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Limits of Agreement

1 Statement of the LME model

Further to a paper published by Laird and Ware in 1982, a linear mixed effects model is a linear model that combined fixed and random effect terms formulated as follows;

$$Y_i = X_i\beta + Z_ib_i + \epsilon_i$$

- Y_i is the $n \times 1$ response vector
- X_i is the $n \times p$ Model matrix for fixed effects
- β is the $p \times 1$ vector of fixed effects coefficients
- Z_i is the $n \times q$ Model matrix for random effects
- b_i is the $q \times 1$ vector of random effects coefficients, sometimes denoted as u_i
- ϵ is the $n \times 1$ vector of observation errors

pkcng generalize this approach to account for situations where the distributions are not identical, which is commonly the case. The TDI is not consistent and may not preserve its asymptotic nominal level, and that the coverage probability approach of lin2002 is overly conservative for moderate sample sizes. This methodology proposed by pkcng is a regression based approach that models the mean and the variance of differences as functions of observed values of the average of the paired measurements.

Maximum likelihood estimation is used to estimate the parameters. The REML estimation is not considered since it does not lead to a joint distribution of the estimates of fixed effects and random effects parameters, upon which the assessment of agreement is based.

2 Random Effects and MCS

The methodology comprises two calculations. The second calculation is for the standard deviation of means. Before the modified Bland and Altman method can be applied for repeated measurement data, a check of the assumption that the variance of the repeated measurements for each subject by each method is independent of the mean of the repeated measures. This can be done by plotting the within-subject standard deviation against the mean of each subject by each method. Mean Square deviation measures the total deviation of a

2.1 Random coefficient growth curve model

(Chincilli 1996) Random coefficient growth curve model, a special type of mixed model have been proposed a single measure of agreement for repeated measurements.

$$\mathbf{d} = \mathbf{X}\mathbf{b} + \mathbf{Z}\mathbf{u} + \mathbf{e} \quad (1)$$

The distributional assumptions also require \mathbf{d} to \mathbf{N}

3 Other Approaches

3.1 Random coefficient growth curve model

(Chincilli 1996) Random coefficient growth curve model, a special type of mixed model have been proposed a single measure of agreement for repeated measurements.

3.2 Marginal Modelling

(Diggle 2002) proposes the use of marginal models as an alternative to mixed models. Marginal models are appropriate when inferences about the mean response are of specific interest.

4 KP

Most residual covariance structures are design for one within-subject factor. However two or more may be present. For such cases, an appropriate approach would be the residual covariance structure using Kronecker product of the underlying within-subject factor specific covariances structure.

5 LME

Consistent with the conventions of mixed models, pkc formulates the measurement y_{ij} from method i on individual j as follows;

$$y_{ij} = P_{ij}\theta + W_{ij}v_i + X_{ij}b_j + Z_{ij}u_j + \epsilon_{ij}, (j = 1, 2, i = 1, 2, \dots, n) \quad (2)$$

The design matrix P_{ij} , with its associated column vector θ , specifies the fixed effects common to both methods. The fixed effect specific to the j th method is articulated by the design matrix W_{ij} and its column vector v_i . The random effects common to both methods is specified in the design matrix X_{ij} , with vector b_j whereas the random effects specific to the i th subject by the j th method is expressed by Z_{ij} , and vector u_j . Noticeably this notation is not consistent with that described previously. The design matrices are specified so as to include a fixed intercept for each method, and a random intercept for each individual. Additional assumptions must also be specified;

$$v_{ij} \sim N(0, \Sigma), \quad (3)$$

These vectors are assumed to be independent for different i s, and are also mutually independent. All Covariance matrices are positive definite. In the above model effects can be classed as those common to both methods, and those that vary with method. When considering differences, the effects common to both effectively cancel each other out. The differences of each pair of measurements can be specified as following;

$$d_{ij} = X_{ij}b_j + Z_{ij}u_j + \epsilon_{ij}, (j = 1, 2, i = 1, 2, \dots, n) \quad (4)$$

This formulation has separate distributional assumption from the model stated previously.

This agreement covariate x is the key step in how this methodology assesses agreement.