RT-MAE 2001-02

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by

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Classificação AMS: 62F05, 62J05.
(AMS Classification)

- Janeiro de 2001 -

Null Intercept Measurement Error Regression Models

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SUMMARY. We consider measurement error regression models with null intercepts for the analysis of pretest/posttest repeated measurements data. The within sample units correlation structure is induced by a mixed model adopted for the observed values of the true covariate. We indicate how the maximum likelihood estimators of the regression parameters may be calculated and derive their asymptotic distribution. The proposed procedures are numerically illustrated with data previously analyzed in the literature via classical regression techniques.

KEY WORDS: Maximum likelihood; pretest/posttest data; random effects.

1 Introduction

In a recent paper, Singer and Andrade (1997) proposed regression models to analyse data from a pretest/posttest study designed to compare two types of toothbrushes with respect to the efficacy in removing dental plaque. In that study, a dental plaque index was obtained on each of 26 (14 female and 12 male) preschoolers, before and after toothbrushing, with a regular and an experimental (hugger) toothbrush. No intercepts were included in the proposed models since null pretest dental plaque indices imply null expected posttest values. The models also allowed for correlated within individual measurements (bringing into perspective the fact that the same subjects were evaluated under two different experimental conditions) as well as for nonlinear relationships between the posttest dental plaque index (taken as the random response variable) and the pretest dental plaque index (considered as a fixed explanatory variable).

Since the amount of dental plaque is evaluated imprecisely and given the similar nature of the pretest and the posttest variables, measurement error models constitute an interesting alternative to analyse the data. We attack the problem under such a perspective, recognizing that at this stage, the proposed models do not encompass the same flexibility as the ones discussed in Singer and Andrade (1997).

A simple linear regression model with measurement errors typically considered in the literature is defined by the equations

$$Y_i = \alpha + \beta x_i + e_i, \tag{1}$$

$$X_i = x_i + u_i, \tag{2}$$

where Y_i and X_i, $i = 1, \ldots, n$ respectively denote the observed values of the response and explanatory variables, α represents the (unknown) intercept, β stands for the (unknown) slope and

$$\begin{pmatrix} e_i \\ u_i \\ x_i \end{pmatrix} \sim N_3 \left[\begin{pmatrix} 0 \\ 0 \\ \mu_x \end{pmatrix}, \begin{pmatrix} \sigma_e^2 & 0 & 0 \\ 0 & \sigma_u^2 & 0 \\ 0 & 0 & \sigma_x^2 \end{pmatrix} \right], \tag{3}$$

are independently distributed, $i = 1, \ldots, n$. It is well known that such a model is not identifiable and to bypass this inconvenience, we must make an extra assumption about the parameters (Kendall and Stuart, 1973). Among the available alternatives, we identify i) σ_e^2 or (and) σ_u^2 known, ii) $\lambda = \sigma_e^2/\sigma_u^2$ known, iii) $k_x = \sigma_x^2/(\sigma_x^2 + \sigma_u^2)$ known or iv) α known. We are particularly interested in situations for which iv) holds and without loss of generality, we take $\alpha = 0$.

Under the model specified by (1), (2) and (3) and taking $\alpha = 0$, the method of moments estimators of $\beta, \mu_x, \sigma_x^2, \sigma_u^2$, λ and σ_e^2 are respectively

$$\begin{aligned} \hat{\beta} &= \frac{\overline{Y}}{\overline{X}}, \ \hat{\mu}_x = \overline{X}, \ \hat{\sigma}_x^2 = \frac{\overline{X}S_{XY}}{\overline{Y}}, \ \hat{\sigma}_u^2 = \frac{\overline{Y}S_{XX} - \overline{X}S_{XY}}{\overline{Y}} \\ \hat{\lambda} &= \frac{\overline{Y}}{\overline{X}}\left(\frac{\overline{X}S_{YY} - \overline{Y}S_{XY}}{\overline{Y}S_{XX} - \overline{X}S_{XY}}\right), \ \hat{\sigma}_e^2 = \frac{\overline{X}S_{YY} - \overline{Y}S_{XY}}{\overline{X}} \end{aligned} \tag{4}$$

where $\overline{Y} = \sum_{i=1}^n Y_i/n$, $S_{XY} = \sum_{i=1}^n (Y_i - \overline{Y})X_i/n$, and similarly for the other sample moments. Chan and Mak (1979) show that $\hat{\theta} = (\hat{\beta}, \hat{\mu_x}, \hat{\sigma}_x^2, \hat{\sigma}_u^2, \hat{\sigma}_e^2)'$ are maximum likelihood estimators (MLE) of the corresponding parameters provided that the variance estimators are nonnegative and present the associated asymptotic covariance matrix. Patefield (1985) also considers the case where both α and λ are known and shows that in such a case, no analytic expressions are available for the MLE of the model parameters. The underlying probability model here is a four-dimensional curved normal distribution as discussed in Lindsey (1996).

Motivated by the example discussed above, we first extend the null intercept version of (1) – (2) to

$$Y_{ij} = \beta_i x_{ij} + e_{ij}, \tag{5}$$

$$X_{ij} = x_{ij} + u_{ij}, \tag{6}$$

where

$$\begin{pmatrix} e_{ij} \\ u_{ij} \\ x_{ij} \end{pmatrix} \sim N_3 \left[\begin{pmatrix} 0 \\ 0 \\ \mu_{xi} \end{pmatrix}, \begin{pmatrix} \sigma_{ei}^2 & 0 & 0 \\ 0 & \sigma_{ui}^2 & 0 \\ 0 & 0 & \sigma_{xi}^2 \end{pmatrix} \right] \tag{7}$$

are independently distributed, $i = 1, 2$, $j = 1, \ldots, n$. Again, referring to the example described above, Y_{ij} (X_{ij}) denotes the dental plaque index observed on the j-th individual after (before) toothbrushing with the conventional ($i = 1$) or the experimental ($i = 2$) toothbrush. Taking into account that no sex effects were detected by Singer and Andrade (1997), we disconsidered that factor here to simplify notation. The main objectives of the analysis are to estimate β_i, $i = 1, 2$ and to test the hypothesis $\beta_1 = \beta_2$. Maximum likelihood estimators of $\beta_i, \mu_{xi}, \sigma_{xi}^2, \sigma_{ui}^2, \sigma_{ei}^2$, or λ_i $(= \sigma_{ei}^2/\sigma_{ui}^2)$, $i = 1, 2$ are as given in (4) with the obvious extra index (i) to accommodate the stratified design structure.

A simpler and more realistic model may be obtained by assuming that only the slopes β_i and the ratios of the error variances, λ_i, vary between the strata, i.e., replacing (7) with

$$\begin{pmatrix} e_{ij} \\ u_{ij} \\ x_{ij} \end{pmatrix} \sim N_3 \left[\begin{pmatrix} 0 \\ 0 \\ \mu_{x} \end{pmatrix}, \begin{pmatrix} \sigma_{ei}^2 & 0 & 0 \\ 0 & \sigma_{u}^2 & 0 \\ 0 & 0 & \sigma_{x}^2 \end{pmatrix} \right] \tag{8}$$

$i = 1, 2$. $j = 1, \ldots, n$. Here, however. the task of finding the MLEs of the parameters is more complicated. since no analytical expressions are available and iterative procedures are required.

Now. still motivated by the dental plaque example. given that each individual is evaluated with both toothbrushes, it seems necessary to consider models that incorporate a possible within subjects correlation structure. In this direction. extending the model specified by (5). (6) and (8), we assume that the true values of the explanatory variables are related through the random effects model

$$x_{ij} = \mu_x + a_j \tag{9}$$

with a_j denoting independent random variables such that $a_j \sim N(0, \sigma_x^2)$, $i = 1, 2$, $j = 1, \ldots, n$ and are independent of u_{ij}. This implies that

$$\rho_{12} = \mathrm{corr}(X_{1j}, X_{2j}) = \frac{\sigma_x^2}{\sigma_x^2 + \sigma_u^2}, \tag{10}$$

$j = 1, \ldots, n$. Under this framework, the distribution of the true value of the pre-treatment plaque index depends exclusively on the individuals. A more general model may include an additional random term which allows the true value of the explanatory variable to depend on the type of toothbrush as well, i.e.,

$$x_{ij} = \mu_x + a_j + \delta_{ij}, \tag{11}$$

with $\delta_{ij} \sim N(0, \sigma_\delta^2)$ independently distributed of a_j and u_{ij}. This implies that

$$\rho_{12} = corr(X_{1j}, X_{2j}) = \frac{\sigma_x^2}{\sigma_x^2 + \sigma_u^2 + \sigma_\delta^2}, \tag{12}$$

$j = 1, \ldots, n$. Note that (9) is a special case of (11) with $\sigma_\delta^2 = 0$.

Tosteson et al. (1998) considered the estimation of random effects parameters in mixed models for longitudinal data with covariate measurement errors. Although, in principle, the models under investigation here could be thought as special cases of the models they deal with, the corrected estimators they propose are only valid when the regression parameters do not vary with time. This corresponds to setting $\beta_1 = \beta_2 = \beta$ in our case. Buonaccorsi et al. (2000), developed pseudo maximum likelihood estimators under similar models, based on the estimation of the measurement error covariate parameters (X_{ij} in our case). After obtaining these estimators they maximize the likelihood function of $Y|X$ as a function of the remaining parameters. The idea behind their proposal is to use standard linear mixed model software. The simplification of the model suggested in their paper does not apply in our case.

In Section 2 we present the log-likelihood function under the correlated model defined by (5), (6), (8) and (9) and display the method of moments estimators which may serve as initial values for the numerical procedures required to obtain the MLEs of the parameters. The first derivatives of the log-likelihood function are detailed in Appendix A and the corresponding Fisher information matrix is presented in Appendix B. These results may be used to construct Wald tests for the hypothesis $\beta_1 = \beta_2$. We also propose a score test for the hypothesis $\sigma_\delta^2 = 0$ which is useful to assess whether the more general framework specified by (5), (6), (8) and (11) is more appropriate to model the data. In Section 3 we illustrate these procedures numerically, and compare the results with those obtained via classical regression techniques.

2 Likelihood inference for the correlated model

Under the model specified by equations (5), (6), (8) and (9), the vector of observations $(X_{1j}, Y_{1j}, X_{2j}, Y_{2j})'$ is distributed according to a four-dimensional normal distribution with mean vector $(\mu_x, \beta_1\mu_x, \mu_x, \beta_2\mu_x)'$ and covariance matrix

$$\mathbf{V} = \begin{bmatrix} \sigma_x^2 + \sigma_u^2 & \beta_1\sigma_x^2 & \sigma_x^2 & \beta_2\sigma_x^2 \\ \beta_1\sigma_x^2 & \beta_1^2\sigma_x^2 + \lambda_1\sigma_u^2 & \beta_1\sigma_x^2 & \beta_1\beta_2\sigma_x^2 \\ \sigma_x^2 & \beta_1\sigma_x^2 & \sigma_x^2 + \sigma_u^2 & \beta_2\sigma_x^2 \\ \beta_2\sigma_x^2 & \beta_1\beta_2\sigma_x^2 & \beta_2\sigma_x^2 & \beta_2^2\sigma_x^2 + \lambda_2\sigma_u^2 \end{bmatrix}.$$

By using general properties of the multivariate normal distribution it follows that the log-likelihood function for $\theta = (\beta_1, \beta_2, \mu_x, \sigma_x^2, \sigma_u^2, \lambda_1, \lambda_2)'$ can be written as

$$
\begin{aligned}
L(\theta) = const - \frac{n}{2}\log[\sigma_u^6\Delta] + \frac{1}{\sigma_u^2\Delta}\Bigg\{\sigma_x^2\Bigg[\lambda_1\lambda_2\sum_{j=1}^{n} X_{1j}X_{2j} + \beta_1\beta_2\sum_{j=1}^{n} Y_{1j}Y_{2j} \\
+\beta_1\lambda_2\left(\sum_{j=1}^{n} X_{1j}Y_{1j} + \sum_{j=1}^{n} X_{2j}Y_{1j}\right) + \beta_2\lambda_1\left(\sum_{j=1}^{n} X_{1j}Y_{2j} + \sum_{j=1}^{n} X_{2j}Y_{2j}\right)\Bigg] \\
+\sigma_u^2\mu\left[\lambda_1\lambda_2\left(\sum_{j=1}^{n} X_{1j} + \sum_{j=1}^{n} X_{2j}\right) + \beta_1\lambda_2\sum_{j=1}^{n} Y_{1j} + \beta_2\lambda_1\sum_{j=1}^{n} Y_{2j}\right] \\
-\frac{1}{2}\Bigg\{n\sigma_u^2\mu^2\Gamma + \left(\Delta - \lambda_1\lambda_2\sigma_x^2\right)\left(\sum_{j=1}^{n} X_{1j}^2 + \sum_{j=1}^{n} X_{2j}^2\right) \qquad (13) \\
-\left[\sigma_u^2\lambda_2 + \left(\beta_2^2 + 2\lambda_2\right)\sigma_x^2\right]\sum_{j=1}^{n} Y_{1j}^2 + \left[\sigma_u^2\lambda_1 + \left(\beta_1^2 + 2\lambda_1\right)\sigma_x^2\right]\sum_{j=1}^{n} Y_{2j}^2\Bigg\}\Bigg\},
\end{aligned}
$$

where $\Gamma = \beta_1^2\lambda_2 + \beta_2^2\lambda_1 + 2\lambda_1\lambda_2$ and $\Delta = \Gamma\ \sigma_x^2 + \sigma_u^2\lambda_1\lambda_2$.

The likelihood equations are obtained by equating the first derivatives of (13) to zero. This requires simple but tedious algebraic manipulations and the results are presented in Apendix A. Since there are no explicit solutions to these equations, we must rely on iterative procedures, based on the Newton-Raphson algorithm, for example, to obtain the MLE of θ. The following method of moments estimators may be employed as initial values for such iterative procedures:

$$
\tilde{\beta}_1 = \frac{2\overline{Y}_1}{\overline{X}_1 + \overline{X}_2}, \quad \tilde{\beta}_2 = \frac{2\overline{Y}_2}{\overline{X}_1 + \overline{X}_2}, \quad \tilde{\mu}_x = \frac{\overline{X}_1 + \overline{X}_2}{2},
$$

$$
\tilde{\sigma}_x^2 = \frac{S_{X_1Y_2}\left(\overline{X}_1 + \overline{X}_2\right)}{2\overline{Y}_2}, \quad \tilde{\sigma}_u^2 = S_{X_1X_1} - \tilde{\sigma}_x^2
$$

$$
\tilde{\lambda}_1 = \frac{1}{\tilde{\sigma}_u^2}\left(S_{Y_1Y_1} - \frac{4\overline{Y}_1^2\tilde{\sigma}_x^2}{\left(\overline{X}_1 + \overline{X}_2\right)^2}\right) \quad \text{and} \quad \tilde{\lambda}_2 = \frac{1}{\tilde{\sigma}_u^2}\left(S_{Y_2Y_2} - \frac{4\overline{Y}_2^2\tilde{\sigma}_x^2}{\left(\overline{X}_1 + \overline{X}_2\right)^2}\right),
$$

where the sample moments $S_{X_1Y_2}$, $S_{Y_1Y_1}$ $S_{Y_2Y_2}$, $\overline{X}_i$ and $\overline{Y}_i$, $i = 1, 2$ are defined as before.

Let $\hat{\theta}$ denote the maximum likelihood estimator of the parameter vector θ. Since the usual regularity conditions (Sen and Singer, 1993) are satisfied for the model specified by (5), (6), (8) and (9), it follows that as $n \to \infty$, $\sqrt{n}(\hat{\theta} - \theta) \xrightarrow{D} N[\mathbf{0}, \mathbf{J}^{-1}(\theta)]$, where $\mathbf{J}(\theta)$ is the Fisher information matrix for $\hat{\theta}$. The derivation of the elements of $\mathbf{J}(\theta)$ require extensive algebraic manipulations and are presented in Appendix B. A consistent estimator of such a matrix may be obtained substituting the elements of $\hat{\theta}$ for the corresponding elements of θ in the expressions given in Appendix B.

To test $H_0 : \beta_1 = \beta_2$ versus the alternative $H_1 : \beta_1 > \beta_2$ we may consider a Wald statistic of the form

$$Q_w = n(\mathbf{C}\hat{\theta})'(\mathbf{C}\mathbf{J}^{-1}(\hat{\theta})\mathbf{C}')^{-1}(\mathbf{C}\hat{\theta}) \tag{14}$$

with $\mathbf{C} = (1, -1, 0, 0, 0, 0, 0)$. Under the null hypothesis, Q_w follows asymptotically a chi-squared distribution with one degree of freedom.

To test whether the model specified by (5), (6), (8) and (11) (in lieu of (9)) is more appropriate for the data, we will consider two approaches. The simpler one involves the asymptotic distribution of the method of moments estimator of σ_δ^2,

$$\tilde{\sigma}_\delta^2 = \frac{S_{X_1Y_1}\left(\overline{X}_1 + \overline{X}_2\right)}{2\overline{Y}_1} - \frac{S_{X_1Y_2}\left(\overline{X}_1 + \overline{X}_2\right)}{2\overline{Y}_2}.$$

Defining

$$\mathbf{m} = \left(\overline{X}_1 - \mu_x, \overline{X}_2 - \mu_x, \overline{Y}_1 - \beta_1\mu_x, \overline{Y}_2 - \beta_2\mu_x, S_{X_1Y_1} - \beta_1\left(\sigma_x^2 + \sigma_\delta^2\right), S_{X_1Y_2} - \beta_2\sigma_x^2\right)'$$

we can show that $\sqrt{n}\mathbf{m} \xrightarrow{D} N\left(0, \Sigma\right)$, with:

$$
\Sigma = \begin{bmatrix}
\sigma_x^2+\sigma_u^2+\sigma_\delta^2 & \sigma_x^2 & \beta_1\left(\sigma_x^2+\sigma_\delta^2\right) & \beta_2\sigma_x^2 & 0 & 0 \\
\sigma_x^2 & \sigma_x^2+\sigma_u^2+\sigma_\delta^2 & \beta_1\sigma_x^2 & \beta_2\left(\sigma_x^2+\sigma_\delta^2\right) & 0 & 0 \\
\beta_1\left(\sigma_x^2+\sigma_\delta^2\right) & \beta_1\sigma_x^2 & \beta_1^2\left(\sigma_x^2+\sigma_\delta^2\right)+\lambda_1\sigma_u^2 & \beta_1\beta_2\sigma_x^2 & 0 & 0 \\
\beta_2\sigma_x^2 & \beta_2\left(\sigma_x^2+\sigma_\delta^2\right) & \beta_1\beta_2\sigma_x^2 & \beta_2^2\left(\sigma_x^2+\sigma_\delta^2\right)+\lambda_2\sigma_u^2 & 0 & 0 \\
0 & 0 & 0 & 0 & \nu & \gamma \\
0 & 0 & 0 & 0 & \gamma & \varepsilon
\end{bmatrix},
$$

$$
\nu = 2\beta_1^2\left(\sigma_x^2+\sigma_\delta^2\right)^2+\sigma_u^2\left[\left(\beta_1^2+\lambda_1\right)\left(\sigma_x^2+\sigma_\delta^2\right)+\lambda_1\sigma_u^2\right],
$$

$$
\gamma = \beta_1\beta_2\sigma_x^2\left[2\left(\sigma_x^2+\sigma_\delta^2\right)+\sigma_u^2\right]
$$

and

$$
\varepsilon = \beta_2^2\sigma_x^4+\left(\sigma_x^2+\sigma_\delta^2+\sigma_u^2\right)\left[\beta_2^2\left(\sigma_x^2+\sigma_\delta^2\right)+\lambda_2\sigma_u^2\right].
$$

Using the delta method, we may show that the asymptotic variance of $\tilde{\sigma}_\delta^2$ is

$$
\begin{aligned}
V_A \;=\; & \frac{\left(\sigma_x^2+\sigma_\delta^2\right)^2}{2\beta_1^2\mu_x^2}\left(\beta_1^2\sigma_\delta^2+2\lambda_1\sigma_u^2\right)+\left(\sigma_x^2+\sigma_u^2+\sigma_\delta^2\right)\left(2\sigma_\delta^2+\frac{\lambda_1\sigma_u^2}{\beta_1^2}+\frac{\lambda_2\sigma_u^2}{\beta_2^2}\right) \\
& +\frac{1}{2\beta_2^2\mu_x^2}\left[\beta_2^2\sigma_\delta^2\left(2\mu_x^2\sigma_\delta^2+\left(\sigma_x^2\left(2\sigma_\delta^2+3\sigma_x^2\right)+\sigma_\delta^2\sigma_u^2\right)\right)+2\lambda_2\sigma_u^2\sigma_x^4\right]. \qquad (15)
\end{aligned}
$$

Thus, the hypothesis $H_0 : \sigma_\delta^2 = 0$ can be tested by constructing the confidence interval $\tilde{\sigma}_\delta^2 \mp 2\sqrt{\hat{V}_A}$, where $\hat{V}_A$ denotes a consistent estimator of V_A, which may be obtained by substituting estimators for the parameters β_1, β_2, μ_x, σ_x^2, σ_u^2, σ_δ^2, λ_1 and λ_2 in (15).

For the same purpose, we may also consider a score type test statistic defined by

$$
Q_R = \frac{1}{n}\mathbf{U}_\delta(\hat{\theta})'\mathbf{J}_\delta^{-1}(\hat{\theta})\mathbf{U}_\delta(\hat{\theta}), \qquad (16)
$$

where $\hat{\theta}$ is the MLE of θ under the simpler model and $\mathbf{U}_\delta(\hat{\theta})$ denotes the score statistic $\partial L(\theta)/\partial\theta$ for the more general model evaluated at $\hat{\theta}$.

Expressions for the elements of $\mathbf{U}_\delta(\theta)$ and $\mathbf{J}_\delta^{-1}(\theta)$ are displayed in Appendices C and D, respectively. Since the estimators of θ under the more general model are computationally harder to obtain, Q_R represents a great simplification for practical applications. Note, however, that for the hypothesis under investigation here ($\sigma_\delta^2 = 0$), the parameter value lies in the boundary of the parameter space, implying that the distribution of Q_R is not easily obtained as indicated in Cox and Hinkley (1974), for example. However, we expect that, for large sample sizes, it may be well approximated by a chi-squared distribution with one degree of freedom. In that direction, to study the behavior of Q_R for moderate and large sample sizes, we considered a limited simulation study. Two thousand samples of sizes $n = 20,\ 30,\ 50$, of pairs of random vectors $(Y_{1j},\ X_{1j})$ and $(Y_{2j},\ X_{2j})$ were generated according to the model defined in (5),(6), (8) and (9) with $\mu = 2.0$, $\lambda_1 = \lambda_2 = 1.0$, $\sigma_x^2 = 1.0$ for each combination of the following levels of the remaining parameters: ($\beta_1 = 0.15$, $\beta_2 = 0.45$), ($\beta_1 = 0.50$, $\beta_2 = 0.75$), and $\sigma_u^2 = 0.5,\ 1.0$ which imply reliability ratios $k_x{=}(\sigma_x^2/(\sigma_x^2 + \sigma_u^2)){=}\ 0.67,\ 0.50$.

Considering a nominal significance level $\alpha = 5\%$ we obtained the corresponding empirical significance levels as the ratio between the number of samples for which $Q_R > 3.84$ and the total number of samples. The results are displayed in Table 1 and do not contradict our conjecture that a chi-squared distribution on one degree of freedom may be employed to assess the significance of Q_R.

Table 1: Empirical significance levels for the Q_R statistic

k_x	β_1	β_2	$n = 20$	$n = 30$	n=50
0.67	0.15	0.45	0.051	0.053	0.050
	0.50	0.75	0.046	0.051	0.051
0.50	0.15	0.45	0.053	0.047	0.048
	0.50	0.75	0.054	0.050	0.045

3 Numerical illustration

As a numerical illustration for the procedures outlined above, we start by fitting the model defined by (5), (6), (8) and (9) to the data presented in Singer and Andrade (1997). Both the method of moments estimators used as initial values for the Newton-Raphson algorithm and the resulting MLEs (as well as the corresponding asymptotic standard errors, within parentheses) are presented in Table 2.

Table 2: Parameter estimates under model (5), (6), (8) and (9)

Estimation Method	Parameter β_1	β_2	μ	σ_x^2	σ_u^2	λ_1	λ_2
Moment	0.156	0.436	1.769	0.408	0.562	0.074	0.363
ML	0.147	0.454	1.758	0.539	0.482	0.102	0.267
	(0.025)	(0.045)	(0.172)	(0.200)	(0.123)	(0.040)	(0.123)

Plugging in the maximum likelihood estimates of the parameters into the expressions for the score statistic and the Fisher information matrix (displayed in Appendix D) associated to the more complex model defined by (5), (6), (8) and (11), we obtain $Q_R = 1.09$, $(p = 0.298)$ which clearly suggests that the simpler model is acceptable. In fact, the iterative algorithm designed to compute the MLE under such a model did not converge for the data under investigation. An approximate 95% confidence interval for the parameter σ_ζ^2 based on the method of moments estimates is (0.000, 1.066), corroborating the above conclusion.

Now, using the expressions given in Appendix A, we may compute a Wald statistic to test the hypothesis $H_0 : \beta_1 = \beta_2$ under the simpler model. Here we obtain $Q_w = 41.88$ $(p < 0.001)$ which is in accordance with the results previously presented by Singer and Andrade (1997) under a different approach.

For comparison purposes, we fitted a classical linear regression model defined by

$$Y_{ij} = \beta_i X_{ij} + e_{ij} \tag{17}$$

$i = 1, 2, j = 1, .., n$, $e_{1j} \sim N(0, \sigma_1^2)$, $e_{2j} \sim N(0, \sigma_2^2)$, $\rho_e = corr(e_{1j}, e_{2j}) = \sigma_{12}/\sigma_1\sigma_2$ to the same data. Under such a model, the MLEs of the variances of the post-toothbrushing dental plaque indices Y_{1j} and Y_{2j} (0.030 and 0.096, respectively) are roughly half those obtained under the measurement error model (0.061 and 0.240, respectively), reflecting the extra variability induced by the uncertainty in the measurement of the pre-toothbrushing dental plaque indices, X_{1j} and X_{2j}. Furthermore, the estimates (standard errors) of dental plaque reduction rates, β_1 and β_2 were 0.169 (0.018) and 0.404 (0.028), respectively. As expected, the standard errors of the parameters of interest are larger than those obtained under the measurement error model (as indicated in Table 2).

Acknowledgements

This research was supported by grants from the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP). and FINEP (PRONEX), Brazil.

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Appendix A: Likelihood equations for model (5), (6), (8) and (9)

The first partial derivatives of the likelihood function (13) are

$$\begin{aligned}\partial L(\theta)/\partial\beta_i &= \Delta^{-1}\Big\{-n\sigma_x^2\beta_i\lambda_{(3-i)} + (\sigma_u^2\Delta)^{-1}\textstyle\sum_{j=1}^n \Big[Y_{ij}\left(B_{(3-i)}\sigma_x^2 + \lambda_{(3-i)}\sigma_u^2\right) \\ &\quad -\beta_i\left(\beta_{(3-i)}\sigma_x^2 y_{(3-i)j} + \lambda_{(3-i)}R_j\right)\Big]\left[\lambda_i\lambda_{(3-i)}R_j + \sigma_x^2 Q_j\right]\Big\}, i = 1,2.\end{aligned}$$

$$\partial L(\theta)/\partial\mu = \Delta^{-1}\left(-n\mu\Gamma + \textstyle\sum_{j=1}^n P_j\right),$$

$$
\begin{aligned}
\partial L(\theta)/\partial\sigma_x^2 &= (2\Delta)^{-1}\left\{-n\Gamma + \Delta^{-1}\textstyle\sum_{j=1}^{n}(P_j-\mu\Gamma)^2\right\},\\
\partial L(\theta)/\partial\sigma_u^2 &= -(\sigma_u^2\Delta)^{-1}\{n/2\,[3\Delta+\lambda_1\lambda_2\sigma_u^2(1-\mu^2\Gamma\Delta^{-1})]+\Delta^{-1}\{\lambda_1\lambda_2\sigma_u^2\\
&\quad\times\left[\mu\textstyle\sum_{j=1}^{n}P_j - 1/2\,(\lambda_1\lambda_2X+\lambda_2u_{1y}+\lambda_1u_{2y})\right]+\sigma_x^2\sigma_u^{-2}(\lambda_1\lambda_2\sigma_u^2\\
&\quad+\Delta)\left[\lambda_1\lambda_2\textstyle\sum_{j=1}^{n}X_{1j}X_{2j}+\beta_1\beta_2\sum_{j=1}^{n}Y_{1j}Y_{2j}+\sum_{j=1}^{n}Q_j(X_{1j}+X_{2j})\right.\\
&\quad\left.-1/2\,((\Gamma-\lambda_1\lambda_2)X+B_2u_{1y}+B_1u_{2y})\right]\}\},\\
\partial L(\theta)/\partial\lambda_i &= (2\Delta)^{-1}\left\{-n\left(B_{(3-i)}\sigma_x^2+\lambda_{(3-i)}\sigma_u^2\right)+(\sigma_u^2\Delta)^{-1}\textstyle\sum_{j=1}^{n}\left[\beta_i\right.\right.\\
&\quad\left.\left.\times\left(\beta_{(3-i)}\sigma_x^2Y_{(3-i)j}+\lambda_{(3-i)}R_j\right)-\left(B_{(3-i)}\sigma_x^2+\lambda_{(3-i)}\sigma_u^2\right)Y_{ij}\right]^2\right\},\\
&\quad i=1,2,
\end{aligned}
$$

where

$B_1=\beta_1^2+2\lambda_1$, $B_2=\beta_2^2+2\lambda_2$, $\Gamma=\beta_1^2\lambda_2+\beta_2^2\lambda_1+2\lambda_1\lambda_2$, $\Delta=\Gamma\sigma_x^2+\lambda_1\lambda_2\sigma_u^2$, $X=\sum_{j=1}^{n}\left(X_{1j}^2+X_{2j}^2\right)$, $u_{1y}=\sum_{j=1}^{n}Y_{1j}^2$, $u_{2y}=\sum_{j=1}^{n}Y_{2j}^2$, $R_j=\mu\sigma_u^2+\sigma_x^2(X_{1j}+X_{2j})$, $Q_j=\beta_1\lambda_2Y_{1j}+\beta_2\lambda_1Y_{2j}$, $P_j=\lambda_1\lambda_2(X_{1j}+X_{2j})+Q_j$, $j=1,\ldots,n$.

Appendix B: Fisher information matrix for model (5), (6), (8) and (9)

Let

$$
\mathbf{J}(\theta)=-E\left(\frac{\partial^2 log f\left(\left(X_1,Y_1,X_2,Y_2\right),\theta\right)}{\partial\theta\partial\theta'}\right)=[I_{ij}]_{7X7}\ ,
$$

with $\theta=(\beta_1,\beta_2,\mu_x,\sigma_x^2,\sigma_u^2.\lambda_1,\lambda_2)'$. Then

$$
\begin{aligned}
I_{11} &= \Delta^{-1}\{(\beta_2^2+2\lambda_2)(\sigma_x^2+\mu^2)\sigma_x^2\sigma_u^{-2}+\lambda_2(\mu^2+2\beta_1^2\lambda_2\sigma_x^4\Delta^{-1})\},\\
I_{12} &= I_{21} = -\beta_1\beta_2\sigma_x^2(\sigma_u^2\Delta)^{-1}[\mu^2-(\lambda_1\lambda_2\sigma_u^2-\sigma_x^2\Gamma)\sigma_x^2\Delta^{-1}].\\
I_{13} &= I_{31} = \mu\beta_1\lambda_2\Delta^{-1},\ I_{14} = I_{41} = \beta_1\lambda_2\sigma_x^2\Gamma\Delta^{-2}.\\
I_{15} &= I_{51} = \beta_1\lambda_1\lambda_2^2\sigma_x^2\Delta^{-2},\ I_{16} = I_{61} = \beta_1\lambda_2\sigma_x^2[(\beta_2^2+2\lambda_2)\sigma_x^2+\lambda_2\sigma_u^2]\Delta^{-2},\\
I_{17} &= I_{71} = -\beta_1\beta_2^2\lambda_1\sigma_x^4\Delta^{-2}.\\
I_{22} &= \Delta^{-1}[(\beta_1^2+2\lambda_1)(\sigma_x^2+\mu^2)\sigma_x^2\sigma_u^{-2}+\lambda_1(\mu^2+2\beta_2^2\lambda_1\sigma_x^4\Delta^{-1})],\\
I_{23} &= I_{32} = \beta_2\lambda_1\mu\Delta^{-1}.\ I_{24} = I_{42} = \beta_2\lambda_1\sigma_x^2\Gamma\Delta^{-2},
\end{aligned}
$$

$$
\begin{aligned}
I_{25} &= I_{52} = \beta_2\lambda_1^2\lambda_2\sigma_x^2\Delta^{-2}, I_{26} = I_{62} = -\beta_1^2\beta_2\lambda_2\sigma_x^4\Delta^{-2}, \\
I_{27} &= I_{72} = \beta_2\lambda_1\sigma_x^2\left[\left(\beta_1^2+2\lambda_1\right)\sigma_x^2+\lambda_1\sigma_u^2\right]\Delta^{-2}, \\
I_{33} &= \Gamma\Delta^{-1}, I_{34} = I_{43} = I_{35} = I_{53} = I_{36} = I_{63} = I_{37} = I_{73} = 0, \\
I_{44} &= \Gamma^2(2\Delta^2)^{-1}, I_{45} = I_{54} = \lambda_1\lambda_2\Gamma(2\Delta^2)^{-1}, \\
I_{46} &= I_{64} = (2\sigma_u^2\Delta^2)^{-1}\left[\left(\beta_2^2+2\lambda_2\right)\left(\Delta+\lambda_1\lambda_2\sigma_u^2\right)\sigma_x^2+\lambda_1\lambda_2^2\sigma_u^4\right], \\
I_{47} &= I_{74} = (2\sigma_u^2\Delta^2)^{-1}\left[\left(\beta_1^2+2\lambda_1\right)\left(\Delta+\lambda_1\lambda_2\sigma_u^2\right)\sigma_x^2+\lambda_1^2\lambda_2\sigma_u^4\right], \\
I_{55} &= \sigma_u^{-2}\left[\Delta^{-1}\left(\lambda_1\lambda_2+\sigma_x^4\Gamma^2(2\sigma_u^2\Delta)^{-1}\right)+\sigma_u^{-2}\right], I_{56} = I_{65} = \beta_1^2\lambda_2^2\sigma_u^2(2\Delta^2)^{-1}, \\
I_{57} &= I_{75} = \beta_2^2\lambda_1^2\sigma_u^2(2\Delta^2)^{-1}, I_{66} = \left[\left(\beta_2^2+2\lambda_2\right)\sigma_x^2+\lambda_2\sigma_u^2\right]^2(2\Delta^2)^{-1}, \\
I_{67} &= I_{76} = \beta_1^2\beta_2^2\sigma_x^4(2\Delta^2)^{-1}, I_{77} = \left[\left(\beta_1^2+2\lambda_1\right)\sigma_x^2+\lambda_1\sigma_u^2\right](2\Delta^2)^{-1},
\end{aligned}
$$

with Δ and Γ as given in Appendix A.

Appendix C: Likelihood equations for model (5), (6), (8) and (11)

The elements of $\mathbf{U}_\delta(\theta)$ are

$$
\begin{aligned}
\partial L(\theta)/\partial\beta_i &= J^{-1}\Big\{-n\beta_i F_{(3-i)} + (\sigma_u^2 J)^{-1}\textstyle\sum_{j=1}^n \Big[S_{(3-i)}Y_{ij} - \beta_i\Big(\mu\sigma_u^2 P_{(3-i)} \\
&\quad + F_{(3-i)}X_{ij} + c_{(3-i)j}\sigma_u^2\sigma_x^2\Big)\Big]\Big[F_{(3-i)}c_{ij} + \lambda_i\sigma_u^2\Big(\mu P_{(3-i)} \\
&\quad + \sigma_x^2 c_{(3-i)j}\Big)\Big]\Big\}, i = 1,2, \\
\partial L(\theta)/\partial\mu &= J^{-1}\left(\left[P_2\textstyle\sum_{j=1}^n c_{1j} + P_1\sum_{j=1}^n c_{2j} - n\mu\left(\sigma_u^2 T_2 + 2\sigma_\delta^2 T_1\right)\right]\right), \\
\partial L(\theta)/\partial\sigma_x^2 &= J^{-1}\Big\{-n\left(\sigma_\delta^2 T_1 + \sigma_u^2 T_2/2\right) + (2J)^{-1}\textstyle\sum_{j=1}^n\Big[P_2 c_{1j} + P_1 c_{2j} - \mu\left(\sigma_u^2 T_2\right. \\
&\quad \left.+ 2\sigma_\delta^2 T_1\right)\Big]^2\Big\}, \\
\partial L(\theta)/\partial\sigma_u^2 &= J^{-1}\Big\{-n/2\left[\left(M\sigma_u^2 + 2J\right)\sigma_u^{-2} + \mu^2\left(T_2 - M\left(\sigma_u^2 T_2 + 2\sigma_\delta^2 T_1\right)J^{-1}\right)\right] \\
&\quad + \mu\left[\left(\lambda_1 - P_1 M J^{-1}\right)\textstyle\sum_{j=1}^n c_{2j} + \left(\lambda_2 - P_2 M J^{-1}\right)\sum_{j=1}^n c_{1j}\right] - (2J)^{-1} \\
&\quad \times\Big\{\left(J - M\sigma_u^2\right)Q + M\left[2\sigma_x^2\textstyle\sum_{j=1}^n c_{1j}c_{2j} + \left(\sigma_\delta^2 + \sigma_x^2\right)R\right] - \sigma_\delta^2\sigma_u^{-4}\left(\sigma_\delta^2\right. \\
&\quad \left.+ 2\sigma_x^2\right)\left(J + \sigma_u^2 M\right)\Big(b_2\textstyle\sum_{j=1}^n a_{1j}^2 + b_1\sum_{j=1}^n a_{2j}^2\Big)\Big\}\Big\}.
\end{aligned}
$$

$$\begin{aligned}\partial L(\theta)/\partial\sigma_\delta^2 &= J^{-1}\{-n\{N/2+\mu^2[b_1b_2-NJ^{-1}(\sigma_\delta^2T_1+\sigma_u^2T_2/2)]\}+\mu[(b_2\\&-P_2NJ^{-1})\textstyle\sum_{j=1}^n c_{1j}+(b_1-P_1NJ^{-1})\sum_{j=1}^n c_{2j}\Big]-[\sigma_x^2+\sigma_\delta^2(1\\&-N(\sigma_\delta^2+2\sigma_x^2)(2J)^{-1})]\left(b2\textstyle\sum_{j=1}^n a_{1j}^2+b_1\sum_{j=1}^n a_{2j}^2\right)\sigma_u^{-2}\\&-NJ^{-1}\left[\sigma_x^2\textstyle\sum_{j=1}^n c_{1j}c_{2j}-\sigma_u^2Q/2\right]+(1-N(\sigma_\delta^2+\sigma_x^2)J^{-1})R/2\Big\},\end{aligned}$$

$$\begin{aligned}\partial L(\theta)/\partial\lambda_i &= (2J)^{-1}\Big\{-nS_{(3-i)}+(\sigma_u^2J)^{-1}\textstyle\sum_{j=1}^n\Big\{Y_{ij}S_{(3-i)}-\beta_i\Big[X_{ij}F_{(3-i)}\\&+\sigma_u^2\left(\mu P_{(3-i)}+\sigma_x^2c_{(3-i)j}\right)\Big]\Big\}^2\Big\},i=1,2,\end{aligned}$$

with

$J=\beta_1^2\beta_2^2\sigma_\delta^2(\sigma_\delta^2+2\sigma_x^2)+\lambda_1\lambda_2\sigma^2(\sigma^2+\sigma_\delta^2+\sigma_x^2)+(\beta_1^2\lambda_2+\beta_2^2\lambda_1+\lambda_1\lambda_2)[\sigma_\delta^2(\sigma_\delta^2+2\sigma_x^2)+\sigma^2\times(\sigma_\delta^2+\sigma_x^2)]$, $b_i=\beta_i^2+\lambda_i$, $F_i=\sigma_u^2\lambda_i(\sigma_\delta^2+\sigma_x^2)+\sigma_\delta^2(\sigma_\delta^2+2\sigma_x^2)b_i$, $S_i=F_i+\sigma_u^2[b_i(\sigma_\delta^2+\sigma_x^2)+\lambda_i\sigma_u^2]$, $i=1,2$, $T_1=\beta_1^2\beta_2^2+\beta_2^2\lambda_1+\beta_1^2\lambda_2+\lambda_1\lambda_2$, $T_2=\beta_2^2\lambda_1+\beta_1^2\lambda_2+2\lambda_1\lambda_2$, $P_1=b_1\sigma_\delta^2+\lambda_1\sigma_u^2$, $P_2=b_2\sigma_\delta^2+\lambda_2\sigma_u^2$, $M=T_2(\sigma_\delta^2+\sigma_x^2)+2\lambda_1\lambda_2\sigma_u^2$, $N=2(\sigma_\delta^2+\sigma_x^2)T_1+\sigma_u^2T_2$, $Q=\lambda_1\lambda_2\sum_{j=1}^n\left(X_{1j}^2+X_{2j}^2\right)+\lambda_2\sum_{j=1}^nY_{1j}^2+\lambda_1\sum_{j=1}^nY_{2j}^2$, $R=2\beta_1\lambda_2\sum_{j=1}^nX_{1j}Y_{1j}+2\beta_2\lambda_1\sum_{j=1}^nX_{2j}Y_{2j}-[(\beta_1^2\lambda_2+\beta_2^2\lambda_1+\lambda_1\lambda_2)\sum_{j=1}^n\left(X_{1j}^2+X_{2j}^2\right)+(b_2+\lambda_2)\sum_{j=1}^nY_{1j}^2+(b_1+\lambda_1)\sum_{j=1}^nY_{2j}^2\Big]$, $a_{1j}=Y_{1j}-\beta_1X_{1j}$, $a_{2j}=Y_{2j}-\beta_2X_{2j}$, $c_{1j}=\lambda_1X_{1j}+\beta_1Y_{1j}$, $c_{2j}=\lambda_2X_{2j}+\beta_2Y_{2j}$, $d_{1j}=\beta_1Y_{1j}-\lambda_1X_{1j}$, $d_{2j}=\beta_2Y_{2j}-\lambda_2X_{2j}$, $j=1,\ldots,n$.

Appendix D: Fisher information matrix for model (5), (6), (8) and (11)

Let

$$\mathbf{J}_5(\theta)=-E\left(\frac{\partial^2 log f\left((X_1,Y_1,X_2,Y_2),\theta\right)}{\partial\theta\partial\theta^t}\right)=\frac{1}{J}[I_{ij}]_{8X8}.$$

where $\theta=(\beta_1,\beta_2,\mu_x,\sigma_x^2,\sigma_u^2,\sigma_\delta^2,\lambda_1,\lambda_2)'$. Thus, it follows that for $i=1,2$.

$$\begin{aligned}I_{ii} &= \sigma_u^{-2}\Big\{\mu_x^2S_{(3-i)}+\Big[2\beta_i^2\sigma_u^2F_{(3-i)}^2+\left(b_{(3-i)}\sigma_x^4\sigma_u^2+(\sigma_\delta^2+\sigma_x^2)F_{(3-i)}\right)\Big(\beta_i^2F_{(3-i)}\\&+\lambda_iS_{(3-i)}\Big)\Big]J^{-1}\Big\}.\end{aligned}$$

$$
\begin{aligned}
I_{12} &= -\beta_1\beta_2\sigma_x^2\left[\mu_x^2+\sigma_x^2-2\sigma_u^4\lambda_1\lambda_2\sigma_x^2J^{-1}\right], I_{i3} \;=\; \mu_x\beta_i\left[\sigma_\delta^2 b_{(3-i)}+\sigma_u^2\lambda_{(3-i)}\right],\\
I_{i4} &= \beta_i\left[\sigma_\delta^2 b_{(3-i)}+\sigma_u^2\lambda_{(3-i)}\right]\left[\sigma_u^2\left\{b_i\sigma_\delta^2\lambda_{(3-i)}+\sigma_x^2T_2\right\}+\sigma_\delta^2T_1\left(\sigma_\delta^2+2\sigma_x^2\right)\right]J^{-1},\\
I_{i5} &= \beta_i\lambda_i\left\{\sigma_\delta^2 b_{(3-i)}\left(\sigma_\delta^2+2\sigma_x^2\right)\left[b_{(3-i)}\left(\sigma_\delta^2+\sigma_x^2\right)+\sigma_u^2\lambda_{(3-i)}\right]+\sigma_u^2\lambda_{(3-i)}F_{(3-i)}\right\}J^{-1},\\
I_{i6} &= \beta_i\left\{T_1\sigma_\delta^2\left[b_{(3-i)}\left(\left(\sigma_\delta^2+\sigma_x^2\right)^2+\sigma_x^2\left(\sigma_x^2+\sigma_\delta^2\right)\right)+2\sigma_u^2\lambda_{(3-i)}\left(\sigma_\delta^2+2\sigma_x^2\right)\right]\right.\\
&\quad\left.+\sigma_u^2\left[b_i\lambda_{(3-i)}^2\sigma_u^2\left(\sigma_\delta^2+\sigma_x^2\right)+\sigma_x^4 b_{(3-i)}\left(\beta_i^2\lambda_{(3-i)}-\beta_{(3-i)}^2\lambda_i\right)\right]\right\}J^{-1},\\
I_{17} &= \beta_1F_2S_2J^{-1}, I_{18} \;=\; -\beta_1\beta_2^2\lambda_1\sigma_u^4\sigma_x^4J^{-1}, I_{27} \;=\; -\beta_1^2\beta_2\lambda_2\sigma_u^4\sigma_x^4J^{-1},\\
I_{28} &= \beta_2F_1S_1J^{-1}, I_{33} \;=\; 2\sigma_\delta^2T_1+\sigma_u^2T_2, I_{34}=I_{35}=I_{36}=I_{37}=I_{38} \;=\; 0,\\
I_{44} &= \left(2\sigma_\delta^2T_1+\sigma_u^2T_2\right)^2(2J)^{-1}, I_{45} \;=\; \left[T_1T_2\sigma_\delta^4+\sigma_u^2\lambda_1\lambda_2\left(4T_1\sigma_\delta^2+\sigma_u^2T_2\right)\right](2J)^{-1},\\
I_{46} &= \left\{\textstyle\sum_{i=1}^2\left[\sigma_\delta^4 b_ib_{(3-i)}\lambda_{(3-i)}\left(\beta_i^2+b_i\right)+\sigma_u^2b_i\left(2\beta_{(3-i)}^4\sigma_\delta^2\lambda_i+\beta_i^2\sigma_u^2\lambda_{(3-i)}^2\right)\right]\right.\\
&\quad+2T_1\sigma_\delta^2\left(\beta_1^2\beta_2^2\sigma_\delta^2+2\sigma_u^2\lambda_1\lambda_2\right)+\lambda_1\lambda_2\sigma_u^2\left[T_2\sigma_u^2+2\sigma_\delta^2\left(2\beta_1^2\beta_2^2+\beta_2^2\lambda_1\right.\right.\\
&\quad\left.\left.\left.+\beta_1^2\lambda_2\right)\right]\right\}(2J)^{-1},\\
I_{47} &= \beta_1^2\sigma_u^2\left(b_2\sigma_\delta^2+\lambda_2\sigma_u^2\right)^2(2J)^{-1}, I_{48} \;=\; \beta_2^2\sigma_u^2\left(b_1\sigma_\delta^2+\lambda_1\sigma_u^2\right)^2(2J)^{-1},\\
I_{55} &= \lambda_1\lambda_2T_1\sigma_x^4J^{-1}+\textstyle\sum_{i=1}^2\left(2\beta_{(3-i)}^2\lambda_{(3-i)}F_i^2+\lambda_{(3-i)}^2S_i^2+W_i^2\right)\left(2\sigma_u^4J\right)^{-1},\\
I_{56} &= \left\{\left[\left(2\beta_1^2\beta_2^2+\beta_1^2\lambda_2+\beta_2^2\lambda_1\right)\lambda_1\lambda_2+T_2\left(\beta_1^2\beta_2^2+\lambda_1\lambda_2\right)+\beta_1^2\lambda_2^2b_1+\beta_2^2\lambda_1^2b_2\right]\right.\\
&\quad\left.\left(\sigma_\delta^2+2\sigma_x^2\right)\sigma_\delta^2+\left[4T_1\left(\sigma_x^2+\sigma_\delta^2\right)+T_2\sigma_u^2\right]\sigma_u^2\lambda_1\lambda_2+2T_1T_2\sigma_x^4\right\}(2J)^{-1},\\
I_{57} &= \left\{\lambda_1S_2^2+\beta_1^2\left[F_2^2+\lambda_2b_2\sigma_u^4\sigma_x^4\right]\right\}\left(2\sigma_u^2J\right)^{-1},\\
I_{58} &= \left\{\lambda_2S_1^2+\beta_2^2\left[F_1^2+\lambda_1b_1\sigma_u^4\sigma_x^4\right]\right\}\left(2\sigma_u^2J\right)^{-1},\\
I_{66} &= \left\{\textstyle\sum_{i=1}^2 b_i^2\left[b_{(3-i)}\left(\sigma_\delta^2+\sigma_x^2\right)+\sigma_u^2\lambda_{(3-i)}\right]^2+2b_1^2b_2^2\sigma_x^4\right\}(2J)^{-1}.\\
I_{67} &= \beta_1^2\sigma_u^2\left\{b_2^2\sigma_x^4+\left[b_2\left(\sigma_x^2+\sigma_\delta^2\right)+\sigma_u^2\lambda_2\right]^2\right\}(2J)^{-1},\\
I_{68} &= \beta_2^2\sigma_u^2\left\{b_1^2\sigma_x^4+\left[b_1\left(\sigma_x^2+\sigma_\delta^2\right)+\sigma_u^2\lambda_1\right]^2\right\}(2J)^{-1}.\\
I_{77} &= S_2^2(2J)^{-1}. I_{78} \;=\; \beta_1^2\beta_2^2\sigma_u^4\sigma_x^4(2J)^{-1}. I_{88} \;=\; S_1^2(2J)^{-1}.
\end{aligned}
$$

with $J, T_1, T_2, b_i, F_i, S_i, i = 1, 2$, as given in Appendix C and $W_i = \beta_i^2 \sigma_\delta^2 \left(\sigma_\delta^2 + 2\sigma_x^2\right) b_{(3-i)}$

$+\sigma_u^2 \left(\beta_i^2 \lambda_{(3-i)} + \beta_{(3-i)}^2 \lambda_i\right) \left(\sigma_\delta^2 + \sigma_x^2\right) + \lambda_i \lambda_{(3-i)} \sigma_u^2 \left(\sigma_\delta^2 + \sigma_u^2 + \sigma_x^2\right)$,

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