

Egger model:  $y = \mu + \epsilon, y/\sigma = \mu/\sigma + \epsilon/\sigma$ . whatever  $\sigma$  is, intercept of regression vs  $1/\sigma$  will be 0 so will control FPR, even under heterogeneity, with no need to account for between-study variance, at least as far as fpr.[actually no because inference requires homoskedasticity—will need to use heteroskedasticity-robust variance]

lin unfair comparison

(1/31) Invariant test. test statistic should be same for any translation of the within variances, besides translations of the effect sizes. so a function of the differences of the within variances, and of the effect sizes. is this maximal invariant? Seems something like concordance test would work: proportion of pairs of effects and variances that concord. This is similar to Begg's test but not using the standardized effect sizes (which depend directly on the variances).

old egger ms has local power calculations and talks about the dependence of egger test power on the location of sigma, unlike begg test. otoh begg test power depends on the dispersion of sigma, whereas egger more sensibly depends on the ratio of the dispersion of  $z$  to that of sigma. update: actually in formula for begg test asymptotic local power there is the term  $E(f(Z))$  which may be viewed as a measure of concentration ie it is small when the dispersion is large, so the situation is perhaps analogous to the egger formula. Eg  $E(\log(f(Z))) \leq \log(E(f(Z))), 1/E(f(Z)) \leq \exp(-E(\log(f(Z))))$ ,  $E(f(Z)) \geq \exp(\text{entropy of } Z)$ . not sure if this is useful direction of inequality. but the distributional parameter  $D(Z) = 1/E(f(Z))$  has properties of a statistical dispersion measure, since  $D(aZ + b) = |a|D(Z)$ . Does  $D(Z) \rightarrow 0$  as  $Z$  approximates a constant? Maybe for continuous densities, which go to impulse function.

Found that simulation showing that begg's/egger's test were inconsistent with heterogeneity, with fpr control worse with sample size, only shows that for  $\text{unif}[0,1]$  as distribution for the within variances. even  $\text{unif}[.1,1.1]$  the tests look OK under heterogeneity. This led me to look back at the old calculations on egger regression fpr under heteogeneity.

(2/1-2/3) Worked on formulas for FPR of egger test under heterogeneity. Got expression 1) without assuming normality. Maybe try to use old calculations to get mean and variance of the statistic in the  $P(\dots | 0)$  statement to say something. And 2) assuming normality, in terms of a weighted sum of chi-square. And 3) assuming normality and  $n \rightarrow \infty$ . Latter suggests FPR could be higher or lower than nominal level depending on moments of precision distribution. Found a linear relationship between beta parameters (as precision distribution) determining whether FPR is higher than lower.

Maybe find similar relationship for uniform prior.

Maybe this dependence on the precision explains some of the conflicting assessments from simulation studies in the literature.

Planning on working on expressions for  $\tau^2$  under selection.

(2/4) [worked on begg manuscript. added simulation for random effects model]

(2/5) Worked out way to implement rlin (sample simulated meta-analysis data sets with pvalue thresholding and randomly keeping some studes that don't meet the threshold) without using the loop. Didn't write out or implement.

Worked on distribution of dersimonian-laird tau.hat under hetrogeneity. Tried to get some inequalities to compare it to the true tau.hat. Realized the data under selection won't be using the true tau.hat either.

[pollard: section on coupling, probably finished with chapter on distribution theory in metric spaces]

(2/6) Partially implemented fast/direct version of Lin algo for sampling ma data subject to p-val pub bias. Managed for mu=0 case but not general mu, which requires sampling from the join distr of (z,s) under a linear constraint. Had forgotten that when  $\mu \neq 0$ , pval selection affects s, just like effect size selection. this was in egger#1 notes, had decides at the time to set aside the  $\mu \neq 0$  case, maybe now too.

(2/7) Tried (starting yesterday) to maximize bias ratio. Found a quad form to maximize over a polytope, but the form is indefinite. [pollard-started chapter on unif convergence]

(2/8) worked more on maximizng bias ratio. a few visualizations for the 2-simplex. guessed form of argmax, couldn't confirm. Begg.R #3 (2022 section).

Added sim to begg manuscript for negative bias (bad FPR) example-t with low df.

(2/9) realized t example from last night was bad since variances are defined so the meta analysis model isn't great. did beta and added to ms. though originally chose t since bimodal study distribution seemed pathological.

(2/12) from simulations found that lin's modification to the egger test (estimating  $\tau^2$ ) is consistent under hard thresholding alternatives-as is the test ignoring heterogeneity. the estimate of  $\tau^2$  usually truncates to 0 except for very large between/within variances anyway.

Tried the alternative method of heteroskedasticity consistent regression with egger's test. Found that it's power was often better but fpr also inflated (sometimes a lot-20rate), just a higher power curve.

(2/13) under pval thresholding, when the grand mean is 0, egger statistic and begg statistic both test whether the mean of the post-selection distribution is 0. egger is testing the intercept in the model  $y^* \sim \beta_0 + \beta_1 1/\sigma^*$  but under pval thresholding  $z$  and  $\sigma$  are independent so  $Ey^* | 1/\sigma^*$  is constant and equals the intercept. begg test is testing for trend  $y/\sigma - \mu/\sigma$  against  $1/\sigma$ . From the above  $y/\sigma$  has no trend vs  $1/\sigma$  so the trend of  $y/\sigma - \mu/\sigma$  is all due to  $\mu$ .

tried resampling on a few statistics. begg stat seemed to do best. then realized lin had anohter paper on using resampling, lin2020.

then tried testing the slope in the egger regression for equality with the mean of  $y$ , looked promising. (2/14) then realized the intercept being 0 is the same as the slope coefficient being equal to the fixed effects summary estimate  $\hat{\theta}$  (since then the slope coefficient is the same as projection onto the  $1/\sigma$  predictor which has size equal to  $\hat{\theta}$ ) so the tests are the same.

found that the regression of the begg lm approximation,  $(y - \hat{\theta}_{fe})/\sigma \sim 1 + 1/\sigma$  gives intercept equal to the egger statistic and intercept is similar to the begg statistic. also have the joint distr here so can compute pval that they are jointly 0. can also add a skewness analysis. however the slope of

the begg-lm statistic, ie the z-statistic regressands above, is nonzero almost exactly when the egger intercept is nonzero in simulations, and give the same pvals of significant difference from 0, so not much power gain it seems, at least in the scenarios tested. if they are the same across all scenarios the question becomes, what is the difference of the slope of the z-statistics and the begg statistic, kendalls tau. The former reduces in the gaussian case to the pearson correlation multiplied by the ratio of the variances of the predictor and response. so that ratio must be driving the difference. (besides robustness of the rank statistic.) (2/15) intercept (=egger stat) and slope of z-stat slope test are almost identical, and the difference between this slope and begg test are due entirely to a) (minor) the  $O(1/n) 1/\sum(1/v)$  terms in begg test and (mainly) b) using kendall vs pearson method of correlation. Tried bounding the difference of the intercept and slope. expression seems related to  $m(1)/\sqrt{m(2)}$ , where  $m$  gives the moments of the precision. would be nice to have a result of the form: The difference between begg's test computed using pearson instead of kendall correlation is a) the  $O(1/n) 1/\sum(1/v)$  terms and the difference between slope and intercept. (latter may actually be large. will need to check the difference for precisions with large  $m(1)/\sqrt{m(2)}$ ); if it is large, that just means we have found a usual combined statistic, the slope and intercept of the z-test...which can hopefully be augmented with the skewness test.)

need to verify lin2018 argument about the independence of their skewness statistic and the egger statistic. the lm residuals are independent of the betahats (or uncorrelated at least) but the test stat isn't the betahats but the t-stats. the se in the denominator uses the residuals. so this would at most be asymptotically independent?

(2/19) comparing pearson-begg test to egger test. found that the pearson-begg test always has a larger p-value than egger test. so i guess egger has higher fpr and power both. expression is given on egger #2.

(2/20) verified egger coef and t-statistic are the intercept estimate and t-stat in the pearson-begg regression (hadn't done this analytically before). did not yet verify analytically that pearson correlation between  $(y - \hat{\theta}_{fe})/\sigma$  and  $1/\sigma$  is the same as the slope in the pearson-begg regression, did a quick google search and found plenty of sources talking about their equivalence of testing.

drew a picture of begg pearson regression to understand why egger stat shows up as the intercept. tried to figure out if it's possible for the intercept to be 0 but not the slope or vice versa; seems they should both be 0 at the same time.

(2/21) verified testing pearson correlation is the same as slope, so begg stat using pearson corr (and without the  $O(1/n)$  sigma corrections in the denominator) is the same as testing slope is 0 in the pearson-begg linear regression. in so doing found a much nicer expression for the t-statistic of the slope than i was using, may try to find something corresponding for the egger statistic, and the difference between the two.

looked at pearson-begg regression under the null, comparing intercept t-stat, slope t-stat, and f-stat. found intercept/egger always more significant

than slope,  $f$  somewhere in between. difference is most dramatic for larger  $E(m^2)/E(m)^2$ .

the discrepancy is a problem with the slope term. the regression does not use iid data because of the  $\theta$  in the regressand. just like in the other manuscript. this leads the slope pvalues to be less significant, a loss of power. looking at the formula previously derived for the difference in magnitudes of the test stats, this difference goes to 0 as  $n \rightarrow \infty$  at least under the null when  $y$ s and  $s$  are orthogonal. unlike the actual begg test, where the bias persists. [does not agree with sims—at least for f-test holds for  $n \geq 1000$ ] (2/22) found in fact pearson-begg slope is asymptotically biased, i was forgetting about a  $\sqrt{n}$  factor. so it is analogous to the kendall begg estimator. found simpler formulas for the egger t-statistic (analogous to the one yesterday for the pearson-begg t-stat). found the coefficients are related by  $\hat{\beta}_0 m_1 = -\hat{\beta}_1 m_2$ . some linear relationship would have to hold between the coefficients since the projection of the regressand onto the design column space  $M(1, s)$  lies in the one dimensional subspace  $M(1, s) \cap s^\perp$ . need to look at asymptotics.

(3/4) Last week when trying to find the local power function for begg's test, I realized I could obtain the asymptotic normality of the begg statistic for general  $Z$  using the stochastic equicontinuity arguments. so i worked on showing that, which will require revising the old begg manuscript.

Two further issues with the old begg ms: first, this approach gives a clearer picture of when the test bias is positive or negative, the sign of  $E(f_Z(Z)) - 2E(ZF_Z(Z))$  for standardized and centered  $Z$ . By looking at beta distributions, found that many but not all bimodal distributions are underconservative. Then focused on unimodal distributions and found that Student's  $t$  with  $df \leq$  around 2.4 is also underconservative. Wondering now if log concavity of the density is a sufficient condition for the test not to be underconservative. second, still working on find the  $S$  distribution that maximizes the bias for fixed  $Z$ . I had looked at discrete approximations and found an approximation that seems to maximize.  $R$ 's optim does not change when started at the distribution.