

## WEB APPENDIX 1

### Stata program for dose-response meta-analysis

Stata code for Example 2 of this paper

```
/* Information about glst command is available here
http://nicolaorsini.altervista.org/stata/tutorial/g/glst.htm
*/

/* two-stage fixed-effect meta-analysis */

. glst logrr dose, se(se) cov(peryears cases) pfirst(study type) ts(f)

Two-stage fixed-effects dose-response model      Number of studies =      4

Generalized least-squares regression              Number of obs =      4
Goodness-of-fit chi2(3) =      6.13              Model chi2(1) =      9.50
Prob > chi2 =      0.1055                       Prob > chi2 =      0.0021
-----+-----
logrr |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-----+-----
dose |      .005548   .0018002    3.08   0.002     .0020197   .0090762
-----+-----

/* Relative risk for 12 grams/day incremental unit */

. lincom dose*12, eform

-----+-----
logrr |      exp(b)   Std. Err.      z    P>|z|     [95% Conf. Interval]
-----+-----
(1) |      1.068842   .023089     3.08   0.002     1.024533   1.115067
-----+-----

/* two-stage random-effect meta-analysis */

. glst logrr dose, se(se) cov(peryears cases) pfirst(study type) ts(r)

Two-stage random-effects dose-response model      Number of studies =      4

Generalized least-squares regression              Number of obs =      4
Goodness-of-fit chi2(3) =      6.13              Model chi2(1) =      4.40
Prob > chi2 =      0.1055                       Prob > chi2 =      0.0358
-----+-----
logrr |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-----+-----
dose |      .0054527   .0025981    2.10   0.036     .0003605   .010545
-----+-----
Moment-based estimate of between-study variance of the slope: tau2 = 0.0000137

/* Relative risk for 12 grams/day incremental unit */

. lincom dose*12, eform

-----+-----
logrr |      exp(b)   Std. Err.      z    P>|z|     [95% Conf. Interval]
-----+-----
(1) |      1.067621   .0332856    2.10   0.036     1.004336   1.134894
-----+-----
```

## WEB APPENDIX 2

### SAS program for dose-response meta-analysis

SAS code for Example 2 of this paper (partial, without revealing the actual data set for protection)

```
/** you need to download this macro from XXX's website in software section
http://www.hsph.harvard.edu/faculty/donna-spiegelman/software/
***/

%include "metadose.sas";

%metadose(dat=all, /** should have variables &ratio, &95UB, &dose, &Ncase, &Ntotal, &studyname **/
  ratio=rr, /** odds ratio for case-control, relative risk for cohort **/
  /*variance=variance,*/
  UB=ul,
  dose=nut_med, /** median dose for each exposure level */
  Ncase=cases, /** number of cases for each exposure level */
  Ntotal =peryears, /** total amount of person-time (cohort) or subjects (case-control) */
  studyname=study, /** study name, character value **/
  studytype=1,
  graphname_g=alc.lung.greenland.ps, /** for greenland method to get var-covar plot **/
  graphname_h=alc.lung.hamling.ps, /** for Hamling method to get var-covar plot **/
  wt=12, unit_wt=g/day, var_covar=GH,linearCheck=1,
  meta=T
);
```

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These are the input data plus the estimated cell counts using both methods

Obs	STUDY	Median dose	RR	UL	Cases	Greenland Est_Cases	Hamling Est_Cases	Actual Person-time	Hamling_Est Person-time
1	at	0.0000	1.00000	.	45	36.678	38.612	5931.51	6254.08
2	at	1.8480	0.82433	1.22406	61	61.897	66.542	12143.00	13074.80
3	at	9.0868	0.87490	1.27234	79	79.373	92.324	14671.52	17092.19
4	at	22.8571	0.80515	1.19664	60	63.998	65.746	12854.30	13226.27
5	at	45.5952	0.82968	1.25888	53	56.054	50.982	10925.75	9952.80
6	hp	0.0000	1.00000	.	51	63.498	56.054	96659.16	87056.06
7	hp	2.1000	0.79991	1.20884	41	52.228	37.638	99390.73	73075.96
8	hp	9.5000	0.96763	1.39726	67	71.036	57.724	111751.78	92648.35
9	hp	18.8000	0.50574	0.86916	18	17.842	17.087	53704.71	52472.27
10	hp	40.3000	1.25836	1.83760	67	39.395	51.256	47656.96	63260.29
11	nt	0.0000	1.00000	.	111	105.078	47.706	1356.69	605.09
12	nt	2.2000	1.10632	1.57168	136	152.761	71.410	1782.74	818.69
13	nt	9.3000	1.19576	1.66387	200	227.500	99.507	2456.36	1055.50
14	nt	22.5000	1.10051	1.53745	193	176.422	93.262	2069.80	1074.87
15	nt	41.3000	1.69433	2.43712	188	166.239	57.408	1266.80	429.75
16	ny	0.0000	1.00000	.	47	47.457	45.646	20756.52	20258.20
17	ny	0.9667	0.72706	1.01658	135	151.156	135.113	90930.18	82476.19
18	ny	11.4000	0.94785	1.35805	86	92.178	84.526	42533.97	39577.95
19	ny	22.8000	0.84882	1.26343	53	49.353	51.656	25430.02	27009.01
20	ny	45.6000	1.16348	1.69670	71	51.856	65.648	19493.39	25041.75

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These are the point estimates and input data using both methods of meta-analysis for dose-response  
RR/OR is given in an increment of 12 g/day

Obs	studyname	G_BSTAR	G_SESTAR	G_RRSTAR	H_BSTAR	H_SESTAR	H_RRSTAR
1	at	-.001846892	.003596107	0.97808	-.001985603	.003636415	0.97645
2	hp	0.006029110	.004387492	1.07503	0.006744383	.004329228	1.08430
3	nt	0.009797354	.003482907	1.12476	0.009525432	.003567898	1.12109
4	ny	0.007576733	.003212849	1.09518	0.007859609	.003127314	1.09891

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The following are the results from the meta regression

test for heterogeneity

Model	Method	Pooled Est (SE)	RR/OR(CI)	Z-score	linear trend p-value	tau**2	p-value	Q	df
fixed	Greenland	0.0055( 0.0018)	1.0688( 1.0245, 1.1151)	3.0820	0.0021		0.1056	6.1279	3
fixed	Hamling	0.0057( 0.0018)	1.0706( 1.0263, 1.1168)	3.1650	0.0016		0.1045	6.1515	3
Random	Greenland	0.0055( 0.0026)	1.0676( 1.0043, 1.1349)	2.0988	0.0358	0.0000			
Random	Hamling	0.0056( 0.0026)	1.0694( 1.0059, 1.1368)	2.1489	0.0316	0.0000			

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 Assessment of non-linearity - p-values  
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	Greenland	Hamling
Test for non-linearity	0.206691	0.1722052
Test for overall significance of curve	0.0017896	0.0011502