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Response to comments on 'Marginalized multi-level hurdle and zero-inflated models for overdispersed and correlated count data with excess zeros'

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1. Introduction

We are grateful to Dr. Inan for pointing out an issue with our original paper. Following up on this, we have identified a few more and offer a solution. First, our paper is based on two sets of normally distributed random effects: one for the probability component, the other for the count model component, that are assumed to be uncorrelated. This was not mentioned in the original paper. Therefore, we now derive a version for the correlated random-effects case. Second, we started from equating algebraic functions of the marginalized hierarchical model and a corresponding marginal model. This, however, is generally not the right approach. Rather, a specific function (typically the mean) of the marginalized hierarchical model should be equated to an algebraically convenient function (typically the mean that would result from a marginally formulated model).

In Section 2, some relevant material pertaining to the non-zero-inflated case is presented. Sections 3 and 4 are devoted to the zero-inflated and hurdle cases, respectively. The data of the original paper are re-analyzed and available in the form of on-line Supplementary Materials. Importantly, the estimates and standard errors that change due to the corrections that need to be applied can be found there.

2. The Non-zero-inflated Model

It is important to realize that the full model specification is of a conditional nature, and not of a marginal nature. Only the marginal mean is assumed to be of a certain parametric form, not the entire marginal distribution. The only latitude comes through the connector function. This means that in the marginal model one (in the non-zero-inflated cases) or two (in the zero-inflated case) identifications can be done. We will illustrate this using the non-zero-inflated combined model.

The specification usually found is:

$$\lambda_{ij}^{c} = \theta_{ij} \exp\left(\Delta_{ij} + \boldsymbol{z}_{ij}'\boldsymbol{b}_i\right), \quad (1)$$

$$\lambda_{ij}^{m} = \exp\left(\boldsymbol{x}_{ij}'\boldsymbol{\xi}\right). \quad (2)$$

We find this in Kassahun *et al*[1], but for example also in Molenberghs *et al.*[2] and in various earlier papers.

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The familiar integral equation, which dates back to the original authors of the marginalized multilevel model (MMM)[3, 4, 5] is:

$$\lambda_{ij}^m = \int\int \lambda_{ij}^c f(\theta_{ij}) f(\boldsymbol{b}_i) d\theta_{ij} d\boldsymbol{b}_i, \quad (3)$$

$$\exp\left(\boldsymbol{x}_{ij}'\boldsymbol{\xi}\right) = \int\int \theta_{ij} \exp\left(\Delta_{ij} + \boldsymbol{z}_{ij}'\boldsymbol{b}_i\right) f(\theta_{ij}) f(\boldsymbol{b}_i) d\theta_{ij} d\boldsymbol{b}_i, \quad (4)$$

$$\boldsymbol{x}_{ij}'\boldsymbol{\xi} = \ln E(\theta_{ij}) + \Delta_{ij} + \frac{1}{2}\boldsymbol{z}_{ij}' D \boldsymbol{z}_{ij}. \quad (5)$$

Hence,

$$\Delta_{ij} = \boldsymbol{x}_{ij}'\boldsymbol{\xi} - \ln E(\theta_{ij}) - \frac{1}{2}\boldsymbol{z}_{ij}' D \boldsymbol{z}_{ij}. \quad (6)$$

Note that there is a minus sign missing in Kassahun *et al.*[1] in the equation following their equation (4). This goes back to Molenberghs *et al.*[6] (their equation (38)). Also, in the same equation following equation (4) in Kassahun *et al.*[1], it would be more common to write $\ln(\alpha/\beta)$ for the logarithm of the mean of the gamma variable, but this is a matter of convention.

In the above derivation, it should be kept in mind that the conditional model is assumed to be of a Poisson type, *given* the random effects. The resulting marginal model is multivariate in nature but *not* of a Poisson type. Rather, it is a Poisson-gamma-normal model, with a joint marginal distribution that is complex. Molenberghs, Verbeke, and Demétrio[6] gave an expression in the form of a multi-indexed series expansion.

Thus, the correct logic is that the joint distribution of the model is specified through its hierarchical formulation. Once this formulation is given, a parametric form is imposed on the univariate marginal mean functions. The fact that this is even possible, results from the connector function.

To see this more clearly, and also to prepare for further developments, we restate the above, but in simplified notation. The hierarchical model is then specified as:

$$P(Y = y|\theta, \boldsymbol{b}) = f(y|\lambda^c) = \frac{e^{-\lambda^c}(\lambda^c)^y}{y!}, \quad (7)$$

$$\lambda^c = \theta \exp(\Delta + \boldsymbol{z}'\boldsymbol{b}), \quad (8)$$

$$\theta \sim \text{Gamma}(\alpha, \beta), \quad (9)$$

$$\boldsymbol{b} \sim N(0, D). \quad (10)$$

It then follows that

$$E(Y|\theta, \boldsymbol{b}) = \sum_{y=0}^{\infty} y \frac{e^{-\lambda^c}(\lambda^c)^y}{y!} = \lambda^c. \quad (11)$$

Hence,

$$E[E(Y|\theta, \boldsymbol{b})] = E(\theta) \exp\left(\Delta + \frac{1}{2}\boldsymbol{z}' D \boldsymbol{z}\right). \quad (12)$$

If we, once again, require this to be equal to $\exp(\boldsymbol{x}'\boldsymbol{\xi})$, then we find

$$\ln E(\theta) + \Delta + \frac{1}{2}\boldsymbol{z}' D \boldsymbol{z} = \boldsymbol{x}'\boldsymbol{\xi},$$

leading to (6), as it should.

3. Zero-inflated Models

Continuing to use simplified notation, consider the ZI model first.

The conditional model specification is:

$$P(Y = y|\theta, \boldsymbol{b}) = \begin{cases} \pi^c + (1-\pi^c) f(0|\lambda^c) & y = 0, \\ (1-\pi^c) f(y|\lambda^c) & y > 0, \end{cases} \quad (13)$$

$$\pi^c = \Phi(\Delta_1 + \boldsymbol{z}_1'\boldsymbol{b}_1), \quad (14)$$

$$\lambda^c = \theta \exp(\Delta_2 + \boldsymbol{z}_2'\boldsymbol{b}_2), \quad (15)$$

$$\theta \sim \text{Gamma}(\alpha, \beta), \quad (16)$$

$$\boldsymbol{b} = \begin{pmatrix} \boldsymbol{b}_1 \\ \boldsymbol{b}_2 \end{pmatrix} \sim N\left[\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} D_{11} & D_{12} \\ D_{21} & D_{22} \end{pmatrix}\right]. \quad (17)$$

It now follows:

$$E(Y|\theta,\boldsymbol{b}) = [\pi^c + (1-\pi^c)f(0|\lambda^c)]\cdot 0 + \sum_{y=1}^{\infty} y\frac{e^{-\lambda^c}(\lambda^c)^y}{y!} = (1-\pi^c)\lambda^c. \tag{18}$$

Now, the above is of the same form that would result, had we specified a marginal Poisson model, i.e., a formulation of the form

$$P(Y=y) = \begin{cases} \pi^* + (1-\pi^*)f(0|\lambda^*) & y=0, \\ (1-\pi^*)f(y|\lambda^*) & y>0. \end{cases} \tag{19}$$

On pages 7 (for the hurdle model) and 8 (for the ZI model) in Kassahun *et al.*[1] it appears that the *entire* models are equated. Rather, what we are allowed to do, in line with earlier comments, is state that the marginal mean is of a specific form, e.g.,

$$E(Y) = (1-\pi^m)\lambda^m. \tag{20}$$

The fact that calculating the mean form (19) results in the form (20) does not imply that the marginal model behind (25)–(17) is equal to (20). In fact, as stated before, we know this is not true.

Nevertheless, equating the mean functions leads to the requirement:

$$\int\int (1-\pi^c)\lambda^c f(\theta)f(\boldsymbol{b})d\theta d\boldsymbol{b} = (1-\pi^m)\lambda^m. \tag{21}$$

While this appears straightforward, there is a caveat: π^c and λ^c are connected through correlated random effects.

In the special but relevant case that $\boldsymbol{b}_1$ and $\boldsymbol{b}_2$ are uncorrelated, and hence that $D_{12}=0$, we can solve the system:

$$\int \pi^c f(\boldsymbol{b}_1)d\boldsymbol{b}_1 = \pi^m, \tag{22}$$

$$\int\int \lambda^c f(\boldsymbol{b}_2)f(\theta)d\boldsymbol{b}_2 d\theta = \lambda^m. \tag{23}$$

Now, (22) is the classical binary connector function integral equation; (23) is the counterpart for the Poisson case. These lead to the solutions on page 4407 of Kassahun *et al.*[1].

Zero-inflated Models with Correlated Normal Random Effects

In case $D_{12}\neq 0$, the integral equation takes the form:

$$\int\int\int (1-\pi^c)\lambda^c f(\theta)f(\boldsymbol{b}_1)f(\boldsymbol{b}_2|\boldsymbol{b}_1)d\theta d\boldsymbol{b}_1 d\boldsymbol{b}_2 = (1-\pi^m)\lambda^m. \tag{24}$$

Given that

$$\boldsymbol{b}_2|\boldsymbol{b}_1 \sim N\left(D_{21}D_{11}^{-1}\boldsymbol{b}_1, \widetilde{D} = D_{22} - D_{21}D_{11}^{-1}D_{12}\right),$$

and with some straightforward algebra, we obtain the following intermediate step:

$$E(\theta)e^{\Delta_2+\frac{1}{2}\boldsymbol{z}_2'\widetilde{D}\boldsymbol{z}_2}\int (1-\pi^c)e^{\boldsymbol{z}_2'D_{21}D_{11}^{-1}\boldsymbol{b}_1}f(\boldsymbol{b}_1)d\boldsymbol{b}_1 = (1-\pi^m)\lambda^m.$$

This, in turn, leads to

$$E(\theta)e^{\Delta_2+\frac{1}{2}\boldsymbol{z}_2'D_{22}\boldsymbol{z}_2}\int (1-\pi^c)f(\boldsymbol{b}_1;\mu = D_{12}\boldsymbol{z}_2)d\boldsymbol{b}_1.$$

Upon applying a final transformation ($\widetilde{\boldsymbol{b}}_1 = \boldsymbol{b}_1 - D_{12}\boldsymbol{z}_2 \sim N(0, D_{11})$), we find that the Poisson connector remains the same, but for the binary connector, we need to solve:

$$\pi^c = \Phi(\Delta_1 + \boldsymbol{z}_1'\widetilde{\boldsymbol{b}}_1 + \boldsymbol{z}_1'D_{12}\boldsymbol{z}_2).$$

Of course, this is equal to the standard binary connector problem, but merely with a shift applied to Δ_1, i.e.,

$$\Delta_1 = -\boldsymbol{z}_1'D_{12}\boldsymbol{z}_2 + \sqrt{1+\boldsymbol{z}_1'D_{11}\boldsymbol{z}_1}\cdot\Phi^{-1}\left[\text{expit}\left(\boldsymbol{x}_1'\boldsymbol{\gamma}^m\right)\right]$$

when the logit link is used, while for the probit link this is:

$$\Delta_1 = -\boldsymbol{z}_1'D_{12}\boldsymbol{z}_2 + \sqrt{1+\boldsymbol{z}_1'D_{11}\boldsymbol{z}_1}\cdot\left(\boldsymbol{x}_1'\boldsymbol{\gamma}^m\right).$$

4. Hurdle Models

Dr. Gul Inan correctly states that there is a modification needed here. However, (5) in Dr. Inan's text is not right because we want to take the conditional mean over the entire distribution, not conditional on a value.

Using the same simplified notation as before, we now have:

$$P(Y=y|\theta,\boldsymbol{b}) \quad = \quad \begin{cases} \pi^c & y=0, \\ (1-\pi^c)\frac{f(y|\lambda^c)}{1-f(0|\lambda^c)} & y>0, \end{cases} \tag{25}$$

with the rest of the model specified by (14)–(17). It now follows:

$$E(Y|\theta,\boldsymbol{b}) = \pi^c\cdot 0 + \frac{1-\pi^c}{1-f(0|\lambda^c)}\sum_{y=1}^{\infty} f(y|\lambda^c) = \frac{1-\pi^c}{1-f(0|\lambda^c)}\cdot\lambda^c = \frac{1-\pi^c}{1-e^{-\lambda^c}}\cdot\lambda^c. \tag{26}$$

This is identical to the expression obtained by Dr. Inan.

Also here, we note that the marginal model is *not* of the form presented in the middle of page 4407 in Kassahun *et al.*[1] but, in keeping with what is done earlier, we can require conditional mean (26) to take the same form marginally:

$$E(Y) = (1-\pi^m)\cdot\frac{\lambda^m}{1-e^{-\lambda^m}}.$$

When $\boldsymbol{b}_1$ and $\boldsymbol{b}_2$ are independent, we find the classical connector integral equation for the binary component:

$$\int \pi^c f(\boldsymbol{b}_1)d\boldsymbol{b}_1 = \pi^m.$$

For the count connector function, we need to solve:

$$\int\int \frac{\lambda^c}{1-e^{-\lambda^c}} f(\boldsymbol{\theta})f(\boldsymbol{b}_2)d\theta d\boldsymbol{b}_2 = \frac{\lambda^m}{1-e^{-\lambda^m}}.$$

More explicitly,

$$\int\int \frac{\theta e^{\Delta_2+\boldsymbol{z}_2'\boldsymbol{b}_2}}{1-e^{-\left[\theta e^{\Delta_2+\boldsymbol{z}_2'\boldsymbol{b}_2}\right]}} f(\boldsymbol{\theta})f(\boldsymbol{b}_2)d\theta d\boldsymbol{b}_2 = \frac{e^{\boldsymbol{x}_2'\boldsymbol{\xi}}}{1-e^{-e^{\boldsymbol{x}_2'\boldsymbol{\xi}}}}.$$

This is the result of Dr. Inan. Dr. Inan's proposal to solve this equation iteratively, through Newton-Raphson, is very sensible. Of course, also here, a further modification is needed when the two normal random effects are correlated.

Hurdle Models With Correlated Normal Random Effects

In line with what we find in the zero-inflated case, we now have:

$$\int\int\int \Phi(\Delta_1+\boldsymbol{z}_1'\boldsymbol{b}_1)\cdot\frac{\theta e^{\Delta_2+\boldsymbol{z}_2'\boldsymbol{b}_2}}{1-e^{-\left[\theta e^{\Delta_2+\boldsymbol{z}_2'\boldsymbol{b}_2}\right]}} f(\boldsymbol{\theta})f(\boldsymbol{b}_1)f(\boldsymbol{b}_2|\boldsymbol{b}_1)d\theta d\boldsymbol{b}_1 d\boldsymbol{b}_2 = \Phi(\boldsymbol{x}_1'\gamma)\cdot\frac{e^{\boldsymbol{x}_2'\boldsymbol{\xi}}}{1-e^{-e^{\boldsymbol{x}_2'\boldsymbol{\xi}}}}.$$

However now, the denominator under the integrand implies that simplification is less straightforward, and hence a Newton-Raphson approach for the pair (Δ_1,Δ_2) is an obvious way forward. Note that in the zero-inflated case, we were able to derive intuitive expressions for Δ_1 and Δ_2, but these are not unique, given that there is one integral equation with two tuning parameters. Here, one can at best hope to find an algebraic expression for Δ_1, because even in the uncorrelated random effects case, there is no closed form for the count connector. Therefore, we can simply set one of the two equal to zero, $\Delta_1\equiv 0$, say, and then solve the reduced integral equation for Δ_2.

5. Concluding Remarks

In summary, the issues discussed are as follows.

First, one should not formulate the entire marginal model, unlike in Kassahun *et al.*[1] (pp. 4407–4408), but only use a convenient marginal mean formulation and equate it to the marginal mean as derived from the fully formulated hierarchical model. It is fine to use this model as inspiration to derive a marginal mean function, but no more than that. Dr. Inan's work is not inconsistent with this observation, but it is not explicitly mentioned. Also, Dr. Inan's equation (5) is better replaced by a more conventional derivation of the marginal mean.

Second, neither the original proposal nor Dr. Inan's derivation is entirely correct when the normal random effects are correlated. Dr. Inan's work is correct for uncorrelated random effects. The original proposal is correct in the zero-inflated case (not in the hurdle case) when the random effects are uncorrelated.

Third, for correlated random effects, we have derived the correction for the ZI case. It is algebraically a minor modification in the ZI case, but nevertheless one that needs to be made and that has important implications for computation.

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Supplementary Materials

A. Data Analysis

Here, we re-analyze both case studies using the marginalized ZI models. Fitting the marginalized hurdle model with correlated normal random effects is very computationally intensive because it requires solving integral equations iteratively for each observation, even for medium size datasets. Therefore, we exemplify the analyses using the marginalized zero-inflated model with correlated normal random effects.

A.1. IRC Data

The data were analyzed using the zero-inflation models ZI(PNG)ℓ, ZI(PNG)p, MZI(PNG)ℓ and MZI(PNG)p. Results are shown in Table A.1. Estimates slightly change from the ones of Kassahun *et al.*[1] in Table II. The conclusions are:

- Comparing ZI(PNG)ℓ, ZI(PNG)p, and their marginalized counterpart, the intercept ξ_0 seems to differ as a result of the marginalization, while the other estimates corresponding to the count part appear similar. This follows from the nature of the connector function. However, estimates corresponding to the zero-inflation component, such as $\gamma_0, \gamma_1, \gamma_2, \gamma_3$, and d_2 show some difference. This is expected from the change of link function.
- The marginalized models lead to estimates of increased precision. In terms of parameter significance, all models suggest that standard deviations of the random intercepts of the positive counts and the excess zeros, overdispersion parameter, zero-inflation intercept, and zero-inflation coefficients of village and season are statistically significant. In addition, the correlation parameter ρ is negative and statistically significant across models.

Note that there is quite some difference in some parameter estimates (intercepts) between the non-marginalized and marginalized versions, even though the likelihood values at maximum do not change. This is in line with theory, because a pair of models is identical in fit, but with parameters expressed on a different scale: conditional on random effects versus marginalized over random effects. For count data, the difference is typically strong for intercept type parameters, while for binary data all parameters would be affected ([2]).

Given that the MH(PNG)ℓ and MH(PNG)p models were not fitted, we interpreted the estimates using the MZI(PNG)ℓ model. However, these do not change compared to the ones presented on page 4406 of Kassahun *et al.*[1]. The MZI(PNG)ℓ as shown in Table A.1 suggests that village at risk had higher expected A. gambiae log-counts $(0.9808, p < 0.0001)$ as compared with the controls. Furthermore, log-counts in the wet season were higher than in the dry season $(2.2404, p < 0.0001)$. However, no statistically significant association was observed for the time effect $(p = 0.9585)$; the same is true for the village-time interaction $(p = 0.6566)$. The zero-inflation estimate corresponding to village $(\widehat{\gamma}_2 = -0.8914, p < 0.0001)$ with $\exp(\widehat{\gamma}) = 0.41$ implies that the odds of zeros in the at-risk villages is nearly one third of what is expected in the control villages. In addition, it was found that the odds of zeros in the wet season is much smaller than that of the dry season $(\widehat{\gamma}_3 = -1.2095, p < 0.0001)$. The correlation of the random effects is negative and significant $(\widehat{\rho} = -0.4322, p = 0.0417)$, suggesting the presence of a strong negative association between the count and zero-inflation processes.

Table A.1. *IRC data: parameter estimates (standard deviation) for the regression coefficients in (1)ZI(PNG)ℓ, (2)MZI(PNG)ℓ,ZI(PNG)p, (2)MZI(PNG)p link for zero-inflation.*

Effect	Parameter	Estimate(s.e.)	Estimate(s.e.)
		$ZI(PNG)_\ell$	$MZI(PNG)_\ell$
Intercept	ξ_0	-0.0085(0.1639)	0.0389(0.1595)
Time	ξ_1	0.0061(0.0988)	0.0051(0.0983)
Village	ξ_2	0.9824(0.1688)	0.9808(0.1683)
Season	ξ_3	2.2418(0.0982)	2.2404(0.0979)
Village × time	ξ_4	-0.0524(0.1163)	-0.0517(0.1160)
Overdispersion	α	1.4472(0.1126)	1.4388(0.1111)
Std. dev. random intercept count	d_1	0.2856(0.0677)	0.2824(0.0667)
Inflation intercept	γ_0	2.2771(0.1634)	1.9131(0.1564)
Inflation time	γ_1	0.0172(0.0568)	0.0129(0.0493)
Inflation village	γ_2	-1.0145(0.1486)	-0.8914(0.1279)
Inflation season	γ_3	-1.3816(0.1039)	-1.2095(0.0914)
Std. dev. random intercept inflation	d_2	0.8597(0.0814)	0.511(0.0472)
Corr. random effects	ρ	-0.4583(0.2058)	-0.4322(0.2105)
-2log-likelihood		12,817	12,815
AIC		12,843	12,841
		$ZI(PNG)_p$	$MZI(PNG)_p$
Intercept	ξ_0	-0.0080(0.1640)	0.03097(0.1598)
Time	ξ_1	0.0098(0.0989)	0.0105(0.0989)
Village	ξ_2	0.9816(0.1687)	0.983(0.1687)
Season	ξ_3	2.2426(0.0983)	2.2427(0.0983)
Village × time	ξ_4	-0.0553(0.1164)	-0.0561(0.1164)
Overdispersion	α	1.4442(0.1119)	1.4442(0.1119)
Std. dev. random intercept count	d_1	0.2835(0.0669)	0.2837(0.0670)
Inflation intercept	γ_0	1.3387(0.0936)	1.1347(0.0886)
Inflation time	γ_1	0.0152(0.0340)	0.0135(0.0303)
Inflation village	γ_2	-0.5954(0.0879)	-0.5300(0.0772)
Inflation season	γ_3	-0.8099(0.0592)	-0.7209(0.0527)
Std. dev. random intercept inflation	d_2	0.5119(0.0474)	0.5119(0.0474)
Corr. random effects	ρ	-0.4394(0.2097)	-0.4397(0.2096)
-2log-likelihood		12,817	12,817
AIC		12,843	12,843

A.2. Jimma Longitudinal Family Survey of Youth

Table A.2 shows the results of fitting the ZI(PN-)ℓ and MZI(PN-)ℓ models. As before, the estimates are almost the same than the ones presented in Kassahun *et al.*[1] in Table VI. Therefore, the findings are the same:

- The marginalized model appears relatively superior in precision. However, estimates corresponding to the count part remain similar, and this is not surprising given the smaller random-effects variance.
- The standard deviation of the random intercept inflation changes substantially among conditional and marginal model, leading to non-negligible differences in the zero-inflation estimates as well.

Table A.2. *Jimma Longitudinal Family Survey of Youth: parameter estimates (standard deviation) for the regression coefficients in (1)ZI(PN-)ℓ, (2)MZI(PN-)ℓ*

Effect	Parameter	Estimate(s.e.)	Estimate(s.e.)
		ZI(PN-)$_\ell$	MZI(PN-)$_\ell$
Intercept	ξ_0	0.8620(0.1440)	0.8686(0.1441)
Time	ξ_1	0.0673(0.0179)	0.0672(0.0179)
Sex	ξ_2	0.0840(0.0272)	0.0841(0.0273)
Age	ξ_3	0.0288(0.0092)	0.0288(0.0092)
Std. dev. random intercept count	d_1	0.1197(0.0321)	0.1198(0.0321)
Inflation intercept	γ_0	2.2627(0.3858)	2.001(0.3486)
Inflation time	γ_1	0.1862(0.0463)	0.1632(0.0416)
Inflation sex	γ_2	-0.4227(0.0731)	-0.3803(0.0654)
Inflation age	γ_3	-0.0605(0.0251)	-0.0539(0.0225)
Std. dev. random intercept inflation	d_2	0.8010(0.0689)	0.4719(0.0403)
Corr. random effects	ρ	-0.1329(0.2888)	-0.1320(0.2946)
-2log-likelihood		13,242	13,242
AIC		13,264	13,264