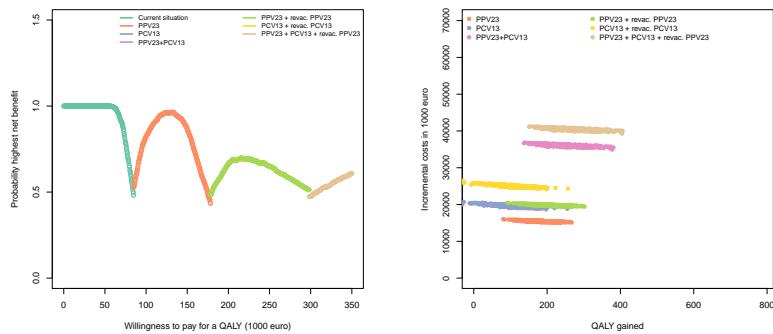
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

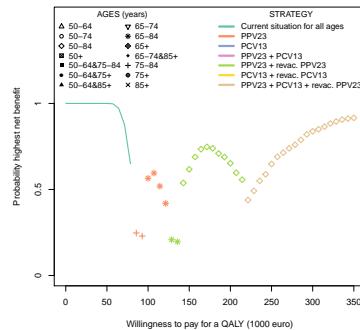
CE plane: age 65y - 74y



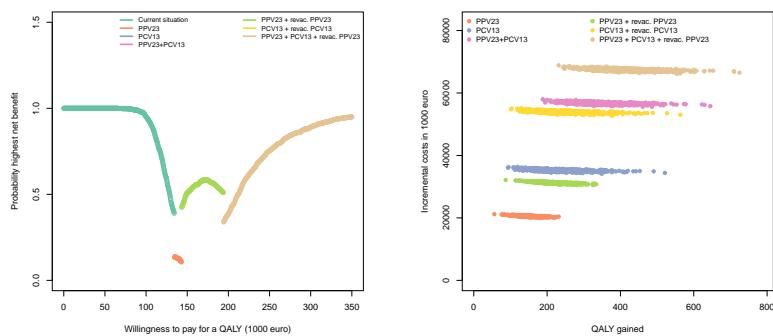
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## 25% reduction of the baseline PCV13 price, baseline PPV23 price

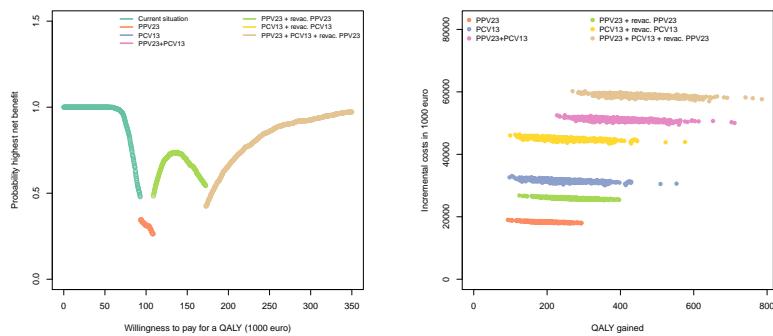


CEAFs: all age groups and strategies



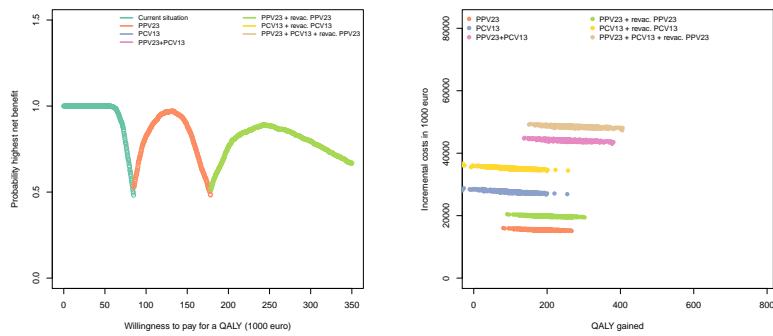
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

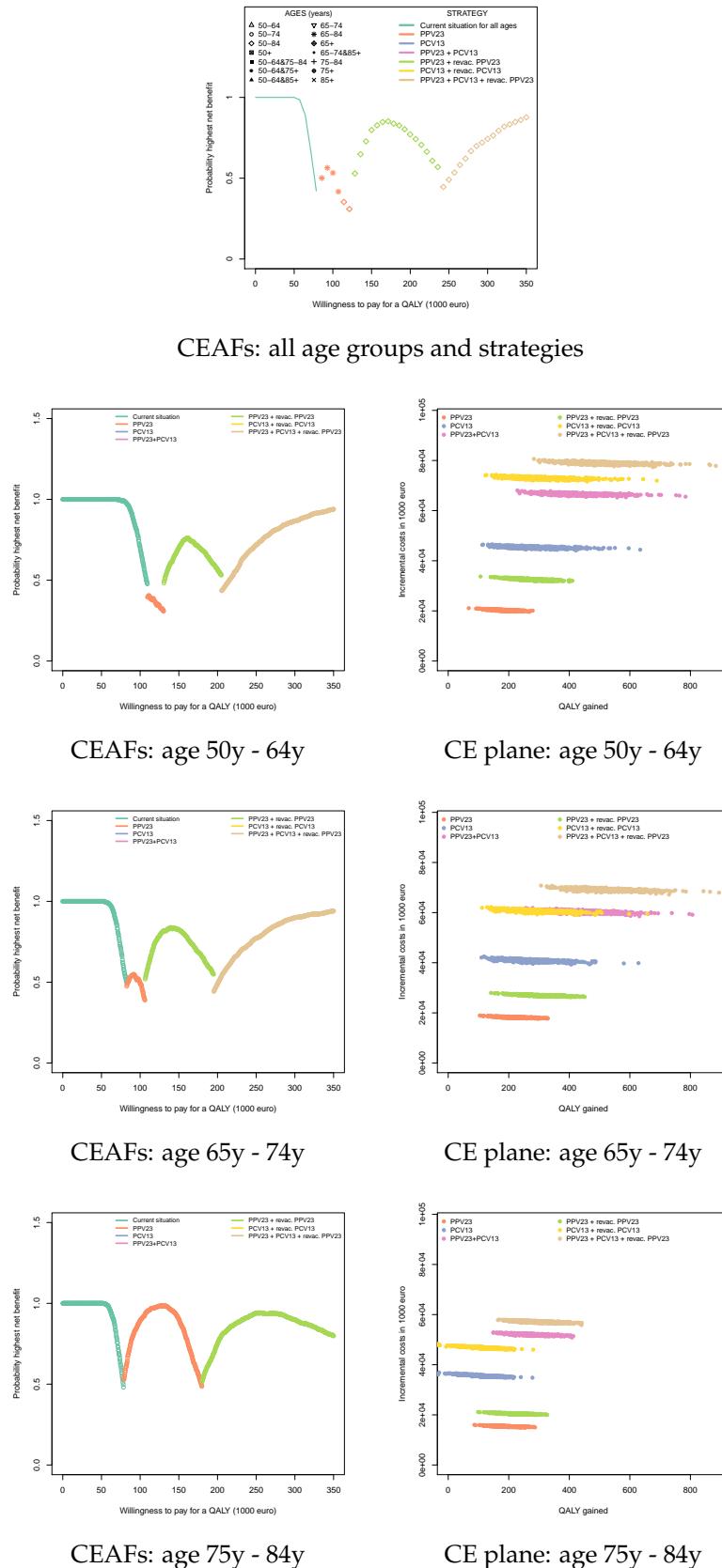
CE plane: age 65y - 74y



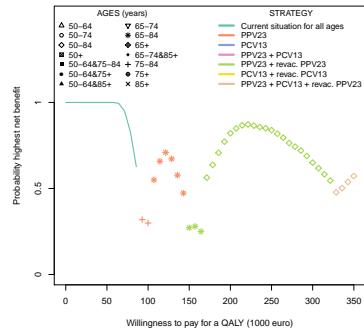
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

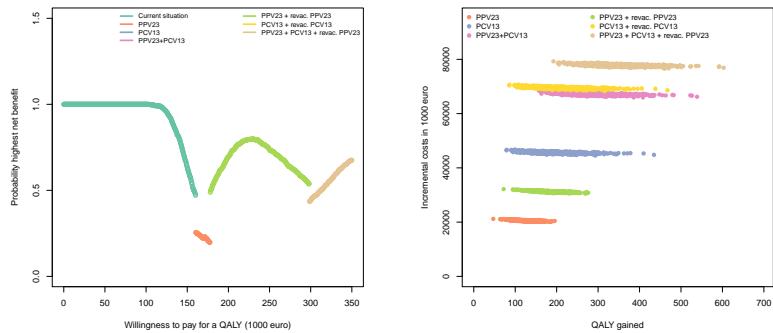
## No discounting: discount rate costs and effects: 0%



## Discount rate for costs and effects: 3%

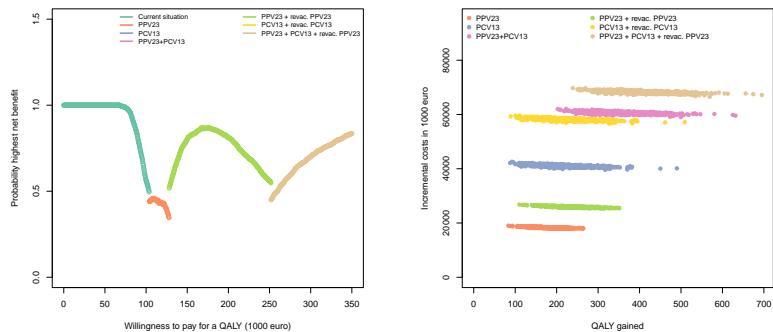


CEAFs: all age groups and strategies



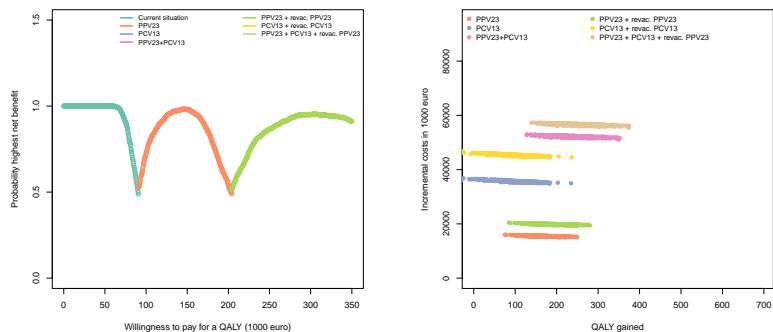
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

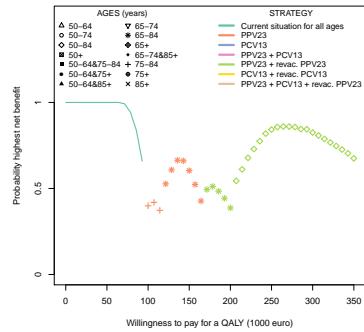
CE plane: age 65y - 74y



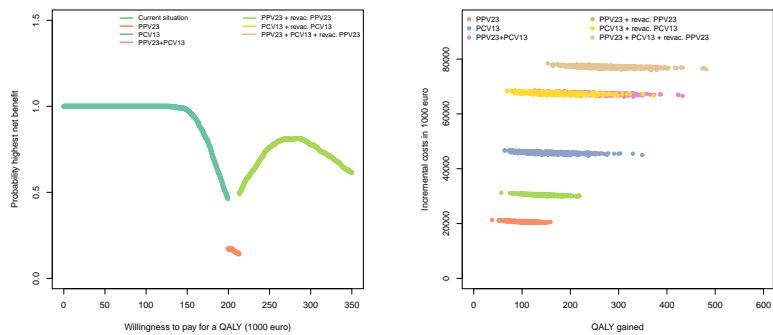
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## Discount rate for costs and effects: 5%

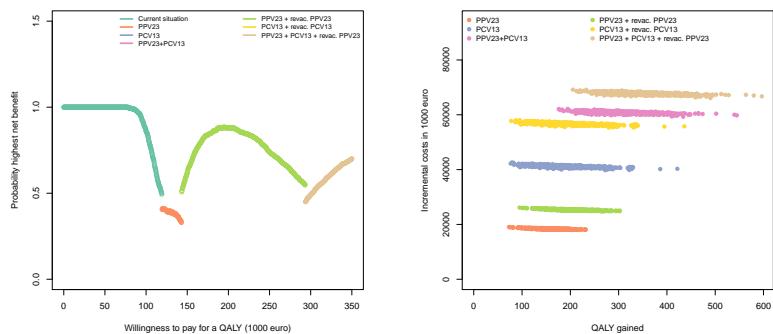


CEAFs: all age groups and strategies



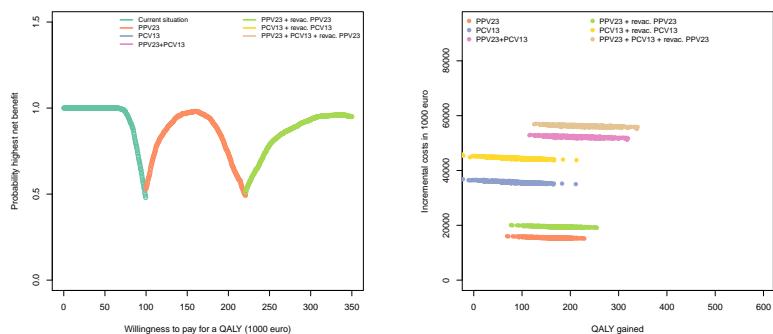
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

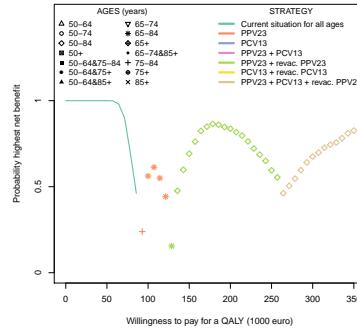
CE plane: age 65y - 74y



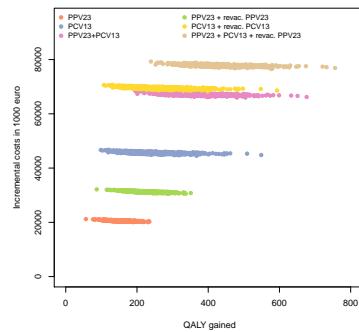
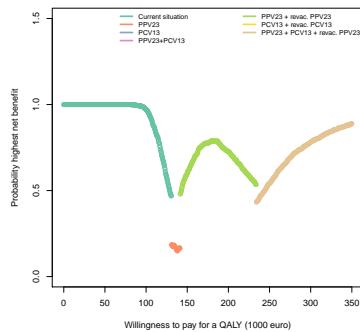
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## Using QALY loss averaged over all risk groups (baseline: low risk group only)

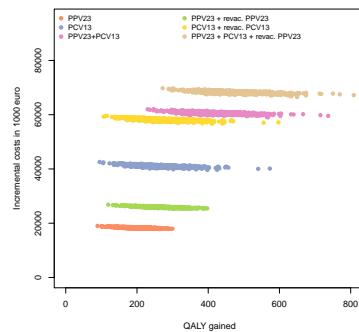
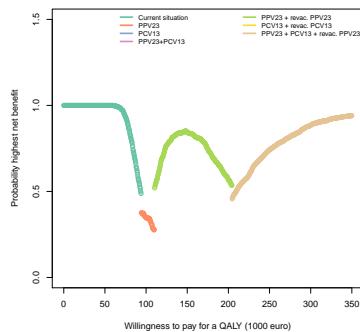


CEAFs: all age groups and strategies



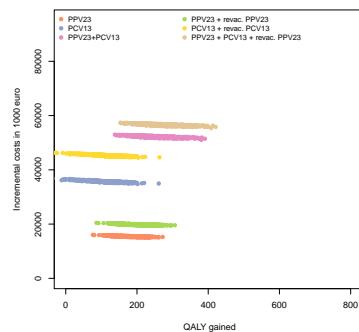
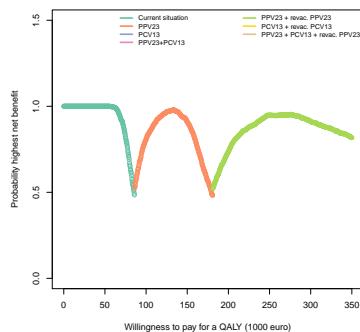
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

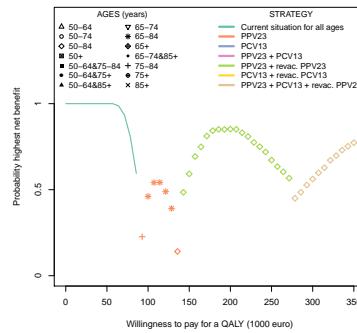
CE plane: age 65y - 74y



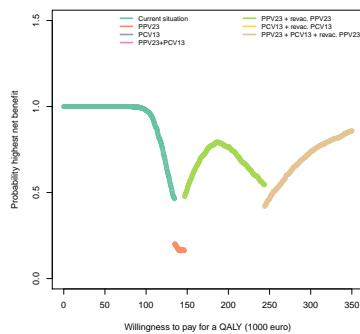
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

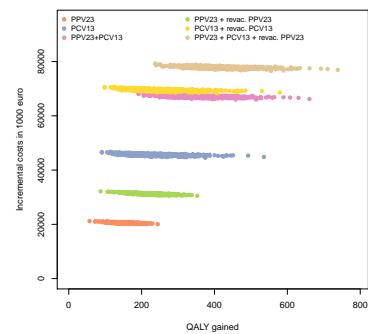
## Using QALY loss of the medium risk group only (baseline: low risk group only)



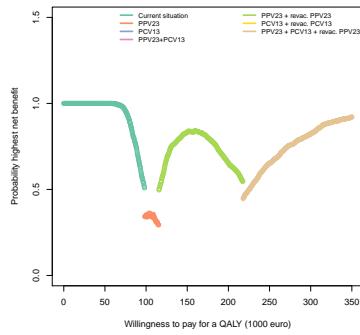
CEAFs: all age groups and strategies



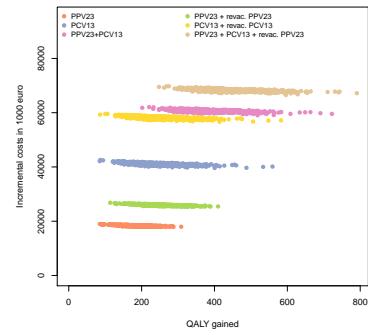
CEAFs: all age groups and strategies



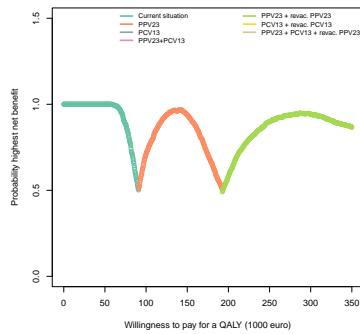
CE plane: all age groups and strategies



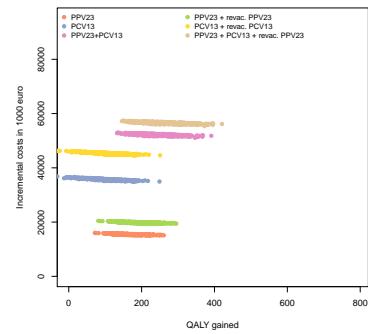
CEAFs: age 50y - 64y



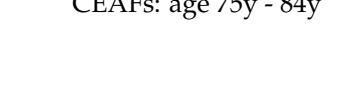
CE plane: age 50y - 64y



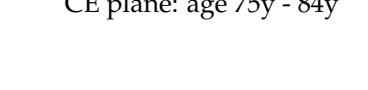
CEAFs: age 65y - 74y



CE plane: age 65y - 74y



CEAFs: age 75y - 84y



CE plane: age 75y - 84y

## Appendix C

### **Univariate sensitivity analysis: Baseline = 0% PCV13 and 0% PPV23 effectiveness against non-invasive CAP**

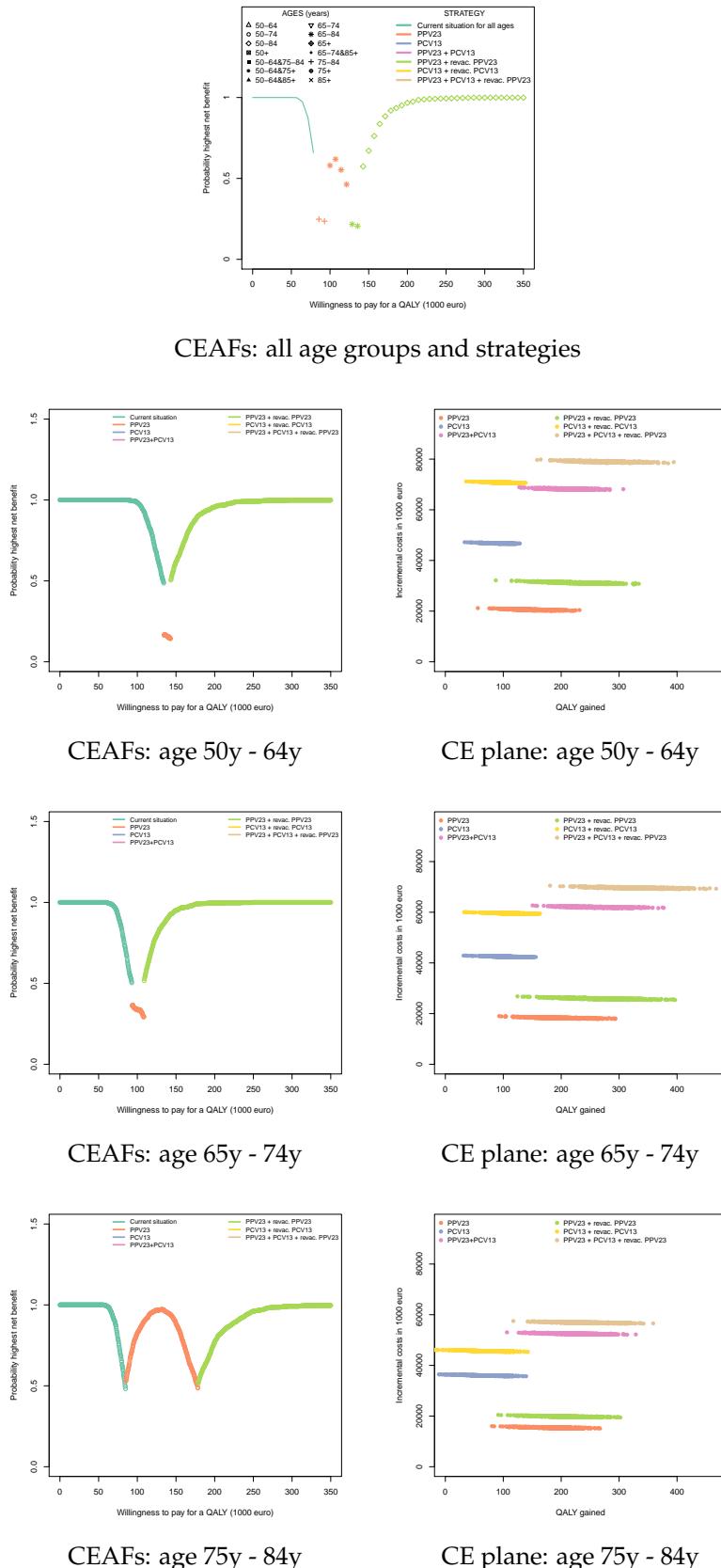
In this supplementary file, we present a visual overview of the effectiveness and cost-effectiveness of the different strategies in the different age groups, assuming 0% PCV13 and 0% PPV23 effectiveness against non-invasive CAP, unless explicitly mentioned otherwise, and show the univariate (or one way) sensitivity of these outcomes.

This supplement shows Cost-Effectiveness Acceptability Frontiers (CEAFs) and cost-effectiveness planes (CE planes) by age group targeted, on each page for a different scenario. Each page or scenario is defined by the change in a single variable or assumption versus the baseline.

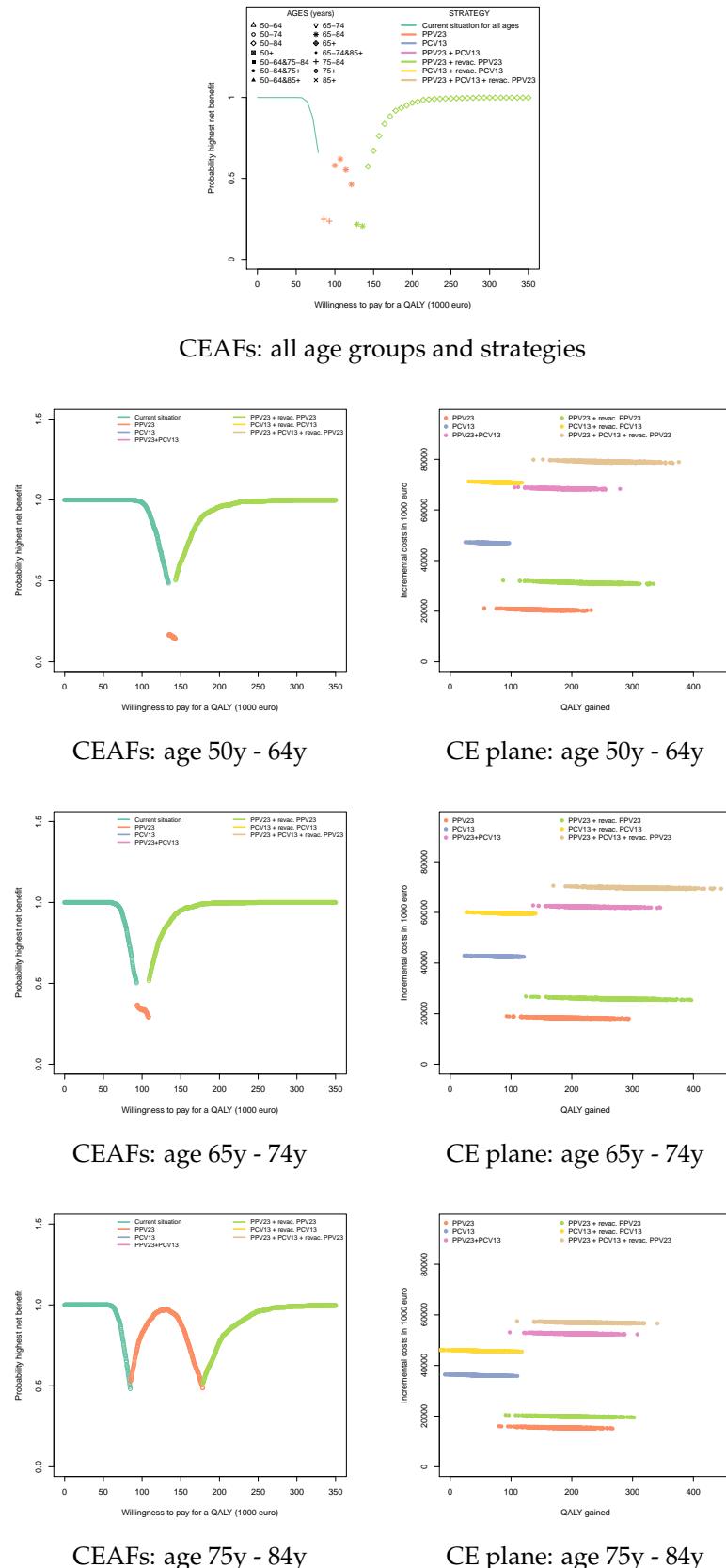
CEAFs have the attractive feature of summarizing parameter uncertainties in the ICERs in relation to a range of willingness to pay values. We use CEAFs showing for each willingness to pay (WTP) level over a wide range, the probability that the strategy depicted at that WTP level is the one strategy (amongst all strategies being compared) that results in the highest net benefit (when a QALY is valued at the WTP level shown). In the CE planes the realizations of 1000 simulations in terms of costs and effects (QALYs), results in clouds of 1000 points - one cloud for each incremental strategy - plotted versus the origin, where the origin of the plane represents the current situation. The further to the right, the more effective, the higher, the more costly a particular strategy is versus the current situation. Note that the same 1000 simulations per strategy are used to produce all the results we present under uncertainty.

For a stated “one way” deviation from the baseline above, each page shows at the top the CEAF over all age groups and strategies combined. Below this summary CEAF, we show more specific CEAFs by one of three age groups (on the left), along with their corresponding CE plane (on the right).

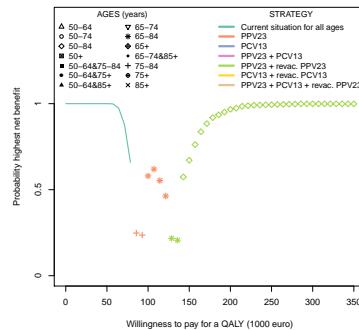
## Baseline: Both PCV13 and PPV23 0% effectiveness against non-invasive CAP



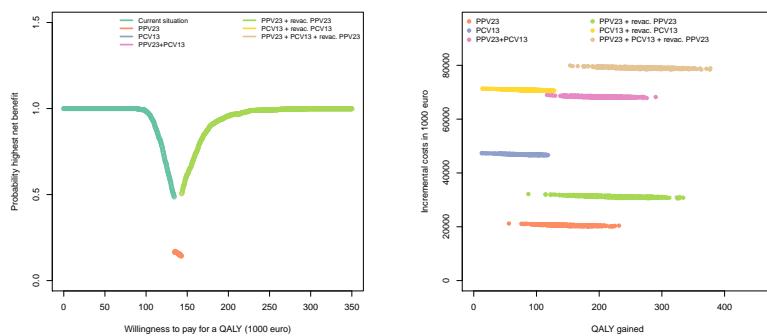
## 5 years of PCV13 protection followed by no protection, and baseline PPV23 protection



## Age independent VE for PCV13 from age 50 to 84y

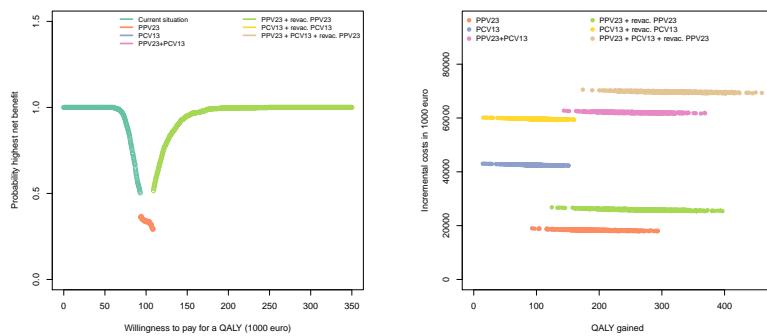


CEAFs: all age groups and strategies



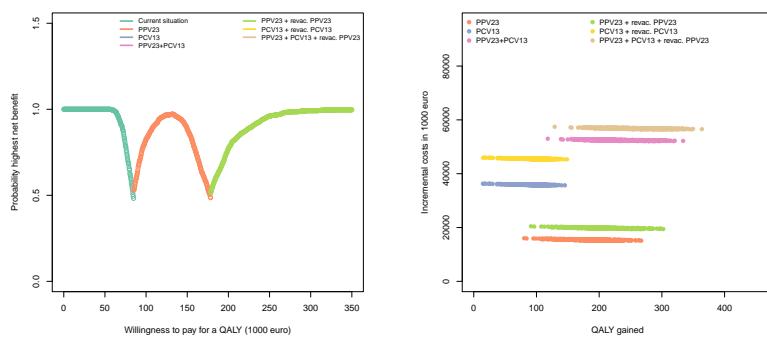
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

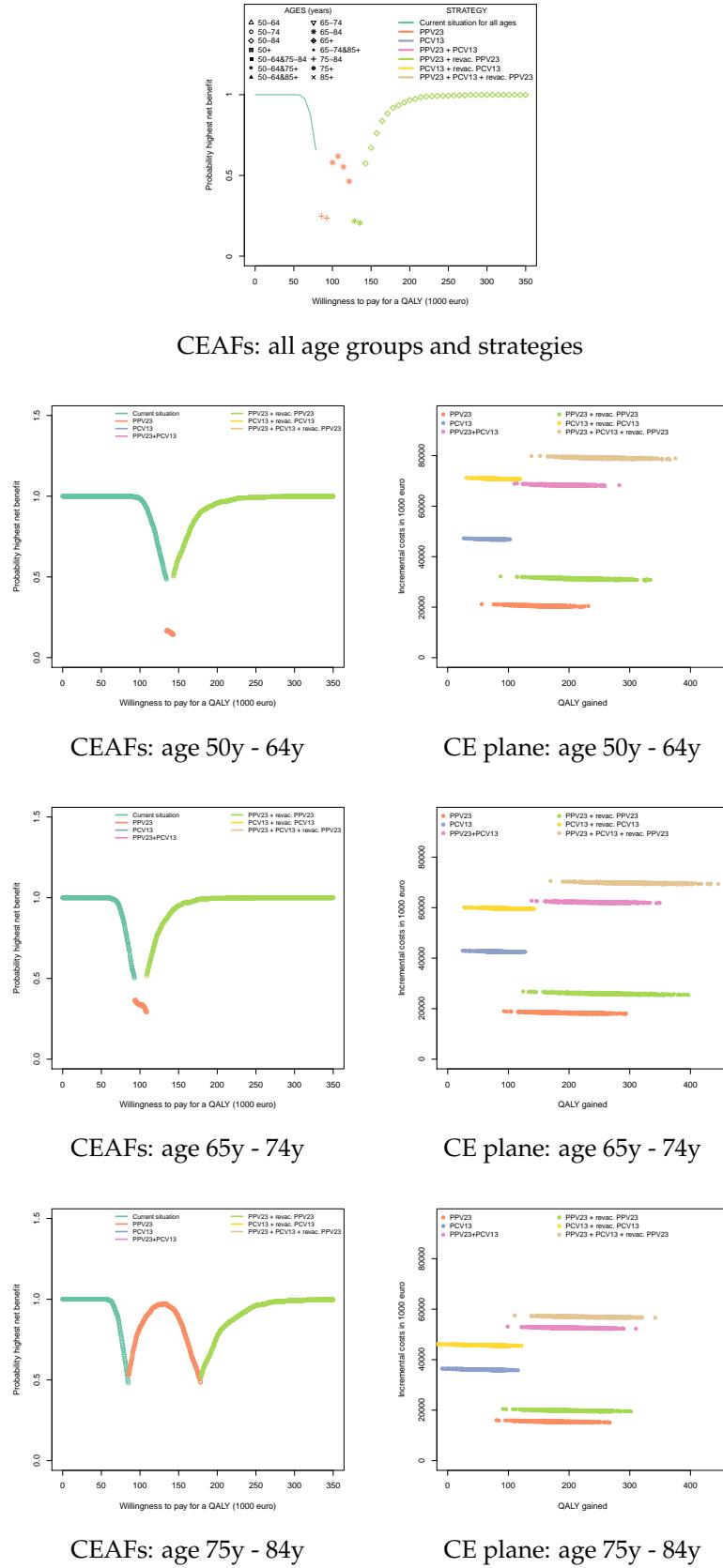
CE plane: age 65y - 74y



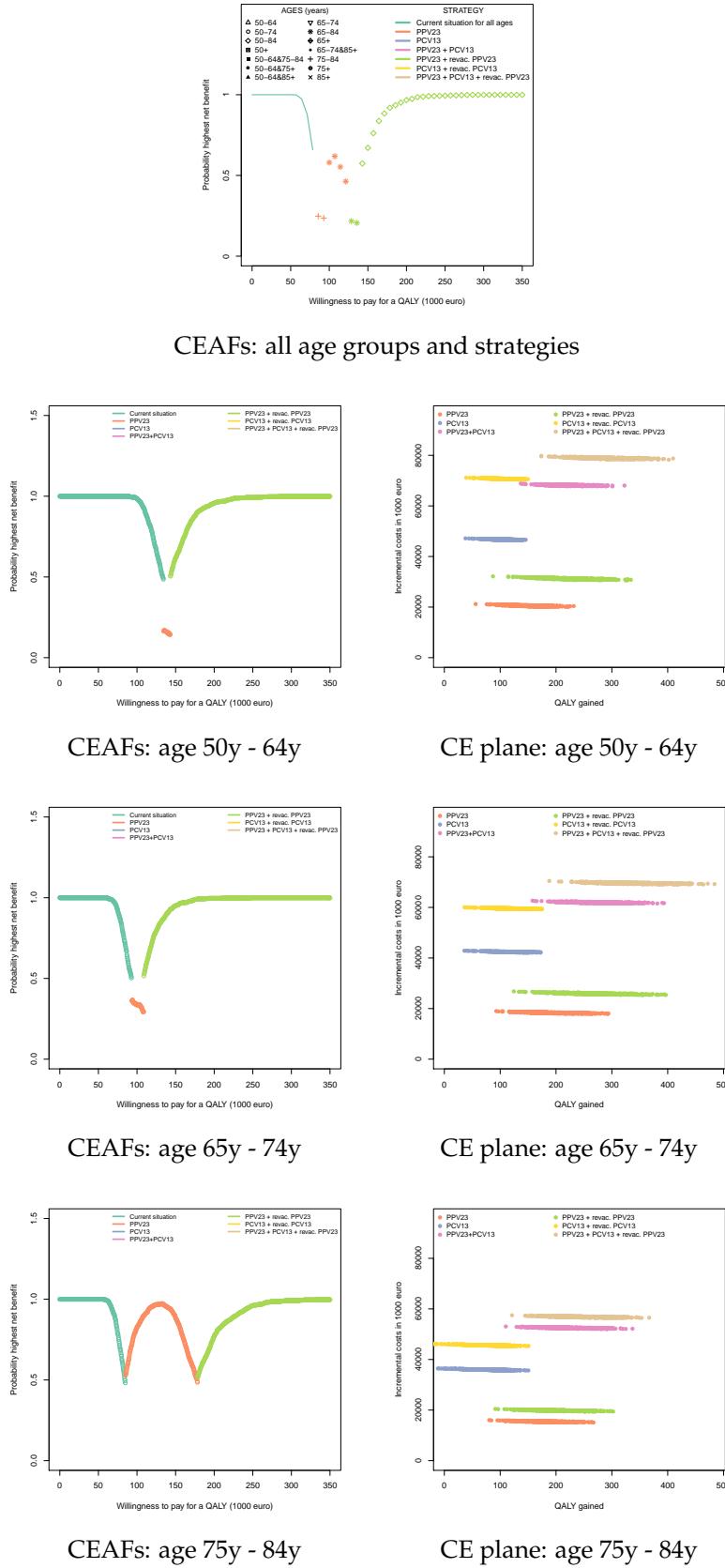
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

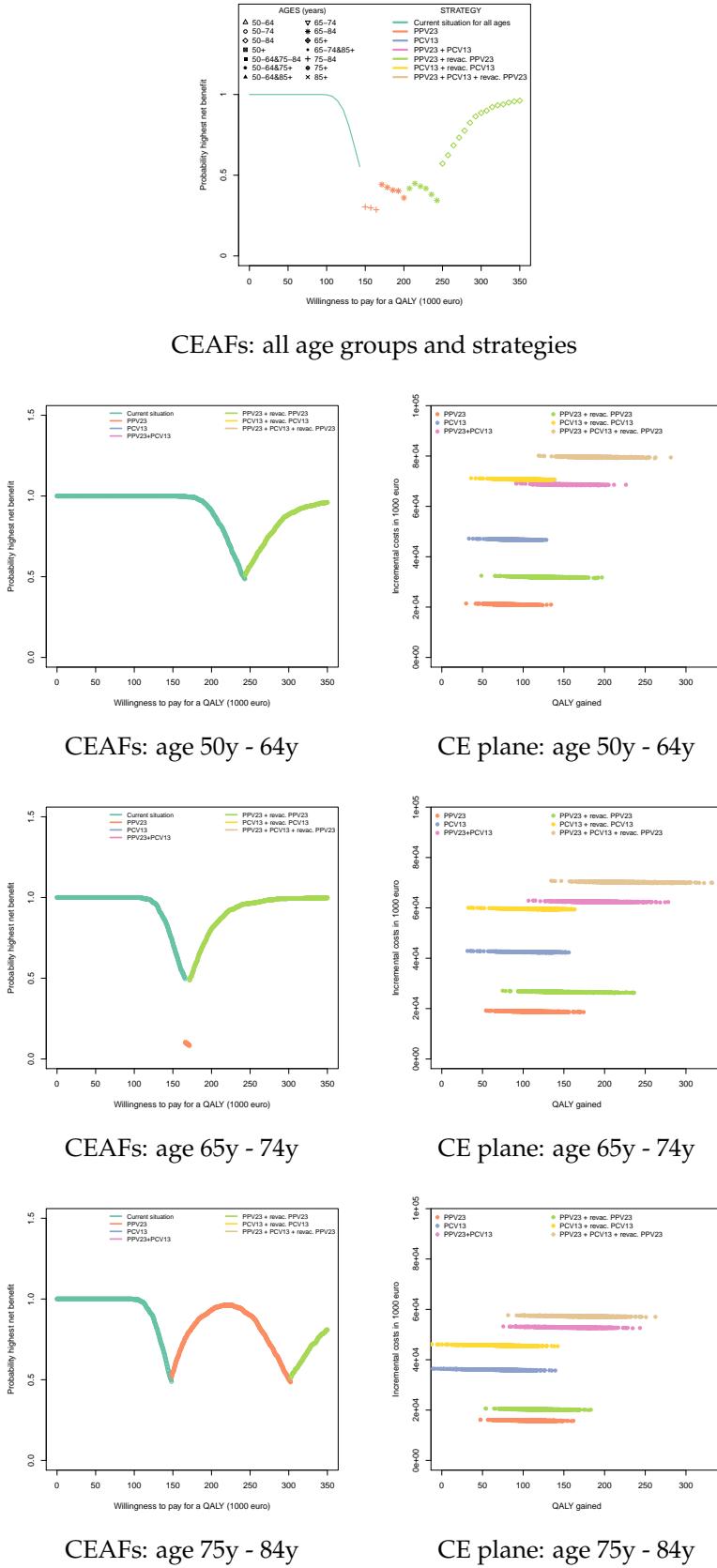
**Minimum duration of PCV13 protection (4 years fixed protection followed by rapid waning to no protection at 10 years), and baseline PPV23 protection**



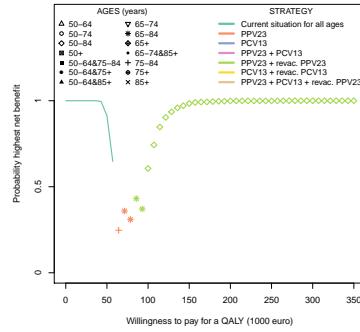
**Maximum duration of PCV13 protection ((9 years fixed protection followed by slow waning to no protection at 20 years), and baseline PPV23 protection**



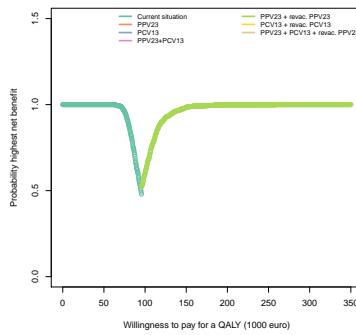
**2 years of complete (without waning) PPV23 protection followed by no protection, and baseline PCV13 vaccine protection**



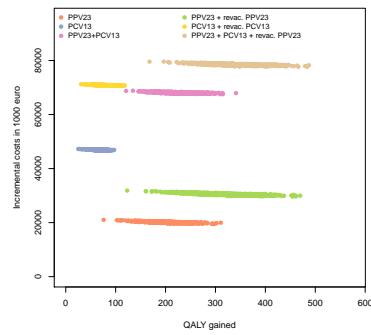
**5 years of complete (without waning) protection followed by no protection for both PCV13 and PPV23**



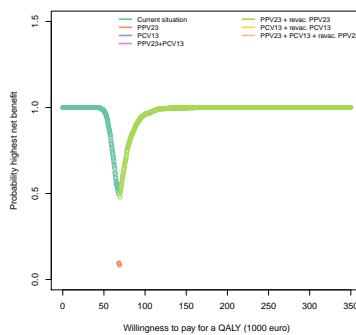
CEAFs: all age groups and strategies



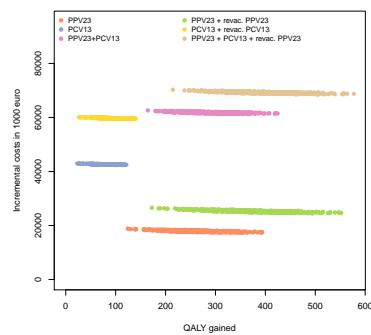
CEAFs: age 50y - 64y



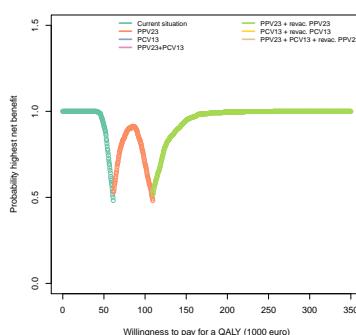
CE plane: age 50y - 64y



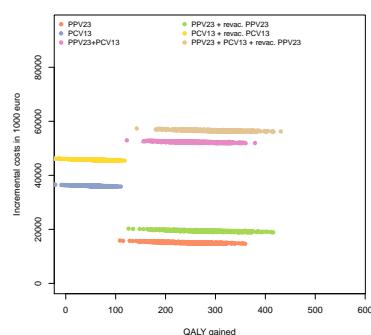
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

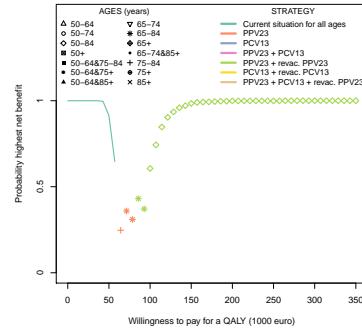


CEAFs: age 75y - 84y

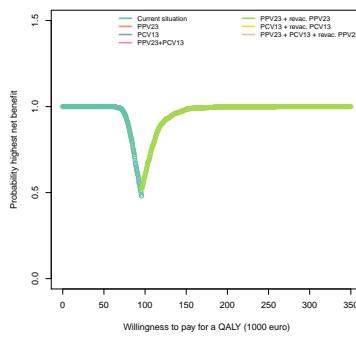


CE plane: age 75y - 84y

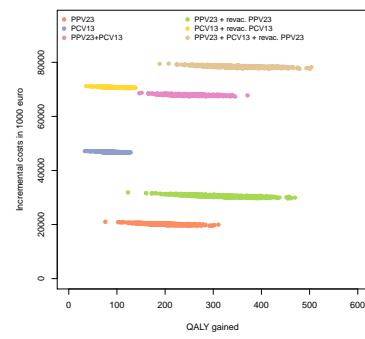
**5 years of complete (without waning) PPV23 protection followed by no protection, and baseline PCV13 vaccine protection**



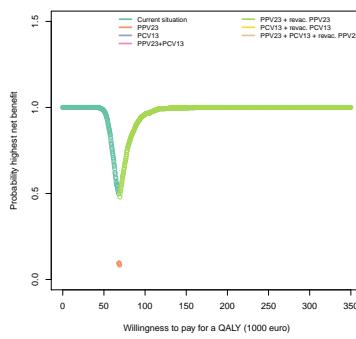
CEAFs: all age groups and strategies



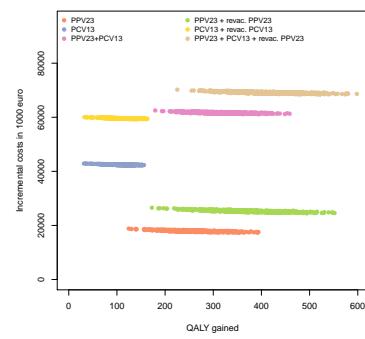
CEAFs: age 50y - 64y



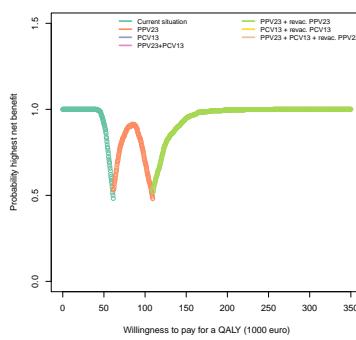
CE plane: age 50y - 64y



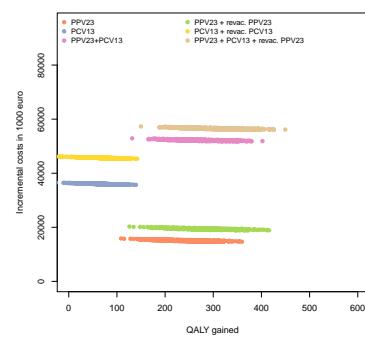
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

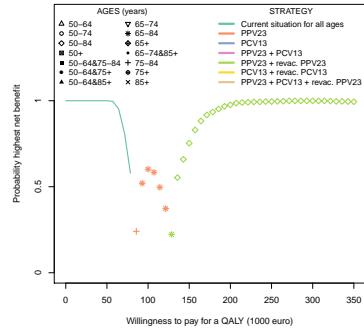


CEAFs: age 75y - 84y

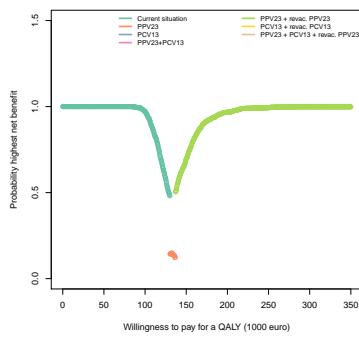


CE plane: age 75y - 84y

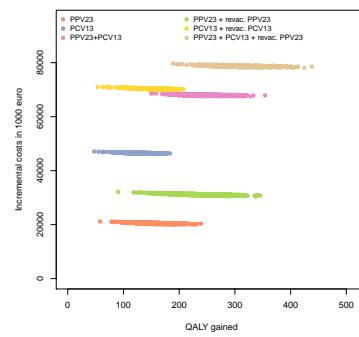
**Minimum PCV13 incidence decline (PCV13 serotype incidence -10% per year, baseline (76%) replacement)**



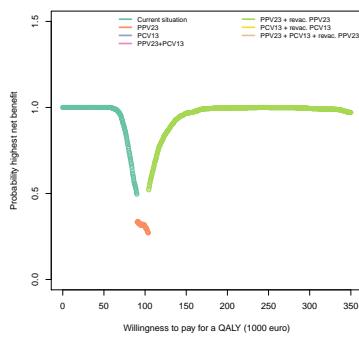
CEAFs: all age groups and strategies



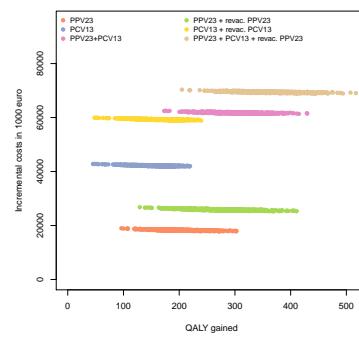
CEAFs: age 50y - 64y



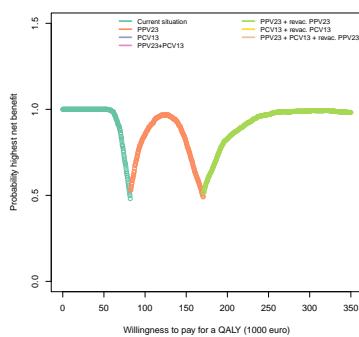
CE plane: age 50y - 64y



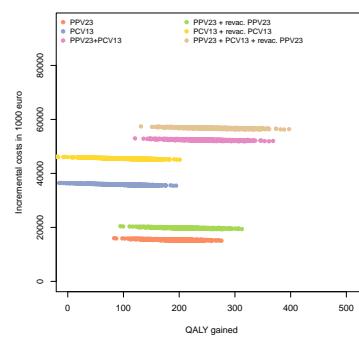
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

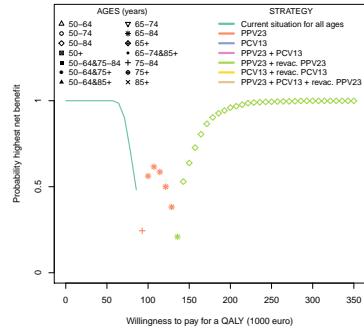


CEAFs: age 75y - 84y

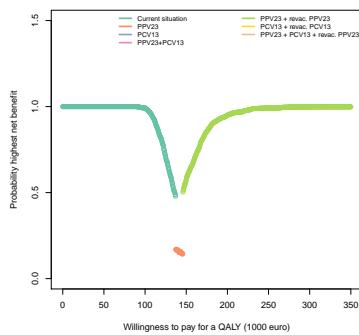


CE plane: age 75y - 84y

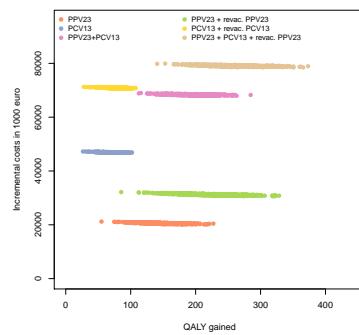
**Maximum PCV13 incidence decline (PCV13 serotype incidence -20% per year, baseline (76%) replacement)**



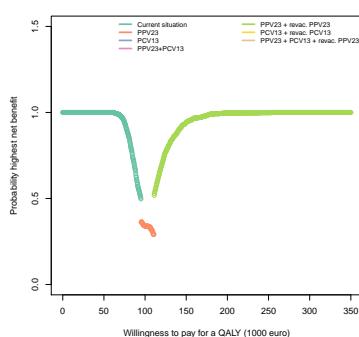
CEAFs: all age groups and strategies



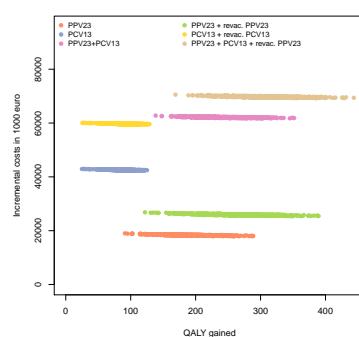
CEAFs: age 50y - 64y



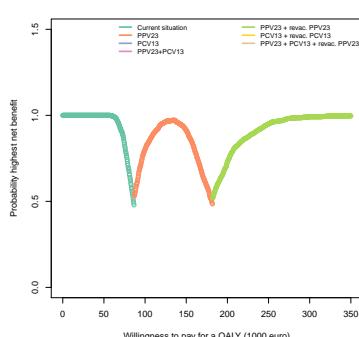
CE plane: age 50y - 64y



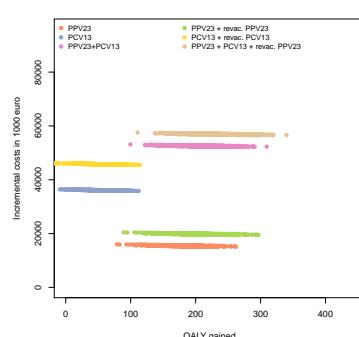
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

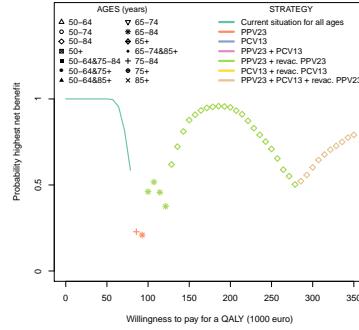


CEAFs: age 75y - 84y

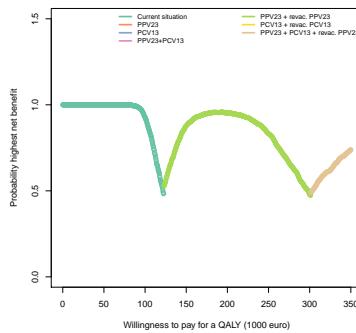


CE plane: age 75y - 84y

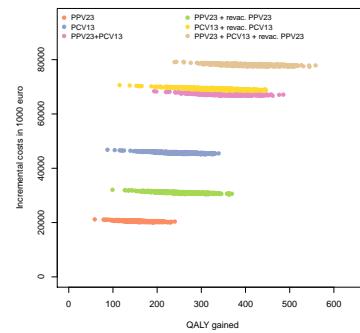
**Quick PCV13 serotype relapse: PCV13 incidence returns to 2015 value within 7 years  
(0% replacement of PCV13 incidence decline by non-PCV13 types)**



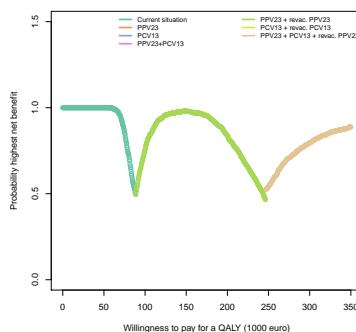
CEAFs: all age groups and strategies



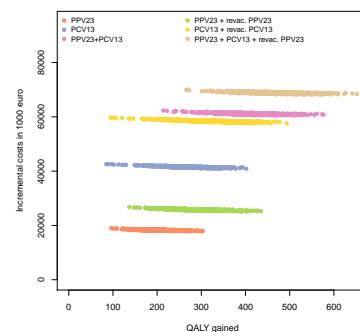
CEAFs: age 50y - 64y



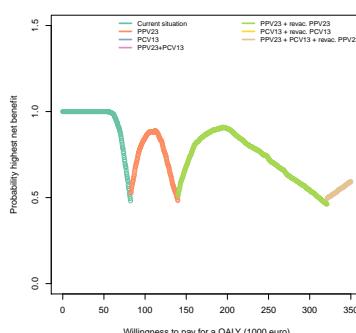
CE plane: age 50y - 64y



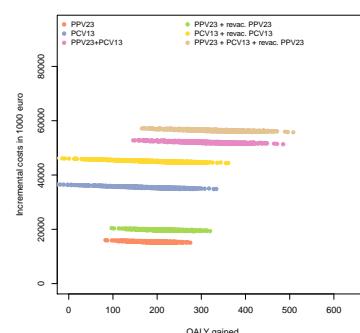
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

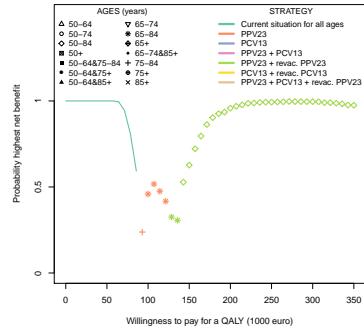


CEAFs: age 75y - 84y

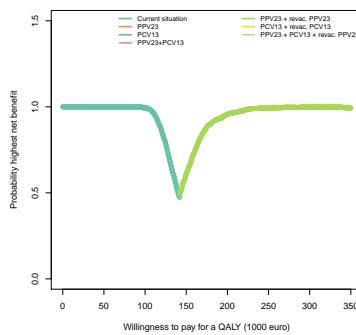


CE plane: age 75y - 84y

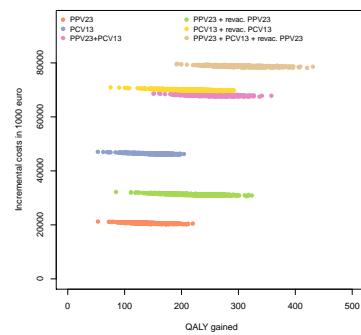
**Slow PCV13 serotype relapse: PCV13 incidence returns to 2015 value within 15 years  
(0% replacement of PCV13 incidence decline by non-PCV13 types)**



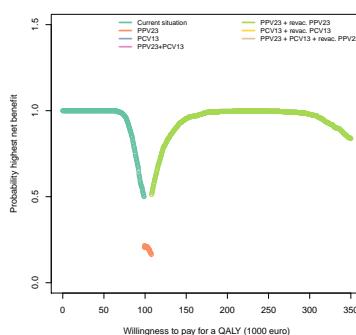
CEAFs: all age groups and strategies



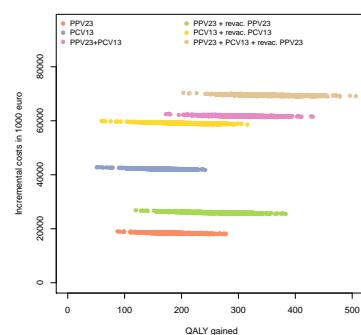
CEAFs: age 50y - 64y



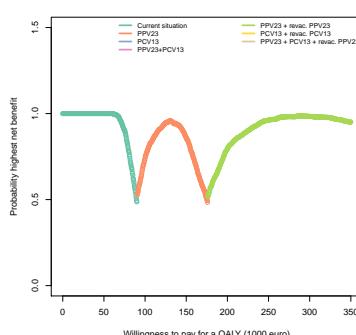
CE plane: age 50y - 64y



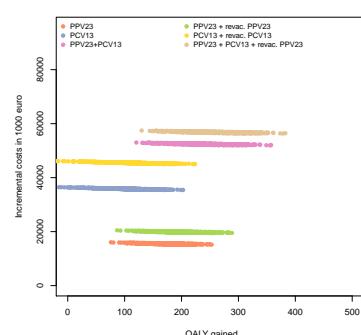
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

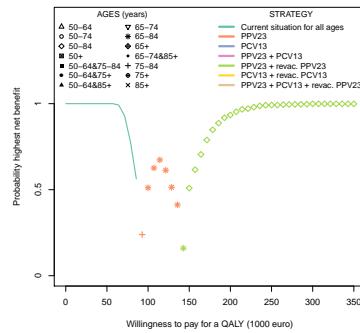


CEAFs: age 75y - 84y

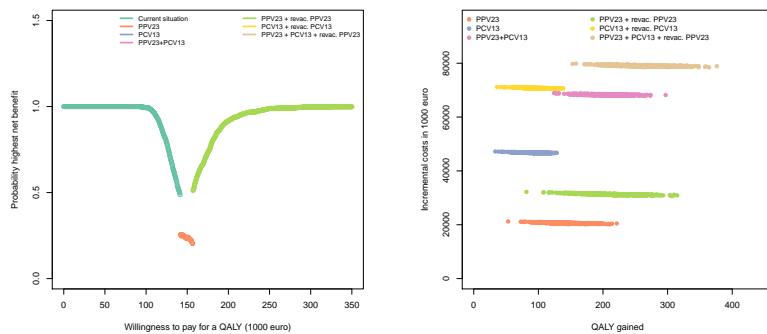


CE plane: age 75y - 84y

## Serotype replacement: 34% (2013 serocoverage data) instead of 76% (2015 baseline)

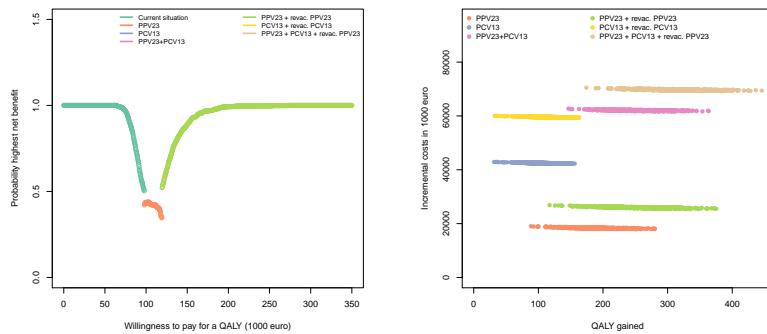


CEAFs: all age groups and strategies



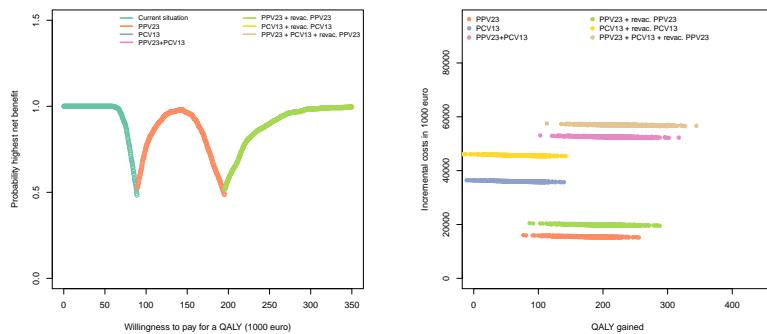
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

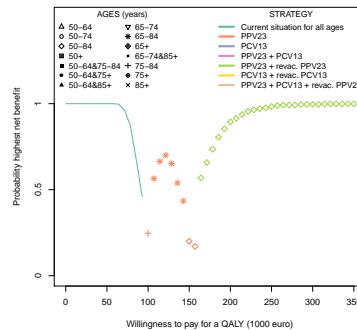
CE plane: age 65y - 74y



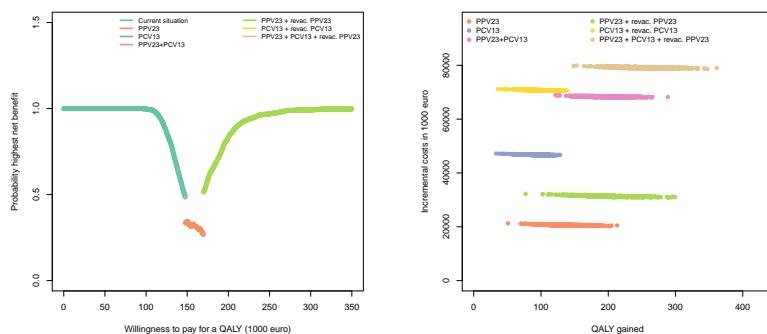
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## Serotype replacement extreme low: 0% instead of 76% (2015 baseline)

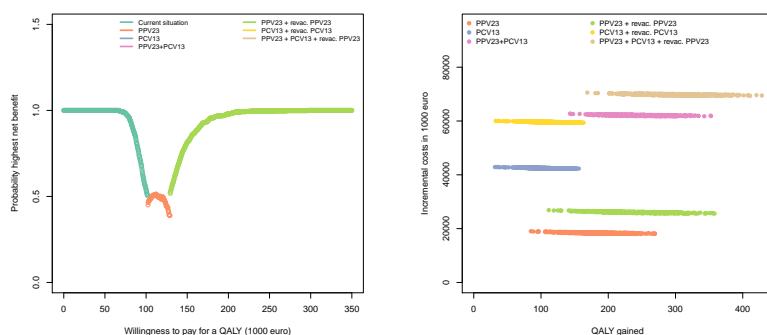


CEAFs: all age groups and strategies



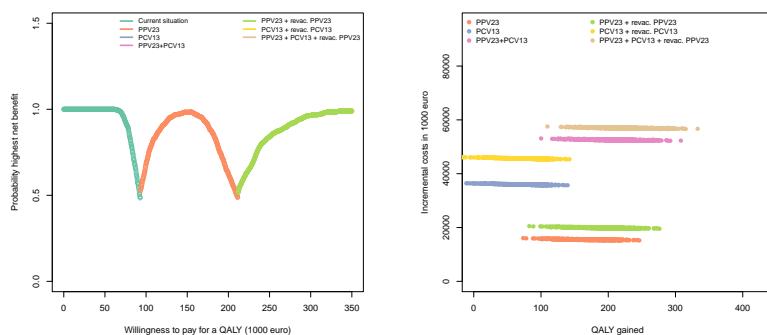
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

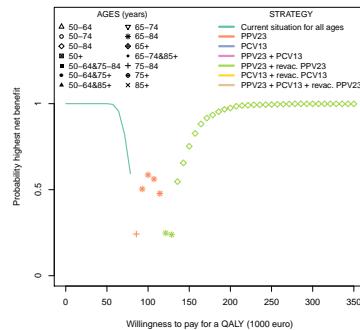
CE plane: age 65y - 74y



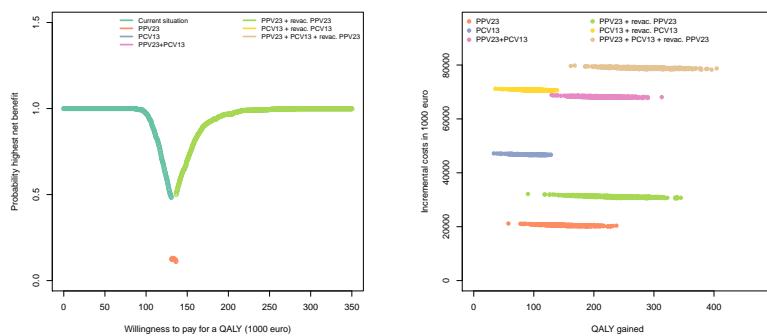
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## Serotype replacement extreme high: 100% instead of 76% (2015 baseline)

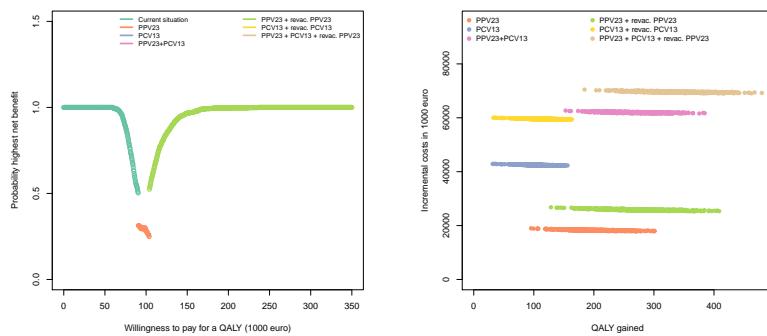


CEAFs: all age groups and strategies



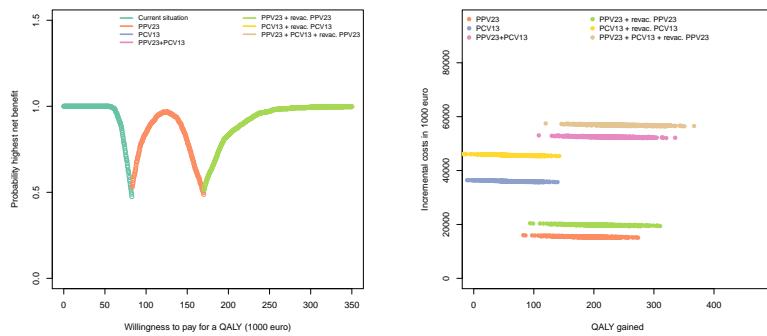
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

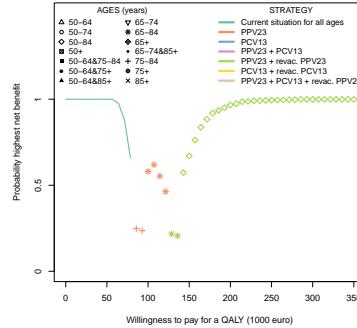
CE plane: age 65y - 74y



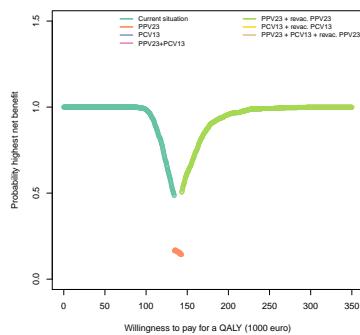
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

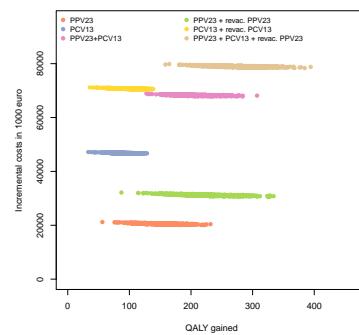
**Higher percentage of pneumococcal pneumonia in outpatient CAP (27% (Said 2013) instead of 10.5%)**



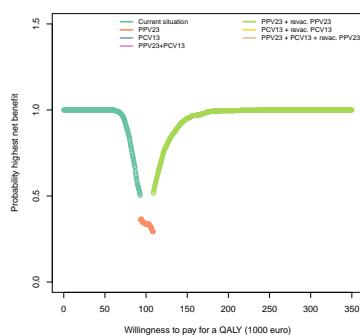
CEAFs: all age groups and strategies



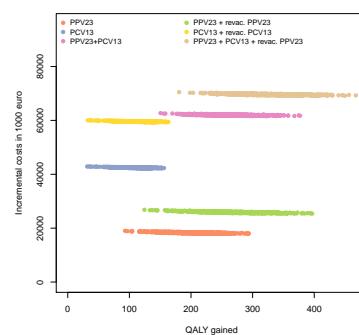
CEAFs: age 50y - 64y



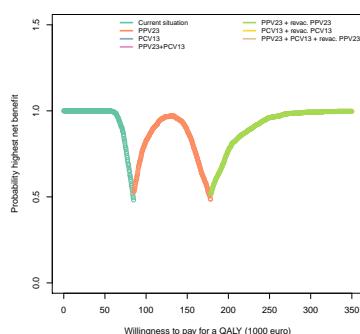
CE plane: age 50y - 64y



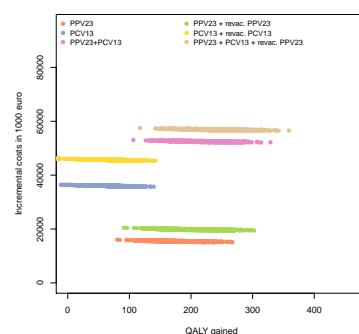
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

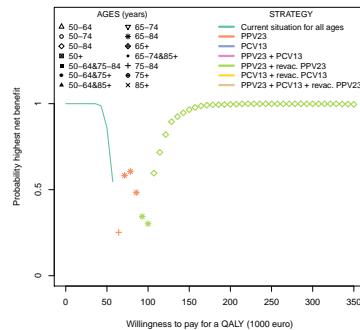


CEAFs: age 75y - 84y

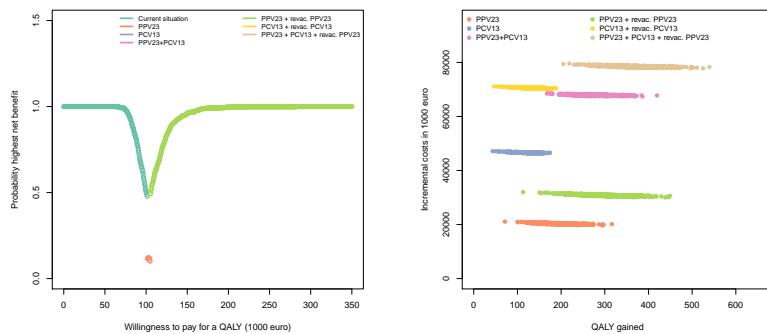


CE plane: age 75y - 84y

## Higher hospitalised pneumococcal pneumonia incidence: 1.5 x baseline

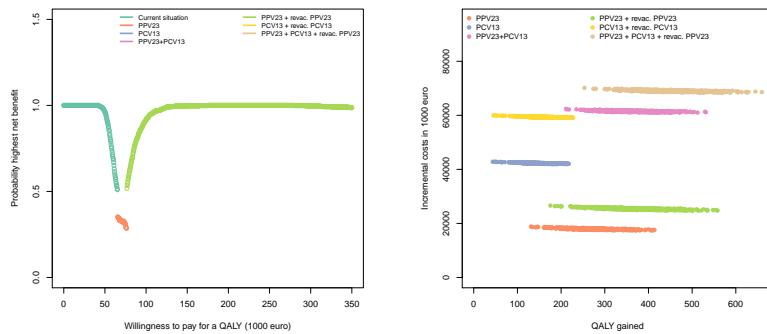


CEAFs: all age groups and strategies



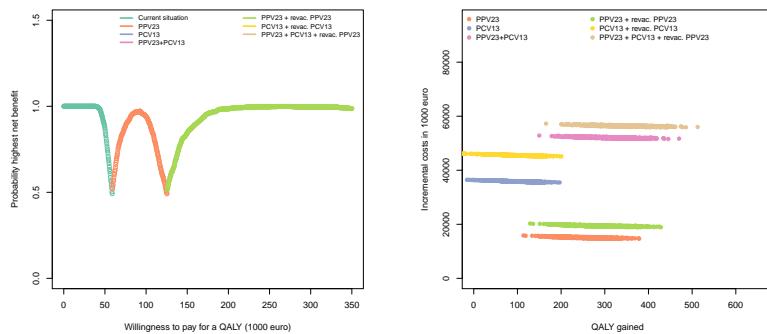
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

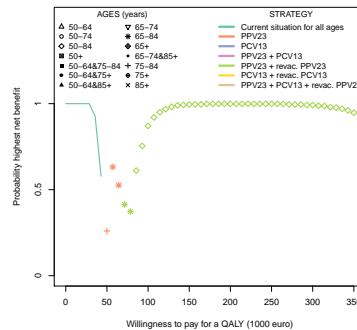
CE plane: age 65y - 74y



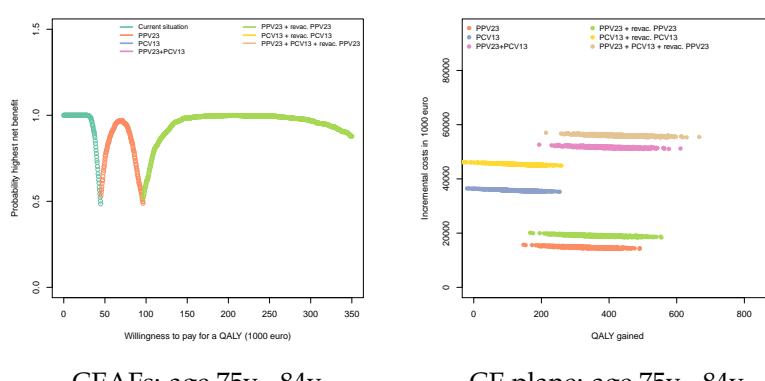
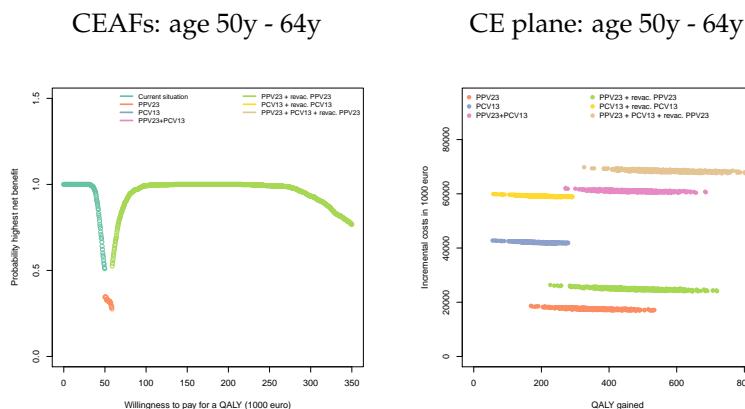
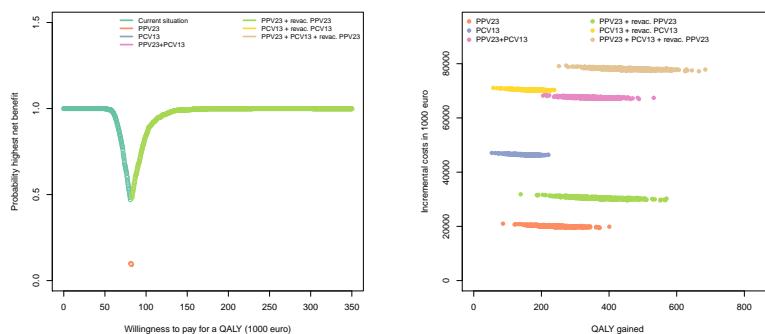
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

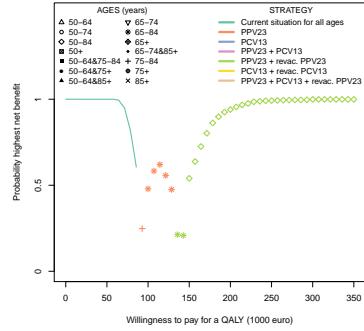
## Higher hospitalised pneumococcal pneumonia incidence: 2 x baseline



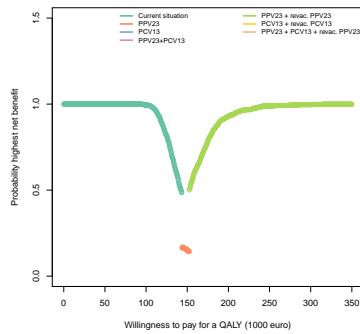
CEAFs: all age groups and strategies



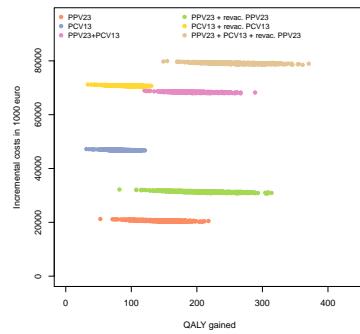
**Lower incidence of hospitalisations (94% of baseline, assuming no underreporting in NRC)**



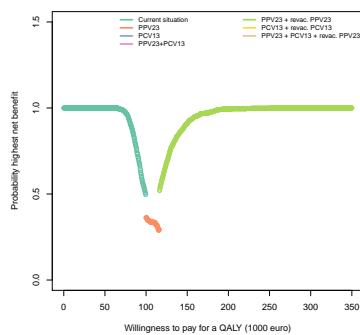
CEAFs: all age groups and strategies



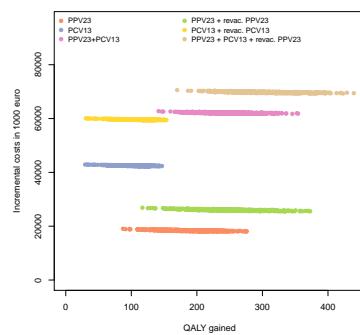
CEAFs: age 50y - 64y



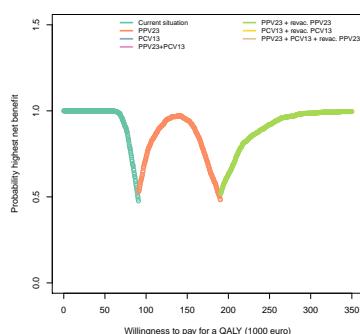
CE plane: age 50y - 64y



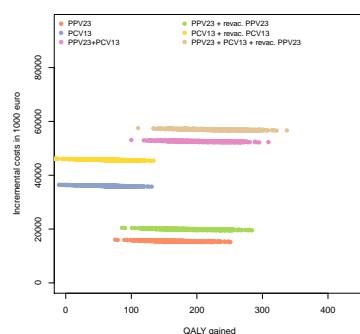
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

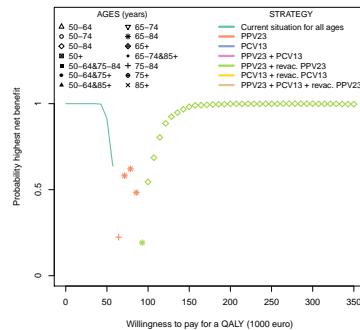


CEAFs: age 75y - 84y

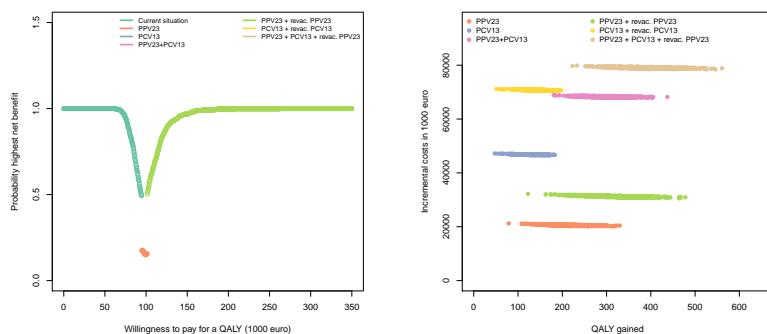


CE plane: age 75y - 84y

## High mortality: Death rate of hospitalised cases: 150% of base

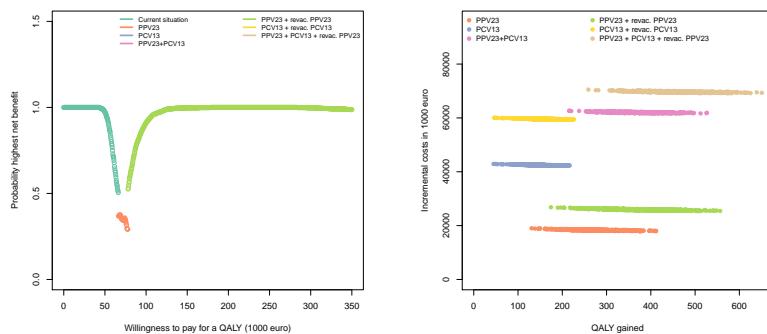


CEAFs: all age groups and strategies



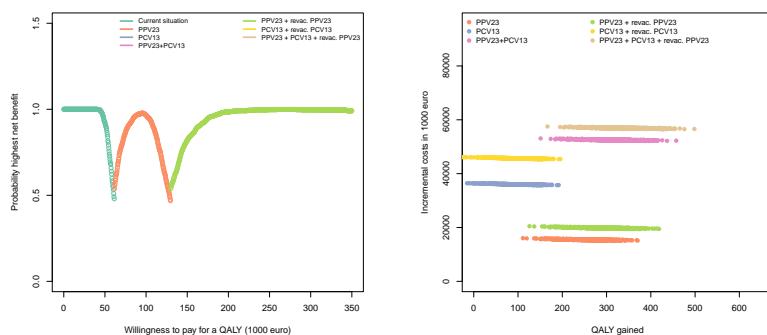
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

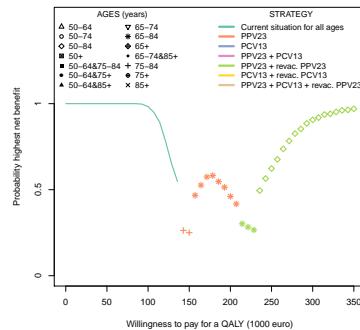
CE plane: age 65y - 74y



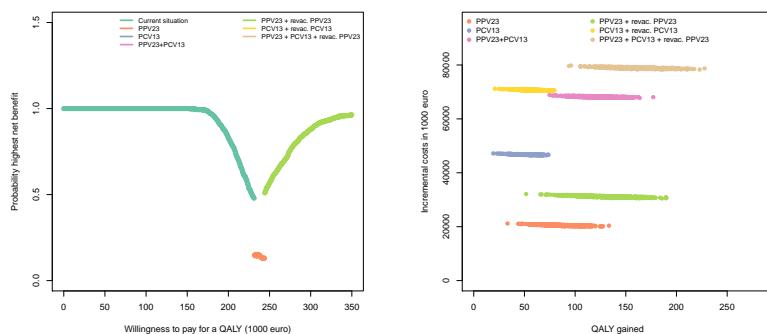
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## Low mortality: Death rate of hospitalised cases: 50% of baseline

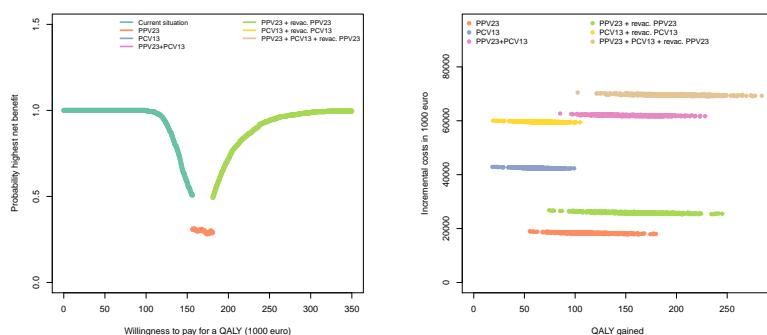


CEAFs: all age groups and strategies



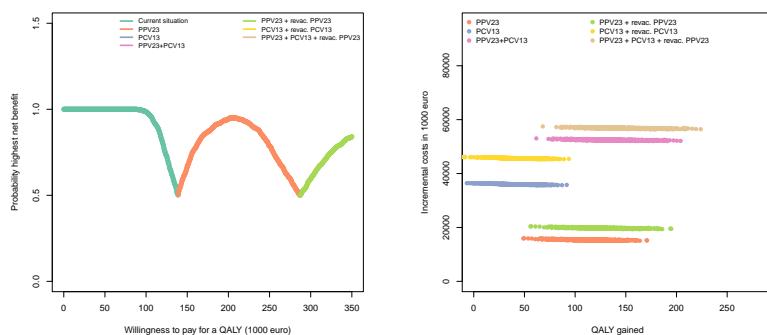
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

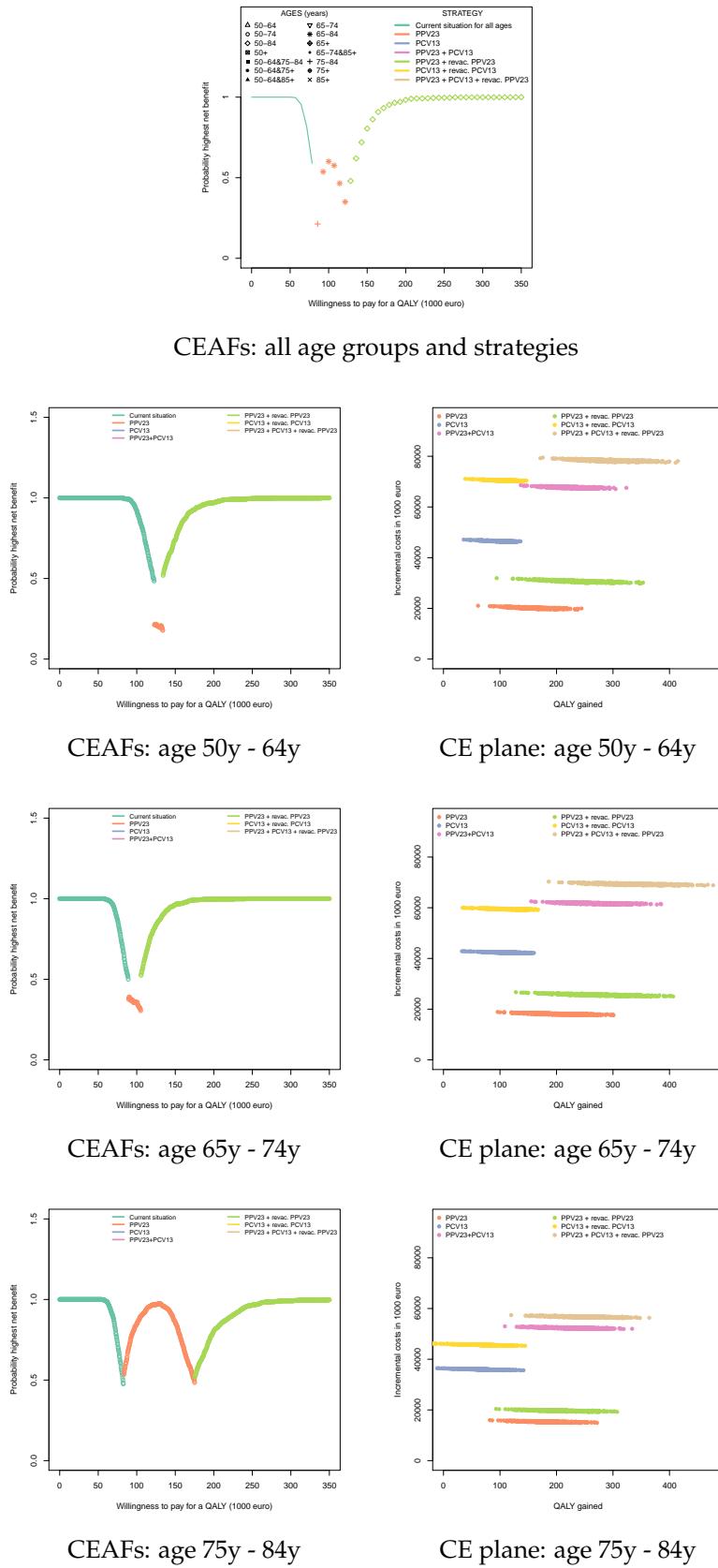
CE plane: age 65y - 74y



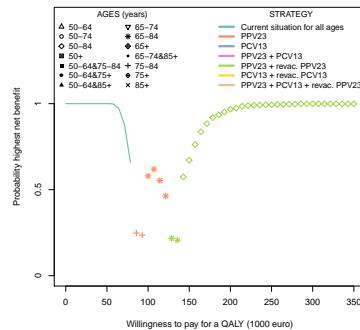
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

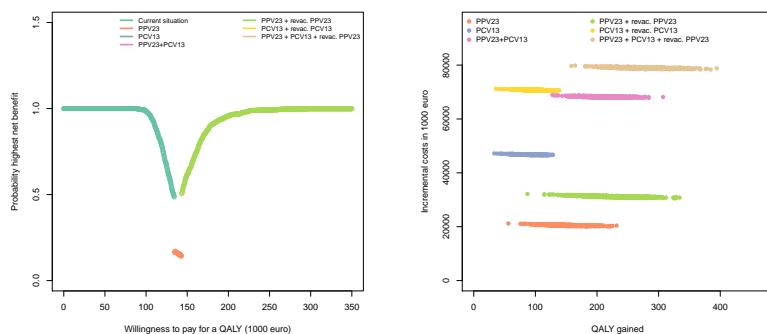
## More meningitis sequelae (probabilities of 20% for hearing loss and 22% for neurological sequelae)



## Higher costs CAP for outpatients (1 extra GP consult per case)

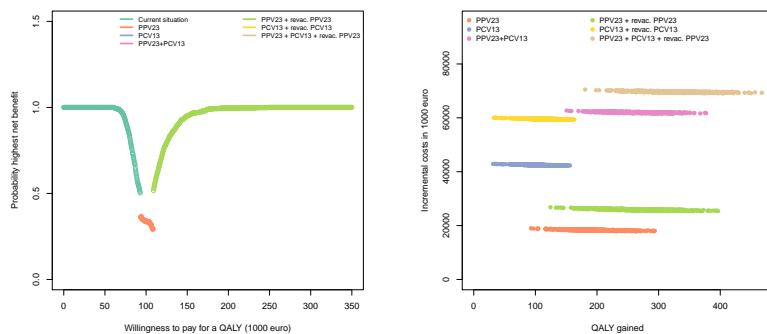


CEAFs: all age groups and strategies



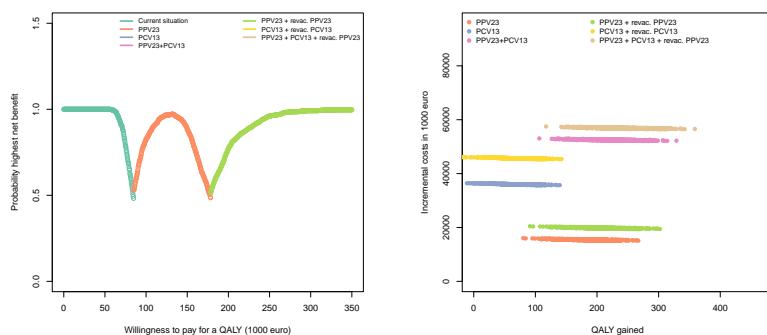
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

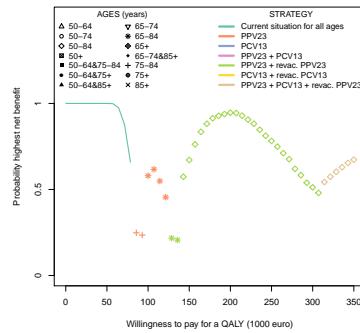
CE plane: age 65y - 74y



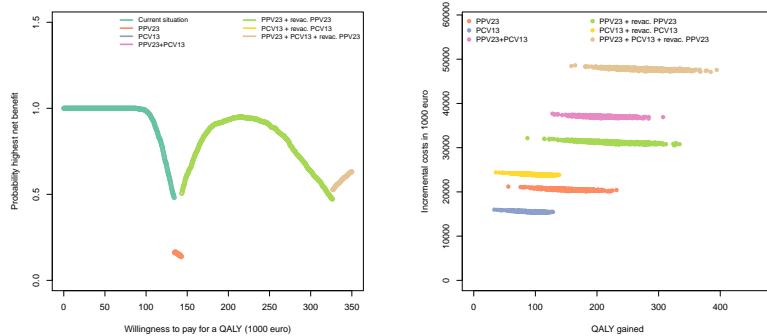
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## 75% reduction of the baseline PCV13 price, baseline PPV23 price

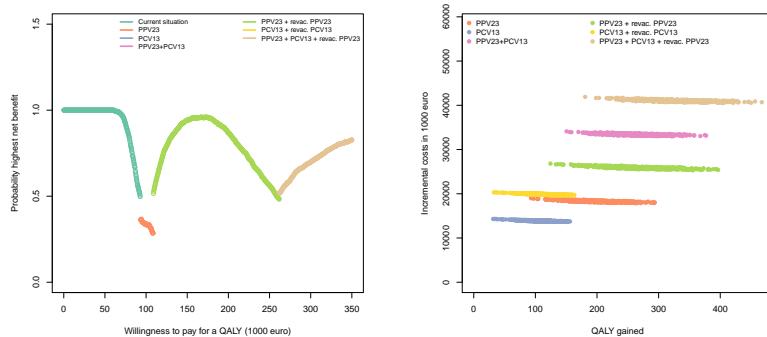


CEAFs: all age groups and strategies



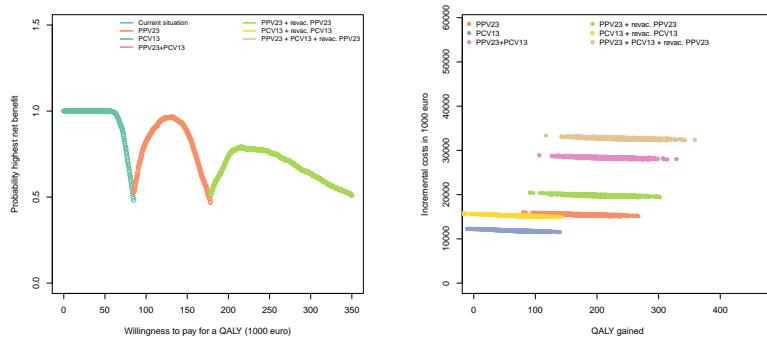
CEAFs: all age groups and strategies

CE plane: all age groups and strategies



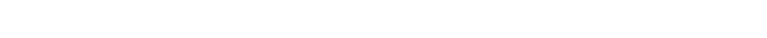
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

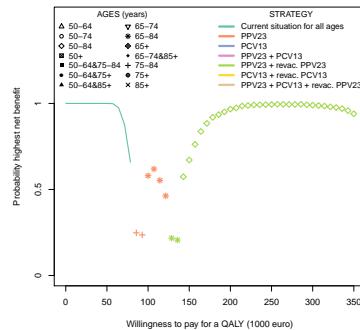
CE plane: age 65y - 74y



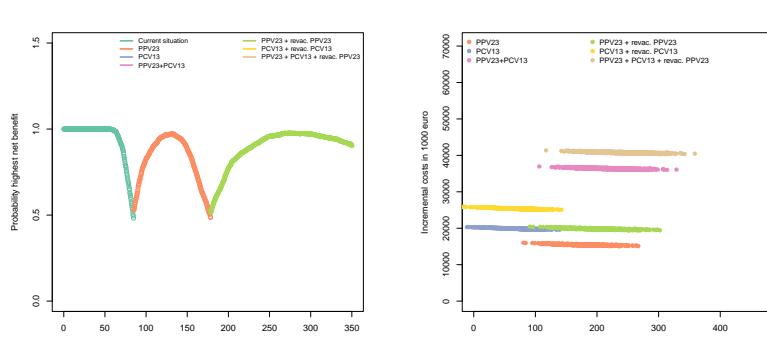
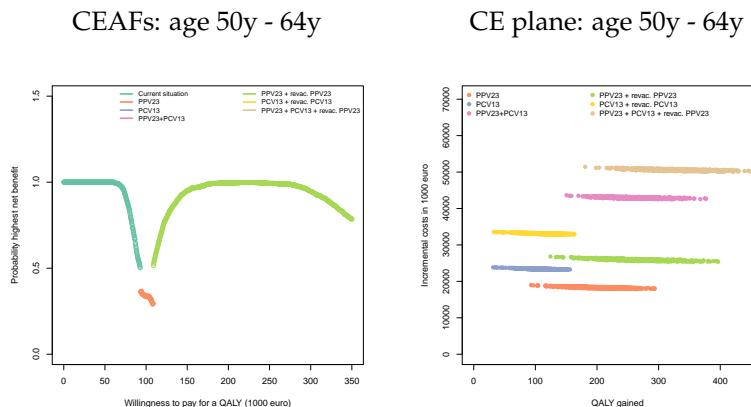
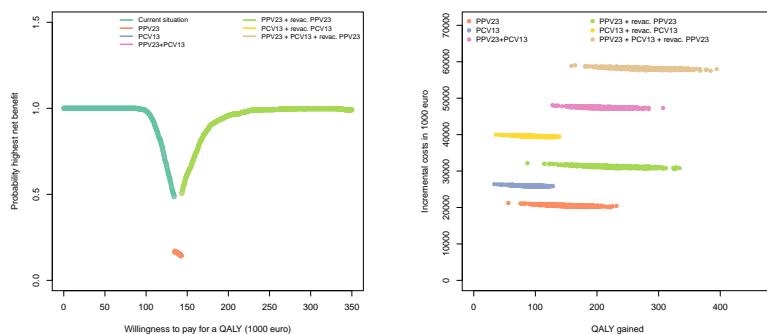
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

## 50% reduction of the baseline PCV13 price, baseline PPV23 price

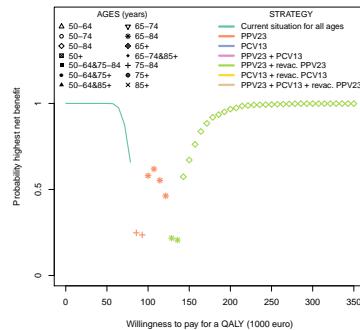


CEAFs: all age groups and strategies

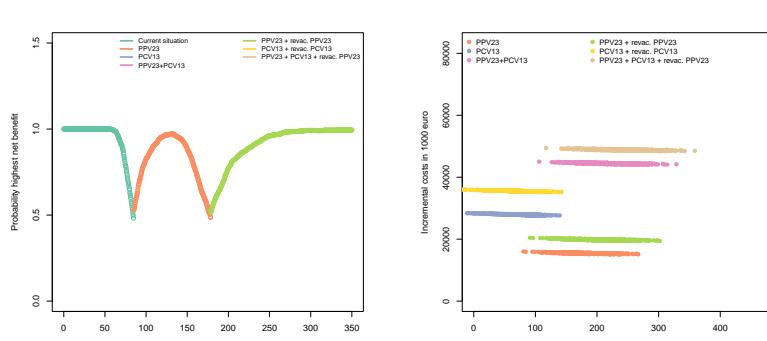
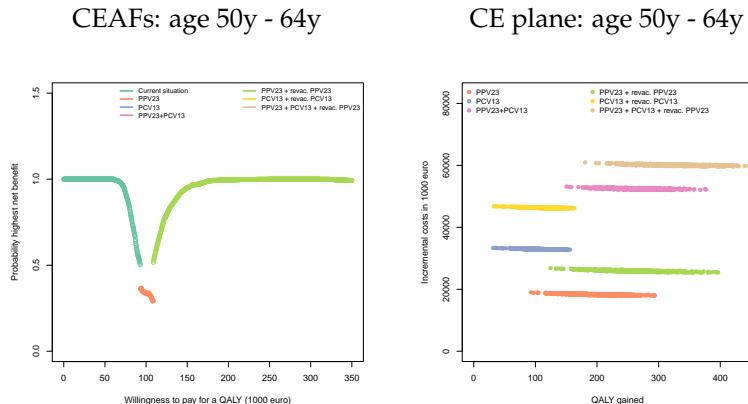
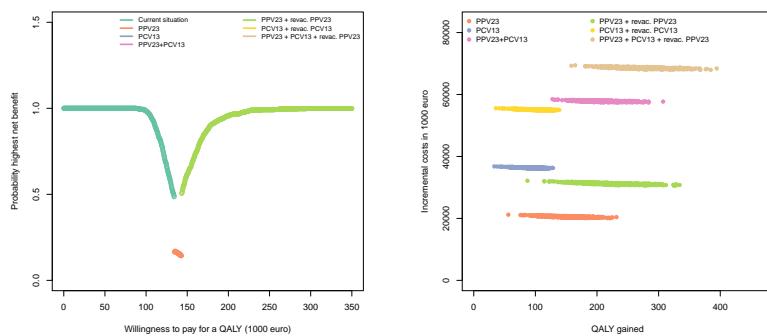


CEAFs: age 75y - 84y      CE plane: age 75y - 84y

## 25% reduction of the baseline PCV13 price, baseline PPV23 price

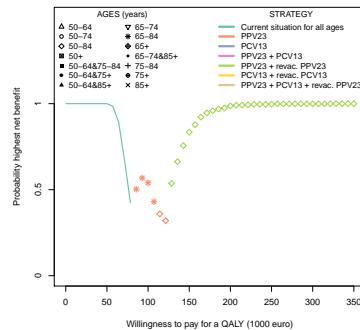


CEAFs: all age groups and strategies

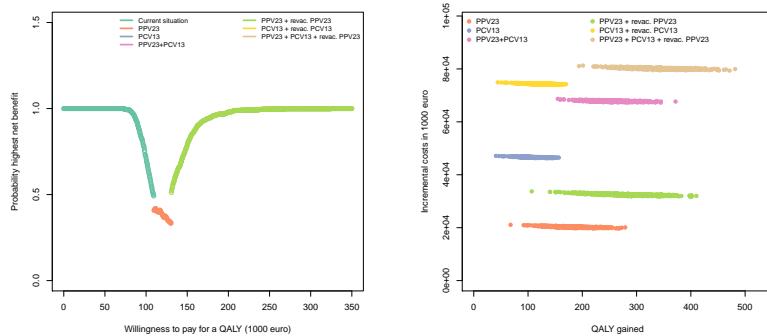


CEAFs: age 75y - 84y      CE plane: age 75y - 84y

## No discounting: discount rate costs and effects: 0%

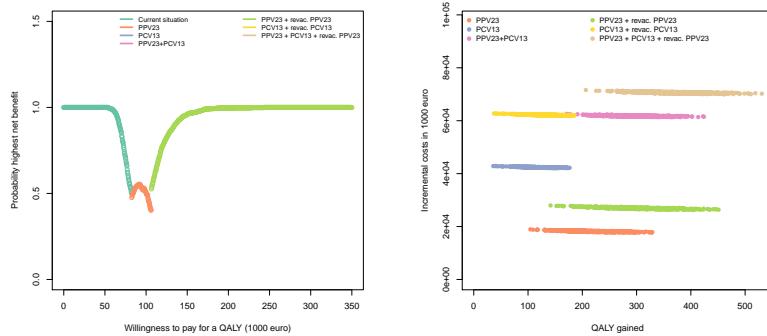


CEAFs: all age groups and strategies



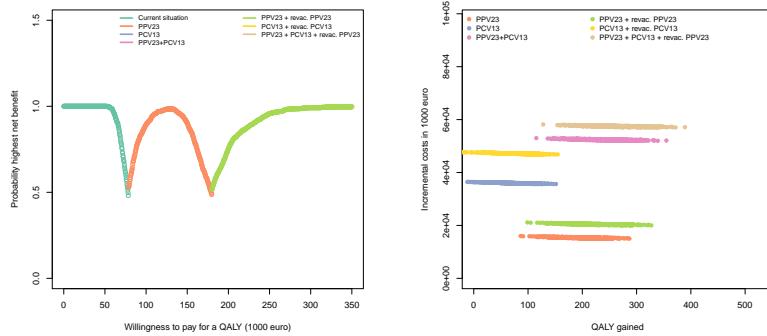
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

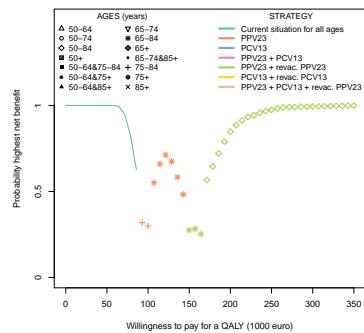
CE plane: age 65y - 74y



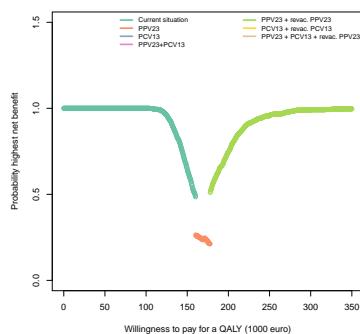
CEAFs: age 75y - 84y

CE plane: age 75y - 84y

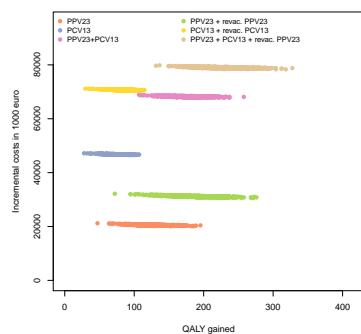
## Discount rate for costs and effects: 3%



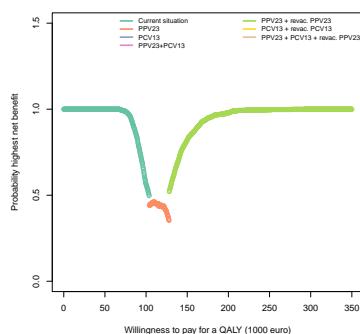
CEAFs: all age groups and strategies



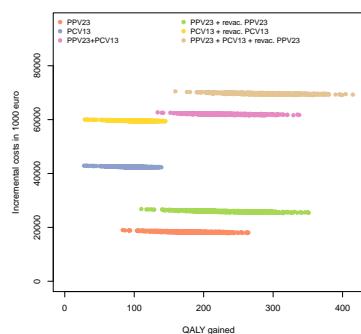
CEAFs: age 50y - 64y



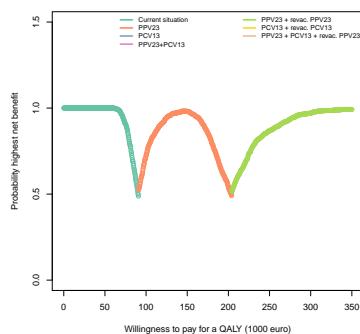
CE plane: age 50y - 64y



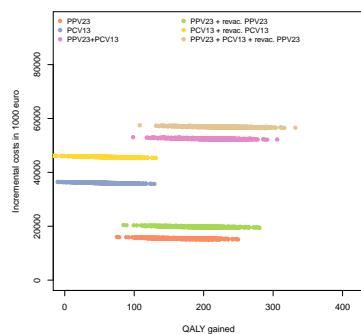
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

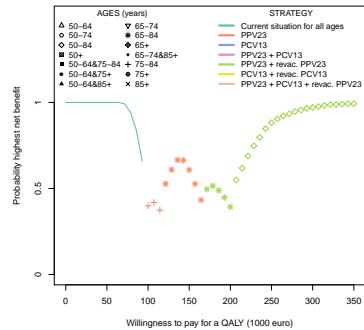


CEAFs: age 75y - 84y

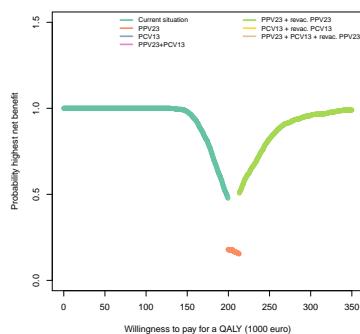


CE plane: age 75y - 84y

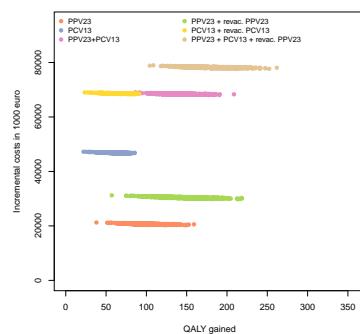
## Discount rate for costs and effects: 5%



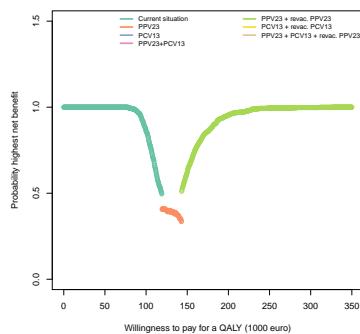
CEAFs: all age groups and strategies



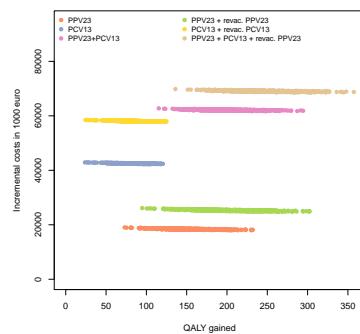
CEAFs: all age groups and strategies



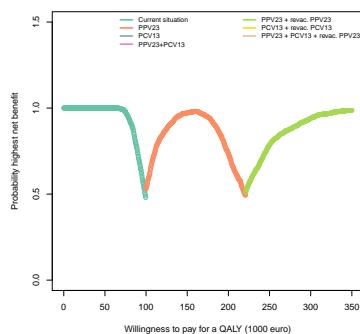
CE plane: all age groups and strategies



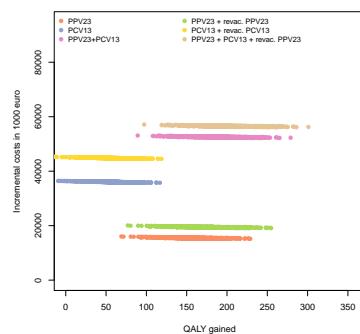
CEAFs: age 50y - 64y



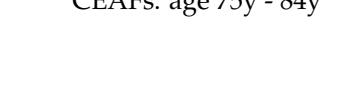
CE plane: age 50y - 64y



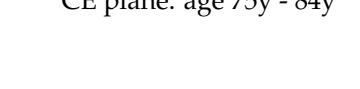
CEAFs: age 65y - 74y



CE plane: age 65y - 74y

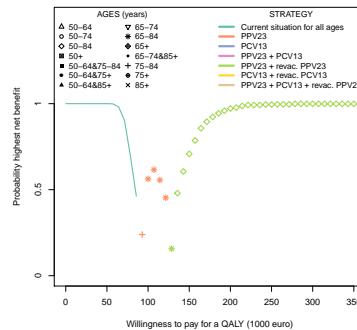


CEAFs: age 75y - 84y

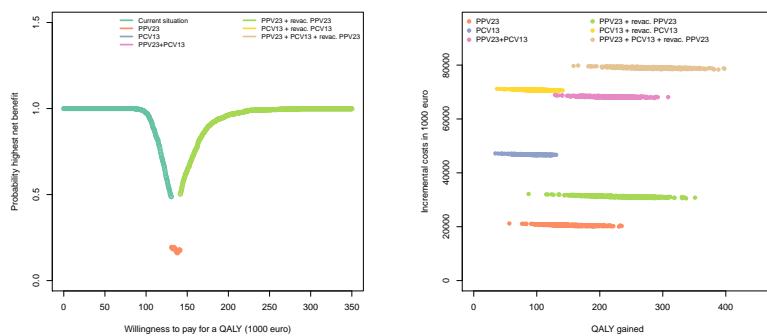


CE plane: age 75y - 84y

## Using QALY loss averaged over all risk groups (baseline: low risk group only)

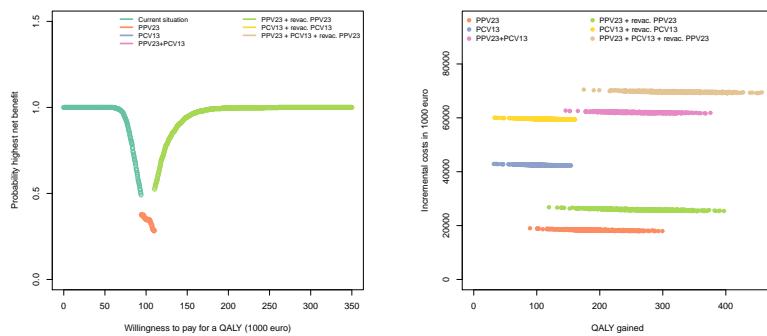


CEAFs: all age groups and strategies

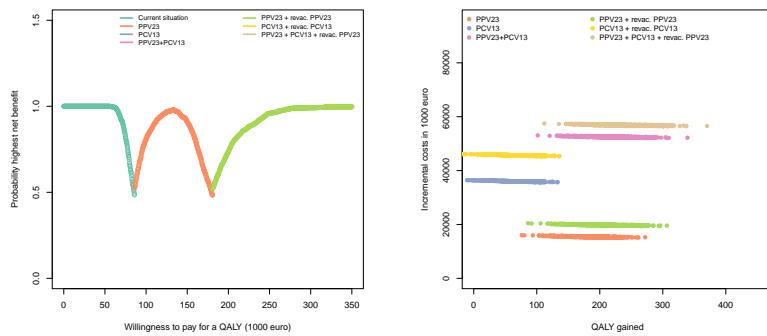


CEAFs: all age groups and strategies

CE plane: all age groups and strategies



CE plane: age 50y - 64y

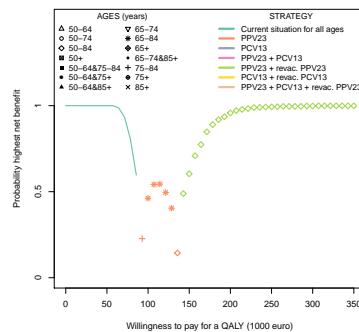


CE plane: age 65y - 74y

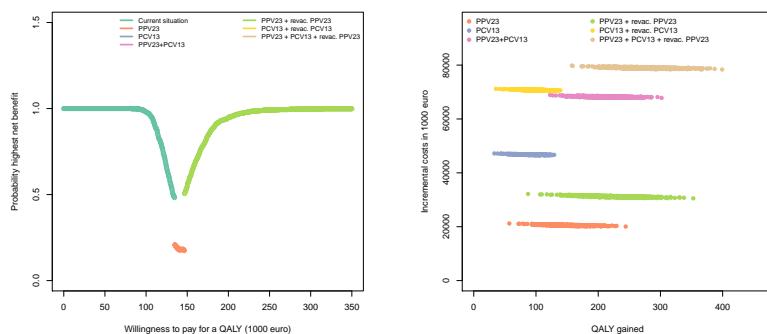
CEAFs: age 65y - 74y

CE plane: age 75y - 84y

## Using QALY loss of the medium risk group only (baseline: low risk group only)

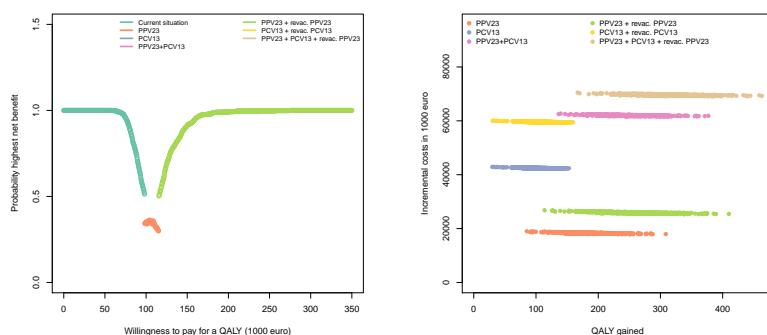


CEAFs: all age groups and strategies



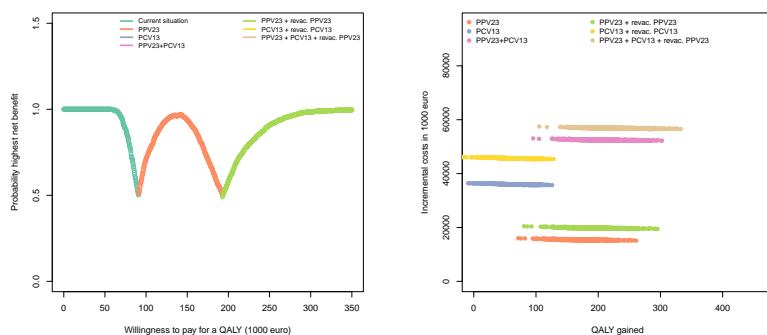
CEAFs: age 50y - 64y

CE plane: age 50y - 64y



CEAFs: age 65y - 74y

CE plane: age 65y - 74y



CEAFs: age 75y - 84y

CE plane: age 75y - 84y