

# Predictors and correlates of adherence to combination antiretroviral therapy (cART): meta-analysis

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# Background

- Adherence to cART important predictor of treatment success
- Adherence influenced by wide range of factors (demographic-, treatment-related, condition-related, patient-related, interpersonal)
- Knowledge of predictors/correlates of adherence could:
  - Help identify patients at risk of low adherence
  - Guide targets for development of adherence enhancing interventions

# Objectives

- To review current evidence on predictors/correlates of adherence to cART.
  - (demographic, treatment-related, condition-related, patient-related, interpersonal).
- To aggregate findings into quantitative estimates (effect sizes) of their impact on adherence
- To investigate whether variation among studies in effect sizes is associated with differences in study design features.

# Search strategy

- **Database:** PubMed
- **Search terms:** predictor OR determinant OR correlate OR influencing factor AND medication adherence OR patient compliance AND HIV infection OR HAART OR antiretroviral therapy

# Inclusion criteria

- Original papers published between July 1996 – April 2012
- Adult, non-pregnant HIV infected persons prescribed cART for chronic HIV infection
- Reporting data that allow for calculating effect size between potential predictor/correlate and adherence

**Excluded:** exclusive focus on the following specific populations: drug users, prison inmates, homeless persons, and psychiatric diseases patients.

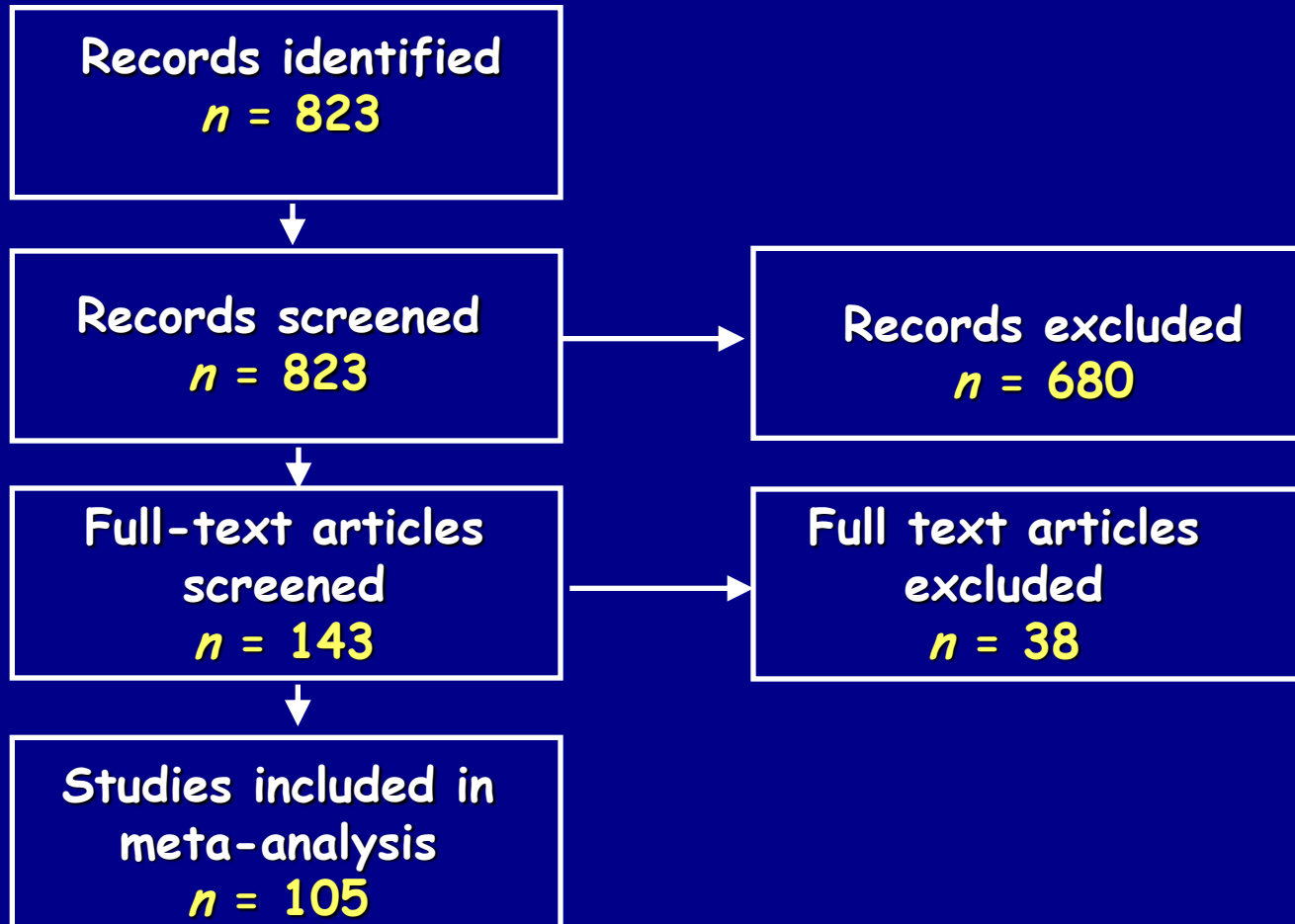
# Impact of Study design features

- Study design (longitudinal vs cross-sectional)
- Treatment status (already on cART vs start/switch)
- Adherence assessment method (self-report vs electronic monitoring device vs other)
- Human Development Index (HDI) of country where study was conducted
  - (United Nations; life expectancy, education, standard of living)

# Data analysis

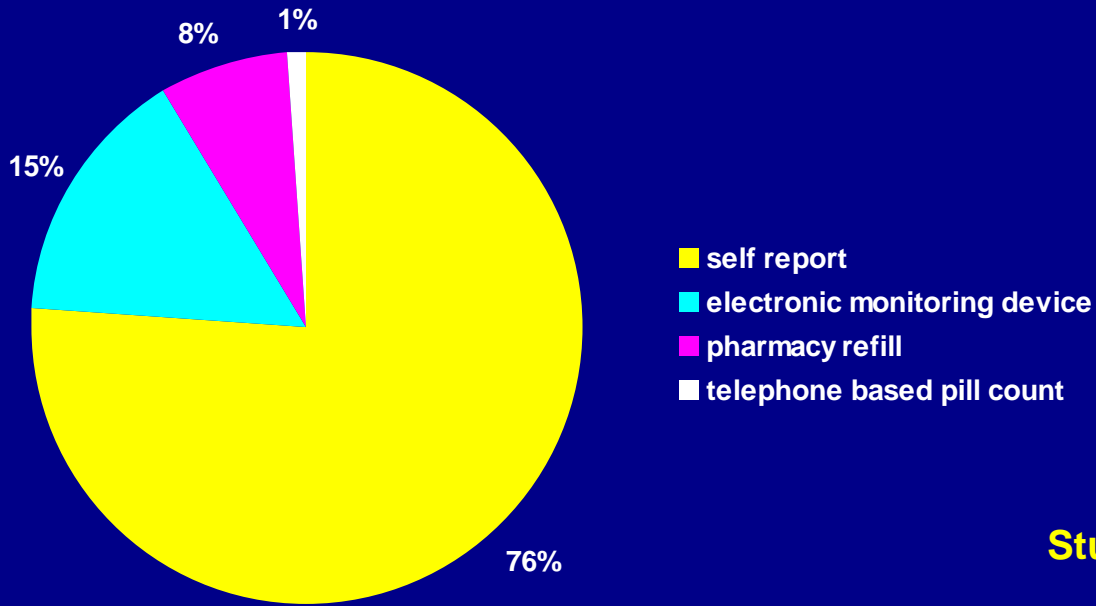
- Common effect size:  $r$ 
  - ( $\leq 0.10$  small, 0.25 medium,  $\geq 0.40$  large)
- Random effect models with inverse variance weights to pool effect sizes
- Mixed-effects meta regression
- Comprehensive Meta Analysis Version 2

# Flow diagram study selection

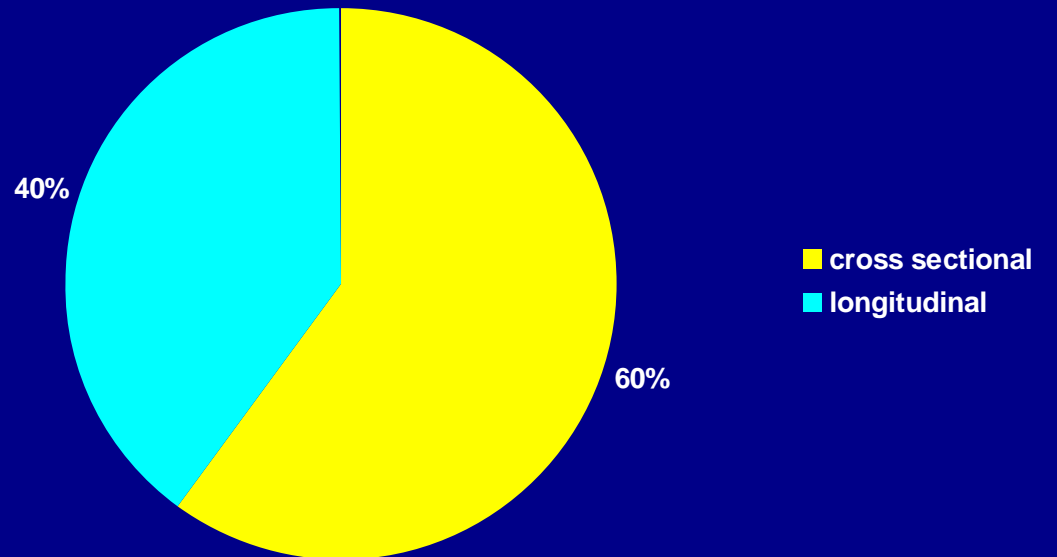




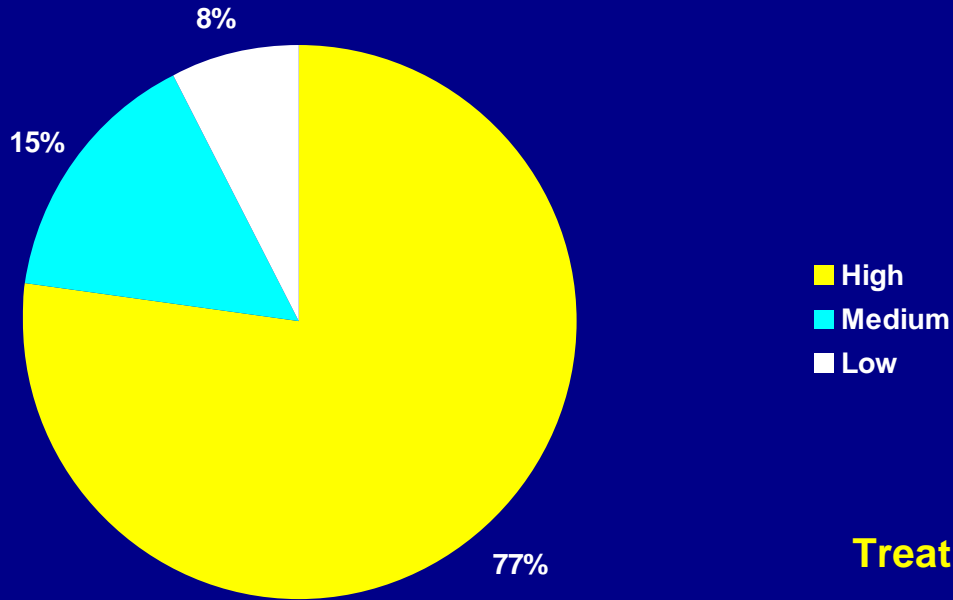
### Adherence assessment method



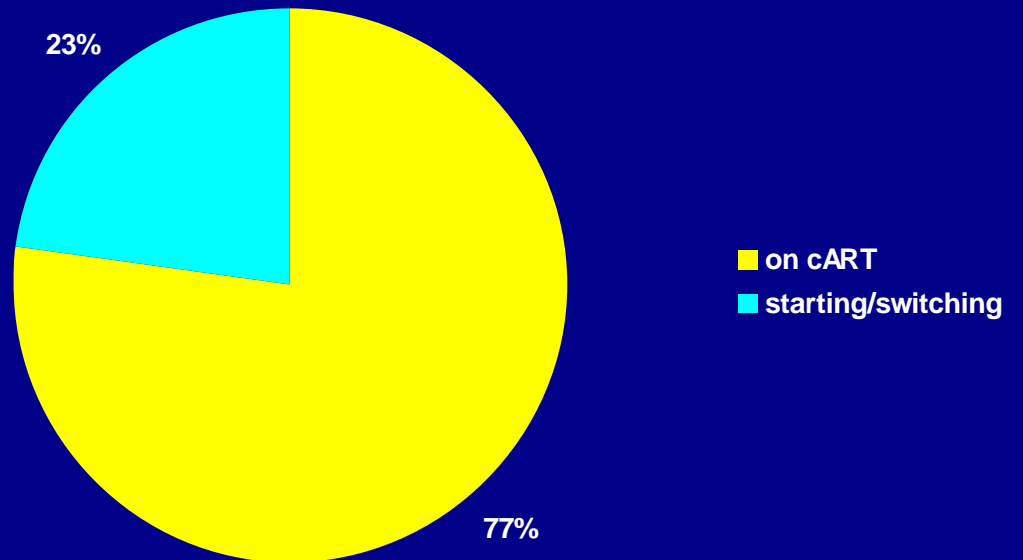
### Study design



## Human Development Index

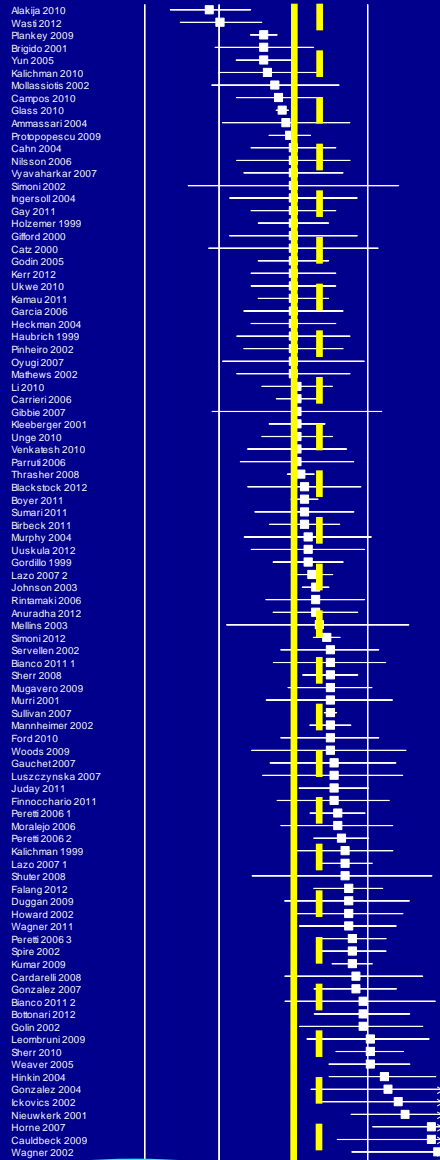


## Treatment status



# Age

Study Correlation and 95% CI



Age:

Point estimate  $r$

0.06

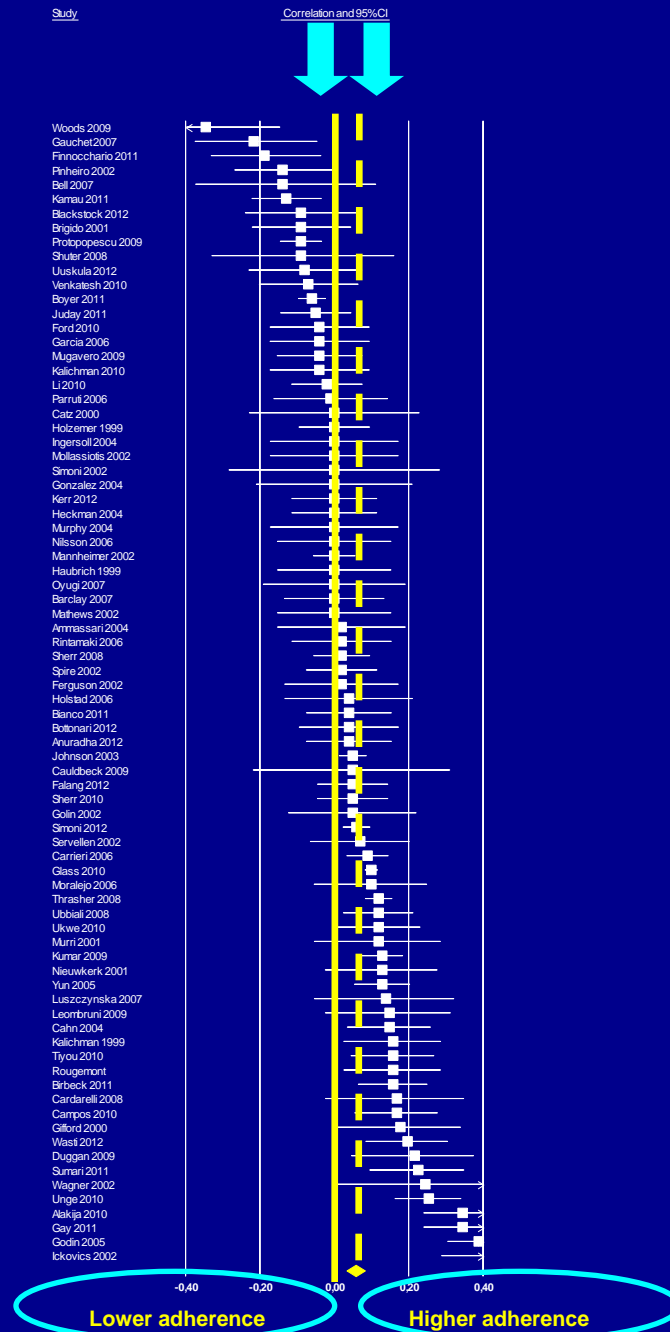
(0.04, 0.08)

$P = < 0.001$

Lower adherence

Higher adherence

# Male gender



**Male gender:**

Point estimate  $r$

0.06

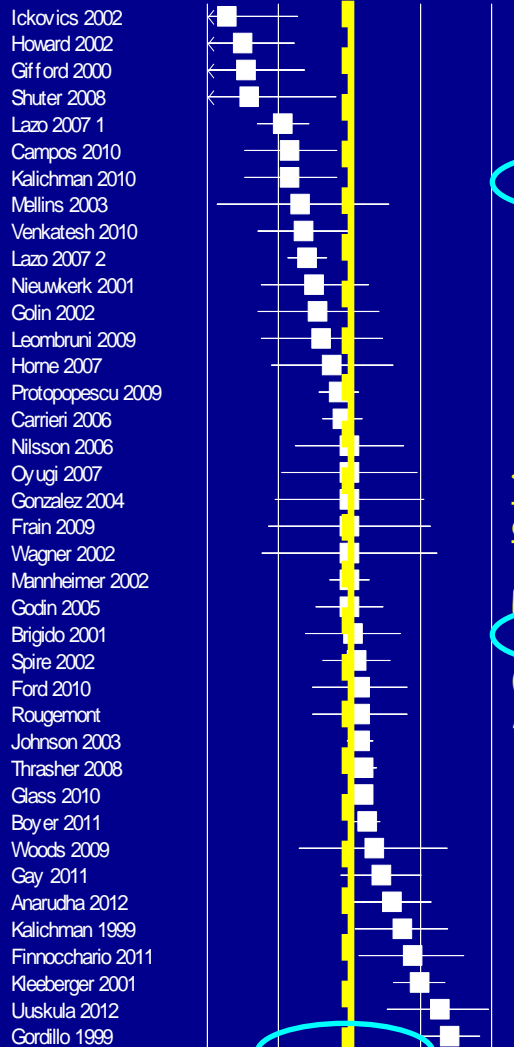
(0.03, 0.08)

$P = <0.001$

# CD4 cell count

Study

Correlation and 95% CI



## CD4 count:

Point estimate  $r$

-0.01

(-0.04, 0.02)

$P = 0.58$

## Time since HIV diagnosis:

Point estimate  $r$

-0.03

(-0.07, 0.01)

$P = 0.15$

-0,40 -0,20 0,00 0,20 0,40

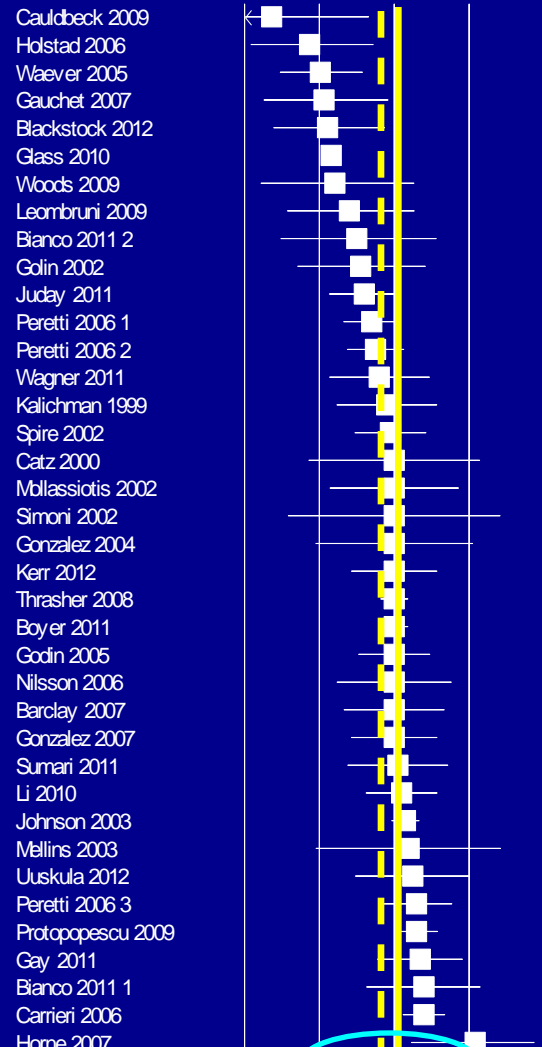
Lower adherence

Higher adherence

# Time since HIV diagnosis

Study

Correlation and 95% CI



-0,40 -0,20 0,00 0,20 0,40

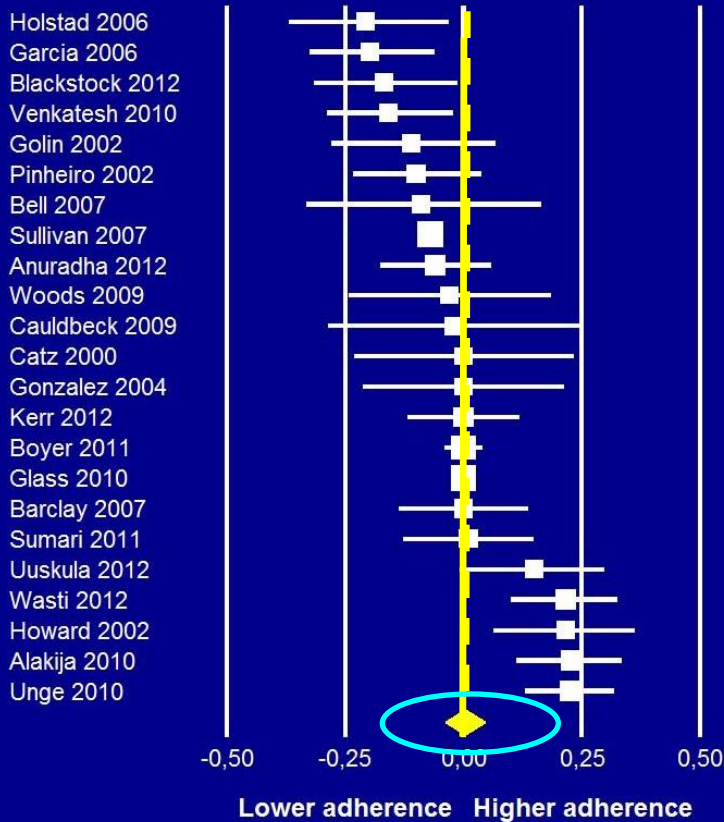
Lower adherence

Higher adherence

# Duration cART

Study

Correlation and 95% CI



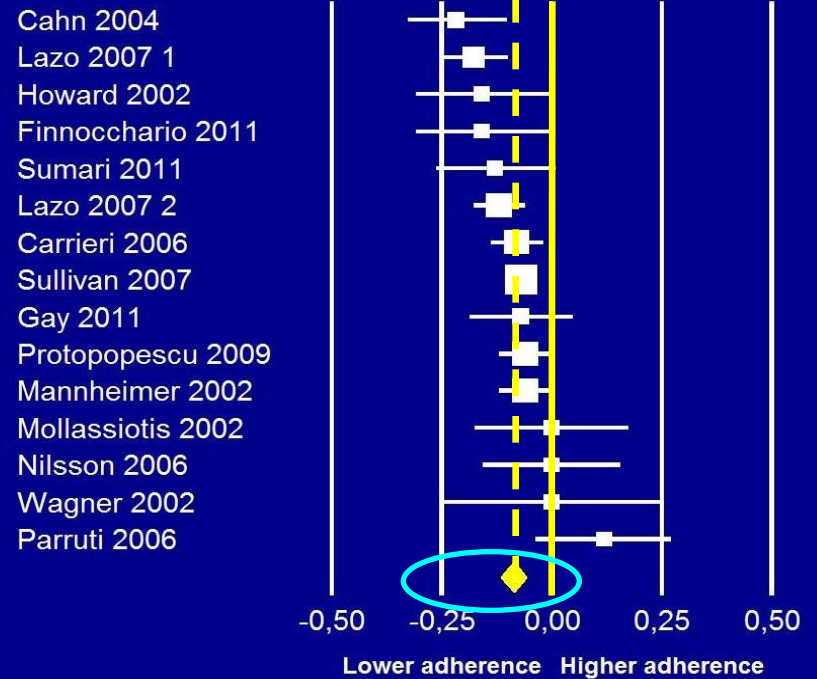
Point estimate  $r$  : -0.01 (-0.04, 0.02)

$P = 0.58$

# PI in regimen

Study

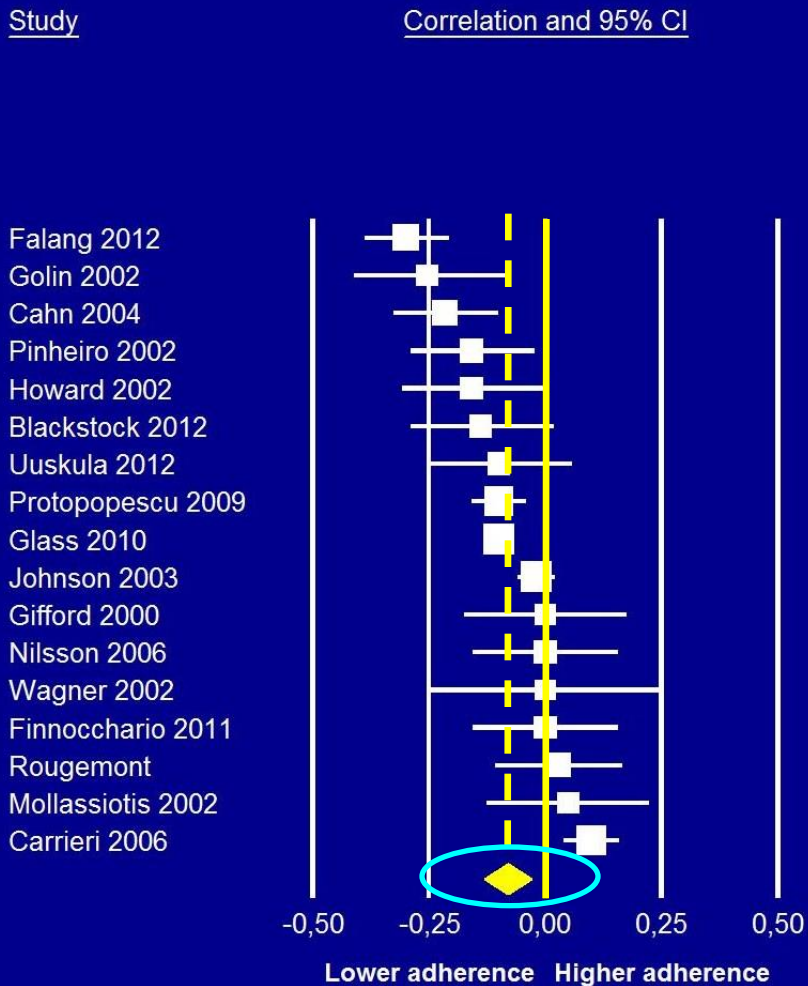
Correlation and 95% CI



Point estimate  $r$  : -0.09 (-0.12, -0.06)

$P = <0.001$

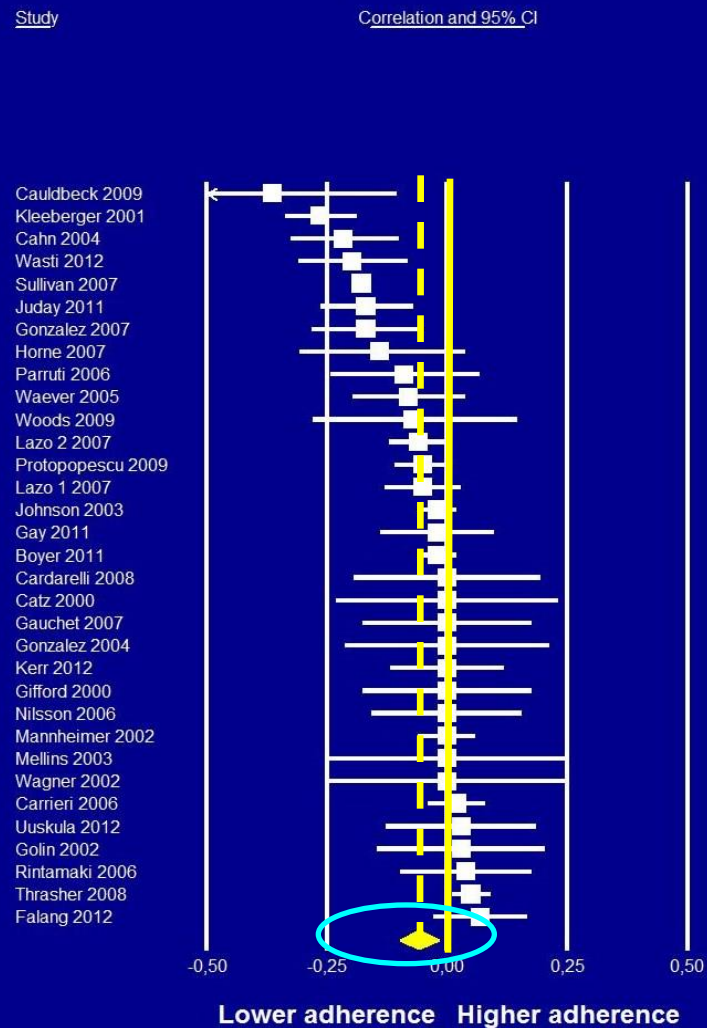
## Daily dosing frequency



Point estimate  $r : -0.08 (-0.13, -0.03)$

$P = 0.001$

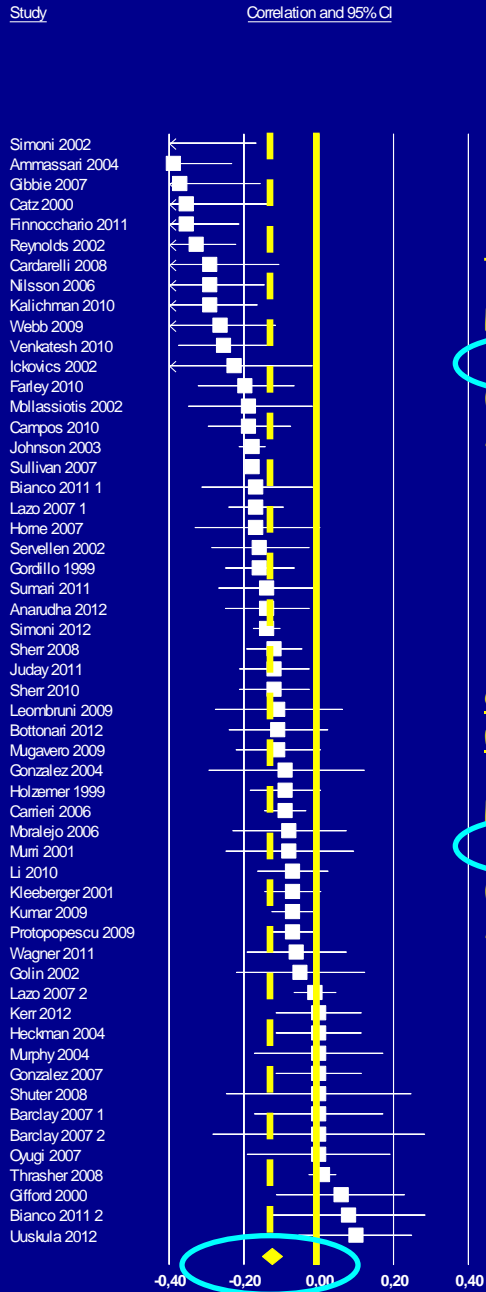
## Pill burden



Point estimate  $r : -0.06 (-0.10, -0.02)$

$P = 0.004$

# Depressive symptoms



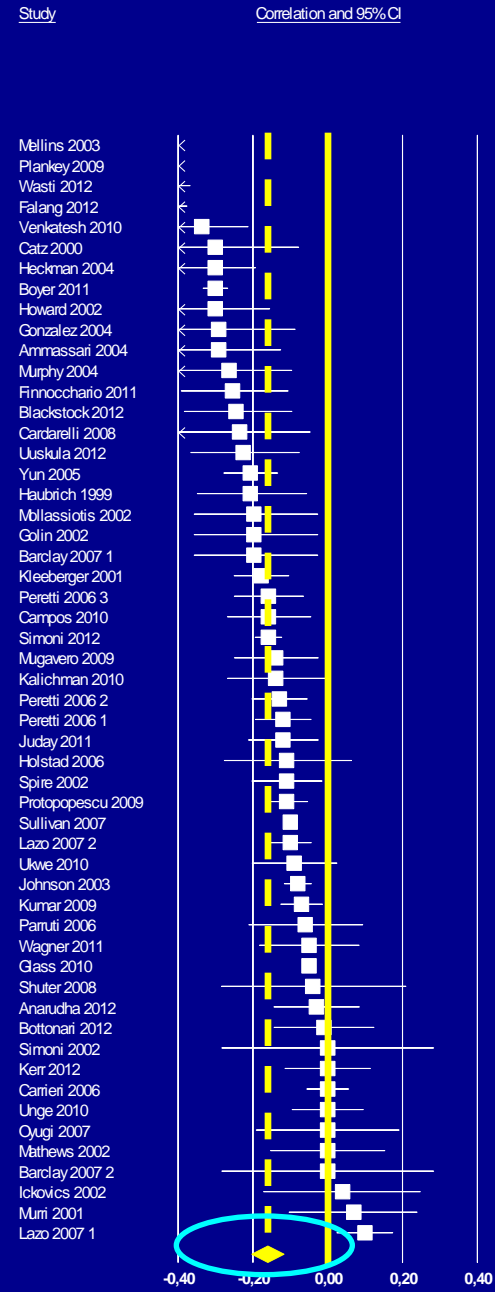
## Depressive symptoms:

Point estimate  $r$   
**-0.13**  
 (-0.15, -0.10)  
 $P = <0.001$

## Concurrent substance use:

Point estimate  $r$   
**-0.16**  
 (-0.21, -0.12)  
 $P = <0.001$

# Concurrent substance use

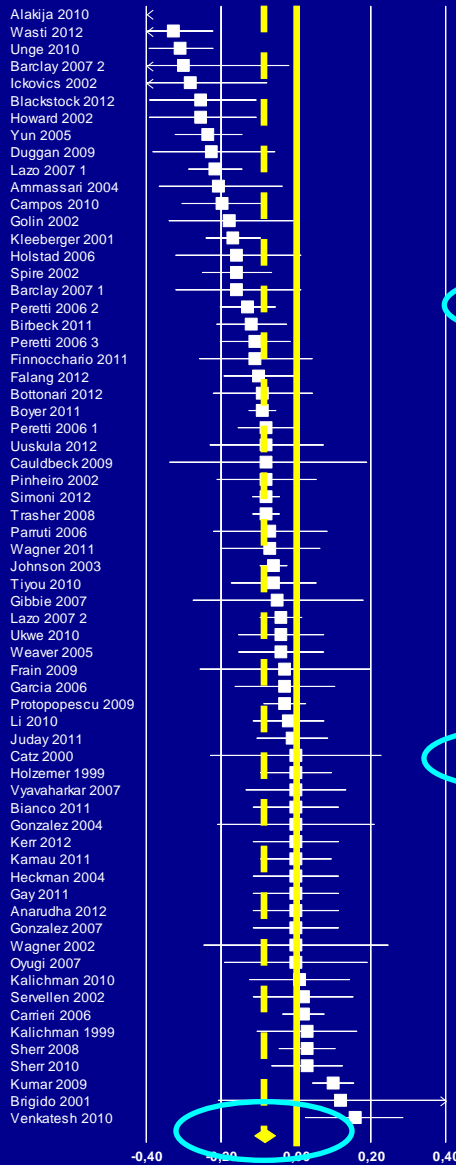




# Financial constraints

Study

Correlation and 95% CI



## Financial constraints:

Point estimate  $r$

**-0.09**  
(-0.11, -0.06)  
 $P = <0.001$

## Social support:

Point estimate  $r$

**0.10**  
(0.06, 0.14)  
 $P = <0.001$

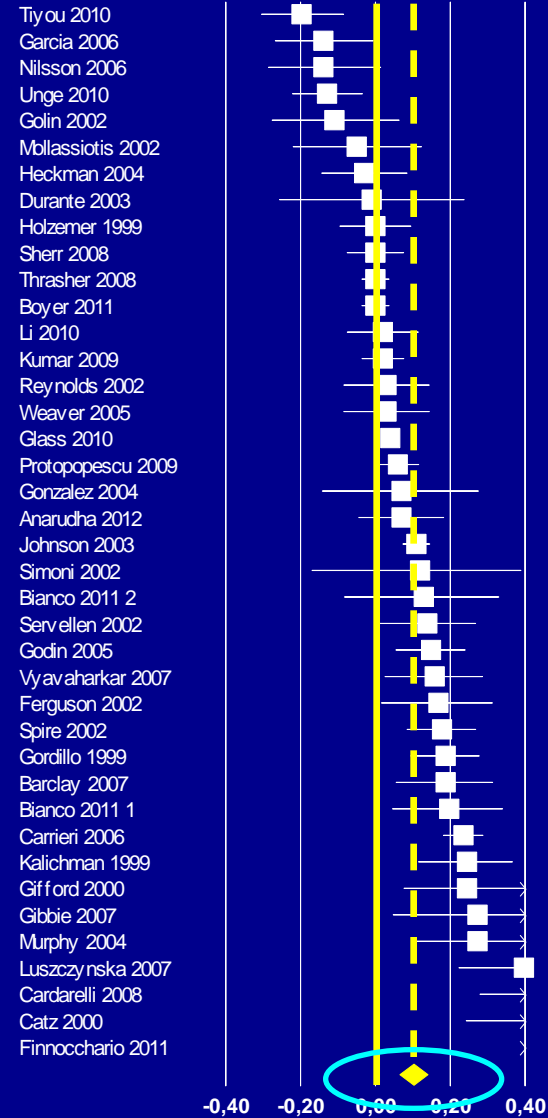
Lower adherence

Higher adherence

# Social support

Study

Correlation and 95% CI



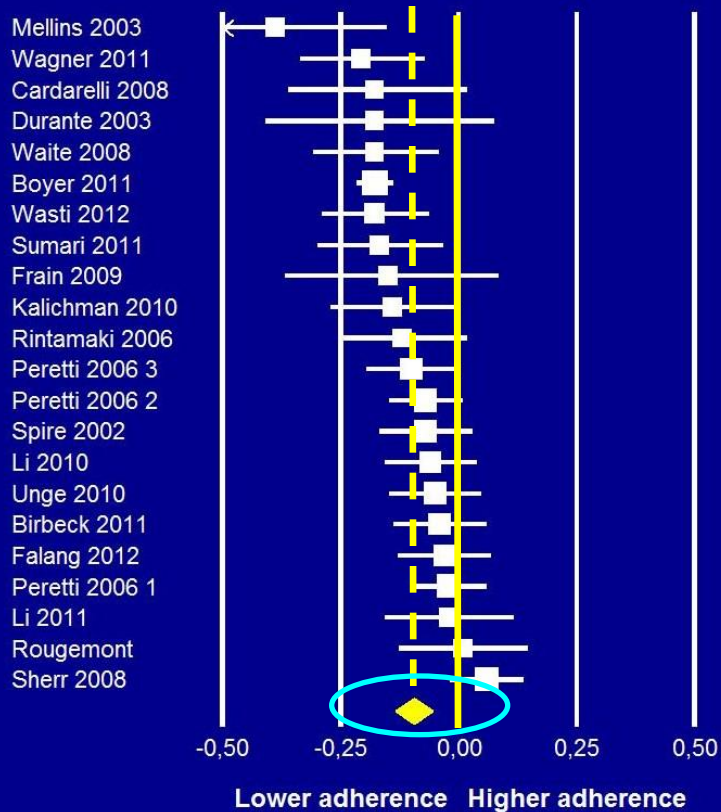
Lower adherence

Higher adherence

## HIV stigma

Study

Correlation and 95% CI



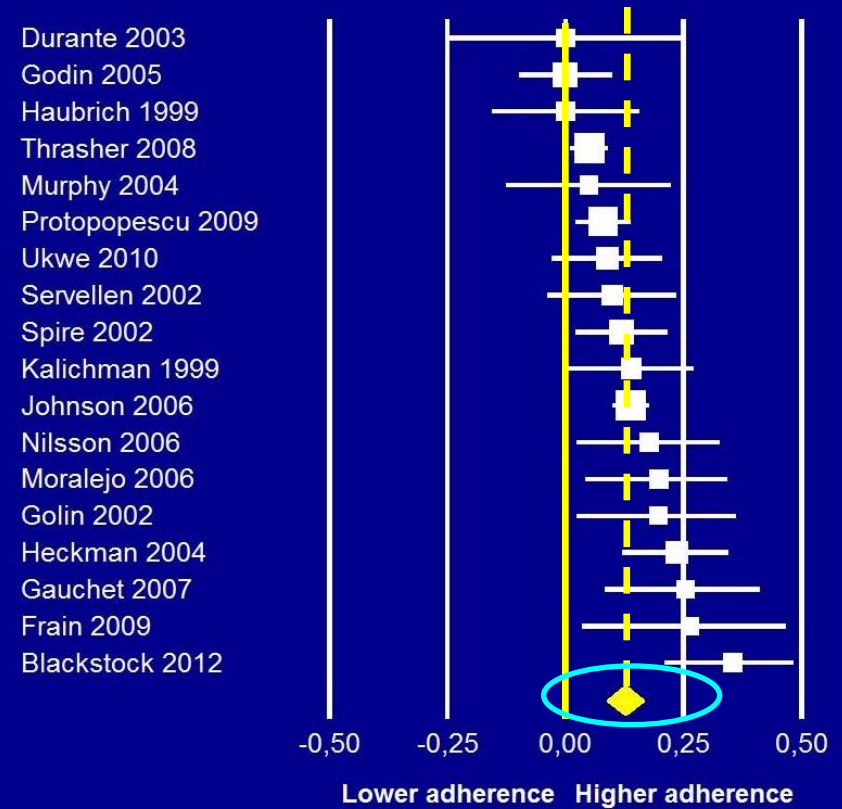
Point estimate  $r$  : -0.10 (-0.13, -0.03)

$P = <0.001$

## Trust / satisfaction health care provider

Study

Correlation and 95% CI



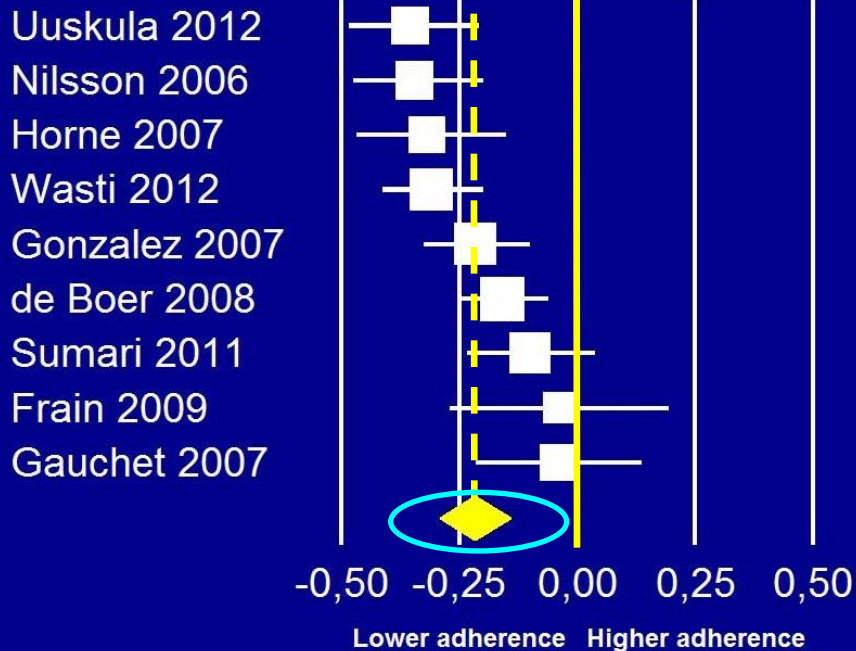
Point estimate  $r$  : 0.13 (0.09, 0.17)

$P = <0.001$

## Beliefs: concerns about cART

Study

Correlation and 95% CI



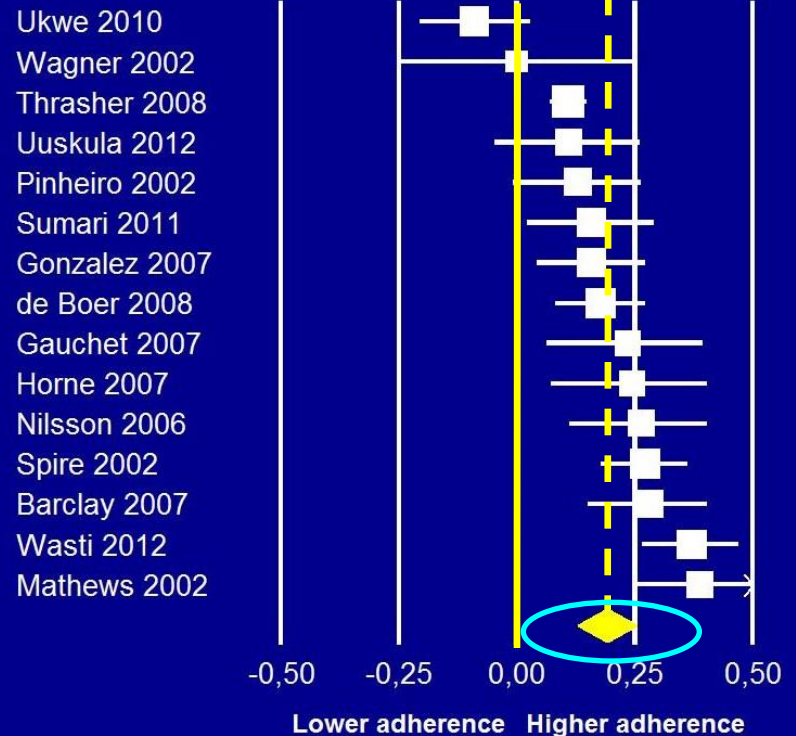
Point estimate  $r$  : -0.22 (-0.29, -0.14)

$P = <0.001$

## Beliefs: necessity /utility of cART

Study

Correlation and 95% CI

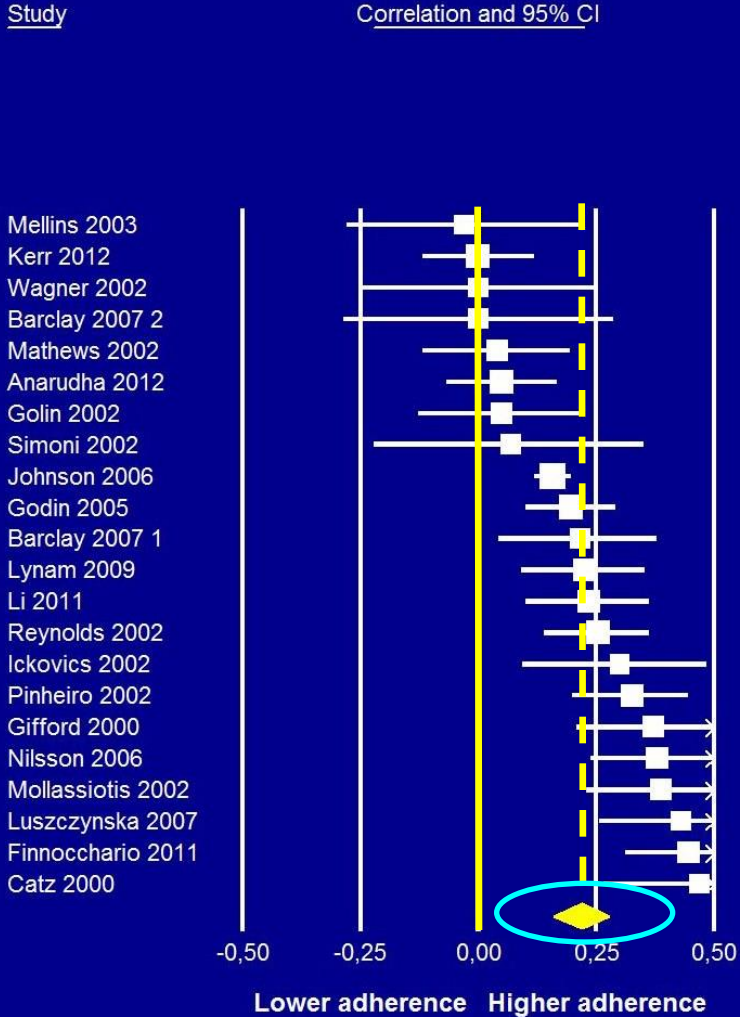


Point estimate  $r$  : 0.19 (0.13, 0.25)

$P = <0.001$

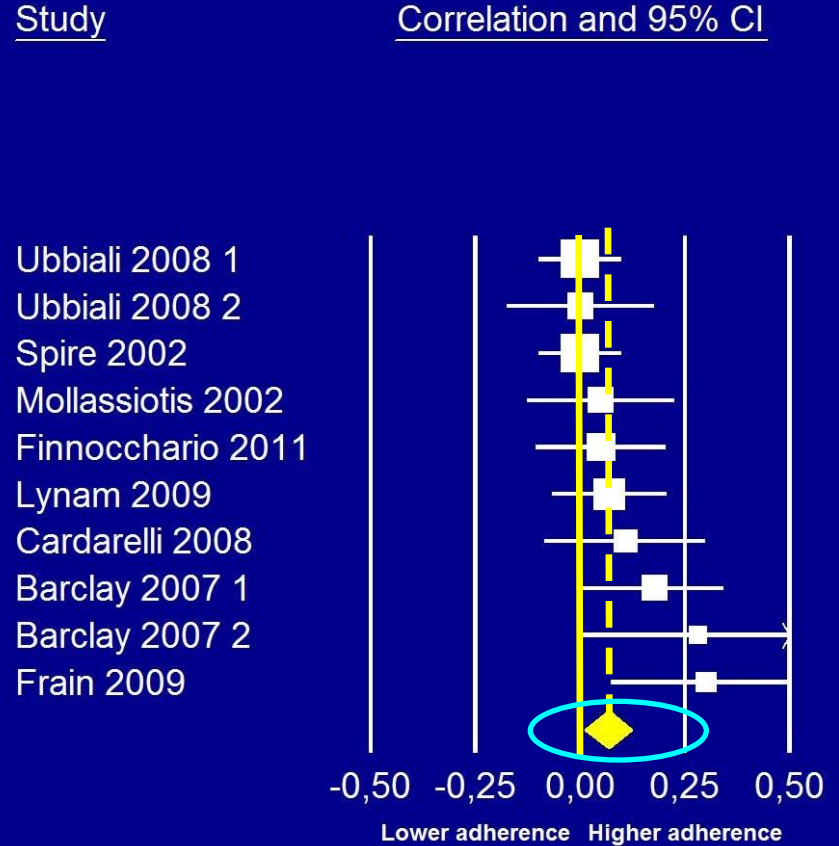
# Beliefs: adherence self-efficacy

# Internal Locus of Control



Point estimate  $r : 0.22 (0.16, 0.28)$

$P = <0.001$

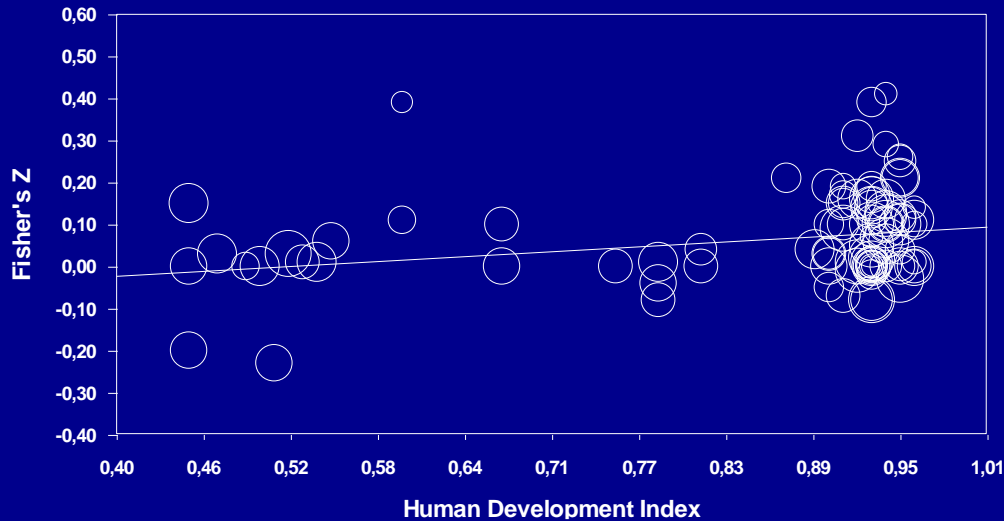


Point estimate  $r : 0.07 (0.01, 0.12)$

$P = 0.02$

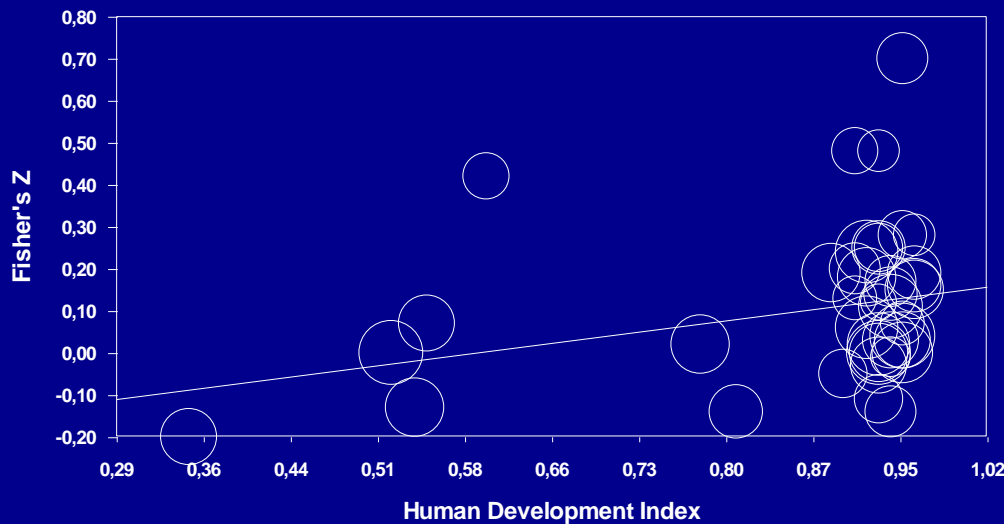
# Moderator analyses

Regression of Human Development Index on Fisher's Z



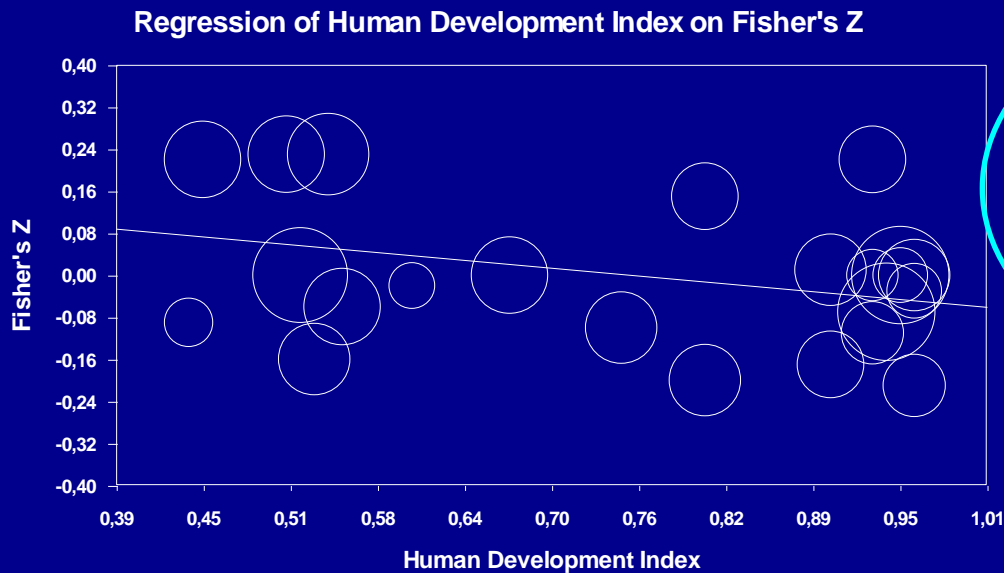
**HDI on correlation  
Age/adherence:**  
slope 0.19  
P value <0.001

Regression of Human Development Index on Fisher's Z



**HDI on correlation  
Social support/adherence:**  
slope 0.37  
P value 0.004

# Moderator analyses cont.



HDI on correlation  
Duration of cART/adherence:  
slope -0.24  
P value 0.03

Adherence assessment method on correlation Age/adherence:  
electronic monitoring device versus others methods  
 $r = 0.14$  versus  $r = 0.05$ ,  $p = <0.001$

Treatment status on correlation current substance use/adherence:  
Already on cART versus starting/switching  
 $r = -0.18$  versus  $r = -0.04$ ,  $p = 0.02$

# Conclusions

## Small effects

Age, Male gender

PI in regimen, Daily dosing frequency, Pill burden

Social support, HIV stigma

Internal Locus of control

## Small -medium sized effects

Depressive symptoms

Concurrent substance use

Trust / satisfaction health care provider

## Medium sized effects

Concerns about cART

Beliefs about necessity /utility of cART

Adherence self-efficacy

# Conclusions

## Adherence enhancing interventions:

- Adherence self-efficacy and patients' beliefs about cART (concerns & necessity).
- Trust/satisfaction with health care provider.
- Simplification of cART regimens expected to have smaller albeit significant effects.
- Findings support current emphasis on reducing depressive symptoms and concurrent substance use.