The SAS meta_subtype_trend Macro

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Abstract

The %meta_subtype_trend macro tests whether the exposure-subtype association has a trend across the ordinal cancer subtypes. The user runs separate Cox (for cohort studies) or conditional logistic models (for nested case-control studies) for each subtype, and then tests the heterogeneity hypothesis using the outputs from the separate models, or the user takes the estimates (and standard errors) from the literature and test the heterogeneity hypothesis. In the subtype-specific analysis, the confounders-disease associations are allowed to be different among the subtypes.

Keywords: SAS, macro, heterogeneity test, subtype, ordinal, meta-regression

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1 Description

%meta_subtype_trend macro tests whether the exposure-subtype association has a trend across the ordinal cancer subtypes.

2 Invocation and Details

In order to run this macro, your program must know where to look for it. You can tell SAS where to look for macros by using the options:

```
options mautosource sasautos=<directories macro is located>;
```

In the Channing servers, the option statements might be

```
options mautosource sasautos='/usr/local/channing/sasautos';
```

Below is a description of the input parameter.

```
%meta_subtype_trend(
logRR = the estimated log relative risk for each cancer subtype in
                 relation to the exposure
var = estimated variance of the estimated log relative risk
score = the ordinal or median score assigned to each cancer subtype
subtype = the cancer subtype
data =  a SAS data set containing all the variables mentioned above
)
```

The data set used in this macro can be created based on the output from the full cohort unconstrained analysis, or the nested or matched case-control unconstrained analysis.

3 Examples

Below is an example illustrating the use of this macro, based on a study of the association of alcohol consumption with colon cancer subtypes defined by LINE-1 methylation level (3 ordinal categories, low, medium and high).

We first create a dataset containing scores for the ordinal subtypes, the subtype-specific $log(\hat{RR})$, representing the exposure-subtype associations, and variances of the subtype-specific $log(\hat{RR})$.

```
data colon;
input subtype $1-11  ESTIMATE    STDERR;
var=STDERR**2;
if subtype eq 'LINE-1-low ' then score=0;
if subtype eq 'LINE-1-med ' then score=1;
if subtype eq 'LINE-1-high' then score=2;

datalines;
LINE-1-low             0.30950  0.13467
LINE-1-med             0.44929  0.10814
LINE-1-high          -0.0007371  0.11743
;
```

The macro call is:

```
%meta_subtype_trend(data = colon, logRR = ESTIMATE, var = var,
subtype = subtype, score = score);
```

The macro printed out the following output.

```
    The P-value for the test that the exposure of interest has an
    increasing or decreasing ordinal association with the relative
    risks for each increasing subtype is:  0.1237
```

This analysis result suggests that there is not sufficient evidence to conclude that the alcohol association with colon cancer monotonically increases or decreases across the low LINE-1, medium LINE-1 and high LINE-1 colon cancer.

4 How should I describe this in my Methods section?

The estimates of the subtype-specific relative risks are based on a fully unconstrained approach in which the confounder effects are allowed to be difference among the subtypes. To test whether the exposure-disease association has a trend across the ordinal subtypes, we used the meta-regression method with a subtype-specific random effect term (XXX, *et al.*, 2014).

5 Correspondence

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6 References

Molin Wang, Donna Spiegelman, Aya Kuchiba, Paul Lochhead, Sehee Kim, Andrew T. Chan, Elizabeth M. Poole, Rulla Tamimi, Shelley S. Tworoger, Edward Giovannucci, Bernard Rosner, Shuji Ogino.
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