

# 1 Methods for the integrated meta-analysis

## 2 of mean and variation effects

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25

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27   [https://github.com/AlistairMcNairSenior/IMAMV\\_Vignette](https://github.com/AlistairMcNairSenior/IMAMV_Vignette).

28

29

## 30 Abstract

31 Meta-analyses in ecology and evolution typically focus on population means *via* effect  
32 sizes such as the log response ratio. Recently, there has been interest in quantifying  
33 effects on variability using the log variability ratio and the log coefficient of variation  
34 ratio. Until now, testing for the effects on group means and variabilities has  
35 necessitated two separate models. We present a workflow for one integrated meta-  
36 analysis of mean and variation effects, or 'IMAMV'. In a worked example, using data  
37 from the diet-mixing literature we show how the focal parameters from IMAMV match  
38 those from the equivalent two-model analysis. A common limitation to meta-analysis of  
39 variation, is unreported variance values in the primary literature. IMAMV can increase  
40 the power to detect effects on variation in meta-analytics datasets with missing  
41 variance values through 'borrowing of strength'. We show, for example, that in a dataset  
42 with 20% missing variance values, IMAMV increased the precision of the meta-analytic  
43 estimate on the variation effect by 10% compared to the conventional two-model  
44 approach. IMAMV can be implemented in commonly used software and requires no  
45 additional data beyond that used in the analysis of group means.

46

## 47 Introduction

48 Meta-analysis is widely used in many fields including ecology and evolutionary biology  
49 <sup>1</sup>. For meta-analysis, the user first quantifies the results from a set of comparable  
50 studies using a common effect-size metric. Analysing these effect sizes, one then  
51 estimates the overall sign and magnitude, as well as replicability, of effects in the  
52 literature <sup>1,2</sup>. The most widely used effect size in ecology is the log ratio of sample means  
53 (a.k.a., the log response ratio, lnRR) <sup>3-5</sup>. The second most popular is the standardised  
54 mean difference <sup>3,4</sup>, which is also a mean-centric effect size. Hence, ecological meta-  
55 analysts have most often studied how phenomena affect group means, such as the  
56 difference between control and experimental treatment groups.

57

58 Over the past decade there has been increasing interest in looking beyond means to  
59 understand effects on inter-individual variability <sup>6-9</sup>. This interest has been supported by  
60 the development of effect sizes for meta-analysing variation effects <sup>10,11</sup>. Differences in  
61 variability between groups may be quantified using effect sizes such as the log  
62 variability ratio (lnVR) and log coefficient of variation ratio (lnCVR) <sup>10,11</sup>. Recent  
63 applications include assessing how inter-individual variation is affected by light  
64 pollution, sexual selection, and immune threats <sup>12-14</sup>. These methods originated in  
65 ecology and evolution <sup>10</sup>, but have now become widespread e.g., in psychiatric  
66 medicine; <sup>15,16-18</sup>.

67

68 Quantifying lnVR or lnCVR requires no additional data to that used for lnRR <sup>10</sup>. Therefore,  
69 any dataset that assesses mean effects *via* lnRR can also test for effects on variability.

70 In rare cases, studies have performed a two step-analysis, first analysing the mean, and  
71 then the variation e.g.,<sup>19,20,21</sup> (Figure 1A). In other instances, the variation effects have  
72 been reported in subsequent re-analyses of data originally gathered to assess mean  
73 effects e.g.,<sup>22,23</sup>. However, compared to lnRR, effect sizes for variation seem to be used  
74 rarely<sup>4,23</sup>, implying that most variation effects go untested or at least unreported.

75 Possible reasons for the underutilisation of the methods might include lack of  
76 awareness, the perceived effort of undertaking a second analysis, and/or under-  
77 reporting of variance values in the primary literature.

78

79 Here, we present an approach for the simultaneous meta-analysis of mean and  
80 variability effects using a single model; we refer to this approach as integrated meta-  
81 analysis of mean and variation effects (IMAMV; Figure 1B). We demonstrate how IMAMV  
82 offers the convenience of a single integrated model and also provides information on  
83 the correlation of mean- and variation-effects. Importantly, we show that for datasets  
84 with missing-variance values IMAMV boosts power to detect effects on the variation  
85 through ‘borrowing of strength’ (Figure 1B). IMAMV can be implemented in freely  
86 available and widely used R packages. For example, all models in the main text have  
87 been implemented in *metafor*<sup>24</sup>, though packages such as *brms* or *MCMCglmm*<sup>24-27</sup>  
88 may also be used for more complex analyses.

89

90 As a case study, we apply IMAMV to the effects of diet-mixing on mean and among-  
91 animal variation in reproductive function. Diet-mixing studies compare the  
92 performance of groups of animals held on single- vs mixed-food diets. These data are  
93 well suited because they contain layers of non-independence typically seen in other

94 eco-evolutionary meta-analyses. The dataset contains data on the sample mean and  
95 sample variability for reproductive function in 282 groups of animals clustered into 69  
96 experiments. *A priori*, we expect single-food diets to decrease means and increase  
97 among-animal variability<sup>28</sup>.

98

99 Accompanying this paper is a vignette that describes the implementation of IMAMV in R  
100 (a pdf has been supplied for review “IMAMV\_Vignette.pdf”), and all code and data are  
101 available at [https://github.com/AlistairMcNairSenior/IMAMV\\_Vignette](https://github.com/AlistairMcNairSenior/IMAMV_Vignette).

102

## 103 Key Effect Sizes and Estimators

104 A relatively unbiased estimator of the log population mean based on the sample mean,  
105 which we refer to as  $\ln\bar{x}$ , and its sampling variance ( $\nu_{\ln\bar{x}}$ ) are<sup>29</sup>:

106

$$107 \ln\bar{x} = \log(\bar{x}) + \frac{1}{2} \left( \frac{(s/\bar{x})^2}{n} \right) = \log(\bar{x}) + \frac{1}{2} \left( \frac{CV^2}{n} \right), \quad (1)$$

108

$$109 \nu_{\ln\bar{x}} = \frac{(s/\bar{x})^2}{n} + \frac{(s/\bar{x})^4}{2n^2} = \frac{CV^2}{n} + \frac{CV^4}{2n^2}, \quad (2)$$

110

111 where  $\bar{x}$  is the sample mean,  $s$  is the sample standard deviation (SD),  $n$  is the sample  
112 size, and  $CV$  is the coefficient of variation (i.e.,  $s/\bar{x}$ ). The  $\ln\text{RR}$  contrasts the sample  
113 means of two groups, and along with its sampling variance, can be calculated as<sup>5</sup>:

114

$$115 \ln\text{RR} = \ln\bar{x}_E - \ln\bar{x}_C, \quad (3)$$

116

117  $v_{\ln RR} = v_{\ln \bar{x}_E} + v_{\ln \bar{x}_C},$  (4)

118

119 where  $\ln \bar{x}_E$  and  $\ln \bar{x}_C$  are the log sample means for the experimental and control groups  
120 and  $v_{\ln \bar{x}_E}$  and  $v_{\ln \bar{x}_C}$  are the sampling variances (note, this formulation assumes the  
121 samples are independent).

122

123 A relatively unbiased estimator of the log population SD, based on the sample SD and  
124 its sampling variance ( $v_{\ln s}$ ) is<sup>11,30</sup>:

125

126  $\ln s = \log(s) + \frac{1}{2(n-1)},$  (5)

127

128  $v_{\ln s} = \frac{1}{2} \frac{n}{(n-1)^2},$  (6)

129

130 where all notation is as above. To quantify the difference in variation between two  
131 samples, such as experimental and control groups, one may use the  $\ln VR$ <sup>10</sup>:

132

133  $\ln VR = \ln s_E - \ln s_C,$  (7)

134

135  $v_{\ln VR} = v_{\ln s_E} + v_{\ln s_C}.$  (8)

136

137 It may be desirable to meta-analyse studies where there is an association between the  
138 mean and the variance of the data. For example, there is a very strong association

139 between the log mean and log SD within the diet-mixing dataset (Figure 2A). Positive  
140 associations persist after correcting for inter-study unitary differences by centring each  
141 group on the within-study averages for log mean and log SD (Figure 2B). Hence, one may  
142 wish to understand how treatments affect variation, after correcting for any effects on  
143 the group mean. In such cases one may analyse the log CV see <sup>31</sup> for a discussion on the use of CV as a  
144 measure of variation<sup>10</sup>. The log CV and its sampling variance can be estimated as <sup>10</sup>:

145

$$146 \quad \ln CV = \ln s - \ln \bar{x}, \quad (9)$$

147

$$148 \quad v_{\ln CV} = v_{\ln s} + v_{\ln \bar{x}}. \quad (10)$$

149

150 Up until now, the most common approach for the meta-analysis of variation has been to  
151 compute an effect size for difference in the log CV of two groups as  $\ln CVR$  <sup>11</sup>:

152

$$153 \quad \ln CVR = \ln CV_E - \ln CV_C = \ln VR - \ln RR, \quad (11)$$

154

$$155 \quad v_{\ln CVR} = v_{\ln CV_E} + v_{\ln CV_C} = v_{\ln RR} + v_{\ln VR}. \quad (12)$$

156

157 We now demonstrate how these effect sizes for the mean and the variance can be  
158 analysed within a single statistical model, ‘IMAMV’.

159

160 **Contrast-Based IMAMV**

161 The standard random-effects meta-analysis for a conventional ‘contrast-based’  
162 analysis of effects on the mean using the  $\ln\text{RR}$  can be written as:

163

164 
$$\ln\text{RR}_j = \theta + a_j + m_j, \quad (13)$$

165

166 
$$a_j \sim N(0, \sigma_a^2), \quad (14)$$

167

168 
$$m_j \sim N(0, v_{\ln\text{RR}_j}), \quad (15)$$

169

170 where  $\ln\text{RR}_j$  is the sampled effect size in the  $j$ th study (i.e.,  $j = 1 \dots J$  effect sizes) as  
171 estimated via eqn. 3,  $\theta$  is the meta-analytic estimate of  $\ln\text{RR}$  (i.e.,  $\mu_{\ln\text{RR}}$ ),  $a$  is the  
172 deviation of the true effect in the  $j$ th study from  $\theta$ , and  $m_j$  is the deviation of  $\ln\text{RR}_j$  from  
173 the true effect due to sampling.  $a_j$  is assumed to be normally distributed as per eqn. 14;  
174  $\sigma_a$  is the estimated SD in effects among studies, and its square is often referred to as  
175 the heterogeneity,  $\tau^2$  (i.e.,  $\tau^2 = \sigma_a^2$ ).  $m_j$  is assumed to be normally distributed with mean  
176 0 and SD  $\sqrt{v_{\ln\text{RR}_j}}$  (eqn. 4). Where one wants to understand effects on variation,  $\ln\text{RR}$  is  
177 substituted for  $\ln\text{CVR}$  (i.e., eqns 11 and 12; Figure 1A).

178

179 We have applied eqn. 13 to the  $\ln\text{RR}$  and  $\ln\text{CVR}$  for the diet-mixing data using *metafor*  
180 (see Vignette). We calculated effects such that negative values indicate lower measures  
181 in the single-food group and *vice versa*. On average, single-food feeding leads to  
182 reductions in mean reproductive output (Two-Model Analysis, Table 1). The effect on

183 mean reproductive output is large, amounting to an 26% reduction on a single-food diet  
184 (i.e.,  $1 - e^{-0.30} = 0.26$ ). In contrast, single-food diets typically increase the CV by around  
185 17% (i.e.,  $e^{0.16} = 1.17$ ). For both lnRR and lnCVR estimated heterogeneity is more than  
186 double the estimated effect (Table 1), suggesting considerable variance in the  
187 distribution of effects reported within the literature<sup>32</sup>.

188

189 IMAMV is an alternative to performing separate analyses of the lnRR and lnCVR. We  
190 propose a bivariate meta-analysis that simultaneously estimates (1) the lnRR and (2)  
191 the paired differences between lnVR and lnRR. Importantly, this difference can be  
192 considered an estimate of lnCVR (see eqn. 11; Figure 1B).

193

194 In the current worked example each pair of samples has both an lnRR and lnVR, and an  
195 IMAMV version of eqn. 13 of these paired effect sizes can be written as:

196

$$197 y_{ij} = \alpha + a_j + (\beta_{\ln VR} + b_j) \times S_{ij} + m_{ij}, \quad (16)$$

198

$$199 \begin{bmatrix} a_k \\ b_k \end{bmatrix} \sim N \left( \begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma_a^2 & \rho_{ab} \sigma_a \sigma_b \\ \rho_{ab} \sigma_a \sigma_b & \sigma_b^2 \end{bmatrix} \right), \quad (17)$$

200

$$201 m_{ij} \sim N(0, v_{y_{ij}}), \quad (18)$$

202

203 where  $y_{ij}$  is the  $i$ th effect type (i.e.,  $i = 1 = \ln RR$ ,  $i = 2 = \ln VR$ ) from the  $j$ th study. Here  $\alpha$  is  
204 the meta-analytic intercept which corresponds to the estimate for lnRR (i.e.,  $\alpha = \mu_{\ln RR}$ ),  
205  $\beta_{\ln VR}$  is the meta-analytic difference between lnVR and lnRR, and  $S_{ij}$  is a dummy

206 predictor coded as 0 if  $y_{ij}$  is a sample lnRR and 1 for lnVR. Because the term  $\beta_{\text{lnVR}}$  is an  
207 estimate of lnVR – lnRR, it is also an estimate of lnCVR (eqn. 11). Note that, the analysis  
208 explicitly pairs instances of lnRR and lnVR from the same samples, and the terms  $a_k$  and  
209  $b_k$  then give deviations of average lnRR and lnCVR for study  $j$  from  $\alpha$  and  $\beta_{\text{lnVR}}$ . The  $j$ th  
210 deviations are assumed bi-variate normally distributed as per eqn. 17:  $\sigma_a$  and  $\sigma_b$  give  
211 the among-study SDs in lnRR and lnCVR. The term  $\rho_{ab}$  gives the correlation between  
212 effects on the mean and variation effects at the between-study level.  $\nu_{y_{ij}}$  is the  
213 sampling variance for  $y_{ij}$ , estimated by eqn. 4 or 8 for instances of lnRR or lnVR,  
214 respectively. We have applied eqn. 16 to the diet mixing data and the estimated point-  
215 estimates for effect magnitude are identical to those from the two-model analysis  
216 (Table 1). In addition, the correlation between lnRR and lnCVR was estimated to be -  
217 0.58, suggesting that as single food diets generate more negative effects on the mean,  
218 they simultaneously generate more variation.

219

## 220 Non-Independence and Random Effects in IMAMV

221 The models in eqns 13 and 16 assume that all effect sizes are independent, such that  
222 each study/experiment only contains one control and one experimental group. In  
223 ecology and evolution this assumption often is invalid because most datasets contain  
224 non-independent effect sizes<sup>3,4,33,34</sup>. For example, in the diet-mixing dataset most  
225 experiments yield more than one effect size. The most widely used solution to this issue  
226 of non-independence is to include an additional term, to form a multi-level meta-  
227 analytic model sensu<sup>3</sup>. In the case of IMAMV, we can formulate a multilevel extension  
228 of eqn. 16 as:

229

230 
$$y_{ijk} = \alpha + a_k + e_{jk} + (\beta_{\ln VR} + b_k + f_{jk}) \times S_{ijk} + m_{ijk}, \quad (19)$$

231

232 
$$\begin{bmatrix} a_k \\ b_k \end{bmatrix} \sim N \left( \begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma_a^2 & \rho_{ab}\sigma_a\sigma_b \\ \rho_{ab}\sigma_a\sigma_b & \sigma_b^2 \end{bmatrix} \right), \quad (20)$$

233

234 
$$\begin{bmatrix} e_{jk} \\ f_{jk} \end{bmatrix} \sim N \left( \begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma_e^2 & \rho_{ef}\sigma_e\sigma_f \\ \rho_{ef}\sigma_e\sigma_f & \sigma_f^2 \end{bmatrix} \right), \quad (21)$$

235

236 
$$m_{ijk} \sim N(0, v_{y_{ijk}}), \quad (22)$$

237

238

239 where  $y_{ijk}$  is the  $i$ th effect type (i.e.,  $i = 1 = \ln RR$ ,  $i = 2 = \ln VR$ ) from the  $j$ th pairwise  
 240 contrast of treatment groups in the  $k$ th study; i.e., the dataset contains  $k = 1 \dots K$   
 241 studies, and the  $k$ th study contains  $j = 1 \dots J$  pairwise contrasts).  $a_k$  and  $b_k$  give  
 242 deviations of average  $\ln RR$  and  $\ln CVR$  for study  $k$  from  $\alpha$  and  $\beta_{\ln VR}$ , while  $e_{jk}$  and  $f_{jk}$  give  
 243 the deviations for the  $j$ th pairwise contrast in experiment  $k$ .  $\sigma_a$  and  $\sigma_b$  give the among-  
 244 study SDs in  $\ln RR$  and  $\ln CVR$  respectively, while  $\sigma_e$  and  $\sigma_f$  give the within-study (i.e.,  
 245 between group) SDs. The terms  $\rho_{ab}$  and  $\rho_{ef}$  give the correlations between effects on the  
 246 mean and variation at the between- and within-study levels, respectively. The total  
 247 heterogeneity for  $\ln RR$  can be estimated as  $\tau_{\ln RR}^2 = \sigma_a^2 + \sigma_e^2$ , and that for  $\ln CVR$  as  
 248  $\tau_{\ln CVR}^2 = \sigma_b^2 + \sigma_f^2$ . Table 1 shows that the application of this model to the diet mixing  
 249 dataset yields similar point estimates to the preceding analyses, though the CIs are  
 250 wider, having accounted for non-independence.

251

252 **Moderator Variables in IMAMV**

253 Most ecological and evolutionary meta-analyses detect high levels of heterogeneity<sup>32,35</sup>.

254 Moderators are meta-variables related to the individual effect sizes that may explain

255 this heterogeneity. For example, in the diet mixing dataset, we have coded effect sizes

256 by whether the focal species is terrestrial or marine dwelling. There are two common

257 approaches to testing moderator variables: (1) stratification, and (2) meta-regression.

258 IMAMV is compatible with both approaches. With stratification one simply subsets the

259 data by the levels of the moderator and analyses each using separate instances of

260 IMAMV.

261

262 Meta-regression involves fitting the moderator variable as a predictor in a model that

263 estimates differences in the overall effect size between levels of the moderator. The

264 IMAMV framework above already uses meta-regression, where the  $\beta_{\ln VR}$  term in eqn. 19,

265 estimates the  $\ln CVR$ . Incorporating a moderator variable involves including an

266 interaction between the moderator and the term estimating  $\ln CVR$ . In the case of the

267 IMAMV in eqns 19 through 22, a meta-regression including a two-level moderator coded

268 as 0 and 1 can be formulated as:

269

$$270 \quad y_{ijk} = \alpha + a_k + e_{jk} + \beta_{\text{Mod}} \times R_{ijk} +$$

$$271 \quad (\beta_{\ln VR} + b_k + f_{jk}) \times S_{ijk} + \beta_{\text{Mod} \Delta \ln VR} \times V_{ijk} + m_{ijk}, \quad (23)$$

272

273 where  $R_{ijk}$  is a dummy predictor coded 0 if  $y_{ijk}$  is an effect size associated with the  
274 reference level of the moderator and 1 otherwise,  $\beta_{Mod}$  is the meta-analytic estimate for  
275 the difference in  $\ln RR$  between levels of the moderator,  $V_{ijk}$  is a dummy predictor coded  
276 as 1 if  $y_{ijk}$  is both an estimate of the  $\ln VR$  and level 1 of the moderator (and coded as 0  
277 otherwise),  $\beta_{Mod\Delta\ln VR}$  is an estimate of the interaction term for the moderator and effect  
278 size type, and all other terms are as in eqn. 19. The term  $\beta_{Mod\Delta\ln VR}$  can be interpreted as  
279 difference in  $\ln CVR$  between levels of the moderator.

280

281 Here, we have applied the meta-regression described in eqn. 23 to habitat differences  
282 in the diet mixing dataset. There are no statistically significant differences among  
283 habitats for  $\ln CVR$  ( $\beta_{Mod\Delta\ln VR} = \ln CVR_{Terrestrial} - \ln CVR_{Marine} = 0.12$ , CI = -0.10 to 0.35).  
284 However, the reductive effect of single food diets on mean reproductive function is  
285 estimated to be stronger in terrestrial than marine habitats ( $\beta_{Mod} = \ln RR_{Terrestrial} -$   
286  $\ln RR_{Marine} = -0.23$ , CI = -0.47 to -0.002).

287

## 288 Borrowing of Strength and Missing Data

289 A limitation to meta-analysis of variation effects is missing data. Unfortunately, it is  
290 relatively common for some of the primary literature to not report the among-replicate  
291 SDs (or related metrics), which are needed to calculate  $\ln VR$  or  $\ln CVR$  (e.g., Figure 1A).  
292 IMAMV can boost power to detect effects on variability in datasets with missing SDs  
293 through ‘borrowing of strength’. Borrowing of strength can occur in multivariate meta-  
294 analyses of the effects of the treatment on a pair of correlated outcomes (e.g., effect of  
295 an intervention on both blood-pressure and the risk of stroke)<sup>36</sup>. In such cases, the

296 correlated outcomes provide indirect information about the effects of the treatment on  
297 one another, potentially increasing the precision on the estimates in the analysis<sup>36,37</sup>.  
298 Borrowing of strength is expected to be particularly beneficial in cases where a random  
299 subset of studies does provide effect sizes one of the outcomes<sup>36,37</sup>, making it a very  
300 valuable phenomenon for meta-analysis of variation where there are missing SDs.

301

302 When faced with a meta-analytic dataset with missing among-replicate SDs, we  
303 propose that the user may estimate the sampling variance of lnRR for studies with  
304 missing SDs using established methods e.g.,<sup>38</sup>, before applying IMAMV to the full lnRR  
305 and partial lnVR dataset. IMAMV is then expected to yield more precise estimate of the  
306 effects on the variation than would be obtained from a univariate analysis of the partial  
307 lnVR or lnCVR dataset.

308

309 To demonstrate this benefit of IMAMV, we have deleted the SD data from a random 20%  
310 of the entries within the diet-mixing dataset. For the complete cases, where SD was not  
311 missing, we estimated lnVR and lnCVR and the associated sampling variances as  
312 above. We estimated the lnRR and its sampling variance for every entry (i.e., including  
313 those with missing SD) following Nakagawa, Noble, Lagisz, Spake, Viechtbauer, Senior  
314<sup>38</sup>. This resulted in a dataset with 331 instances of lnRR, but just 265 instances of lnCVR  
315 and lnVR. We then compared the results of the two-model analysis of lnRR and lnCVR  
316 with IMAMV (following eqn. 16). Both analyses provide comparable estimates of effect  
317 magnitude (Table 2). The estimates for lnRR also have the same standard error (SE;  
318 Table 2). However, the SE and CIs for the estimate of the lnCVR are narrower in IMAMV  
319 than in the two model analysis, despite the models containing the same effect sizes.

320 These differences in SE translate into a 10% gain in precision and an increase in  
321 efficiency for the IMAMV analysis (i.e., relative efficiency =  $1.1 = \frac{1/\text{SE}_{\text{IMAMV}}^2}{1/\text{SE}_{\text{2-model}}^2}$ ).

322

### 323 Additional Sources of Non-Independence

324 Beyond hierarchical data structures, eco-evolutionary datasets often contain other  
325 sources of non-independence. For example, by calculating multiple pair-wise effect  
326 sizes using the same control-group data contrast-based analyses can induce  
327 correlations among effect sizes; sometimes termed ‘stochastic dependency’<sup>33,39,40</sup>. In  
328 the case of diet-mixing, consider a study that contains two single-food groups, A and B,  
329 and one mixed food group, C. In this case we have pairwise effect sizes contrasting AC  
330 and BC, duplicating the use of group C data. To a degree, contrast-based analyses can  
331 be corrected for stochastic dependency by including the estimated covariance among-  
332 correlated effect sizes<sup>34,40</sup>. Another solution to stochastic-dependency is to use an  
333 ‘arm-based’ model. Arm-based models circumvent the calculation of pairwise effect  
334 sizes prior to fitting the model. Rather, one fits the sample statistics from individual  
335 groups as outcomes (i.e.,  $\ln\bar{x}$  and  $\ln s$  rather than  $\ln RR$  and  $\ln VR$ ) and uses a meta-  
336 regression model to estimate the difference between treatment conditions. IMAMV is  
337 compatible with both different corrections for stochastic dependency, and the vignette  
338 gives a worked example of an arm-based IMAMV applied to the diet-mixing dataset (see  
339 Supplementary Materials and Vignette).

340

341 Another common problem in eco-evolutionary meta-analyses is phylogenetic non-  
342 independence<sup>34,41</sup>, where we might expect more closely related taxa to display more

343 similar effect sizes. A solution, with which IMAMV is compatible, is to apply a  
344 phylogenetic meta-analysis. The vignette associated with this paper contains code for a  
345 phylogenetic IMAMV. The phylogenetic effects were accounted for by creating a  
346 phylogenetic covariance matrix for all species within each analysis *rotr* package <sup>42</sup>, and  
347 including that matrix as a term in the model e.g., as in <sup>27</sup>. We have implemented the  
348 phylogenetic IMAMV using the package *metafor*, but note that there are limits to the  
349 complexity of the IMAMV that can be fitted in this package. More complex models could  
350 be implemented in *brms* or *MCMCglmm* <sup>25</sup> (see supplementary materials and Vignette).  
351

## 352 Discussion

353 Here, we present a framework for the integrated meta-analysis of mean and variation  
354 effects (IMAMV). This approach allows the user to simultaneously meta-analyse effects  
355 on group means and variabilities, which previously necessitated two analyses. While  
356 the bivariate models presented here appear complex, the key terms from IMAMV can be  
357 interpreted equivalently to those coming from the univariate models of lnRR and lnCVR  
358 currently in use. What is more, the models themselves are very closely related to two  
359 analyses with which ecologists and evolutionary biologists may already be familiar. The  
360 first is the linear mixed-effects model (LMM) <sup>43,44</sup>; the most basic IMAMV in eqn. 16 has a  
361 structural similarity to a LMM containing a random-regression at a single-level. The  
362 second method with which IMAMV is similar is network meta-analysis (NMA). NMA is  
363 increasingly common in medical research <sup>45</sup>, but still emerging in ecology and evolution  
364 c.f., <sup>46</sup>. Through NMA one estimates the effects of different factors/treatments on an  
365 outcome of interest, even if those factors/treatments are not directly compared in

366 underlying literature; e.g., one may estimate the effects of B vs C, from studies  
367 comparing A vs B and A vs C through their common control treatment A. The IMAMV  
368 model in eqn. 16 is structurally comparable to NMA model <sup>47</sup>, but rather than fitting  
369 effect sizes from different treatments on the same outcomes, one fits mean and  
370 variance effect sizes from the same samples.

371

372 We have shown that IMAMV can be compatible with many of the tools that eco-  
373 evolutionary meta-analysts use to account for complex data structures (e.g.,  
374 hierarchical and phylogenetic non-independence) <sup>34</sup>. Additionally, the usual frameworks  
375 for reporting meta-analyses are transferable. For example, tools for visualisation of  
376 contrasts-based effect sizes, such as forest plots and orchard plots <sup>48,49</sup>, can be applied  
377 to lnRR and lnCVR. With regards to reporting heterogeneity statistics, the usual  
378 heterogeneity statistics, such as  $Q$  and  $I^2$ , are estimable. However, we urge users to also  
379 think about direct derivatives of the estimated variation itself, such as the prediction  
380 intervals e.g., in orchard plots; <sup>49</sup>, the ‘coefficient of heterogeneity’ and the closely  
381 related ‘M statistic’ <sup>32</sup>. These metrics convey a sense of the expected distribution of  
382 future effect sizes.

383

384 In addition to offering the convenience of a single analysis, IMAMV offers two explicit  
385 benefits over the two-model approach. The first is that the user gets an estimate of the  
386 correlation between effects on the mean and the variance. In some cases, this  
387 correlation itself may be of biological relevance. For example, correlations between  
388 effects on intra-genomic trait means and variances maybe indicative adaptation to a  
389 fluctuating environment through bet-hedging <sup>50</sup>. The second benefit of IMAMV (which

390 flows indirectly from the estimated correlation) is borrowing of strength. Through  
391 borrowing of strength IMAMV can supply more precise estimates of effects on  
392 variability, thus yielding increased power. As we demonstrate these benefits manifest  
393 where there are missing SDs in the dataset. The problem of missing SDs is pervasive in  
394 meta-analysis. One survey found around 70% of meta-analytic datasets in ecology and  
395 evolution contain missing SDs, with the rate of missingness in a given dataset affecting  
396 up to 30% of effect sizes<sup>38,51</sup>. Methods have been developed to deal with missing SD  
397 data reviewed in<sup>51</sup>. However, these methods are designed to estimate the sampling  
398 variance for mean-focussed effect sizes (e.g., lnRR and SMD) when SDs are missing and  
399 are not considered appropriate when the SD is focus of the point estimate (e.g., lnVR or  
400 lnCVR). As far as we can tell IMAMV is the first method proposed to help boost the  
401 power of variation-focussed analyses in the presence of missing SDs. Note that to gain  
402 this benefit of IMAMV the user must collect data on sample means from all studies,  
403 including those that do not report SD data. Put another way, counterintuitively missing  
404 SDs should not be considered an exclusion criteria for meta-analysis of the variation *via*  
405 IMAMV.

406

407 Biologists work hard to gather and curate their meta-analytic datasets. However, many  
408 of these datasets have not been used to their full potential by testing for effects on  
409 variability. This is particularly surprising in the eco-evolutionary space, where biological  
410 variability underpins core theoretical concepts e.g., niche breadth, and natural  
411 selection<sup>52</sup>. We hope that IMAMV will allow eco-evolutionary users of meta-analysis to  
412 conveniently test for the effects on both population means and within-population  
413 variability.

414

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418 **Author Contributions**

419 AMS and SN conceived the study. TD and AMS collected data. ML and YY contributed to

420 the development of the code. AMS write the first draft of the paper. All authors

421 contributed to the final draft and interpretation of results.

422

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561 **Tables**

562 **Table 1. Estimated parameters from different analyses of the  $\ln\text{RR}$  and  $\ln\text{CVR}$  including contrast-based integrated meta-analyses**  
563 **of mean and variation effects (IMAMV). CI = 95% confidence interval,  $\tau$ = heterogeneity.**

| Analysis                        | $\ln\text{RR}$ (CI)    | $\tau_{\ln\text{RR}}$ | $\ln\text{CVR}$ (CI) | $\tau_{\ln\text{CVR}}$ |
|---------------------------------|------------------------|-----------------------|----------------------|------------------------|
| Two-Model Analysis              | -0.30 (-0.37 to -0.22) | 0.68                  | 0.16 (0.09 to 0.22)  | 0.53                   |
| Contrast-Based IMAMV            | -0.30 (-0.37 to -0.22) | 0.67                  | 0.16 (0.09 to 0.22)  | 0.52                   |
| Multilevel Contrast-Based IMAMV | -0.31 (-0.43 to -0.20) | 0.69                  | 0.17 (0.06 to 0.28)  | 0.54                   |

564

565 **Table 2. Estimated parameters from two-model analyses and contrast-based integrated meta-analyses of mean and variation**

566 **effects (IMAMV) with 20% missing standard-deviation data. SE = standard error, CI = 95% confidence interval.**

| Analysis             | lnRR (CI)              | SE <sub>lnRR</sub> | lnCVR (CI)          | SE <sub>lnCVR</sub> |
|----------------------|------------------------|--------------------|---------------------|---------------------|
| Two-Model Analysis   | -0.32 (-0.40 to -0.24) | 0.040              | 0.18 (0.10 to 0.26) | 0.040               |
| Contrast-Based IMAMV | -0.32 (-0.40 to -0.24) | 0.040              | 0.18 (0.11 to 0.26) | 0.038               |

567

568

569 **Figures**

**A) Traditional Two-Model Analysis**

|         | Control |           |    | Treatment |           |    | Effect Sizes |      |                            |
|---------|---------|-----------|----|-----------|-----------|----|--------------|------|----------------------------|
|         | n       | $\bar{x}$ | SD | n         | $\bar{x}$ | SD | InRR         | InVR | $\lnCVR (= \lnVR - \lnRR)$ |
| Study 1 | 5       | 5         | 3  | 5         | 8         | 4  | 0.5          | 0.3  | -0.2                       |
| Study 2 | 8       | 8         | 4  | 8         | 13        | 10 | 0.5          | 0.9  | -0.4                       |
| Study 3 | 15      | 7         | NA | 15        | 5         | NA | -0.3         | NA   | NA                         |

- Two separate models.
- Correlation between mean and variation effects not estimated.
- Study 3 excluded from analysis of variation effects.

Univariate fit of mean effects.  
 $\mu_{\lnRR}$

Univariate fit of Variation effects.  
 $\mu_{\lnCVR}$

**B) IMAMV**

|         | Control |           |    | Treatment |           |    | Effect Sizes |      |
|---------|---------|-----------|----|-----------|-----------|----|--------------|------|
|         | n       | $\bar{x}$ | SD | n         | $\bar{x}$ | SD | y            | Stat |
| Study 1 | 5       | 5         | 3  | 5         | 8         | 4  | 0.5          | InRR |
| Study 2 | 8       | 8         | 4  | 8         | 13        | 10 | 0.5          | InRR |
| Study 3 | 15      | 7         | NA | 15        | 5         | NA | -0.3         | InRR |
| Study 1 | 5       | 5         | 3  | 5         | 8         | 4  | 0.3          | InVR |
| Study 2 | 8       | 8         | 4  | 8         | 13        | 10 | 0.9          | InVR |

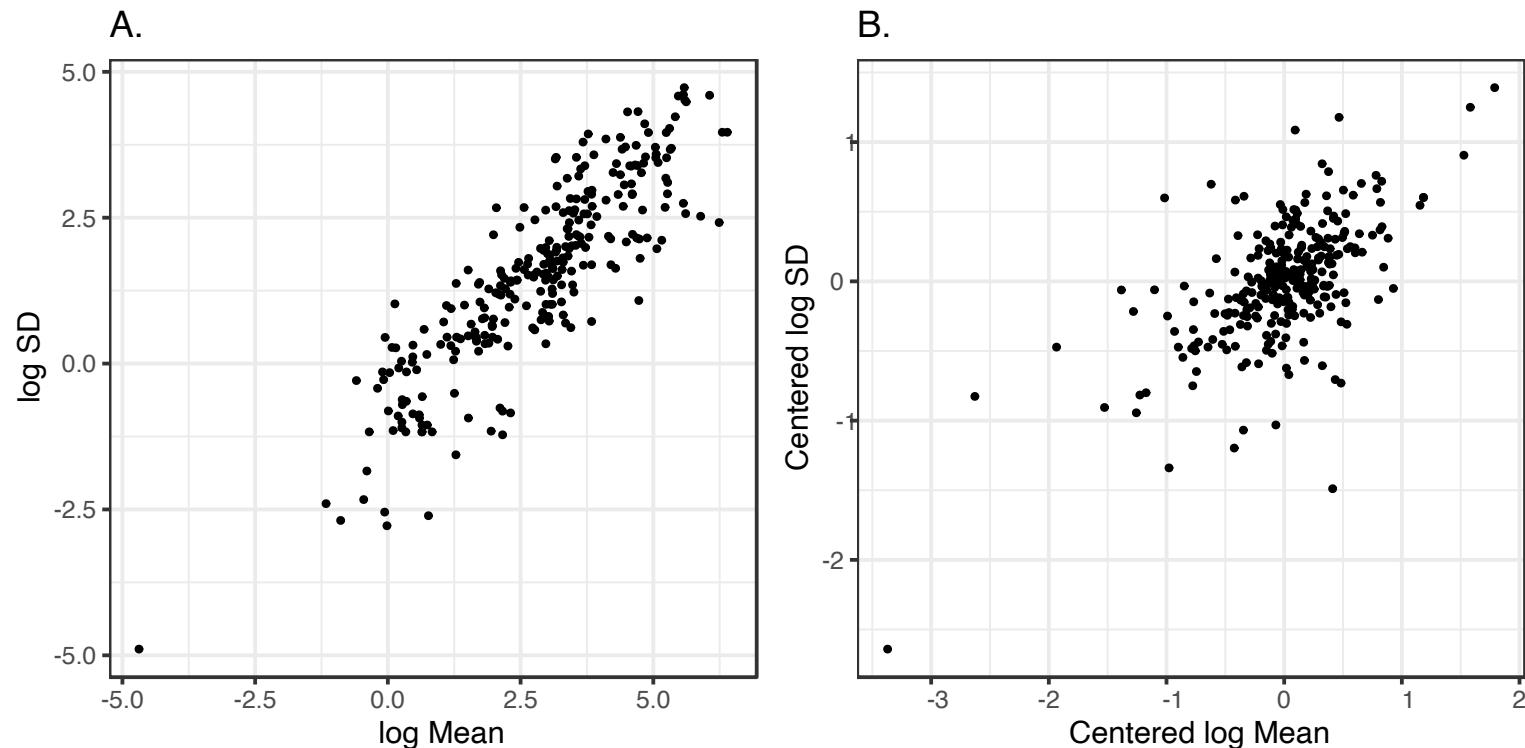
- One model.
- Correlation between mean and variation effects estimated.
- Borrowing of strength from study 3 InRR increases power to detect variation effects.

Pairwise Bivariate fit.  
 $\mu_{\lnRR} + \beta_{\lnVR - \lnRR} (\text{i.e.,} \lnCVR)$

570

571 **Figure 1. Hypothetical contrast of the current and proposed approach. A) the traditional method independently analyses effects**  
 572 **on the mean and variation, overlooking any correlations among effect types. B) IMAMV uses bivariate meta-analysis to analyse**  
 573 **mean and variation effects at the same time, thereby estimating any correlations and increasing strength for datasets with**  
 574 **missing variance values.**

575



576

577 **Figure 2. Association between log mean and log SD for reproductive data in the diet-mixing data set. In A) the data are in reported**  
**578 units. In B) the data have been mean-centred within each experiment.**

579

# Supplement Information for the Integrated Meta-Analysis of Mean and Variation Effects in Ecology and Evolution

## Arm-Based IMAMV

As discussed in the main text, contrast-based analyses is that they can induce an additional layer of non-independence by calculating multiple pair-wise effect sizes using the same control-group data; sometimes termed ‘stochastic dependency’ (1-3). Arm-based models are free from this issue as one fits the sample statistics from individual groups as outcomes (i.e.,  $\ln\bar{x}$  and  $\ln s$  rather than  $\ln RR$  and  $\ln CV$ ) and uses a meta-regression model to estimate the difference between treatment conditions. An arm-based multi-level IMAMV can be written as:

$$y_{ijk} = \alpha + a_k + e_{jk} + (\beta_{\ln s} + b_k + f_{jk}) \times S_{ijk} + (\beta_E + c_k + g_{jk}) \times T_{ijk} + (\beta_{\ln s \Delta E} + d_k + h_{jk}) \times U_{ik} + m_{ik}, \quad (S1)$$

$$\begin{bmatrix} a_k \\ \vdots \\ d_k \end{bmatrix} \sim N \left( \begin{bmatrix} 0 \\ \vdots \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma_a^2 & \cdots & \rho_{ad}\sigma_a\sigma_d \\ \vdots & \ddots & \vdots \\ \rho_{ad}\sigma_a\sigma_d & \cdots & \sigma_d^2 \end{bmatrix} \right), \quad (S2)$$

$$\begin{bmatrix} e_{jk} \\ \vdots \\ h_{jk} \end{bmatrix} \sim N \left( \begin{bmatrix} 0 \\ \vdots \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma_e^2 & \cdots & \rho_{eh}\sigma_e\sigma_h \\ \vdots & \ddots & \vdots \\ \rho_{eh}\sigma_e\sigma_h & \cdots & \sigma_h^2 \end{bmatrix} \right), \quad (S3)$$

$$m_{ik} \sim N(0, \nu_{y_{ik}}), \quad (S4)$$

where,  $y_{ijk}$  is the  $i$ th sample statistic (i.e.,  $i = 1 = \ln\bar{x}$ ,  $i = 2 = \ln s$ ) of the  $j$ th sample in the  $k$ th experiment. Here, the  $\alpha$  and  $\beta_{\ln s}$  are interpretable as meta-analytic estimates of the log mean and log CV (i.e.,  $\beta_{\ln s} = \mu_{\ln s - \ln\bar{x}} = \mu_{\ln CV}$ ; eqn. 9) under the control condition, and  $S_{ijk}$  is a dummy predictor coded as 0 if  $y_{ijk}$  is a sample  $\ln\bar{x}$  and 1 if  $y_{ijk}$  is  $\ln s$ .  $\beta_E$  is a meta-analytic estimate of difference in  $\ln\bar{x}$  in the experimental and control conditions and can thus be equivalent to  $\ln RR$  (i.e.,  $\beta_E = \mu_{\ln\bar{x}_E - \ln\bar{x}_C} = \mu_{\ln CV}$ ; eqn. 3), and  $T_{ijk}$  is a dummy predictor coded as 0 if  $y_{ijk}$  is from a control condition and 1 for an experimental group.  $\beta_{\ln s \Delta E}$  is an interaction term giving the difference in  $\beta_{\ln s}$  under the experimental and control conditions, and is therefore equivalent to  $\ln CV$  ( $\beta_{\ln s \Delta E} = \ln CV_E - \ln CV_C = \ln CV$ ; eqn. 11), with  $U_{ik}$  as a third dummy predictor coded as 1 if  $y_{ijk}$  is an estimate of  $\ln s$  under the experimental condition, and 0 otherwise.  $a_k$  through  $d_k$  give deviations of the true values of each group from estimated parameters, and  $e_{jk}$  through  $h_{jk}$  give the within-sample deviations. Finally,  $m_{ik}$  gives the deviation of the sample from the group-specific effect, which has a SD estimated as  $\nu_{y_{ik}}$  (eqn. 2 if  $y_{ijk}$  is  $\ln\bar{x}$  and eqn. 6 for  $\ln s$ ). The key variance components for meta-analytic interpretation are  $\sigma_c$  and  $\sigma_d$ , which give the among-experiment SD in  $\ln RR$  and  $\ln CV$ , while the within-experiment SDs are  $\sigma_g$  and  $\sigma_h$ ;  $\tau_{\ln RR}^2 = \sigma_c^2 + \sigma_d^2$  and  $\tau_{\ln CV}^2 = \sigma_g^2 + \sigma_h^2$ .

We have applied the arm-based IMAMV shown in eqn. S1 to the diet-mixing data using *metafor*. The point estimates and statistical significance of the overall effects of diet mixing on the log mean and log CV of traits are nearly identical using all methods (Table

S1). However, the arm-based estimates of heterogeneity are lower than those estimated by the contrast-based models in all cases but one. The most likely explanation for this difference is that the contrast-based model has treated a relatively large number of dependent effect sizes as independent, thereby inflating the variation among effects.

One can also include moderators in an arm-based IMAMV. We have not written the equation in full here, but the key terms of interest added to eqn. S1 would be:  $\beta_{\text{Mod}\Delta E}$ , which is an interaction interpretable as the difference in  $\text{LnRR}$  between levels of the moderator; and  $\beta_{\text{Mod}\Delta \text{Ins}\Delta E}$ , which is a three-way interaction that is interpretable as the difference in  $\text{LnCVR}$  between levels of the moderator.

## Dual Formula Implementation of Integrated Meta-Analysis of Mean and Variation Effects (IMAMV)

In the main text we have implemented IMAMV models by simultaneously fitting statistics related to the log group means and SDs as a single response and using a moderator variable or fixed effect with appropriate error structure (e.g., a random-slope) to induce a bivariate model. The advantage of this approach is that these models can be implemented in any software that can fit multi-level meta regression, such as the popular R package *metafor*.

An alternative offered by some software is to implement a bivariate model using a ‘dual-formula’ specification. One such example is the Bayesian R package *brms* (4), which offers dual-formula model specification.

A dual formula specification for a simple random-effects contrast-based IMAMV for the  $\text{LnRR}$  and  $\text{LnCVR}$  is:

$$\begin{pmatrix} \text{LnRR}_i \\ \text{LnCVR}_i \end{pmatrix} = \begin{pmatrix} \theta_{\text{LnRR}} + a_i + p_i \\ \theta_{\text{LnCVR}} + c_i + q_i \end{pmatrix}, \quad (\text{S5})$$

$$\begin{pmatrix} a_i \\ c_i \end{pmatrix} \sim N \left( \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_a^2 & \sigma_{ac} \\ \sigma_{ac} & \sigma_c^2 \end{pmatrix} \right), \quad (\text{S6})$$

$$\begin{pmatrix} p_i \\ q_i \end{pmatrix} \sim N \left( \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \nu_{\text{LnRR}_i} \\ \nu_{\text{LnCVR}_i} \end{pmatrix} \right), \quad (\text{S7})$$

where  $\text{LnRR}_i$  and  $\text{LnCVR}_i$  are the effect sizes in the  $i$ th study as estimated by eqns 3 and 11 in the main text,  $\theta_{\text{LnRR}}$  and  $\theta_{\text{LnCVR}}$  are the meta-analytic overall effects as estimated by the model,  $a_i$  and  $c_i$  give the deviation of the population effect from  $\theta_{\text{LnRR}}$  and  $\theta_{\text{LnCVR}}$  in the  $i$ th study  $p_i$  and  $q_i$  give the deviations of the sampled effects from the population effects due to sampling in the  $i$ th study. Both  $a_i$  and  $c_i$  are assumed to be multi-variate normally distributed as shown in eqn. S2, where  $\sigma_a^2$  and  $\sigma_c^2$  give the among-study heterogeneity in  $\text{LnRR}$  and  $\text{LnCVR}$ , respectively, as estimated by the model, and  $\sigma_{ac}$  gives the covariance between effects at the level of the study. Also  $p_i$  and  $q_i$  are assumed to

be normally distributed as per eqn. S3, where the sampling variances are estimated via eqns 4 and 12 in the main text.

An arm-based IMAMV may also be implemented in a dual formula context as:

$$\begin{pmatrix} \ln\bar{x}_{ij} \\ \ln CV_{ij} \end{pmatrix} = \begin{pmatrix} \alpha_{\ln\bar{x}} + a_i + (\beta_{\ln\bar{x}} + b_i) \times T_{ij} + p_{ij} \\ \alpha_{\ln CV} + c_i + (\beta_{\ln CV} + d_i) \times T_{ij} + q_{ij} \end{pmatrix}, \quad (S8)$$

$$\begin{pmatrix} a_i \\ \vdots \\ d_i \end{pmatrix} \sim N \left( \begin{pmatrix} 0 \\ \vdots \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_a^2 & \dots & \sigma_{ad} \\ \vdots & \ddots & \vdots \\ \sigma_{da} & \dots & \sigma_d^2 \end{pmatrix} \right), \quad (S9)$$

$$\begin{pmatrix} p_{ij} \\ q_{ij} \end{pmatrix} \sim N \left( \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \nu_{\ln\bar{x}_{ij}} \\ \nu_{\ln CV_{ij}} \end{pmatrix} \right), \quad (S10)$$

where  $\ln\bar{x}_{ij}$  and  $\ln CV_{ij}$  are the log mean and log CV from the  $j$ th group (i.e.,  $j = 1, 2$ , where 1 = control and 2 = treatment) in the  $i$ th study as estimated by eqns 1 and 9 in the main text,  $\alpha_{\ln\bar{x}}$  and  $\alpha_{\ln CV}$  are the meta-analytic overall estimates of  $\ln x$  and  $\ln CV$  in the control condition, and  $\beta_{\ln\bar{x}}$  and  $\beta_{\ln CV}$  are the effects of the treatment on  $\ln x$  and  $\ln CV$ .  $I_{ij}$  is a dummy predictor, coded as 0 where  $\ln\bar{x}_{ij}$  and  $\ln s_{ij}$  is from a control group and 1 otherwise.  $a_i$  and  $c_i$  give the deviation of the population effect from  $\alpha_{\ln\bar{x}}$  and  $\alpha_{\ln CV}$  in the  $i$ th study, while  $b_i$  and  $d_i$  give the deviation of the population effect from  $\beta_{\ln\bar{x}}$  and  $\beta_{\ln CV}$  in the  $i$ th study.  $p_{ij}$  and  $q_{ij}$  give the deviations of the sampled statistics from the population statistic due to sampling in the  $i$ th study for the  $j$ th group.  $a_i$  through  $d_i$  are assumed to be multi-variate normally distributed as shown in eqn. S5, where  $\sigma_a^2$  through  $\sigma_d^2$  give the among-study heterogeneities, with  $\sigma_b^2$  through  $\sigma_d^2$  respectively, being interpretable as the estimated heterogeneity in the effect size. Also,  $p_{ij}$  and  $q_{ij}$  are assumed to be normally distributed as per eqn. S6, where the sampling variances are estimated via eqns 2 and 10 in the main text.

## Table S1

**Example of full reporting of all terms from an arm-based integrated meta-analysis of mean and variation effects (IMAMV). Results comes from the multi-level arm-based IMAMV in the diet-mixing dataset. For each term we report the interpretation and equivalent term in eqn. 24 in the main text. For fixed effects we also include 95% confidence intervals (CIs).**

| Fixed Effects  |                          |       |                |
|--|--------------------------|-------|----------------|
| Interpretation   | Eqn. 24                  | Est.  | CI             |
| $\ln\bar{x}_{\text{Control}}$  | $\alpha$                 | 2.92  | 2.52 to 3.32   |
| $(\ln s - \ln\bar{x})_{\text{Control}} = \ln CV_{\text{Control}}$                      | $\beta_{\ln s}$          | -1.40 | -0.32 to -0.19 |
| $\ln\bar{x}_{\text{Exp.}} - \ln\bar{x}_{\text{Control}} = \ln RR$                      | $\beta_E$                | 0.34  | -0.47 to -0.20 |
| $(\ln s - \ln\bar{x})_{\text{Exp.}} - (\ln s - \ln\bar{x})_{\text{Control}} = \ln CVR$ | $\beta_{\ln s \Delta E}$ | 0.19  | 0.07 to 0.30   |
| Random Effects / Correlations  |                          |       |                |
| Interpretation   | Eqn. 24                  | Est.  |                |
| Among-study variance in $\alpha$   | $\sigma_a^2$             | 2.72  |                |
| Among-study variance in $\beta_{\ln s}$  | $\sigma_b^2$             | 0.50  |                |
| Among-study variance in $\beta_E$  | $\sigma_c^2$             | 0.03  |                |
| Among-study variance in $\beta_{\ln s \Delta E}$                                       | $\sigma_d^2$             | 0.04  |                |
| Among-study correlation between $\alpha$ and $\beta_{\ln s}$                           | $\rho_{ab}$              | -0.13 |                |
| Among-study correlation between $\alpha$ and $\beta_E$                                 | $\rho_{ac}$              | 0.83  |                |
| Among-study correlation between $\alpha$ and $\beta_{\ln s \Delta E}$                  | $\rho_{ad}$              | -0.57 |                |
| Among-study correlation between $\beta_{\ln s}$ and $\beta_E$                          | $\rho_{bc}$              | -0.66 |                |
| Among-study correlation between $\beta_{\ln s}$ and $\beta_{\ln s \Delta E}$           | $\rho_{bd}$              | -0.10 |                |
| Among-study correlation between $\beta_E$ and $\beta_{\ln s \Delta E}$                 | $\rho_{cd}$              | -0.41 |                |
| Within-study variance in $\alpha$  | $\sigma_e^2$             | 0.14  |                |
| Within-study variance in $\beta_{\ln s}$   | $\sigma_f^2$             | 0.08  |                |
| Within-study variance in $\beta_E$   | $\sigma_g^2$             | 0.42  |                |
| Within-study variance in $\beta_{\ln s \Delta E}$                                      | $\sigma_h^2$             | 0.09  |                |
| Within-study correlation between $\alpha$ and $\beta_{\ln s}$                          | $\rho_{ef}$              | -0.39 |                |
| Within-study correlation between $\alpha$ and $\beta_E$                                | $\rho_{eg}$              | -0.26 |                |
| Within-study correlation between $\alpha$ and $\beta_{\ln s \Delta E}$                 | $\rho_{eh}$              | 0.38  |                |
| Within-study correlation between $\beta_{\ln s}$ and $\beta_E$                         | $\rho_{fg}$              | -0.31 |                |
| Within-study correlation between $\beta_{\ln s}$ and $\beta_{\ln s \Delta E}$          | $\rho_{fh}$              | -0.11 |                |
| Within-study correlation between $\beta_E$ and $\beta_{\ln s \Delta E}$                | $\rho_{gh}$              | -0.73 |                |

## References

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# Integrated Meta-Analysis of Mean and Variation Effects (IMAMV) Vignette

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## Overview

This vignette is written to accompany the paper “Methods for the Integrated Meta-analysis of Mean and Variation Effects in Ecology and Evolution”.

Integrated meta-analysis of mean and variation effects (IMAMV) is a proposed analytical framework for simultaneously meta-analysing effects of treatments/groupings on sample means and sample variation. The method proposes to use a bivariate meta-analysis that analyses mean effects via the log ratio of sample means ( $\ln RR$ ), and variation via the log variance ratio ( $\ln VR$ ) and log coefficient of variation ratio ( $\ln CVR$ ). The method exploits the fact that  $\ln VR - \ln RR = \ln CVR$ , and that this difference is estimable via meta-regression.

This vignette works through three different approaches to the meta-analysis of variation: (1) the standard two-model approach, which uses separate meta-analyses of the  $\ln RR$  and  $\ln CVR$ , (2) contrast-based IMAMV, and (3) arm-based IMAMV. Versions of each analysis that account for non-independence and test for moderator variables are explored, as are phylogenetic models. Mathematical descriptions of the models are made available in the accompanying paper.

As a working example, we study a meta-analytic dataset of experiments on diet-mixing. The models here are implemented in `metafor` and `brms`, both of which are often used for meta-analysis in the eco-evo fields. However, they can be implemented in any package that allows for meta-regression with random-effects, such as `MCMCglmm`.

## Dataset

Diet mixing experiments test for the effects of single- vs mixed-food diets on animal performance. We have compiled a database of diet-mixing studies looking at reproductive data from 282 groups of animals in 69 experiments. The dataset was compiled by searching and updating the dataset analysed in “An Overlooked Consequence of Dietary Mixing: A Varied Diet Reduces Interindividual Variance in Fitness. Am. Nat. 2015. 186, 649-659. DOI: 10.1086/683182”. The data contains several layers of non-independence, including that most experiments contain more than two treatment groups that can be justifiably contrasted with one another (i.e., more than two effect sizes per experiment).

For the sake of this vignette, effects sizes have already been calculated and the data processed in different ways for the different variants of the analyses presented. Effect sizes were calculated using the formulas in the main text of the accompanying paper. There are four different data formats: contrast- vs arm-based, and each in long- vs wide-format. The processed dataframes have been stored in a list in the Rdata file `data_list.Rda`. In any given analysis a user of IMAMV would only need to format their data in one of these ways, depending on the analysis of choice.

Finally, the `data_list` object also contains a phylogenetic covariance matrix, used in the models toward the end of this vignette. The full contents of the list is shown here.

```
load("data_list.Rda")
names(data_list)

## [1] "arm_wide"      "arm_long"       "contrast_wide" "contrast_long"
## [5] "phylo"
```

## Analysis 1: The Two-Model Approach

The conventional approach to meta-analysis of variation has most often used contrast-based effect sizes. The effects on the mean being estimated via the `lnRR`, then the effects on the variation using a separate model applied to the `lnCVR` (or in some instances the `lnVR`).

For the diet-mixing data, we have pre-processed data in format amenable to these analyses. It can be accessed in the data list via `data_list$contrast_wide`.

```
head(data_list$contrast_wide)
```

```
##   Article.ID Author           Journal Year Consumer.Sp
## 1          art1 Aquaculture Research 2015 Parvocalanus_crassirostris
## 2          art1 Aquaculture Research 2015 Parvocalanus_crassirostris
## 3          art1 Aquaculture Research 2015 Parvocalanus_crassirostris
## 4          art1 Aquaculture Research 2015 Parvocalanus_crassirostris
## 5          art1 Aquaculture Research 2015 Parvocalanus_crassirostris
## 6          art1 Aquaculture Research 2015 Parvocalanus_crassirostris
##   Habitat Experiment.ID Data.ID      lnRR      v_lnRR      lnVR      v_lnVR
## 1  Marine           c1  dat1  0.9387648  0.039645511 -0.7375989  0.1946240
## 2  Marine           c1  dat2  0.3849543  0.047678185 -0.3022809  0.1946240
## 3  Marine           c1  dat3  0.7386473  0.039141741 -1.1895841  0.1946240
## 4  Marine           c1  dat4 -0.3069166  0.003327347 -0.5465437  0.1583058
## 5  Marine           c1  dat5 -0.8607272  0.011360020 -0.1112256  0.1583058
## 6  Marine           c1  dat6 -0.5070341  0.002823576 -0.9985288  0.1583058
##   lnCVR      v_lnCVR
## 1 -1.6763638  0.2342695
## 2 -0.6872352  0.2423021
## 3 -1.9282314  0.2337657
## 4 -0.2396271  0.1616331
## 5  0.7495015  0.1696658
## 6 -0.4914947  0.1611294
```

```
dim(data_list$contrast_wide)
```

```
## [1] 331 14
```

The most relevant columns for now are:

- `lnRR` gives the effect of a single-food diet relative to a mixed-food diet on the sample mean.
- `lnCVR` gives the effect of a single-food diet relative to a mixed-food diet on the sample CV.
- `v_lnRR` gives the sampling variances for the `lnRR`.
- `v_lnCVR` gives the sampling variances for the `lnCVR`.
- `Data.ID` is a unit-level variable with 1:n effect sizes.

Other columns give meta-variables related to the article and species associated with each effect size.

A pair of random-effects meta-analyses using the package `metafor` can be specified as follows.

```
library(metafor)
```

```
rma.mv(yi = lnRR, V = v_lnRR, random = list(~1|Data.ID), data = data_list$contrast_wide)
```

```
##  
## Multivariate Meta-Analysis Model (k = 331; method: REML)  
##  
## Variance Components:  
##  
##           estim     sqrt  nlevels  fixed  factor  
## sigma^2    0.4564   0.6755     331     no  Data.ID  
##  
## Test for Heterogeneity:  
## Q(df = 330) = 23693.7200, p-val < .0001  
##  
## Model Results:  
##  
##           estimate      se     zval    pval    ci.lb    ci.ub  
## -0.2961  0.0381  -7.7721  <.0001  -0.3707  -0.2214  ***  
##  
## ---  
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
rma.mv(yi = lnCVR, V = v_lnCVR, random = list(~1|Data.ID), data = data_list$contrast_wide)
```

```

## 
## Multivariate Meta-Analysis Model (k = 331; method: REML)
## 
## Variance Components:
## 
##           estim     sqrt  nlevels  fixed   factor
## sigma^2    0.2798  0.5290     331     no  Data.ID
## 
## Test for Heterogeneity:
## Q(df = 330) = 1561.2967, p-val < .0001
## 
## Model Results:
## 
## estimate     se     zval   pval   ci.lb   ci.ub
## 0.1590  0.0332  4.7826  <.0001  0.0938  0.2241  ***
## 
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

The model estimates give a negative lnRR ( estimate =  $-0.2961$  ), which is statistically significant (i.e., the CI does not span 0). This estimate suggests that single food diets decrease mean reproductive function to around 74% of that on mixed-diets (i.e.,  $\exp(-0.2961) = 0.7437$  ). However, there is a positive lnCVR ( estimate =  $0.1590$  ), suggesting single food diets increase the CV by around 17% (i.e.,  $\exp(0.1590) = 1.1723$  ). For lnRR the heterogeneity is  $0.6755$  , while that for lnCVR is  $0.5290$  , and in both cases this can be considered substantial (i.e.,  $\sqrt(\sigma^2) > \text{abs}(\text{estimate})$  )

## Analysis 2: Contrast-Based IMAMV

IMAMV is an alternative to implementing two separate analyses. Rather a bivariate model is fitted to both the lnRR and lnVR data. The model uses a meta-regression (similar to a ‘random-regression’) to estimate paired differences between lnVR and lnRR from the same samples, thus yielding an estimate of lnCVR.

The data for a contrast based IMAMV are effectively the same as those for the two-model analysis above, but in long format. This means that effect sizes of different types (i.e., lnRR and lnVR) are mixed in the same column, with type identified by a dummy variable.

In the case of the diet-mixing dataset, we have formatted these data and they are available in the data list as follows.

```
head(data_list$contrast_long)
```

```

##          yi      vi stat Experiment.ID Data.ID          Consumer.Sp
## 1  0.9387648 0.039645511 lnRR          c1    dat1 Parvocalanus_crassirostris
## 2  0.3849543 0.047678185 lnRR          c1    dat2 Parvocalanus_crassirostris
## 3  0.7386473 0.039141741 lnRR          c1    dat3 Parvocalanus_crassirostris
## 4 -0.3069166 0.003327347 lnRR          c1    dat4 Parvocalanus_crassirostris
## 5 -0.8607272 0.011360020 lnRR          c1    dat5 Parvocalanus_crassirostris
## 6 -0.5070341 0.002823576 lnRR          c1    dat6 Parvocalanus_crassirostris
##   Habitat
## 1  Marine
## 2  Marine
## 3  Marine
## 4  Marine
## 5  Marine
## 6  Marine

```

```
dim(data_list$contrast_long)
```

```
## [1] 662    7
```

The key columns for analysis are:

- `yi` contains a mix of lnRR and lnVR data.
- `vi` is the associated sampling variances.
- `stat` is a dummy variable indicating whether the row contains an instance of lnRR or lnVR.
- `Data.ID` indicates those lnRR and lnVR that are calculated from the same pair of samples.

We can implement a contrast-based IMAMV in `metafor` as follows.

```
rma.mv(yi=yi, V=vi, mods=~stat, random=list(~stat|Data.ID), struct="GEN", data = data_list$contrast_long)
```

```

## 
## Multivariate Meta-Analysis Model (k = 662; method: REML)
## 
## Variance Components:
## 
## outer factor: Data.ID (nlvls = 331)
## inner term: ~stat (nlvls = 2)
## 
##          estim   sqrt  fixed  rho:  intr      stVR
## intrcpt  0.4504  0.6711    no       - -0.5805
## statlnVR  0.2751  0.5245    no       no      -
## 
## Test for Residual Heterogeneity:
## QE(df = 660) = 26176.4495, p-val < .0001
## 
## Test of Moderators (coefficient 2):
## QM(df = 1) = 22.8889, p-val < .0001
## 
## Model Results:
## 
##          estimate      se     zval   pval    ci.lb    ci.ub
## intrcpt   -0.2940  0.0378 -7.7757 <.0001  -0.3681  -0.2199 *** 
## statlnVR   0.1574  0.0329  4.7842 <.0001   0.0929   0.2219 *** 
## 
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

The estimates for the effect of diet mixing on the mean, as quantified by `lnRR`, are given as the `intrcpt`. The effect on variation, as quantified by `lnCVR`, are given as `statlnVR`. The overall effects are almost identical to that estimated by the two-model analysis; here we have  $\text{lnRR} = -0.2940$  and  $\text{lnCVR} = 0.1574$ , and again the CIs exclude 0. The total heterogeneity estimates are also nearly identical to those from a two-model analysis. For `lnRR` this is `0.6711` and for `lnCVR` `0.5245`.

We have fitted `lnVR`, so how is the model output is interpretable as `lnCVR`?

The model here has fitted the `stat` dummy variable in a meta-regression, estimating the difference in magnitude between effect sizes that are coded as `lnVR` and those coded as `lnRR`, which is another way of estimating `lnCVR`;  $\text{lnVR} - \text{lnRR} = \text{lnCVR}$ . Importantly, when we specified the model, we ensured that the `lnVR`-`lnRR` differences were estimated at the level of the individual sample pairs. The argument `struct = "GEN"` specifies a model that is similar to 'random-regression' mixed effects model, estimating the slopes for `lnVR`-`lnRR` at the level of individual sample pairs (i.e., via `~stat | Data.ID`).

The contrast-based IMAMV has estimated similar to terms to those from the two-model analysis, but also yields additional estimates of the correlation between `lnRR` and `lnCVR`; `stVR = -0.5805`. One can interpret this as more negative estimates of `lnRR` are associated with more positive effects of `lnCVR`. Put another way, the bigger the reductive effect of the diet on mean reproductive function, the more variation it generates.

## Non-Independence and Multi-Level IMAMV

This basic random-effects model has assumed independence of effect sizes. However, it is common in eco-evolutionary meta-analyses for the same experiment to generate multiple effects sizes, meaning those effects from the same experiment are non-independent. Multi-level models can be used to account for this non-independence by clustering effect sizes based on some level of grouping.

In the diet-mixing dataset, the column `Experiment.ID` codes each effect size by its experiment of origin. This can be added to our contrast-based IMAMV under the `random` argument to create a multi-level model as follows.

```
rma.mv(yi=yi, V=vi, mods=~stat, random=list(~stat|Experiment.ID, ~stat|Data.ID), stru
ct="GEN", data = data_list$contrast_long)

## 
## Multivariate Meta-Analysis Model (k = 662; method: REML)
## 
## Variance Components:
## 
## outer factor: Experiment.ID (nlvls = 69)
## inner term: ~stat (nlvls = 2)
## 
##          estim   sqrt  fixed  rho:  intr      stVR
## intrcpt  0.1152  0.3395    no       - -0.3896
## statlnVR  0.1402  0.3745    no       no      -
## 
## outer factor: Data.ID (nlvls = 331)
## inner term: ~stat (nlvls = 2)
## 
##          estim   sqrt  fixed  phi:  intr      stVR
## intrcpt  0.3570  0.5975    no       - -0.6992
## statlnVR  0.1491  0.3862    no       no      -
## 
## Test for Residual Heterogeneity:
## QE(df = 660) = 26176.4495, p-val < .0001
## 
## Test of Moderators (coefficient 2):
## QM(df = 1) = 8.7982, p-val = 0.0030
## 
## Model Results:
## 
##          estimate      se     zval    pval    ci.lb    ci.ub
## intrcpt -0.3145  0.0596 -5.2734 <.0001 -0.4314 -0.1976 ***
## statlnVR  0.1706  0.0575  2.9662  0.0030  0.0579  0.2833 **
## 
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The sign and statistical significance of the estimates in the multi-level models match those in the random-effects model, though the magnitude of the effects are slightly larger (i.e., deviate more from 0) and precision slightly lower (i.e., the CIs are wider). Here the heterogeneity has been partitioned between the among- and within-experiment levels (i.e., `Experiment.ID` vs `Data.ID`). The total estimated heterogeneity can be calculated as the square root of the sum of the `sigma^2` estimates from the two levels. For `InRR` this is `sqrt(0.1152 + 0.3570) = 0.6872` and for `InCVR` it is `sqrt(0.1402 + 0.1491) = 0.5379`, largely matching the estimates from the random-effects model above.

## Meta-Regression in Contrast-Based IMAMV

Moderator variables, which might explain heterogeneity in effects, can be included in IMAMV. In the diet-mixing dataset, for example, we have coded effect sizes by whether the focal species is terrestrial vs marine dwelling in the column `Habitat`.

In `metafor` we can include the moderator by specifying it in interaction with the `stat` variable in the `mods` argument.

```
rma.mv(yi=yi, V=vi, mods=~stat + Habitat + stat:Habitat, random=list(~stat|Experiment.ID, ~stat|Data.ID), struct="GEN", data = data_list$contrast_long)
```

```
##
## Multivariate Meta-Analysis Model (k = 662; method: REML)
##
## Variance Components:
##
## outer factor: Experiment.ID (nlvls = 69)
## inner term: ~stat (nlvls = 2)
##
##          estim   sqrt  fixed  rho:  intr      stVR
## intrcpt  0.1170  0.3421    no      - -0.3591
## statlnVR  0.1383  0.3720    no      no      -
##
## outer factor: Data.ID (nlvls = 331)
## inner term: ~stat (nlvls = 2)
##
##          estim   sqrt  fixed  phi:  intr      stVR
## intrcpt  0.3532  0.5943    no      - -0.6984
## statlnVR  0.1490  0.3860    no      no      -
##
## Test for Residual Heterogeneity:
## QE(df = 658) = 26171.7780, p-val < .0001
##
## Test of Moderators (coefficients 2:4):
## QM(df = 3) = 12.7709, p-val = 0.0052
##
## Model Results:
##
##          estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt      -0.1910  0.0867 -2.2014  0.0277 -0.3610  -0.0209  *
## statlnVR       0.1055  0.0857  1.2302  0.2186 -0.0626  0.2735
## HabitatTerrestrial -0.2361  0.1197 -1.9732  0.0485 -0.4707 -0.0016  *
## statlnVR:HabitatTerrestrial  0.1248  0.1153  1.0825  0.2790 -0.1011  0.3507
##          ci.ub
## intrcpt      -0.0209  *
## statlnVR       0.2735
## HabitatTerrestrial -0.0016  *
## statlnVR:HabitatTerrestrial  0.3507
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

In the meta-regression the marine category has been fitted as the reference group, and so the different estimates can be interpreted as follows.

- `intrcpt = -0.1910` is the lnRR in marine animals.
- `statlnVR = 0.1055` is the lnCVR in marine animals.

- `HabitatTerrestrial = -0.2361` gives the difference in `lnRR` between terrestrial and marine organisms. The estimate is negative and statistically significant, suggesting that single-food diets reduce the mean reproductive function in terrestrial more than in marine habitats.
- `statlnVR:HabitatTerrestrial = 0.1248` is the interaction between the `stat` term and the `Habitat` moderator. Although it is an interaction it can quite straightforwardly be interpreted as the difference in `lnCVR` between habitats. While the estimate is positive, suggesting a larger effect of the diet on the CV in the terrestrial habitat, it is non-significant.

## Analysis 3: Arm-Based IMAMV

It is common for contrast-based analyses to contain an additional layer of non-independence that arises when two effect sizes are based on the same control sample, sometimes termed ‘stochastic dependency’. In the diet-mixing dataset, for instance, we calculated all pair-wise effect sizes within the same experiment. Therefore, two effect sizes that compare different single-food treatments to the same mixed-food treatment are correlated.

Stochastic dependency arises because contrast-based models calculate effect-sizes prior to model fitting. Arm-based models circumvent this non-independence by fitting the sample statistic from each group as the outcome, and using the model to estimate differences between treatment groups.

For an arm-based analysis the individual sample log means and log SDs or log CVs for each group are fitted, and a dummy variable specifies, which treatment the group was exposed to. We have formatted the diet-mixing data this way in the data list here.

```
head(data_list$arm_wide)
```

```
##   Article.ID Author          Journal Year Consumer.Sp
## 1      art1 Alajmi Aquaculture Research 2015 Parvocalanus_crassirostris
## 2      art1 Alajmi Aquaculture Research 2015 Parvocalanus_crassirostris
## 3      art1 Alajmi Aquaculture Research 2015 Parvocalanus_crassirostris
## 4      art1 Alajmi Aquaculture Research 2015 Parvocalanus_crassirostris
## 5      art1 Alajmi Aquaculture Research 2015 Parvocalanus_crassirostris
## 6      art1 Alajmi Aquaculture Research 2015 Parvocalanus_crassirostris
##   Habitat Experiment.ID      mean n      sd treat      lnX      v_lnX
## 1  Marine             c1 89.03226 5 7.096774 single 4.489634 0.0012715488
## 2  Marine             c1 50.96774 5 10.967742 single 3.935824 0.0093042225
## 3  Marine             c1 72.90323 5 4.516129 single 4.289517 0.0007677783
## 4  Marine             c1 34.19355 5 14.838710     mix 3.550869 0.0383739623
## 5  Marine             c1 120.96774 5 12.258065     mix 4.796551 0.0020557977
## 6  Marine             c1 19.35484 5 6.451613     mix 2.974054 0.0224691358
##   lnSD v_lnSD      lnCV      v_lnCV Data.ID
## 1 2.084640 0.15625 -2.4049938 0.1575215     dat1
## 2 2.519958 0.15625 -1.4158652 0.1655542     dat2
## 3 1.632655 0.15625 -2.6568614 0.1570178     dat3
## 4 2.822239 0.15625 -0.7286300 0.1946240     dat4
## 5 2.631184 0.15625 -2.1653667 0.1583058     dat5
## 6 1.989330 0.15625 -0.9847234 0.1787191     dat6
```

```
dim(data_list$arm_wide)
```

```
## [1] 282 18
```

Each row contains the sample statistics from an individual group of animals, with the variable `treat` specifying whether the group was exposed to a single- or mixed-food diet.

A very basic arm-based analysis of the mean effects using the `lnX` and `v_lnX` data can be specified in `metafor` as here.

```
rma.mv(yi = lnX, V = v_lnX, mods=~treat, random = list(~treat|Experiment.ID, ~treat|Data.ID), struct="GEN", data = data_list$arm_wide)
```

```
##  
## Multivariate Meta-Analysis Model (k = 282; method: REML)  
##  
## Variance Components:  
##  
## outer factor: Experiment.ID (nlvls = 69)  
## inner term: ~treat (nlvls = 2)  
##  
##          estim   sqrt  fixed  rho:  intr   trts  
## intrcpt    2.7342  1.6535   no      -  1.0000  
## treatsingle  0.0183  0.1353   no      no     -  
##  
## outer factor: Data.ID (nlvls = 282)  
## inner term: ~treat (nlvls = 2)  
##  
##          estim   sqrt  fixed  phi:  intr   trts  
## intrcpt    0.1387  0.3725   no      - -0.1968  
## treatsingle  0.3868  0.6219   no      no     -  
##  
## Test for Residual Heterogeneity:  
## QE(df = 280) = 612141.6429, p-val < .0001  
##  
## Test of Moderators (coefficient 2):  
## QM(df = 1) = 23.1014, p-val < .0001  
##  
## Model Results:  
##  
##          estimate      se     zval    pval    ci.lb    ci.ub  
## intrcpt      2.9053  0.2027  14.3297  <.0001   2.5079   3.3027  ***  
## treatsingle -0.3279  0.0682 -4.8064  <.0001  -0.4616  -0.1942  ***  
##  
## ---  
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The estimate for `intrcpt` is the average log mean of control groups, and is somewhat meaningless as we have averaged over many different species and measures of reproductive function. However, the estimate for `treatsingle` is the difference in log sample means between single- and mixed-food groups, and thus interpretable as the `lnRR`. Note samples from the same experiment etc. were paired in the analysis, thus retaining the principle of concurrent control. The value `-0.3228` is similar to those coming from the contrast-based models above, though this analysis can be considered to have better accounted for non-independence as it is free of stochastic dependency. The heterogeneity can be estimated by adding up the `treatsingle` rows in the `Experiment.ID` and `Data.ID` parts of the output;  $\sqrt{0.0183 + 0.3868} = 0.6365$

For an arm-based IMAMV we need combine the above approach with bivariate model. For this analysis the arm-based data are best transformed in to long-format with the log sample means (`lnX`) and log sample SDs (`lnSD`) in the same column and a dummy variable specifying which is which.

For the diet mixing data, these are available pre-formatted here.

```
head(data_list$arm_long)
```

```
##   Article.ID Author          Journal Year Consumer.Sp
## 1      art1 Alajmi Aquaculture Research 2015 Parvocalanus_crassirostris
## 2      art1 Alajmi Aquaculture Research 2015 Parvocalanus_crassirostris
## 3      art1 Alajmi Aquaculture Research 2015 Parvocalanus_crassirostris
## 4      art1 Alajmi Aquaculture Research 2015 Parvocalanus_crassirostris
## 5      art1 Alajmi Aquaculture Research 2015 Parvocalanus_crassirostris
## 6      art1 Alajmi Aquaculture Research 2015 Parvocalanus_crassirostris
##   Habitat Experiment.ID treat Data.ID      yi      vi stat
## 1  Marine            c1 single   dat1 2.084640 0.15625 lnSD
## 2  Marine            c1 single   dat2 2.519958 0.15625 lnSD
## 3  Marine            c1 single   dat3 1.632655 0.15625 lnSD
## 4  Marine            c1   mix   dat4 2.822239 0.15625 lnSD
## 5  Marine            c1   mix   dat5 2.631184 0.15625 lnSD
## 6  Marine            c1   mix   dat6 1.989330 0.15625 lnSD
```

```
dim(data_list$arm_long)
```

```
## [1] 564 12
```

The columns `yi` and `vi` give the log sample statistics and their sampling variances, `stat` is a dummy variable identifying whether the sample statistic is an instance of the log mean or the log SD, and `treat` specifies whether the sample is from a group on a single- or mixed-food diet. Here `Data.ID` pairs instances of the log mean and log SD that are from the same sample.

A multi-level arm-based IMAMV can be fit as follows.

```
rma.mv(yi = yi, V = vi, mods=~treat*stat, random = list(~treat*stat|Experiment.ID, ~treat*stat|Data.ID), struct="GEN", data = data_list$arm_long)
```

```

##  

## Multivariate Meta-Analysis Model (k = 564; method: REML)  

##  

## Variance Components:  

##  

## outer factor: Experiment.ID (nlvls = 69)  

## inner term: ~treat * stat (nlvls = 4)  

##  

##          estim  sqrt  fixed  rho:  intr  trts  stSD  

## intrcpt      2.7207 1.6494    no     -  0.8294 -0.1341  

## treatsingle   0.0288 0.1698    no     no     - -0.6633  

## statlnSD      0.5015 0.7082    no     no     no    -  

## treatsingle:statlnSD 0.0438 0.2092    no     no     no    no  

##          t:SD  

## intrcpt      -0.5710  

## treatsingle   -0.4058  

## statlnSD      -0.1024  

## treatsingle:statlnSD      -  

##  

## outer factor: Data.ID      (nlvls = 282)  

## inner term: ~treat * stat (nlvls = 4)  

##  

##          estim  sqrt  fixed  phi:  intr  trts  stSD  

## intrcpt      0.1389 0.3727    no     - -0.2607 -0.3852  

## treatsingle   0.4198 0.6479    no     no     - -0.3122  

## statlnSD      0.0776 0.2786    no     no     no    -  

## treatsingle:statlnSD 0.0913 0.3021    no     no     no    no  

##          t:SD  

## intrcpt      0.3795  

## treatsingle   -0.7280  

## statlnSD      -0.1100  

## treatsingle:statlnSD      -  

##  

## Test for Residual Heterogeneity:  

## QE(df = 560) = 629739.6516, p-val < .0001  

##  

## Test of Moderators (coefficients 2:4):  

## QM(df = 3) = 306.6336, p-val < .0001  

##  

## Model Results:  

##  

##          estimate    se    zval    pval    ci.lb    ci.ub  

## intrcpt      2.9207 0.2022 14.4430 <.0001   2.5244   3.3171 ***  

## treatsingle   -0.3358 0.0691 -4.8575 <.0001  -0.4713 -0.2003 ***  

## statlnSD      -1.4072 0.0929 -15.1505 <.0001 -1.5892 -1.2252 ***  

## treatsingle:statlnSD 0.1870 0.0581   3.2190  0.0013   0.0731   0.3008 **  

##  

## ---  

## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

This model is arguably more free of (or corrected for) non-independence than any of the preceding analyses.

The output looks quite complex, but actually has a relatively easy interpretation that maps on to the contrast-based models above.

- `intrcpt = 2.9207` is the log sample mean for control, in this instance mixed-food, groups. The estimate is somewhat meaningless.
- `treatsingle = -0.3358` is the lnRR, here the difference in log means between single- and mixed-food groups. The sign and magnitude of effect is consistent with all other analyses of the lnRR above, and remains statistically significant.
- `statlnSD = -1.4072` is the log CV for the control group (actually log SD - log mean, but that is equal to the log CV), and again the value is a bit meaningless.
- `treatsingle:statlnSD = 0.1870` is the estimate of the lnCVR, which again matches the contrast-based analyses above in terms of sign, magnitude and statistical significance.

The relevant heterogeneities for the lnRR and lnCVR are available in the rows labelled `treatsingle` and `treatsingle:statlnSD` in the `Experiment.ID` and `Data.ID` parts of the analysis. Correlations between effect sizes at the among- and within-study levels have also been estimated, and can be found by reading across the row `treatsingle` to the column `t:SD`. At both levels the correlations are negative (among-experiment = `-0.4058`, within-experiment = `-0.7280`), matching the estimates from the contrast-based analyses.

## Meta-Regression in Arm-Based IMAMV

Again we can include/test moderator variables in an arm-based IMAMV. Here is an arm-based model that tests the moderating effect of Habitat again.

```
rma.mv(yi = yi, V = vi, mods=~treat*stat*Habitat, random = list(~treat*stat|Experiment.ID, ~treat*stat|Data.ID), struct="GEN", data = data_list$arm_long)
```

```

##  

## Multivariate Meta-Analysis Model (k = 564; method: REML)  

##  

## Variance Components:  

##  

## outer factor: Experiment.ID (nlvls = 69)  

## inner term: ~treat * stat (nlvls = 4)  

##  

##  

## estim sqrt fixed rho: intr trts stSD  

## intrcpt 2.7234 1.6503 no - 0.8385 -0.1125  

## treatsingle 0.0236 0.1537 no no - -0.6358  

## statlnSD 0.4880 0.6986 no no no -  

## treatsingle:statlnSD 0.0441 0.2099 no no no no  

##  

## t:SD  

## intrcpt -0.5511  

## treatsingle -0.3476  

## statlnSD -0.1458  

## treatsingle:statlnSD -  

##  

## outer factor: Data.ID (nlvls = 282)  

## inner term: ~treat * stat (nlvls = 4)  

##  

##  

## estim sqrt fixed phi: intr trts stSD  

## intrcpt 0.1406 0.3750 no - -0.0060 -0.3903  

## treatsingle 0.2919 0.5403 no no - -0.3167  

## statlnSD 0.0778 0.2789 no no no -  

## treatsingle:statlnSD 0.0298 0.1726 no no no no  

##  

## t:SD  

## intrcpt -0.4041  

## treatsingle -0.8601  

## statlnSD 0.4447  

## treatsingle:statlnSD -  

##  

## Test for Residual Heterogeneity:  

## QE(df = 556) = 589589.8407, p-val < .0001  

##  

## Test of Moderators (coefficients 2:8):  

## QM(df = 7) = 313.0065, p-val < .0001  

##  

## Model Results:  

##  

##  

## estim se zval pval  

## intrcpt 3.1690 0.3224 9.8304 <.0001  

## treatsingle -0.2257 0.0985 -2.2898 0.0220  

## statlnSD -1.5932 0.1454 -10.9538 <.0001  

## HabitatTerrestrial -0.4043 0.4142 -0.9761 0.3290  

## treatsingle:statlnSD 0.1380 0.0860 1.6057 0.1084  

## treatsingle:HabitatTerrestrial -0.2007 0.1374 -1.4610 0.1440  

## statlnSD:HabitatTerrestrial 0.3043 0.1876 1.6221 0.1048  

## treatsingle:statlnSD:HabitatTerrestrial 0.0908 0.1169 0.7767 0.4373  

## ci.lb ci.ub  

## intrcpt 2.5372 3.8009 ***  

## treatsingle -0.4188 -0.0325 *  

## statlnSD -1.8782 -1.3081 ***  

## HabitatTerrestrial -1.2161 0.4075

```

```

## treatsingle:statlnSD          -0.0305  0.3065
## treatsingle:HabitatTerrestrial -0.4701  0.0686
## statlnSD:HabitatTerrestrial   -0.0634  0.6721
## treatsingle:statlnSD:HabitatTerrestrial -0.1383  0.3198
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

The long list of interaction terms in the model looks daunting, but again can be directly mapped on to a contrast-based model in terms of effect size. The most important terms to look at are:

- `treatsingle` = `-0.2257`, which gives the `lnRR` for marine species.
- `treatsingle:statlnSD` = `0.1380`, which gives the `lnCVR` in the marine species.
- `treatsingle:HabitatTerrestrial` = `-0.2007` is the difference in `lnRR` between terrestrial and marine species. This estimate is similar in magnitude to the contrast-based meta-regression, but is non-significant.
- `treatsingle:statlnSD:HabitatTerrestrial` = `0.0908` (the three-way-interactive term) is the difference in `lnCVR` between the different habitats.

The less interesting terms can be interpreted as follows. `intrcpt` and `statlnSD` is the average log mean and log CV of the control groups for all marine species, while `HabitatTerrestrial` and `statlnSD:HabitatTerrestrial` are differences between terrestrial and marine taxa for those log means and log CVs.

## Phylogenetic Models

Multi-species meta-analyses such as are explored here contain phylogenetic non-independence as some of the species are more closely related, while others are more distantly related. It is common for ecologists and evolutionary biologists to correct for this non-independence using a phylogenetic model. IMAMV is compatible with such models. We now demonstrate two options for fitting phylogenetic IMAMV.

First we must load and solve a matrix which gives the relatedness among the different species in the diet-mixing dataset, which we created using the R package `rotl`. The matrix is stored at the end of the data list.

```

phyloM<-data_list$phylo
A<-solve(as(phyloM, "dgCMatrix"))

```

The matrix contains a row/column for each of the species in the dataset listed under the column `Consumer.Sp`. A phylogenetic correction can then be applied to the arm-based IMAMV in `metafor` as follows using the `R` argument.

```

rma.mv(yi = yi, V = vi, mods=~treat*stat, random = list(~treat*stat|Consumer.Sp, ~treat*stat|Data.ID), struct="GEN", data = data_list$arm_long, R = list(Consumer.Sp = A))

```

```

##  

## Multivariate Meta-Analysis Model (k = 564; method: REML)  

##  

## Variance Components:  

##  

## outer factor: Consumer.Sp (nlvls = 51)  

## inner term: ~treat * stat (nlvls = 4)  

##  

##          estim  sqrt  fixed  rho:  intr  trts  stSD  

## intrcpt    2.2229 1.4909    no     -  0.9429 -0.2335  

## treatsingle  0.0278 0.1666    no     no     - -0.5441  

## statlnSD    0.5236 0.7236    no     no     no    -  

## treatsingle:statlnSD  0.0206 0.1435    no     no     no    no  

##          t:SD  

## intrcpt    -0.9760  

## treatsingle -0.8478  

## statlnSD    0.0163  

## treatsingle:statlnSD    -  

##  

## outer factor: Data.ID      (nlvls = 282)  

## inner term: ~treat * stat (nlvls = 4)  

##  

##          estim  sqrt  fixed  phi:  intr  trts  stSD  

## intrcpt    0.7893 0.8884    no     - -0.0302 0.0159  

## treatsingle  0.3247 0.5698    no     no     - -0.2615  

## statlnSD    0.1518 0.3896    no     no     no    -  

## treatsingle:statlnSD  0.1534 0.3917    no     no     no    no  

##          t:SD  

## intrcpt    -0.3784  

## treatsingle -0.2281  

## statlnSD    -0.2183  

## treatsingle:statlnSD    -  

##  

## Test for Residual Heterogeneity:  

## QE(df = 560) = 629739.6516, p-val < .0001  

##  

## Test of Moderators (coefficients 2:4):  

## QM(df = 3) = 166.7641, p-val < .0001  

##  

## Model Results:  

##  

##          estimate    se    zval    pval    ci.lb    ci.ub  

## intrcpt      3.0229 0.2275 13.2904 <.0001   2.5771   3.4687 ***  

## treatsingle   -0.3305 0.1220 -2.7092  0.0067 -0.5696 -0.0914 **  

## statlnSD     -1.3713 0.1121 -12.2311 <.0001 -1.5910 -1.1515 ***  

## treatsingle:statlnSD  0.1829 0.0659  2.7740  0.0055  0.0537  0.3121 **  

##  

## ---  

## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

The key estimates from for the main effects (treatsingle = -0.3305 for lnRR and treatsingle:statlnSD = 0.1829 for lnCVR) match those from the non-phylogenetic model.

The user may have noted that here we swapped the experiment-level random effect for the species. This is a limit of the current implementation of `rma.mv`, which only permits two random effects with the inner terms (i.e., `inner|outer`) used to pair data from the same samples.

We now demonstrate how to implement an IMAMV model with more than two random effects using `brms`. See `?brms` to get started with this package.

```
library(brms)
```

`brms` allows ‘dual-formula’ specification, which some users may find more straight forward. Here we are implementing an arm-based model and thus we specify an equation for the log mean and for the log SD. The data are best suited to this function in wide format (i.e., with the mean and variance-related statistics in separate columns).

The formula for the model is specified here. Important parts to note are that (1) the `treat` is fitted as a fixed effect, and random slope at each of the multiple levels, (2) that the phylogenetic correlation matrix is associated with the `Consumer.Sp` level of the model, (3) we have specified `lnCV` as the variation-related metric and (4) that the formula is duplicated for both the log mean and log CV

```
arm_form<-bf(lnX |se(sqrt(v_lnX)) ~ treat + (1+treat|a|gr(Consumer.Sp, cov=A)) + (1+treat|b|Experiment.ID) + (1+treat|c|Data.ID)) +
bf(lnCV |se(sqrt(v_lnCV)) ~ treat + (1+treat|a|gr(Consumer.Sp, cov=A)) + (1+treat|b|Experiment.ID) + (1+treat|c|Data.ID)) +
set_rescor(FALSE)
```

The model fits using an MCMC algorithm. The user must specify how long the model runs for (`iter` and `warmup` arguments), how frequently samples are taken (`thin` argument), and how many replicate chains are run (`chains` argument). Here we have specified a model that will run relatively quickly for the sake of the vignette. MCMC algorithms must be checked in a series of diagnostic tests for behavior and convergence (e.g., see `?gelman.diag`). A robust analysis that passes all such checks would likely need a longer run and with chains run in, at least, triplicate.

Finally we run the model, noting I have set the seed to increase the reproducibility of results.

```
set.seed(123)
phylo_IMAMV<-brm(formula=arm_form, data=data_list$arm_wide, data2=list(A=A), family=gaussian, cores=1, chains=1, iter=3000, warmup=2000, thin=1)
```

```
summary(phylo_IMAMV)
```

```
## Warning: Parts of the model have not converged (some Rhats are > 1.05). Be
## careful when analysing the results! We recommend running more iterations and/or
## setting stronger priors.
```

```
## Warning: There were 38 divergent transitions after warmup. Increasing
## adapt_delta above 0.8 may help. See
## http://mc-stan.org/misc/warnings.html#divergent-transitions-after-warmup
```

```

##  Family: MV(gaussian, gaussian)
##  Links: mu = identity; sigma = identity
##          mu = identity; sigma = identity
##  Formula: lnX | se(sqrt(v_lnX)) ~ treat + (1 + treat | a | gr(Consumer.Sp, cov =
A)) + (1 + treat | b | Experiment.ID) + (1 + treat | c | Data.ID)
##          lnCV | se(sqrt(v_lnCV)) ~ treat + (1 + treat | a | gr(Consumer.Sp, cov =
A)) + (1 + treat | b | Experiment.ID) + (1 + treat | c | Data.ID)
##  Data: data_list$arm_wide (Number of observations: 282)
##  Draws: 1 chains, each with iter = 3000; warmup = 2000; thin = 1;
##          total post-warmup draws = 1000
##
## Multilevel Hyperparameters:
## ~Consumer.Sp (Number of levels: 51)
##                                         Estimate Est.Error l-95% CI u-95% CI Rhat
## sd(lnX_Intercept)                  0.18     0.10    0.01    0.38 1.00
## sd(lnX_treatsingle)                0.03     0.02    0.00    0.08 1.00
## sd(lnCV_Intercept)                 0.08     0.05    0.01    0.18 1.00
## sd(lnCV_treatsingle)                0.06     0.03    0.01    0.13 1.00
## cor(lnX_Intercept,lnX_treatsingle)  0.05     0.44   -0.77    0.83 1.00
## cor(lnX_Intercept,lnCV_Intercept)   -0.05    0.41   -0.76    0.77 1.00
## cor(lnX_treatsingle,lnCV_Intercept) -0.01    0.46   -0.82    0.81 1.00
## cor(lnX_Intercept,lnCV_treatsingle) -0.24    0.43   -0.91    0.71 1.00
## cor(lnX_treatsingle,lnCV_treatsingle) -0.23    0.43   -0.89    0.72 1.00
## cor(lnCV_Intercept,lnCV_treatsingle) -0.07    0.44   -0.82    0.77 1.00
##
##                                         Bulk_ESS Tail_ESS
## sd(lnX_Intercept)                  59      171
## sd(lnX_treatsingle)                154     369
## sd(lnCV_Intercept)                 105     178
## sd(lnCV_treatsingle)                78      308
## cor(lnX_Intercept,lnX_treatsingle)  398     476
## cor(lnX_Intercept,lnCV_Intercept)   242     255
## cor(lnX_treatsingle,lnCV_Intercept) 185     182
## cor(lnX_Intercept,lnCV_treatsingle)  156     248
## cor(lnX_treatsingle,lnCV_treatsingle) 193     328
## cor(lnCV_Intercept,lnCV_treatsingle) 198     481
##
## ~Data.ID (Number of levels: 282)
##                                         Estimate Est.Error l-95% CI u-95% CI Rhat
## sd(lnX_Intercept)                  0.38     0.04    0.31    0.46 1.01
## sd(lnX_treatsingle)                0.50     0.14    0.25    0.74 1.01
## sd(lnCV_Intercept)                 0.30     0.05    0.21    0.40 1.04
## sd(lnCV_treatsingle)                0.26     0.13    0.03    0.55 1.13
## cor(lnX_Intercept,lnX_treatsingle)  0.19     0.37   -0.40    0.91 1.03
## cor(lnX_Intercept,lnCV_Intercept)   -0.57    0.13   -0.80   -0.30 1.01
## cor(lnX_treatsingle,lnCV_Intercept) -0.47    0.33   -0.94    0.41 1.04
## cor(lnX_Intercept,lnCV_treatsingle) -0.35    0.37   -0.88    0.48 1.02
## cor(lnX_treatsingle,lnCV_treatsingle) -0.49    0.34   -0.95    0.30 1.00
## cor(lnCV_Intercept,lnCV_treatsingle)  0.12    0.39   -0.61    0.83 1.05
##
##                                         Bulk_ESS Tail_ESS
## sd(lnX_Intercept)                  216     370
## sd(lnX_treatsingle)                 15      170
## sd(lnCV_Intercept)                  55      76
## sd(lnCV_treatsingle)                 15      36
## cor(lnX_Intercept,lnX_treatsingle)   14      62
## cor(lnX_Intercept,lnCV_Intercept)   126     255

```

```

## cor(lnX_treatsingle,lnCV_Intercept)      24      41
## cor(lnX_Intercept,lnCV_treatsingle)      44     112
## cor(lnX_treatsingle,lnCV_treatsingle)    53     127
## cor(lnCV_Intercept,lnCV_treatsingle)    53     117
##
## ~Experiment.ID (Number of levels: 69)
##                                         Estimate Est.Error l-95% CI u-95% CI Rhat
## sd(lnX_Intercept)                      1.61     0.19    1.23    2.01 1.00
## sd(lnX_treatsingle)                   0.12     0.08    0.01    0.30 1.02
## sd(lnCV_Intercept)                   0.68     0.09    0.50    0.84 1.01
## sd(lnCV_treatsingle)                  0.10     0.07    0.01    0.26 1.00
## cor(lnX_Intercept,lnX_treatsingle)    0.23     0.37   -0.56    0.83 1.00
## cor(lnX_Intercept,lnCV_Intercept)    -0.17    0.15   -0.44    0.14 1.01
## cor(lnX_treatsingle,lnCV_Intercept) -0.30     0.42   -0.89    0.64 1.03
## cor(lnX_Intercept,lnCV_treatsingle) -0.17     0.40   -0.83    0.66 1.01
## cor(lnX_treatsingle,lnCV_treatsingle) -0.10     0.43   -0.84    0.75 1.00
## cor(lnCV_Intercept,lnCV_treatsingle) -0.15     0.43   -0.84    0.76 1.00
##
##                                         Bulk_ESS Tail_ESS
## sd(lnX_Intercept)                      141      339
## sd(lnX_treatsingle)                   73       327
## sd(lnCV_Intercept)                   216      286
## sd(lnCV_treatsingle)                  165      302
## cor(lnX_Intercept,lnX_treatsingle)    527      544
## cor(lnX_Intercept,lnCV_Intercept)    179      357
## cor(lnX_treatsingle,lnCV_Intercept)  18       61
## cor(lnX_Intercept,lnCV_treatsingle)  436      623
## cor(lnX_treatsingle,lnCV_treatsingle) 355      533
## cor(lnCV_Intercept,lnCV_treatsingle)  349      508
##
## Regression Coefficients:
##                                         Estimate Est.Error l-95% CI u-95% CI Rhat Bulk_ESS Tail_ESS
## lnX_Intercept      2.93     0.21    2.54    3.35 1.00      123     200
## lnCV_Intercept    -1.39     0.10   -1.59   -1.19 1.00      269     517
## lnX_treatsingle   -0.34     0.07   -0.48   -0.20 1.02      189     378
## lnCV_treatsingle   0.21     0.07    0.08    0.35 1.00      311     522
##
## Further Distributional Parameters:
##                                         Estimate Est.Error l-95% CI u-95% CI Rhat Bulk_ESS Tail_ESS
## sigma_lnX        0.00     0.00    0.00    0.00   NA     NA     NA
## sigma_lnCV       0.00     0.00    0.00    0.00   NA     NA     NA
##
## Draws were sampled using sampling(NUTS). For each parameter, Bulk_ESS
## and Tail_ESS are effective sample size measures, and Rhat is the potential
## scale reduction factor on split chains (at convergence, Rhat = 1).

```

The first thing to note is the warnings at the top of the output. This model would clearly need a good deal of tinkering with the MCMC specifications before we would consider the results robust. The fixes to these issues will be data set specific and do not affect dual formula specification for IMAMV. Hence, we do not present a full exploration of how to adjust the MCMC part of the model. Some solutions to explore might include adjusting `max_treedepth` via the `control` argument, running the model for longer (`iter`, `warmup` and `thin` arguments), and specifying a different prior (`prior` argument). There are many good tutorials on using the `brms` package that cover model specification in detail; see here <https://ayumi-495.github.io/multinomial-GLMM-tutorial/>.

Putting these concerns aside for the sake of the vignette, we can interpret the results as follows. The main overall estimates for the effects of diet mixing can be found under the `Regresson Coefficients` part of the output. The term `lnX_treatsingle = -0.35` is the `lnRR`, while `lnCV_treatsingle = 0.21` is the `lnCVR`. Again these estimates are similar to those seen in the phylogenetic model from `metafor`. The heterogeneity estimates can be found under the `Multilevel Hyperparameters` part of the output. The rows labelled `sd(lnX_treatsingle)` and `sd(lnCV_treatsingle)` give the SD among `lnRR` and `lnCVR` at different levels of the analysis. Note the estimates for `Consumer.Sp` are considerably smaller than those at other levels of the analysis, indicating that phylogenetic effects are likely to be weak.

## Data Visualization

Contrast-based IMAMV can use the already wide array of tools for data-visualization (e.g., forest plots and orchard plots). These must just be applied to the `lnRR` and `lnCVR` (or `lnVR` if that is the analysis of choice).

There are no widely used formats for the visualization of arm-based meta-analyses. Here we propose a new tool, based on estimation plots and orchard plots. We have written a function called `gg_mestimation`, which requires the packages `ggplot2` and `ggbeeswarm` to work.

The function can be loaded from the header file `mestimation_functions.R`.

```
source("mestimation_function.R")
```

The key arguments to pass to the function are as follows:

- `data` : a dataframe containing, at least, the sample statistics to be plotted, the group of each statistic (e.g., control or experimental) and the sample size of each.
- `group` : the column name in `data` giving the group for each statistic being plotted.
- `stat` : the column name in `data` giving the sample statistics being plotted.
- `n` : the column name in `data` giving the sample sizes for each statistic being plotted.
- `control_mu` : the estimate of the meta-analytic mean in the control group.
- `mu` : the overall effect estimated by meta-analysis.
- `ci_l` and `ci_u` : the confidence intervals on `mu`.
- `tau` : the total heterogeneity associated with `mu`.

Here for example, we plot the analysis in the first arm-based IMAMV from above. This model was specified as:

```
rma.mv(yi = yi, V = vi, mods=~treat*stat, random = list(~treat*stat|Experiment.ID, ~treat*stat|Data.ID), struct="GEN", data = data_list$arm_long)
```

```

##  

## Multivariate Meta-Analysis Model (k = 564; method: REML)  

##  

## Variance Components:  

##  

## outer factor: Experiment.ID (nlvls = 69)  

## inner term: ~treat * stat (nlvls = 4)  

##  

##          estim  sqrt  fixed  rho:  intr  trts  stSD  

## intrcpt      2.7207 1.6494    no     -  0.8294 -0.1341  

## treatsingle   0.0288 0.1698    no     no     - -0.6633  

## statlnSD      0.5015 0.7082    no     no     no    -  

## treatsingle:statlnSD 0.0438 0.2092    no     no     no    no  

##          t:SD  

## intrcpt      -0.5710  

## treatsingle   -0.4058  

## statlnSD      -0.1024  

## treatsingle:statlnSD      -  

##  

## outer factor: Data.ID      (nlvls = 282)  

## inner term: ~treat * stat (nlvls = 4)  

##  

##          estim  sqrt  fixed  phi:  intr  trts  stSD  

## intrcpt      0.1389 0.3727    no     - -0.2607 -0.3852  

## treatsingle   0.4198 0.6479    no     no     - -0.3122  

## statlnSD      0.0776 0.2786    no     no     no    -  

## treatsingle:statlnSD 0.0913 0.3021    no     no     no    no  

##          t:SD  

## intrcpt      0.3795  

## treatsingle   -0.7280  

## statlnSD      -0.1100  

## treatsingle:statlnSD      -  

##  

## Test for Residual Heterogeneity:  

## QE(df = 560) = 629739.6516, p-val < .0001  

##  

## Test of Moderators (coefficients 2:4):  

## QM(df = 3) = 306.6336, p-val < .0001  

##  

## Model Results:  

##  

##          estimate    se     zval    pval    ci.lb    ci.ub  

## intrcpt      2.9207 0.2022 14.4430 <.0001  2.5244  3.3171 ***  

## treatsingle   -0.3358 0.0691 -4.8575 <.0001 -0.4713 -0.2003 ***  

## statlnSD      -1.4072 0.0929 -15.1505 <.0001 -1.5892 -1.2252 ***  

## treatsingle:statlnSD 0.1870 0.0581  3.2190  0.0013  0.0731  0.3008 **  

##  

## ---  

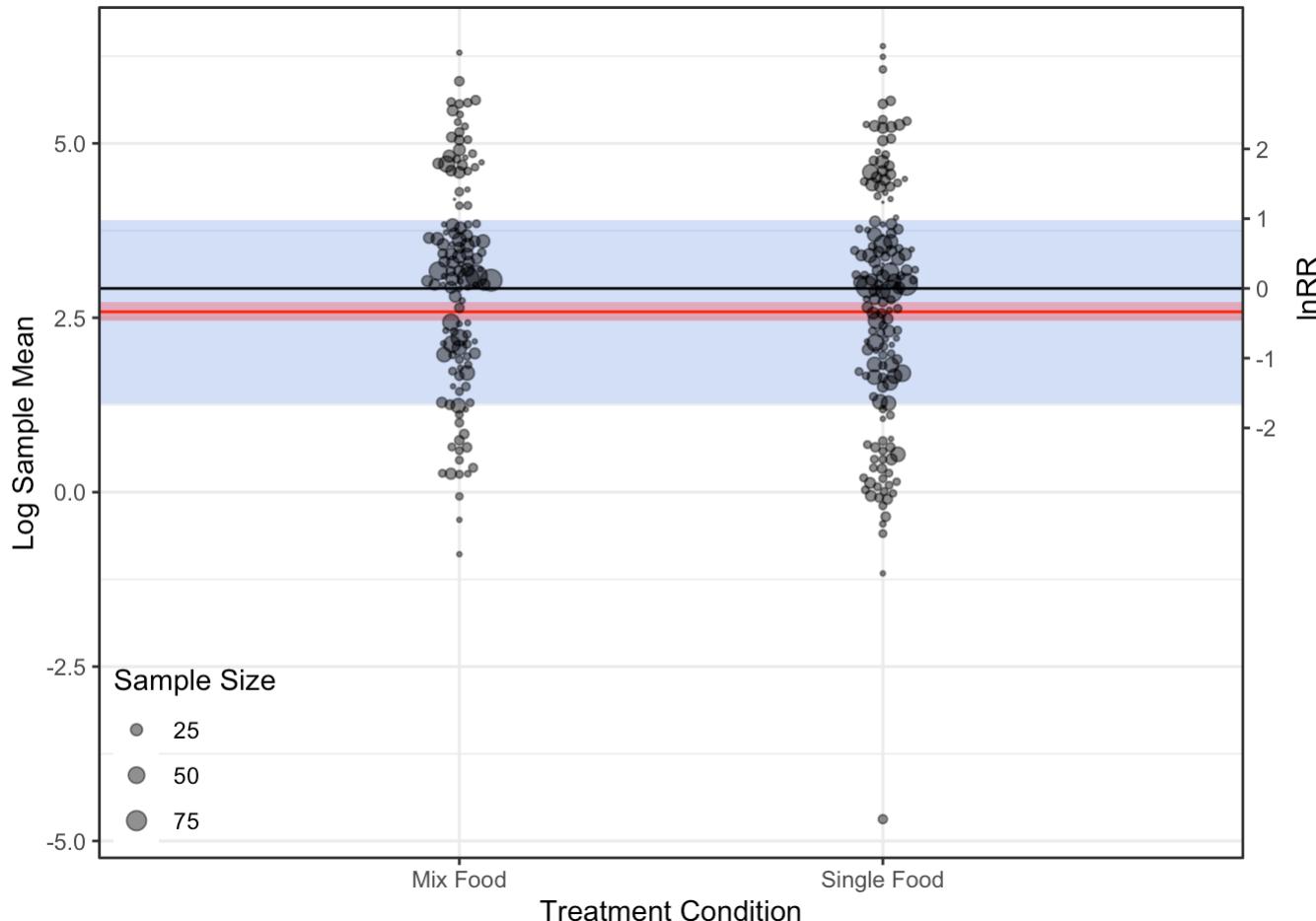
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

Data in wide-format are well suited for use in this function, and we start by plotting the effects on the log mean (data in `lnX`). The estimate for the mean in the control group for `control_mu` is given under the analysis `intrcpt = 2.9207`. The effect of diet mixing on the mean (i.e., the `lnRR`) for the `mu` argument is

given under `treatsingle = -0.3358`, along with its CIs (`ci_lb = -0.4713`, `ci_ub = -0.2003`). The total heterogeneity for `tau`, estimated as the sum of the `treatsingle` terms at the two levels of the analysis, is  $\sqrt{0.4198 + 0.0288} = 0.6698$ .

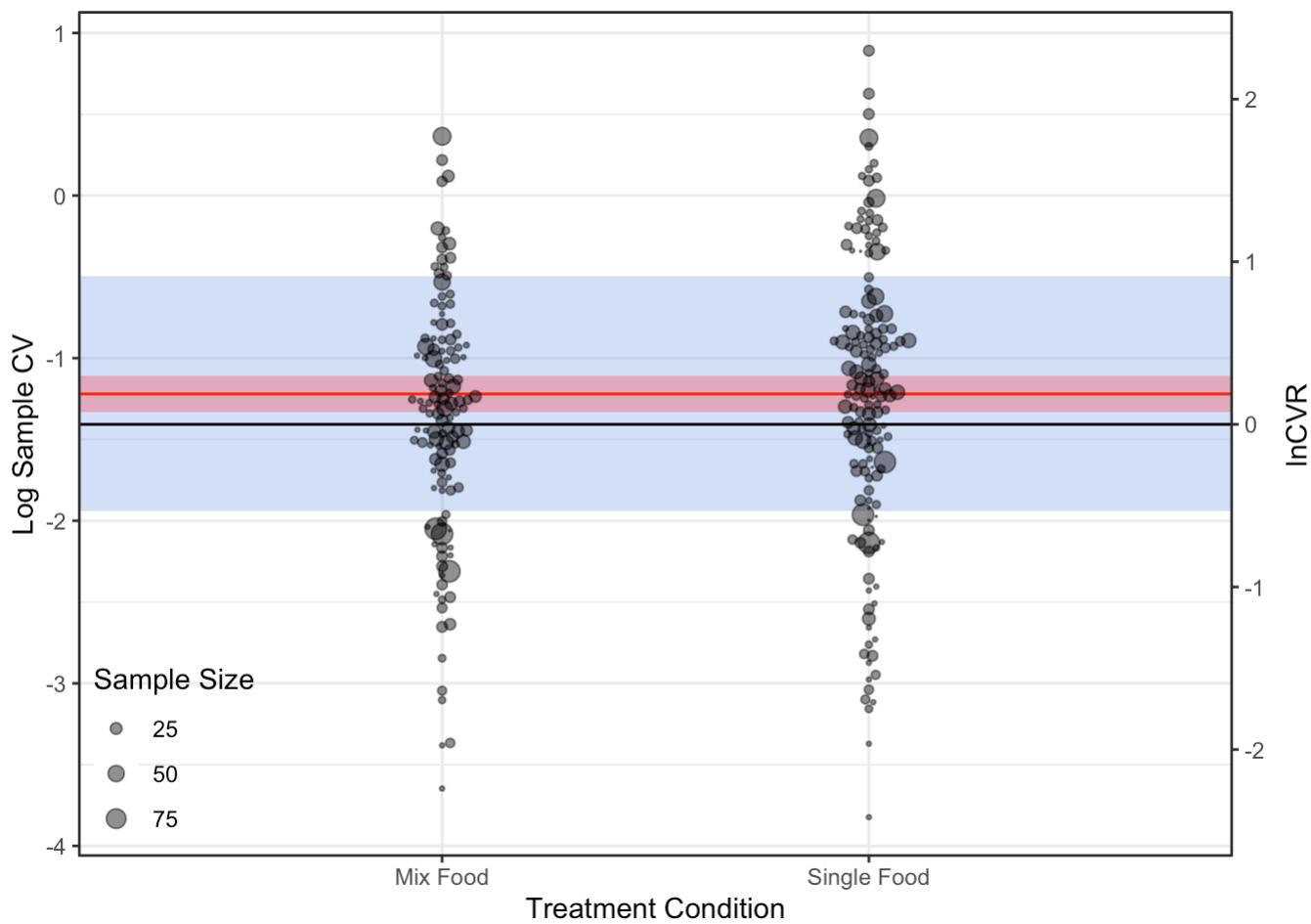
```
gg_mestimation(data = data_list$arm_wide, group = "treat", stat = "lnX", n = "n", control_mu = 2.9207, mu = -0.3358, ci_l = -0.4713, ci_u = -0.2003, tau = 0.6698)
```



We see the log mean (y-axis) as a function of the dietary treatment (x-axis). Individual sample statistics are scaled by their sample size. The right-hand axis gives the projection in to the effect size (lnRR) space. In the effect size space, the line of no effect is the black horizontal line, while the estimated effect is the red horizontal line. The red shading gives the 95% CI on the effect on the mean, which excludes 0 in this case. The blue shaded zone visualizes the 95% prediction interval for future effects, which is based on the estimated heterogeneity ( `tau` ).

We can then reapply this to the lnCVR, using the estimates for `statlnSD` in the model as the `control_mu`, and `treatsingle:statlnSD` in the model as `mu`. The heterogeneity is  $\sqrt{0.0913 + 0.0438} = 0.3676$ .

```
gg_mestimation(data = data_list$arm_wide, group = "treat", stat = "lnCV", n = "n", control_mu = -1.4072, mu = 0.1870, ci_l = 0.0731, ci_u = 0.3008, tau = 0.3676)
```



## Session Info

```
library(sessioninfo)
session_info()
```

```

## - Session info
## setting value
## version R version 4.5.1 (2025-06-13)
## os      macOS Sequoia 15.5
## system aarch64, darwin20
## ui      X11
## language (EN)
## collate en_US.UTF-8
## ctype   en_US.UTF-8
## tz      Australia/Sydney
## date    2025-07-31
## pandoc  3.4 @ /Applications/RStudio.app/Contents/Resources/app/quarto/bin/tools/
##          aarch64/ (via rmarkdown)
## quarto   1.6.42 @ /Applications/RStudio.app/Contents/Resources/app/quarto/bin/qua
##          rto
##
## - Packages
##   package * version  date (UTC) lib source
##   abind      1.4-8    2024-09-12 [1] CRAN (R 4.5.0)
##   backports   1.5.0    2024-05-23 [1] CRAN (R 4.5.0)
##   bayesplot   1.13.0   2025-06-18 [1] CRAN (R 4.5.0)
##   beeswarm    0.4.0    2021-06-01 [1] CRAN (R 4.5.0)
##   bridgesampling 1.1-2   2021-04-16 [1] CRAN (R 4.5.0)
##   brms        * 2.22.0   2024-09-23 [1] CRAN (R 4.5.0)
##   Brobdingnag 1.2-9    2022-10-19 [1] CRAN (R 4.5.0)
##   bslib        0.9.0    2025-01-30 [1] CRAN (R 4.5.0)
##   cachem       1.1.0    2024-05-16 [1] CRAN (R 4.5.0)
##   callr        3.7.6    2024-03-25 [1] CRAN (R 4.5.0)
##   checkmate    2.3.2    2024-07-29 [1] CRAN (R 4.5.0)
##   cli          3.6.5    2025-04-23 [1] CRAN (R 4.5.0)
##   coda          0.19-4.1  2024-01-31 [1] CRAN (R 4.5.0)
##   codetools    0.2-20   2024-03-31 [1] CRAN (R 4.5.1)
##   digest        0.6.37   2024-08-19 [1] CRAN (R 4.5.0)
##   distributional 0.5.0    2024-09-17 [1] CRAN (R 4.5.0)
##   dplyr        1.1.4    2023-11-17 [1] CRAN (R 4.5.0)
##   evaluate     1.0.4    2025-06-18 [1] CRAN (R 4.5.0)
##   farver        2.1.2    2024-05-13 [1] CRAN (R 4.5.0)
##   fastmap      1.2.0    2024-05-15 [1] CRAN (R 4.5.0)
##   generics      0.1.4    2025-05-09 [1] CRAN (R 4.5.0)
##   ggbeeswarm   * 0.7.2    2023-04-29 [1] CRAN (R 4.5.0)
##   ggplot2      * 3.5.2    2025-04-09 [1] CRAN (R 4.5.0)
##   glue          1.8.0    2024-09-30 [1] CRAN (R 4.5.0)
##   gridExtra     2.3      2017-09-09 [1] CRAN (R 4.5.0)
##   gtable        0.3.6    2024-10-25 [1] CRAN (R 4.5.0)
##   htmltools     0.5.8.1   2024-04-04 [1] CRAN (R 4.5.0)
##   inline        0.3.21   2025-01-09 [1] CRAN (R 4.5.0)
##   jquerylib     0.1.4    2021-04-26 [1] CRAN (R 4.5.0)
##   jsonlite      2.0.0    2025-03-27 [1] CRAN (R 4.5.0)
##   knitr         1.50     2025-03-16 [1] CRAN (R 4.5.0)
##   labeling      0.4.3    2023-08-29 [1] CRAN (R 4.5.0)
##   lattice       0.22-7   2025-04-02 [1] CRAN (R 4.5.1)
##   lifecycle     1.0.4    2023-11-07 [1] CRAN (R 4.5.0)
##   loo            2.8.0    2024-07-03 [1] CRAN (R 4.5.0)
##   magrittr      2.0.3    2022-03-30 [1] CRAN (R 4.5.0)
##   mathjaxr     1.8-0    2025-04-30 [1] CRAN (R 4.5.0)

```

```

##  Matrix          * 1.7-3    2025-03-11 [1] CRAN (R 4.5.1)
##  matrixStats     1.5.0     2025-01-07 [1] CRAN (R 4.5.0)
##  metadat        * 1.4-0    2025-02-04 [1] CRAN (R 4.5.0)
##  metafor         * 4.8-0    2025-01-28 [1] CRAN (R 4.5.0)
##  mvtnorm        1.3-3     2025-01-10 [1] CRAN (R 4.5.0)
##  nlme           3.1-168   2025-03-31 [1] CRAN (R 4.5.1)
##  numDeriv        * 2016.8-1.1 2019-06-06 [1] CRAN (R 4.5.0)
##  pillar          1.10.2    2025-04-05 [1] CRAN (R 4.5.0)
##  pkgbuild        1.4.8     2025-05-26 [1] CRAN (R 4.5.0)
##  pkgconfig       2.0.3     2019-09-22 [1] CRAN (R 4.5.0)
##  plyr            1.8.9     2023-10-02 [1] CRAN (R 4.5.0)
##  posterior       1.6.1     2025-02-27 [1] CRAN (R 4.5.0)
##  processx        3.8.6     2025-02-21 [1] CRAN (R 4.5.0)
##  ps              1.9.1     2025-04-12 [1] CRAN (R 4.5.0)
##  QuickJSR        1.8.0     2025-06-09 [1] CRAN (R 4.5.0)
##  R6              2.6.1     2025-02-15 [1] CRAN (R 4.5.0)
##  RColorBrewer    1.1-3     2022-04-03 [1] CRAN (R 4.5.0)
##  Rcpp            * 1.0.14   2025-01-12 [1] CRAN (R 4.5.0)
##  RcppParallel    5.1.10    2025-01-24 [1] CRAN (R 4.5.0)
##  reshape2         1.4.4     2020-04-09 [1] CRAN (R 4.5.0)
##  rlang            1.1.6     2025-04-11 [1] CRAN (R 4.5.0)
##  rmarkdown        2.29      2024-11-04 [1] CRAN (R 4.5.0)
##  rstan            2.32.7    2025-03-10 [1] CRAN (R 4.5.0)
##  rstantools      2.4.0     2024-01-31 [1] CRAN (R 4.5.0)
##  sass             0.4.10    2025-04-11 [1] CRAN (R 4.5.0)
##  scales           1.4.0     2025-04-24 [1] CRAN (R 4.5.0)
##  sessioninfo     * 1.2.3    2025-02-05 [1] CRAN (R 4.5.0)
##  StanHeaders     2.32.10   2024-07-15 [1] CRAN (R 4.5.1)
##  stringi          1.8.7     2025-03-27 [1] CRAN (R 4.5.0)
##  stringr          1.5.1     2023-11-14 [1] CRAN (R 4.5.0)
##  tensorA          0.36.2.1  2023-12-13 [1] CRAN (R 4.5.0)
##  tibble           3.3.0     2025-06-08 [1] CRAN (R 4.5.0)
##  tidyselect        1.2.1     2024-03-11 [1] CRAN (R 4.5.0)
##  vctrs            0.6.5     2023-12-01 [1] CRAN (R 4.5.0)
##  vipor            0.4.7     2023-12-18 [1] CRAN (R 4.5.0)
##  withr            3.0.2     2024-10-28 [1] CRAN (R 4.5.0)
##  xfun             0.52      2025-04-02 [1] CRAN (R 4.5.0)
##  yaml             2.3.10    2024-07-26 [1] CRAN (R 4.5.0)
##
## [1] /Library/Frameworks/R.framework/Versions/4.5-arm64/Resources/library
## * — Packages attached to the search path.
##
## -----

```