

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.

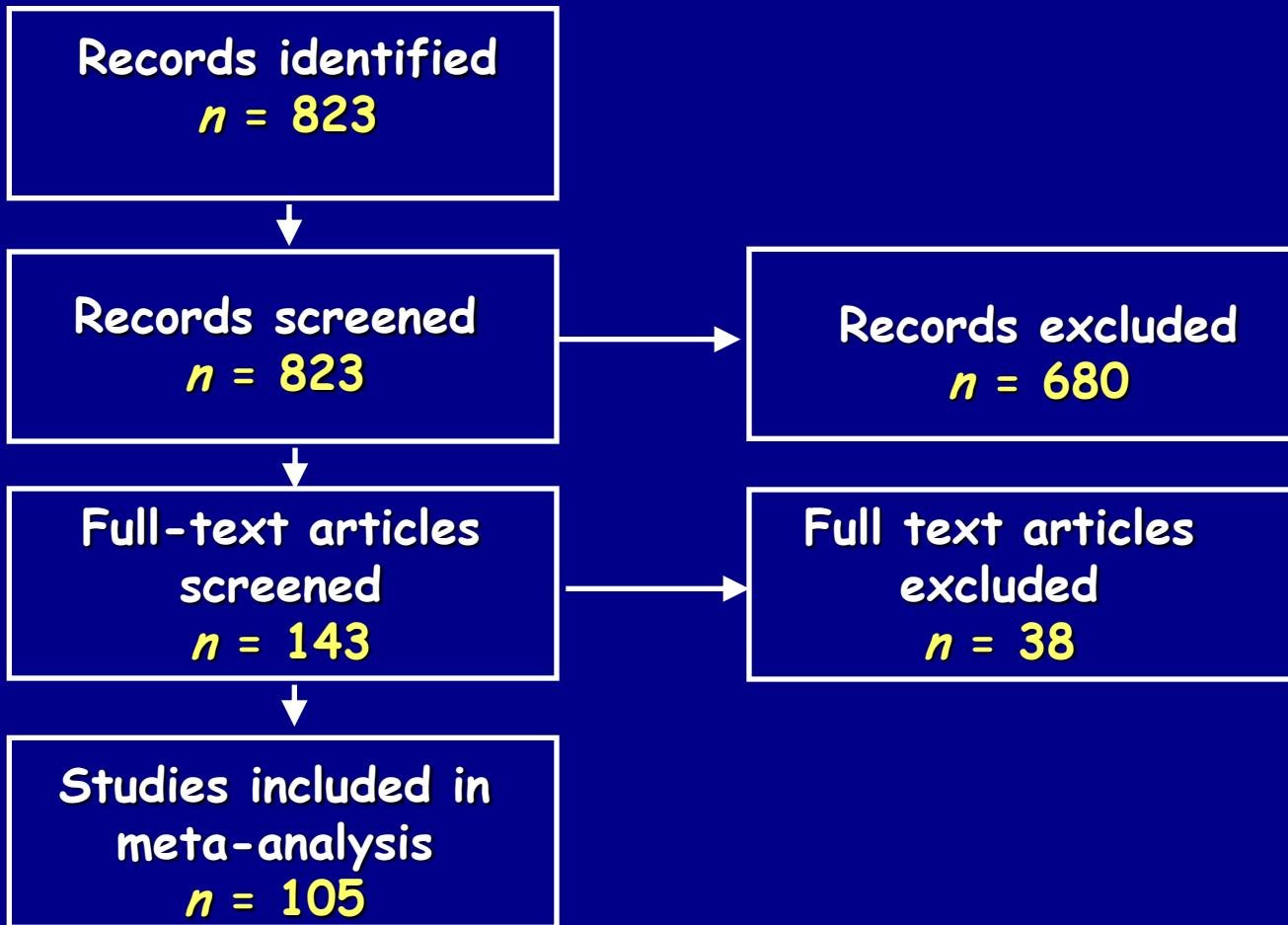
Impact of Study design features

- 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)

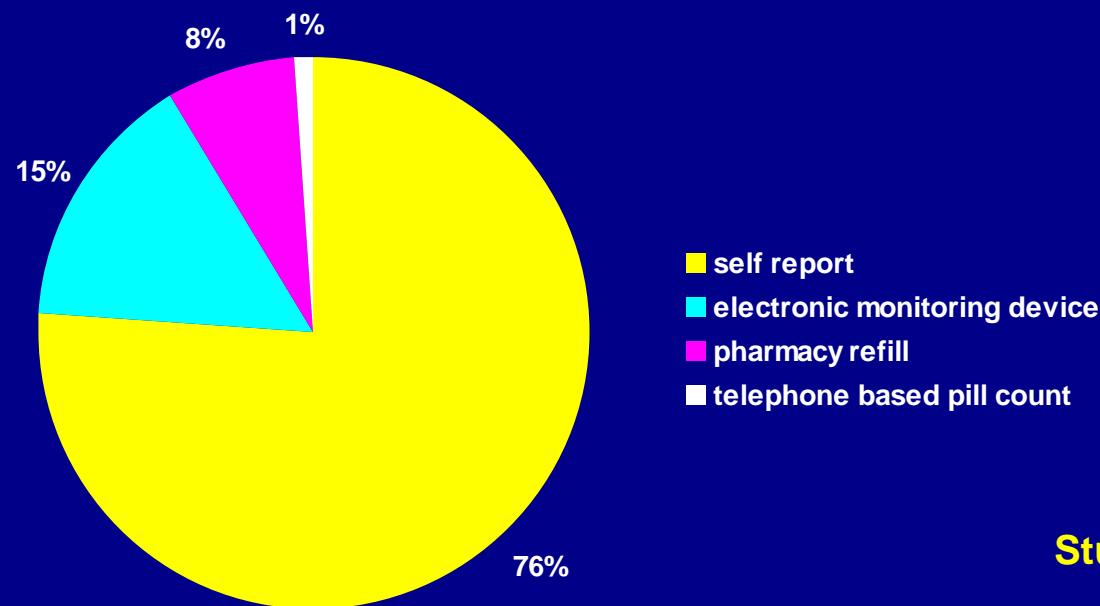
Data analysis

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

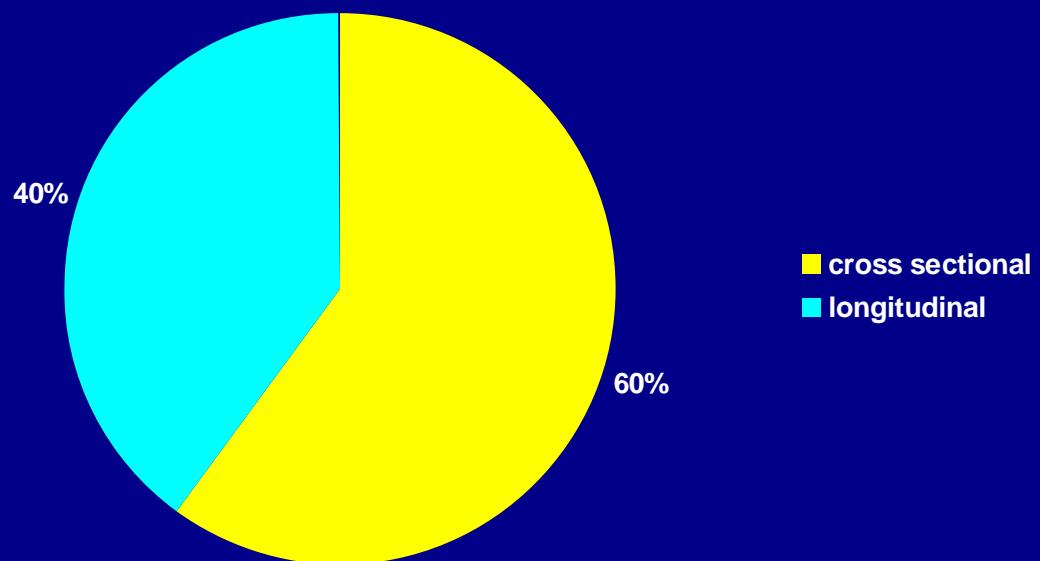
Flow diagram study selection



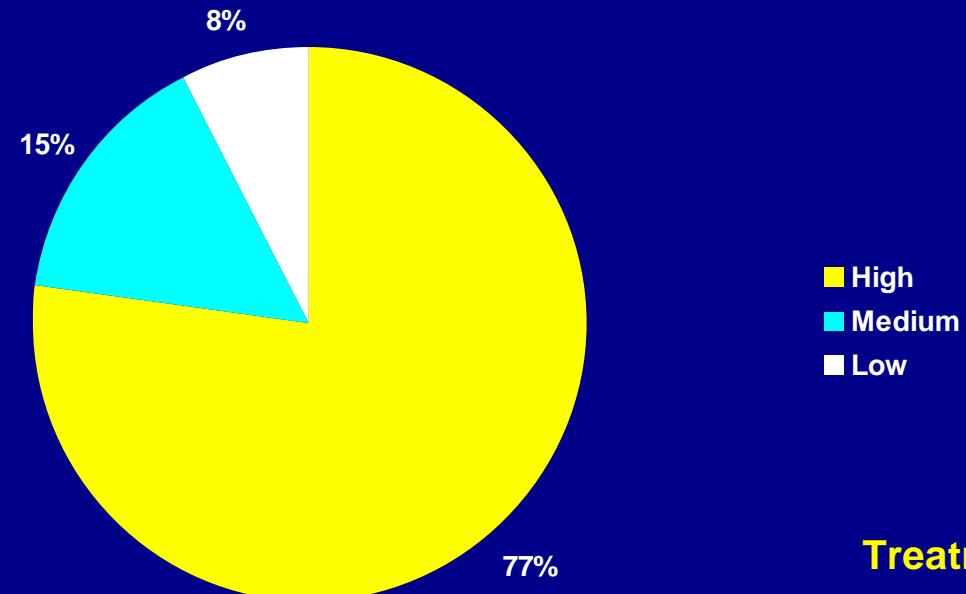
Adherence assessment method



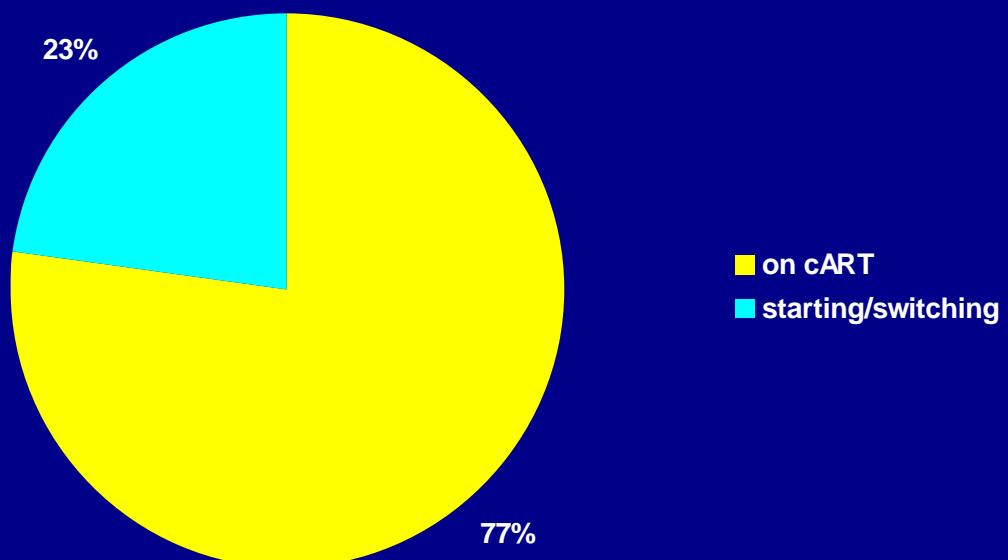
Study design



Human Development Index



Treatment status

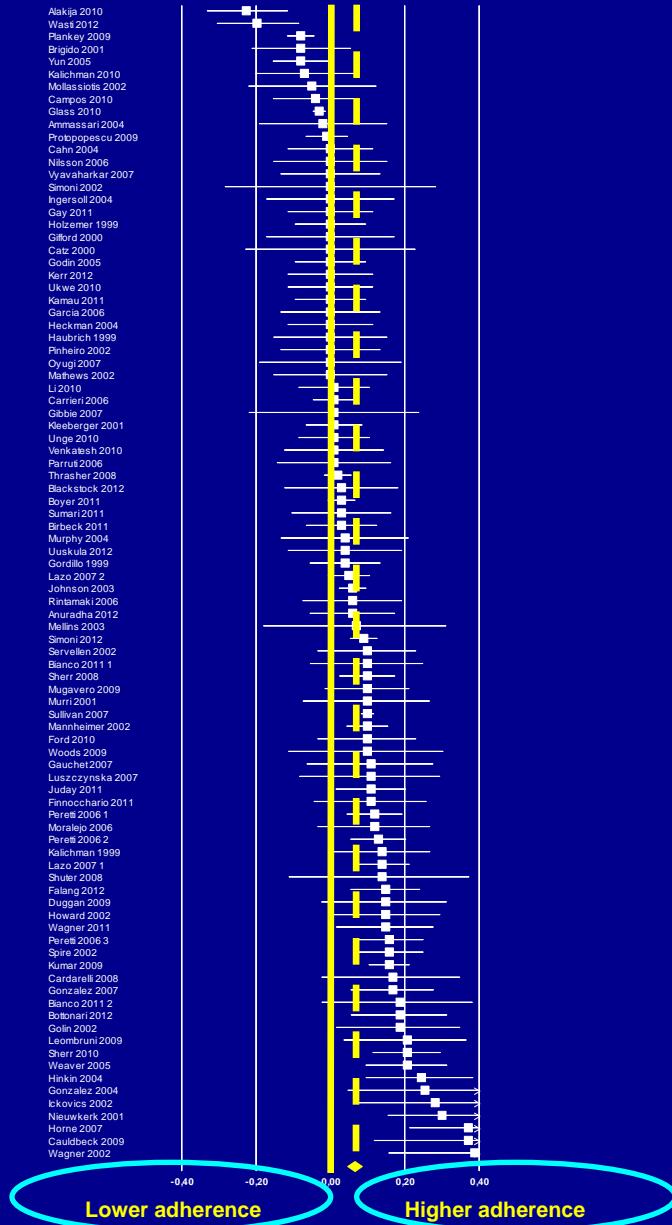


Age

Study

Correlation and 95%CI

Alakija 2010
Wasz 2012
Pankay 2009
Brigido 2001
Yun 2005
Kalechman 2010
Molassas 2002
Garcia 2010
Glass 2010
Ammassari 2004
Popopescu 2009
Cain 2004
Nilsson 2006
Wyawaharkar 2007
Simo 2002
Ingersoll 2004
Gaynor 2011
Holzemer 1999
Gifford 2000
Cato 2000
Goon 2005
Kerr 2012
Ukwe 2010
Kamau 2011
Garnett 2006
Heckman 2004
Haubrich 1999
Pinheiro 2002
Ovugui 2007
Matthews 2002
Li 2010
Carrión 2006
Gibbie 2007
Keller 2001
Ung 2010
Venkatesh 2010
Parr 2006
Thrasher 2008
Blackstock 2012
Boyer 2011
Sumari 2011
Brueck 2011
Mirelles 2004
Ujukata 2012
Gordillo 1999
Lazo 2007 2
Johnson 2003
Rintamaki 2006
Anuradha 2012
Mellins 2003
Simo 2012
Simo 2002
Bastico 2011 1
Sher 2008
Musavero 2009
Muri 2001
Sullivan 2007
Mannheimer 2002
Ford 2010
Woods 2009
Gifford 2007
Luz 2007
Judy 2011
Finnocchiaro 2011
Peres 2006 1
Moralejo 2006
Peres 2006 2
Kalechman 1999
Lazo 2007 1
Shrivastava 2008
Palang 2012
Dugan 2009
Howard 2002
Wagner 2011
Peres 2006 3
Spira 2002
Kumar 2009
Cardarelli 2008
Gordon 2007
Bastico 2011 2
Botonari 2012
Golin 2002
Leonbruni 2009
Sher 2010
Weaver 2005
Hinkin 2004
Gonzalez 2004
Ickowicz 2002
Nisarukhan 2001
Horne 2007
Cauldbeck 2009
Wagner 2002

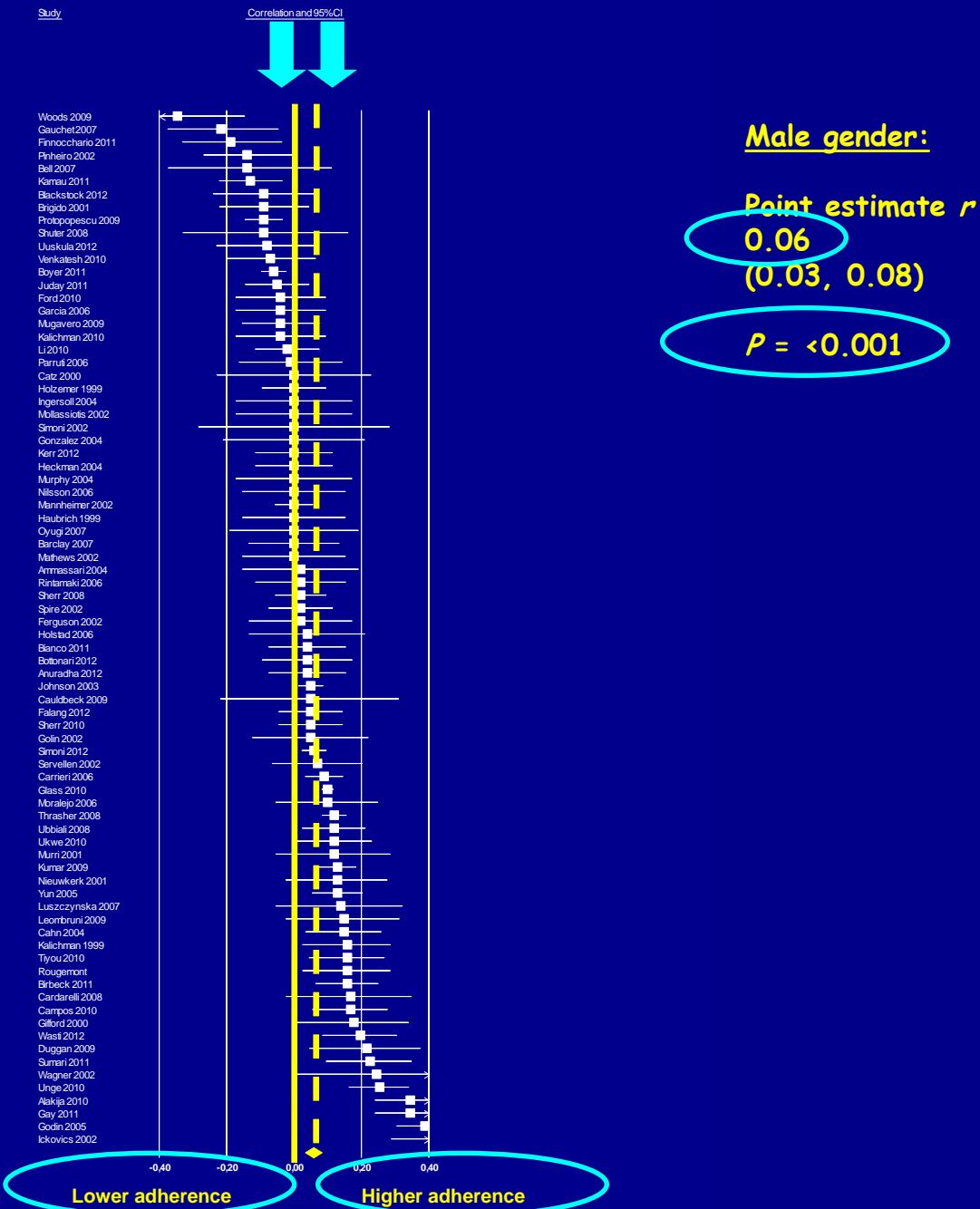


Age:

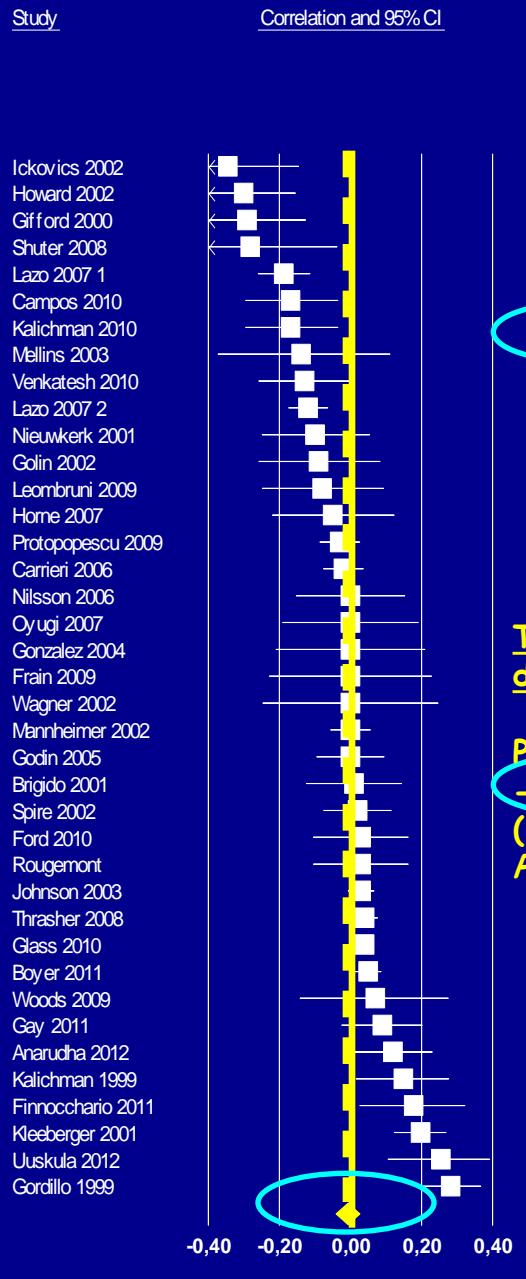
Point estimate r
0.06
(0.04, 0.08)

$P = <0.001$

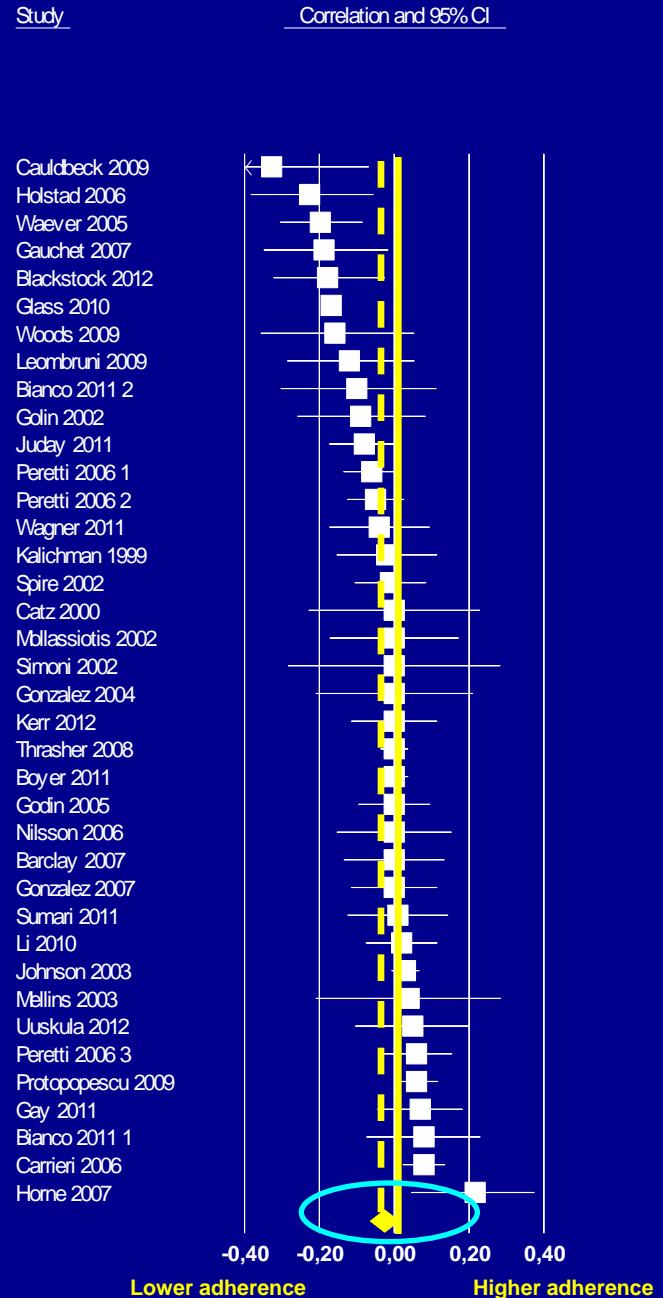
Male gender



CD4 cell count



Time since HIV diagnosis

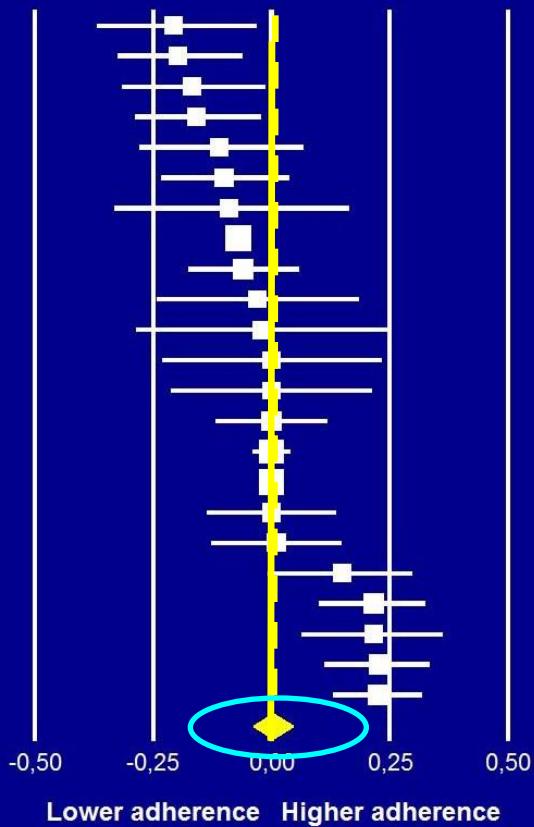


Duration cART

Study

Correlation and 95% CI

Holstad 2006
Garcia 2006
Blackstock 2012
Venkatesh 2010
Golin 2002
Pinheiro 2002
Bell 2007
Sullivan 2007
Anuradha 2012
Woods 2009
Cauldbeck 2009
Catz 2000
Gonzalez 2004
Kerr 2012
Boyer 2011
Glass 2010
Barclay 2007
Sumari 2011
Uuskula 2012
Wasti 2012
Howard 2002
Alakija 2010
Unge 2010



Point estimate $r : 0.00 (-0.04, 0.02)$

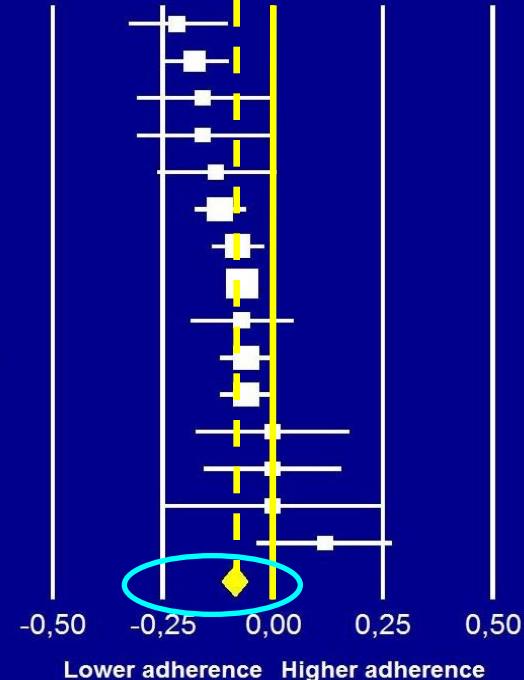
$P = 0.58$

PI in regimen

Study

Correlation and 95% CI

Cahn 2004
Lazo 2007 1
Howard 2002
Finnocchiaro 2011
Sumari 2011
Lazo 2007 2
Carrieri 2006
Sullivan 2007
Gay 2011
Protopopescu 2009
Mannheimer 2002
Mollassiotis 2002
Nilsson 2006
Wagner 2002
Parruti 2006



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

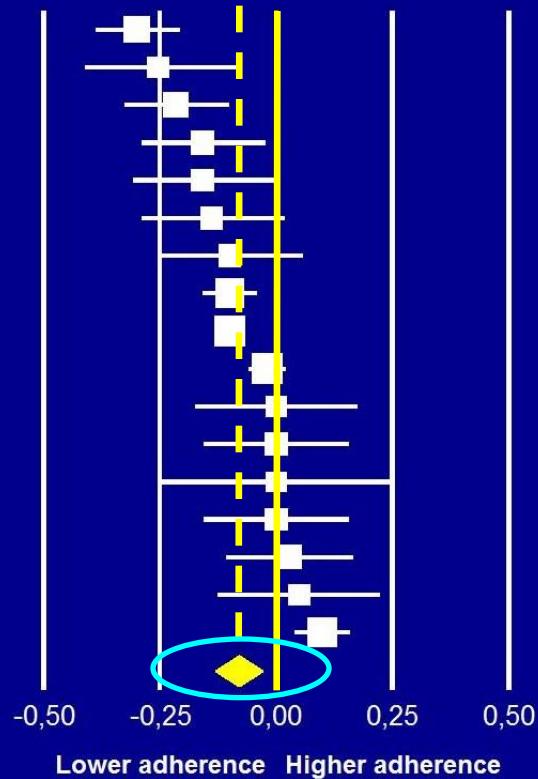
$P < 0.001$

Daily dosing frequency

Study

Correlation and 95% CI

Falang 2012
Golin 2002
Cahn 2004
Pinheiro 2002
Howard 2002
Blackstock 2012
Uuskula 2012
Protopopescu 2009
Glass 2010
Johnson 2003
Gifford 2000
Nilsson 2006
Wagner 2002
Finnocchiaro 2011
Rougemont
Mollasiotis 2002
Carrieri 2006



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

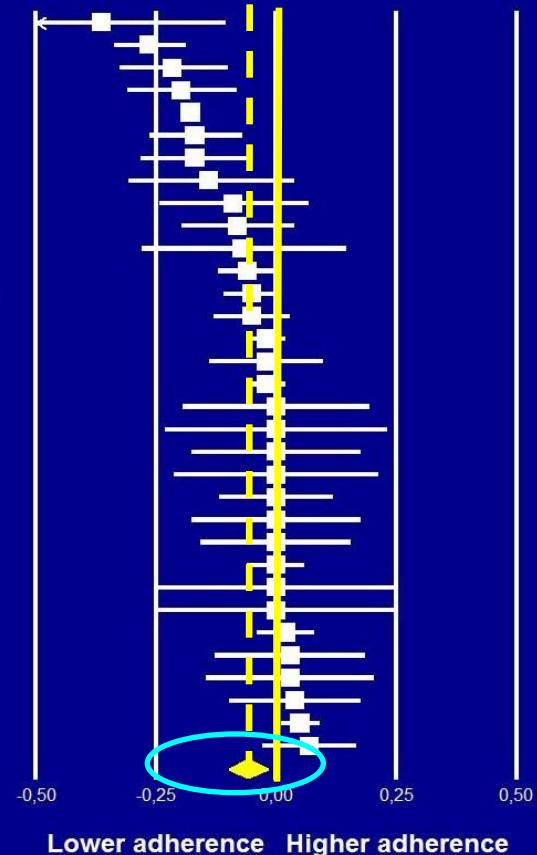
$P = 0.001$

Pill burden

Study

Correlation and 95% CI

Cauldbeck 2009
Kleeberger 2001
Cahn 2004
Wasti 2012
Sullivan 2007
Juday 2011
Gonzalez 2007
Home 2007
Parruti 2006
Waever 2005
Woods 2009
Lazo 2 2007
Protopopescu 2009
Lazo 1 2007
Johnson 2003
Gay 2011
Boyer 2011
Cardarelli 2008
Catz 2000
Gauchet 2007
Gonzalez 2004
Kerr 2012
Gifford 2000
Nilsson 2006
Mannheimer 2002
Mellins 2003
Wagner 2002
Carrieri 2006
Uuskula 2012
Golin 2002
Rintamaki 2006
Thrasher 2008
Falang 2012

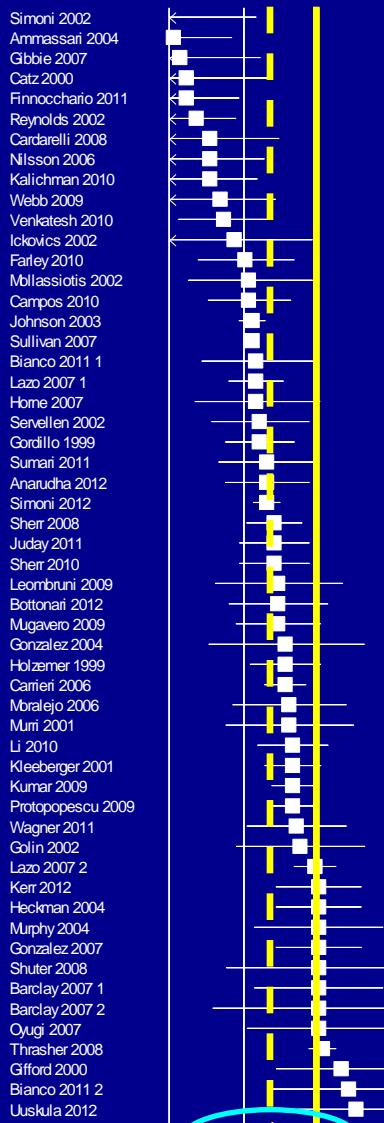


Point estimate $r : -0.06 (-0.10, -0.02)$

$P = 0.004$

Depressive symptoms

Study Correlation and 95% CI



Depressive symptoms:

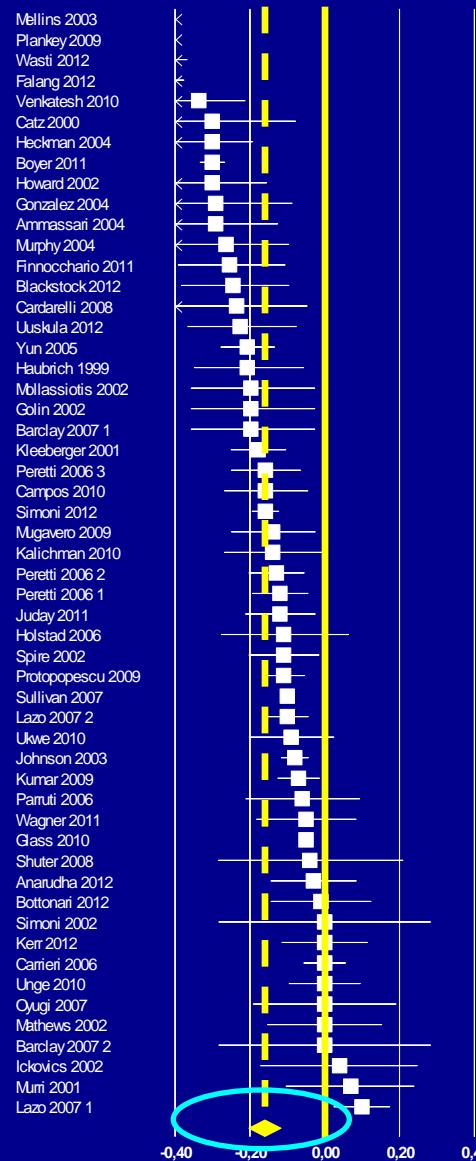
Point estimate r
-0.13
 $(-0.15, -0.10)$
 $P = <0.001$

Concurrent substance use:

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

Concurrent substance use

Study Correlation and 95% CI



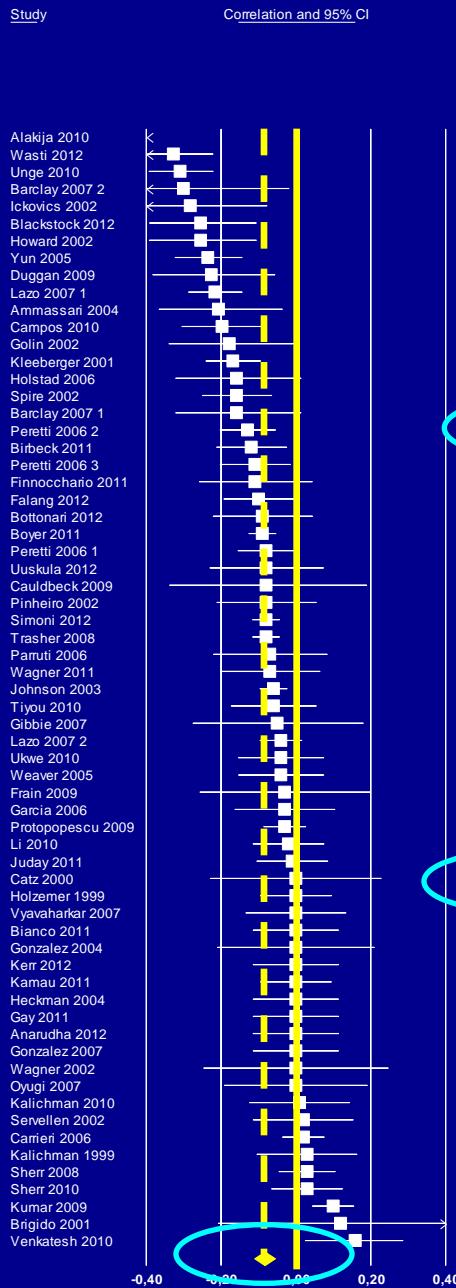
Lower adherence

Higher adherence

Lower adherence

Higher adherence

Financial constraints



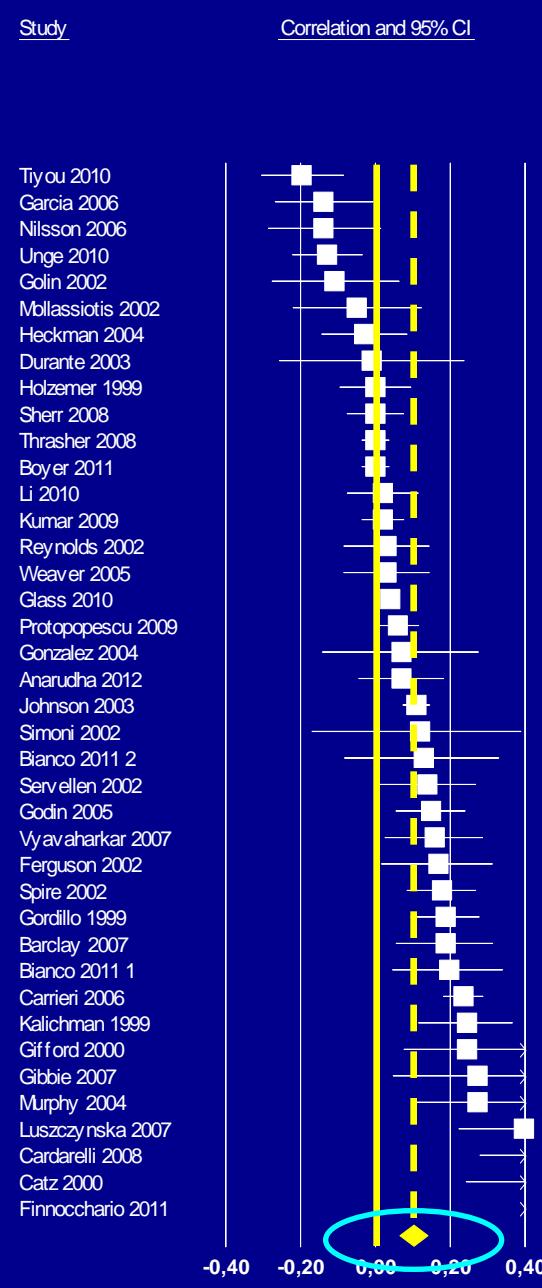
Financial constraints:

Point estimate r
-0.09
 $(-0.11, -0.06)$
 $P = <0.001$

Social support:

Point estimate r
0.10
 $(0.06, 0.14)$
 $P = <0.001$

Social support



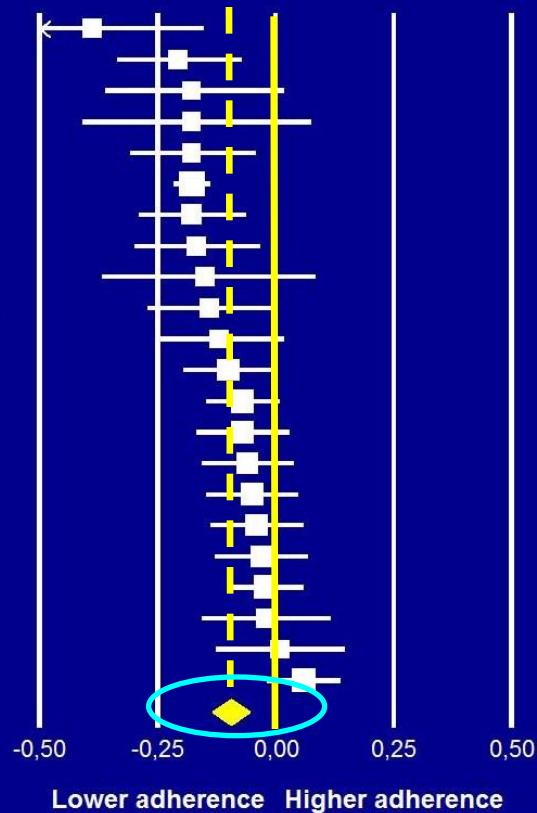
Lower adherence Higher adherence

HIV stigma

Study

Correlation and 95% CI

Mellins 2003
Wagner 2011
Cardarelli 2008
Durante 2003
Waite 2008
Boyer 2011
Wasti 2012
Sumari 2011
Frain 2009
Kalichman 2010
Rintamaki 2006
Peretti 2006 3
Peretti 2006 2
Spire 2002
Li 2010
Unge 2010
Birbeck 2011
Falang 2012
Peretti 2006 1
Li 2011
Rougemont
Sherr 2008



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

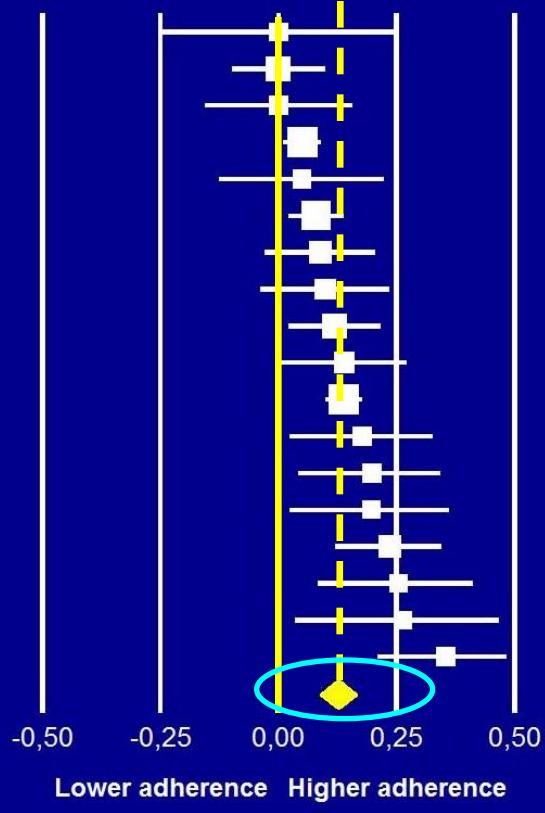
$P < 0.001$

Trust / satisfaction health care provider

Study

Correlation and 95% CI

Durante 2003
Godin 2005
Haubrich 1999
Thrasher 2008
Murphy 2004
Protopopescu 2009
Ukwe 2010
Servellen 2002
Spire 2002
Kalichman 1999
Johnson 2006
Nilsson 2006
Moralejo 2006
Golin 2002
Heckman 2004
Gauchet 2007
Frain 2009
Blackstock 2012



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

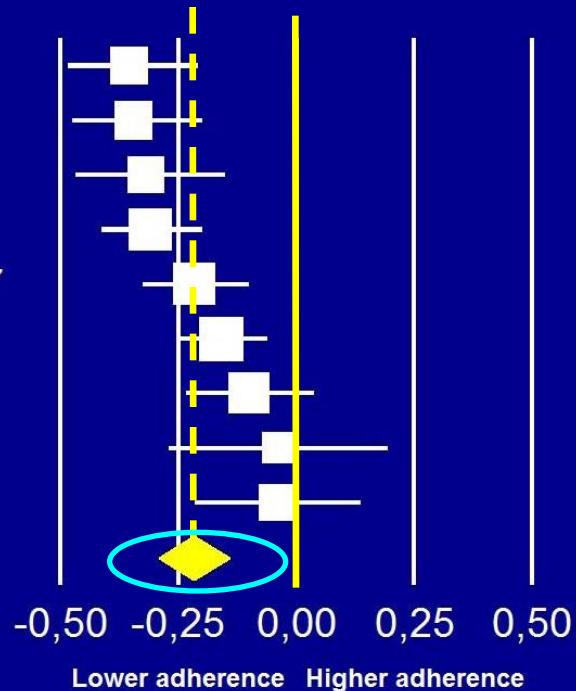
$P < 0.001$

Beliefs: concerns about cART

Study

Correlation and 95% CI

Uuskula 2012
Nilsson 2006
Horne 2007
Wasti 2012
Gonzalez 2007
de Boer 2008
Sumari 2011
Frain 2009
Gauchet 2007

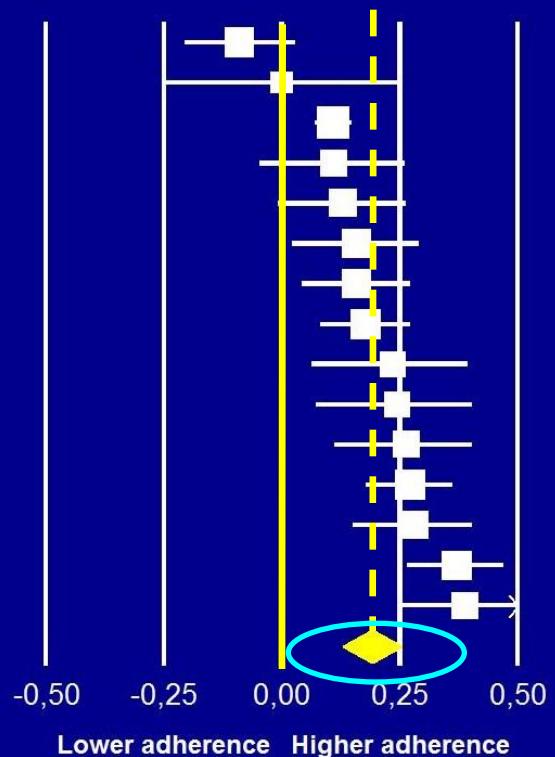


Beliefs: necessity /utility of cART

Study

Correlation and 95% CI

Ukwe 2010
Wagner 2002
Thrasher 2008
Uuskula 2012
Pinheiro 2002
Sumari 2011
Gonzalez 2007
de Boer 2008
Gauchet 2007
Horne 2007
Nilsson 2006
Spire 2002
Barclay 2007
Wasti 2012
Mathews 2002



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

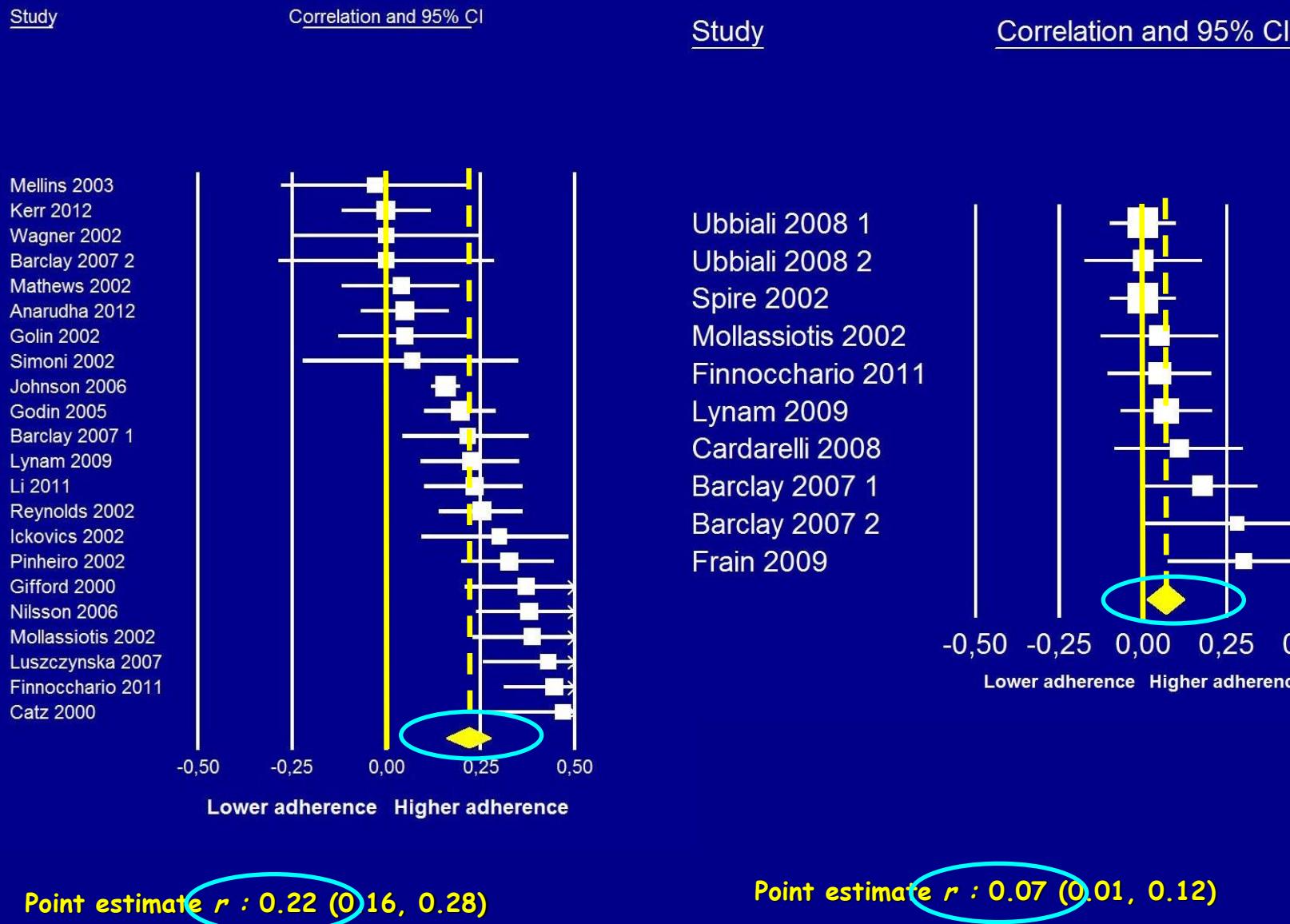
$P < 0.001$

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

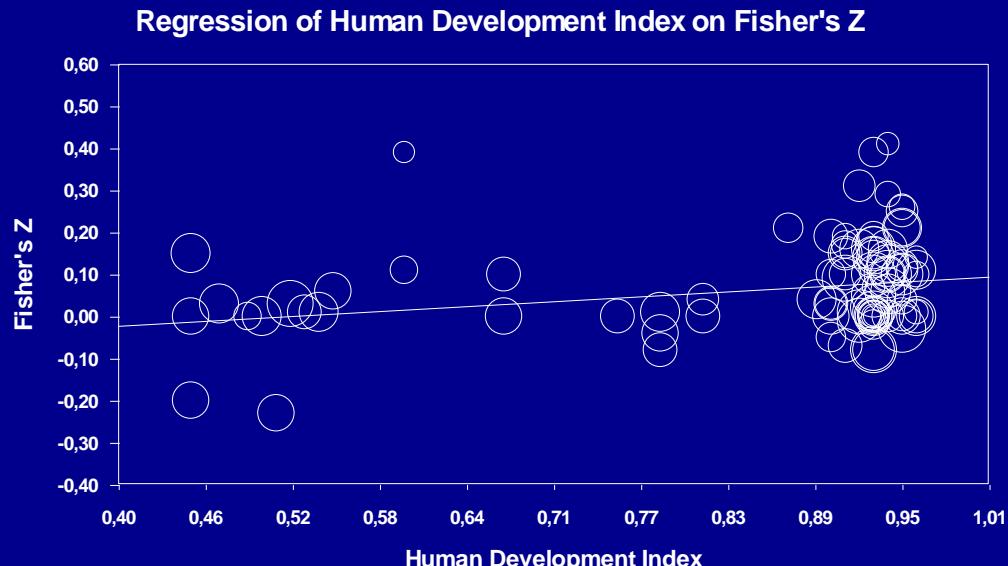
$P < 0.001$

Beliefs: adherence self-efficacy

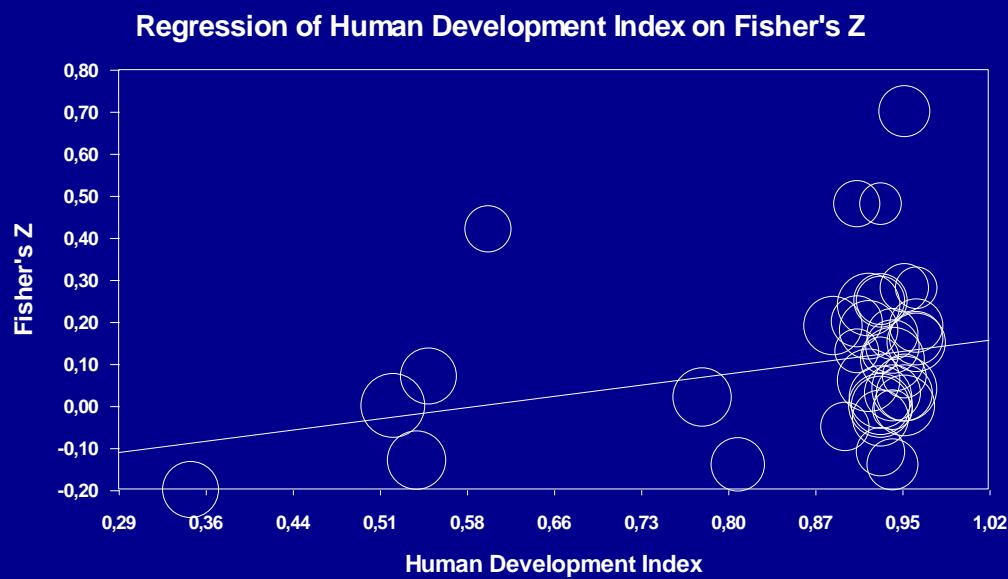
Internal Locus of Control



Moderator analyses

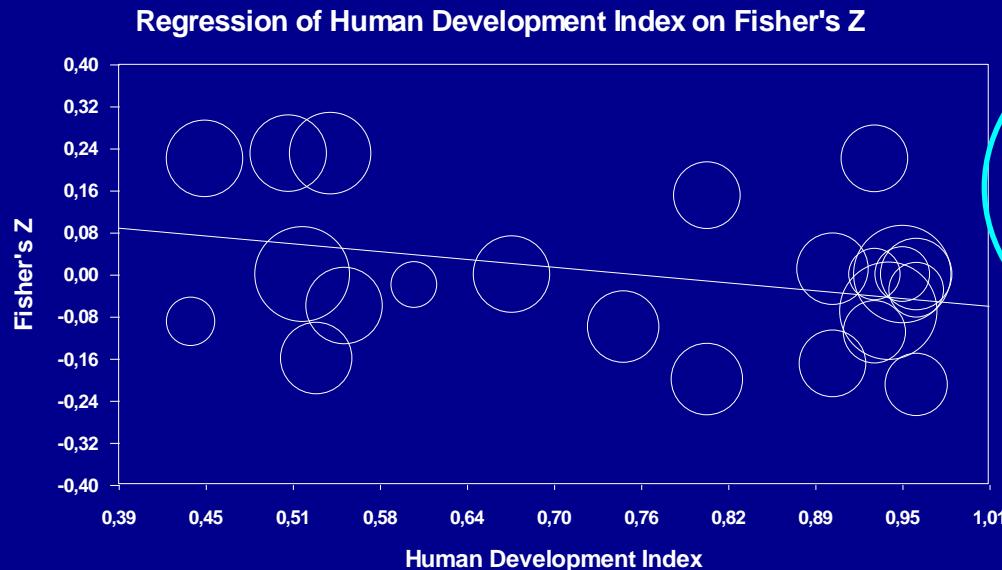


HDI on correlation
Age/adherence:
slope 0.19
P value <0.001



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.