**Supplementary material**

Parameters used in the model are follows:

$a\_{c}$ = observed risk of all-cause pneumonia (ACP) in unvaccinated individuals.

$a\_{v}$ = observed risk of ACP in vaccinated individuals.

$p\_{c}$ = observed risk of pneumococcal pneumonia (PP) in unvaccinated individuals.

$p\_{v}$ = observed risk of PP in vaccinated individuals.

$π\_{c}$ = true risk of PP in unvaccinated individuals.

$π\_{v}$ = true risk of PP in vaccinated individuals.

$Se$ = test sensitivity for diagnosing PP.

$Sp$ = test specificity for diagnosing PP.

Followings are our assumptions:

Assumption 1 (A1): the misclassification in the diagnosis of ACP is non-differential.

Assumption 2 (A2): the pneumococcal vaccine does not change the risk of non-pneumococcal pneumonia.

Assumption 3 (A3): the directions of $ve\_{a}$ and $ve\_{p}$ are identical, and the value of $ve\_{p}$ is equal to or greater than that of $ve\_{a}$ (i.e., $0<ve\_{a}\leq ve\_{p}$ or $ve\_{p} \leq ve\_{a}<0$).

Assumption 4 (A4): the pneumococcal vaccine does not affect $Se$ and $Sp$.

The observed VE against ACP ($ve\_{a})$, observed VE against PP ($ve\_{p}$), and true VE against PP ($ve\_{π})$ are given as follows:

$ve\_{a}=1-\frac{a\_{v}}{a\_{c}}$,

$ve\_{p}=1-\frac{p\_{v}}{p\_{c}}$,

$ve\_{π}=1-\frac{π\_{v}}{π\_{c}}$*.*

According to the assumptions A1 and A2, the risk differences for ACP and true PP are identical [[25](#_ENREF_25)].

$a\_{c}-a\_{v}=π\_{c}-π\_{v}$. (1)

Thus, the true proportion of PP among ACP in unvaccinated individuals is given as:

$\frac{π\_{c}}{a\_{c}}=\frac{π\_{c}\*(a\_{c}-a\_{v})}{a\_{c}\*(π\_{c}-π\_{v})}=\frac{ve\_{a}}{ve\_{π}}$*.* (2)

According to the supplementary table, the proportion of tested positive is:

$p=π\*Se+\left(a-π\right)\*\left(1-Sp\right)$. (3)

Thus,

$Se=\frac{p-(a-π)\*(1-Sp)}{π}$. (4)

By (1), (2), and (3), $ve\_{p}$ is rewritten as follows:

$ve\_{p}=1-\frac{p\_{v}}{p\_{c}}=1-\frac{π\_{v}\*Se+\left(a\_{v}-π\_{v}\right)\*\left(1-Sp\right)}{π\_{c}\*Se+\left(a\_{c}-π\_{c}\right)\*\left(1-Sp\right)}$

$=\frac{π\_{c}\*Se+\left(a\_{c}-π\_{c}\right)\*\left(1-Sp\right)-π\_{v}\*Se-\left(a\_{v}-π\_{v}\right)\*\left(1-Sp\right)}{π\_{c}\*Se+\left(a\_{c}-π\_{c}\right)\*\left(1-Sp\right)}$

$=\frac{(π\_{c}-π\_{v})\*Se+\left(a\_{c}-a\_{v}-π\_{c}+π\_{v}\right)\*\left(1-Sp\right)}{π\_{c}\*Se+\left(a\_{c}-π\_{c}\right)\*\left(1-Sp\right)}$

$=\frac{(π\_{c}-π\_{v})\*Se}{π\_{c}\*Se+\left(a\_{c}-π\_{c}\right)\*\left(1-Sp\right)}$

$=\frac{π\_{c}\*ve\_{π}\*Se}{π\_{c}\*Se+\left(a\_{c}-π\_{c}\right)\*\left(1-Sp\right)}$*.* (5)

Thus,

$\frac{ve\_{p}}{ve\_{π}}=\frac{π\_{c}\*Se}{π\_{c}\*Se+\left(a\_{c}-π\_{c}\right)\*\left(1-Sp\right)}$

Because $a\_{c}\geq π\_{c}$, $\left|ve\_{π}\right|\geq \left|ve\_{p}\right|$.

By (2) and (5), $Se$ is given as follows:

$Se=\frac{p\_{c}\*ve\_{p}}{π\_{c}\*ve\_{π}}=\frac{p\_{c}\*ve\_{p}}{a\_{c}\*ve\_{a}}=\frac{p\_{c}-p\_{v}}{a\_{c}-a\_{v}}$. (6)

By (4),

$\frac{p\_{c}-\left(a\_{c}-π\_{c}\right)\*(1-Sp)}{π\_{c}}=\frac{p\_{v}-\left(a\_{v}-π\_{v}\right)\*(1-Sp)}{π\_{v}}$,

$π\_{v}\*p\_{c}-π\_{v}\*\left(a\_{c}-π\_{c}\right)\*\left(1-Sp\right)=π\_{c}\*p\_{v}-π\_{c}\*\left(a\_{v}-π\_{v}\right)\*(1-Sp)$.

Thus, $Sp$ is given as follows:

$Sp=1-\frac{π\_{v}\*p\_{c}-π\_{c}\*p\_{v}}{π\_{v}\*a\_{c}-π\_{c}\*a\_{v}}$

$=1-\frac{p\_{c}}{a\_{c}}\*\frac{\frac{π\_{v}\*p\_{c}-π\_{c}\*p\_{v}}{π\_{c}\*p\_{c}}}{\frac{π\_{v}\*a\_{c}-π\_{c}\*a\_{v}}{π\_{c}\*a\_{c}}}$

$=1-\frac{p\_{c}}{a\_{c}}\*\frac{\frac{π\_{v}}{π\_{c}}-\frac{p\_{v}}{p\_{c}}}{\frac{π\_{v}}{π\_{c}}-\frac{a\_{v}}{a\_{c}}}$

$=1-\frac{p\_{c}}{a\_{c}}\*\frac{\left(1-\frac{π\_{v}}{π\_{c}}\right)-\left(1-\frac{p\_{v}}{p\_{c}}\right)}{\left(1-\frac{π\_{v}}{π\_{c}}\right)-\left(1-\frac{a\_{v}}{a\_{c}}\right)}$

$=1-\frac{p\_{c}}{a\_{c}}\*\frac{ve\_{π}-ve\_{p}}{ve\_{π}-ve\_{a}}$ (7)

$=1-\frac{p\_{c}}{a\_{c}}\*\frac{(ve\_{π}-ve\_{a})+(ve\_{a}-ve\_{p})}{ve\_{π}-ve\_{a}}$

$=-\frac{p\_{c}}{a\_{c}}\*\frac{ve\_{p}-ve\_{a}}{ve\_{π}-ve\_{a}}+\left(1-\frac{p\_{c}}{a\_{c}}\right)$ (8)

As other values are given as observed values in trials, $Sp$ is a linear rational function of $ve\_{π}$ (see supplementary figure).

If $0<ve\_{a}\leq ve\_{p}\leq ve\_{π}\leq 1$, $Sp$ becomes minimum at $ve\_{π}$=1. By (7),

$Sp\_{min}=1-\frac{p\_{c}\*(1-ve\_{p})}{a\_{c}\*(1-ve\_{a})}=1-\frac{p\_{v}}{a\_{v}}$.

If $ve\_{π}\leq ve\_{p}\leq ve\_{a}<0$, $Sp$ becomes minimum at $ve\_{π}\rightarrow -\infty $. By (8),

$Sp\_{min}=1-\frac{p\_{c}}{a\_{c}}$.

**Supplementary table**

True and observed risks of pneumococcal pneumonia and diagnostic test accuracy.

|  |  |  |  |
| --- | --- | --- | --- |
|  | True pneumococcal pneumonia | True non-pneumococcal pneumonia | Total |
| Tested positive | $$π\*Se$$ | $$\left(a-π\right)\*(1-Sp)$$ | $$p$$ |
| Tested negative | $$π\*(1-Se)$$ | $$\left(a-π\right)\*Sp$$ | $$a-p$$ |
| Total | $$π$$ | $$a-π$$ | $$a$$ |

$π$, true risk of pneumococcal pneumonia (PP) in total individuals; $p$, observed risk of PP in total individuals; $a$, observed risk of all-cause pneumonia in total individuals; $Se$, test sensitivity for diagnosing PP; $Sp$, test specificity for diagnosing PP.

**Supplementary figure**

Association between specificity and true vaccine efficacy for pneumococcal pneumonia.

$ve\_{a}$, observed vaccine efficacy (VE) against all-cause pneumonia (ACP); $ve\_{p}$, observed VE against pneumococcal pneumonia (PP); $ve\_{π}$, true VE against PP;$ Se$, sensitivity; $Sp$, specificity;$ a\_{c}$, observed risk of ACP in unvaccinated individuals; $a\_{v}$, observed risk of ACP in vaccinated individuals; $p\_{c}$, observed risk of PP in unvaccinated individuals; $p\_{v}$, observed risk of PP in vaccinated individuals.

The x-axis shows $ve\_{π}$, and the y-axis shows $Sp$. $Sp$ is given as a linear rational function of $ve\_{π}$ (solid line). A. When $0<ve\_{a}\leq ve\_{p}\leq ve\_{π}<1$, the function has branches in the upper right and lower left. Because $ve\_{π}$ can take values between $ve\_{a}$ and 1 (unshaded area), $Sp$ becomes minimum at $ve\_{π}$=1. B. When $ve\_{π}\leq ve\_{p}\leq ve\_{a}<0$, the function has branches in the upper left and lower right. Because $ve\_{π}$ can take values between $-\infty $ and $ve\_{a}$ (unshaded area), $Sp$ becomes minimum at $ve\_{π}\rightarrow -\infty $.

