

# **A Meta-analysis of Determinants and Outcomes of Medication Adherence in Adult Solid Organ Transplantation**

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# Disclosures

- Cynthia L. Russell has no disclosures.

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- *on behalf of the B-serious consortium*

# Objectives

- Describe the background of determinants and outcomes of medication adherence in the adult transplant population.
- Discuss the methods used in this meta-analysis.
- Analyze the results of the meta-analysis.
- Evaluate the conclusions reached from the meta-analysis.

# Definitions

## Adherence

- The extent to which a person's behavior (taking medications, following a recommended diet and/or executing life-style changes) corresponds with the *agreed* recommendations of a health care provider <sup>1</sup>

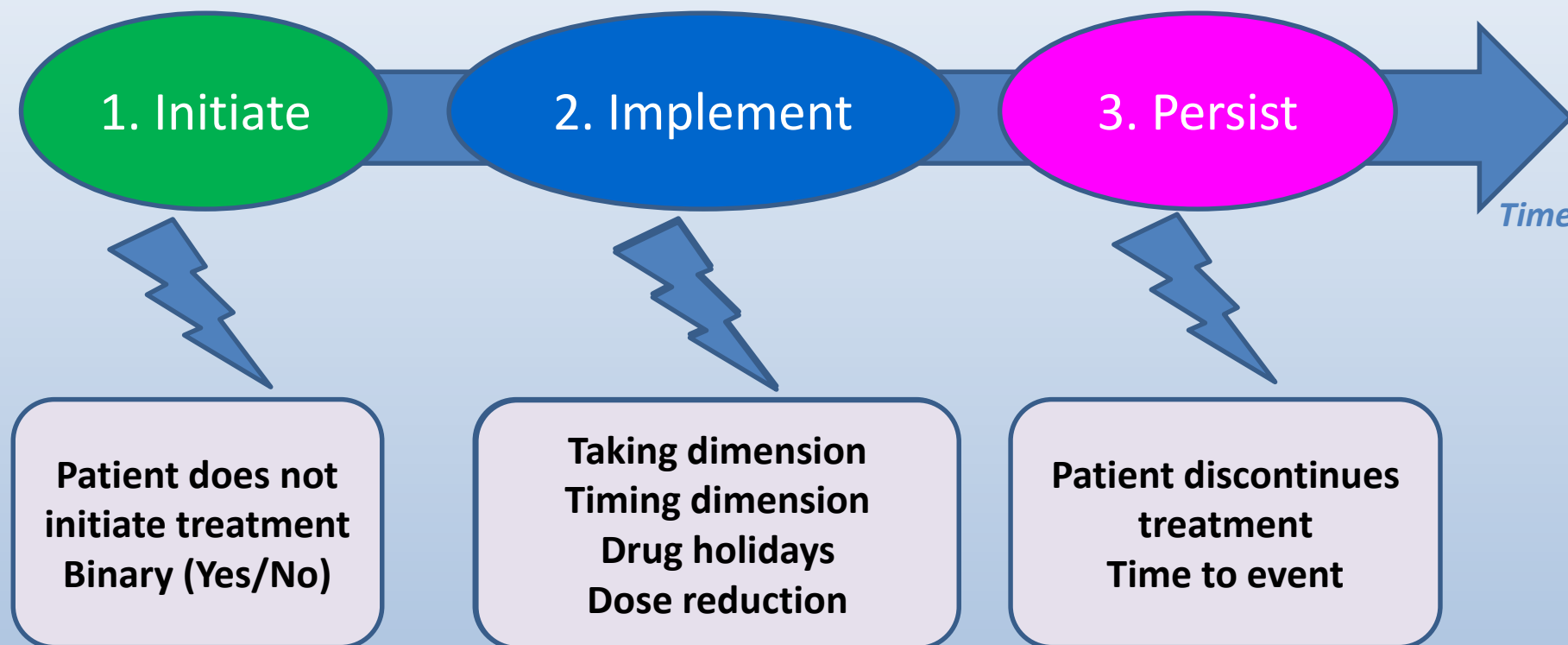
## Medication Non-Adherence

- Deviation from the prescribed medication regimen sufficient to influence adversely the regimen's intended effect <sup>2</sup>

1. Sabate et al. Adherence to Long-Term Therapies Evidence for Action. 2003; World Health Organization. 2. Fine et al. *Am J Transpl.* 2009; 9:35–41.

# Medication Adherence

The process by which patients take their medications as prescribed



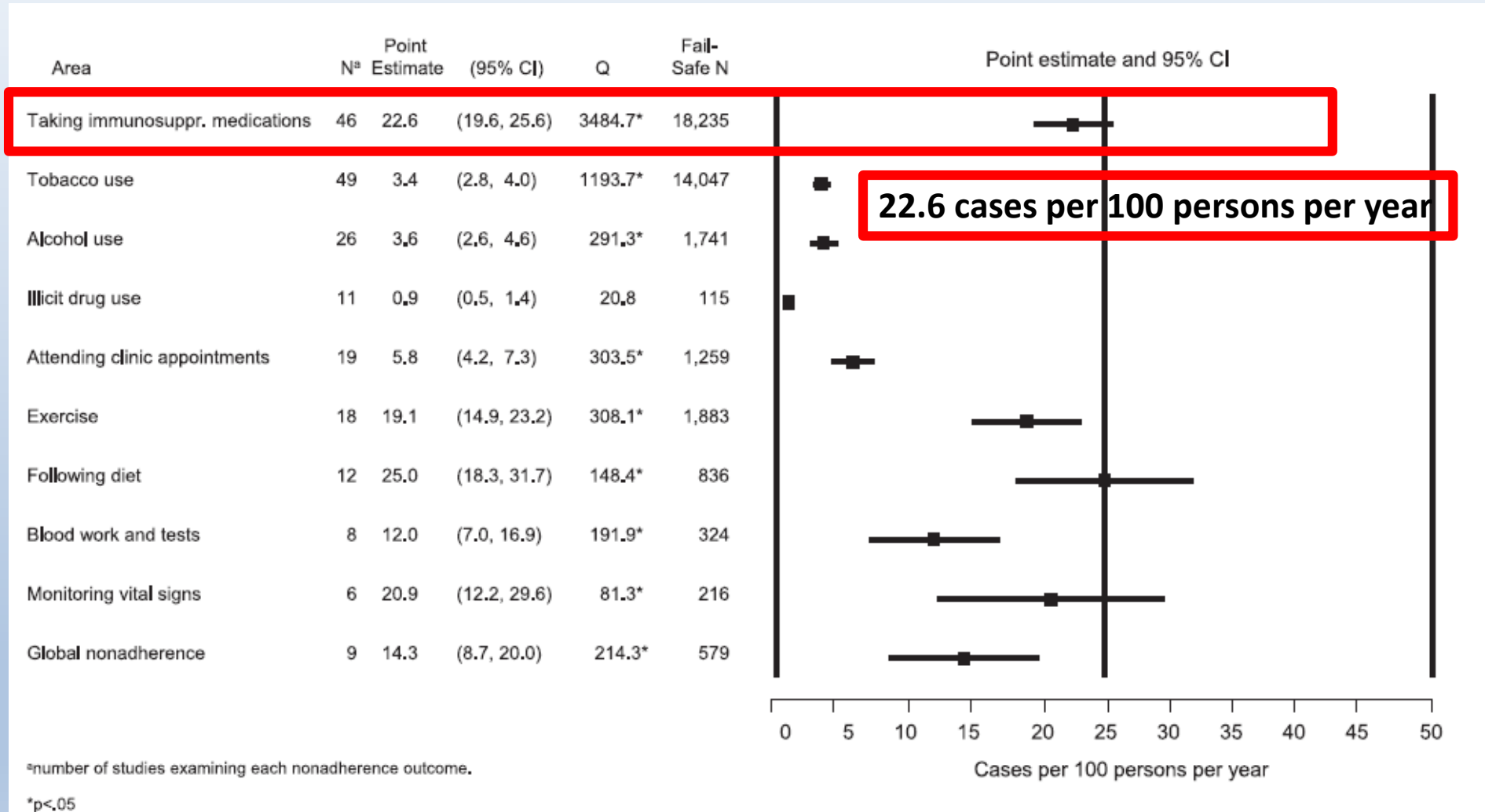
Vrijens et al., British Journal of Clinical Pharmacology,  
2012; 73(5):691-705

# The Scope of the Problem

- **Medication non-adherence**
  - **\$300 billion/year in avoidable costs of hospitalizations, nursing home admissions, and premature deaths <sup>1</sup>**
  - **33-69% of hospital admissions due to medication non-adherence - \$100 billion a year <sup>1</sup>**
  - **Transplant medical costs - \$33,000 in first 3 years after transplant <sup>2</sup>**
  - **Graft failure – increased 6 to 7 fold <sup>3-5</sup>**

1. Osterberg & Blaschke. *N Engl J Med* 2005; 353:487-497 2. Pinsky et al. *American Journal of Transplantation* 2009; 9: 2597–2606; 3. Desmyttere A et al. *Acta Gastroenterol Belg.* 2005;68:347-352. 4. Prihodova et al. *JAN* 2014; doi: 10.1111/jan.12447. 5. Butler et al. *Transplantation.* 2004; 77:769–789.

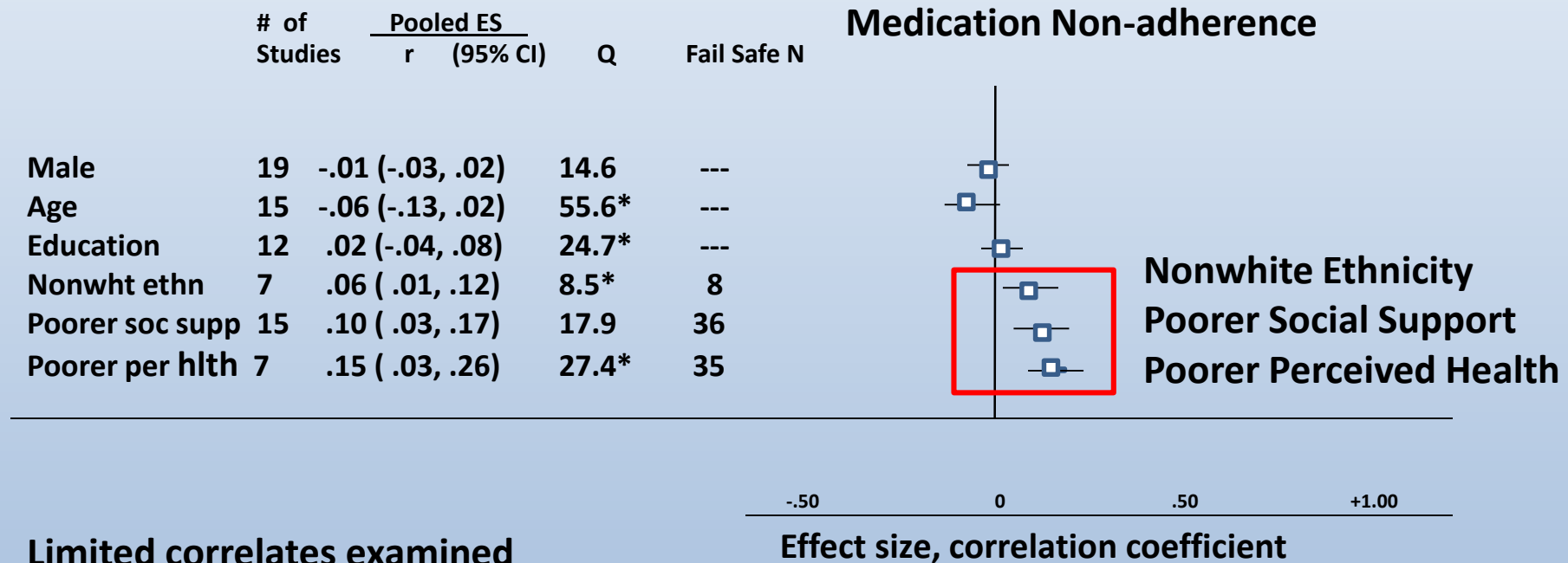
# Prevalence of Medication Non-Adherence



Dew et al. *Transplantation* 2007; 83: 858-873.



# Factors Associated with Medication Non-Adherence in Adult Transplantation



Limited correlates examined  
Outcomes not explored

# Research Gap

- Numerous primary studies have examined determinants and outcomes of medication adherence in adults with solid organ transplant, however no meta-analyses have examined both determinants and outcomes in this population.
- World Health Organization's Multi-level Model nested within Socio-ecological theory was used to guide this study.

# Aims of Study

- To investigate the relationship between socio-economic, patient-related, treatment-related, condition-related, and health care team/system-related **factors** and post-transplant medication non-adherence in adults with lung, heart, liver and kidney organ transplantation
- To investigate the relationship between post-transplant medication non-adherence and clinical, economic **outcomes** & health-related quality of life in adults with lung, heart, liver and kidney organ transplantation

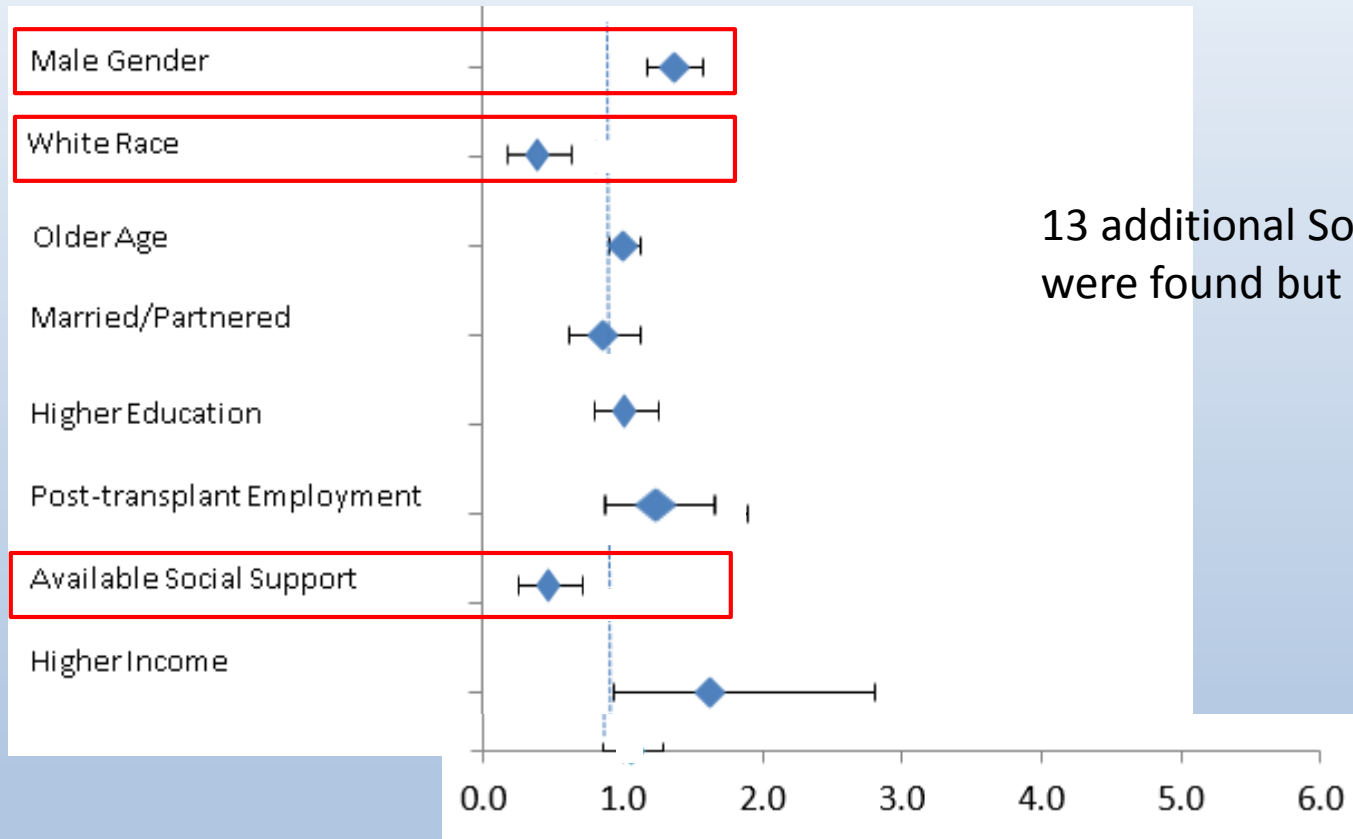
# Methods

- Following standard methodology for systematic review and meta-analysis (<http://www.crd.york.ac.uk/PROSPERO>), we conducted electronic searches of PubMed (1947-2012), Ebscohost CINAHL (1981-2012), Ovid PsycINFO (1967-2012) and EMBASE.COM (1947-2012). No language limits were used.
- From 4060 citations meeting inclusion criteria, 3324 abstracts were screened. Of these, 482 full-text articles were accessed and reviewed for eligibility.
- After eliminating 408 studies, 68 studies were included in the review. Data were abstracted from each article by pairs of the authors. Meta-analyses were conducted on factors/outcomes of NA examined in 5 or more studies.

# Study Characteristics (N=74)

| Characteristic               |                        | Results         |
|------------------------------|------------------------|-----------------|
| Organ Transplant Type        | Liver (%)              | 10.4            |
|                              | Kidney (%)             | 74.0            |
|                              | Heart (%)              | 13.0            |
|                              | Lung (%)               | 2.6             |
| Continent                    | North-America (%)      | 55.8            |
|                              | Europe (%)             | 33.8            |
|                              | Asia (%)               | 3.9             |
|                              | Other (%)              | 5.2             |
| Sample Size                  | Median                 | 137             |
|                              | IQ Range               | 20 - 15,525     |
| Participant % Male<br>Gender | Mean $\pm$ SD          | 63.1 $\pm$ 12.0 |
|                              | 25th and 75th IQ Range | 82-255          |
| Participant Mean Age         | Mean $\pm$ SD          | 48.1 $\pm$ 7.2  |
|                              | Range                  | 32.2 – 61.7     |

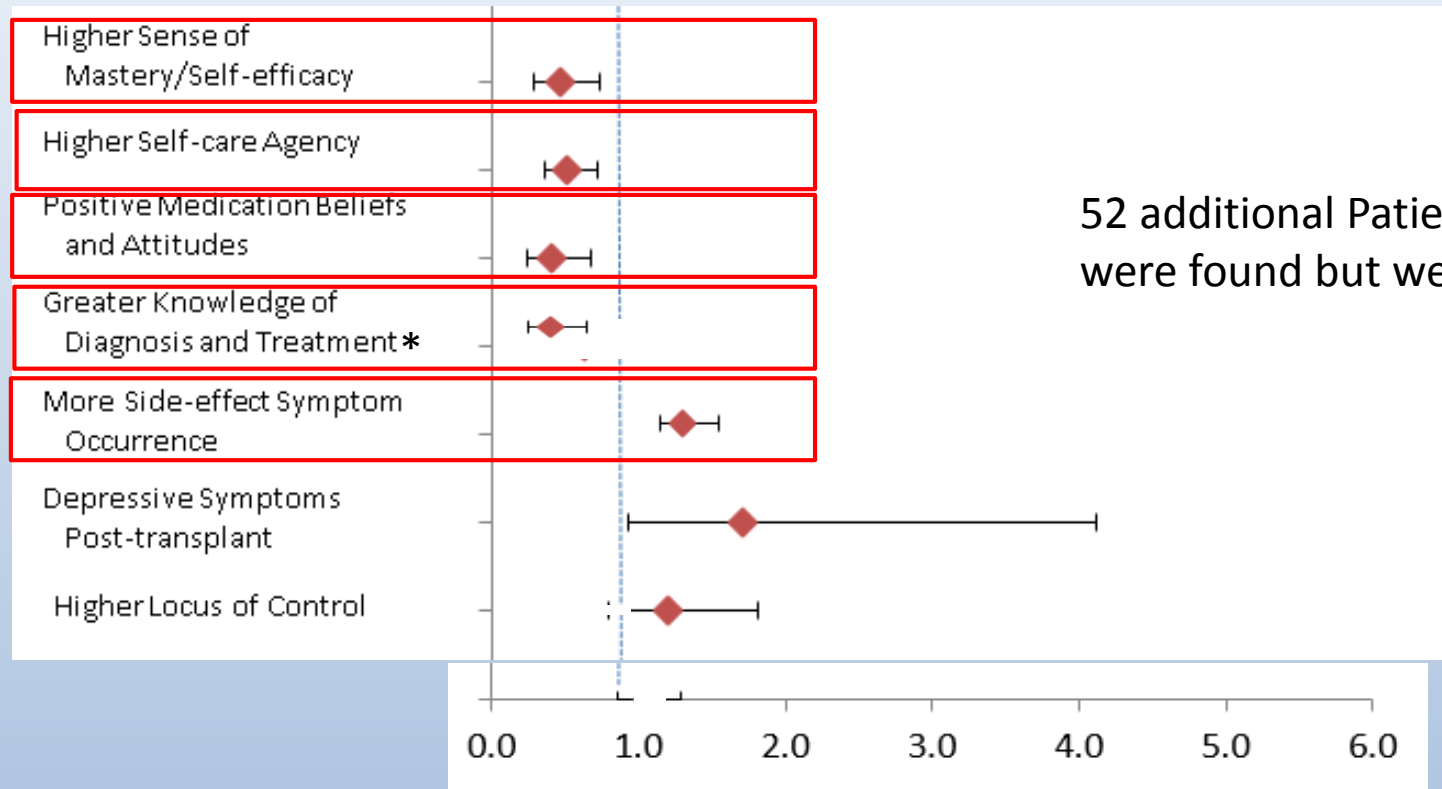
# Results: Sociodemographic Factors



13 additional Sociodemographic factors were found but were studied < 5 times

p<.05

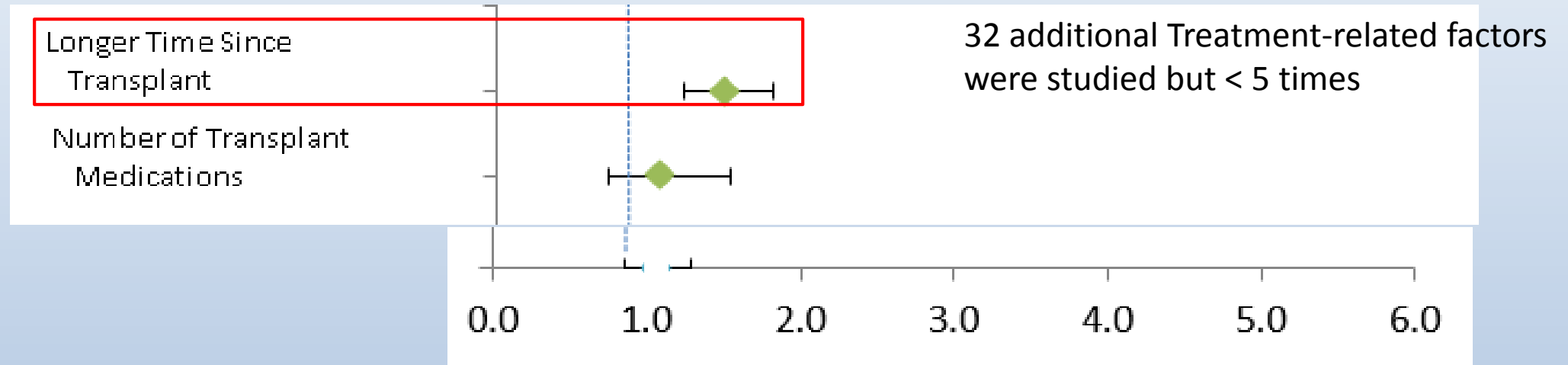
# Results: Patient-Related Factors



52 additional Patient-related factors were found but were studied < 5 times

p<.001  
\*p<.05

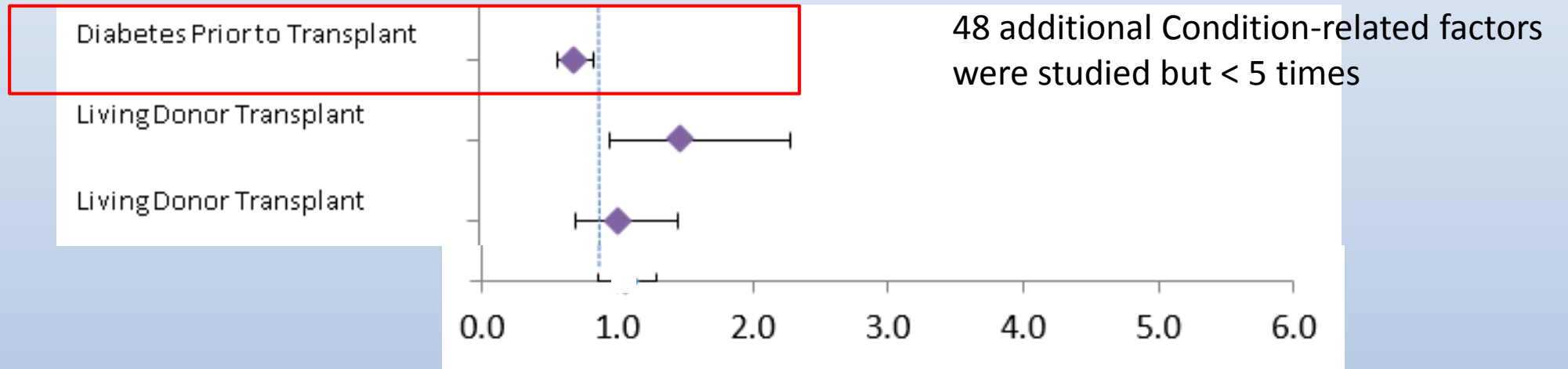
# Results: Treatment-Related Factors



$p < .001$

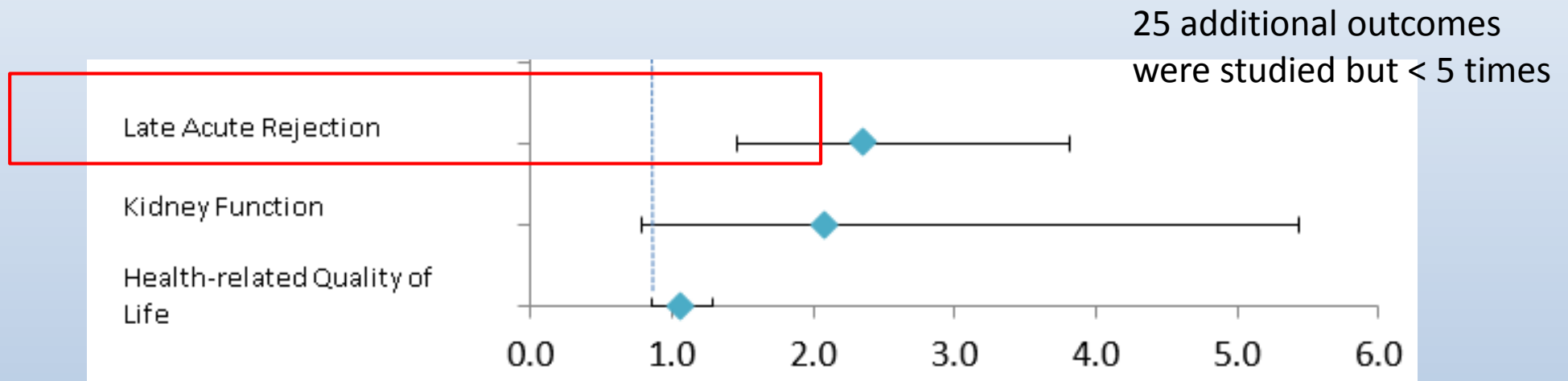


# Results: Condition-Related Factors



$p < .001$

# Association of Medication Non-Adherence with Outcomes



$p < .001$

# Results: Healthcare/System-Related Factors

| Factors   | # of papers |
|---|-------------|
| Support from the healthcare provider              | 2           |
| Type of health insurance                          | 2           |
| Continent of transplant surgery                   | 1           |
| State or country of transplant surgery            | 2           |
| Transplant center                                 | 3           |
| Distance from the transplant center (travel time) | 1           |
| Having health insurance                           | 1           |
| Frequency of follow-up (number of visits)         | 1           |

**Total = 11**

# Summary

## Medication Non-Adherence

### Protective

- Higher sense of mastery/self-efficacy
- Higher self-care agency/ability
- Greater knowledge of diagnosis and treatment
- Positive medication beliefs/attitudes
- Having diabetes pre-transplant

### Increased Risk

- More side-effect symptom occurrence
- Longer time since transplant

### Medication Non-adherence

- Late acute rejection (2.356 times as likely)

# Discussion

- **Support multilevel determinants' contributions to NA-WHO model as an organizing framework is supported.**
- **Published research continues to remain focused on the patient- and micro-level (health care provider, social support).**

# Discussion

- **First to provide strong evidence that medication non-adherence worsens the longer the recipient is from the transplant date and that having diabetes prior to transplant is protective for medication non-adherence.**
- **Medication non-adherence results in a 2.3 times increased risk for late acute rejection.**
- **Many factors with heterogeneity in study findings**
  - **Varied instruments used to measure factors and medication non-adherence**
- **Most study statistics were correlations (r-values) – estimates were made in conversion to odds ratios**

# Conclusions

- WHO organizing framework nested within Socio-ecological theory is supported.
- Future research should focus on health care organization and health care system influences.
- All potential correlates and outcomes of medication non-adherence should be included in future intervention studies.
- Standardized definitions of correlates and outcomes should be developed to decrease heterogeneity across studies.

# Thank you!!

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**Questions?**