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Models of clustering and their implementation

(a) The independence model

$$y_i \sim Binomial(1, \pi_i)$$

$$\text{logit}(\pi_i) = \alpha + \beta t_i \qquad (1)$$

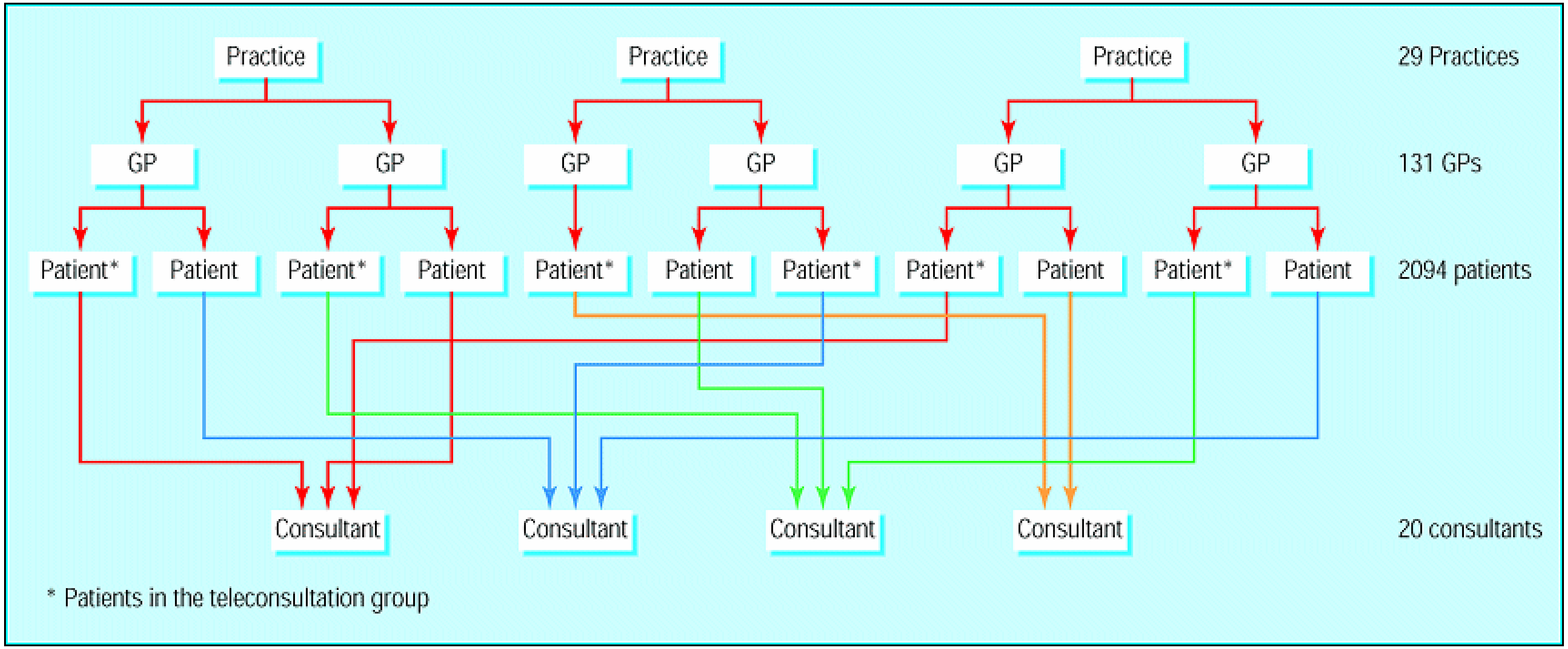
where y_i = the outcome for the *i*th patient

π_i = probability of being offered a follow-up appointment

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

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

β = 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

$$y_{ij} \sim Binomial(1, \pi_{ij})$$

$$\text{logit}(\pi_{ij}) = \alpha + \beta t_{ij} + u_j \qquad (2)$$

$$u_j \sim Normal(0, \sigma_u^2)$$

where y_{ij} = response of the *i*th patient in the *j*th cluster

u_j = random effect of the *j*th cluster

σ_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

$$y_{ij} \sim Binomial(1, \pi_{ij})$$

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

$$\begin{pmatrix} u_{aj} \\ u_{bj} \end{pmatrix} \sim Bivariate\ Normal\left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_a^2 & \sigma_{ab} \\ \sigma_{ab} & \sigma_b^2 \end{pmatrix}\right) \qquad (3)$$

where u_{aj} = random effect in the *j*th cluster across all patients

u_{bj} = treatment-by-cluster interaction for the *j*th cluster

σ_a^2 = between cluster variance in the outcomes

σ_b^2 = between cluster variance in the intervention effect

σ_{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[w1] and a Bayesian approach in WinBUGS.[w2] 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.[w3]

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.[w4]

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±2×0.48 = –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±2×0.84; 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.

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

	Assuming independence	**Clustering of the outcomes**	**Clustering of the intervention effect**
BCV for the outcomes	NA	0.23 (0.14)	0.39 (0.24)
BCV for the intervention effect	NA	NA	0.71 (0.40)
Correlation	NA	NA	-0.25 (0.24)
DIC	2661.5	2614.6	2556.0

NA = not applicable

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