



Assessment of the Quality of Life Impact of Medical Devices

David W. Feigal, Jr., M.D., M.P.H.

Director

Center for Devices and Radiological Health

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Quality of Life

Definitional Elements

- ▶ Prolonging Life
- ▶ Relieving Distress
- ▶ Restoring Function
- ▶ Preventing Disability

Lembke, 1952



FDA and New Therapeutics

Responsibilities

- ▶ Approve Initial Marketing **efficacy** Claims based on *Clinical Benefit*
 - Prevent
 - Cure
 - Ameliorate
 - Alter Body Function
- Note: change in test or lab result is not sufficient unless the lab result has well established clinical meaning

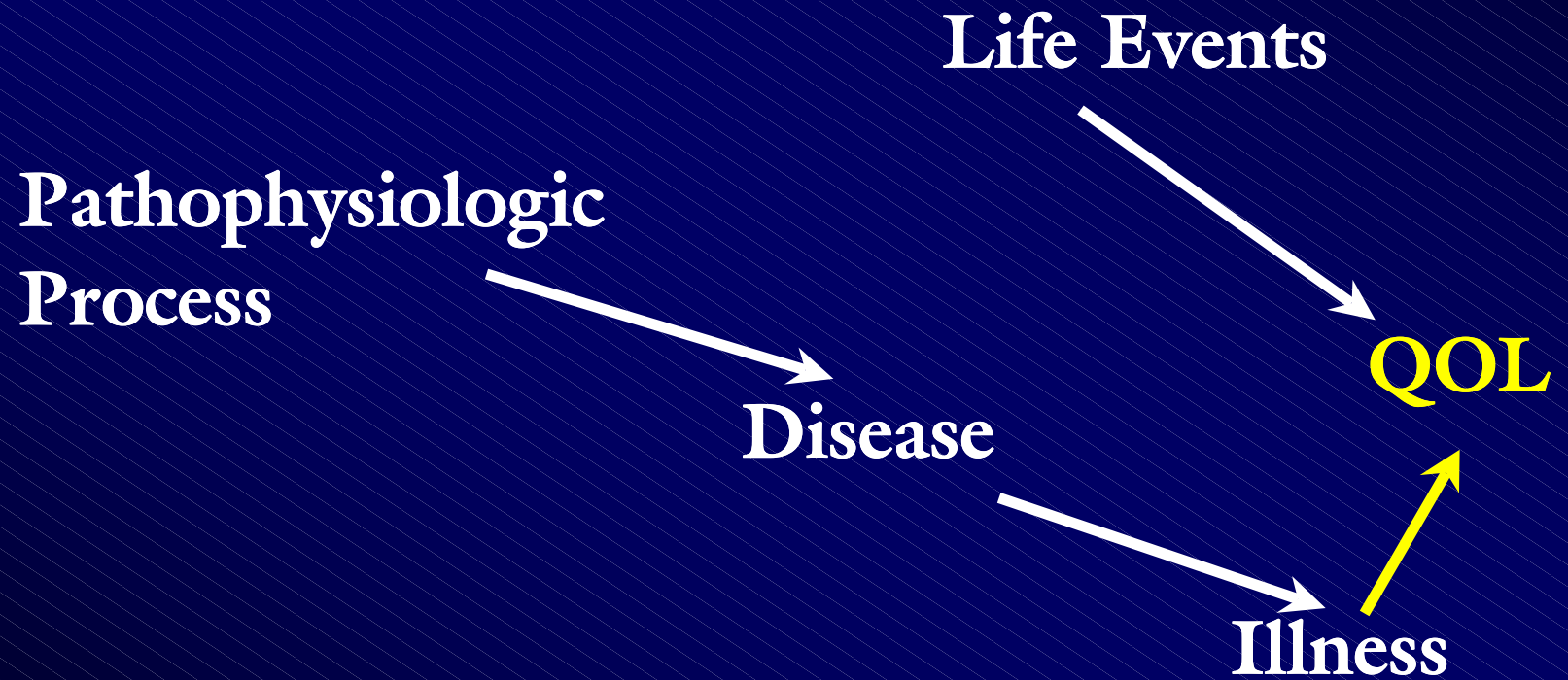
Quality of Life Scales

What do they measure?

- ▶ Improved Survival ?
 - Disease free survival
 - Quality adjusted survival
- ▶ Improved symptom profiles ?
 - Disease specific symptoms
 - Disability assessment
- ▶ Global perception of function ?

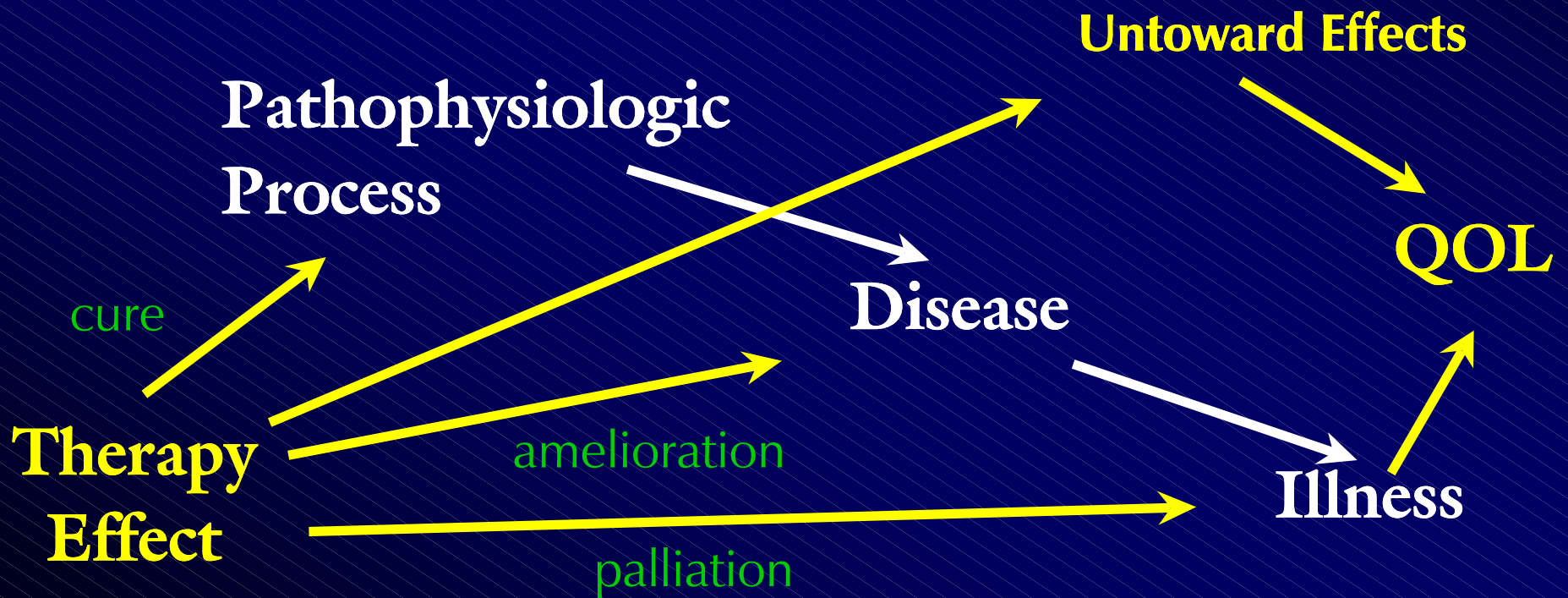
Quality of Life

Disease –Therapy Model



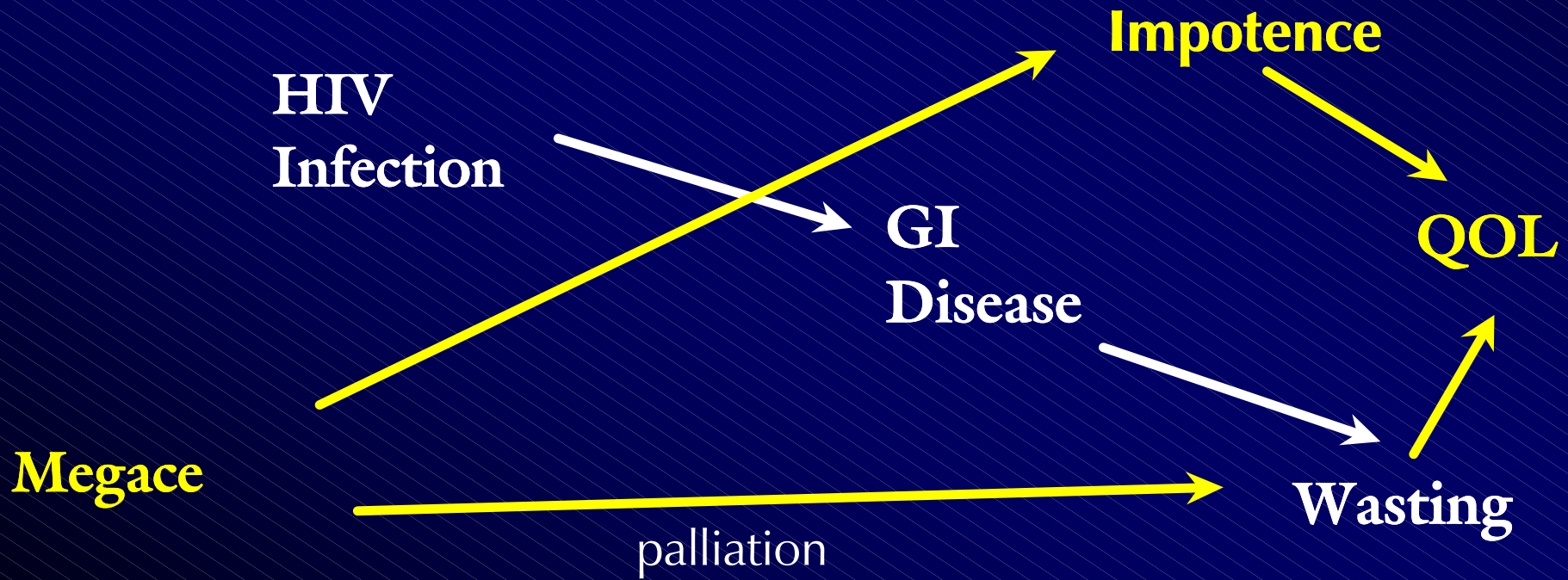
Quality of Life

Disease –Therapy Model



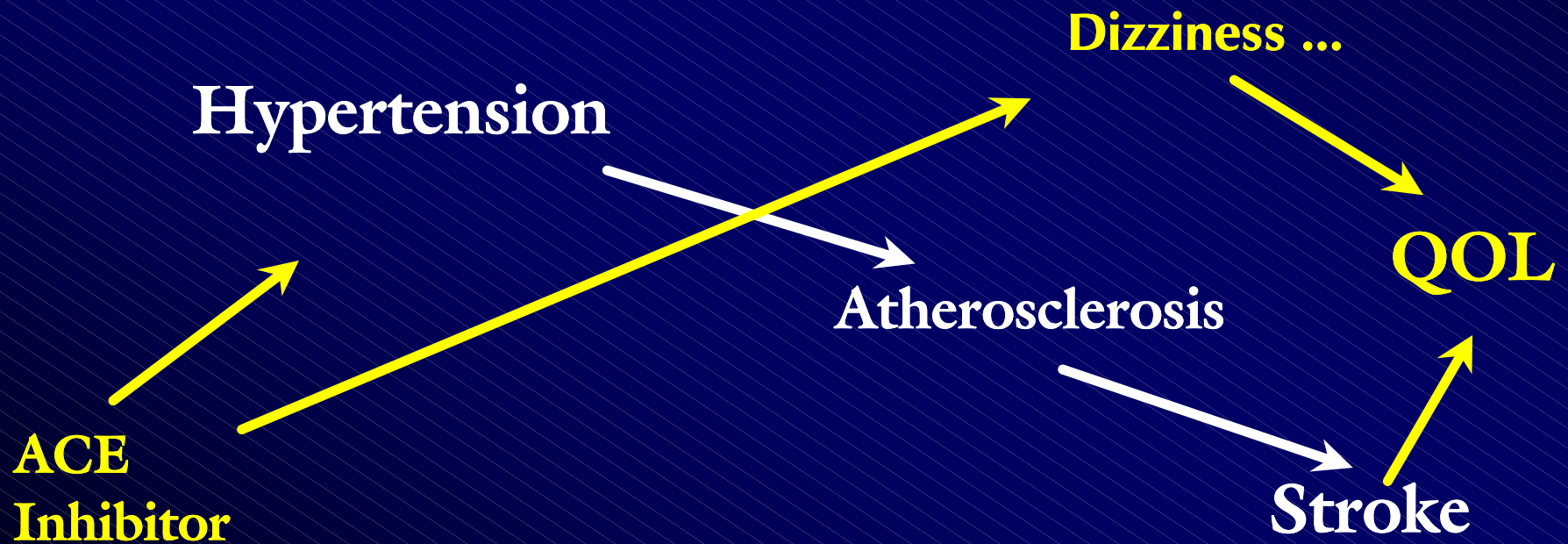
Quality of Life

Disease - Therapy Model



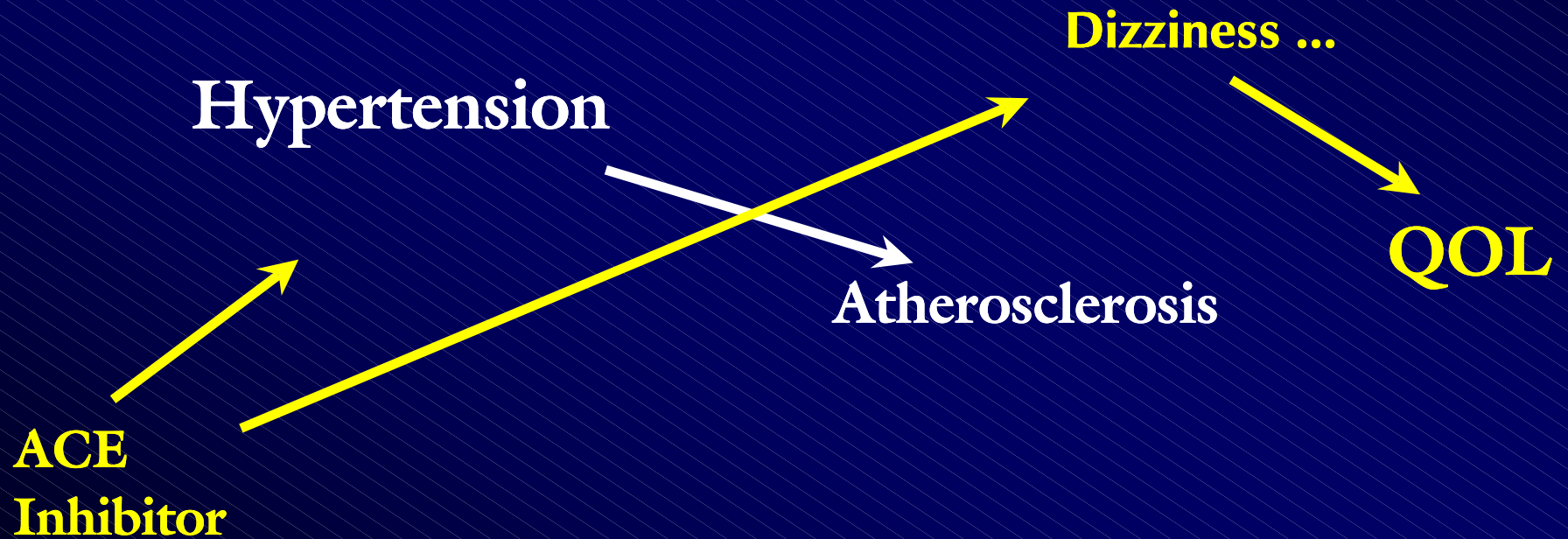
Quality of Life

Disease – Therapy Model



Quality of Life

Disease – Therapy Model



Quality of Life: A Case Study

New Antiviral vs. Continued AZT

- ▶ Randomized double blind study
- ▶ 500 participants followed 6 months
- ▶ Antiviral effects assessed by change in CD4 count, quantitative viral culture
- ▶ Quality of Life assessed with
 - Karnofsky Performance Status
 - MOS
 - Spitzer

Quality of Life

Karnofsky Scale

- 100 Asymptomatic, normal Function
- 80-90 Symptomatic, fully ambulatory
- 60-70 Symptomatic, in bed <50% of day
- 40-50 Symptomatic, in bed >50% of day
- 20-30 Bedridden
- 0 Death

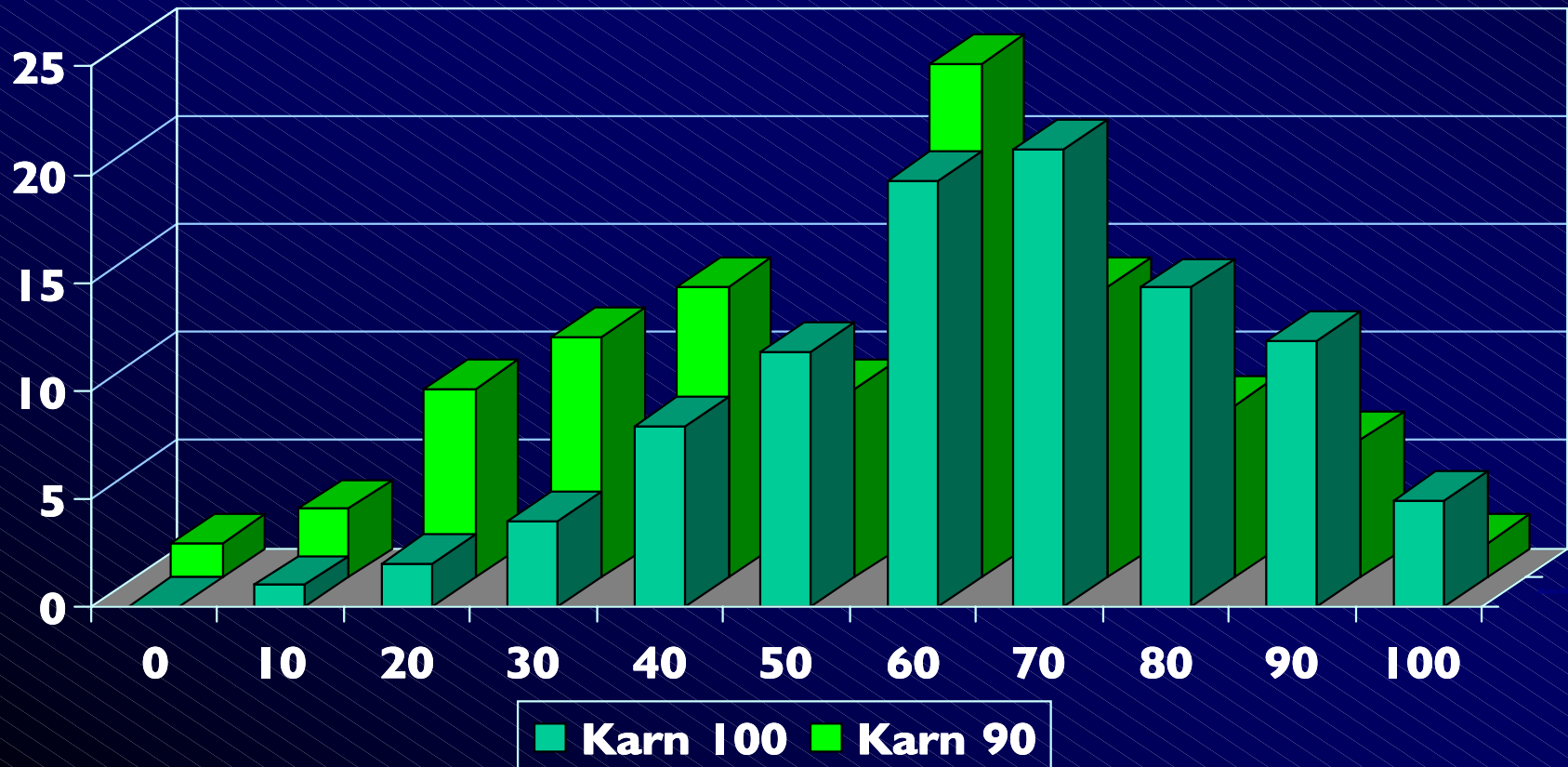
Quality of Life

MOS Framework of Health Indicators

- ▶ Clinical Status
- ▶ Physical functioning and well-being
- ▶ Mental functioning and well-being
- ▶ Social/role functioning and well-being
- ▶ General health perceptions and satisfaction

Quality of Life Scales

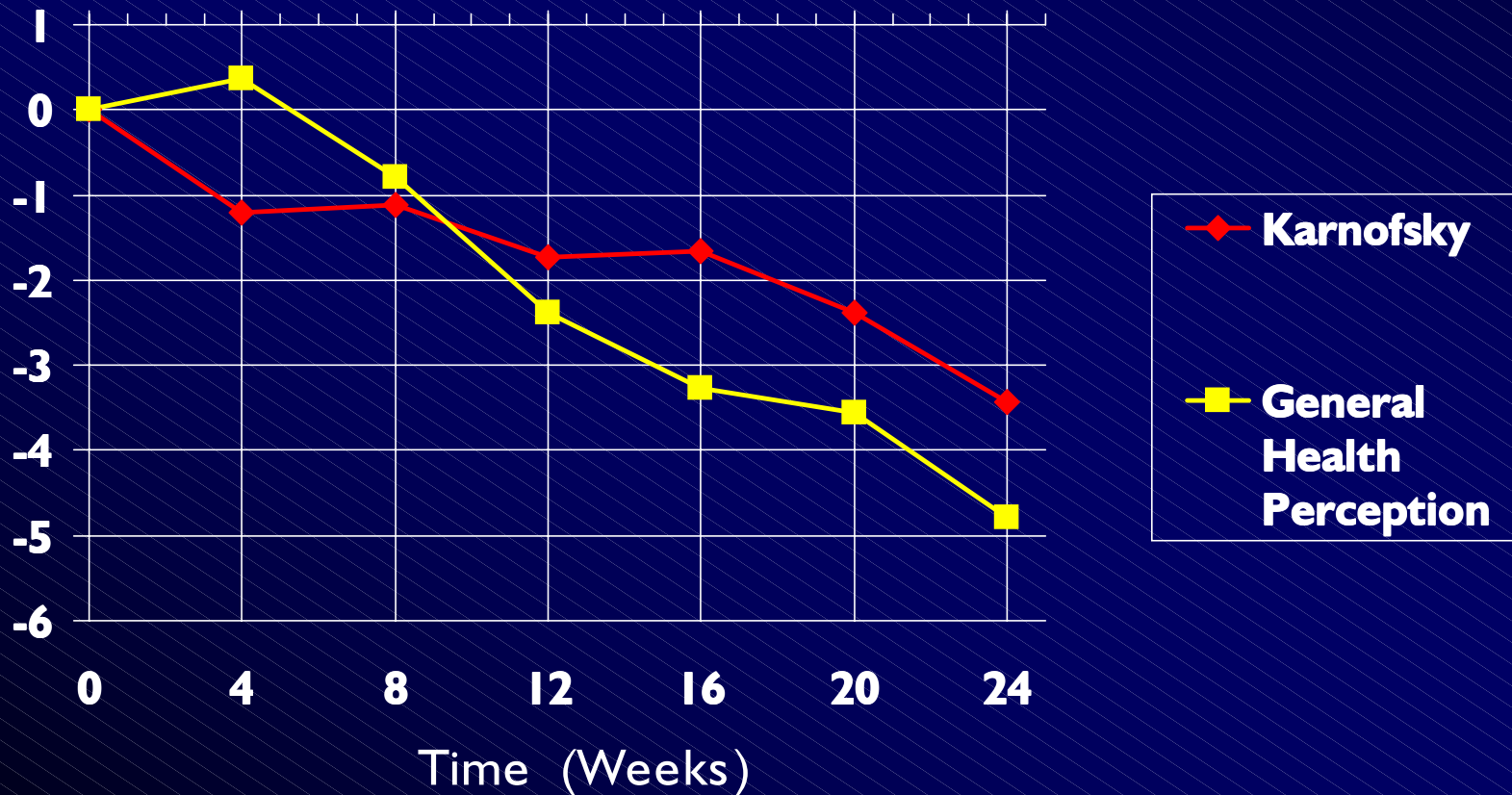
General Health Perception Scale



Quality of Life Scales

Karnofsky and General Health Perception

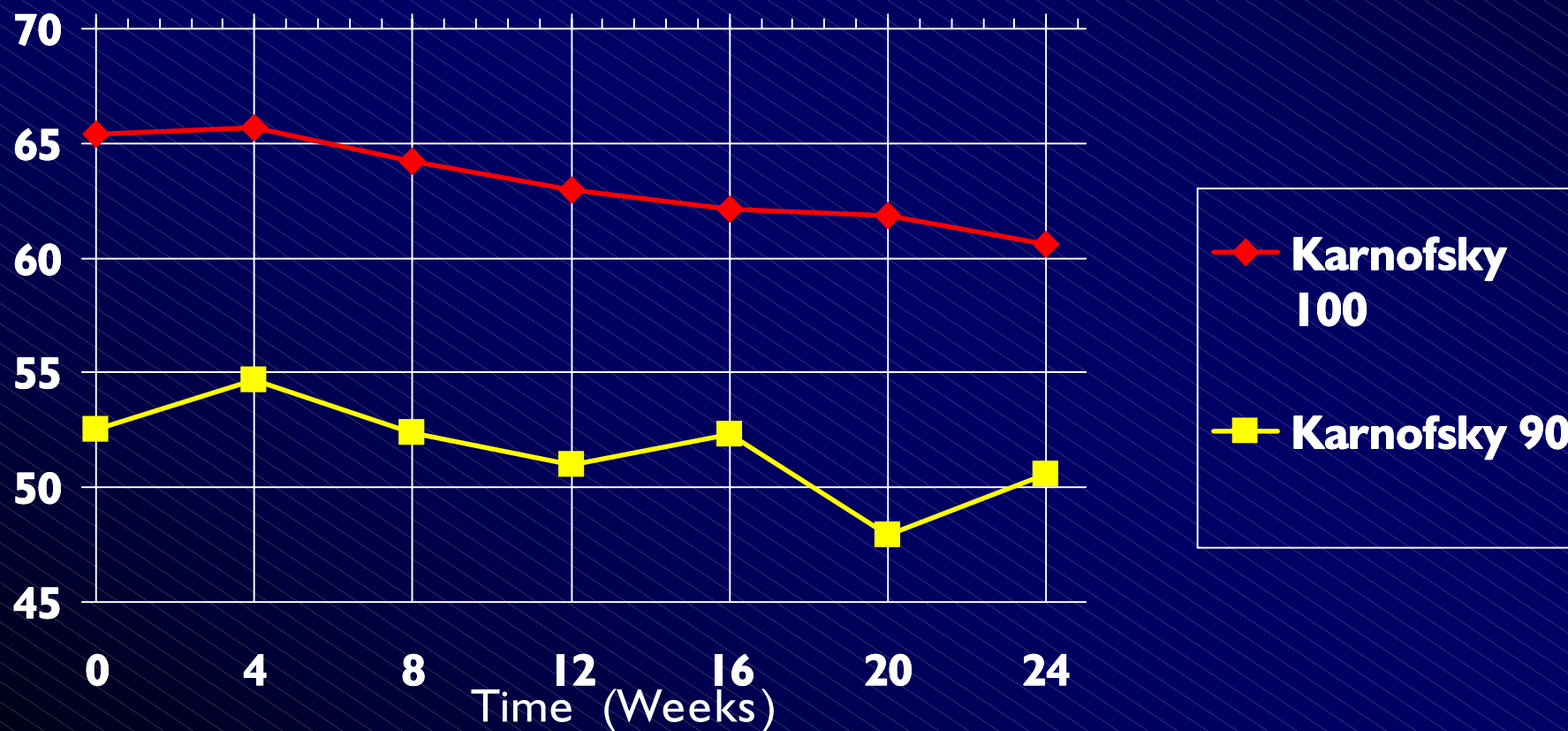
Change from Baseline in subgroup with Karnofsky = 100 at Baseline



Quality of Life Scales

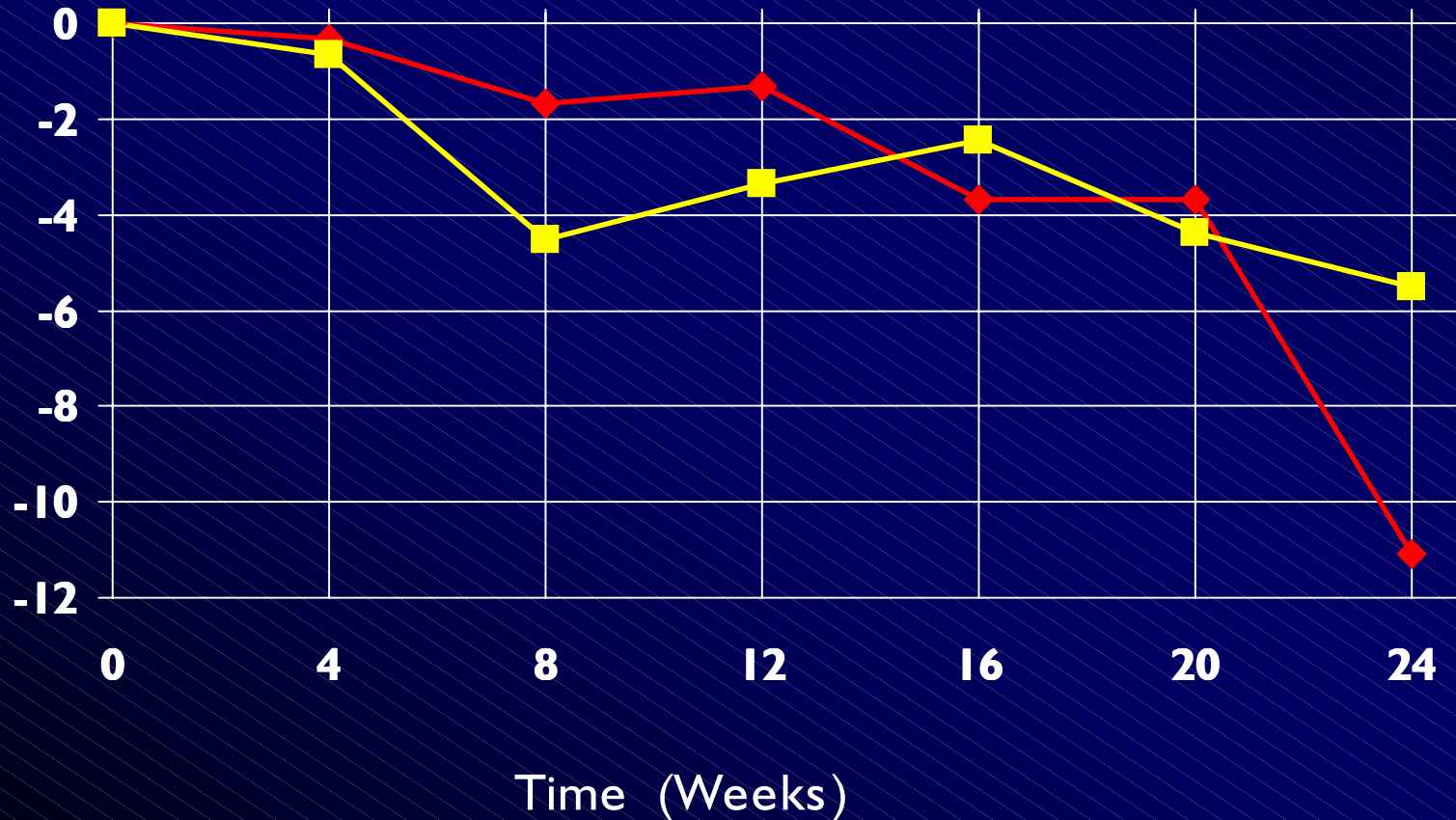
General Health Perception

Change from Baseline Stratified by Karnofsky at Baseline



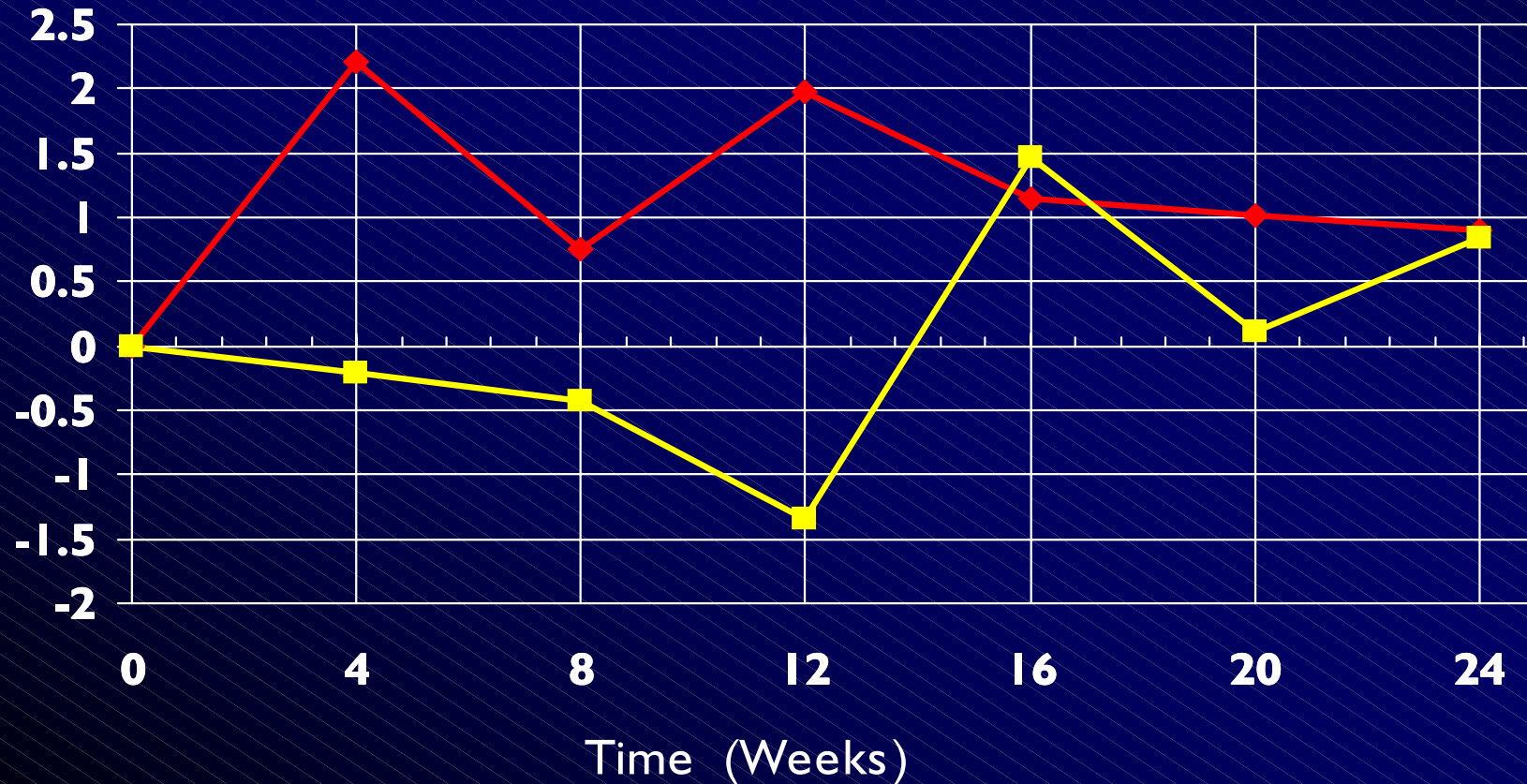
Quality of Life Scales

Pain Scale: Change in baseline by Drug



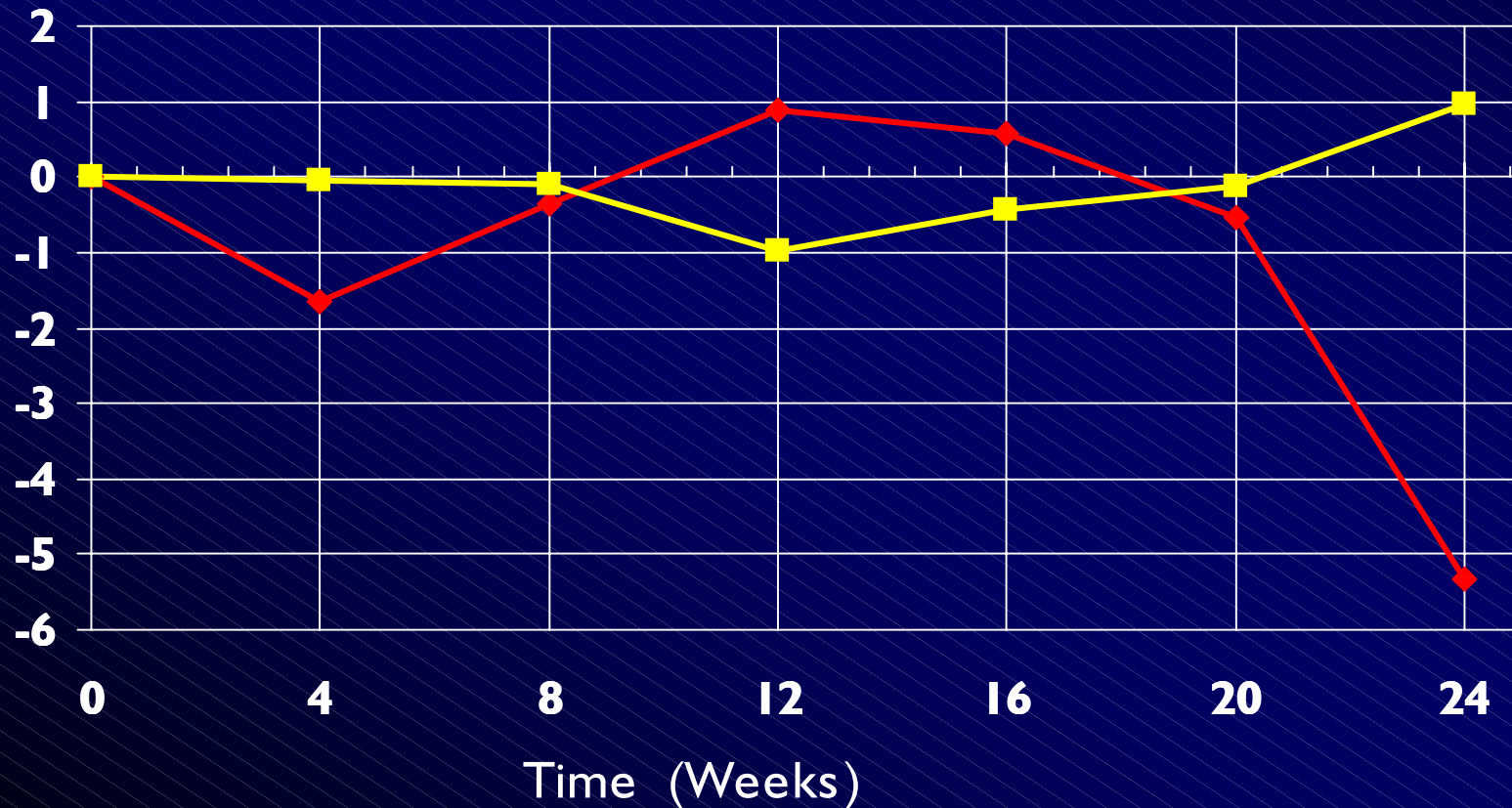
Quality of Life Scales

Mental Health Index: Change in baseline by Drug



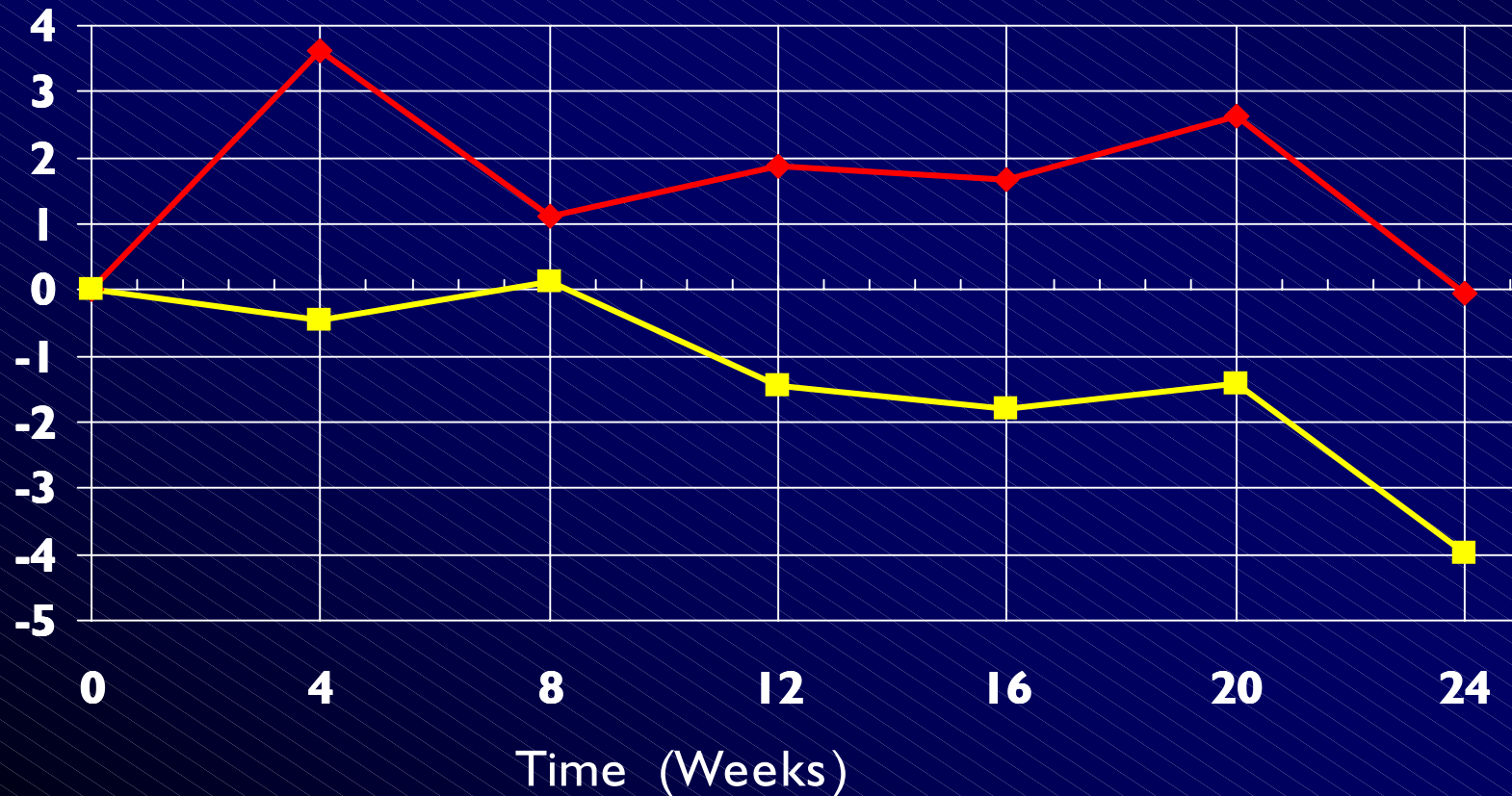
Quality of Life Scales

Physical Function Index: Change in baseline by Drug



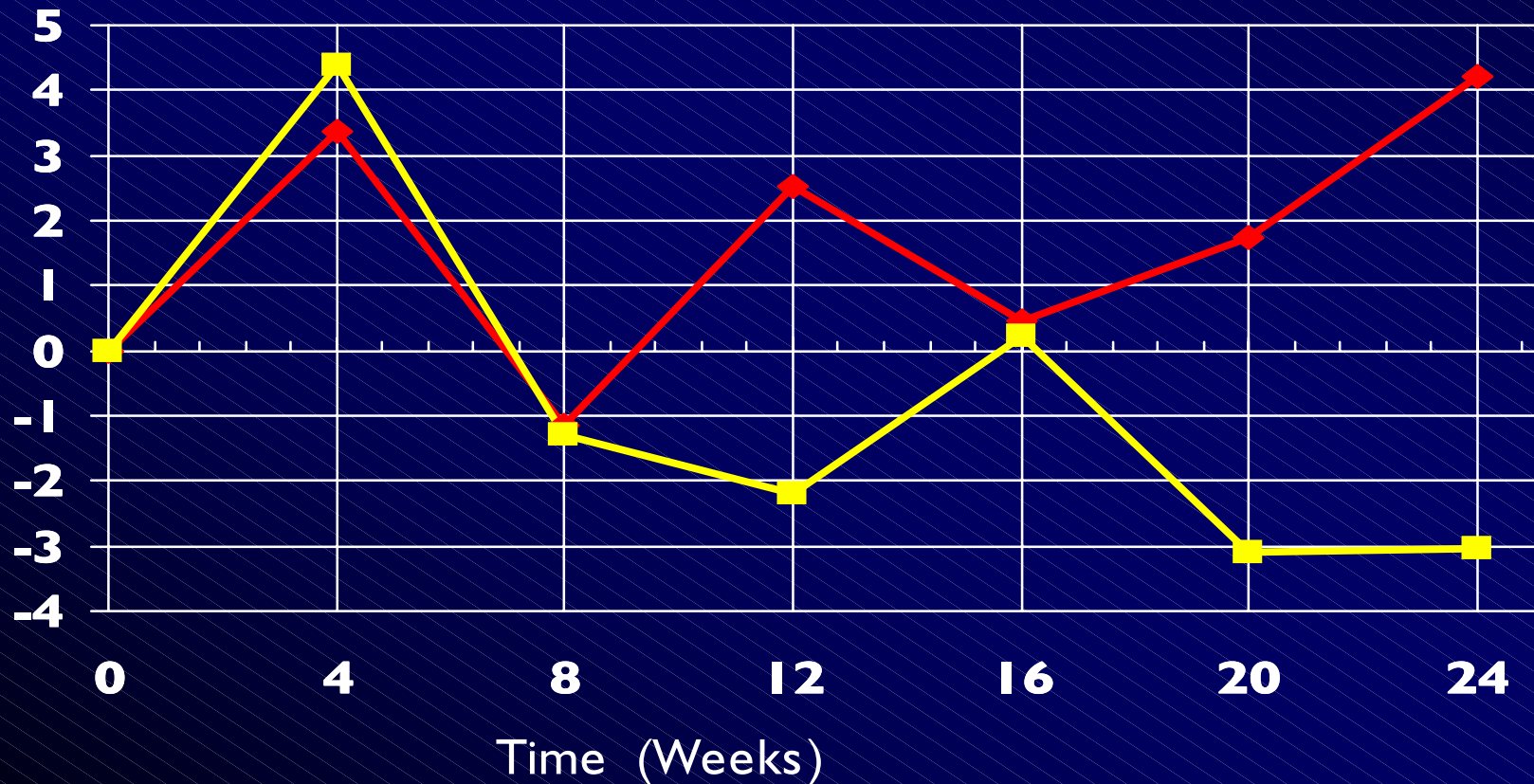
Quality of Life Scales

Vitality: Change in baseline by Drug



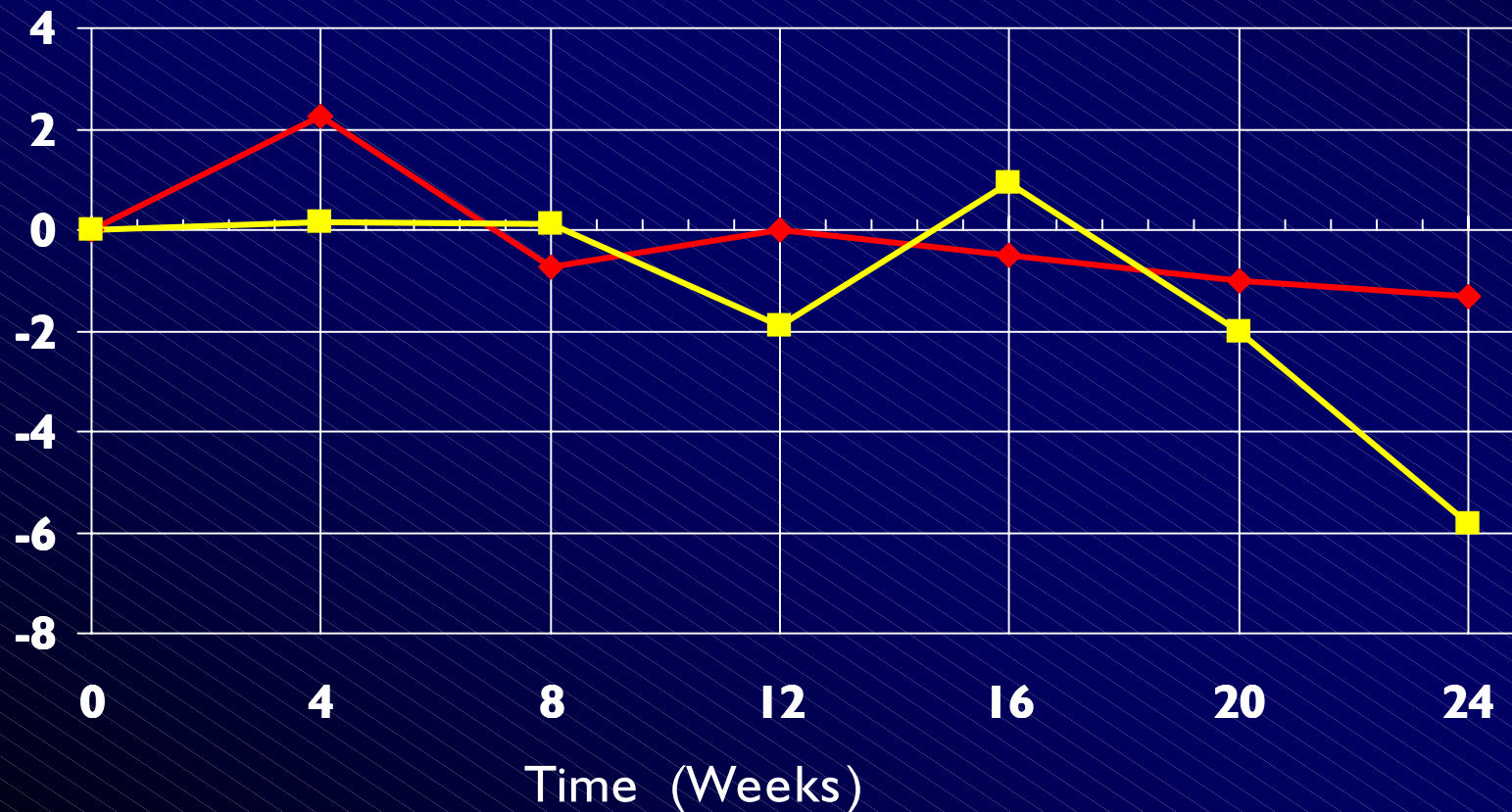
Quality of Life Scales

Role Emotional: Change in baseline by Drug



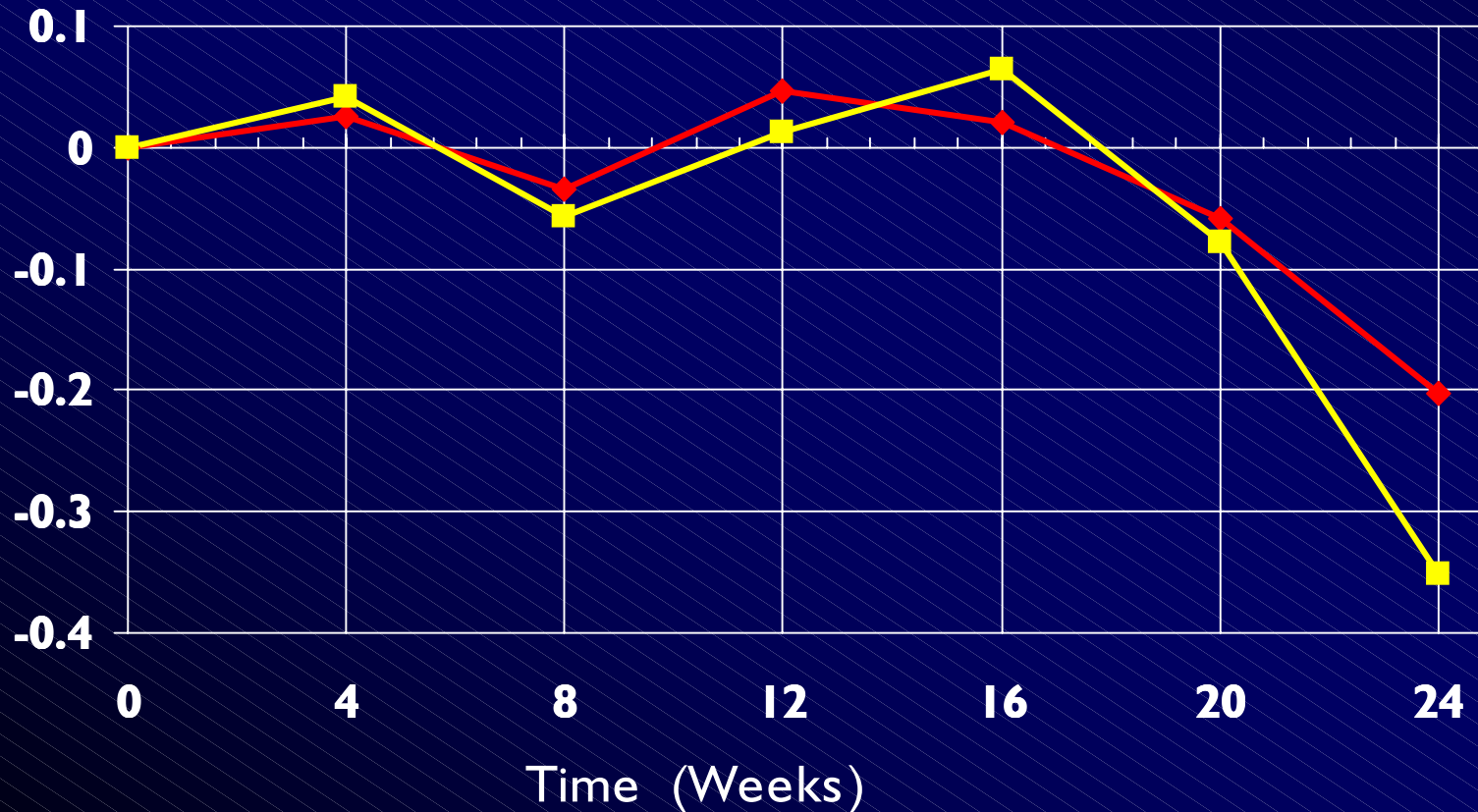
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Social Functioning: Change in baseline by Drug



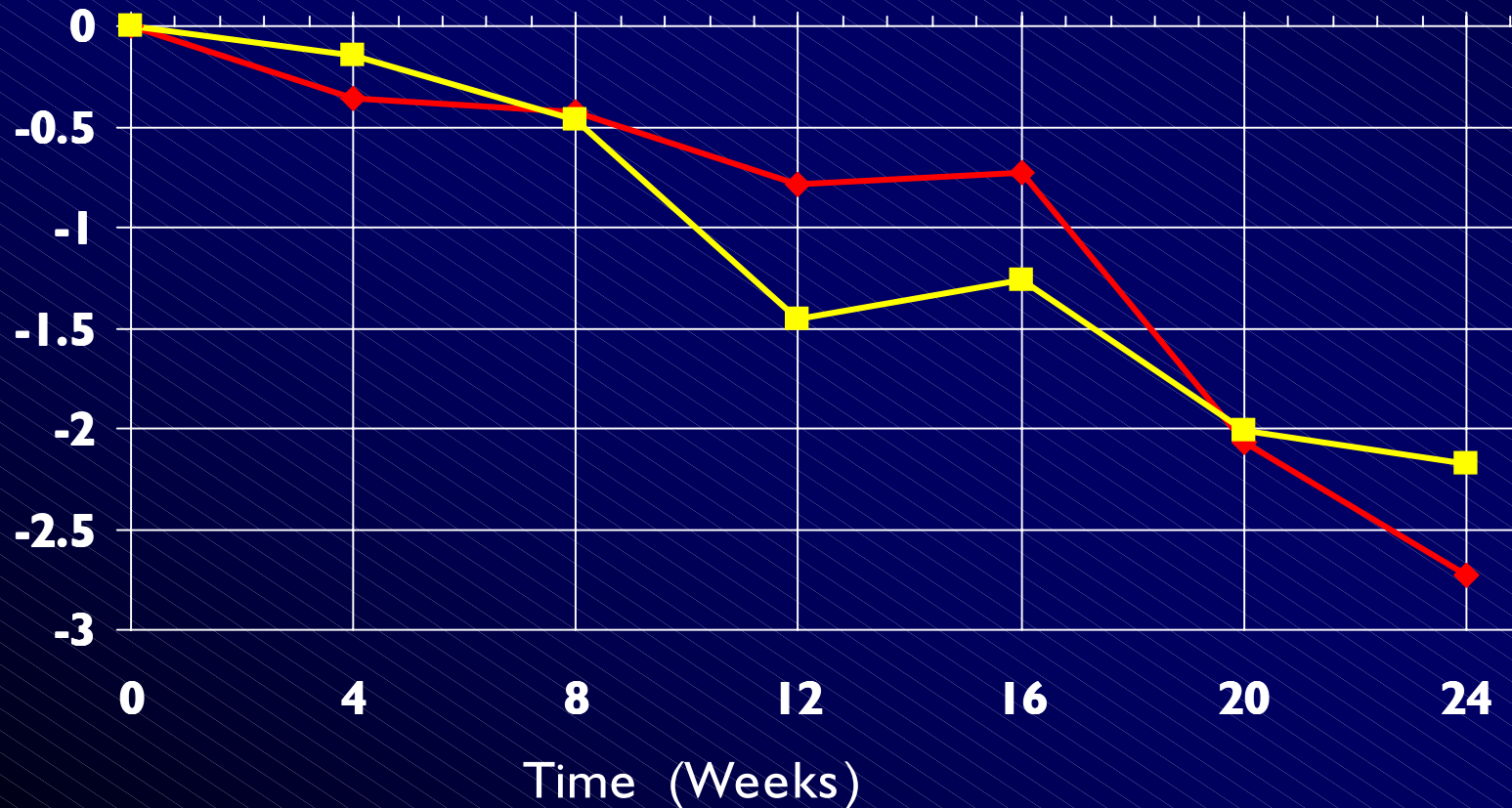
Quality of Life Scales

Spitzer: Change in baseline by Drug



Quality of Life Scales

Karnofsky: Change in baseline by Drug



Clinical Study Results

New Drug compared to Continued AZT

- ▶ CD4 counts were about 40 cells higher in the new drug group over the first 24 weeks of the study
- ▶ Other than study discontinuation for adverse reactions there were few clinical differences between the two study groups
- ▶ With 18 month follow-up there was a trend for a survival advantage and fewer hospitalizations for the new drug group

Quality of Life

Bio-Psycho-Social Model

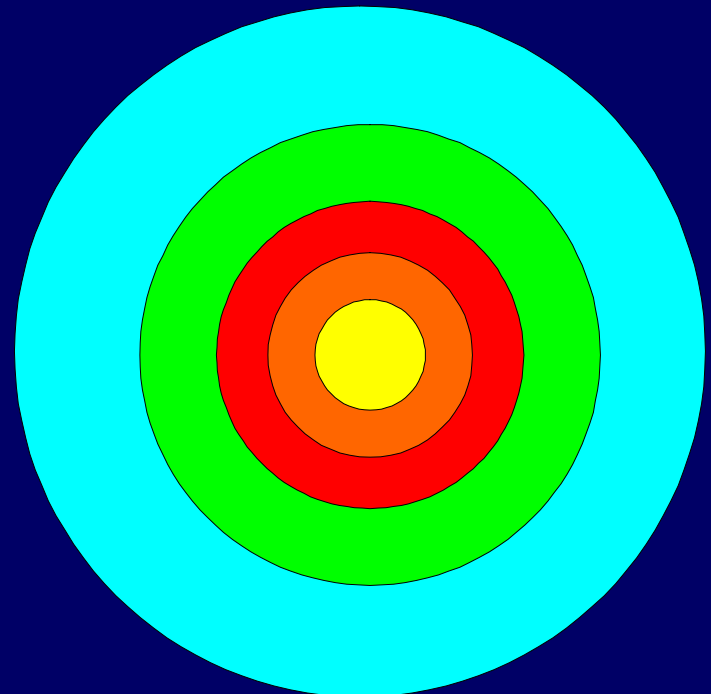
Organelle

Cell

Organ

Person

Family / Society



George Engle

Quality of Life

Bio-Psycho-Social Model

Organelle

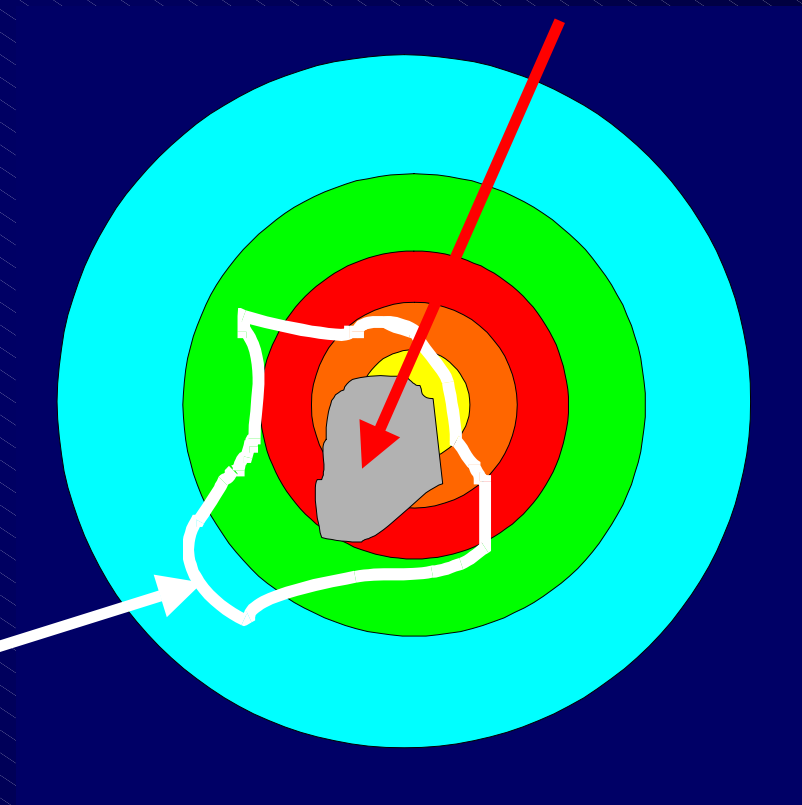
Cell

Organ

Person

Family / Society

Therapy Effect



Disease Effect

Quality of Life

Concerns

▶ Global Measures may be Less Sensitive

- e.g., a drug developed to relieve edema should have a larger impact on a congestive heart failure symptoms than on a QOL measure that edema effects indirectly
- e.g., adverse experiences will be better detected directly than through their effects on QOL

Quality of Life

Concerns

▶ Lack of Standardized Instruments

- Many clinical trials have "custom" instruments that might be tailored to favor the sponsor's treatment
- Lack of interpretability by clinicians and patients
- Lack of comparative experience across trials

Quality of Life

Concerns

- ▶ Potential to integrate risks and benefits

Conceptual

- Is the integration meaningful to the patient ?
 - e.g., wearing corrective lenses and death on the same scale
 - e.g., considering social functioning and symptoms together rather than separately

Quality of Life

Concerns

► Potential to integrate risks and benefits

Temporal

- Adverse experiences mostly occur early
Clinical benefits mostly occur late
- Methods may not adequately distinguish reversible from irreversible adverse experiences
- Results may be sensitive to duration of follow-up
- Study drop out after adverse experiences is common and creates analysis problems

Quality of Life

Advantages

- ▶ Focus on illness rather than disease
 - patient centered, not laboratory based
- ▶ Potential for standardized assessment method
- ▶ Potential to assess relative impact of events
 - Traditional clinical end-points may be mixtures of events
 - The events in the mixtures do not have the same impact
- ▶ Potential to integrate risks and benefits
 - Traditional approach considers efficacy and adverse experiences separately

Quality of Life

Proposed Uses*

- ▶ A basis for choice between two agents with similar efficacy
- ▶ A tool to study compliance by learning the impact of treatment on QOL
- ▶ A method to quantify pain, distress and other subjective outcomes
- ▶ A measure of utility in cost-effectiveness studies

Quality of Life

Role in Therapeutic Development

- ▶ Primary endpoint ?
- ▶ Secondary measure to support primary finding ?
- ▶ Basis for comparative claim for equally effective drugs ?
(which implies measuring adverse experiences)
- ▶ Advertising claim ?

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