IZSTO

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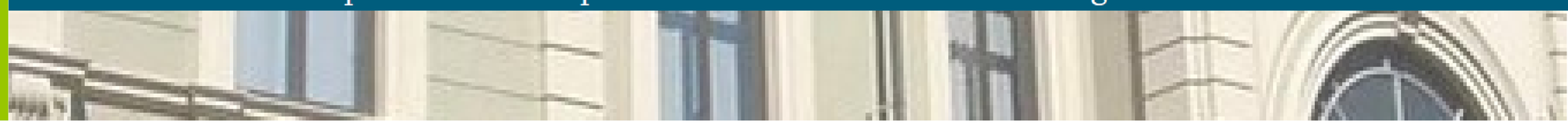

CAN NETWORK META-ANALYSIS HELP IN EXPLAINING THE RISKS FOR SCRAPIE?

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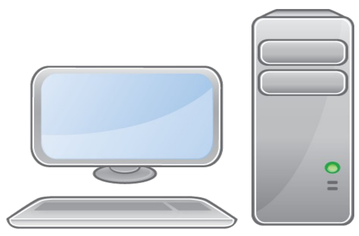
INTRODUCTION & AIM

Network meta-analysis (NMA) is a multivariate extension of meta-analysis. NMA synthesizes data from a network of trials about more than two competing healthcare interventions. The integration of direct evidence (from studies directly comparing interventions) with indirect evidence (information about two treatments derived via a common comparator) increases the precision in the estimates and produces a relative ranking of all treatments for the studied outcome. Although commonly applied to randomized clinical trials evaluation, NMA can be applied to a set of different estimates of a risk. Therefore we applied NMA to classical scrapie, a transmissible spongiform encephalopathy of small ruminants, strongly influenced by polymorphisms of the prion protein gene (PRNP). Our aim was to assess the shape of association between multiple exposures (different genotypes with different level of resistance to scrapie in sheep) and a baseline genotype (homozygosis at ARQ).

MATERIAL AND METHODS

STEP 1:Systematic review



http://www.ncbi.nlm.nih.gov/pubmed/
http://www.neuroprion.org
3 leading books reference lists

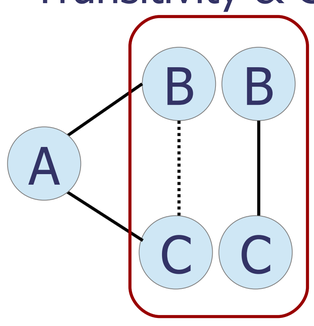
Genetic variables:
4 studies
12 genotypes

P=12-1=11
comparisons

NMA

- allows a joint synthesis of the multiple end points, describing their multivariate relationship as well
- Correlation is separated into two components: within and between studies correlation

STEP2:Assumptions
Transitivity & Consistency



Direct comparison
Indirect comparison

μBC = μAC − μAB

STEP3:The model

General model under consistency

$$y_i \approx N(\mu i, Si)$$

$$\mu_i \approx N(\beta, \sum\ )$$

yi vector of log(OR) from the i[th] study
μ_i study-specific mean vector
β vector of overall meta-analytical estimates

Between-studies variance–covariance matrix

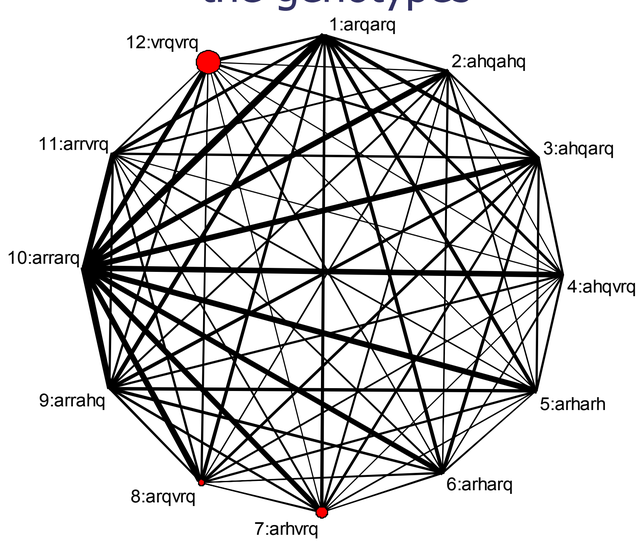
$$Z = \tau^2 \sum_0$$

τ unknown parameter
Σ_0 a matrix with elements proportional to

$$\sigma_{rs} = \begin{cases} 1 & if \quad r = s \\ 0.5 & if \quad r \neq s \end{cases}$$

RESULTS

The network obtained among the genotypes



Consistency model(ref:ARQ/ARQ)

Overall_mean	OR	SE	Z	P>z	95% CI	
AHQ/AHQ	0.174413	0.092253	-3.3	0.001	0.061852	0.49182
AHQ/ARQ	0.241817	0.123471	-2.78	0.005	0.088892	0.657821
AHQ/VRQ	0.052039	0.030639	-5.02	0	0.016412	0.165001
ARH/ARH	0.104623	0.058369	-4.05	0	0.035054	0.312255
ARH/ARQ	0.150009	0.081107	-3.51	0	0.051987	0.432856
ARH/VRQ	9.728385	5.23403	4.23	0	3.38907	27.92551
ARQ/VRQ	5.452524	2.776536	3.33	0.001	2.00978	14.79268
ARR/AHQ	0.008578	0.004749	-8.6	0	0.002898	0.025388
ARR/ARQ	0.00948	0.004956	-8.91	0	0.003403	0.026412
ARR/VRQ	0.301581	0.154814	-2.34	0.02	0.110267	0.824824
VRQ/VRQ	20.38705	10.5219	5.84	0	7.413838	56.06162

Between studies variance and heterogeneity and I^2

Genotype	T	95% CI		I^2	95% CI	
AHQ/AHQ	1.01543	0.73434	1.29651	93	87	95
AHQ/ARQ				99	99	100
AHQ/VRQ				86	77	91
ARH/ARH				91	84	94
ARH/ARQ				94	90	96
ARH/VRQ				95	92	97
ARQ/VRQ				100	99	100
ARR/AHQ				86	76	91
ARR/ARQ				96	93	97
ARR/VRQ				99	98	100
VRQ/VRQ				97	95	98

Probability of being the *Best* estimate of scrapie

STUDY	AHQ/AHQ	AHQ/ARQ	AHQ/VRQ	ARH/ARH	ARH/ARQ	ARH/VRQ	ARQ/VRQ	ARR/AHQ	ARR/ARQ	ARR/VRQ	VRQ/VRQ
1	0	0	0	0	0	21.5	8	0	0	0	70.5
2	0	0	0	0	0	21.5	8	0	0	0	70.5
3	0	0	0	0	0	21.5	8	0	0	0	70.5
4	0	0	0	0	0	21.5	8	0	0	0	70.5

CONCLUSION

Multivariate meta-analysis has an abundance of potential and promise over its univariate counterpart. Network meta-analysis represents a new method to combine evidence from direct and indirect comparisons among a set of different estimates of a risk in a unique network of treatments. Our new approach to genetic veterinary data (i.e. the risk of becoming a scrapie diseased animal) has underlined the importance of genotypes other than the best known ARR/ARR in the decline of the disease. In the network we have obtained, we can visually realize that heterozygosis ARR/* may have the same meaning as homozygosis, whereas other genotypes such as ARH/VRQ are very good predictors of the disease.

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