SUPPLEMENTARY MATERIALS

To accompany the article in BMC Infectious Diseases:

Title: An evidence synthesis approach to estimating the incidence of symptomatic pertussis infection in the Netherlands, 2005–2011
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In this supplementary materials document, OpenBUGS code for the model is provided, further information is supplied regarding the Markov model developed to adjust seroconversion probabilities for the 1-4 years and 5-9 years age-groups for vaccination-related high Ptx-IgG titres, and a graphical comparison of the prior and posterior distributions for the probability of being symptomatic given infection is made.
model {

  ## Vague Beta prior on d_SI and random-walk prior on c_S|Pop
  ## NG is number of age-groups; NY is number of years
  for (a in 1:NG) {
    d.SI[a] ~ dbeta(1,1)       # Detection probability
  }
  for (y in 1:NY) {
    logit(c.SgivenPop[a, y]) <- logit(c.SgivenPop[a, y])
  }
  logit(c.SgivenPop[a, 1]) ~ dnorm(0,0.0001)
  tau[a] ~ dgamma(0.001,0.001)
  for (y in 2:NY) {
    logit(c.SgivenPop[a, y]) ~ dnorm(logit(c.SgivenPop[a, y-1]),tau[a])
  }

  ## Beta priors on c_SI|I: PIENTER-2 (ages 10-60+) and expert opinion(<1 yr)
  ## Parameters of beta prior (a and b) supplied as Prop.Sympt.a and Prop.Sympt.b
  c.SIgivenI[1] ~ dbeta(Prop.Sympt.a[1],Prop.Sympt.b[1])

  ## Vague Beta priors on c_SI|I for 1-4 and 5-9 yrs
  for (a in 2:3) {
    c.SIgivenI[a] ~ dbeta(1,1)
  }

  ## Update c_SI|I with data: BINKI (age-groups 1-4 through 20-59 yrs only)
  ## Data supplied as positives (y.Obs.Prop.Sympt) and total (n.Obs.Prop.Sympt)
  for (a in 2:5) {
    y.Obs.Prop.Sympt[a] ~ dbin(c.SIgivenI[a],n.Obs.Prop.Sympt[a])
  }

  ## Loop for likelihood and functional expressions
  ## Seroconversion data inform c_S|Pop for year=3 (2007) only:
  for (a in 1:NG) {
    y.Obs.Prop.Pienter2[a, 3] ~ dbin(c.SIgivenPop[a, 3],n.Obs.Prop.Pienter2[a, 3])
  }

  MF[a] <- (1/d.SI[a])              # Define multiplication factor

  for (y in 1:NY) {
    y.Obs.Num.Notif[a, y] ~ dbin(d.SI[a],n.SI[a, y])
    SIAR[a, y] <- (c.SIgivenI[a]*c.IgivenPop[a, y]) # Define SI attack rate

    # Adjust c_I|Pop for vaccination-related seroconversions
    c.IgivenPop[a, y] <- (c.SIgivenPop[a, y] * (1 - adjVacc[a]))
  }

  # Numbers in S, I and SI subpopulations
  n.S[a, y] <- (c.SIgivenPop[a, y] * n.Pop[a, y])
  n.I[a, y] <- (c.IgivenPop[a, y] * n.Pop[a, y])
  n.SI[a, y] <- (c.SIgivenI[a] * n.I[a, y])
}

## Aggregated-over-age values in index (NG+1)
for (y in 1:NY) {
  n.I[(NG+1), y] <- sum(n.I[1:NG, y])
  n.SI[(NG+1), y] <- sum(n.SI[1:NG, y])
  SIAR[(NG+1), y] <- n.SI[(NG+1), y]/sum(n.Pop[1:NG, y])
}
Adjustment for vaccination-related high Ptx-IgG titres

In the following, we describe how the seroconversion probabilities for the age-groups 1-4 and 5-9 years were adjusted, to account for the proportion of each age-group with a high Ptx-IgG titre attributable to previous vaccination. We constructed a simple Markov model of the waning titre expected using the recommended immunization schedule: a series of four infant vaccinations is administered at 2, 3, 4, and 11 months of age, with a booster vaccination given at four years of age [1, 2].

Fig. S1 shows the multi-state Markov model. The flow of children aged one through nine years, over the period 1995 through 2011, was modelled. One-year olds enter one of two compartments: Vaccinated (Infant), with probability \( \beta \); or Unvaccinated with probability \((1 - \beta)\). \( \beta \) is the vaccination coverage (i.e., percentage with base immunity) for the relevant simulation year. For convenience, immune response to the vaccine is assumed to result in an Ptx-IgG titre of ≥125 EU/ml. Titres are then assumed to wane with an annual probability of 69%. This annual transition probability, \( P_\gamma \), was derived from predictions of a statistical model fitted to longitudinal data on natural pertussis infection [3]. Specifically, the transition probability \( P_\gamma \) approximates the rate by which the fraction of infected persons with titre ≥125 declines as a function of time since infection. When children turn four years of age, they receive a booster vaccination; thus children of this age only who are in the Vaccinated (Infant) and Titre < 125 EU/ml compartments can move to the Vaccinated (Booster) compartment with probability \( P_\psi \), where is \( P_\psi \) represents the booster vaccination coverage for the relevant year.

The simulation provided estimates of the proportion of children aged one through nine years with a vaccination-related Ptx-IgG titre ≥125 EU/ml, for the years 2005 through 2011 (Table S1). There was little variation across time, except for the oldest ages in 2005 and 2006, which is due to the four-year booster being introduced in 2002 (e.g., children who were eight or nine years old in 2005 would have been too old to receive the booster in 2002). For use in the evidence synthesis model, we estimated separate proportions with Ptx-IgG titre ≥125 due to vaccination for the 1-4 years and 5-9 years age-groups, by averaging together the values for the individual ages in each age-group for the simulation, and then averaging over years. The
resulting estimated proportions of vaccination-related high titres are 0.687 and 0.185 for age-groups 1-4 and 5-9 years, respectively.

To establish the extent to which the model-estimated proportions of vaccination-related high titres are sensitive to the value used for the annual transition probability \( P_\gamma \) we re-ran the Markov model using 10% higher and 10% lower values of \( P_\gamma \), and derived the estimated proportions of vaccination-related high titres for the age-groups 1-4 and 5-9 years, as before (see Table S2). Then, we repeated the evidence synthesis using these modified values of \( \text{propVaccRel} \), and report the posterior median symptomatic infection (SI) incidence rates (per 10,000) for these two age groups, comparing with the posterior median SI incidence rates obtained using the baseline value for \( P_\gamma \) (Table S2). There were only small differences apparent; depending on year, there was a maximum 3% increase in estimated SI incidence rate if the higher value for \( P_\gamma \) was adopted, and up to a 6% decrease if the lower value was used.

**Table S1.** Modelled percentage of children with Ptx-IgG titre ≥125 EU/ml due to vaccination, 2005-2011, as estimated using vaccination uptake data and model-derived waning antibody rates.

<table>
<thead>
<tr>
<th>Calendar year</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>94.0</td>
<td>94.5</td>
<td>95.2</td>
<td>95.0</td>
<td>95.4</td>
<td>95.4</td>
<td>95.5</td>
</tr>
<tr>
<td>2</td>
<td>57.1</td>
<td>57.0</td>
<td>57.2</td>
<td>57.5</td>
<td>57.4</td>
<td>57.5</td>
<td>57.5</td>
</tr>
<tr>
<td>3</td>
<td>41.3</td>
<td>41.0</td>
<td>40.9</td>
<td>41.0</td>
<td>41.1</td>
<td>41.1</td>
<td>41.2</td>
</tr>
<tr>
<td>4</td>
<td>82.6</td>
<td>83.2</td>
<td>82.9</td>
<td>82.7</td>
<td>83.0</td>
<td>83.4</td>
<td>83.4</td>
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<tr>
<td>5</td>
<td>33.6</td>
<td>33.7</td>
<td>33.8</td>
<td>33.6</td>
<td>33.6</td>
<td>33.7</td>
<td>33.8</td>
</tr>
<tr>
<td>6</td>
<td>19.0</td>
<td>19.4</td>
<td>19.3</td>
<td>19.2</td>
<td>19.1</td>
<td>19.1</td>
<td>19.1</td>
</tr>
<tr>
<td>7</td>
<td>14.2</td>
<td>14.1</td>
<td>14.6</td>
<td>14.4</td>
<td>14.3</td>
<td>14.2</td>
<td>14.2</td>
</tr>
<tr>
<td>8</td>
<td>17.0</td>
<td>12.2</td>
<td>12.0</td>
<td>12.5</td>
<td>12.3</td>
<td>12.2</td>
<td>12.1</td>
</tr>
<tr>
<td>9</td>
<td>15.2</td>
<td>15.2</td>
<td>11.0</td>
<td>10.9</td>
<td>11.3</td>
<td>11.1</td>
<td>11.1</td>
</tr>
</tbody>
</table>
**Table S2.** Results of sensitivity analysis to baseline and 10% lower and 10% higher values assumed for the annual transition probability of waning high Ptx-IgG titre ($P_\gamma$). $propVaccRel$ refers to the model-derived proportion of vaccination-related high titres.

<table>
<thead>
<tr>
<th>$P_\gamma$</th>
<th>$propVaccRel$</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age-group 1-4 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>69.0%</td>
<td>0.687</td>
<td>257</td>
<td>149</td>
<td>147</td>
<td>121</td>
<td>79</td>
<td>57</td>
<td>70</td>
</tr>
<tr>
<td>62.7%</td>
<td>0.704</td>
<td>243</td>
<td>141</td>
<td>138</td>
<td>114</td>
<td>74</td>
<td>54</td>
<td>66</td>
</tr>
<tr>
<td>75.9%</td>
<td>0.678</td>
<td>264</td>
<td>153</td>
<td>151</td>
<td>124</td>
<td>81</td>
<td>58</td>
<td>72</td>
</tr>
<tr>
<td>Age-group 5-9 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>69.0%</td>
<td>0.185</td>
<td>386</td>
<td>196</td>
<td>193</td>
<td>197</td>
<td>160</td>
<td>82</td>
<td>182</td>
</tr>
<tr>
<td>62.7%</td>
<td>0.206</td>
<td>377</td>
<td>191</td>
<td>188</td>
<td>192</td>
<td>156</td>
<td>81</td>
<td>178</td>
</tr>
<tr>
<td>75.9%</td>
<td>0.164</td>
<td>395</td>
<td>201</td>
<td>197</td>
<td>202</td>
<td>164</td>
<td>84</td>
<td>187</td>
</tr>
</tbody>
</table>

**Fig. S1.** Multi-state Markov model for pertussis vaccination and waning anti-Ptx-IgG titre.
Fig. S2. Prior (i.e., reflecting both PIENTER-2 and BINKI data) and posterior distributions for the parameter $c_{a,SII}$. 
References

