



Depressie en cardiovasculaire stoornissen: Is er wel een causale relatie?

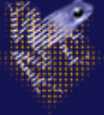
**Symposium ziekenhuispsychiatrie: Samen in beweging
25 november 2011**

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De tien ziekten met wereldwijd
de grootste ziektelast in 2020 (Lancet, 1998)

	ziekte	DALYs	%
1	<i>ischemische hartziekte</i>	82.3	5.9
2	<i>depressie</i>	78.7	5.7
3	verkeersongevallen	71.2	5.1
4	cerebrovasculaire ziekte	61.4	4.4
5	chronische obstructieve longziekte	57.6	4.2
6	luchtweg infecties	42.7	3.1
7	tuberculose	42.5	3.0
8	oorlogsverwondingen	41.3	3.0
9	diarree	37.1	2.7
10	HIV	36.3	2.6



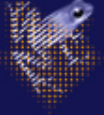
Waar hebben we het over in NL?

Stemmingsstoornis: 650.000 mensen

Isschemische hartziekten: 700.000 mensen

Prevalentie depressie verhoogd bij mensen met hartziekten en omgekeerd.

40-80.000 mensen met depressie en hartziekten (en angst:
70-90.000) in NL



De belangrijkste thema's:

Psychosociale factoren => hart- en vaatziekte?

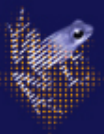
Leidt depressie tot mortaliteit?

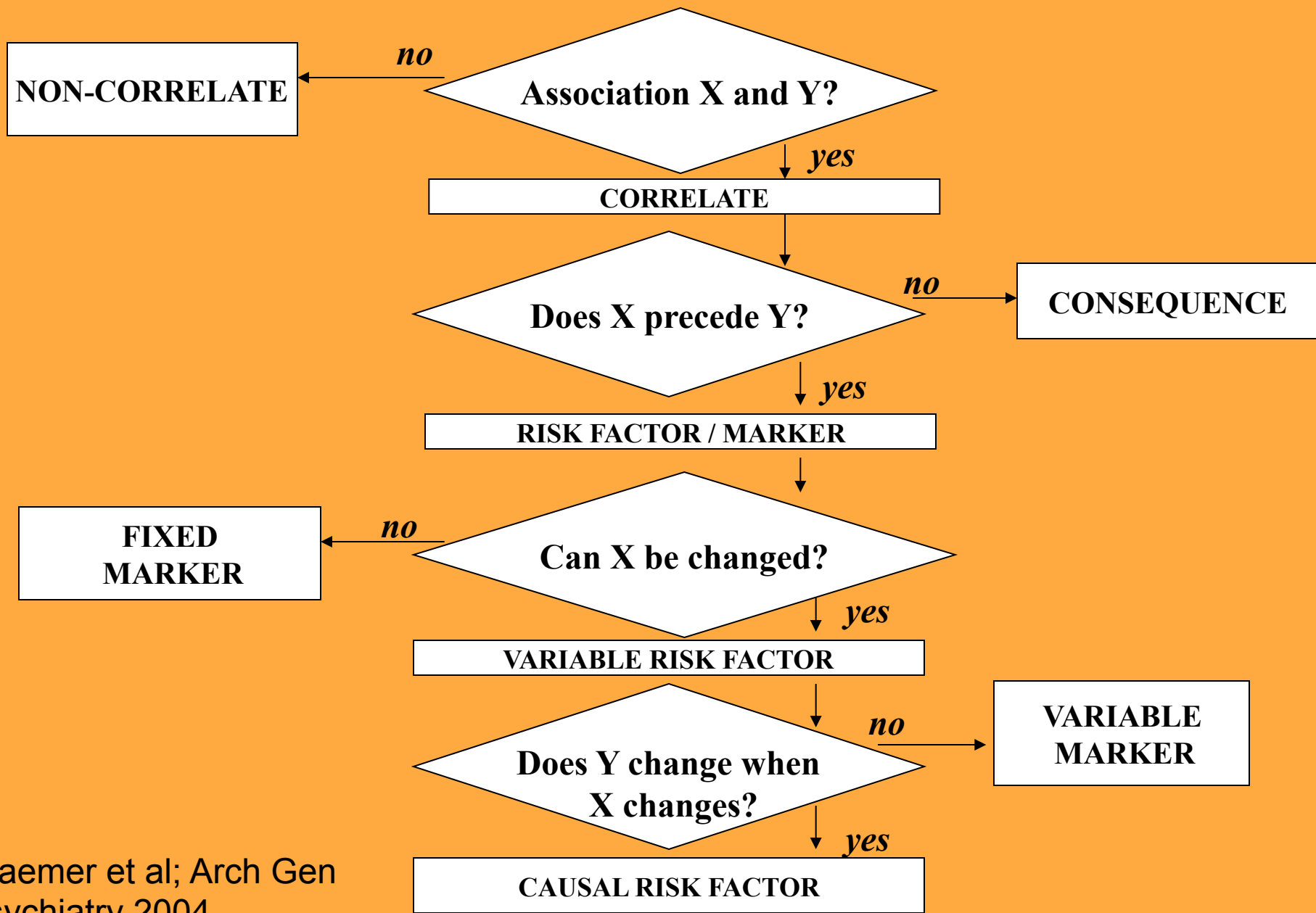
Behandeling van psychosociale problemen bij hartziekte

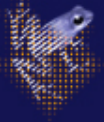
Leidt behandeling van depressie tot betere prognose?

Mechanismen die verband depressie – hartziekte verklaren

Screenen op depressie bij hartziekte





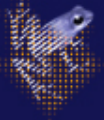


Leidt behandeling van depressie tot minder
cardiovasculaire morbiditeit/mortaliteit?

Twee studies (RCTs): ENRICHD
(N>2,000) and MIND-IT (N=331)

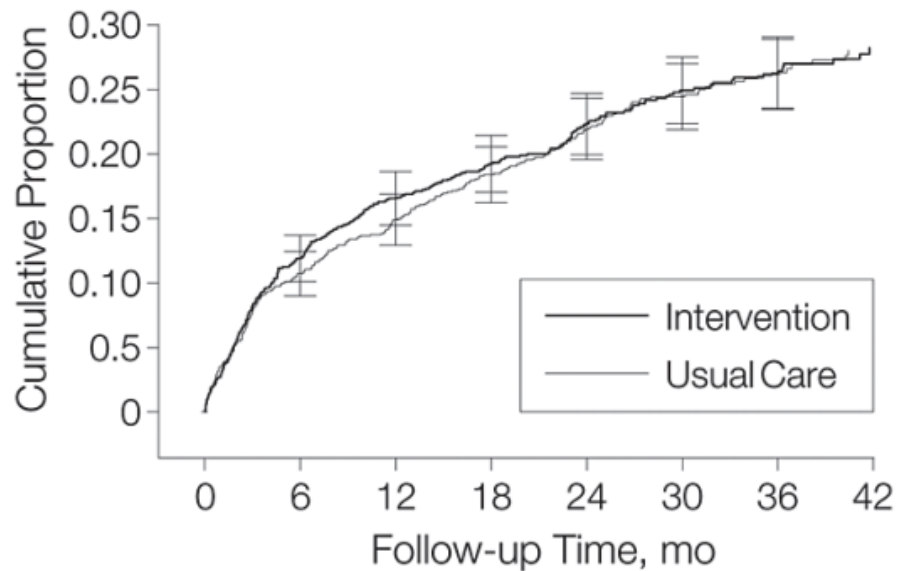
Wat waren de belangrijkste
resultaten?





Behandeling van depressie om cardioprognose te verbeteren: ENRICHD

Estimated Probability of Death or Nonfatal Myocardial Infarction



No. at Risk

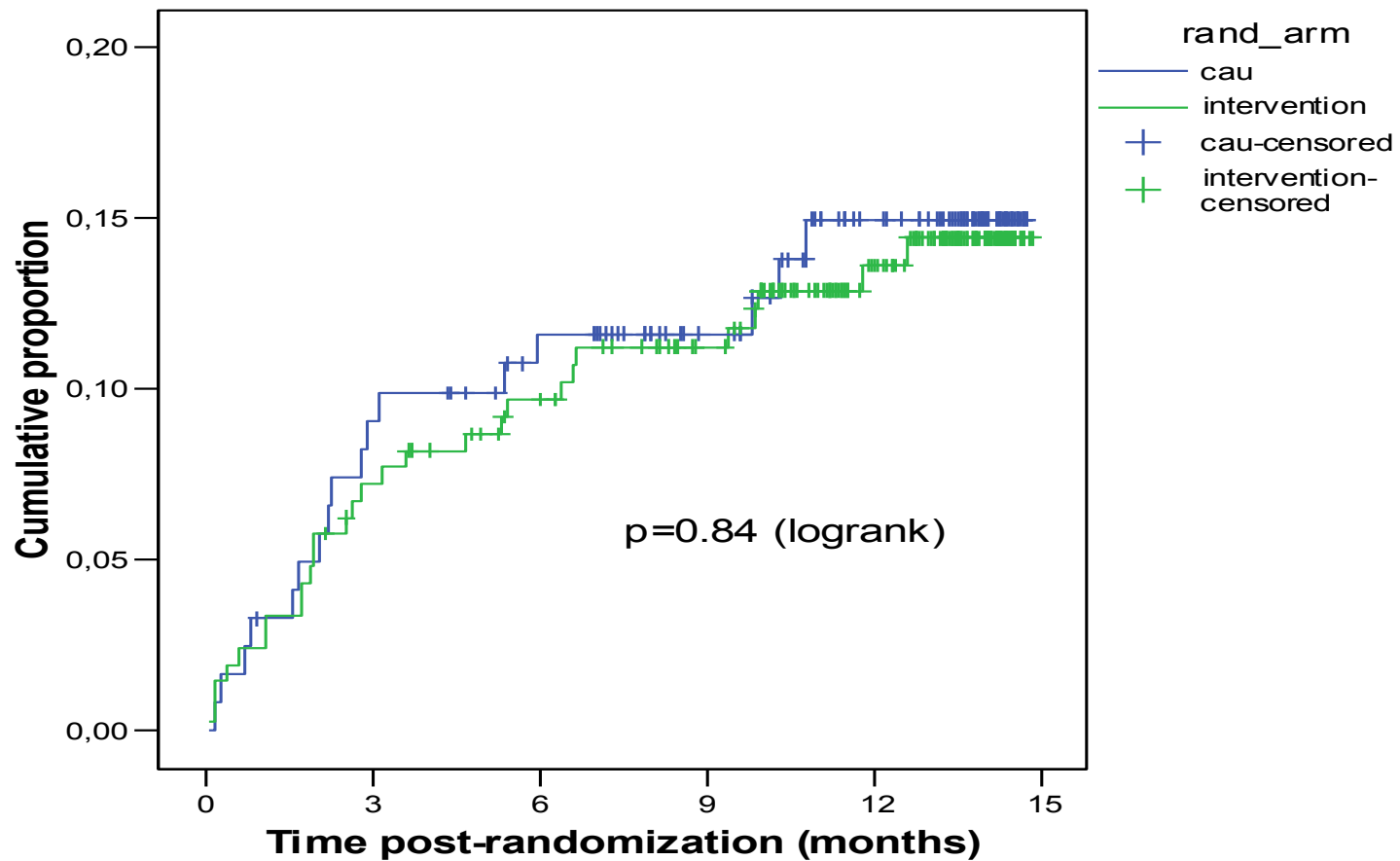
Usual Care	1243	1099	1031	898	670	460	265	130
Intervention	1238	1083	1010	886	669	439	280	122

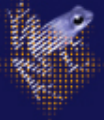
Writing Committee for the ENRICHD Investigators, JAMA 2003; 289:3106-3116.



Behandeling van depressie om cardioprognose te verbeteren: ENRICHD

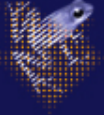
Estimated probability of cardiac events





Bescheiden effecten op depressie

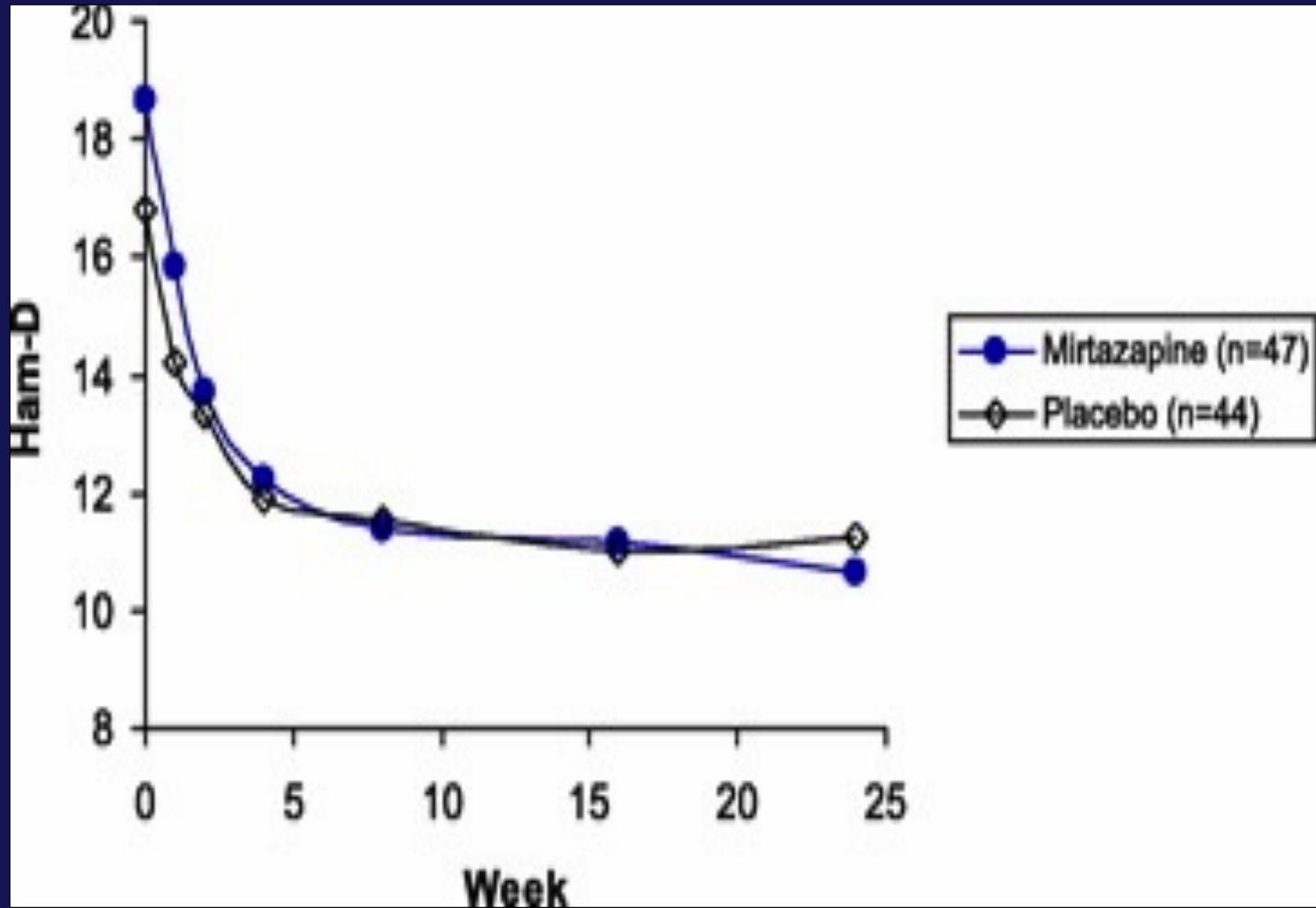
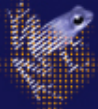
Study	N	Control	Treatment	Relative effect	P-value
SADHART	369	Placebo	Sertraline	-0.8	NS
MIND-IT	91	Placebo	Mirtazapine	-2.4	NS
ENRICHD	2481	Usual care	CBT	-1.7	P<0.001

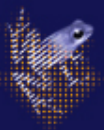


Verandering in HAM-D scores na behandeling (24 weken)

	INTERVENTION	CONTROL	DIFFERENCE
Strik et al	22->12 10	21->14 7	2.8
SADHART	20.6->11.2 8.4	19.8->12.2 7.6	0.8
ENRICHD	17.7->7.6 10.1	17.8->9.4 8.3	1.7
MIND-IT	18.7->10.7 8.0	16.8->11.2 5.6	2.4

Met andere woorden, 70-90% van de geobserveerde effecten worden al bereikt in de controle condities!





Screenen voor depressie in hartpatiënten?

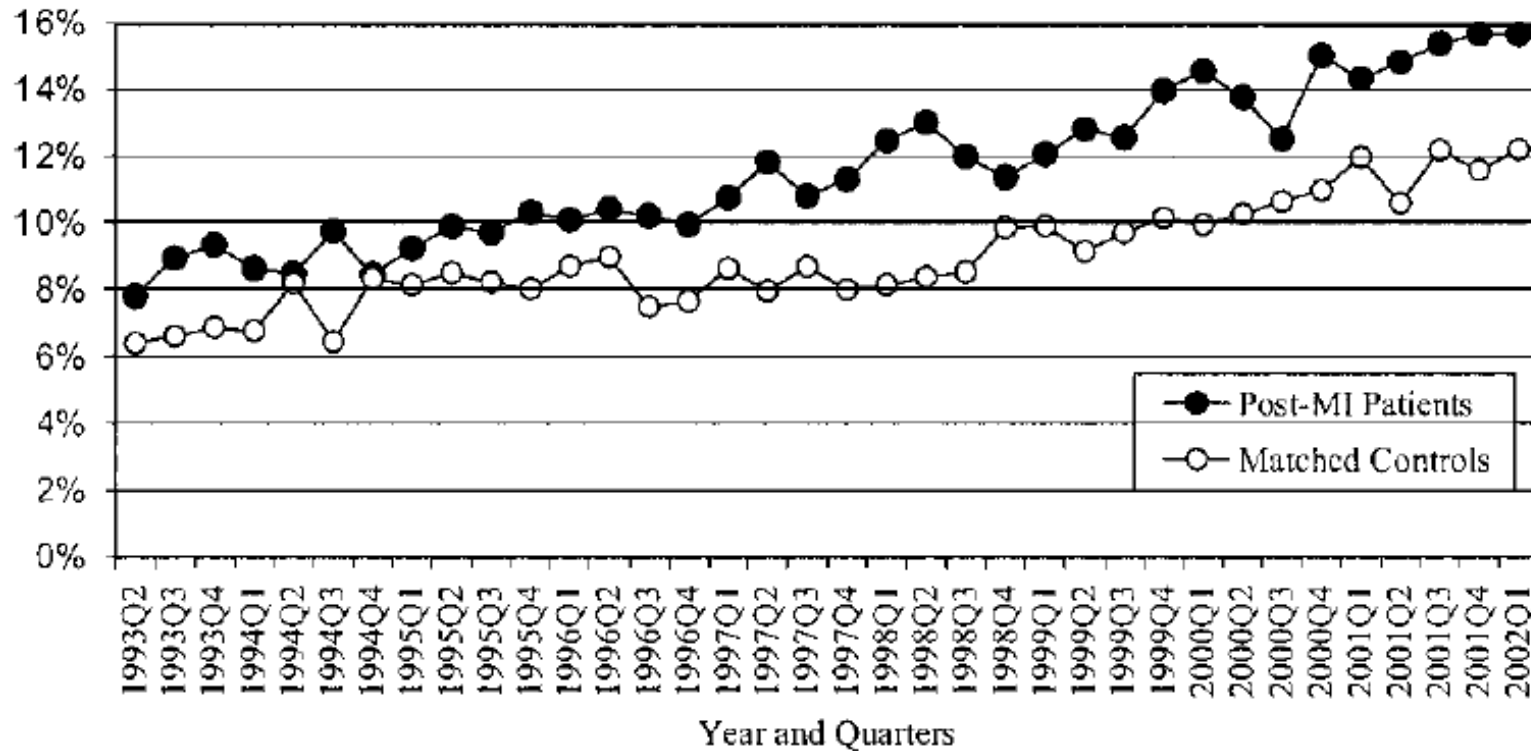
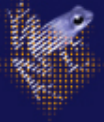
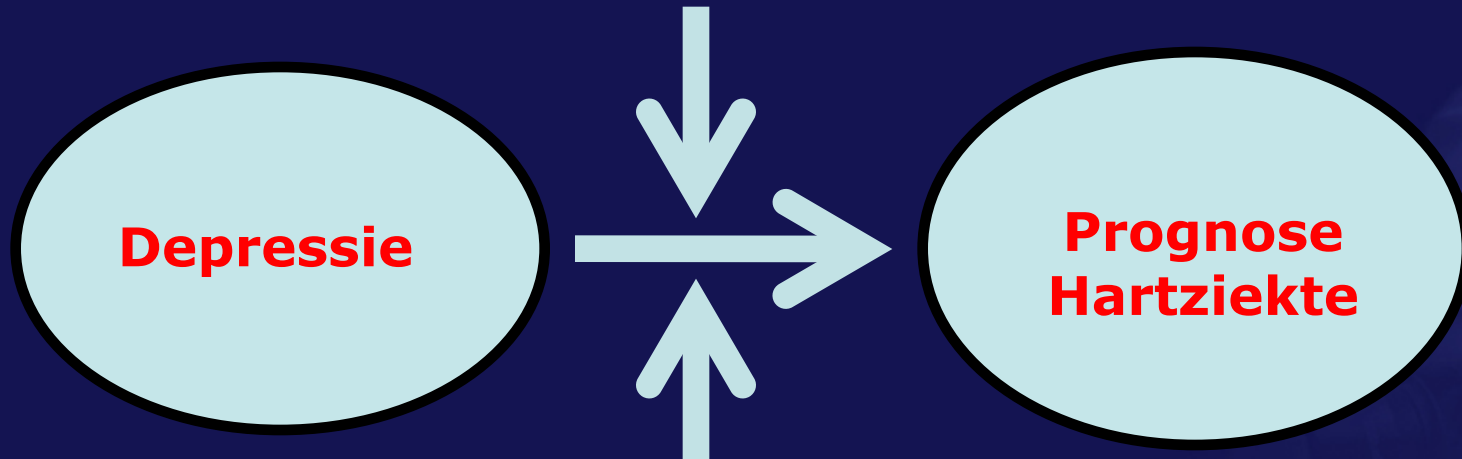


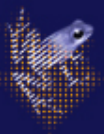
Figure 1. Proportion of post-MI and matched controls using antidepressants in a population-based study of elderly Ontario residents, 1993–2002.



- Gedragmatige factoren:
- Lichaamsbeweging
- Therapietrouw
- Toegang tot cardiovasc zorg

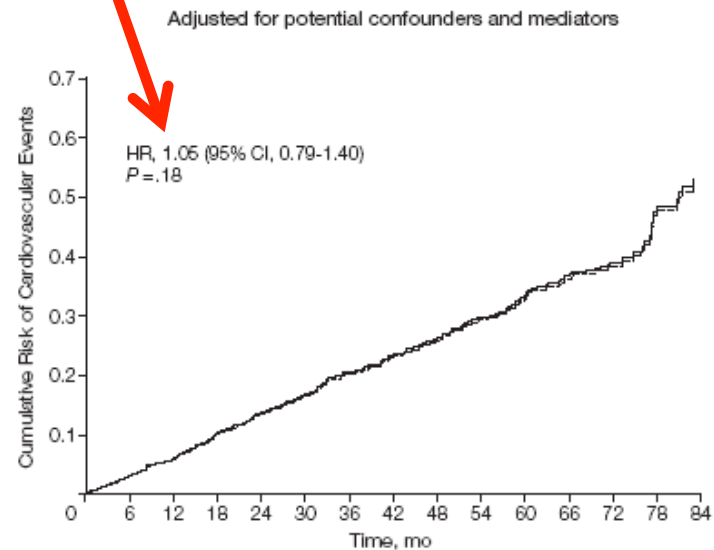
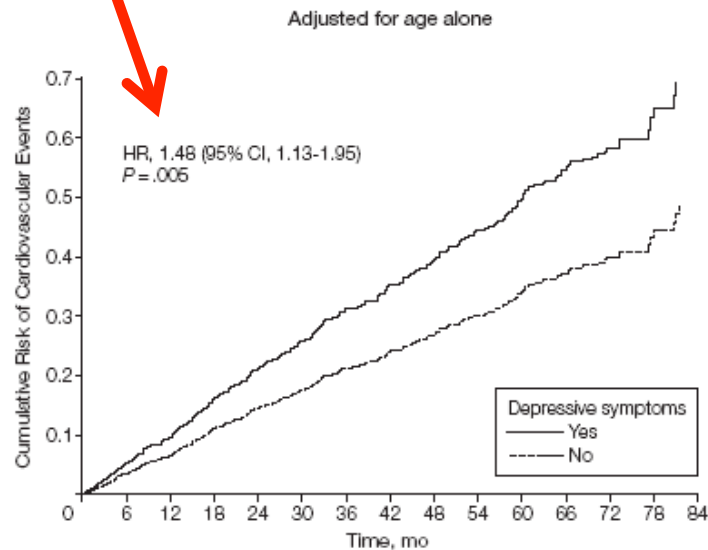


- Fysiologische factoren:
- Inflammatie
- Autonome Zenuw systeem activiteit
- Bloedplaatjes functioneren
- HPA-as activiteit
- Serotonine metabolisme
- Onverzadigde vetzuren



Association depression and cardiac outcomes: unadjusted and adjusted

Figure 1. Cumulative Risk of Cardiovascular Events








No. at risk

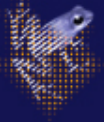
Depressive symptoms

Yes	186	164	149	135	116	48	39	7	186	164	149	135	116	48	39	7
No	768	723	660	612	534	273	214	36	768	723	660	612	534	273	214	36

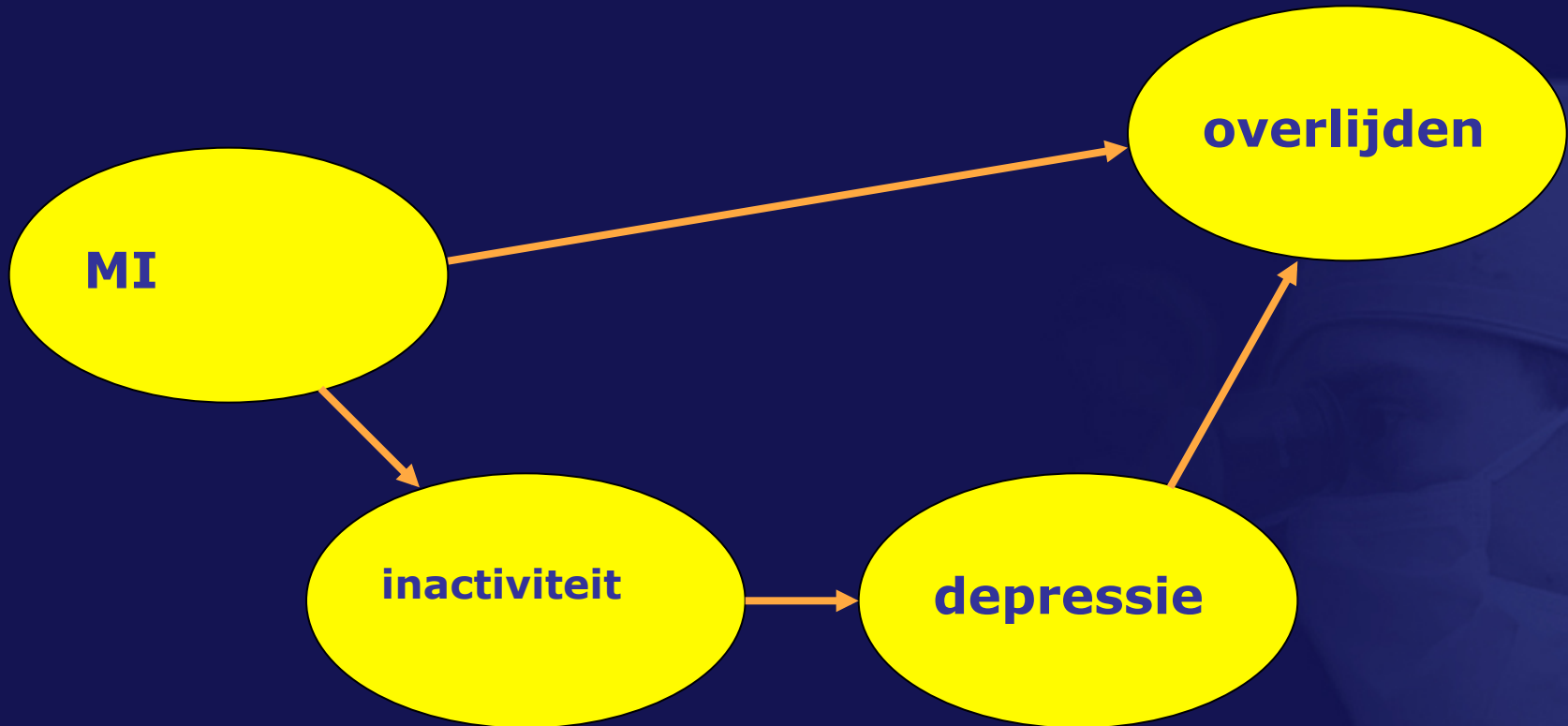
Data are stratified by depressive symptoms before and after adjustment for health behaviors in 954 participants with complete data. The adjusted hazard ratio (HR) differs slightly from Table 4 because 63 patients with incomplete data were excluded from the analysis. CI indicates confidence interval.

Table 3. Change in the Strength of Association Between Depressive Symptoms and Cardiovascular Events (Expressed as the Percent Change in the Age-Adjusted Log Hazard Ratio) After Adjustment for Potential Confounders and Mediators

Covariate	Change in Effect Size After Adjustment, % ^a
Demographic characteristics	
Male sex	3.1
White	0.5
High school graduate	-2.5
Body mass index	0.7
Comorbid conditions	
Hypertension	-1.1
Myocardial infarction	-7.8 ^a
Stroke	-5.4 ^a
Revascularization	-0.4
Congestive heart failure	 -15.7 ^a
Diabetes mellitus	-8.4 ^a
Cardiac disease severity and risk factors	
Left ventricular ejection fraction	 -19.0 ^a
Diastolic dysfunction	-2.7
Low-density lipoprotein cholesterol level	-0.8
High-density lipoprotein cholesterol level	-4.4
Medication use	
Aspirin	-2.7
β-Blocker	-0.1
Renin-angiotensin system inhibitor	-0.7
Tricyclic antidepressant	-3.1
SSRI	-1.3
Other antidepressant	-8.8 ^a
Potential biological mediators	
Heart rate variability, SDANN	4.5
Heart rate variability, lnVLF	4.1
Serotonin level among nonusers of SSRIs	-1.5
Cortisol excretion	0.5
Norepinephrine excretion	-0.5
Log C-reactive protein level	 -11.3 ^a
Omega-3 fatty acid levels	-1.5
Potential behavioral mediators	
Regular alcohol use	-0.5
Smoking	 -10.9 ^a
Medication nonadherence	-5.3 ^a
Self-reported physical activity	 -31.7 ^a



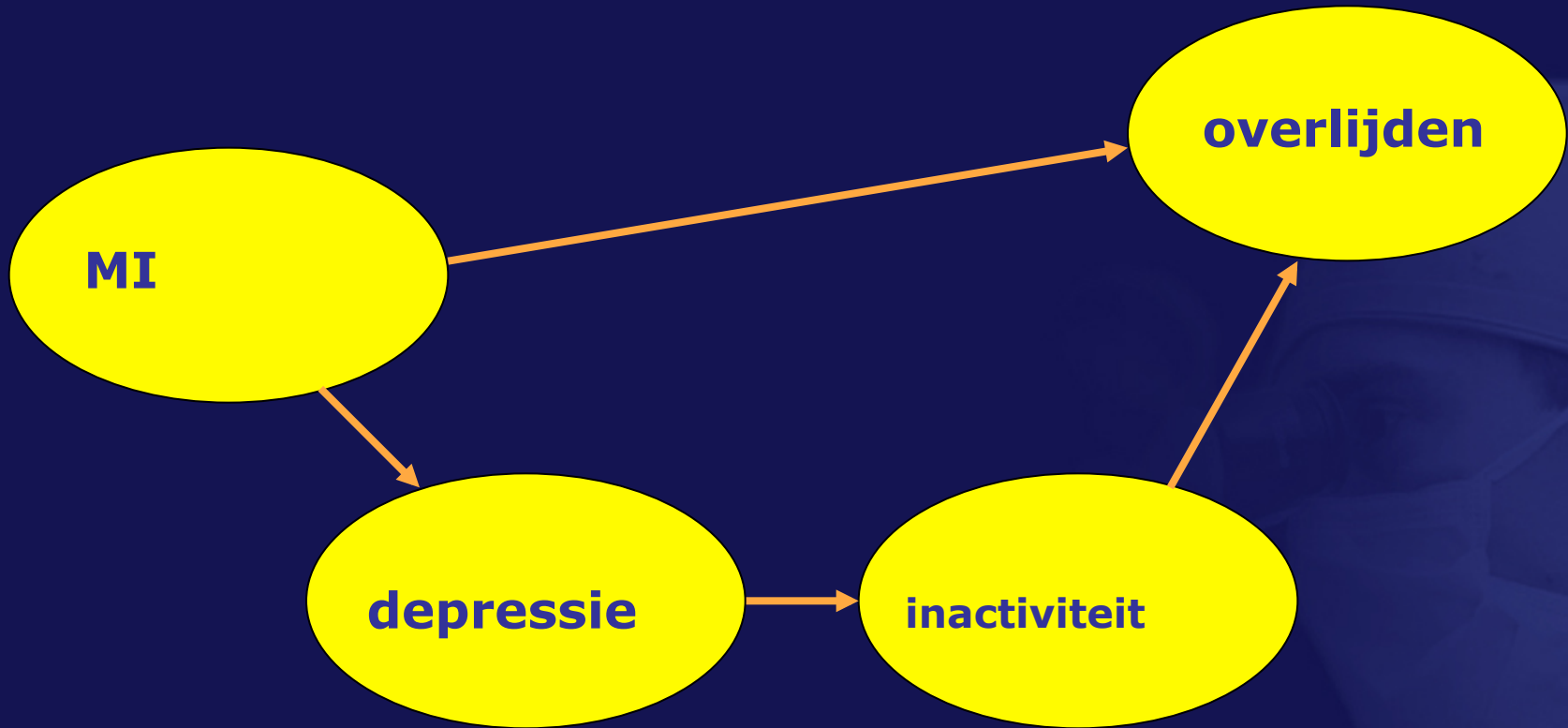
Causaal model van depressie en inactiviteit



confounding

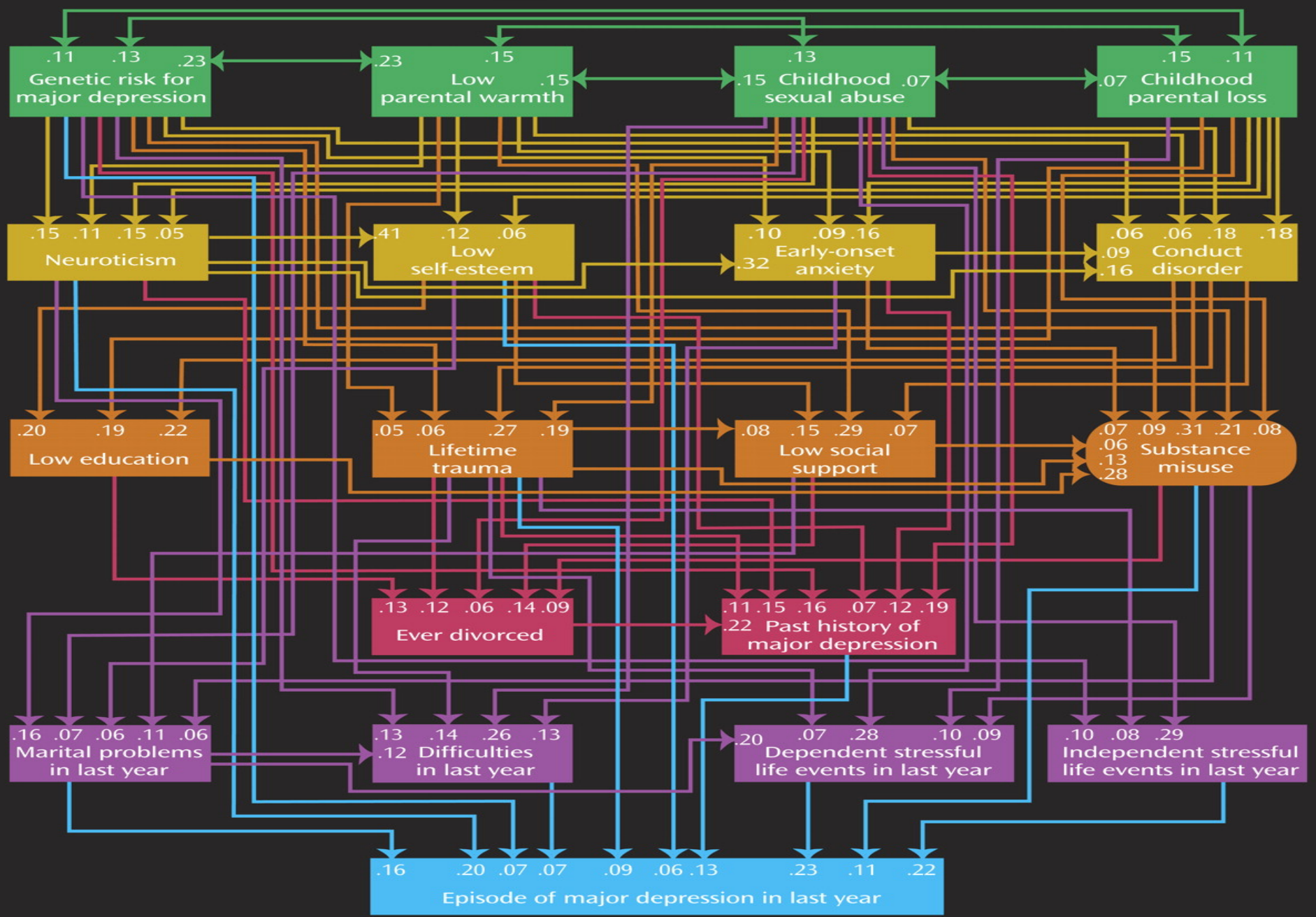


Causaal model depressie en inactiviteit



mediatie

■ Childhood ■ Late adolescence ■ Last year
■ Early adolescence ■ Adulthood ■ Depressive episode in last year

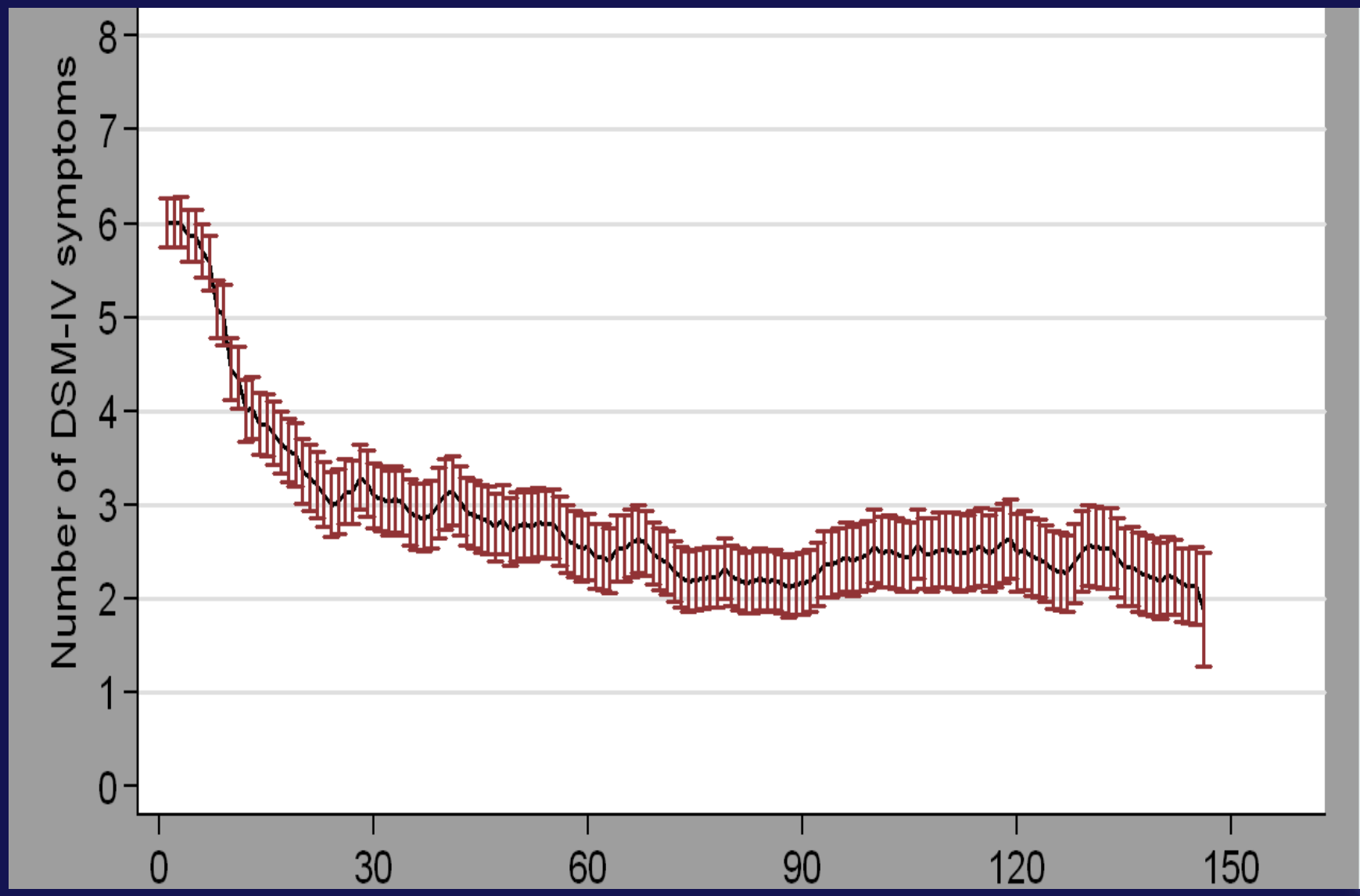
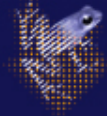




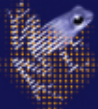
Dit krijg je als je de aanname doet dat:

MAR DAT ZIJN WE NIET !

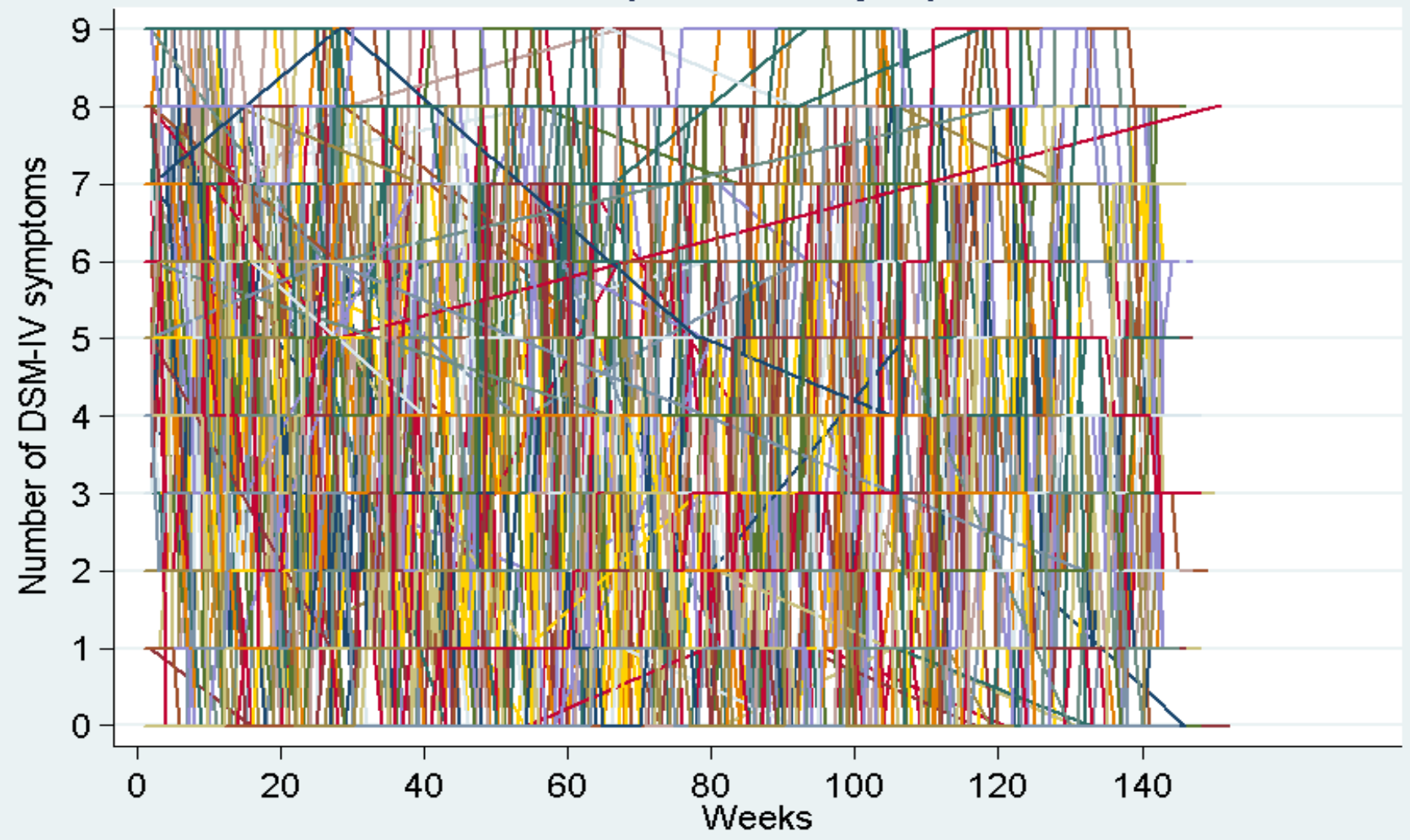
we allemaal uitwisselbaar zijn

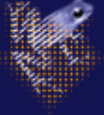


weken



CIDI depressive symptoms



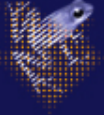


Ideographisch onderzoek

Steekproefgrootte $N \rightarrow$ power om effecten
aan te kunnen tonen

Grote $N \rightarrow$ power om kleine (irrelevante?)
effecten te kunnen vinden

Associaties representeren 'gemiddelde'
causaliteit



Nomothetisch vs. idiographisch

Nomothetisch

Populatie

N groot, T klein

Groep gemiddelden

Inter-individuele variabiliteit

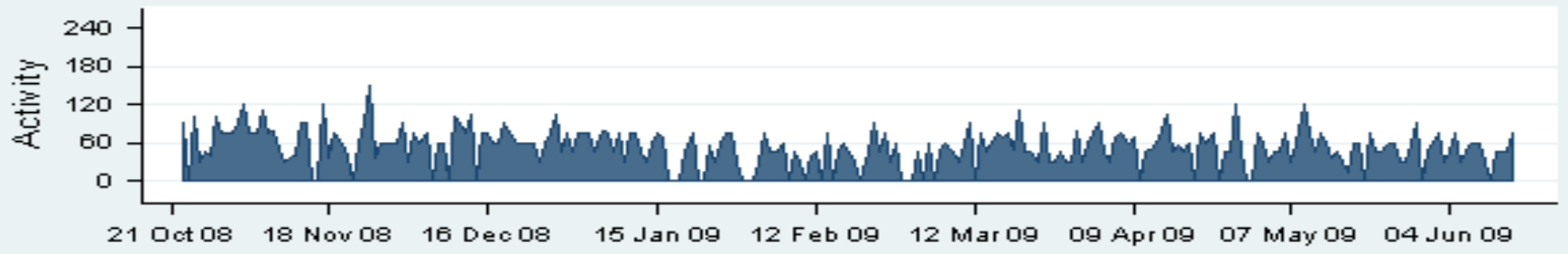
Idiographisch

Individuen

N klein, T groot

Individuele gemiddelden (over tijd)

Intra-individuele variabiliteit





Voorspelling van angstklachten

Belangrijkste risico factor !

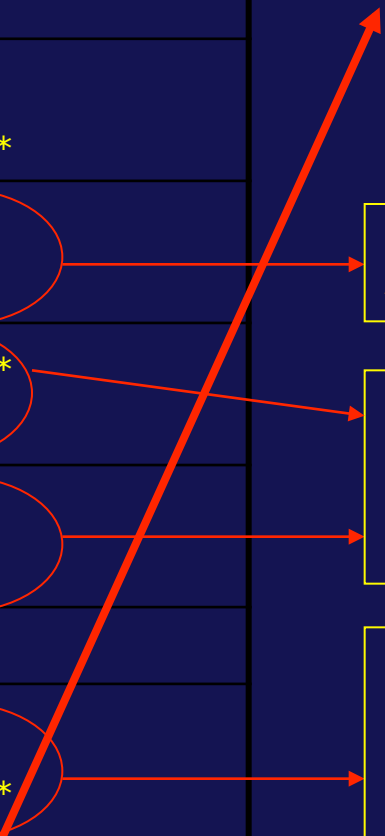
Voorspellers	
Energie (lag 1)	0
Energie (lag 2)	-0.23*
Angst (lag 1)	0.44*
Angst (lag 2)	0.24*
Ontspanning (lag 1)	-0.06*
Ontspanning (lag 2)	0
Activiteit (lag 1)	0.06*
Activiteit (lag 2)	0
Controle variabelen	
Alprazolam	0.14*
Alprazolam (lag 1)	-0.11*
Kerstmis	0.28*
Verklaarde variantie	
	0.85

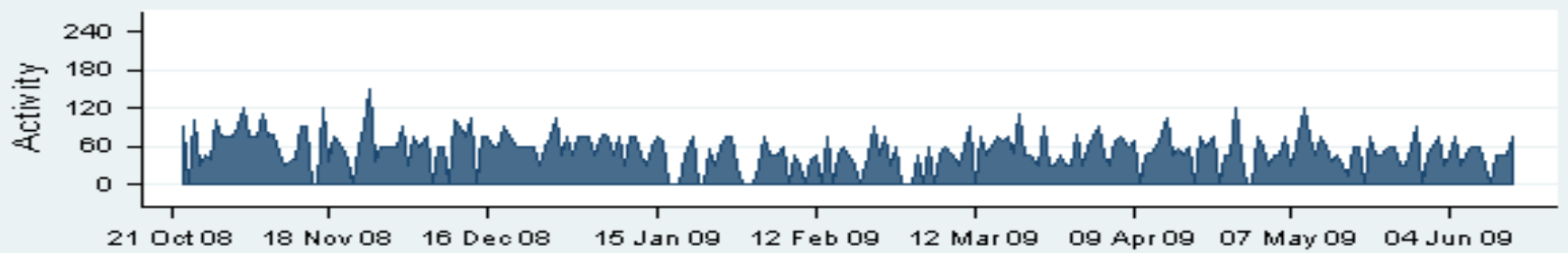
Autocorrelatie

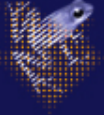
(Contra)productieve interventie

Successvolle zelf-administratie

Vergelijk met nomothetische studies !

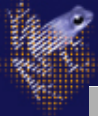






Extended N=1 studie

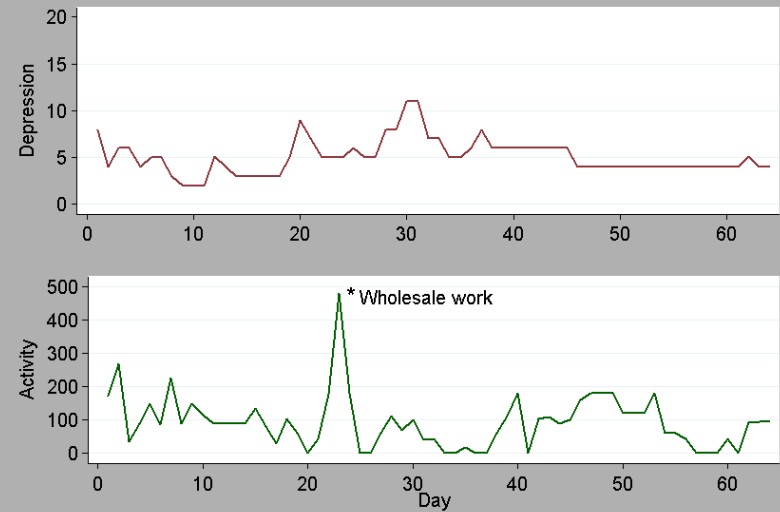
- 4 infarctpatienten, man, lft 50-60, BDI 14-24,
- 59-85 dagen achter elkaar gemeten: BDI en minuten fysieke activiteit



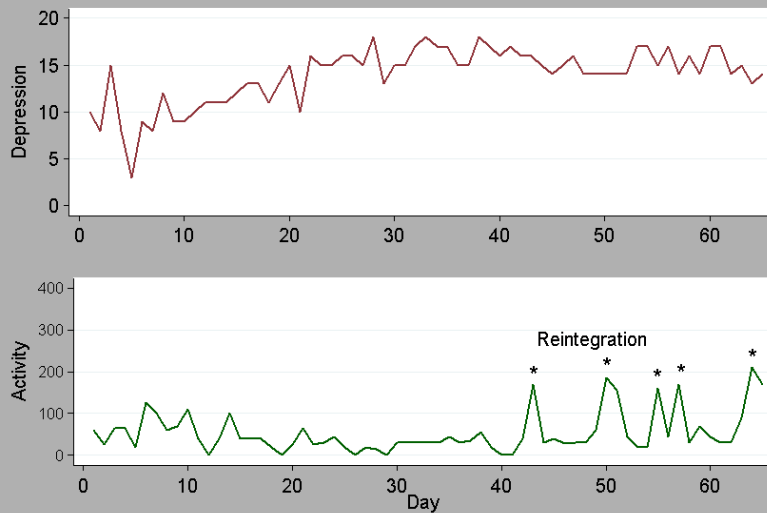
Participant 1



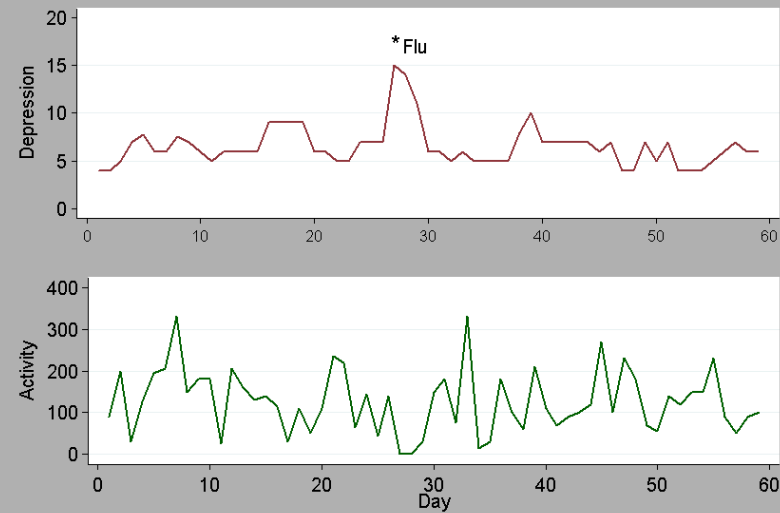
Participant 2



Participant 4



Participant 5





Patient 1

Independent variables	Depression
Depression (lag 1)	0.397***
Depression (lag 2)	0.090
Activity (lag 1)	-0.183*
Activity (lag 2)	0
Control variables	
PEP course	-8.114***
Road trip	-5.424***
Explained variance	0.39

Autocorrelatie

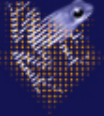
Mooi zo!

Betekenisvol voor deze patient



Uitbreiding naar andere patienten?

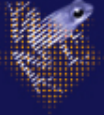
	Patient 1	Patient 2	Patient 3	Patient 4
	Dep -> Act	-----	Act -> Dep	Act -> Dep



Paradigma verschuiving naar idiographisch onderzoek

- Voordelen:
 - echte causaliteit in plaats van gemiddelde causaliteit
 - nieuwe interventies uitproberen zonder dure RCTs
 - wetenschappelijke kennisvergaring versnellen
 - integreren onderzoek en kliniek





En is er nou een causale relatie?

- Laten we eerst maar eens wat doen aan het fenotype depressie....



Deconstructing depression, reconstructing reality

Peter de Jonge

- We gaan geen doorbraak creëren met nog meer fancy biomarkers
- Of met ‘revolutionaire’ nieuwe interventies

Hoe dan wel?

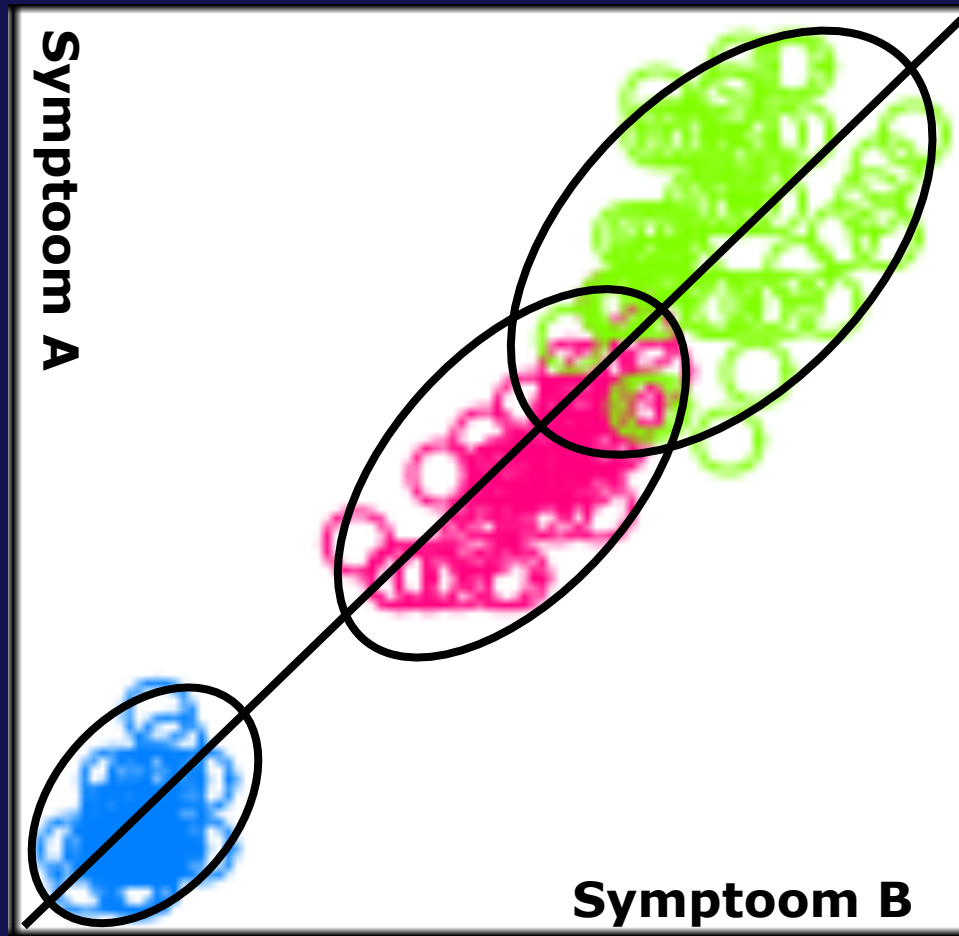
- Empirische herorientatie op het fenotype zelf
- De massale inter-individuele heterogeniteit uitbuiten in plaats van uitmiddelen



Deconstructing depression, reconstructing reality

Peter de Jonge

Mixed Measurement Item Response Theory (MM-IRT)

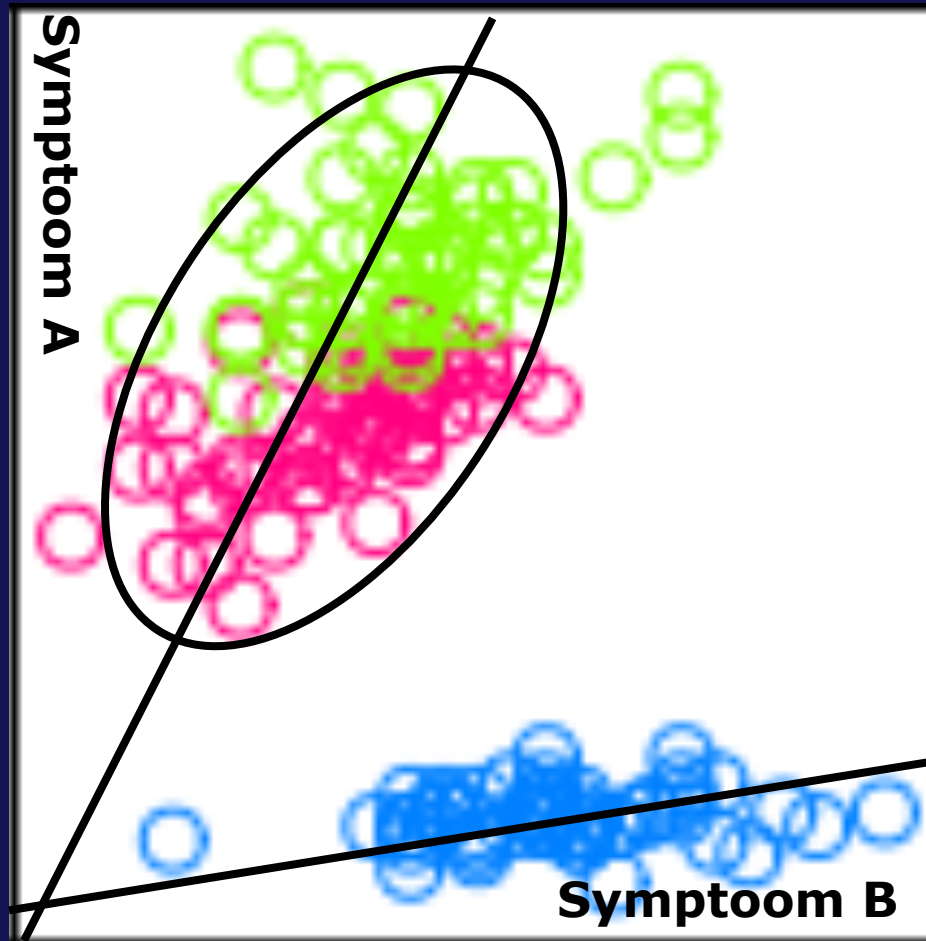


Unidimensionele variatie: Latente Klasse Analyse

Deconstructing depression, reconstructing reality

Peter de Jonge

Mixed Measurement Item Response Theory (MM-IRT)

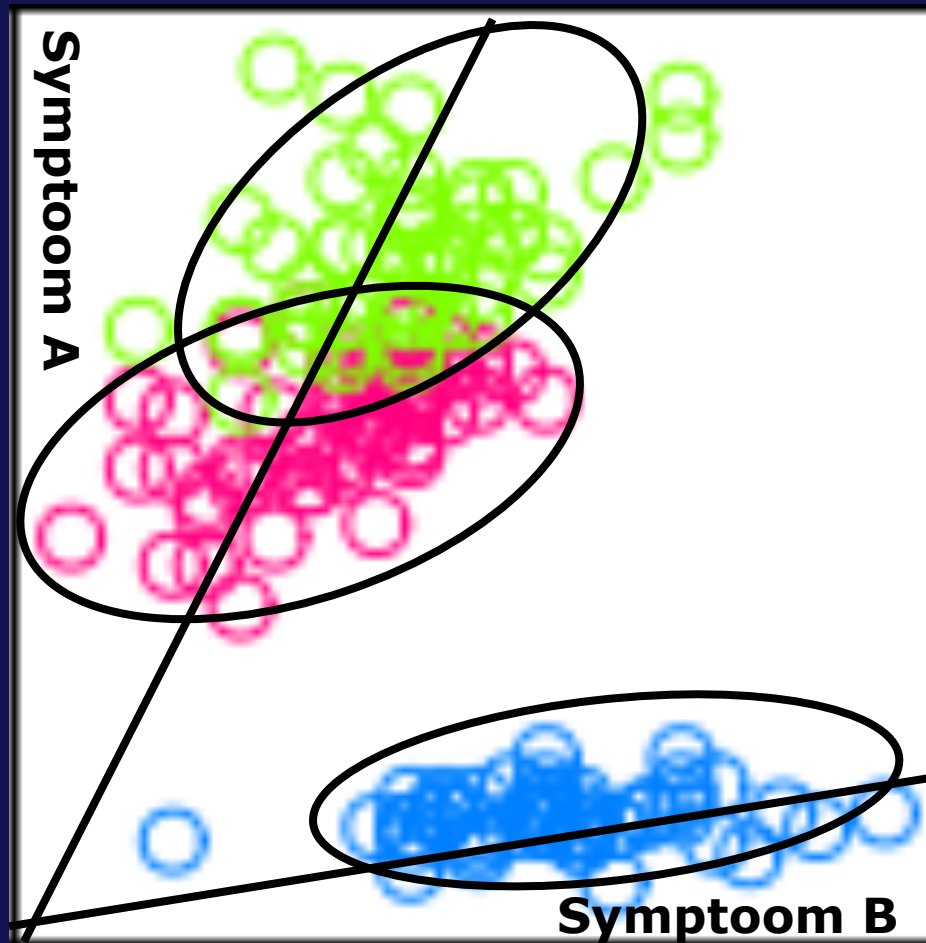


Multidimensionele variatie: Factor Analyse

Deconstructing depression, reconstructing reality

Peter de Jonge

Mixed Measurement Item Response Theory (MM-IRT)



Multidimensionale variatie plus subgroepen: MM-IRT