

Two postestimation commands for assessing confounding

Zhiqiang Wang

Centre for Chronic Disease

School of Medicine



**THE UNIVERSITY
OF QUEENSLAND**



Confounding

- A situation in which a measure of the effect of an exposure on risk is distorted because the association with other factor(s) that influence the outcome under study. (Last 1995)
- A bias due to the imbalanced distribution of extraneous risk factor(s) among study groups.



Approaches to handling confounding

- Restriction
- Randomisation
- Matching
- Stratification
- Multiple regression analysis



Practical approach to assessing confounding

- To compare adjusted with crude effect estimates



Multiple regression

- Number of possible effect estimates
 - Number = 2^n
(where n = number of confounders)



Regression analysis

- Stepwise (P value)
- Bayesian (BIC)
- Akaike (AIC)
- Deviance (DIC)
- Focussed (FIC)
- Bayesian model averaging
- Frequentist model averaging
- Propensity score (two stages)

Command: help confall

help for **confall****plot and display all possible effect estimates after estimation**

```
confall [, eform(string) lockterms(varlist) format(%fmt) xis(string) xformat(%fmt) addaic addbic notable
         graph_options ]
```

Description

confall plots and displays effect estimates from models with all possible combinations of potential confounders. The first independent variable is the exposure of interest and all other independent variables are potential confounders.

options

eform reports the estimated coefficients transformed to odds ratios, hazard ratios, relative risk i.e., $\exp(b)$ rather than b . Confidence intervals are similarly transformed.

format(%fmt) specifies the display format for presenting numbers in graph and table. **format(%9.0g)** is the default

xformat(%fmt) specifies the display format for presenting numbers in x axis. **format(%9.0g)** is the default

lockterms(varlist) specifies variables to be included in all models.

xis() specifies values for x-axis. The default is p representing p values. Alternatives include *aic* (Akaike Information Criterion), *bic* (Bayesian Information Criterion), *r2* (R^2 or Pseudo R^2), and *n* (the number of confounders)

addaic and **addbic** mark the effect estimate from the model with the minimum AIC and BIC, respectively.

notable suppresses the display of the table.

graph_options refers to options of `graph twoway scatter`.

Examples

```
. logistic diabetes bmi age sex cholesterol sbp crp smoking drinking
. confall, lockterm(age sex) eform(OR)
. confall, eform(OR) xline(0.05) yline(1)
. confall, eform(OR) yline(1) xis(aic)
```

Author

Zhiqiang Wang <z.wang@uq.edu.au>
The University of Queensland

Acknowledgments

This work was supported by the NHMRC Australia (301024).

Results

```
. stset time, id(id) failure(diabincident==1)
```

```
      id:      id
failure event: diabincident == 1
obs. time interval: (time[_n-1], time]
exit on or before: failure
```

```
714 total obs.
  0 exclusions
```

```
714 obs. remaining, representing
714 subjects
126 failures in single failure-per-subject data
6725.955 total analysis time at risk, at risk from t =      0
          earliest observed entry t =      0
          last observed exit t = 12.81862
```




All possible effect estimates: syntax

Exposure variable

Potential confounding variables

```
Command
stcox CRP BMI Age Sex IGT weight SBP Cholesterol Diastolic Smoking Drinking GGT ACR
```

```
Command
confall, lockterms(Age Sex) xis(p) eform(Hazard ratio) addbic addaic /* graphic options
```

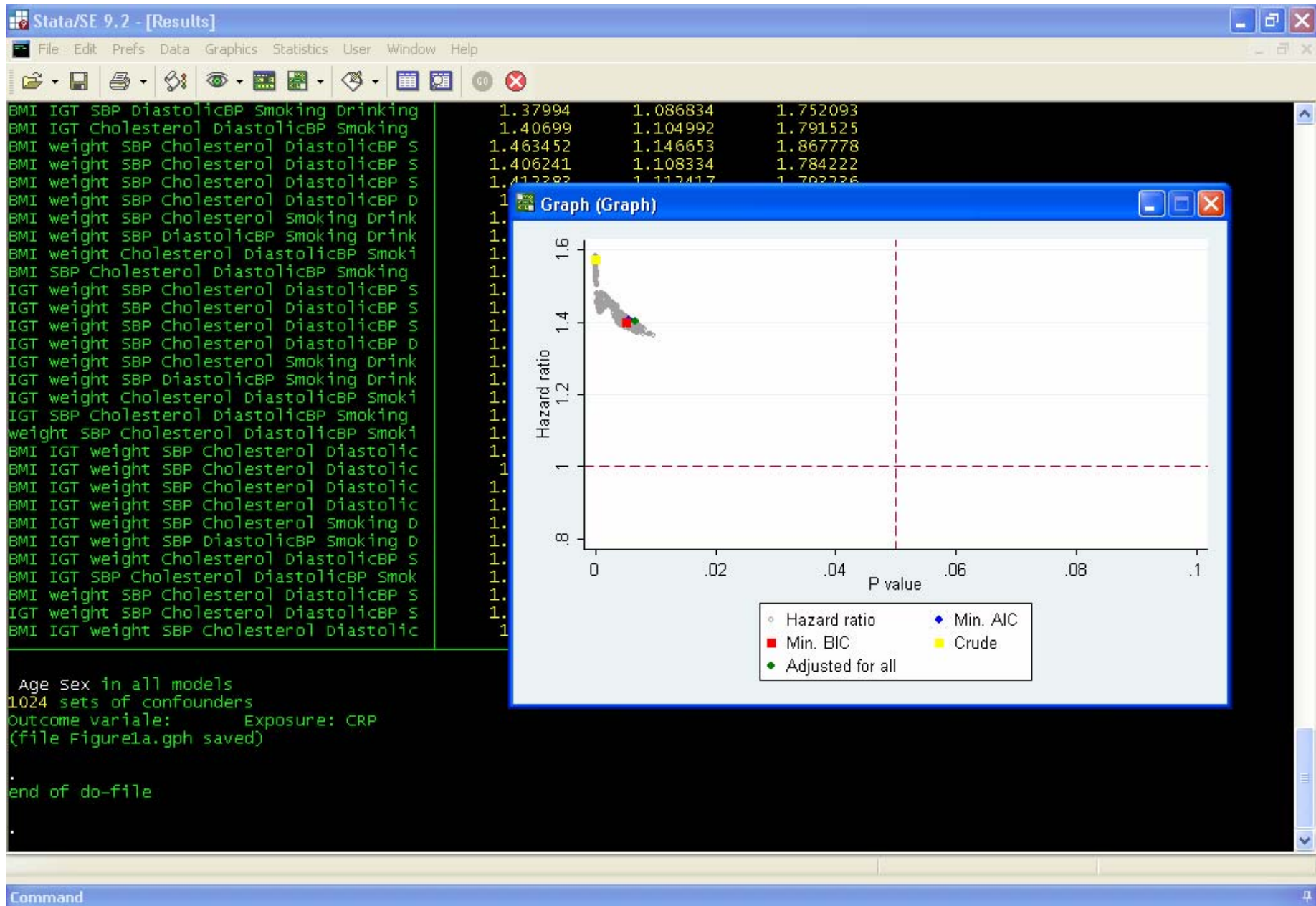
aic bic civ r2 n

```
. confall, eform(Hazard ratio) lock(Age sex)
Please wait.....
```

Var.adj.	Hazard ratio	[95% Conf.	Interval]
Null	1.571584	1.282775	1.925417
BMI	1.477466	1.169968	1.865783
IGT	1.54539	1.252523	1.906736
weight	1.452142	1.153083	1.828765
SBP	1.565356	1.277288	1.918391
Cholesterol	1.584887	1.277	1.967006
DiastolicBP	1.562158	1.274784	1.914314
Smoking	1.570658	1.281828	1.924569
BMI IGT	1.443765	1.138398	1.831045
BMI weight	1.479657	1.170326	1.870746
BMI SBP	1.477475	1.169934	1.86586
BMI Cholesterol	1.475168	1.160456	1.875228
BMI DiastolicBP	1.478016	1.171629	1.864526
BMI Smoking	1.475407	1.168039	1.863659
IGT weight	1.425284	1.127072	1.802401
IGT SBP	1.545571	1.252514	1.907195
IGT Cholesterol	1.548682	1.238458	1.936616
IGT DiastolicBP	1.533699	1.241384	1.894845
IGT smoking	1.542997	1.250355	1.904131
weight SBP	1.451516	1.152536	1.828055
weight Cholesterol	1.452017	1.144587	1.842021
weight DiastolicBP	1.444242	1.147921	1.817055
weight Smoking	1.451014	1.152078	1.827518
SBP Cholesterol	1.583499	1.275891	1.965269
SBP DiastolicBP	1.563755	1.276235	1.91605
SBP Smoking	1.564698	1.276611	1.917796
Cholesterol DiastolicBP	1.576616	1.271765	1.954544
Cholesterol Smoking	1.582786	1.274874	1.965065
DiastolicBP smoking	1.562158	1.274784	1.914315
BMI IGT weight	1.449142	1.141555	1.839605
BMI IGT SBP	1.443855	1.138549	1.83103
BMI IGT Cholesterol	1.445286	1.132155	1.845023
BMI IGT DiastolicBP	1.441919	1.137307	1.828118
BMI IGT smoking	1.44311	1.137493	1.830837
BMI weight SBP	1.479675	1.170292	1.870848
BMI weight Cholesterol	1.47696	1.160258	1.880108

Command

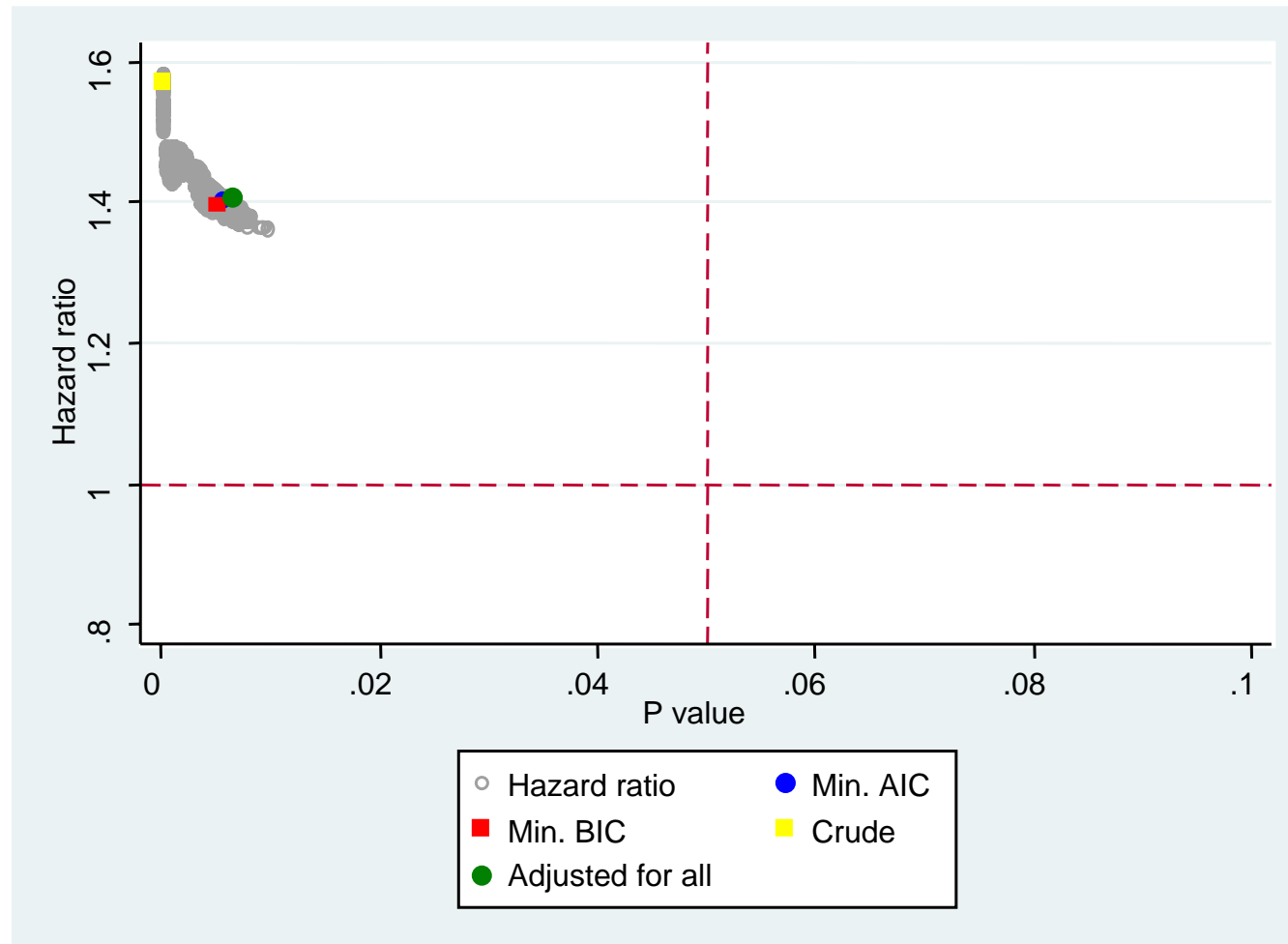
confall, eform(Hazard ratio) lock(Age Sex)





Example 1: C-reactive protein and Diabetes

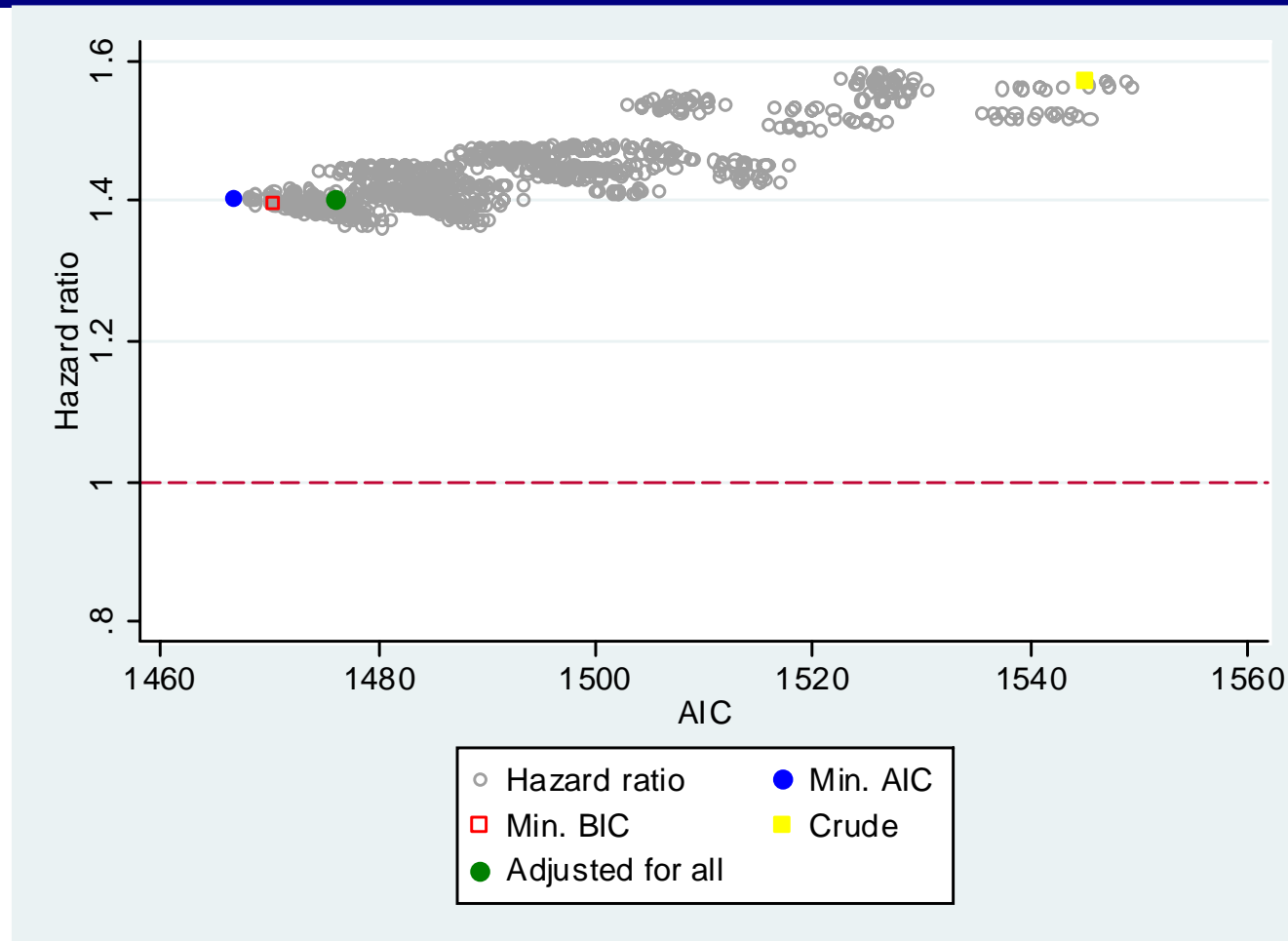
All effect estimates





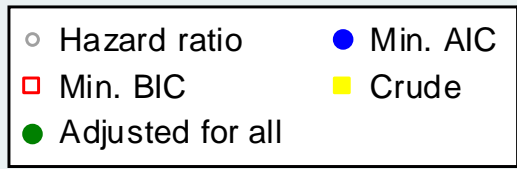
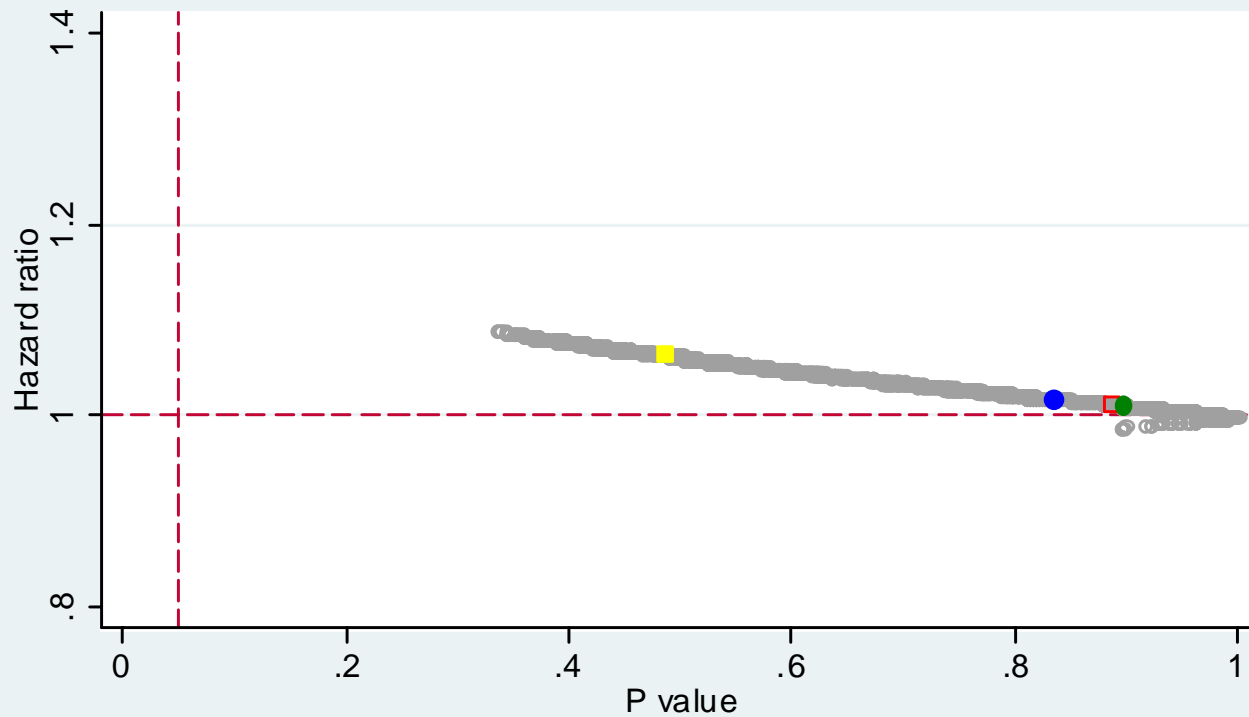
Example 1: CRP and Diabetes

All effect estimates





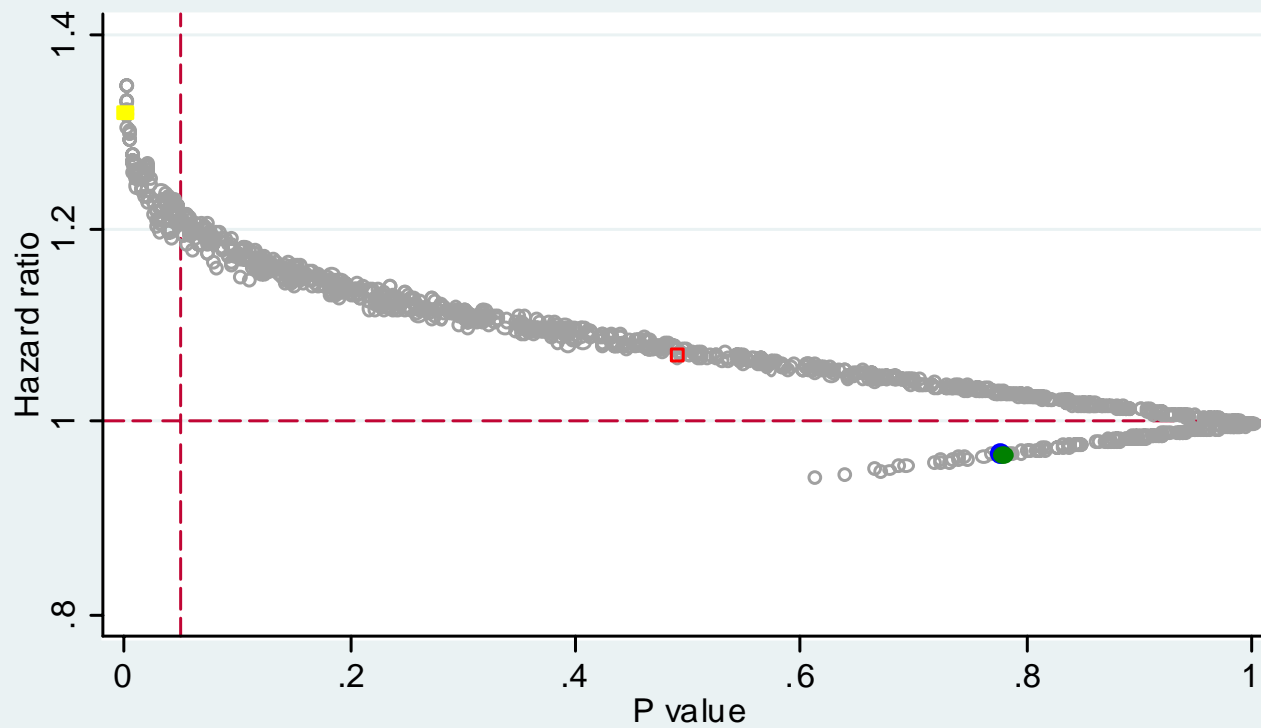
Example 2: No Association and No Confounding All effect estimates





Example 3: GGT and Diabetes

All effect estimates



- Hazard ratio
- Min. BIC
- Min. AIC
- Crude
- Adjusted for all

help for **confnd**

plot and display change-in-effect estimates after estimation

```
confnd [, eform forward lockterms(varlist) format(%fmt) notable graph_options ]
```

Description

confnd plots and displays effect estimates using stepwise change-in-estimate method for assessing confounding. The first independent variable is the exposure of interest and all other independent variables are potential confounders.

Options

eform reports the estimated coefficients transformed to odds ratios, hazard ratios, relative risk i.e., $\exp(b)$ rather than b . Confidence intervals are similarly transformed.

format(%fmt) specifies the display format for presenting numbers in graph and table. **format(%9.0g)** is the default.

forward specifies the forward method, the backward method is the default.

lockterms(varlist) specifies variables to be included in all models.

notable suppresses the display of the table.

graph_options refers to options of `graph twoway scatter`.

Examples

```
. logistic diabetes bmi age sex cholesterol sbp crp smoking drinking  
. confnd, eform  
. confnd, eform(Odds ratio) xline(1)
```

Author

Zhiqiang Wang <zwang@ccs.uq.edu.au>
The University of Queensland

Acknowledgments

This work was supported by the NHMRC Australia (301024).

Also see

On-line: help for `confall` (if installed)



Change-in-effect estimates: syntax

Command

```
stcox CRP BMI Age Sex IGT weight SBP Cholesterol Diastolic Smoking Drinking GGT ACR
```

Command

```
confnd, lockterms(Age Sex) eform(Hazard ratio) forward /* graphic options |
```

Default: backward

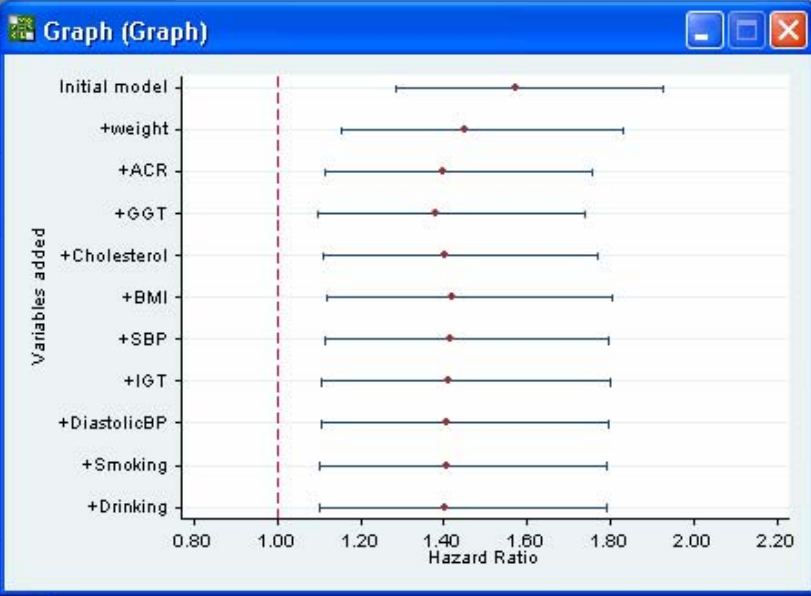
```

Results
stcox regression.           Outcome:
number of obs = 714       Exposure: CRP

Variables added           Hazard Ratio   [95% Conf. Interval]   Change, %
-----
Initial model            1.57           1.28           1.93
+weight                  1.45           1.15           1.83      7.60
+ACR                     1.40           1.12           1.76      3.64
+GGT                    1.38           1.10           1.74      1.26
+Cholesterol            1.40           1.11           1.77      1.37
+BMI                    1.42           1.12           1.80      1.47
+SBP                    1.42           1.11           1.80      0.40
+IGT                    1.41           1.11           1.80      0.34
+DiastolicBP           1.41           1.10           1.80      0.21
+Smoking                1.41           1.10           1.79      0.15
+Drinking                1.40           1.10           1.79      0.19

Age Sex in all models

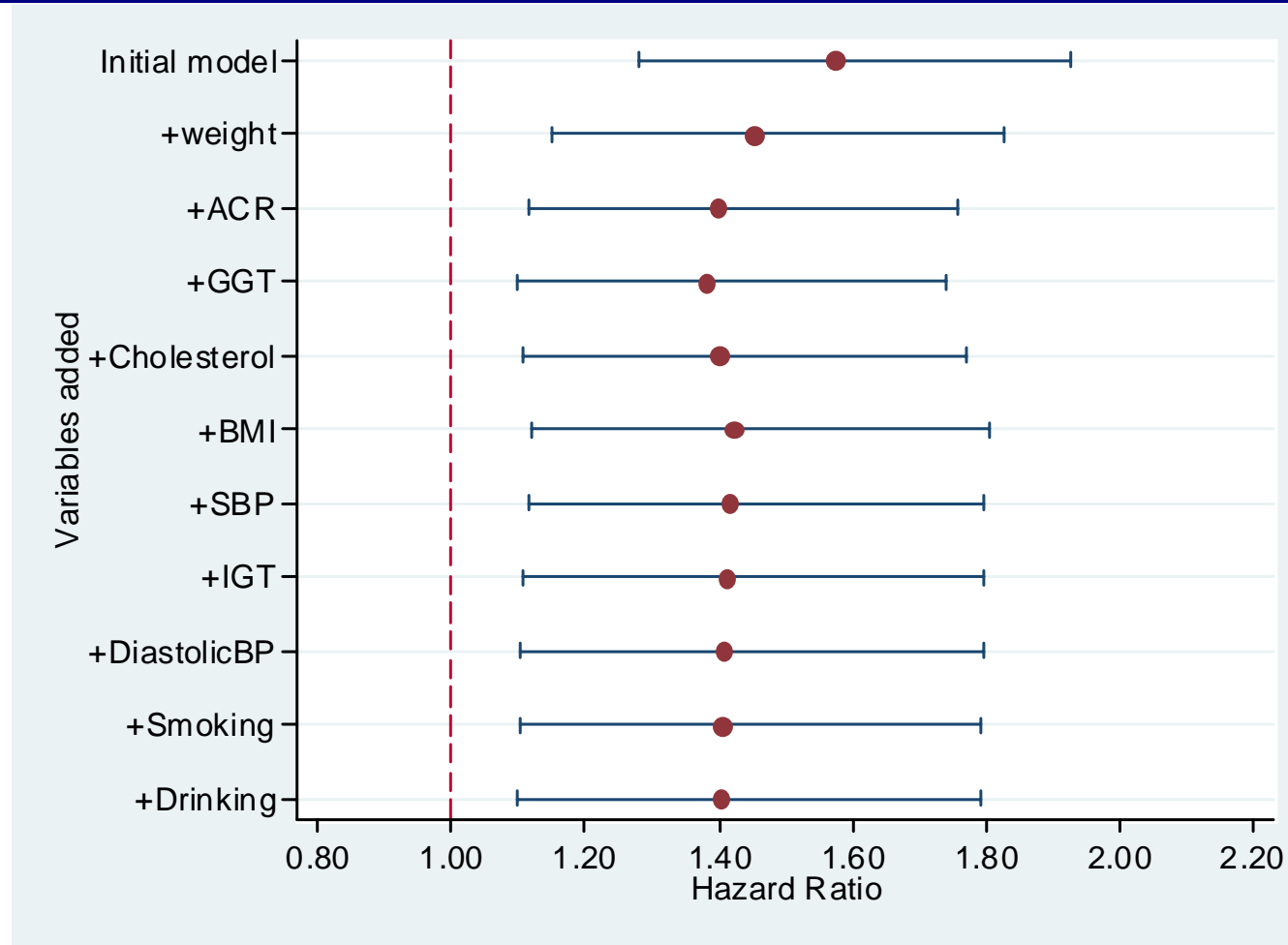
end of do-file
    
```



Command



Example 1: CRP and diabetes change-in-effect estimates: confnd



Stata/SE 9.2

File Edit Prefs Data Graphics Statistics User Window Help

Results


Change-in-estimate
 stcox regression. Outcome:
 number of obs = 714 Exposure: CRP

Variables added	Hazard Ratio	[95% Conf. Interval]	Change, %
Initial model	1.57	1.28 1.93	
+weight	1.45	1.15 1.83	7.60
+ACR	1.40	1.12 1.76	3.64
+GGT	1.38	1.10 1.74	1.26
+Cholesterol	1.40	1.11 1.77	1.37
+BMI	1.42	1.12 1.80	1.47
+SBP	1.42	1.11 1.80	0.40
+IGT	1.41	1.11 1.80	0.34
+DiastolicBP	1.41	1.10 1.80	0.21
+Smoking	1.41	1.10 1.79	0.15
+Drinking	1.40	1.10 1.79	0.19

Age Sex in all models

end of do-file

Command

Slide 20 of 28 uq English (Australia) 

Stata/SE 9.2

File Edit Prefs Data Graphics Statistics User Window Help

Results

```
. confnd, for format(%6.2f)
Change-in-estimate
stcox regression.           Outcome:
number of obs = 714         Exposure: CRP
```

Variables added	Coef.	[95% Conf. Interval]	Change, %
Crude	0.49	0.30 0.68	
+ACR	0.36	0.17 0.56	26.10
+weight	0.34	0.12 0.55	7.87
+Sex	0.35	0.13 0.57	4.21
+GGT	0.33	0.11 0.56	5.33
+Cholesterol	0.35	0.12 0.58	5.43
+Age	0.34	0.10 0.57	3.68
+BMI	0.35	0.11 0.59	4.33
+SBP	0.35	0.11 0.59	1.14
+IGT	0.34	0.10 0.59	0.99
+DiastolicBP	0.34	0.10 0.59	0.60
+Smoking	0.34	0.10 0.58	0.45
+Drinking	0.34	0.09 0.58	0.57

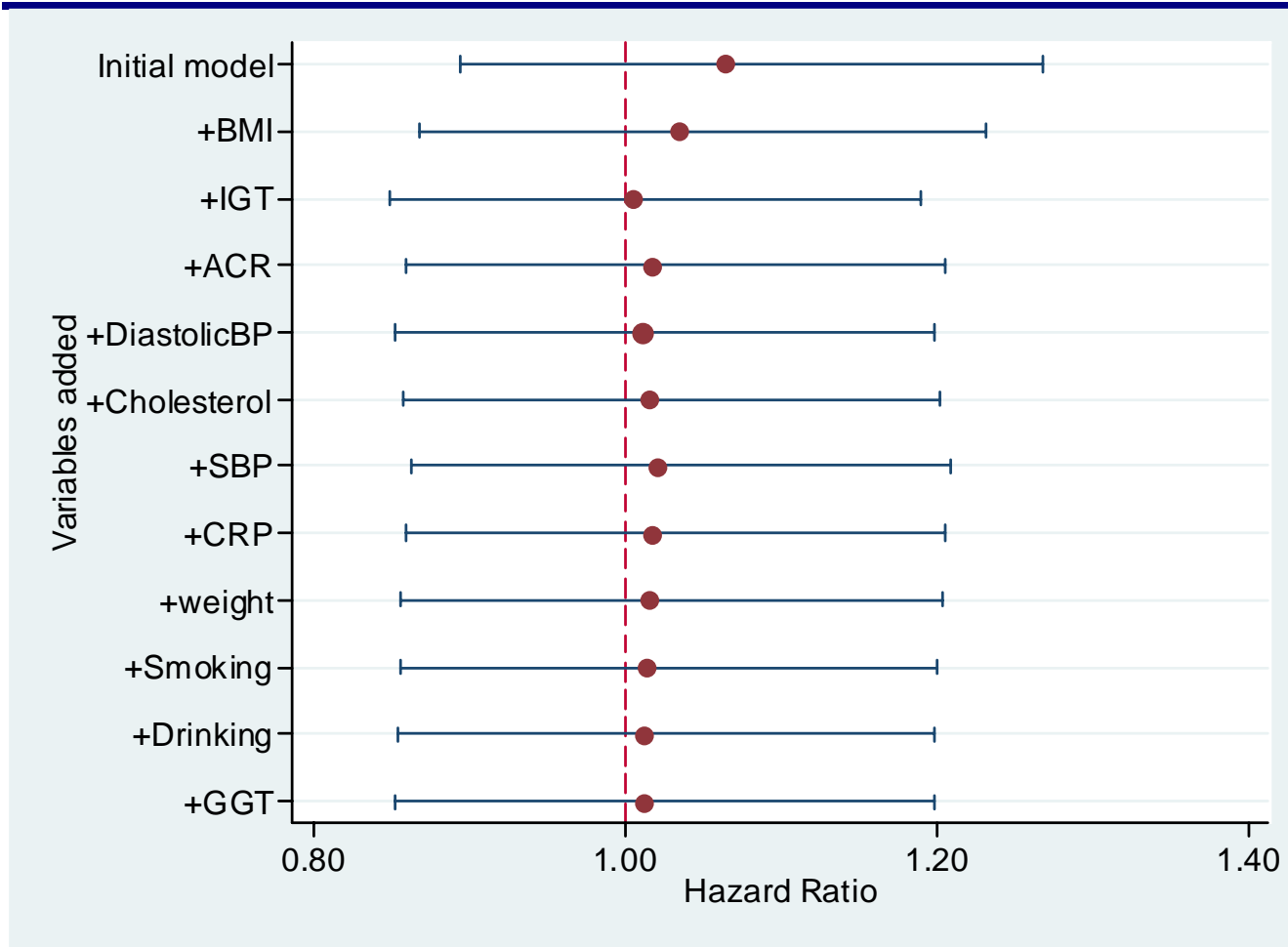
Command

Slide 20 of 28 uq English (Australia)



Example 2: No Association and No Confounding

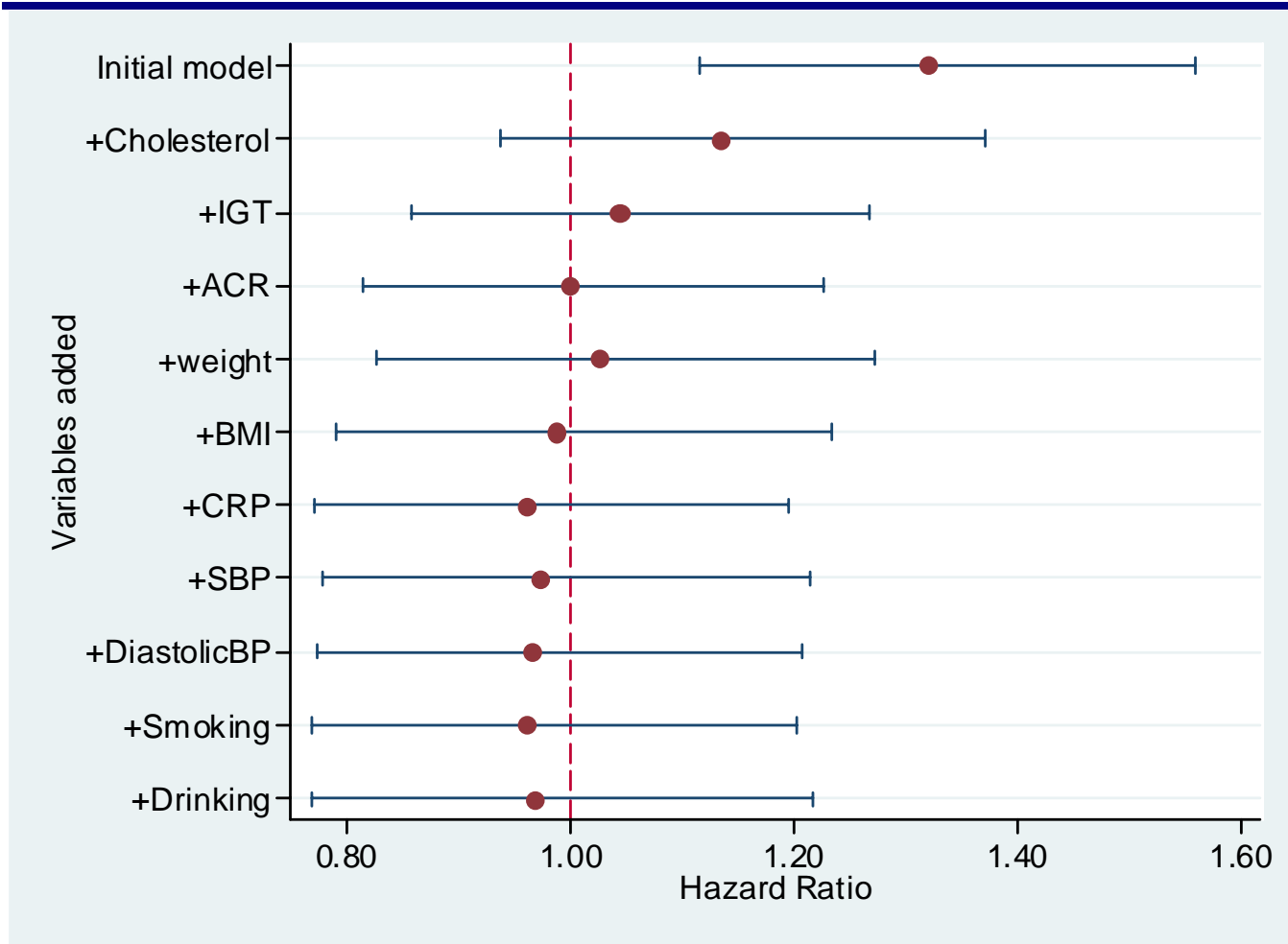
Change-in-effect estimates: confnd





Example 3: GGT and Diabetes

Change-in-effect estimates: confnd



Stata/SE 9.2

File Edit Prefs Data Graphics Statistics User Window Help

Results

Change-in-estimate
 stcox regression. Outcome:
 number of obs = 714 Exposure: GGT

Variables added	Hazard Ratio	[95% Conf. Interval]	Change, %
Initial model	1.32	1.12 1.56	
+Cholesterol	1.13	0.94 1.37	14.03
+IGT	1.04	0.86 1.27	7.97
+ACR	1.00	0.82 1.23	4.17
+weight	1.03	0.83 1.27	2.62
+BMI	0.99	0.79 1.23	3.71
+CRP	0.96	0.77 1.20	2.85
+SBP	0.97	0.78 1.22	1.30
+DiastolicBP	0.97	0.77 1.21	0.70
+Smoking	0.96	0.77 1.20	0.43
+Drinking	0.97	0.77 1.22	0.57

Age Sex in all models

end of do-file

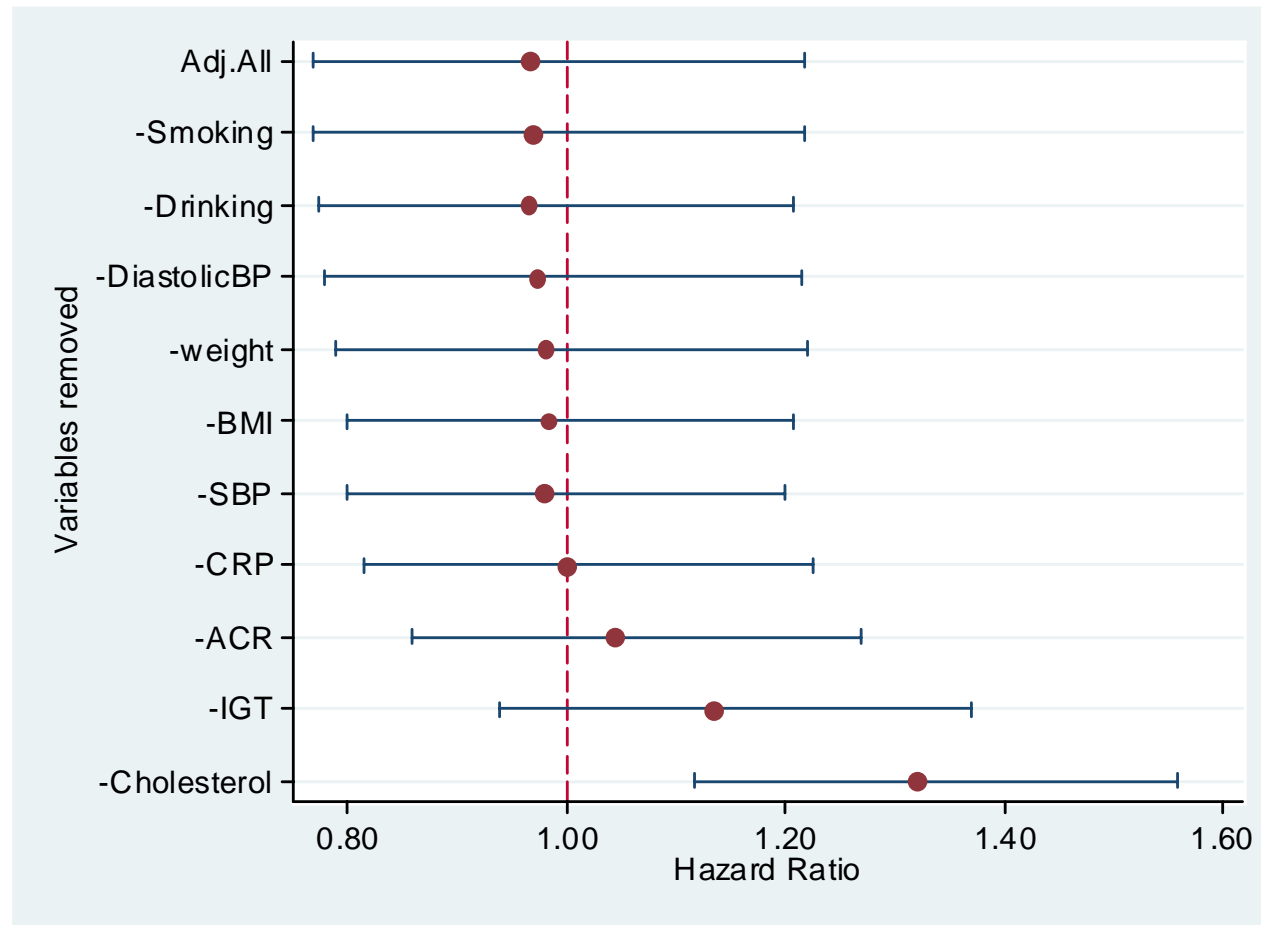
Command

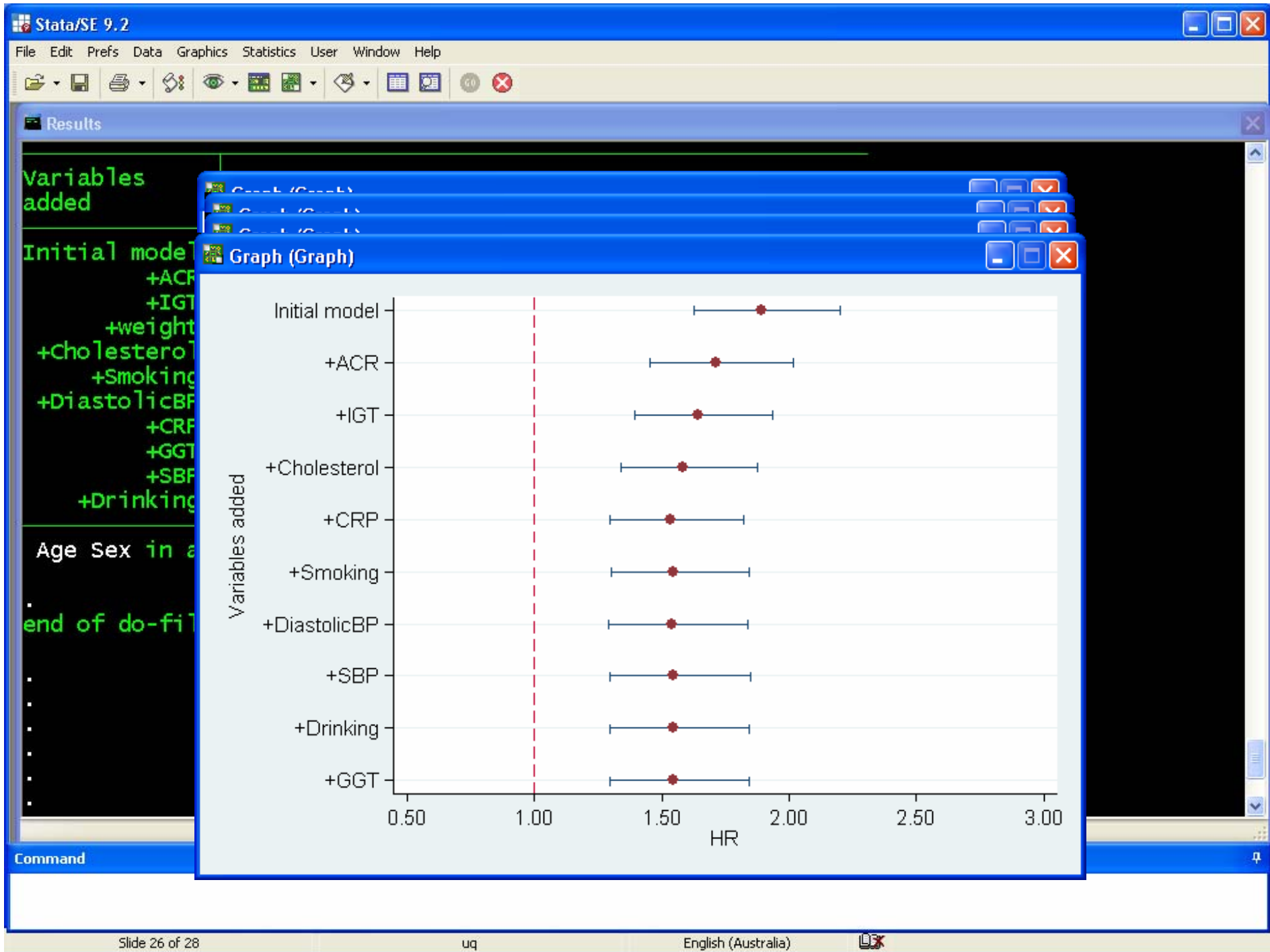
Slide 23 of 28 uq English (Australia)



Example 3: GGT and Diabetes

Change-in-effect estimates: confnd, backward







Conclusions

- Tools are useful for identifying the presence of confounding
- Not a substitute for careful incorporation of available knowledge to select confounding factors in the design stage, or careful data analysis.



Acknowledgements

This work was supported by the National Health and Medical Research Council (NHMRC) of Australia (301024, 320860).