WEB MATERIAL

Time-Varying Exposures and Miscarriage: A Comparison of Statistical Models Through Simulation

Alexandra C. Sundermann, James C. Slaughter, Digna R. Velez Edwards, and Katherine E. Hartmann

Table of Contents

Web Table 1. Characteristics of participants in Right From the Start, 2000–2012

Characteristic	No.	%
Maternal age, years		
<20	190	3.5
20–24	886	16.3
25–29	1,859	34.3
30–34	1,729	31.9
≥35	760	14.0
Ethnicity/race		
White, non-Hispanic	3,791	69.9
Black, non-Hispanic	1.026	18.9
Hispanic	366	6.7
Other	238	4.4
Refused	3	0.1
Body mass index[a]		
Underweight	135	2.5
Normal weight	2,865	52.8
Overweight	1,269	23.4
Obese	1,092	20.1
Missing	63	1.2
Marital status		
Married, cohabitating	4,839	89.2
Other	585	10.8
History of miscarriage		
Yes	4,137	76.3
No	1,207	22.3
Missing	80	1.5
Annual income, $		
≤ 40,000	1,654	30.5
40,001–80,000	1,947	35.9
>80,000	1,637	30.2
Missing/Refused	186	3.4
Education		
High school or less	986	17.8
Some college	976	18.0
College or more	3,479	64.1
Missing	1	0.0
Alcohol use[b]		
Never exposed/distant quit	2,422	44.7
Recent quit	2,710	50.0
Current user	292	5.4
Pregnancy intention		
Intended	3,559	65.6
Unintended	1,470	27.1
Missing	395	7.3
Pregnancy outcome		
Miscarriage	649	12.0
Other	4,775	88.0

[a] Institute of Medicine classifications: underweight <18.5 kg/m^{2,}, normal weight 18.5–24.9 kg/m^{2,}, overweight 25.0–29.9 kg/m^{2,}, obese ≥30.0 kg/m^2.

[b] Recent quitting was defined as cessation of alcohol use within 4 months of the first-trimester interview.

WEB APPENDIX 1

Questionnaire Items About Alcohol Consumption in the First-Trimester Interview

- Have you ever had alcoholic beverages, like beer, wine, or liquor including gin, whiskey, rum, or mixed drinks?
- At this time, do you drink any alcoholic beverages, like beer, wine, or liquor including gin, whiskey, rum, or mixed drinks?
- How often do you drink an alcoholic beverage, by that I mean at least one beer, one glass of wine, one mixed drink, or one shot of liquor? *(# times per day, week, or month, or less than once per month).*
- On those occasions that you drink alcoholic beverages, how many drinks do you usually have?
- At this time, what type(s) of alcohol do you usually drink? To make it easier for you to respond, I'm going to read you a list of options: beer, wine, mixed drinks, shot of liquor, other alcohol _____.
- Did you stop drinking alcoholic beverages in the past 4 months or more than 4 months ago?
- In the past 4 months, have you changed how often and/or how many alcoholic beverages you drink?
- When did this change occur?
- Do you remember what week in [month] that was, the first, second, third, fourth, or fifth?
- Before this change, how often did you drink? *(# times per day, week, or month, or less than once per month).*
- Before this change, on those occasions when you drank alcoholic beverages, how many drinks did you usually have on each occasion?
- What type(s) of alcohol did you usually drink? Did you drink beer, wine, mixed drinks, shot of liquor, other alcohol _____.
- In the past four months, have you had more than four drinks on any one occasion?
- How many times in the past four months have you had more than four drinks on any occasion?
- On those occasions when you had more than four drinks, what type(s) of alcohol did you usually drink? Did you drink beer, wine, mixed drinks, shot of liquor, other alcohol _____.

Web Table 2. Parameter assignment in simulation studies

Parameter	Assignment Rule	Comments
Same across all simulations		
Exposure status at time t=0	$X \sim B(1, 0.5500)$	
Exposure status at time t=140	$X \sim B(1, 0.0900)$	Given an individual was exposed at time t=0
Timing of change in exposure (days' gestation)	$\left(X \sim \text{Beta}(7, 5)\right) \cdot 100 - 30$	Negative values denote a change that occurred prior to last menstrual period.
Outcome timing (days' gestation)	$(X \sim \text{Beta}(4.5, 8.6) \cdot 126 + 14$	Given pregnancy ends in miscarriage
Specific to Relationship 1. Exposure not related to miscarriage risk		
Miscarriage risk	$X \sim B(1, 0.1235)$	
Outcome timing (days' gestation)	$(X \sim \text{Beta}(4.5, 8.6) \cdot 126 + 14$	Given pregnancy ends in miscarriage
Specific to Relationship 2. Any exposure increases risk		
Miscarriage risk given exposed in pregnancy	$X \sim B(1, 0.0969)$	
Miscarriage risk given unexposed in pregnancy	$X \sim B(1, 0.1453)$	
Specific to Relationship 3. Exposure in week five increases risk		
Miscarriage risk given exposed in week five of pregnancy	$X \sim B(1, 0.1698)$	
Miscarriage risk given unexposed in week five of pregnancy	$X \sim B(1, 0.1132)$	Includes both individuals who were unexposed and those whose exposure status change prior to week five
Specific to Relationship 4. Cumulative exposure associates with risk		
Miscarriage risk given exposed in pregnancy	$X \sim B(1, 0.1060 \cdot 1.0137^{t-14})$	*t* equals outcome time if exposure change occurs after outcome or *t* equals time of exposure change if exposure change occurs before outcome
Miscarriage risk given unexposed in pregnancy	$X \sim B(1, 0.1060)$	Includes individuals who were unexposed throughout pregnancy and whose exposure status change prior to day 14

Specific to Relationship 5. Exposure increases risk during the following week

Miscarriage risk given exposure within seven days of outcome	$X \sim B(1, 0.1960)$
Miscarriage risk given no exposure within seven days of outcome	$X \sim B(1, 0.1130)$

WEB APPENDIX 2

Simulation Code

```
*Time-Varying Exposures and Miscarriage: A Comparison of Approaches Through Simulation
*Written for Stata
*******************************************************************************
set more off
clear all
*******************************************************************************
*Relationship 1: Exposure not related to risk
program define null_p, rclass
clear
set obs 1500

gen id=_n

**Define Time-Varying Exposure Variables
gen early_exposed=rbinomial(1, 0.55)
gen late_exposed=rbinomial(1, 0.09) if early_exposed==1
replace late_exposed=0 if early_exposed==0

gen change_consump_time=rbeta(7,5)*100-30 if early_exposed==1

gen days=.
replace days=ceil(change_consump_time)-14
replace days=0 if days<0|days==.

gen gestwkchange=.
replace gestwkchange=0 if change_consump_time>=0 & change_consump_time<7
replace gestwkchange=1 if change_consump_time>=7 & change_consump_time<14
replace gestwkchange=2 if change_consump_time>=14 & change_consump_time<21
replace gestwkchange=3 if change_consump_time>=21 & change_consump_time<28
replace gestwkchange=4 if change_consump_time>=28 & change_consump_time<35
replace gestwkchange=5 if change_consump_time>=35 & change_consump_time<42
replace gestwkchange=6 if change_consump_time>=42 & change_consump_time<49
replace gestwkchange=7 if change_consump_time>=49 & change_consump_time<56
replace gestwkchange=8 if change_consump_time>=56 & change_consump_time<63
replace gestwkchange=9 if change_consump_time>=63 & change_consump_time<70
replace gestwkchange=10 if change_consump_time>=70 & change_consump_time<77
replace gestwkchange=11 if change_consump_time>=77 & change_consump_time<84
replace gestwkchange=12 if change_consump_time>=84 & change_consump_time<91
replace gestwkchange=13 if change_consump_time>=91 & change_consump_time<98
replace gestwkchange=14 if change_consump_time>=98 & change_consump_time~=.
replace gestwkchange=0 if  change_consump_time<0 | (change_consump_time==. & late_exposed==0)
label define wkchanges 0 "No pregnancy exposure" 1 "0-6" 2 "7-13" 3 "14-20" 4 "21-27" 5 "28-34" 6 "35-41"  ///
7 "42-48" 8 "49-55" 9 "56-62" 10 "63-69" 11 "70-76" 12 "77-83" 13 "84-90" 14 "No change or after 1st Tri"
label values gestwkchange wkchanges

**Week specific exposure
gen expose1=.
replace expose1=1 if gestwkchange>=1|late_exposed==1
replace expose1=0 if early_exposed==0|(gestwkchange<1 & late_exposed==0)

gen expose2=.
```

```
replace expose2=1 if gestwkchange>=2|late_exposed==1
replace expose2=0 if early_exposed==0|(gestwkchange<2 & late_exposed==0)

gen expose3=.
replace expose3=1 if gestwkchange>=3|late_exposed==1
replace expose3=0 if early_exposed==0|(gestwkchange<3 & late_exposed==0)

gen expose4=.
replace expose4=1 if gestwkchange>=4|late_exposed==1
replace expose4=0 if early_exposed==0|(gestwkchange<4 & late_exposed==0)

gen expose5=.
replace expose5=1 if gestwkchange>=5|late_exposed==1
replace expose5=0 if early_exposed==0|(gestwkchange<5 & late_exposed==0)

gen expose6=.
replace expose6=1 if gestwkchange>=6|late_exposed==1
replace expose6=0 if early_exposed==0|(gestwkchange<6 & late_exposed==0)

gen expose7=.
replace expose7=1 if gestwkchange>=7|late_exposed==1
replace expose7=0 if early_exposed==0|(gestwkchange<7 & late_exposed==0)

gen expose8=.
replace expose8=1 if gestwkchange>=8|late_exposed==1
replace expose8=0 if early_exposed==0|(gestwkchange<8 & late_exposed==0)

gen expose9=.
replace expose9=1 if gestwkchange>=9|late_exposed==1
replace expose9=0 if early_exposed==0|(gestwkchange<9 & late_exposed==0)

gen expose10=.
replace expose10=1 if gestwkchange>=10|late_exposed==1
replace expose10=0 if early_exposed==0|(gestwkchange<10 & late_exposed==0)

gen expose11=.
replace expose11=1 if gestwkchange>=11|late_exposed==1
replace expose11=0 if early_exposed==0|(gestwkchange<11 & late_exposed==0)

gen expose12=.
replace expose12=1 if gestwkchange>=12|late_exposed==1
replace expose12=0 if early_exposed==0|(gestwkchange<12 & late_exposed==0)

gen expose13=.
replace expose13=1 if gestwkchange>=13|late_exposed==1
replace expose13=0 if early_exposed==0|(gestwkchange<13 & late_exposed==0)

gen expose14=.
replace expose14=1 if gestwkchange>=14|late_exposed==1
replace expose14=0 if early_exposed==0|(gestwkchange<14 & late_exposed==0)

**Outcome
gen outcome=rbinomial(1, 0.1235)

**Outcome Timing
gen gaad=round(rbeta(4.5,8.6)*126+14) if outcome==1
```

```
replace gaad=140 if outcome==0
                                                    **************
*Run models to measure performance

stset gaad, id(id) failure(outcome)

*Simple Cox PH
stcox early_exposed
return scalar sr_b=_b[early_exposed]
return scalar sr_se=_se[early_exposed]
return scalar sr_test=1-chi2(e(df_m), e(chi2))

test _b[early_exposed]==0
return scalar sr_p=r(p)

*Sequential logistic
quietly logistic outcome expose3 if outcome==0|(outcome==1 & gaad>21)
estimate store week_3
return scalar sm_b3=_b[expose3]
return scalar sm_se3=_se[expose3]
test _b[expose3]==0
return scalar sm_p3=r(p)

quietly logistic outcome expose4 if outcome==0|(outcome==1 & gaad>28)
estimate store week_4
return scalar sm_b4=_b[expose4]
return scalar sm_se4=_se[expose4]
return scalar sm_test4=1-chi2(e(df_m), e(chi2))
test _b[expose4]==0
return scalar sm_p4=r(p)

quietly logistic outcome expose5  if outcome==0|(outcome==1 & gaad>35)
estimate store week_5
return scalar sm_b5=_b[expose5]
return scalar sm_se5=_se[expose5]
return scalar sm_test5=1-chi2(e(df_m), e(chi2))
test _b[expose5]==0
return scalar sm_p5=r(p)

quietly logistic outcome expose6 if outcome==0|(outcome==1 & gaad>42)
estimate store week_6
return scalar sm_b6=_b[expose6]
return scalar sm_se6=_se[expose6]
return scalar sm_test6=1-chi2(e(df_m), e(chi2))
test _b[expose6]==0
return scalar sm_p6=r(p)

quietly logistic outcome expose7 if outcome==0|(outcome==1 & gaad>49)
estimate store week_7
return scalar sm_b7=_b[expose7]
return scalar sm_se7=_se[expose7]
return scalar sm_test7=1-chi2(e(df_m), e(chi2))
test _b[expose7]==0
return scalar sm_p7=r(p)

quietly logistic outcome expose8 if outcome==0|(outcome==1 & gaad>56)
```

```
estimate store week_8
return scalar sm_b8=_b[expose8]
return scalar sm_se8=_se[expose8]
return scalar sm_test8=1-chi2(e(df_m), e(chi2))
test _b[expose8]==0
return scalar sm_p8=r(p)

quietly logistic outcome expose9 if outcome==0|(outcome==1 & gaad>63)
estimate store week_9
return scalar sm_b9=_b[expose9]
return scalar sm_se9=_se[expose9]
test _b[expose9]==0
return scalar sm_p9=r(p)

quietly logistic outcome expose10 if outcome==0|(outcome==1 & gaad>70)
estimate store week_10
return scalar sm_b10=_b[expose10]
return scalar sm_se10=_se[expose10]
test _b[expose10]==0
return scalar sm_p10=r(p)

quietly logistic outcome expose11 if outcome==0|(outcome==1 & gaad>77)
estimate store week_11
return scalar sm_b11=_b[expose11]
return scalar sm_se11=_se[expose11]
test _b[expose11]==0
return scalar sm_p11=r(p)

quietly logistic outcome expose12 if outcome==0|(outcome==1 & gaad>84)
estimate store week_12
return scalar sm_b12=_b[expose12]
return scalar sm_se12=_se[expose12]
test _b[expose12]==0
return scalar sm_p12=r(p)

quietly logistic outcome expose13 if outcome==0|(outcome==1 & gaad>91)
estimate store week_13
return scalar sm_b13=_b[expose13]
return scalar sm_se13=_se[expose13]
test _b[expose13]==0
return scalar sm_p13=r(p)

suest week_3 week_4 week_5 week_6 week_7 week_8 week_9 week_10 week_11 week_12 week_13

test (expose3=0) (expose4=0) (expose5=0) (expose6=0) (expose7=0) (expose8=0) ///
 (expose9=0) (expose10=0) (expose11=0) (expose12=0) (expose13=0)

 return scalar sm_exp3_13=r(p)

 test (expose4=0) (expose5=0) (expose6=0) (expose7=0) (expose8=0)

 return scalar sm_exp4_8=r(p)

*Cox with lag
stsplit split, at(1(1)140)
```

```
gen split_exposed=.
replace split_exposed=0 if early_exposed==0
replace split_exposed=1 if early_exposed==1 & late_exposed==0 & change_consump_time > (_t-7)
replace split_exposed=0 if early_exposed==1 & late_exposed==0  & change_consump_time < (_t-7)
replace split_exposed=1 if late_exposed==1

stcox split_exposed
return scalar lr_b1=_b[split_exposed]
return scalar lr_se1=_se[split_exposed]
return scalar lr_test=1-chi2(e(df_m), e(chi2))
test _b[split_exposed]==0
return scalar lr_p1=r(p)

*Cumulative Cox regression
gen exp_dur=.
replace exp_dur=_t-13 if days>=_t
replace exp_dur=days if _t>days
replace exp_dur=0 if exp_dur<0
replace exp_dur=0 if change_consump_time<14|change_consump_time==.

stcox exp_dur
return scalar cc_b=_b[exp_dur]
return scalar cc_se=_se[exp_dur]
test _b[exp_dur]==0
return scalar cc_p=r(p)

*Poisson regression with time ineraction
gen split_exposed2=.
replace split_exposed2=0 if early_exposed==0
replace split_exposed2=1 if early_exposed==1 & late_exposed==0 & change_consump_time > (_t)
replace split_exposed2=0 if early_exposed==1 & late_exposed==0  & change_consump_time < (_t)
replace split_exposed2=1 if late_exposed==1

gen time = _t

fp generate double time^(-1 3), center scale replace

summ time_1 if time==28, meanonly
scalar t1_28=r(mean)

summ time_1 if time==35, meanonly
scalar t1_35=r(mean)

summ time_1 if time==42, meanonly
scalar t1_42=r(mean)

summ time_1 if time==49, meanonly
scalar t1_49=r(mean)

summ time_1 if time==56, meanonly
scalar t1_56=r(mean)

summ time_2 if time==28, meanonly
scalar t2_28=r(mean)

summ time_2 if time==35, meanonly
```

```
scalar t2_35=r(mean)

summ time_2 if time==42, meanonly
scalar t2_42=r(mean)

summ time_2 if time==49, meanonly
scalar t2_49=r(mean)

summ time_2 if time==56, meanonly
scalar t2_56=r(mean)

gen int1 = split_exposed2*time_1
gen int2 = split_exposed2*time_2

poisson _d split_exposed2 time_1 time_2 int1 int2, exposure(gaad)

lincom split_exposed2+int1*t1_28 +int2 * t2_28
return scalar pf2_b4=r(estimate)
return scalar pf2_se4=r(se)

lincom split_exposed2+int1*t1_35 +int2 * t2_35
return scalar pf2_b5=r(estimate)
return scalar pf2_se5=r(se)

lincom split_exposed2+int1*t1_42 +int2 * t2_42
return scalar pf2_b6=r(estimate)
return scalar pf2_se6=r(se)

lincom split_exposed2+int1*t1_49 +int2 * t2_49
return scalar pf2_b7=r(estimate)
return scalar pf2_se7=r(se)

lincom split_exposed2+int1*t1_56 +int2 * t2_56
return scalar pf2_b8=r(estimate)
return scalar pf2_se8=r(se)

test split_exposed2 int1 int2
return scalar pf2_p=r(p)

end
*************************************************************************
*Relationship 1 Simulation
simulate sr_b=r(sr_b) sr_se=r(sr_se) sr_p=r(sr_p) sm_b4=r(sm_b4) sm_se4=r(sm_se4) sm_p4=r(sm_p4) ///
sm_b5=r(sm_b5) sm_se5=r(sm_se5) sm_p5=r(sm_p5) sm_b6=r(sm_b6) sm_se6=r(sm_se6) sm_p6=r(sm_p6) ///
sm_b7=r(sm_b7) sm_se7=r(sm_se7) sm_p7=r(sm_p7) sm_b8=r(sm_b8) sm_se8=r(sm_se8) sm_p8=r(sm_p8) ///
cc_b=r(cc_b) cc_se=r(cc_se) cc_p=r(cc_p) ///
lr_b1=r(lr_b1) lr_se1=r(lr_se1) lr_p1=r(lr_p1) sr_test=r(sr_test) sm_test4=r(sm_test4) ///
sm_test5=r(sm_test5) sm_test6=r(sm_test6) sm_test7=r(sm_test7) sm_test8=r(sm_test8) ///
sm_exp3_13=r(sm_exp3_13) sm_exp4_8=r(sm_exp4_8) lr_test=r(lr_test) ///
pf2_b4=r(pf2_b4) pf2_se4=r(pf2_se4) pf2_b5=r(pf2_b5) pf2_se5=r(pf2_se5) pf2_p=r(pf2_p) ///
pf2_b6=r(pf2_b6) pf2_se6=r(pf2_se6)pf2_b7=r(pf2_b7) pf2_se7=r(pf2_se7) pf2_b8=r(pf2_b8) pf2_se8=r(pf2_se8)
///
, reps(1000) seed(1714): null_p

clear
*************************************************************************
```

```
*******************************************************************************
*******************************************************************************
*Relationship 2: Any exposure uniformly increases risk of loss
program define any_p, rclass
clear
set obs 1500

gen id=_n

**Define Time-Varying Exposure Variables
gen early_exposed=rbinomial(1, 0.55)
gen late_exposed=rbinomial(1, 0.09) if early_exposed==1
replace late_exposed=0 if early_exposed==0

gen change_consump_time=rbeta(7,5)*100-30 if early_exposed==1

gen days=.
replace days=ceil(change_consump_time)-14
replace days=0 if days<0|days==.

gen gestwkchange=.
replace gestwkchange=0 if change_consump_time>=0 & change_consump_time<7
replace gestwkchange=1 if change_consump_time>=7 & change_consump_time<14
replace gestwkchange=2 if change_consump_time>=14 & change_consump_time<21
replace gestwkchange=3 if change_consump_time>=21 & change_consump_time<28
replace gestwkchange=4 if change_consump_time>=28 & change_consump_time<35
replace gestwkchange=5 if change_consump_time>=35 & change_consump_time<42
replace gestwkchange=6 if change_consump_time>=42 & change_consump_time<49
replace gestwkchange=7 if change_consump_time>=49 & change_consump_time<56
replace gestwkchange=8 if change_consump_time>=56 & change_consump_time<63
replace gestwkchange=9 if change_consump_time>=63 & change_consump_time<70
replace gestwkchange=10 if change_consump_time>=70 & change_consump_time<77
replace gestwkchange=11 if change_consump_time>=77 & change_consump_time<84
replace gestwkchange=12 if change_consump_time>=84 & change_consump_time<91
replace gestwkchange=13 if change_consump_time>=91 & change_consump_time<98
replace gestwkchange=14 if change_consump_time>=98 & change_consump_time~=.
replace gestwkchange=0 if  change_consump_time<0 | (change_consump_time==. & late_exposed==0)
label define wkchanges 0 "No pregnancy exposure" 1 "0-6" 2 "7-13" 3 "14-20" 4 "21-27" 5 "28-34" 6 "35-41"  ///
7 "42-48" 8 "49-55" 9 "56-62" 10 "63-69" 11 "70-76" 12 "77-83" 13 "84-90" 14 "No change or after 1st Tri"
label values gestwkchange wkchanges

**Week specific exposure
gen expose1=.
replace expose1=1 if gestwkchange>=1|late_exposed==1
replace expose1=0 if early_exposed==0|(gestwkchange<1 & late_exposed==0)

gen expose2=.
replace expose2=1 if gestwkchange>=2|late_exposed==1
replace expose2=0 if early_exposed==0|(gestwkchange<2 & late_exposed==0)

gen expose3=.
replace expose3=1 if gestwkchange>=3|late_exposed==1
replace expose3=0 if early_exposed==0|(gestwkchange<3 & late_exposed==0)

gen expose4=.
replace expose4=1 if gestwkchange>=4|late_exposed==1
```

```
replace expose4=0 if early_exposed==0|(gestwkchange<4 & late_exposed==0)

gen expose5=.
replace expose5=1 if gestwkchange>=5|late_exposed==1
replace expose5=0 if early_exposed==0|(gestwkchange<5 & late_exposed==0)

gen expose6=.
replace expose6=1 if gestwkchange>=6|late_exposed==1
replace expose6=0 if early_exposed==0|(gestwkchange<6 & late_exposed==0)

gen expose7=.
replace expose7=1 if gestwkchange>=7|late_exposed==1
replace expose7=0 if early_exposed==0|(gestwkchange<7 & late_exposed==0)

gen expose8=.
replace expose8=1 if gestwkchange>=8|late_exposed==1
replace expose8=0 if early_exposed==0|(gestwkchange<8 & late_exposed==0)

gen expose9=.
replace expose9=1 if gestwkchange>=9|late_exposed==1
replace expose9=0 if early_exposed==0|(gestwkchange<9 & late_exposed==0)

gen expose10=.
replace expose10=1 if gestwkchange>=10|late_exposed==1
replace expose10=0 if early_exposed==0|(gestwkchange<10 & late_exposed==0)

gen expose11=.
replace expose11=1 if gestwkchange>=11|late_exposed==1
replace expose11=0 if early_exposed==0|(gestwkchange<11 & late_exposed==0)

gen expose12=.
replace expose12=1 if gestwkchange>=12|late_exposed==1
replace expose12=0 if early_exposed==0|(gestwkchange<12 & late_exposed==0)

gen expose13=.
replace expose13=1 if gestwkchange>=13|late_exposed==1
replace expose13=0 if early_exposed==0|(gestwkchange<13 & late_exposed==0)

gen expose14=.
replace expose14=1 if gestwkchange>=14|late_exposed==1
replace expose14=0 if early_exposed==0|(gestwkchange<14 & late_exposed==0)

**Outcome
gen outcome=rbinomial(1, 0.0968627) if early_exposed==0
replace outcome=rbinomial(1, 0.14529412) if early_exposed==1

**Outcome Timing
gen gaad=round(rbeta(4.5,8.6)*126+14) if outcome==1
replace gaad=140 if outcome==0
                                        **********

*Run models to measure performance
stset gaad, id(id) failure(outcome)

*Simple Cox PH
stcox early_exposed
```

```
return scalar sr_b=_b[early_exposed]
return scalar sr_se=_se[early_exposed]
return scalar sr_test=1-chi2(e(df_m), e(chi2))

test _b[early_exposed]==0
return scalar sr_p=r(p)

*Sequential logistic
quietly logistic outcome expose3 if outcome==0|(outcome==1 & gaad>21)
estimate store week_3
return scalar sm_b3=_b[expose3]
return scalar sm_se3=_se[expose3]
test _b[expose3]==0
return scalar sm_p3=r(p)

quietly logistic outcome expose4 if outcome==0|(outcome==1 & gaad>28)
estimate store week_4
return scalar sm_b4=_b[expose4]
return scalar sm_se4=_se[expose4]
return scalar sm_test4=1-chi2(e(df_m), e(chi2))
test _b[expose4]==0
return scalar sm_p4=r(p)

quietly logistic outcome expose5  if outcome==0|(outcome==1 & gaad>35)
estimate store week_5
return scalar sm_b5=_b[expose5]
return scalar sm_se5=_se[expose5]
return scalar sm_test5=1-chi2(e(df_m), e(chi2))
test _b[expose5]==0
return scalar sm_p5=r(p)

quietly logistic outcome expose6 if outcome==0|(outcome==1 & gaad>42)
estimate store week_6
return scalar sm_b6=_b[expose6]
return scalar sm_se6=_se[expose6]
return scalar sm_test6=1-chi2(e(df_m), e(chi2))
test _b[expose6]==0
return scalar sm_p6=r(p)

quietly logistic outcome expose7 if outcome==0|(outcome==1 & gaad>49)
estimate store week_7
return scalar sm_b7=_b[expose7]
return scalar sm_se7=_se[expose7]
return scalar sm_test7=1-chi2(e(df_m), e(chi2))
test _b[expose7]==0
return scalar sm_p7=r(p)

quietly logistic outcome expose8 if outcome==0|(outcome==1 & gaad>56)
estimate store week_8
return scalar sm_b8=_b[expose8]
return scalar sm_se8=_se[expose8]
return scalar sm_test8=1-chi2(e(df_m), e(chi2))
test _b[expose8]==0
return scalar sm_p8=r(p)

quietly logistic outcome expose9 if outcome==0|(outcome==1 & gaad>63)
```

```
estimate store week_9
return scalar sm_b9=_b[expose9]
return scalar sm_se9=_se[expose9]
test _b[expose9]==0
return scalar sm_p9=r(p)

quietly logistic outcome expose10 if outcome==0|(outcome==1 & gaad>70)
estimate store week_10
return scalar sm_b10=_b[expose10]
return scalar sm_se10=_se[expose10]
test _b[expose10]==0
return scalar sm_p10=r(p)

quietly logistic outcome expose11 if outcome==0|(outcome==1 & gaad>77)
estimate store week_11
return scalar sm_b11=_b[expose11]
return scalar sm_se11=_se[expose11]
test _b[expose11]==0
return scalar sm_p11=r(p)

quietly logistic outcome expose12 if outcome==0|(outcome==1 & gaad>84)
estimate store week_12
return scalar sm_b12=_b[expose12]
return scalar sm_se12=_se[expose12]
test _b[expose12]==0
return scalar sm_p12=r(p)

quietly logistic outcome expose13 if outcome==0|(outcome==1 & gaad>91)
estimate store week_13
return scalar sm_b13=_b[expose13]
return scalar sm_se13=_se[expose13]
test _b[expose13]==0
return scalar sm_p13=r(p)

suest week_3 week_4 week_5 week_6 week_7 week_8 week_9 week_10 week_11 week_12 week_13

test (expose3=0) (expose4=0) (expose5=0) (expose6=0) (expose7=0) (expose8=0) ///
 (expose9=0) (expose10=0) (expose11=0) (expose12=0) (expose13=0)

 return scalar sm_exp3_13=r(p)

 test (expose4=0) (expose5=0) (expose6=0) (expose7=0) (expose8=0)

 return scalar sm_exp4_8=r(p)

*Cox with lag
stsplit split, at(1(1)140)

gen split_exposed=.
replace split_exposed=0 if early_exposed==0
replace split_exposed=1 if early_exposed==1 & late_exposed==0 & change_consump_time > (_t-7)
replace split_exposed=0 if early_exposed==1 & late_exposed==0  & change_consump_time < (_t-7)
replace split_exposed=1 if late_exposed==1

stcox split_exposed
return scalar lr_b1=_b[split_exposed]
```

```
return scalar lr_se1=_se[split_exposed]
return scalar lr_test=1-chi2(e(df_m), e(chi2))
test _b[split_exposed]==0
return scalar lr_p1=r(p)

*Cumulative Cox regression
gen exp_dur=.
replace exp_dur=_t-13 if days>=_t
replace exp_dur=days if _t>days
replace exp_dur=0 if exp_dur<0
replace exp_dur=0 if change_consump_time<14|change_consump_time==.

stcox exp_dur
return scalar cc_b=_b[exp_dur]
return scalar cc_se=_se[exp_dur]
test _b[exp_dur]==0
return scalar cc_p=r(p)

*Poisson regression with time ineraction
gen split_exposed2=.
replace split_exposed2=0 if early_exposed==0
replace split_exposed2=1 if early_exposed==1 & late_exposed==0 & change_consump_time > (_t)
replace split_exposed2=0 if early_exposed==1 & late_exposed==0  & change_consump_time < (_t)
replace split_exposed2=1 if late_exposed==1

gen time = _t

fp generate double time^(-1 3), center scale replace

summ time_1 if time==28, meanonly
scalar t1_28=r(mean)

summ time_1 if time==35, meanonly
scalar t1_35=r(mean)

summ time_1 if time==42, meanonly
scalar t1_42=r(mean)

summ time_1 if time==49, meanonly
scalar t1_49=r(mean)

summ time_1 if time==56, meanonly
scalar t1_56=r(mean)

summ time_2 if time==28, meanonly
scalar t2_28=r(mean)

summ time_2 if time==35, meanonly
scalar t2_35=r(mean)

summ time_2 if time==42, meanonly
scalar t2_42=r(mean)

summ time_2 if time==49, meanonly
scalar t2_49=r(mean)
```

```
summ time_2 if time==56, meanonly
scalar t2_56=r(mean)

gen int1 = split_exposed2*time_1
gen int2 = split_exposed2*time_2

poisson _d split_exposed2 time_1 time_2 int1 int2, exposure(gaad)

lincom split_exposed2+int1*t1_28 +int2 * t2_28
return scalar pf2_b4=r(estimate)
return scalar pf2_se4=r(se)

lincom split_exposed2+int1*t1_35 +int2 * t2_35
return scalar pf2_b5=r(estimate)
return scalar pf2_se5=r(se)

lincom split_exposed2+int1*t1_42 +int2 * t2_42
return scalar pf2_b6=r(estimate)
return scalar pf2_se6=r(se)

lincom split_exposed2+int1*t1_49 +int2 * t2_49
return scalar pf2_b7=r(estimate)
return scalar pf2_se7=r(se)

lincom split_exposed2+int1*t1_56 +int2 * t2_56
return scalar pf2_b8=r(estimate)
return scalar pf2_se8=r(se)

test split_exposed2 int1 int2
return scalar pf2_p=r(p)

end
**********************************************************************
*Relationship 2 Simulation
simulate sr_b=r(sr_b) sr_se=r(sr_se) sr_p=r(sr_p) sm_b4=r(sm_b4) sm_se4=r(sm_se4) sm_p4=r(sm_p4) ///
sm_b5=r(sm_b5) sm_se5=r(sm_se5) sm_p5=r(sm_p5) sm_b6=r(sm_b6) sm_se6=r(sm_se6) sm_p6=r(sm_p6) ///
sm_b7=r(sm_b7) sm_se7=r(sm_se7) sm_p7=r(sm_p7) sm_b8=r(sm_b8) sm_se8=r(sm_se8) sm_p8=r(sm_p8) ///
cc_b=r(cc_b) cc_se=r(cc_se) cc_p=r(cc_p) ///
lr_b1=r(lr_b1) lr_se1=r(lr_se1) lr_p1=r(lr_p1) sr_test=r(sr_test) sm_test4=r(sm_test4) ///
sm_test5=r(sm_test5) sm_test6=r(sm_test6) sm_test7=r(sm_test7) sm_test8=r(sm_test8) ///
sm_exp3_13=r(sm_exp3_13) sm_exp4_8=r(sm_exp4_8) lr_test=r(lr_test) ///
pf2_b4=r(pf2_b4) pf2_se4=r(pf2_se4) pf2_b5=r(pf2_b5) pf2_se5=r(pf2_se5) pf2_p=r(pf2_p) ///
pf2_b6=r(pf2_b6) pf2_se6=r(pf2_se6)pf2_b7=r(pf2_b7) pf2_se7=r(pf2_se7) pf2_b8=r(pf2_b8) pf2_se8=r(pf2_se8)
///
, reps(1000) seed(1714): any_p

clear
**********************************************************************
**********************************************************************
**********************************************************************
*Relationship 3: Exposure in week five of gestation increases risk
program define week5_p, rclass
clear
set obs 1500

gen id=_n
```

```
**Define Time-Varying Exposure Variables
gen early_exposed=rbinomial(1, 0.55)
gen late_exposed=rbinomial(1, 0.09) if early_exposed==1
replace late_exposed=0 if early_exposed==0

gen change_consump_time=rbeta(7,5)*100-30 if early_exposed==1

gen days=.
replace days=ceil(change_consump_time)-14
replace days=0 if days<0|days==.

gen gestwkchange=.
replace gestwkchange=0 if change_consump_time>=0 & change_consump_time<7
replace gestwkchange=1 if change_consump_time>=7 & change_consump_time<14
replace gestwkchange=2 if change_consump_time>=14 & change_consump_time<21
replace gestwkchange=3 if change_consump_time>=21 & change_consump_time<28
replace gestwkchange=4 if change_consump_time>=28 & change_consump_time<35
replace gestwkchange=5 if change_consump_time>=35 & change_consump_time<42
replace gestwkchange=6 if change_consump_time>=42 & change_consump_time<49
replace gestwkchange=7 if change_consump_time>=49 & change_consump_time<56
replace gestwkchange=8 if change_consump_time>=56 & change_consump_time<63
replace gestwkchange=9 if change_consump_time>=63 & change_consump_time<70
replace gestwkchange=10 if change_consump_time>=70 & change_consump_time<77
replace gestwkchange=11 if change_consump_time>=77 & change_consump_time<84
replace gestwkchange=12 if change_consump_time>=84 & change_consump_time<91
replace gestwkchange=13 if change_consump_time>=91 & change_consump_time<98
replace gestwkchange=14 if change_consump_time>=98 & change_consump_time~=.
replace gestwkchange=0 if  change_consump_time<0 | (change_consump_time==. & late_exposed==0)
label define wkchanges 0 "No pregnancy exposure" 1 "0-6" 2 "7-13" 3 "14-20" 4 "21-27" 5 "28-34" 6 "35-41"  ///
7 "42-48" 8 "49-55" 9 "56-62" 10 "63-69" 11 "70-76" 12 "77-83" 13 "84-90" 14 "No change or after 1st Tri"
label values gestwkchange wkchanges

**Week specific exposure
gen expose1=.
replace expose1=1 if gestwkchange>=1|late_exposed==1
replace expose1=0 if early_exposed==0|(gestwkchange<1 & late_exposed==0)

gen expose2=.
replace expose2=1 if gestwkchange>=2|late_exposed==1
replace expose2=0 if early_exposed==0|(gestwkchange<2 & late_exposed==0)

gen expose3=.
replace expose3=1 if gestwkchange>=3|late_exposed==1
replace expose3=0 if early_exposed==0|(gestwkchange<3 & late_exposed==0)

gen expose4=.
replace expose4=1 if gestwkchange>=4|late_exposed==1
replace expose4=0 if early_exposed==0|(gestwkchange<4 & late_exposed==0)

gen expose5=.
replace expose5=1 if gestwkchange>=5|late_exposed==1
replace expose5=0 if early_exposed==0|(gestwkchange<5 & late_exposed==0)

gen expose6=.
replace expose6=1 if gestwkchange>=6|late_exposed==1
```

```
replace expose6=0 if early_exposed==0|(gestwkchange<6 & late_exposed==0)

gen expose7=.
replace expose7=1 if gestwkchange>=7|late_exposed==1
replace expose7=0 if early_exposed==0|(gestwkchange<7 & late_exposed==0)

gen expose8=.
replace expose8=1 if gestwkchange>=8|late_exposed==1
replace expose8=0 if early_exposed==0|(gestwkchange<8 & late_exposed==0)

gen expose9=.
replace expose9=1 if gestwkchange>=9|late_exposed==1
replace expose9=0 if early_exposed==0|(gestwkchange<9 & late_exposed==0)

gen expose10=.
replace expose10=1 if gestwkchange>=10|late_exposed==1
replace expose10=0 if early_exposed==0|(gestwkchange<10 & late_exposed==0)

gen expose11=.
replace expose11=1 if gestwkchange>=11|late_exposed==1
replace expose11=0 if early_exposed==0|(gestwkchange<11 & late_exposed==0)

gen expose12=.
replace expose12=1 if gestwkchange>=12|late_exposed==1
replace expose12=0 if early_exposed==0|(gestwkchange<12 & late_exposed==0)

gen expose13=.
replace expose13=1 if gestwkchange>=13|late_exposed==1
replace expose13=0 if early_exposed==0|(gestwkchange<13 & late_exposed==0)

gen expose14=.
replace expose14=1 if gestwkchange>=14|late_exposed==1
replace expose14=0 if early_exposed==0|(gestwkchange<14 & late_exposed==0)

**Outcome
gen outcome=rbinomial(1, 0.1131766227) if (early_exposed==0| early_exposed==1 & change_consump_time<35)
replace outcome=rbinomial(1, 0.169764934) if early_exposed==1 & change_consump_time>=35
*Found the right proportion with http://homepage.divms.uiowa.edu/~mbognar/applets/beta.html

**Outcome Timing
gen gaad=round(rbeta(4.5,8.6)*126+14) if outcome==1
replace gaad=140 if outcome==0
                                        **********

*Run models to measure performance
stset gaad, id(id) failure(outcome)

*Simple Cox PH
stcox early_exposed
return scalar sr_b=_b[early_exposed]
return scalar sr_se=_se[early_exposed]
return scalar sr_test=1-chi2(e(df_m), e(chi2))

test _b[early_exposed]==0
return scalar sr_p=r(p)
```

```
*Sequential logistic
quietly logistic outcome expose3 if outcome==0|(outcome==1 & gaad>21)
estimate store week_3
return scalar sm_b3=_b[expose3]
return scalar sm_se3=_se[expose3]
test _b[expose3]==0
return scalar sm_p3=r(p)

quietly logistic outcome expose4 if outcome==0|(outcome==1 & gaad>28)
estimate store week_4
return scalar sm_b4=_b[expose4]
return scalar sm_se4=_se[expose4]
return scalar sm_test4=1-chi2(e(df_m), e(chi2))
test _b[expose4]==0
return scalar sm_p4=r(p)

quietly logistic outcome expose5  if outcome==0|(outcome==1 & gaad>35)
estimate store week_5
return scalar sm_b5=_b[expose5]
return scalar sm_se5=_se[expose5]
return scalar sm_test5=1-chi2(e(df_m), e(chi2))
test _b[expose5]==0
return scalar sm_p5=r(p)

quietly logistic outcome expose6 if outcome==0|(outcome==1 & gaad>42)
estimate store week_6
return scalar sm_b6=_b[expose6]
return scalar sm_se6=_se[expose6]
return scalar sm_test6=1-chi2(e(df_m), e(chi2))
test _b[expose6]==0
return scalar sm_p6=r(p)

quietly logistic outcome expose7 if outcome==0|(outcome==1 & gaad>49)
estimate store week_7
return scalar sm_b7=_b[expose7]
return scalar sm_se7=_se[expose7]
return scalar sm_test7=1-chi2(e(df_m), e(chi2))
test _b[expose7]==0
return scalar sm_p7=r(p)

quietly logistic outcome expose8 if outcome==0|(outcome==1 & gaad>56)
estimate store week_8
return scalar sm_b8=_b[expose8]
return scalar sm_se8=_se[expose8]
return scalar sm_test8=1-chi2(e(df_m), e(chi2))
test _b[expose8]==0
return scalar sm_p8=r(p)

quietly logistic outcome expose9 if outcome==0|(outcome==1 & gaad>63)
estimate store week_9
return scalar sm_b9=_b[expose9]
return scalar sm_se9=_se[expose9]
test _b[expose9]==0
return scalar sm_p9=r(p)

quietly logistic outcome expose10 if outcome==0|(outcome==1 & gaad>70)
```

```
estimate store week_10
return scalar sm_b10=_b[expose10]
return scalar sm_se10=_se[expose10]
test _b[expose10]==0
return scalar sm_p10=r(p)

quietly logistic outcome expose11 if outcome==0|(outcome==1 & gaad>77)
estimate store week_11
return scalar sm_b11=_b[expose11]
return scalar sm_se11=_se[expose11]
test _b[expose11]==0
return scalar sm_p11=r(p)

quietly logistic outcome expose12 if outcome==0|(outcome==1 & gaad>84)
estimate store week_12
return scalar sm_b12=_b[expose12]
return scalar sm_se12=_se[expose12]
test _b[expose12]==0
return scalar sm_p12=r(p)

quietly logistic outcome expose13 if outcome==0|(outcome==1 & gaad>91)
estimate store week_13
return scalar sm_b13=_b[expose13]
return scalar sm_se13=_se[expose13]
test _b[expose13]==0
return scalar sm_p13=r(p)

suest week_3 week_4 week_5 week_6 week_7 week_8 week_9 week_10 week_11 week_12 week_13

test (expose3=0) (expose4=0) (expose5=0) (expose6=0) (expose7=0) (expose8=0) ///
 (expose9=0) (expose10=0) (expose11=0) (expose12=0) (expose13=0)

 return scalar sm_exp3_13=r(p)

 test (expose4=0) (expose5=0) (expose6=0) (expose7=0) (expose8=0)

 return scalar sm_exp4_8=r(p)

*Cox with lag
stsplit split, at(1(1)140)

gen split_exposed=.
replace split_exposed=0 if early_exposed==0
replace split_exposed=1 if early_exposed==1 & late_exposed==0 & change_consump_time > (_t-7)
replace split_exposed=0 if early_exposed==1 & late_exposed==0  & change_consump_time < (_t-7)
replace split_exposed=1 if late_exposed==1

stcox split_exposed
return scalar lr_b1=_b[split_exposed]
return scalar lr_se1=_se[split_exposed]
return scalar lr_test=1-chi2(e(df_m), e(chi2))
test _b[split_exposed]==0
return scalar lr_p1=r(p)

*Cumulative Cox regression
gen exp_dur=.
```

```
replace exp_dur=_t-13 if days>=_t
replace exp_dur=days if _t>days
replace exp_dur=0 if exp_dur<0
replace exp_dur=0 if change_consump_time<14|change_consump_time==.

stcox exp_dur
return scalar cc_b=_b[exp_dur]
return scalar cc_se=_se[exp_dur]
test _b[exp_dur]==0
return scalar cc_p=r(p)

*Poisson regression with time ineraction
gen split_exposed2=.
replace split_exposed2=0 if early_exposed==0
replace split_exposed2=1 if early_exposed==1 & late_exposed==0 & change_consump_time > (_t)
replace split_exposed2=0 if early_exposed==1 & late_exposed==0  & change_consump_time < (_t)
replace split_exposed2=1 if late_exposed==1

gen time = _t

fp generate double time^(-1 3), center scale replace

summ time_1 if time==28, meanonly
scalar t1_28=r(mean)

summ time_1 if time==35, meanonly
scalar t1_35=r(mean)

summ time_1 if time==42, meanonly
scalar t1_42=r(mean)

summ time_1 if time==49, meanonly
scalar t1_49=r(mean)

summ time_1 if time==56, meanonly
scalar t1_56=r(mean)

summ time_2 if time==28, meanonly
scalar t2_28=r(mean)

summ time_2 if time==35, meanonly
scalar t2_35=r(mean)

summ time_2 if time==42, meanonly
scalar t2_42=r(mean)

summ time_2 if time==49, meanonly
scalar t2_49=r(mean)

summ time_2 if time==56, meanonly
scalar t2_56=r(mean)

gen int1 = split_exposed2*time_1
gen int2 = split_exposed2*time_2

*Poisson with interaction
```

```
poisson _d split_exposed2 time_1 time_2 int1 int2, exposure(gaad)

lincom split_exposed2+int1*t1_28 +int2 * t2_28
return scalar pf2_b4=r(estimate)
return scalar pf2_se4=r(se)

lincom split_exposed2+int1*t1_35 +int2 * t2_35
return scalar pf2_b5=r(estimate)
return scalar pf2_se5=r(se)

lincom split_exposed2+int1*t1_42 +int2 * t2_42
return scalar pf2_b6=r(estimate)
return scalar pf2_se6=r(se)

lincom split_exposed2+int1*t1_49 +int2 * t2_49
return scalar pf2_b7=r(estimate)
return scalar pf2_se7=r(se)

lincom split_exposed2+int1*t1_56 +int2 * t2_56
return scalar pf2_b8=r(estimate)
return scalar pf2_se8=r(se)

test split_exposed2 int1 int2
return scalar pf2_p=r(p)

end
**************************************************************************
*Relationship 3 Simulation
simulate sr_b=r(sr_b) sr_se=r(sr_se) sr_p=r(sr_p) sm_b4=r(sm_b4) sm_se4=r(sm_se4) sm_p4=r(sm_p4) ///
sm_b5=r(sm_b5) sm_se5=r(sm_se5) sm_p5=r(sm_p5) sm_b6=r(sm_b6) sm_se6=r(sm_se6) sm_p6=r(sm_p6) ///
sm_b7=r(sm_b7) sm_se7=r(sm_se7) sm_p7=r(sm_p7) sm_b8=r(sm_b8) sm_se8=r(sm_se8) sm_p8=r(sm_p8) ///
cc_b=r(cc_b) cc_se=r(cc_se) cc_p=r(cc_p) ///
lr_b1=r(lr_b1) lr_se1=r(lr_se1) lr_p1=r(lr_p1) sr_test=r(sr_test) sm_test4=r(sm_test4) ///
sm_test5=r(sm_test5) sm_test6=r(sm_test6) sm_test7=r(sm_test7) sm_test8=r(sm_test8) ///
sm_exp3_13=r(sm_exp3_13) sm_exp4_8=r(sm_exp4_8) lr_test=r(lr_test) ///
pf2_b4=r(pf2_b4) pf2_se4=r(pf2_se4) pf2_b5=r(pf2_b5) pf2_se5=r(pf2_se5) pf2_p=r(pf2_p) ///
pf2_b6=r(pf2_b6) pf2_se6=r(pf2_se6)pf2_b7=r(pf2_b7) pf2_se7=r(pf2_se7) pf2_b8=r(pf2_b8) pf2_se8=r(pf2_se8)
///
, reps(1000) seed(1714): week5_p

clear
**************************************************************************
**************************************************************************
**************************************************************************
*Relationship 4: Cumulative exposure associates with risk
program define cumulative, rclass
clear
set obs 1500

gen id=_n

**Define Time-Varying Exposure Variables
gen early_exposed=rbinomial(1, 0.55)
gen late_exposed=rbinomial(1, 0.09) if early_exposed==1
replace late_exposed=0 if early_exposed==0
```

```
gen change_consump_time=rbeta(7,5)*100-30 if early_exposed==1

gen days=.
replace days=ceil(change_consump_time)-14
replace days=0 if days<0|days==.

gen gestwkchange=.
replace gestwkchange=0 if change_consump_time>=0 & change_consump_time<7
replace gestwkchange=1 if change_consump_time>=7 & change_consump_time<14
replace gestwkchange=2 if change_consump_time>=14 & change_consump_time<21
replace gestwkchange=3 if change_consump_time>=21 & change_consump_time<28
replace gestwkchange=4 if change_consump_time>=28 & change_consump_time<35
replace gestwkchange=5 if change_consump_time>=35 & change_consump_time<42
replace gestwkchange=6 if change_consump_time>=42 & change_consump_time<49
replace gestwkchange=7 if change_consump_time>=49 & change_consump_time<56
replace gestwkchange=8 if change_consump_time>=56 & change_consump_time<63
replace gestwkchange=9 if change_consump_time>=63 & change_consump_time<70
replace gestwkchange=10 if change_consump_time>=70 & change_consump_time<77
replace gestwkchange=11 if change_consump_time>=77 & change_consump_time<84
replace gestwkchange=12 if change_consump_time>=84 & change_consump_time<91
replace gestwkchange=13 if change_consump_time>=91 & change_consump_time<98
replace gestwkchange=14 if change_consump_time>=98 & change_consump_time~=.
replace gestwkchange=0 if  change_consump_time<0 | (change_consump_time==. & late_exposed==0)
label define wkchanges 0 "No pregnancy exposure" 1 "0-6" 2 "7-13" 3 "14-20" 4 "21-27" 5 "28-34" 6 "35-41"  ///
7 "42-48" 8 "49-55" 9 "56-62" 10 "63-69" 11 "70-76" 12 "77-83" 13 "84-90" 14 "No change or after 1st Tri"
label values gestwkchange wkchanges

**Week specific exposure
gen expose1=.
replace expose1=1 if gestwkchange>=1|late_exposed==1
replace expose1=0 if early_exposed==0|(gestwkchange<1 & late_exposed==0)

gen expose2=.
replace expose2=1 if gestwkchange>=2|late_exposed==1
replace expose2=0 if early_exposed==0|(gestwkchange<2 & late_exposed==0)

gen expose3=.
replace expose3=1 if gestwkchange>=3|late_exposed==1
replace expose3=0 if early_exposed==0|(gestwkchange<3 & late_exposed==0)

gen expose4=.
replace expose4=1 if gestwkchange>=4|late_exposed==1
replace expose4=0 if early_exposed==0|(gestwkchange<4 & late_exposed==0)

gen expose5=.
replace expose5=1 if gestwkchange>=5|late_exposed==1
replace expose5=0 if early_exposed==0|(gestwkchange<5 & late_exposed==0)

gen expose6=.
replace expose6=1 if gestwkchange>=6|late_exposed==1
replace expose6=0 if early_exposed==0|(gestwkchange<6 & late_exposed==0)

gen expose7=.
replace expose7=1 if gestwkchange>=7|late_exposed==1
replace expose7=0 if early_exposed==0|(gestwkchange<7 & late_exposed==0)
```

```
gen expose8=.
replace expose8=1 if gestwkchange>=8|late_exposed==1
replace expose8=0 if early_exposed==0|(gestwkchange<8 & late_exposed==0)

gen expose9=.
replace expose9=1 if gestwkchange>=9|late_exposed==1
replace expose9=0 if early_exposed==0|(gestwkchange<9 & late_exposed==0)

gen expose10=.
replace expose10=1 if gestwkchange>=10|late_exposed==1
replace expose10=0 if early_exposed==0|(gestwkchange<10 & late_exposed==0)

gen expose11=.
replace expose11=1 if gestwkchange>=11|late_exposed==1
replace expose11=0 if early_exposed==0|(gestwkchange<11 & late_exposed==0)

gen expose12=.
replace expose12=1 if gestwkchange>=12|late_exposed==1
replace expose12=0 if early_exposed==0|(gestwkchange<12 & late_exposed==0)

gen expose13=.
replace expose13=1 if gestwkchange>=13|late_exposed==1
replace expose13=0 if early_exposed==0|(gestwkchange<13 & late_exposed==0)

gen expose14=.
replace expose14=1 if gestwkchange>=14|late_exposed==1
replace expose14=0 if early_exposed==0|(gestwkchange<14 & late_exposed==0)

**Outcome Timing
gen gaad=round(rbeta(4.5,8.6)*126+14)

**Outcome
gen outcome=.
replace outcome=rbinomial(1, 0.106*1.0137^(change_consump_time-14)) if early_exposed==1 &
change_consump_time>=14 & gaad>change_consump_time
replace outcome=rbinomial(1, 0.106*1.0137^(gaad-14)) if early_exposed==1 & change_consump_time>=14 &
gaad<=change_consump_time
replace outcome=rbinomial(1, 0.106) if early_exposed==0 | (early_exposed==1 & change_consump_time<14)

replace gaad=140 if outcome==0
                                                    **********
*Run models to measure performance
stset gaad, id(id) failure(outcome)

*Simple Cox PH
stcox early_exposed
return scalar sr_b=_b[early_exposed]
return scalar sr_se=_se[early_exposed]
return scalar sr_test=1-chi2(e(df_m), e(chi2))

test _b[early_exposed]==0
return scalar sr_p=r(p)

*Sequential logistic
quietly logistic outcome expose3 if outcome==0|(outcome==1 & gaad>21)
estimate store week_3
```

```
return scalar sm_b3=_b[expose3]
return scalar sm_se3=_se[expose3]
test _b[expose3]==0
return scalar sm_p3=r(p)

quietly logistic outcome expose4 if outcome==0|(outcome==1 & gaad>28)
estimate store week_4
return scalar sm_b4=_b[expose4]
return scalar sm_se4=_se[expose4]
return scalar sm_test4=1-chi2(e(df_m), e(chi2))
test _b[expose4]==0
return scalar sm_p4=r(p)

quietly logistic outcome expose5  if outcome==0|(outcome==1 & gaad>35)
estimate store week_5
return scalar sm_b5=_b[expose5]
return scalar sm_se5=_se[expose5]
return scalar sm_test5=1-chi2(e(df_m), e(chi2))
test _b[expose5]==0
return scalar sm_p5=r(p)

quietly logistic outcome expose6 if outcome==0|(outcome==1 & gaad>42)
estimate store week_6
return scalar sm_b6=_b[expose6]
return scalar sm_se6=_se[expose6]
return scalar sm_test6=1-chi2(e(df_m), e(chi2))
test _b[expose6]==0
return scalar sm_p6=r(p)

quietly logistic outcome expose7 if outcome==0|(outcome==1 & gaad>49)
estimate store week_7
return scalar sm_b7=_b[expose7]
return scalar sm_se7=_se[expose7]
return scalar sm_test7=1-chi2(e(df_m), e(chi2))
test _b[expose7]==0
return scalar sm_p7=r(p)

quietly logistic outcome expose8 if outcome==0|(outcome==1 & gaad>56)
estimate store week_8
return scalar sm_b8=_b[expose8]
return scalar sm_se8=_se[expose8]
return scalar sm_test8=1-chi2(e(df_m), e(chi2))
test _b[expose8]==0
return scalar sm_p8=r(p)

quietly logistic outcome expose9 if outcome==0|(outcome==1 & gaad>63)
estimate store week_9
return scalar sm_b9=_b[expose9]
return scalar sm_se9=_se[expose9]
test _b[expose9]==0
return scalar sm_p9=r(p)

quietly logistic outcome expose10 if outcome==0|(outcome==1 & gaad>70)
estimate store week_10
return scalar sm_b10=_b[expose10]
return scalar sm_se10=_se[expose10]
```

```
test _b[expose10]==0
return scalar sm_p10=r(p)

quietly logistic outcome expose11 if outcome==0|(outcome==1 & gaad>77)
estimate store week_11
return scalar sm_b11=_b[expose11]
return scalar sm_se11=_se[expose11]
test _b[expose11]==0
return scalar sm_p11=r(p)

quietly logistic outcome expose12 if outcome==0|(outcome==1 & gaad>84)
estimate store week_12
return scalar sm_b12=_b[expose12]
return scalar sm_se12=_se[expose12]
test _b[expose12]==0
return scalar sm_p12=r(p)

quietly logistic outcome expose13 if outcome==0|(outcome==1 & gaad>91)
estimate store week_13
return scalar sm_b13=_b[expose13]
return scalar sm_se13=_se[expose13]
test _b[expose13]==0
return scalar sm_p13=r(p)

suest week_3 week_4 week_5 week_6 week_7 week_8 week_9 week_10 week_11 week_12 week_13

test (expose3=0) (expose4=0) (expose5=0) (expose6=0) (expose7=0) (expose8=0) ///
 (expose9=0) (expose10=0) (expose11=0) (expose12=0) (expose13=0)

 return scalar sm_exp3_13=r(p)

 test (expose4=0) (expose5=0) (expose6=0) (expose7=0) (expose8=0)

 return scalar sm_exp4_8=r(p)

*Cox with lag
stsplit split, at(1(1)140)

gen split_exposed=.
replace split_exposed=0 if early_exposed==0
replace split_exposed=1 if early_exposed==1 & late_exposed==0 & change_consump_time > (_t-7)
replace split_exposed=0 if early_exposed==1 & late_exposed==0  & change_consump_time < (_t-7)
replace split_exposed=1 if late_exposed==1

stcox split_exposed
return scalar lr_b1=_b[split_exposed]
return scalar lr_se1=_se[split_exposed]
return scalar lr_test=1-chi2(e(df_m), e(chi2))
test _b[split_exposed]==0
return scalar lr_p1=r(p)

*Cumulative Cox regression
gen exp_dur=.
replace exp_dur=_t-13 if days>=_t
replace exp_dur=days if _t>days
replace exp_dur=0 if exp_dur<0
```

```
replace exp_dur=0 if change_consump_time<14|change_consump_time==.

stcox exp_dur
return scalar cc_b=_b[exp_dur]
return scalar cc_se=_se[exp_dur]
test _b[exp_dur]==0
return scalar cc_p=r(p)

*Poisson regression with time ineraction
gen split_exposed2=.
replace split_exposed2=0 if early_exposed==0
replace split_exposed2=1 if early_exposed==1 & late_exposed==0 & change_consump_time > (_t)
replace split_exposed2=0 if early_exposed==1 & late_exposed==0  & change_consump_time < (_t)
replace split_exposed2=1 if late_exposed==1

gen time = _t

fp generate double time^(-1 3), center scale replace

summ time_1 if time==28, meanonly
scalar t1_28=r(mean)

summ time_1 if time==35, meanonly
scalar t1_35=r(mean)

summ time_1 if time==42, meanonly
scalar t1_42=r(mean)

summ time_1 if time==49, meanonly
scalar t1_49=r(mean)

summ time_1 if time==56, meanonly
scalar t1_56=r(mean)

summ time_2 if time==28, meanonly
scalar t2_28=r(mean)

summ time_2 if time==35, meanonly
scalar t2_35=r(mean)

summ time_2 if time==42, meanonly
scalar t2_42=r(mean)

summ time_2 if time==49, meanonly
scalar t2_49=r(mean)

summ time_2 if time==56, meanonly
scalar t2_56=r(mean)

gen int1 = split_exposed2*time_1
gen int2 = split_exposed2*time_2

poisson _d split_exposed2 time_1 time_2 int1 int2, exposure(gaad)

lincom split_exposed2+int1*t1_28 +int2 * t2_28
return scalar pf2_b4=r(estimate)
```

```
return scalar pf2_se4=r(se)

lincom split_exposed2+int1*t1_35 +int2 * t2_35
return scalar pf2_b5=r(estimate)
return scalar pf2_se5=r(se)

lincom split_exposed2+int1*t1_42 +int2 * t2_42
return scalar pf2_b6=r(estimate)
return scalar pf2_se6=r(se)

lincom split_exposed2+int1*t1_49 +int2 * t2_49
return scalar pf2_b7=r(estimate)
return scalar pf2_se7=r(se)

lincom split_exposed2+int1*t1_56 +int2 * t2_56
return scalar pf2_b8=r(estimate)
return scalar pf2_se8=r(se)

test split_exposed2 int1 int2
return scalar pf2_p=r(p)

end
**********************************************************************************
*Relationship 4 Simulation
simulate sr_b=r(sr_b) sr_se=r(sr_se) sr_p=r(sr_p) sm_b4=r(sm_b4) sm_se4=r(sm_se4) sm_p4=r(sm_p4) ///
sm_b5=r(sm_b5) sm_se5=r(sm_se5) sm_p5=r(sm_p5) sm_b6=r(sm_b6) sm_se6=r(sm_se6) sm_p6=r(sm_p6) ///
sm_b7=r(sm_b7) sm_se7=r(sm_se7) sm_p7=r(sm_p7) sm_b8=r(sm_b8) sm_se8=r(sm_se8) sm_p8=r(sm_p8) ///
cc_b=r(cc_b) cc_se=r(cc_se) cc_p=r(cc_p) ///
lr_b1=r(lr_b1) lr_se1=r(lr_se1) lr_p1=r(lr_p1) sr_test=r(sr_test) sm_test4=r(sm_test4) ///
sm_test5=r(sm_test5) sm_test6=r(sm_test6) sm_test7=r(sm_test7) sm_test8=r(sm_test8) ///
sm_exp3_13=r(sm_exp3_13) sm_exp4_8=r(sm_exp4_8) lr_test=r(lr_test) ///
pf2_b4=r(pf2_b4) pf2_se4=r(pf2_se4) pf2_b5=r(pf2_b5) pf2_se5=r(pf2_se5) pf2_p=r(pf2_p) ///
pf2_b6=r(pf2_b6) pf2_se6=r(pf2_se6)pf2_b7=r(pf2_b7) pf2_se7=r(pf2_se7) pf2_b8=r(pf2_b8) pf2_se8=r(pf2_se8)
///
, reps(1000) seed(1714): cumulative

clear
**********************************************************************************
**********************************************************************************
**********************************************************************************
*Relationship 5: Exposure increases risk during the following week
program define steady, rclass
*Starting
clear
set obs 1500

gen id=_n

**Define Time-Varying Exposure Variables
gen early_exposed=rbinomial(1, 0.55)
gen late_exposed=rbinomial(1, 0.09) if early_exposed==1
replace late_exposed=0 if early_exposed==0

gen change_consump_time=rbeta(7,5)*100-30 if early_exposed==1

gen days=.
```

```
replace days=ceil(change_consump_time)-14
replace days=0 if days<0|days==.

gen gestwkchange=.
replace gestwkchange=0 if change_consump_time>=0 & change_consump_time<7
replace gestwkchange=1 if change_consump_time>=7 & change_consump_time<14
replace gestwkchange=2 if change_consump_time>=14 & change_consump_time<21
replace gestwkchange=3 if change_consump_time>=21 & change_consump_time<28
replace gestwkchange=4 if change_consump_time>=28 & change_consump_time<35
replace gestwkchange=5 if change_consump_time>=35 & change_consump_time<42
replace gestwkchange=6 if change_consump_time>=42 & change_consump_time<49
replace gestwkchange=7 if change_consump_time>=49 & change_consump_time<56
replace gestwkchange=8 if change_consump_time>=56 & change_consump_time<63
replace gestwkchange=9 if change_consump_time>=63 & change_consump_time<70
replace gestwkchange=10 if change_consump_time>=70 & change_consump_time<77
replace gestwkchange=11 if change_consump_time>=77 & change_consump_time<84
replace gestwkchange=12 if change_consump_time>=84 & change_consump_time<91
replace gestwkchange=13 if change_consump_time>=91 & change_consump_time<98
replace gestwkchange=14 if change_consump_time>=98 & change_consump_time~=.
replace gestwkchange=0 if  change_consump_time<0 | (change_consump_time==. & late_exposed==0)
label define wkchanges 0 "No pregnancy exposure" 1 "0-6" 2 "7-13" 3 "14-20" 4 "21-27" 5 "28-34" 6 "35-41"  ///
7 "42-48" 8 "49-55" 9 "56-62" 10 "63-69" 11 "70-76" 12 "77-83" 13 "84-90" 14 "No change or after 1st Tri"
label values gestwkchange wkchanges

**Week specific exposure
gen expose1=.
replace expose1=1 if gestwkchange>=1|late_exposed==1
replace expose1=0 if early_exposed==0|(gestwkchange<1 & late_exposed==0)

gen expose2=.
replace expose2=1 if gestwkchange>=2|late_exposed==1
replace expose2=0 if early_exposed==0|(gestwkchange<2 & late_exposed==0)

gen expose3=.
replace expose3=1 if gestwkchange>=3|late_exposed==1
replace expose3=0 if early_exposed==0|(gestwkchange<3 & late_exposed==0)

gen expose4=.
replace expose4=1 if gestwkchange>=4|late_exposed==1
replace expose4=0 if early_exposed==0|(gestwkchange<4 & late_exposed==0)

gen expose5=.
replace expose5=1 if gestwkchange>=5|late_exposed==1
replace expose5=0 if early_exposed==0|(gestwkchange<5 & late_exposed==0)

gen expose6=.
replace expose6=1 if gestwkchange>=6|late_exposed==1
replace expose6=0 if early_exposed==0|(gestwkchange<6 & late_exposed==0)

gen expose7=.
replace expose7=1 if gestwkchange>=7|late_exposed==1
replace expose7=0 if early_exposed==0|(gestwkchange<7 & late_exposed==0)

gen expose8=.
replace expose8=1 if gestwkchange>=8|late_exposed==1
replace expose8=0 if early_exposed==0|(gestwkchange<8 & late_exposed==0)
```

```
gen expose9=.
replace expose9=1 if gestwkchange>=9|late_exposed==1
replace expose9=0 if early_exposed==0|(gestwkchange<9 & late_exposed==0)

gen expose10=.
replace expose10=1 if gestwkchange>=10|late_exposed==1
replace expose10=0 if early_exposed==0|(gestwkchange<10 & late_exposed==0)

gen expose11=.
replace expose11=1 if gestwkchange>=11|late_exposed==1
replace expose11=0 if early_exposed==0|(gestwkchange<11 & late_exposed==0)

gen expose12=.
replace expose12=1 if gestwkchange>=12|late_exposed==1
replace expose12=0 if early_exposed==0|(gestwkchange<12 & late_exposed==0)

gen expose13=.
replace expose13=1 if gestwkchange>=13|late_exposed==1
replace expose13=0 if early_exposed==0|(gestwkchange<13 & late_exposed==0)

gen expose14=.
replace expose14=1 if gestwkchange>=14|late_exposed==1
replace expose14=0 if early_exposed==0|(gestwkchange<14 & late_exposed==0)

**Outcome
gen gaad=round(rbeta(4.5,8.6)*126+14)

gen outcome=.
replace outcome=rbinomial(1, 0.19645) if change_consump_time>=gaad-7 & early_exposed==1
replace outcome=rbinomial(1, 0.11335) if early_exposed==0|(change_consump_time<gaad-7 & early_exposed==1)

**Outcome Timing
replace gaad=140 if outcome==0

                                                    **********
*Run models to measure performance
stset gaad, id(id) failure(outcome)

*Simple Cox PH
stcox early_exposed
return scalar sr_b=_b[early_exposed]
return scalar sr_se=_se[early_exposed]
return scalar sr_test=1-chi2(e(df_m), e(chi2))

test _b[early_exposed]==0
return scalar sr_p=r(p)

*Sequential logistic
quietly logistic outcome expose3 if outcome==0|(outcome==1 & gaad>21)
estimate store week_3
return scalar sm_b3=_b[expose3]
return scalar sm_se3=_se[expose3]
test _b[expose3]==0
return scalar sm_p3=r(p)
```

```
quietly logistic outcome expose4 if outcome==0|(outcome==1 & gaad>28)
estimate store week_4
return scalar sm_b4=_b[expose4]
return scalar sm_se4=_se[expose4]
return scalar sm_test4=1-chi2(e(df_m), e(chi2))
test _b[expose4]==0
return scalar sm_p4=r(p)

quietly logistic outcome expose5  if outcome==0|(outcome==1 & gaad>35)
estimate store week_5
return scalar sm_b5=_b[expose5]
return scalar sm_se5=_se[expose5]
return scalar sm_test5=1-chi2(e(df_m), e(chi2))
test _b[expose5]==0
return scalar sm_p5=r(p)

quietly logistic outcome expose6 if outcome==0|(outcome==1 & gaad>42)
estimate store week_6
return scalar sm_b6=_b[expose6]
return scalar sm_se6=_se[expose6]
return scalar sm_test6=1-chi2(e(df_m), e(chi2))
test _b[expose6]==0
return scalar sm_p6=r(p)

quietly logistic outcome expose7 if outcome==0|(outcome==1 & gaad>49)
estimate store week_7
return scalar sm_b7=_b[expose7]
return scalar sm_se7=_se[expose7]
return scalar sm_test7=1-chi2(e(df_m), e(chi2))
test _b[expose7]==0
return scalar sm_p7=r(p)

quietly logistic outcome expose8 if outcome==0|(outcome==1 & gaad>56)
estimate store week_8
return scalar sm_b8=_b[expose8]
return scalar sm_se8=_se[expose8]
return scalar sm_test8=1-chi2(e(df_m), e(chi2))
test _b[expose8]==0
return scalar sm_p8=r(p)

quietly logistic outcome expose9 if outcome==0|(outcome==1 & gaad>63)
estimate store week_9
return scalar sm_b9=_b[expose9]
return scalar sm_se9=_se[expose9]
test _b[expose9]==0
return scalar sm_p9=r(p)

quietly logistic outcome expose10 if outcome==0|(outcome==1 & gaad>70)
estimate store week_10
return scalar sm_b10=_b[expose10]
return scalar sm_se10=_se[expose10]
test _b[expose10]==0
return scalar sm_p10=r(p)

quietly logistic outcome expose11 if outcome==0|(outcome==1 & gaad>77)
estimate store week_11
```

```
return scalar sm_b11=_b[expose11]
return scalar sm_se11=_se[expose11]
test _b[expose11]==0
return scalar sm_p11=r(p)

quietly logistic outcome expose12 if outcome==0|(outcome==1 & gaad>84)
estimate store week_12
return scalar sm_b12=_b[expose12]
return scalar sm_se12=_se[expose12]
test _b[expose12]==0
return scalar sm_p12=r(p)

quietly logistic outcome expose13 if outcome==0|(outcome==1 & gaad>91)
estimate store week_13
return scalar sm_b13=_b[expose13]
return scalar sm_se13=_se[expose13]
test _b[expose13]==0
return scalar sm_p13=r(p)

suest week_3 week_4 week_5 week_6 week_7 week_8 week_9 week_10 week_11 week_12 week_13

test (expose3=0) (expose4=0) (expose5=0) (expose6=0) (expose7=0) (expose8=0) ///
 (expose9=0) (expose10=0) (expose11=0) (expose12=0) (expose13=0)

 return scalar sm_exp3_13=r(p)

 test (expose4=0) (expose5=0) (expose6=0) (expose7=0) (expose8=0)

 return scalar sm_exp4_8=r(p)

*Cox with lag
stsplit split, at(1(1)140)

gen split_exposed=.
replace split_exposed=0 if early_exposed==0
replace split_exposed=1 if early_exposed==1 & late_exposed==0 & change_consump_time > (_t-7)
replace split_exposed=0 if early_exposed==1 & late_exposed==0  & change_consump_time < (_t-7)
replace split_exposed=1 if late_exposed==1

stcox split_exposed
return scalar lr_b1=_b[split_exposed]
return scalar lr_se1=_se[split_exposed]
return scalar lr_test=1-chi2(e(df_m), e(chi2))
test _b[split_exposed]==0
return scalar lr_p1=r(p)

*Cumulative Cox regression
gen exp_dur=.
replace exp_dur=_t-13 if days>=_t
replace exp_dur=days if _t>days
replace exp_dur=0 if exp_dur<0
replace exp_dur=0 if change_consump_time<14|change_consump_time==.

stcox exp_dur
return scalar cc_b=_b[exp_dur]
return scalar cc_se=_se[exp_dur]
```

```
test _b[exp_dur]==0
return scalar cc_p=r(p)

*Poisson regression with time ineraction
gen split_exposed2=.
replace split_exposed2=0 if early_exposed==0
replace split_exposed2=1 if early_exposed==1 & late_exposed==0 & change_consump_time > (_t)
replace split_exposed2=0 if early_exposed==1 & late_exposed==0  & change_consump_time < (_t)
replace split_exposed2=1 if late_exposed==1

gen time = _t

fp generate double time^(-1 3), center scale replace

summ time_1 if time==28, meanonly
scalar t1_28=r(mean)

summ time_1 if time==35, meanonly
scalar t1_35=r(mean)

summ time_1 if time==42, meanonly
scalar t1_42=r(mean)

summ time_1 if time==49, meanonly
scalar t1_49=r(mean)

summ time_1 if time==56, meanonly
scalar t1_56=r(mean)

summ time_2 if time==28, meanonly
scalar t2_28=r(mean)

summ time_2 if time==35, meanonly
scalar t2_35=r(mean)

summ time_2 if time==42, meanonly
scalar t2_42=r(mean)

summ time_2 if time==49, meanonly
scalar t2_49=r(mean)

summ time_2 if time==56, meanonly
scalar t2_56=r(mean)

gen int1 = split_exposed2*time_1
gen int2 = split_exposed2*time_2

poisson _d split_exposed2 time_1 time_2 int1 int2, exposure(gaad)

lincom split_exposed2+int1*t1_28 +int2 * t2_28
return scalar pf2_b4=r(estimate)
return scalar pf2_se4=r(se)

lincom split_exposed2+int1*t1_35 +int2 * t2_35
return scalar pf2_b5=r(estimate)
return scalar pf2_se5=r(se)
```

```
lincom split_exposed2+int1*t1_42 +int2 * t2_42
return scalar pf2_b6=r(estimate)
return scalar pf2_se6=r(se)

lincom split_exposed2+int1*t1_49 +int2 * t2_49
return scalar pf2_b7=r(estimate)
return scalar pf2_se7=r(se)

lincom split_exposed2+int1*t1_56 +int2 * t2_56
return scalar pf2_b8=r(estimate)
return scalar pf2_se8=r(se)

test split_exposed2 int1 int2
return scalar pf2_p=r(p)

end
*************************************************************************
*Relationship 5 Simulation
simulate sr_b=r(sr_b) sr_se=r(sr_se) sr_p=r(sr_p) sm_b4=r(sm_b4) sm_se4=r(sm_se4) sm_p4=r(sm_p4) ///
sm_b5=r(sm_b5) sm_se5=r(sm_se5) sm_p5=r(sm_p5) sm_b6=r(sm_b6) sm_se6=r(sm_se6) sm_p6=r(sm_p6) ///
sm_b7=r(sm_b7) sm_se7=r(sm_se7) sm_p7=r(sm_p7) sm_b8=r(sm_b8) sm_se8=r(sm_se8) sm_p8=r(sm_p8) ///
cc_b=r(cc_b) cc_se=r(cc_se) cc_p=r(cc_p) ///
lr_b1=r(lr_b1) lr_se1=r(lr_se1) lr_p1=r(lr_p1) sr_test=r(sr_test) sm_test4=r(sm_test4) ///
sm_test5=r(sm_test5) sm_test6=r(sm_test6) sm_test7=r(sm_test7) sm_test8=r(sm_test8) ///
sm_exp3_13=r(sm_exp3_13) sm_exp4_8=r(sm_exp4_8) lr_test=r(lr_test) ///
pf2_b4=r(pf2_b4) pf2_se4=r(pf2_se4) pf2_b5=r(pf2_b5) pf2_se5=r(pf2_se5) pf2_p=r(pf2_p) ///
pf2_b6=r(pf2_b6) pf2_se6=r(pf2_se6)pf2_b7=r(pf2_b7) pf2_se7=r(pf2_se7) pf2_b8=r(pf2_b8) pf2_se8=r(pf2_se8)
///
, reps(1000) seed(1714): steady

clear
```

Web Table 3. Performance of four models under relationship 1 (exposure not related to miscarriage risk)

	Simple	Lag	Sequential					Poisson					Cumulative				
Week	**N/A**	**N/A**	**4**	**5**	**6**	**7**	**8**	**4**	**5**	**6**	**7**	**8**	**4**	**5**	**6**	**7**	**8**
True effect [a,b]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean effect [a,b]	0.00	-0.02	0.00	-0.01	-0.02	-0.06	-0.12	-0.26	-0.07	0.01	0.02	-0.04	0.00	0.00	-0.01	-0.01	-0.01
Bias [c]	0.00	-0.02	0.00	-0.01	-0.02	-0.06	-0.12	-0.26	-0.07	0.01	0.02	-0.04	0.00	0.00	-0.01	-0.01	-0.01
RMSE	0.15	0.24	0.17	0.20	0.26	0.37	0.54	0.67	0.39	0.34	0.49	0.88	0.08	0.13	0.17	0.21	0.25
Coverage	0.94	0.96	0.96	0.95	0.95	0.96	0.97	0.99	0.96	0.93	0.94	0.96	0.93	0.93	0.93	0.93	0.93
Power [d]	0.06	0.04	0.04	0.05	0.05	0.04	0.03	0.02	0.04	0.07	0.06	0.04	0.07	0.07	0.07	0.07	0.07

Abbreviation: RMSE, root mean squared error.

[a] On the natural log scale.

[b] Effect estimate is β_1 for the simple, lag, and sequential models and a linear combination for the Poisson and cumulative models.

[c] Mean ln(effect estimate) – ln(effect estimate).

[d] Proportion of confidence intervals not including the null.

Web Table 4. Comparison of confidence interval coverage[a] of estimates for gestational weeks 4–8 from 5 modeling approaches across 4 simulated relationships between exposure and outcome

Scenario	Simple	Lag	Sequential	Poisson	Cumulative
Relationship 2-Any exposure increases risk					
Week 4	0.965	0.876	0.886	0.972	0.091
Week 5	0.965	0.876	0.870	0.934	0.696
Week 6	0.965	0.876	0.896	0.930	0.907
Week 7	0.965	0.876	0.933	0.954	0.934
Week 8	0.965	0.876	0.972	0.953	0.926
Relationship 3-Exposure in week five increases risk					
Week 4	0.817	0.764	0.563	0.943	0.442
Week 5	0.626	0.897	0.954	0.936	0.716
Week 6	0.817	0.764	0.719	0.819	0.442
Week 7	0.817	0.764	0.881	0.828	0.442
Week 8	0.817	0.764	0.949	0.881	0.442
Relationship 4-Cumulative exposure associates with risk					
Week 4	0.943	0.947	0.887	0.975	0.919
Week 5	0.916	0.955	0.941	0.957	0.919
Week 6	0.808	0.904	0.943	0.943	0.919
Week 7	0.621	0.809	0.939	0.920	0.919
Week 8	0.400	0.657	0.927	0.849	0.919
Relationship 5-Exposure increases risk during the following week					
Week 4	0.543	0.965	0.760	0.987	0.022
Week 5	0.543	0.965	0.837	0.965	0.492
Week 6	0.543	0.965	0.865	0.954	0.794
Week 7	0.543	0.965	0.906	0.964	0.902
Week 8	0.543	0.965	0.965	0.960	0.931

[a] Coverage was defined as the proportion of simulations where the confidence intervals for the effect estimates included the true effect.