Trials included in the review


Multicentre Aneurysm Screening study group. Multicentre aneurysm screening study (MASS): cost effectiveness analysis of screening for abdominal aortic aneurysms based on four year results from randomised controlled trial. *BMJ* 2002;325:1135.


Williams C, Northstone K, Harrad RA, Sparrow JM, Harvey I. Amblyopia treatment outcomes after screening before or at age 3 years: follow up from randomised trial. *BMJ* 2002;324:1549.


**Models of clustering and their implementation**

(a) The independence model

\[ y_i \sim \text{Binomial}(1, \pi_i) \]

\[ \logit(\pi_i) = \alpha + \beta t_i \]  \hspace{1cm} (1)

where \( y_i \) = the outcome for the \( i \)th patient

\( \pi_i \) = probability of being offered a follow-up appointment

\( t_i \) = indicator for intervention (1= teleconsultation, 0=control)

\( \alpha \) = mean outcome (log odds of a follow-up appointment) in the control group

\( \beta \) = intervention effect (log odds ratio of a follow-up appointment in the teleconsultation group compared to the control).
The model assumes that all observations are independent.

(b) Clustering of the outcomes

\[ y_{ij} \sim \text{Binomial}(1, \pi_{ij}) \]

\[ \logit(\pi_{ij}) = \alpha + \beta_{ij} + u_j \quad (2) \]

\[ u_j \sim \text{Normal}(0, \sigma_u^2) \]

where \( y_{ij} \) = response of the \( i \)th patient in the \( j \)th cluster

\( u_j \) = random effect of the \( j \)th cluster

\( \sigma_u^2 \) = between cluster variance
This model adjusts for clustering by the inclusion of a random effect. It allows responses to vary by cluster but assumes that the variability in the cluster effects is the same in both treatment groups, hence giving a pooled estimate of the between cluster variance. It also assumes that the intervention effect is the same across all clusters.

(c) Clustering of the intervention effects

\[ y_{ij} \sim \text{Binomial}(1, \pi_{ij}) \]

\[ \logit(\pi_{ij}) = \alpha + \beta t_{ij} + u_{aj} + u_{bj} t_{ij} \]

\[ \begin{pmatrix} u_{aj} \\ u_{bj} \end{pmatrix} \sim \text{Bivariate Normal} \left( \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_{a}^2 & \sigma_{ab} \\ \sigma_{ab} & \sigma_{b}^2 \end{pmatrix} \right) \]  

where  

- \( u_{aj} \) = random effect in the \( j \)th cluster across all patients  
- \( u_{bj} \) = treatment-by-cluster interaction for the \( j \)th cluster  
- \( \sigma_{a}^2 \) = between cluster variance in the outcomes  
- \( \sigma_{b}^2 \) = between cluster variance in the intervention effect  
- \( \sigma_{ab} \) = correlation between the two

This is an extension to the model in equation (2) that fits two random effects, one across all patients, and a second in the teleconsultation group only representing the treatment-by-cluster interaction. This model allows the intervention effect, as well as the outcomes, to vary over clusters. It can also be thought of as allowing the variability between clusters to be different in the two intervention arms.

A similar model can be used where the clustering is imposed and each cluster is only in one intervention group, hence nested within treatment groups. In this case there is no correlation between the two random effects. Equivalently the random effects can be modelled by two independent normal distributions.

(d) Model fitting

The models were fitted using a classical approach in MLwiN and a Bayesian approach in WinBUGS. These gave similar results, and only the Bayesian results have been reported here. Vague priors were chosen for all parameters so that they had little influence on the results obtained: Normal(0,1000) priors for regression parameters, Uniform(0,10) priors for standard deviations (square root of variance terms) and Uniform(-1, 1) for the correlation between the random effects, as suggested by Turner, et al.
Full results from the fitted models

Table A1 gives the estimates of the between cluster variances (BCV) for the models discussed which allow for the heterogeneity in the outcome and the intervention effect between clusters. It also includes the deviance information criteria (DIC), which is a Bayesian measure used for model selection that trades-off model complexity and fit.\textsuperscript{4}

The BCV of 0.23 for the clustering of the outcomes model represents a standard deviation of 0.48. So the 95% range of the intercept term (log odds) across consultants is –0.34 $\pm$ 0.48 = −1.30 to 0.62; this corresponds to a wide range of probabilities from 0.21 to 0.65, compatible with Figure 3a. More importantly, the BCV of 0.71 for the clustering of the intervention effects represents a standard deviation of 0.84. So the 95% range of intervention effects (log odds ratios) across consultants is 0.31 $\pm$ 0.84; this corresponds to a wide range of odds ratios from 0.25 to 7.3, as seen in Figure 3b. This variation between the clusters explains the difference in the estimate of the overall odds ratio and, in particular, the inflated width of the confidence interval when the clustering is taken into account.

The heterogeneity in the outcomes and the intervention effects can also be seen in the DIC, which is substantially reduced when clustering is taken into account; the models allowing for clustering are therefore more appropriate for the data.

\textit{Table A1 Between cluster variances (BCV), their standard errors, and the deviance information criteria (DIC), from the models fitted to the telemedicine trial data}

<table>
<thead>
<tr>
<th></th>
<th>Assuming independence</th>
<th>Clustering of the outcomes</th>
<th>Clustering of the intervention effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCV for the outcomes</td>
<td>NA</td>
<td>0.23 (0.14)</td>
<td>0.39 (0.24)</td>
</tr>
<tr>
<td>BCV for the intervention effect</td>
<td>NA</td>
<td>NA</td>
<td>0.71 (0.40)</td>
</tr>
<tr>
<td>Correlation</td>
<td>NA</td>
<td>NA</td>
<td>-0.25 (0.24)</td>
</tr>
<tr>
<td>DIC</td>
<td>2661.5</td>
<td>2614.6</td>
<td>2556.0</td>
</tr>
</tbody>
</table>

NA = not applicable

References

