Medication Adherence and Outcomes in High Risk Cardiovascular Patients in the ONTARGET Trial

M. Böhm,
H. Schumacher, U. Laufs, P. Sleight,
R. Schmieder, T. Unger, K. Koon, S. Yusuf
on behalf of the ONTARGET-Investigators

Disclosures

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Background

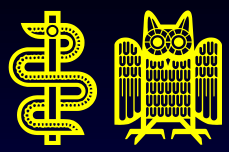
Nonadherence to medications

- is a problem in high risk patients
- associated with multidrug treatment
- related to outcomes in several conditions
  - Hypertension
  - Hyperlipidemia
  - CAD
  - CHF

-Associated with-health related life style characteristics

(„healthy adherer phenomenom“)

Objectives of ONTARGET



Patients:

CV high risk patients after MI, Stroke, PAD, or DM + 2RF

Questions:

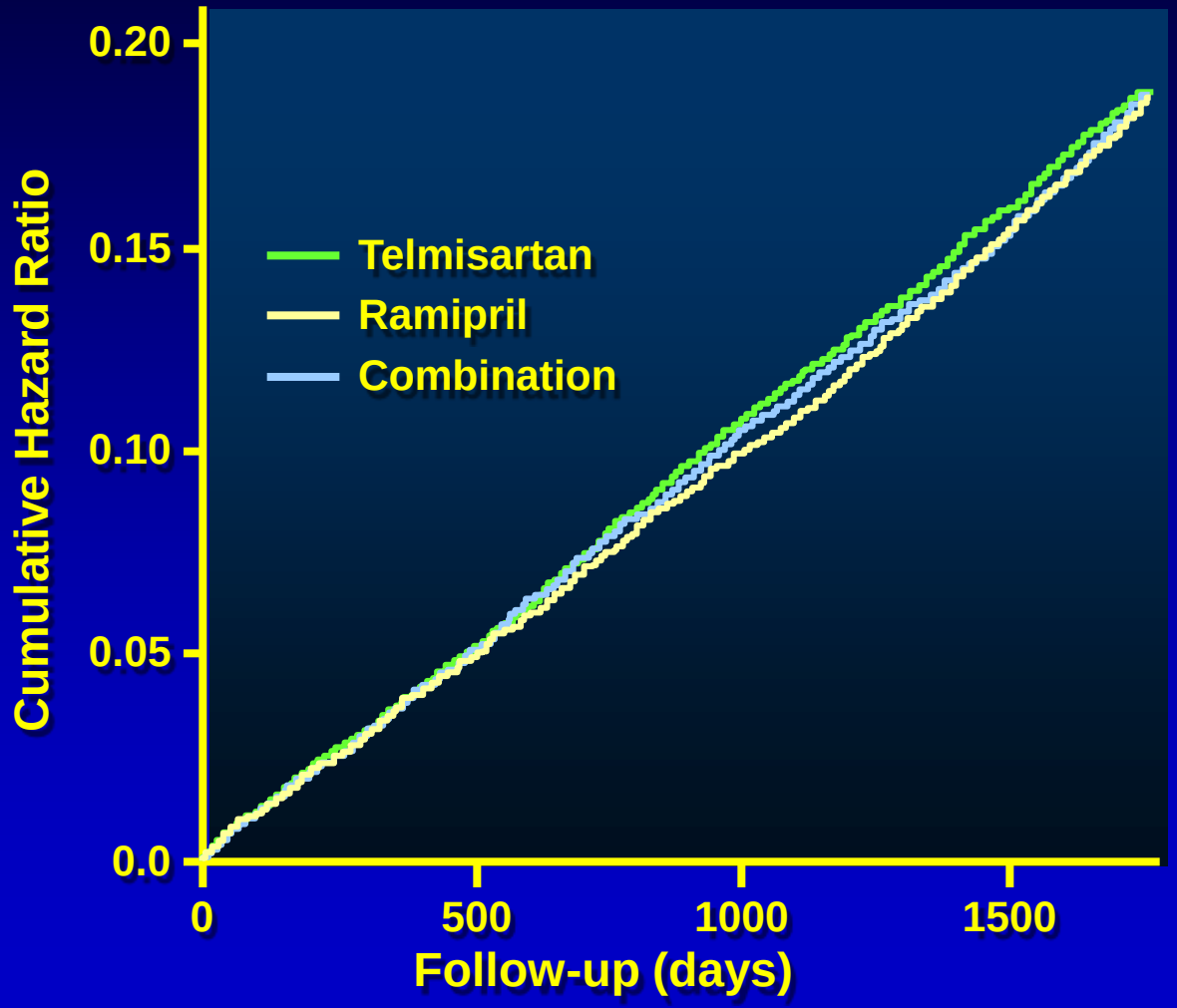
1. Is telmisartan “non-inferior” to ramipril?
2. Is the combination superior to ramipril?

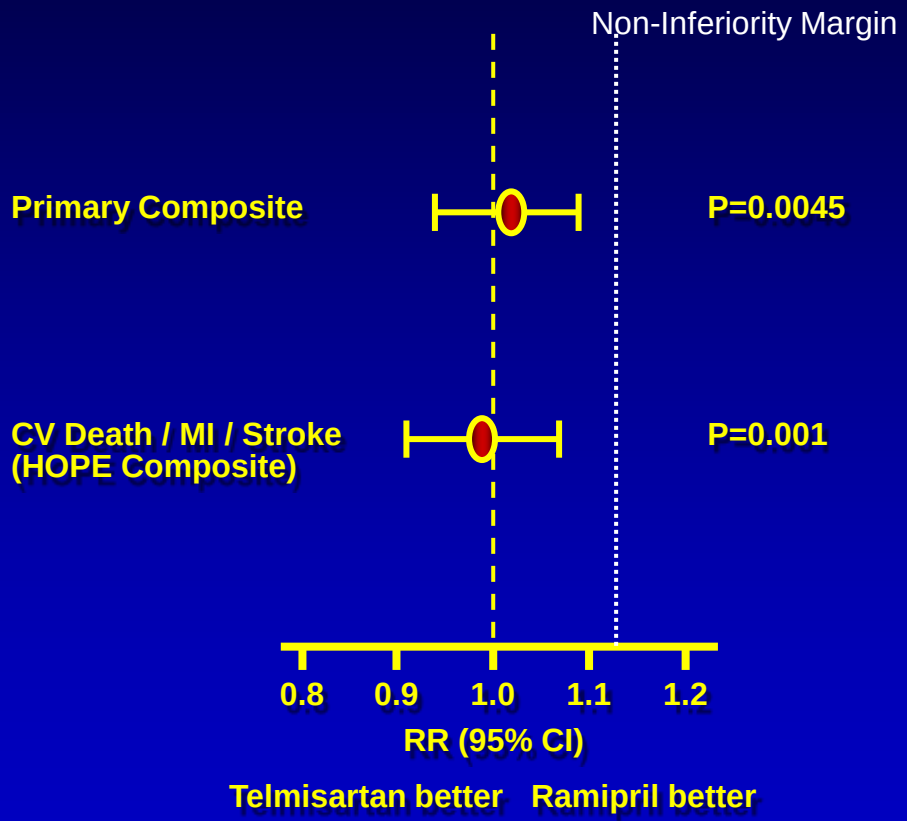
Outcome:

1. Primary: CV death, MI, stroke, CHF hosp
2. Key secondary: CV death, MI, stroke (HOPE trial outcome)
3. Single Components of the primary

ONgoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial, Am Heart J 148: 52-61, 2004

Primary Outcome
Telmisartan vs. Ramipril vs. Combination





ONgoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial, N Engl J Med 358: 1547-1559, 2008

Objective of Current Analysis

- Identification of patient characteristics for nonadherence

- Effect of nonadherence on outcomes

- Effect of CV-outcomes on adherence

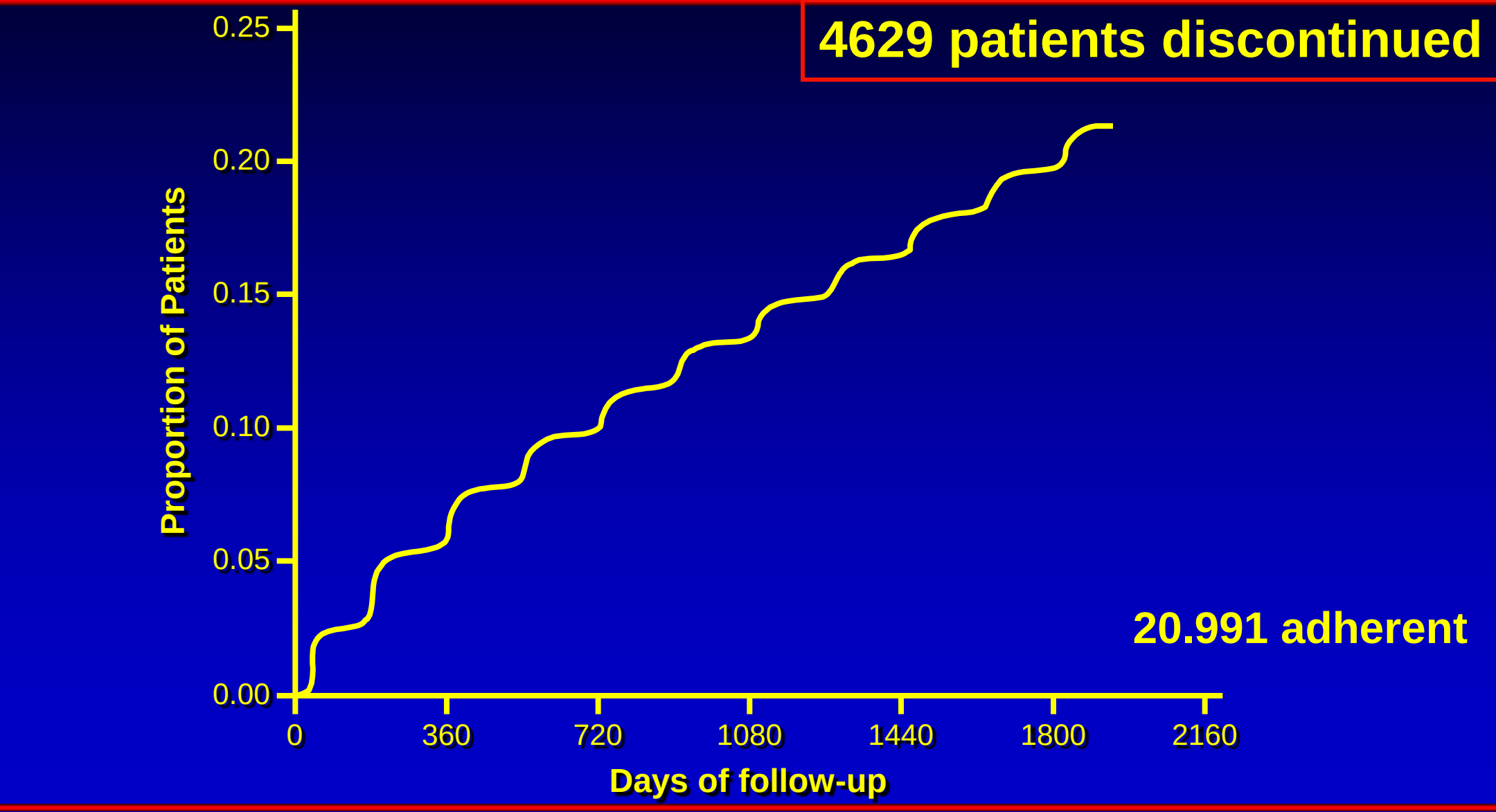
Definitions and Methods

Nonadherence: Complete and Permanent Discontinuation of All Study Medications

Statistical Analysis:

- differences tested by Chi-square (categorical) or Student`s t-test (continuous)
- Cox propotional hazard model
- nonadherence as time-dependent covariate
- multiple regression
- $p<0.01$

Permanent Stop of Study Medication Continuously Increased Over Time



Cox Regression on Time to Permanent Stop of Study Medication (Non-Adherence, adjusted)

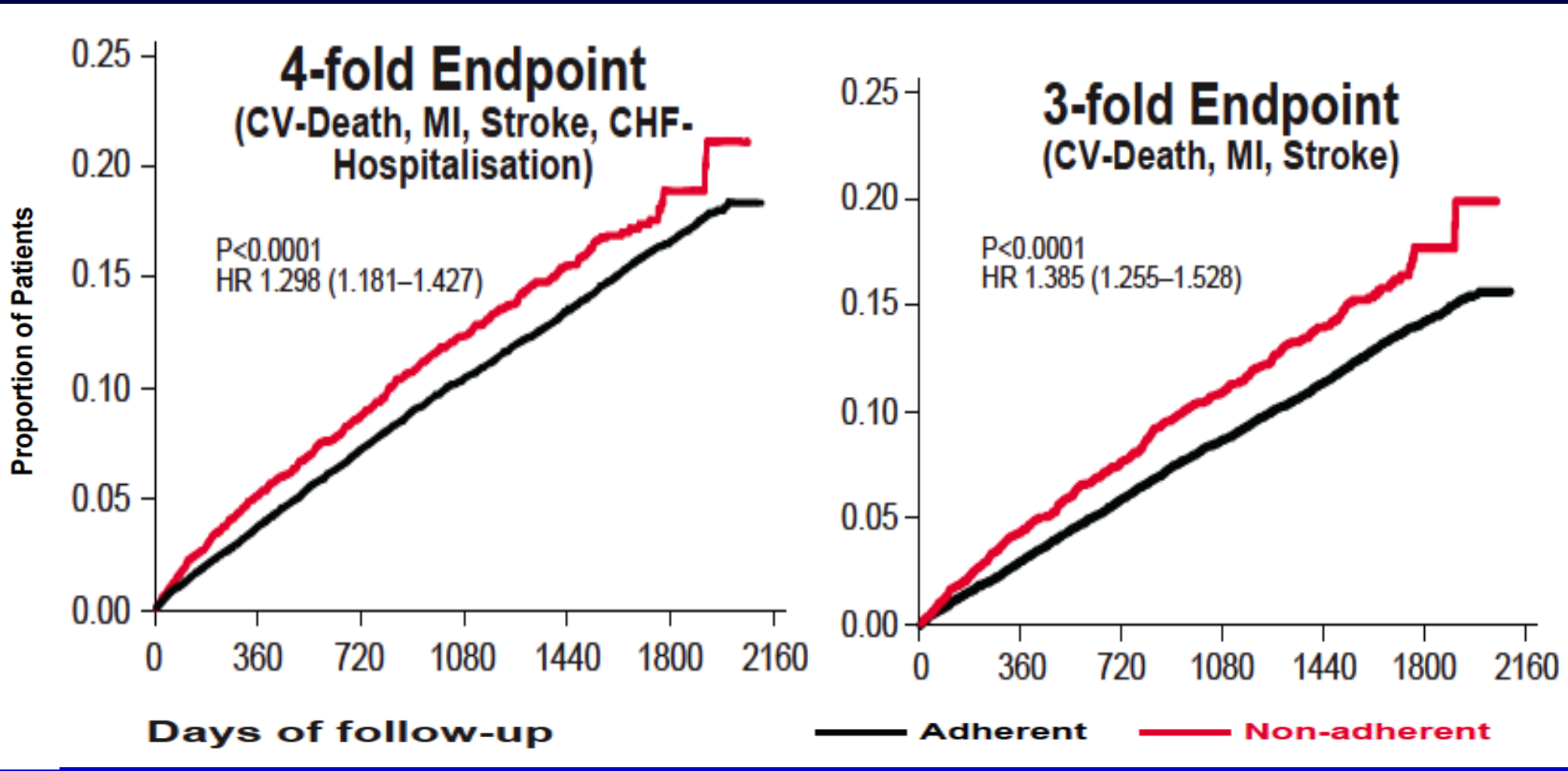
Variable	*Pr > ChiSq*	*HR*	*95% CI*
Age, linear	<0.0001	1.035	(1.030 – 1.039)
Female vs Male	<0.0001	1.200	(1.117 – 1.289)
Black vs White	0.0009	1.302	(1.115 – 1.521)
Asian vs White	<0.0001	0.569	(0.511 – 0.639)
Other vs White	<0.0001	0.645	(0.574 – 0.726)
Activity 2-6/week vs ≤ 1/week	<0.0001	0.863	(0.804 – 0.927)
Every day vs ≤ 1/week	<0.0001	0.806	(0.750 – 0.865)
Smoking Current vs Never	0.0005	1.193	(1.080 – 1.316)
Smoking Formerly vs Never	0.0026	1.113	(1.038 – 1.192))
Stroke / TIA	0.0013	1.128	(0.974 – 1.128)
History of diabetes	<0.0001	1.223	(0.927 – 1.104)
Episodes of depression	<0.0001	1.111	(0.867 – 1.036)

Age, Gender, Ethnics, Physical Activity, Smoking, Diabetes, neuro-psychiatric disorders

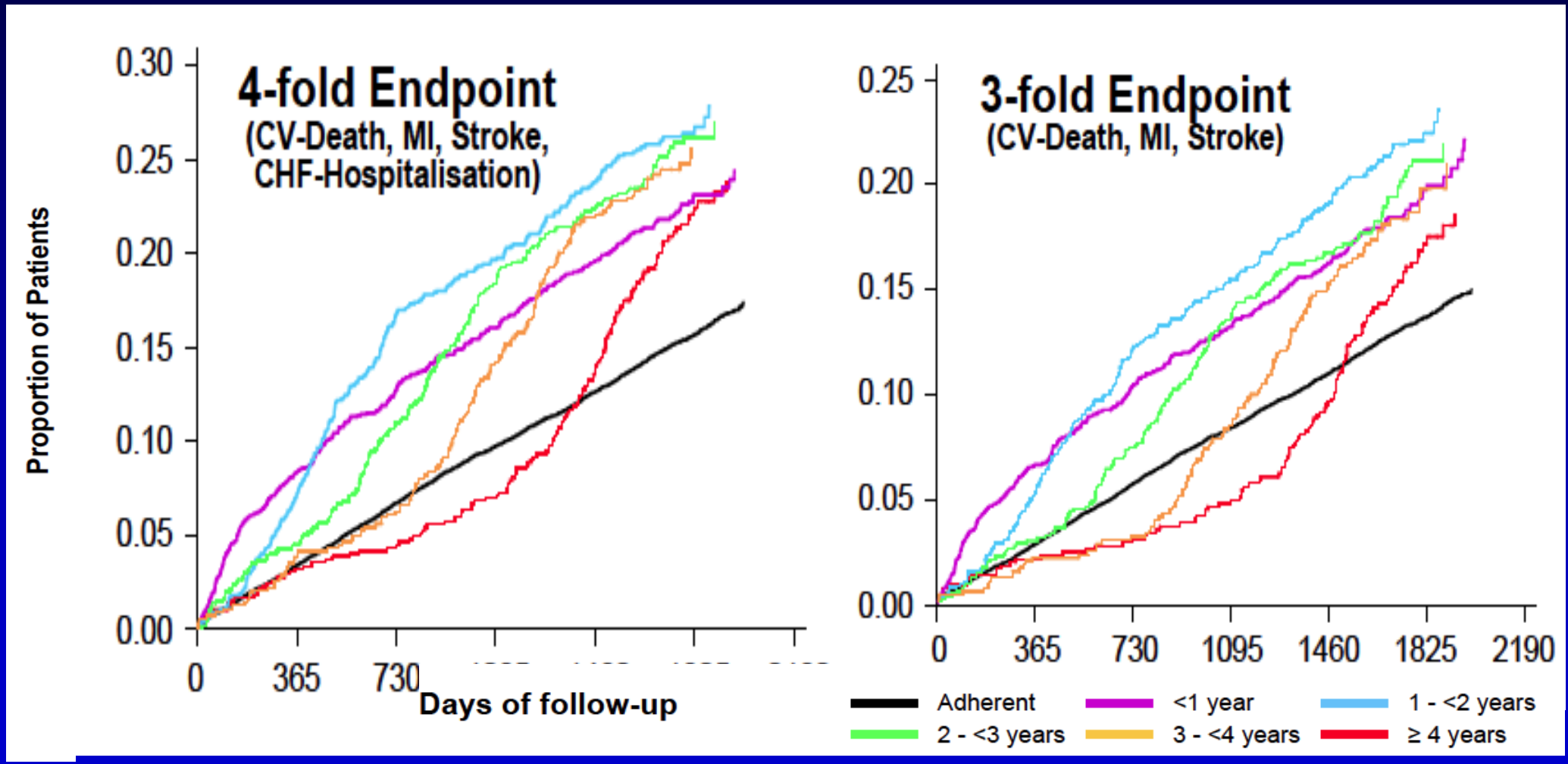
Distribution of Premature Permanent Discontinuations of Study Medication - By Time

Permanent discontinuation	Frequency	Percent	Cumulative Frequency	Cumulative Percent
< 6 weeks	354	7.7	354	7.7
6w - < 6 months	585	12.6	939	20.3
6m - < 1 year	619	13.4	1558	33.7
1y - < 2 years	1038	22.4	2596	56.1
2y - < 3 years	785	17.0	3381	73.0
3y - < 4 years	613	13.2	3994	86.3
≥ 4 years	635	13.7	4629	100.0

Nonadherence Increases Overall Event Rates



Rapid Increase of Events by Year After Permanent Discontinuation of Study Medication



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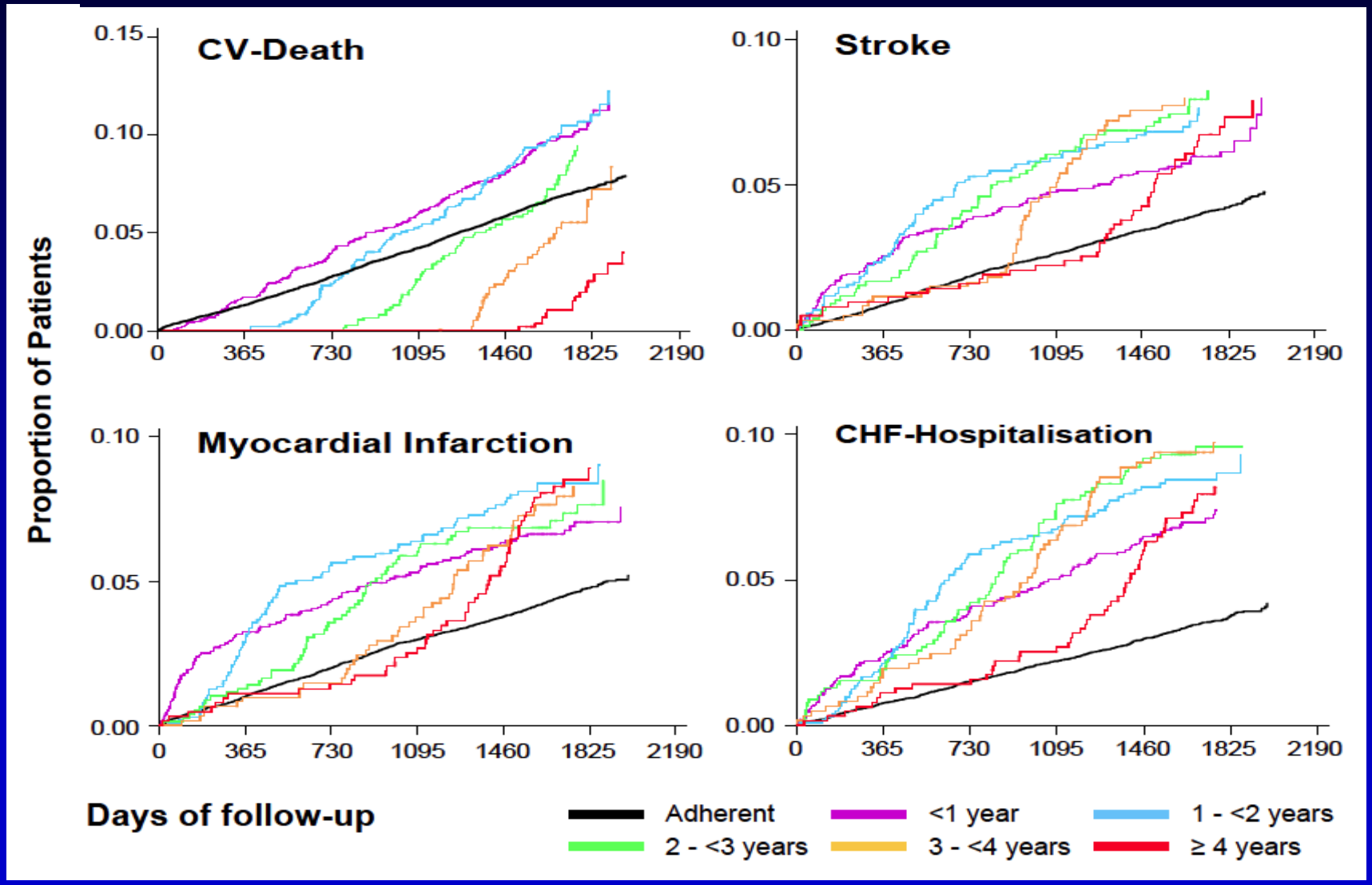
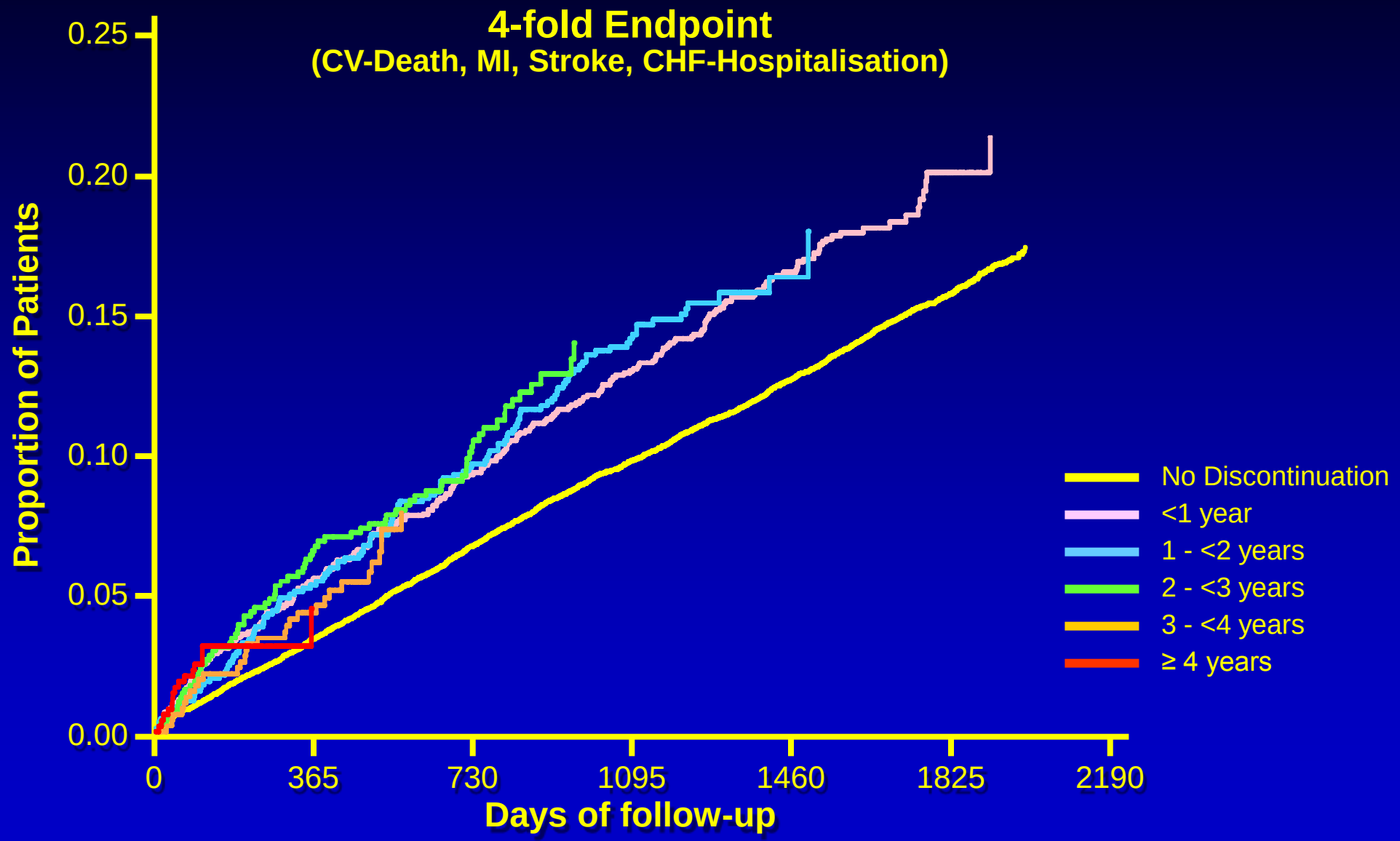


Cox Model with Time-Dependent Covariate

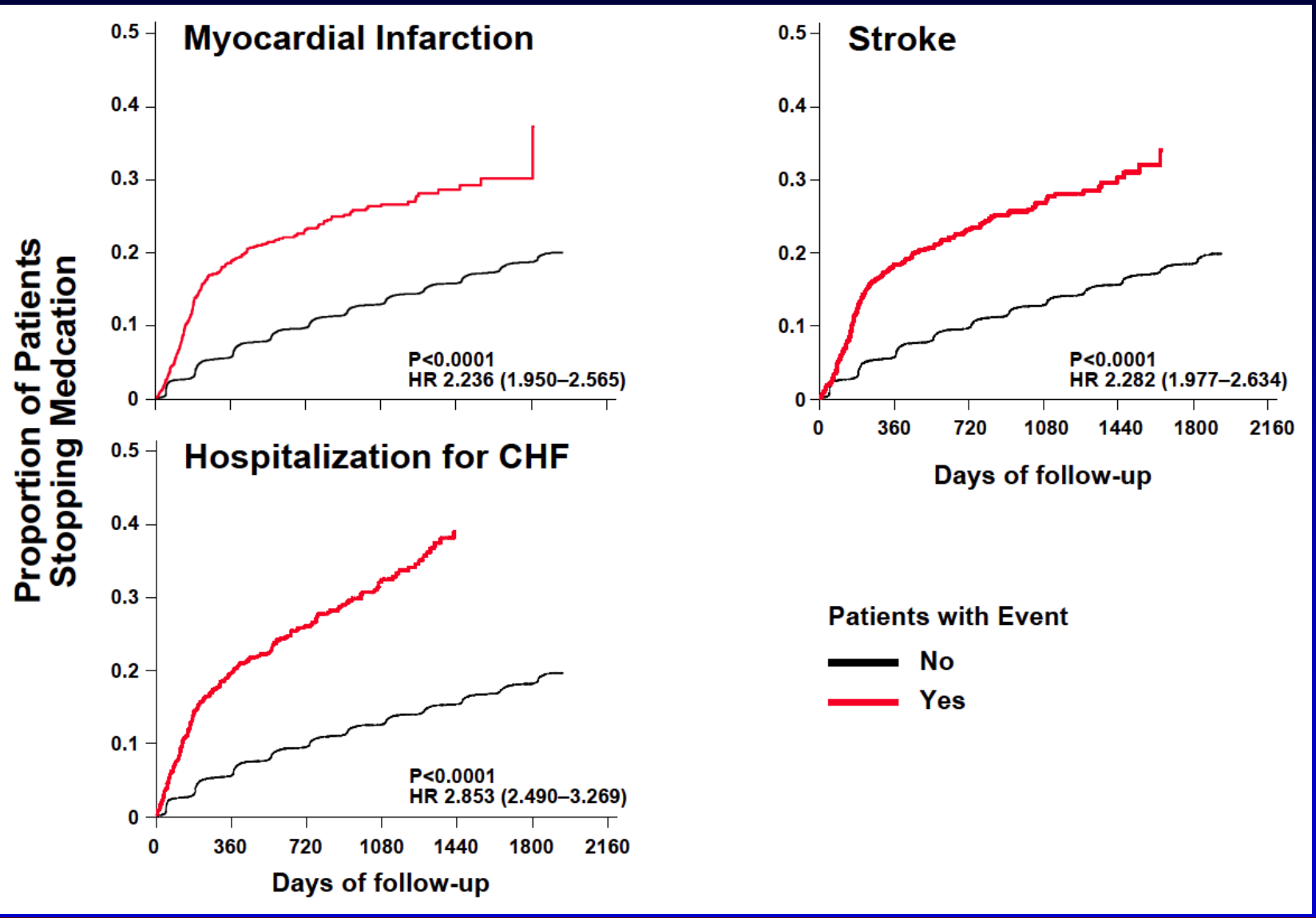
Time-dependent
(HR for being off medication)

	p	*Hazard Ratio (CI)*
4-fold endpoint	<.0001	1.298 (1.181 – 1.427)
3-fold endpoint	<.0001	1.385 (1.255 – 1.528)
CV death	<.0001	2.050 (1.824 – 2.303)
MI	0.6569	1.043 (0.866 – 1.256)
Stroke	0.5171	1.066 (0.879 – 1.293)
CHF Hospitalisation	<.0001	1.464 (1.228 – 1.745)

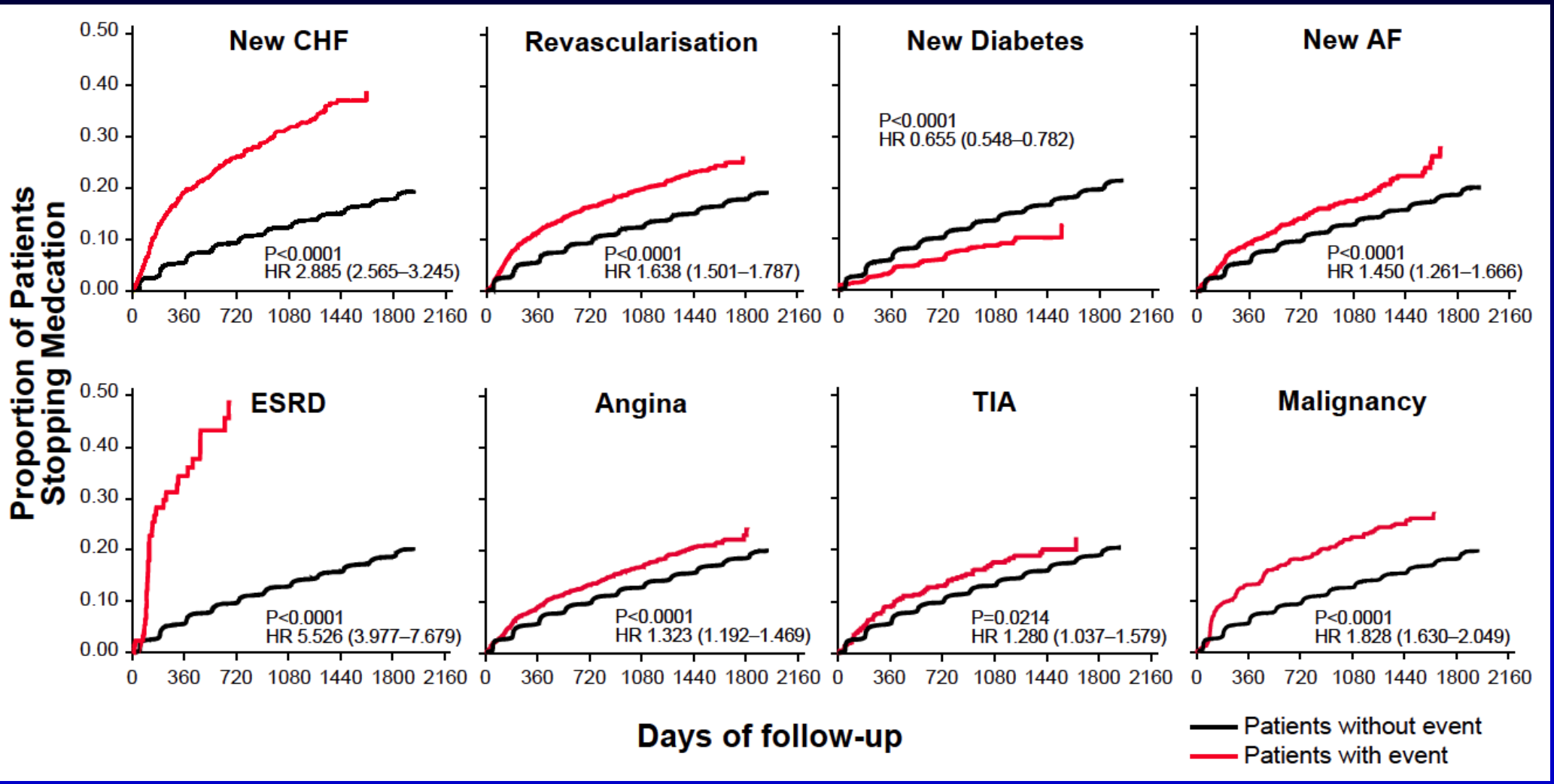
Rate of Rise of Event Rates after Stop of Study Medication is Similiar Between Years of Discontinuation



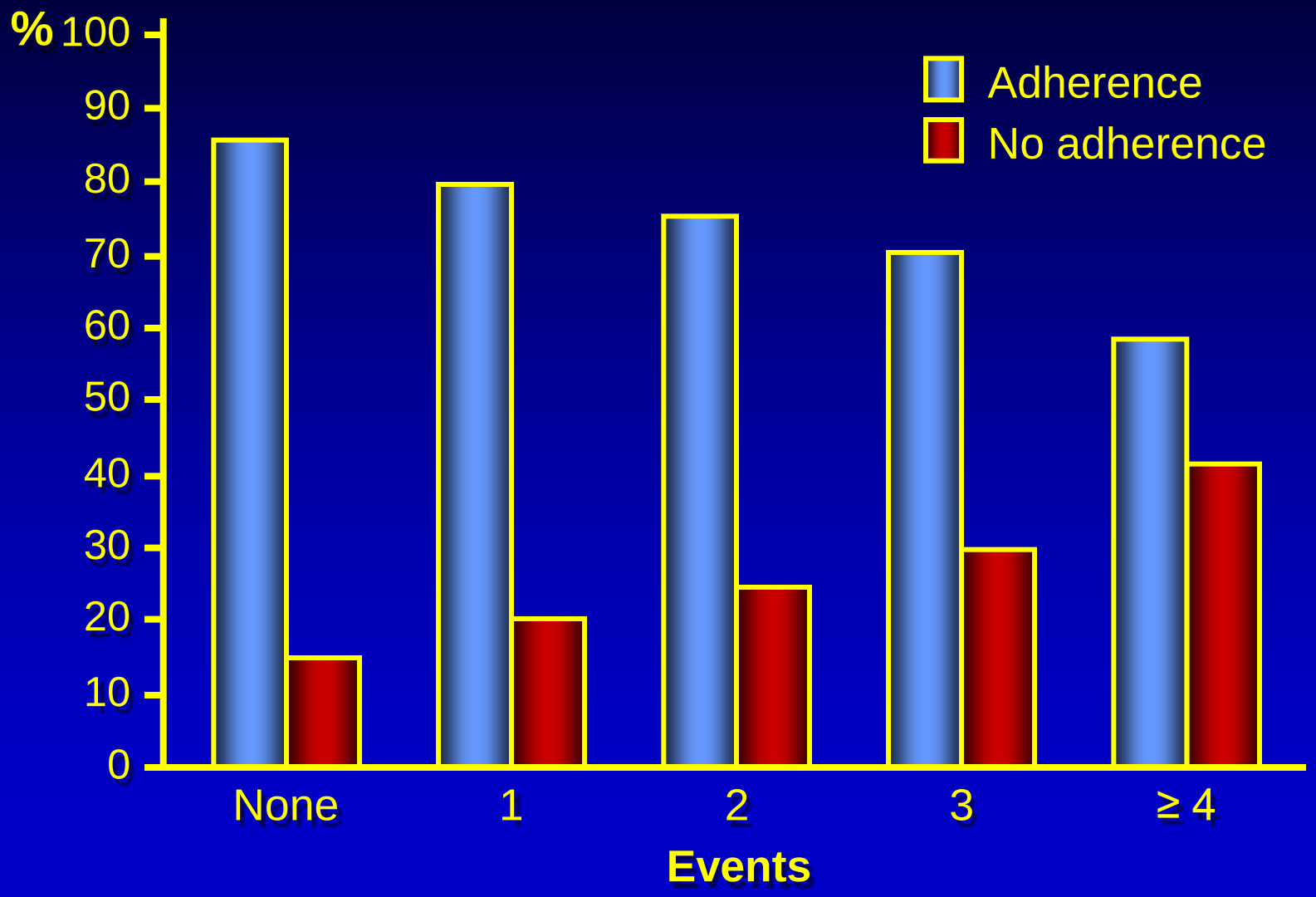
Risk for Discontinuation of Medication is Increased After Nonfatal Primary Event



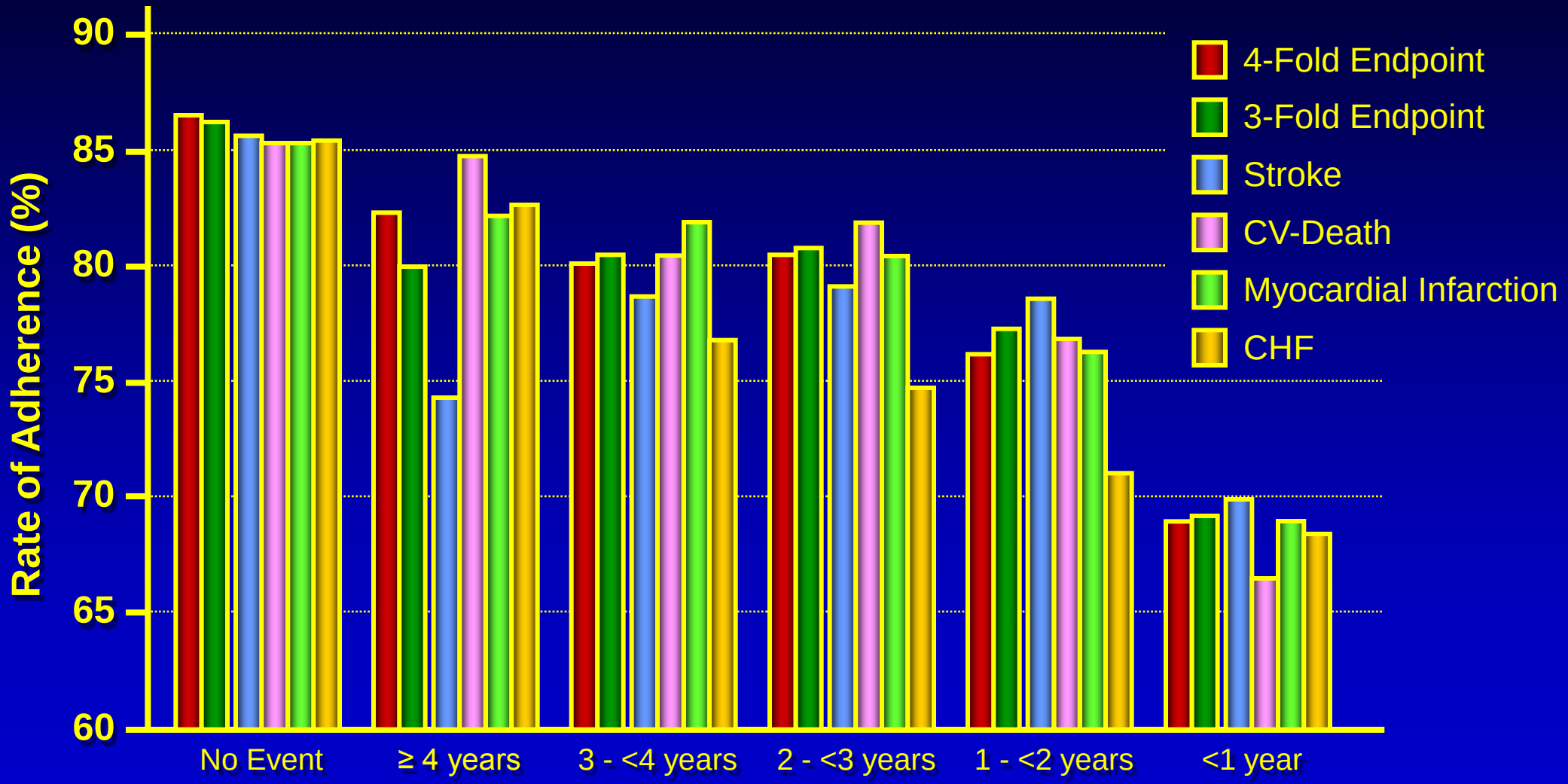
Risk for Discontinuation of Medication is Increased After Nonfatal Other Events



Number of Events Increases Nonadherence



Patients with an Early Event Have Worse Mean Adherence Rates



Conclusions:

- Ageing, females, ethnics, low physical activity, smoking, diabetes, neuro-psychiatric disorders are predictors of nonadherence

- becoming nonadherent rapidly increases events

- the event itself reduces adherence leading into a vicious cycle!

Concept: Nonadherence-Event Vicious Cycle

Age, Gender, Ethnics,
Physical Activity,
Smoking, Diabetes,
neuro-psychiatric disorders

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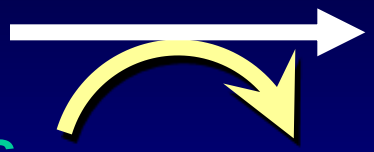

Nonadherence

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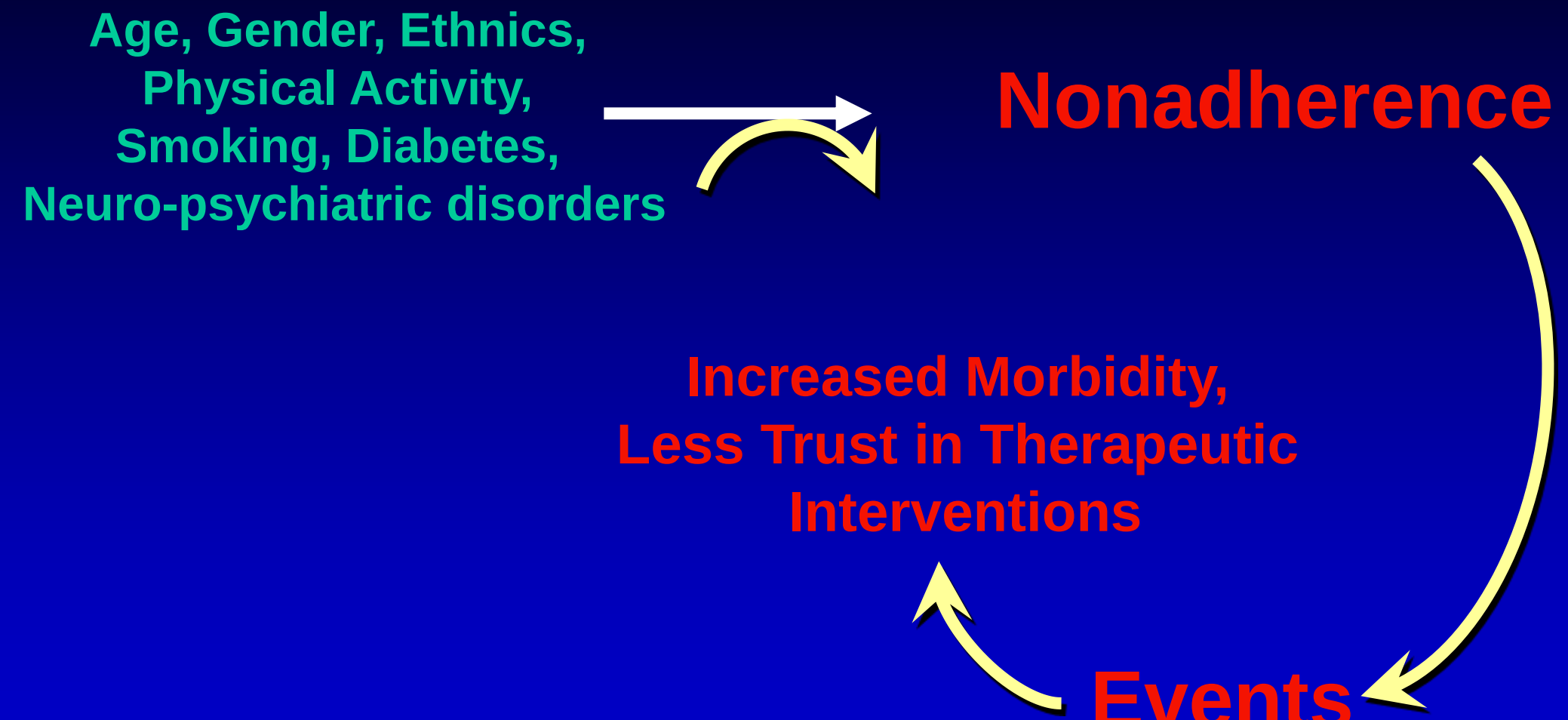

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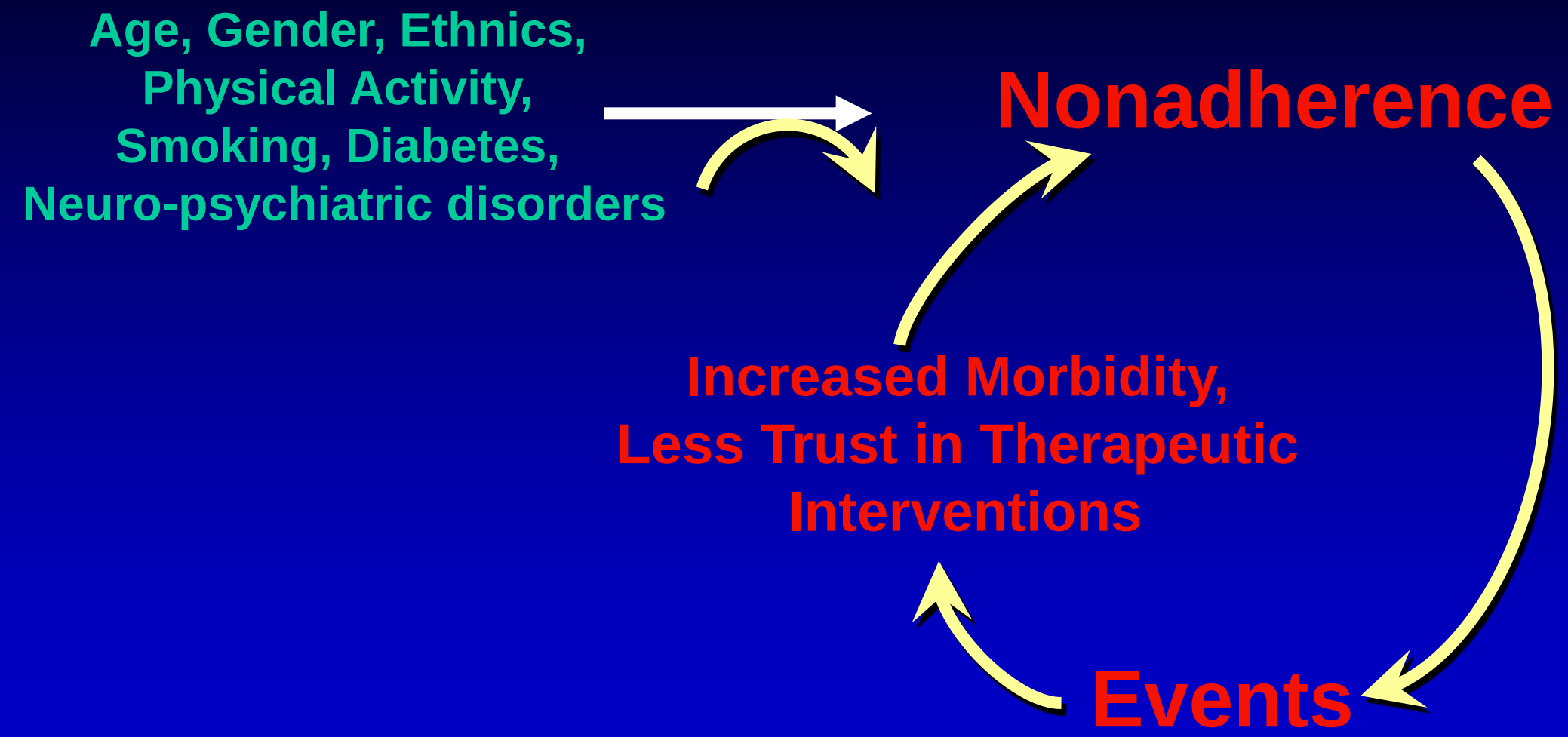

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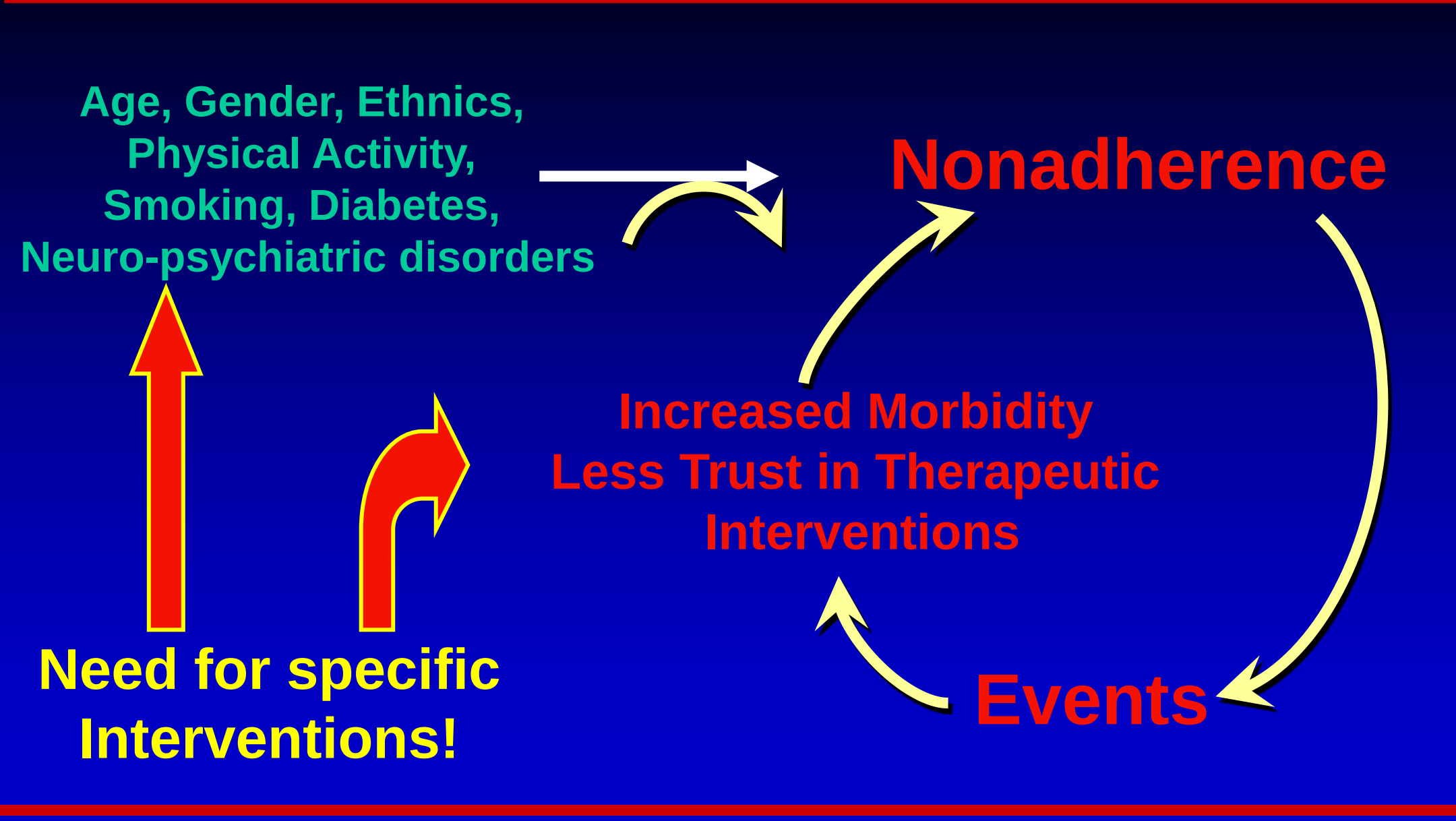

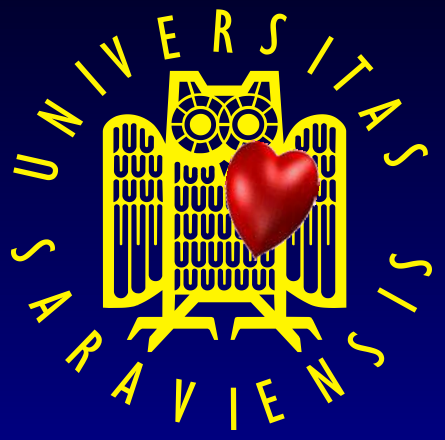

Thank You!

M. Böhm
Innere Medizin III (Kardiologie / Angiologie / Internistische Intensivmedizin)
Universitätsklinikum des Saarlandes
Homburg/Saar