

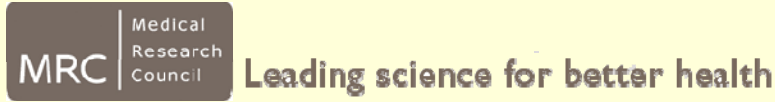
# Cognitive remediation therapy for schizophrenia: an update on efficacy and intervention(s)

Vyv Huddy\*

Prof. Til Wykes\*, Clare Reeder\* and Caroline Cellard\*\*

*\* Department of Psychology,  
Institute of Psychiatry, London.  
vyv.huddy@kcl.ac.uk*

*\*\*Clinical and Cognitive Neurosciences,  
Centre de recherche Université Laval  
Robert-Giffard, Quebec City, Canada*





**Thomas Snyder**

“Community functioning is the ultimate goal....improving cognition in schizophrenia is *not* the end in itself”

Editorial in American Journal of Psychiatry

Michael Green (2009)

# Service user views

Personal experiences (Rethink 2010):

“from a bedroom in a hostel to an independent flat with support available if I needed it ”

***Greater Independence***

“get back to a normal routine....and I hope one day to regain part-time employment”.

***Purpose and role***

“12 years on, I’m married and content”.

***Relationships and support***

- 1. Why is cognition important?**
2. What is cognitive remediation therapy (CRT)?
3. What is the evidence that CRT benefits cognition?
4. Do benefits generalise to community functioning?
5. What about mechanisms for transferring therapy gains to community outcomes?

# Schizophrenia: a DSM IV perspective

Definition includes

- Social Occupational Dysfunction
- Characteristic symptoms
- **Cognitive function**

(1887 to present day e.g. DSM V)

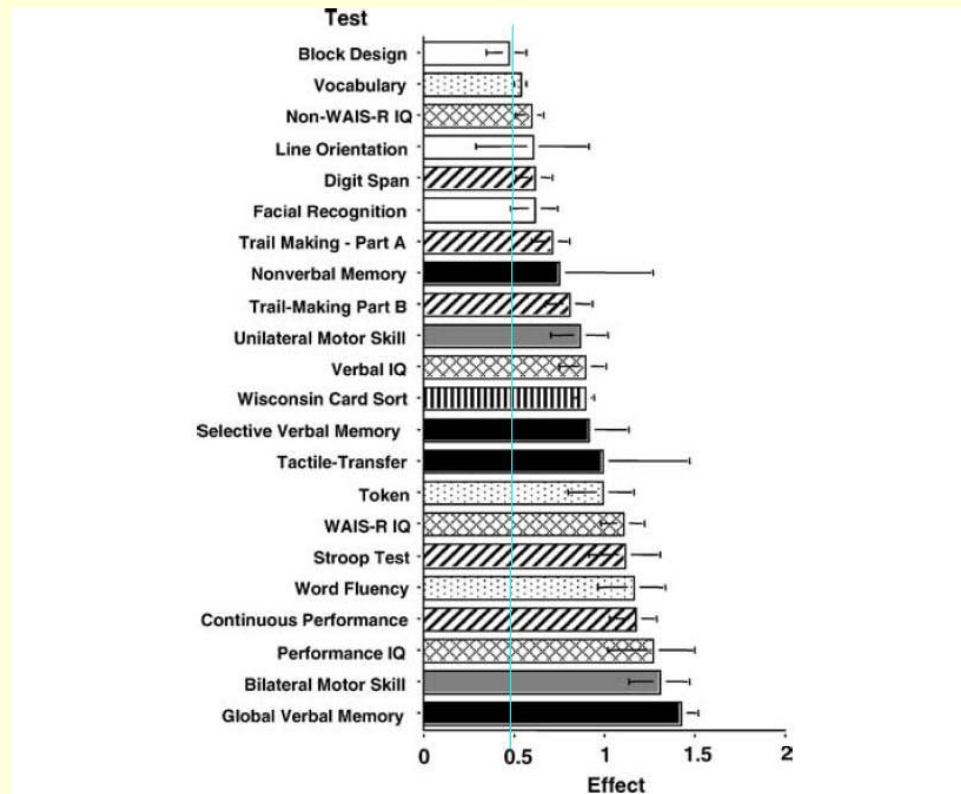
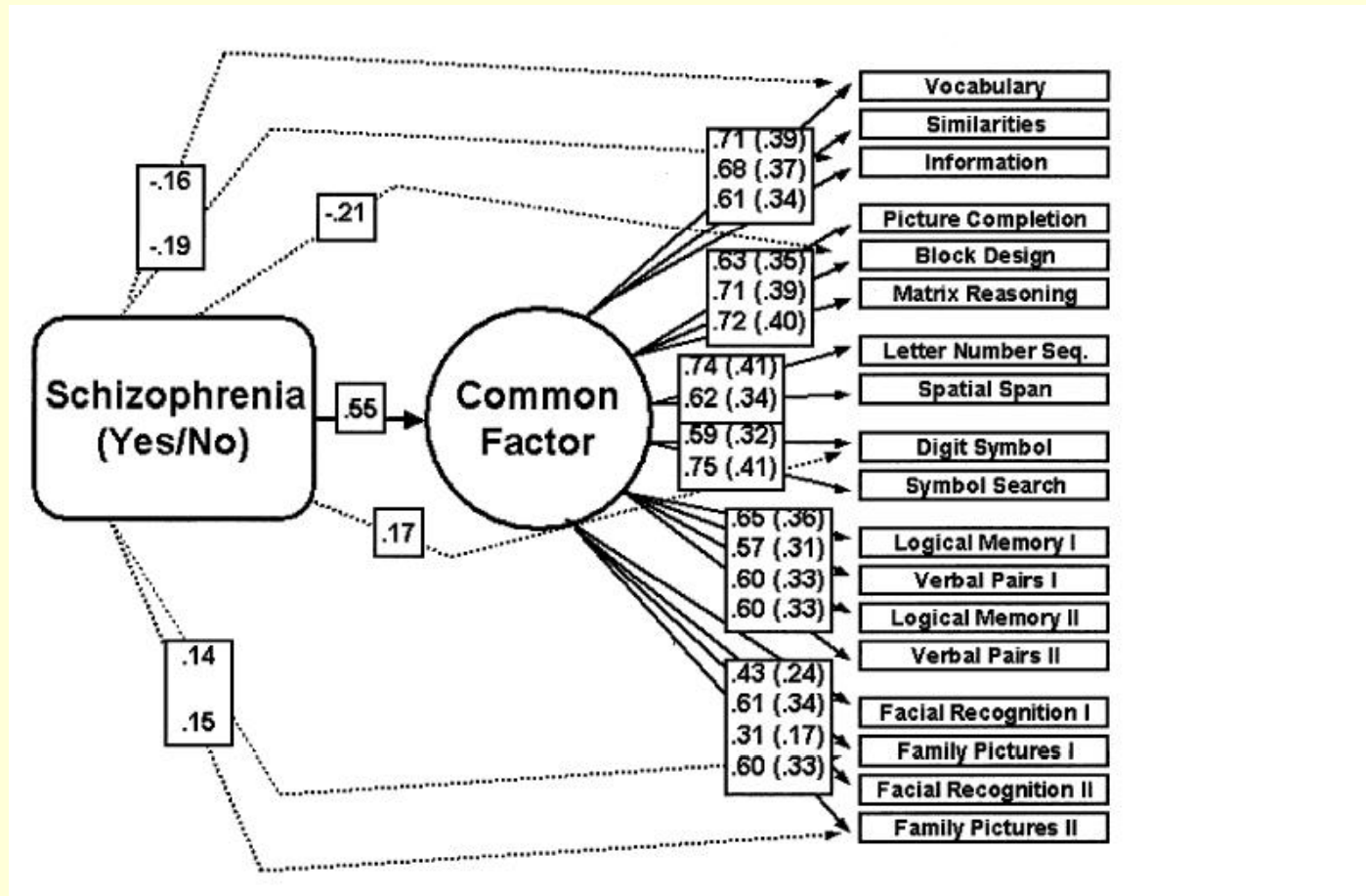
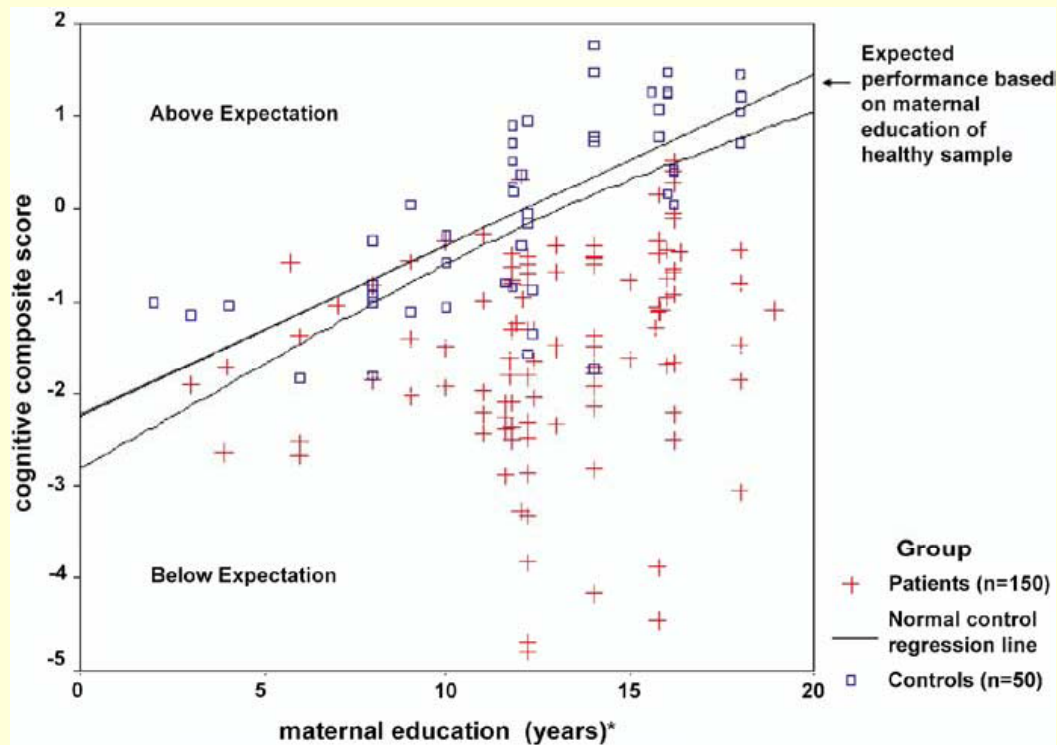


Fig. 1. Mean (and *SE*) of effect sizes calculated based on 509 effects from 204 studies comparing patients with schizophrenia to controls. Shading reflects putative cognitive domains (Heinrichs & Zakzanis, 1998) as follows: white – spatial ability; stippled – language ability; hashed – intelligence; diagonal striped – attention; black – memory; grey – motor skill; and vertical striped – executive.

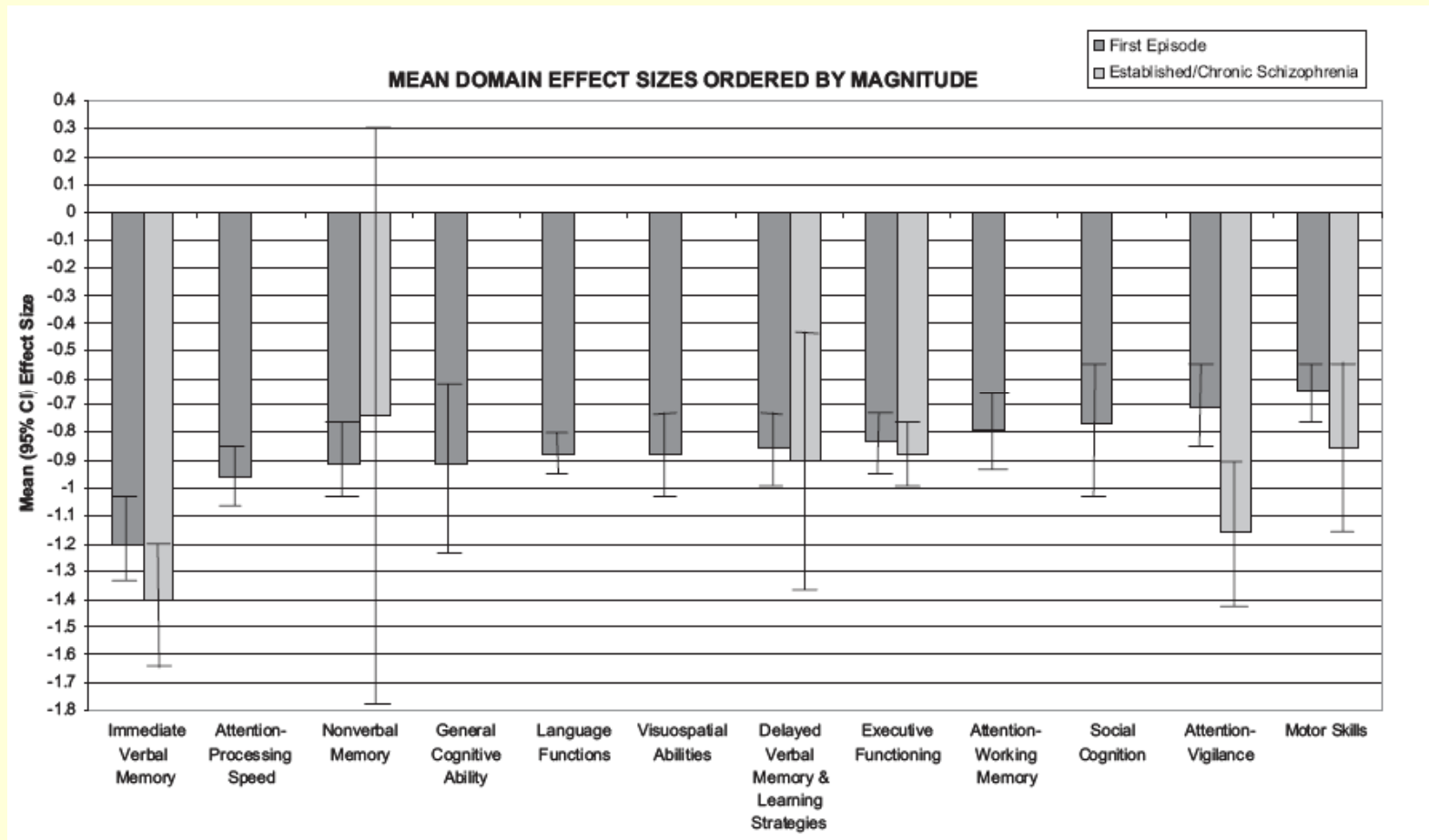
Impairment across multiple domains (e.g. Heinrichs et al. 1998; Dickinson et al. 2008)



Impairments tend to be associated with each other (e.g. Dickinson et al. 2004).



Impairments - when defined as “failure to reach expected level” based on maternal education level – affect 98.1 % of patients (Keefe et al. 2005)



Present at onset (e.g. Mesholam-Gately. 2009) or earlier (e.g. Cannon et al. 2000) and stable (e.g. Szoke et al. 2008)

**“Real World”  
Outcomes**

**Symptoms**

**Cognitive skills**

## What Are the Functional Consequences of Neurocognitive Deficits in Schizophrenia?

Michael Foster Green, Ph.D.

---

*Objective: It has been well established that schizophrenic patients have neurocognitive deficits, but it is not known how these deficits influence the daily lives of patients. The goal of this review was to determine which, if any, neurocognitive deficits restrict the functioning of schizophrenic patients in the outside world. Method: The author reviewed studies that have evaluated neurocognitive measures as predictors and correlates of functional outcome for schizophrenic patients. The review included 1) studies that have prospectively evaluated specific aspects of neurocognition and community (e.g., social and vocational) functioning (six studies), 2) all known studies of neurocognitive correlates of social problem solving (five studies), and 3) all*

**WOS: 150 citations per year**

**“Real World”  
Outcomes**

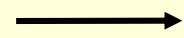
**Symptoms**

**Cognitive skills**

**“Real World”  
Outcomes**

**Cognitive skills**

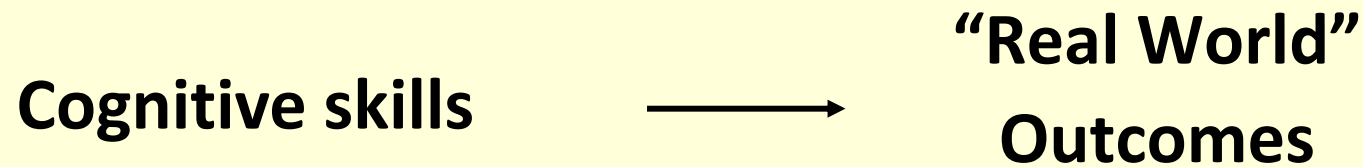
**Cognitive skills**



**(0.2–0.4)**

**“Real World”  
Outcomes**

**Green et al. (1996, 2000)**



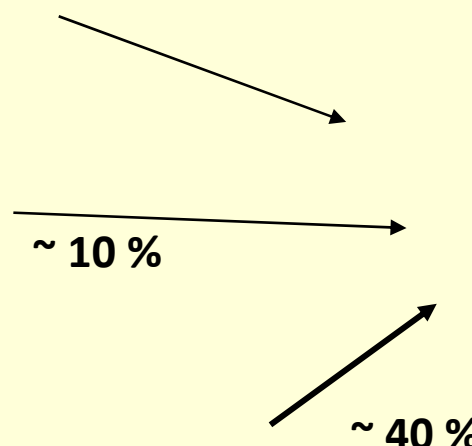
A group of more recent prospective studies support this link:

(Brekke et al., 2005; Bryson and Bell, 2003; Dickerson et al., 1999; Fujii and Wylie, 2003; Gold, 2004; Jaeger et al., 2003; Prouteau et al., 2005; Smith et al., 2002; Velligan et al., 2000; Woonings et al., 2003)

**Symptoms**

**Depression**

**Cognitive skills**  
Via "functional ability"



**Community  
Activities**

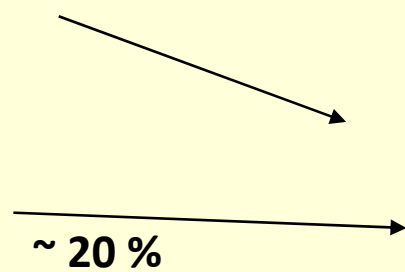
**Cross sectional study: Bowie et al. 2006**

**Symptoms**

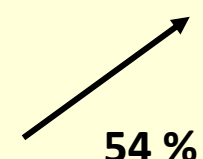
**Depression**

**Cognitive skills**

Via "functional ability"



~ 20 %



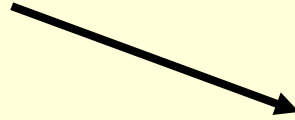
54 %

**Work skills**

**Cross sectional study: Bowie et al. 2006**

**-ve symptoms**

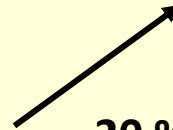
40 %



**Interpersonal  
outcomes**

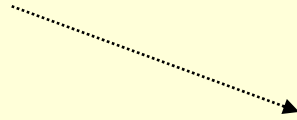
**Cognitive skills**  
Via "functional ability"

20 %



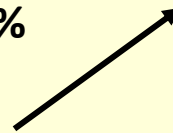
**Cross sectional study: Bowie et al. 2006**

**+ve Symptoms**



**Subsequent need for  
care**

**60%**



**Cognitive skills /  
length of illness**

**Prospective: Netherne series (1990 –1994)**

1. Why is cognition important?
2. **What is cognitive remediation therapy (CRT)?**
3. What is the evidence that CRT benefits cognition?
4. Do benefits generalise to community functioning?
5. What about mechanisms for transferring therapy gains to community outcomes?

# Spoilt for choice?

## **Cognitive remediation programs (some examples):**

Neurocognitive Enhancement Therapy (NET)

Cognitive Enhancement Therapy (CET)

Computer Assisted Cognitive Remediation (CACR)

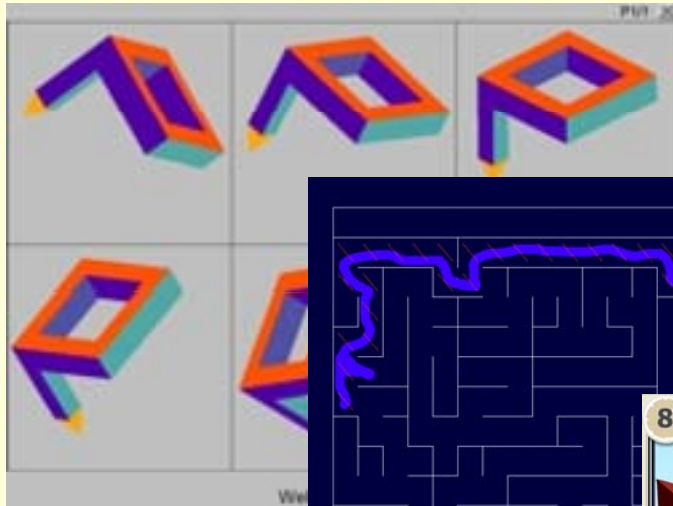
Neuropsychological Educational Approach to Remediation (NEAR)

Integrative Psychological Therapy (IPT)

Posit Science (CRIS)

Cognitive Remediation Therapy (CIRCuiTS)

**Some therapies are  
computerised..  
Practice.. practice..  
practice..**



# Some CRTS are focused on teaching strategy plus practice



# Other variations....

standard vs. “tailored” tasks

duration (< 10 sessions to 2 years)

transfer of cognitive skills to daily activities, work or  
social skills via groups (Keefe et al. 2010; Bell et al. 2002;  
Hogarty et al. 2004; IPT: Brenner, Roder etc)

# Defining CRT for schizophrenia

CREW\*\* (2010) definition:

**“is a behavioural training-based intervention that aims to improve cognitive processes\* with the goal of durable benefits on community functioning”.**

\*(attention, memory, executive function, social cognition or meta cognition)

\*\* Cognitive Remediation Expert Working Group

1. Why is cognition important?
2. What is cognitive remediation therapy (CRT)?
3. **What is the evidence that CRT benefits cognition?**
4. **Do benefits generalise to community functioning?**
5. What about mechanisms for transferring therapy gains to community outcomes?

## A Meta-Analysis of Cognitive Remediation for Schizophrenia: Methodology and Effect Sizes

Til Wykes, Ph.D.

Vyv Huddy, Ph.D.

Caroline Cellard, Ph.D.

Susan R. McGurk, Ph.D.

Pál Czobor, Ph.D.

**Objective:** Cognitive remediation therapy for schizophrenia was developed to treat cognitive problems that affect functioning, but the treatment effects may depend on the type of trial methodology adopted. The present meta-analysis will determine the effects of treatment and whether study method or potential moderators influence the estimates.

**Method:** Electronic databases were searched up to June 2009 using variants of the key words “cognitive,” “training,” “remediation,” “clinical trial,” and “schizophrenia.” Key researchers were contacted to ensure that all studies meeting the criteria were included. This produced 109 reports of 40 studies in which  $\geq 70\%$  of participants had a diagnosis of schizophrenia, all of whom received standard care. There was a comparison group and allocation procedure in these studies. Data were available to calculate effect sizes on cognition and/or functioning. Data were independently extracted by two reviewers with excellent reliability. Methodological moderators were extracted through the Clinical Trials Assessment Measure and verified by authors in 94% of cases.

**Results:** The meta-analysis (2,104 participants) yielded durable effects on global cognition and functioning. The symptom effect was small and disappeared at follow-up assessment. No treatment element (remediation approach, duration, computer use, etc.) was associated with cognitive outcome. Cognitive remediation therapy was more effective when patients were clinically stable. Significantly stronger effects on functioning were found when cognitive remediation therapy was provided together with other psychiatric rehabilitation, and a much larger effect was present when a strategic approach was adopted together with adjunctive rehabilitation. Despite variability in methodological rigor, this did not moderate any of the therapy effects, and even in the most rigorous studies there were similar small-to-moderate effects.

**Conclusions:** Cognitive remediation benefits people with schizophrenia, and when combined with psychiatric rehabilitation, this benefit generalizes to functioning, relative to rehabilitation alone. These benefits cannot be attributed to poor study methods.

*(Am J Psychiatry Wykes et al.; AiA:1–16)*

# CRT Meta Analysis: Sample

- 2104 participants in 39 CRT trials spanning 37 years (1973 – 2010)
- Outcomes: cognition, functioning and symptom outcomes

# CRT Meta Analysis

Data Sources: Electronic databases (Embase, Medline, Current Contents, Web of Science, PsychInfo, and Cochrane Register)

Search Terms: COGNITIVE, TRAINING, REMEDIATION, CLINICAL TRIAL AND SCHIZOPHRENIA

# CRT Meta Analysis: Inclusion criteria

- 1) a intervention is described that aims to improve cognition
- 2) majority (>70%) of participants had a diagnosis of schizophrenia
- 3) all participants received standard care including appropriate medication
- 4) there was a control group and allocation procedure
- 5) there was a cognitive or functional outcome **distinct** from the trained tasks.

# CRT Meta Analysis

## Moderators effects

1. Trial characteristics (training approach, dose [duration and intensity], adjunctive rehabilitation)
2. Participant characteristics (sex, baseline symptoms, age)
3. Methodological rigour >>

# Trial methodology

- Used Clinical Trials Assessment Measure (Tarrier and Wykes, 2004) to rate trials on:
  - Method of randomisation
  - Assessment measures, independence and masking
  - Control group
  - Statistical procedures (including drop out)
  - Treatment protocol and fidelity

# What are the cognitive outcomes?

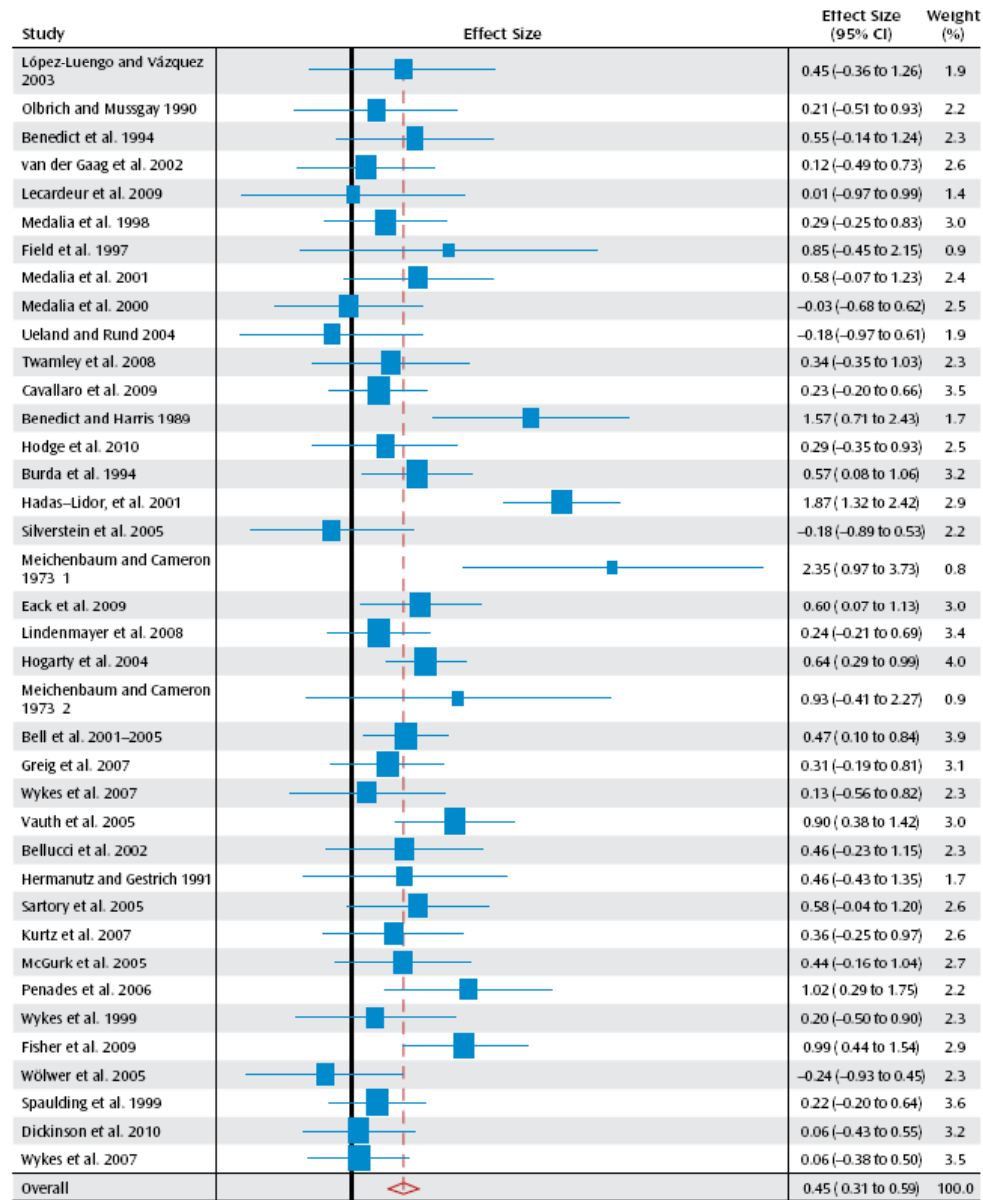
- Effect sizes derived from neuropsychological test scores
- 101 outcomes converted into composites
- Classified to MATRICS (2005) consensus:

(attention, speed of processing, working memory, learning and memory, reasoning / problem solving, social cognition)

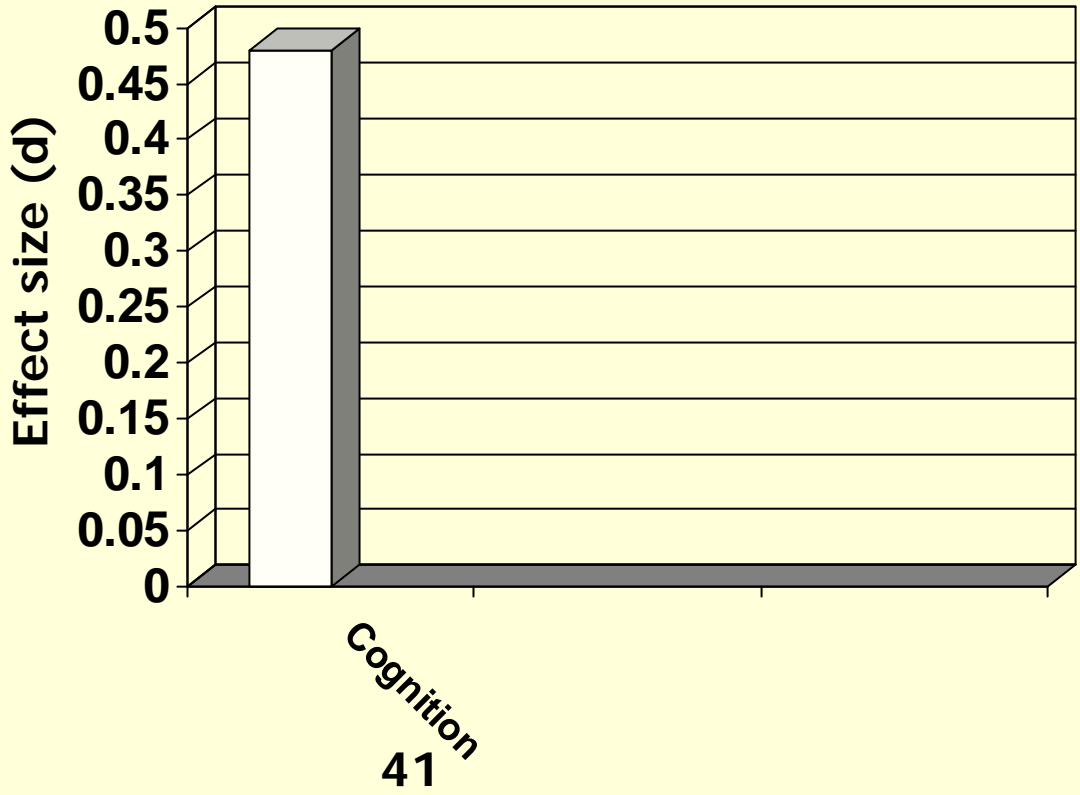
# What are the other outcomes?

- Broad based functioning outcomes (Work skills, functional performance measures, observational measures, GAF scores, work performance and hours, QOL)
- Also, symptom outcomes (e.g. PANSS scores, BPRS)

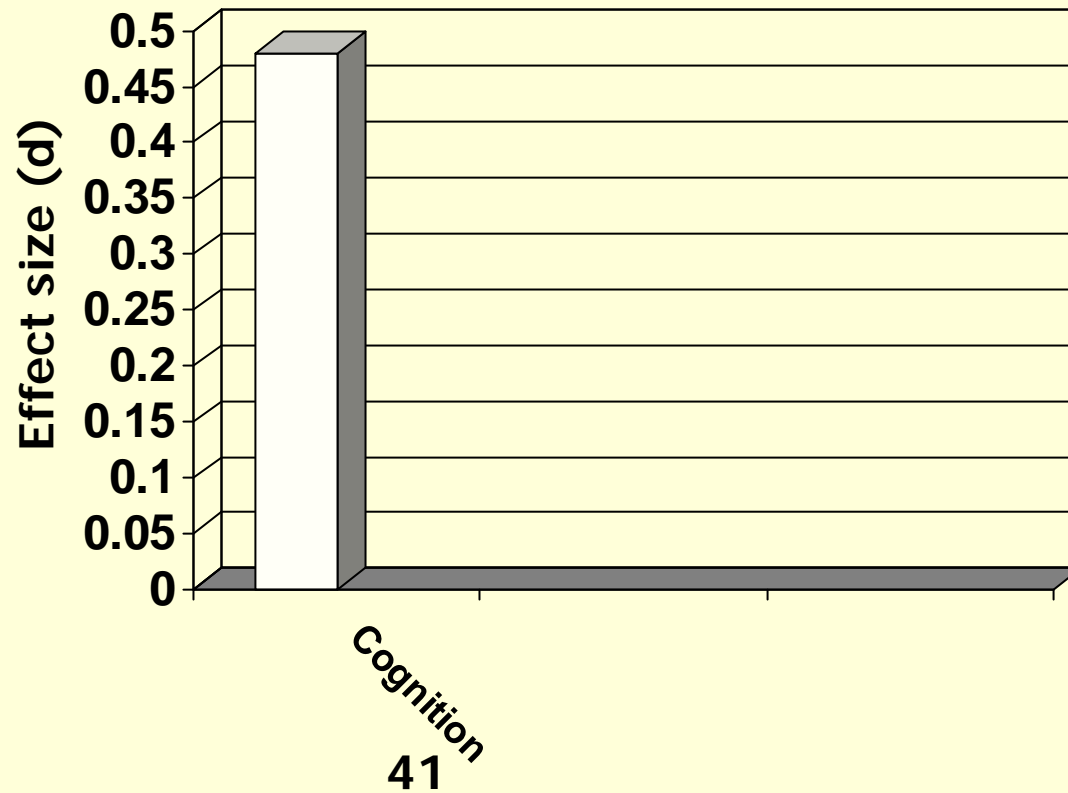
Figure 1. Forest Plot of Global Cognition Among Studies in Cognitive Remediation Therapy\*



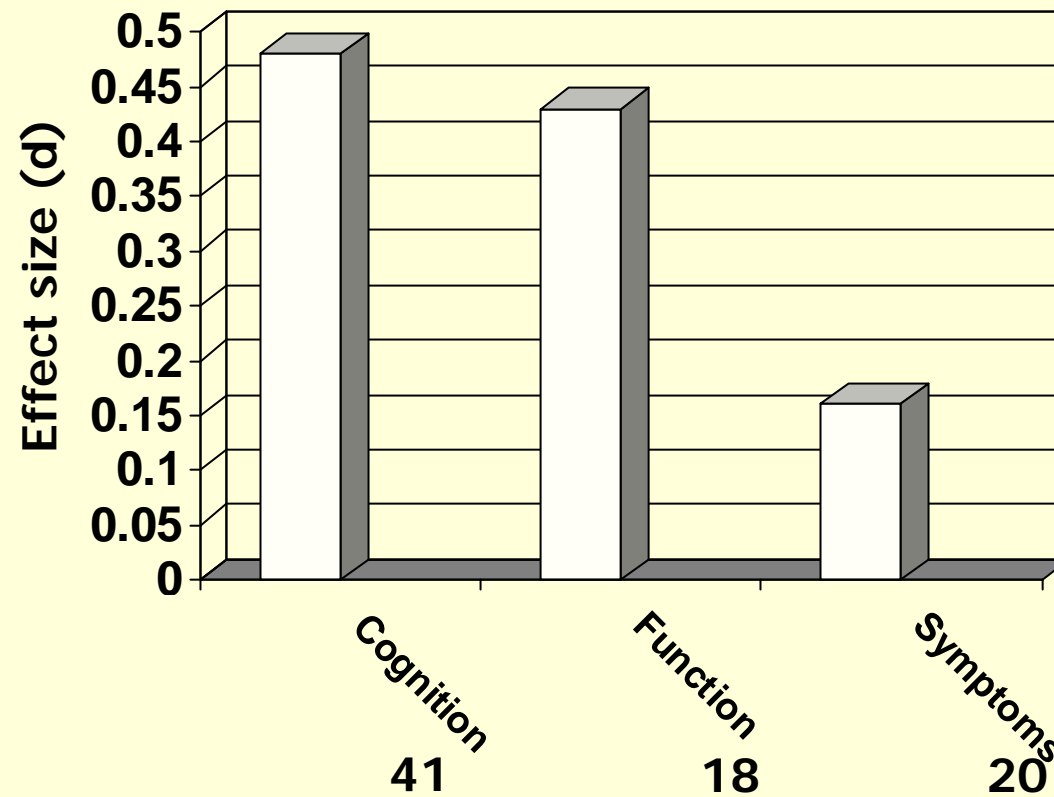
# Does CRT change cognition?



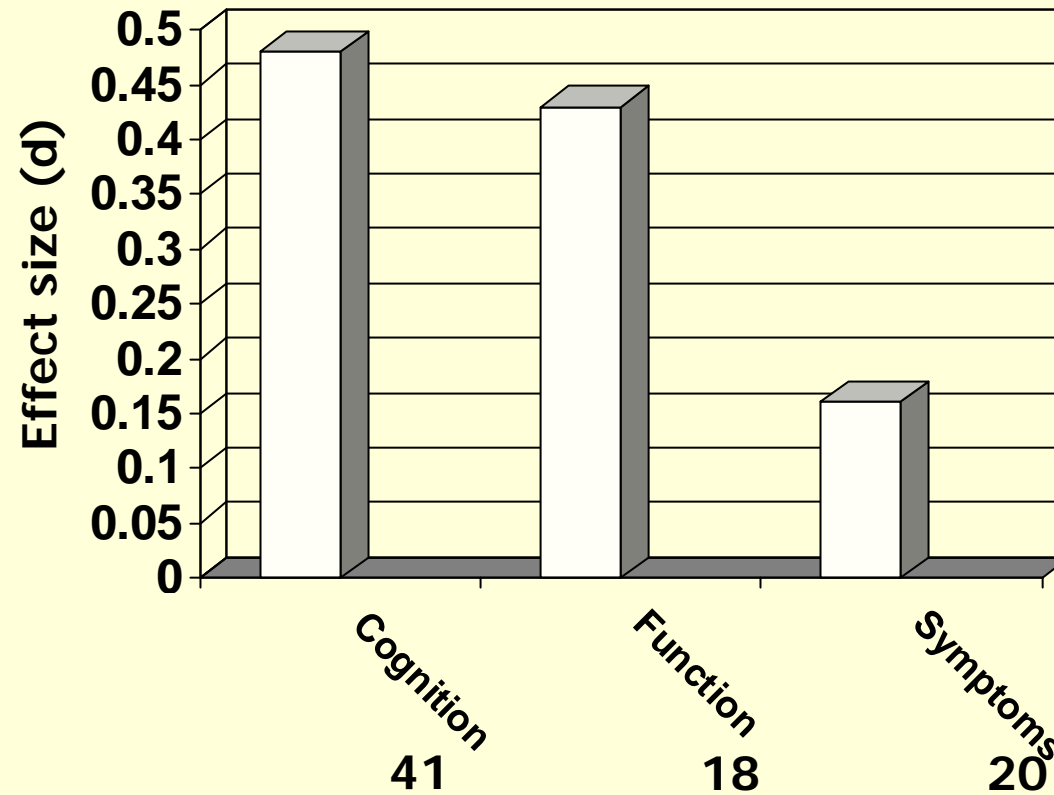
## Is there an effect on function and symptoms?



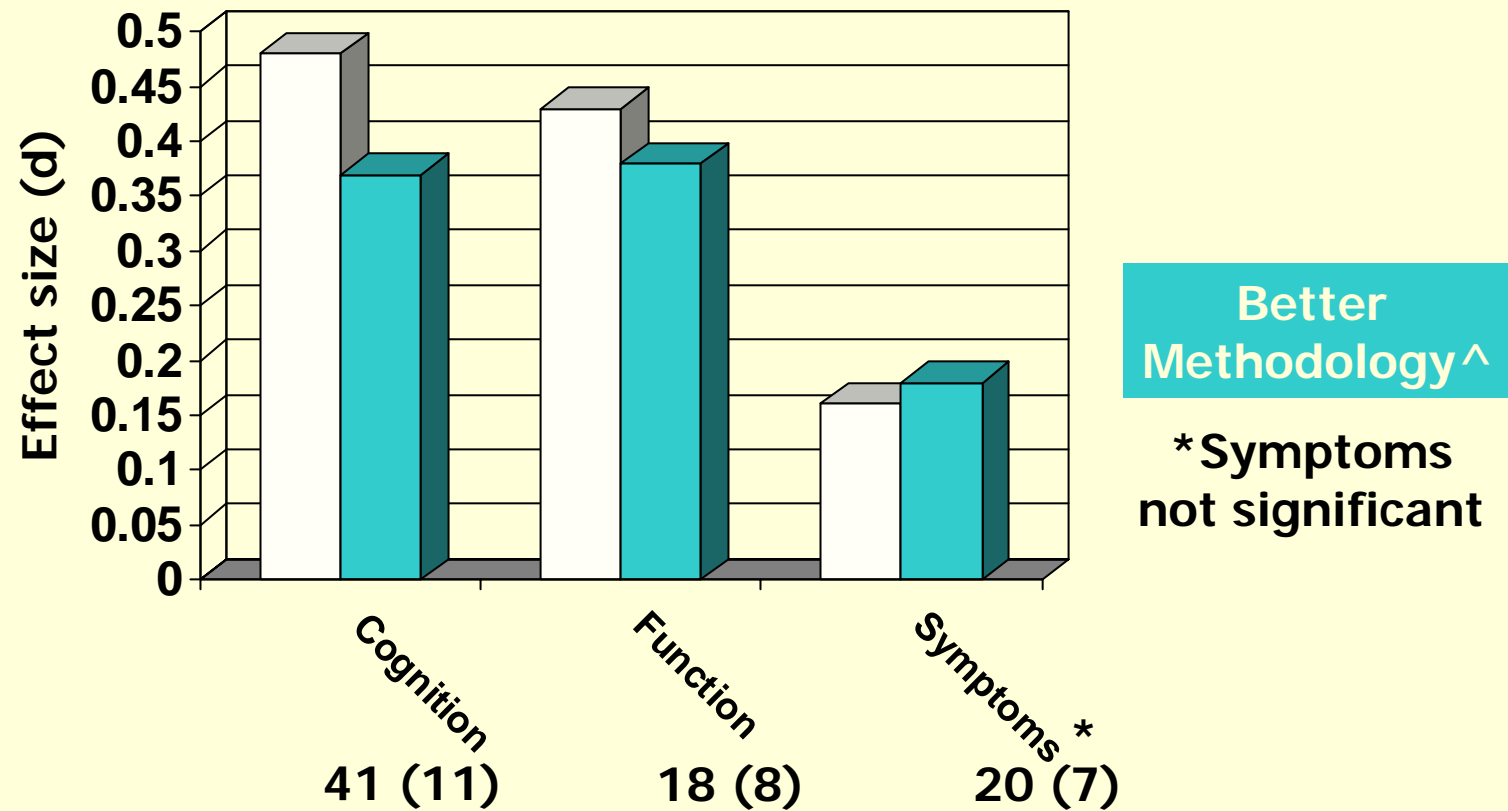
## Is there an effect on function and symptoms?



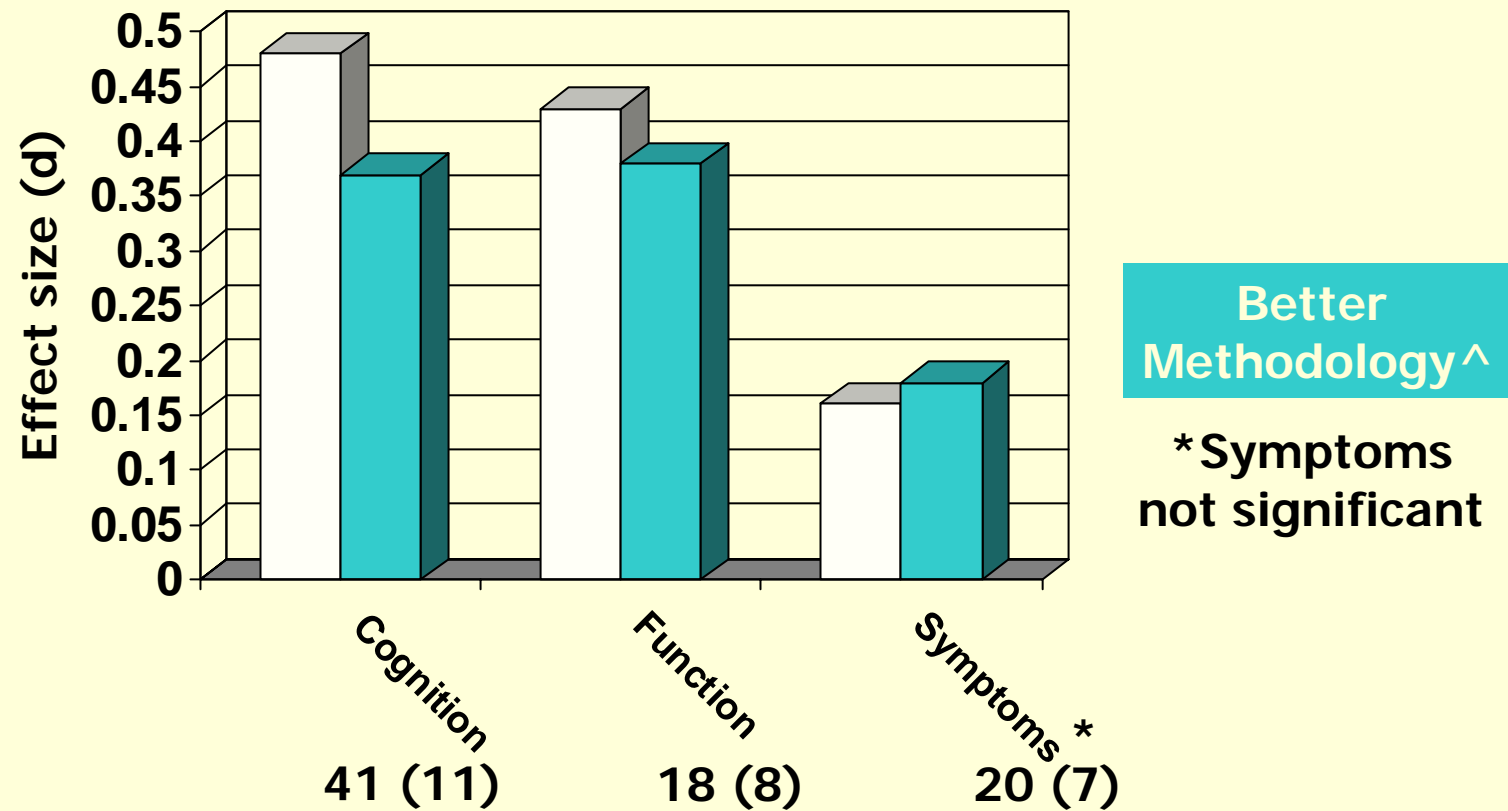
## Is methodology important?



## Is methodology important?

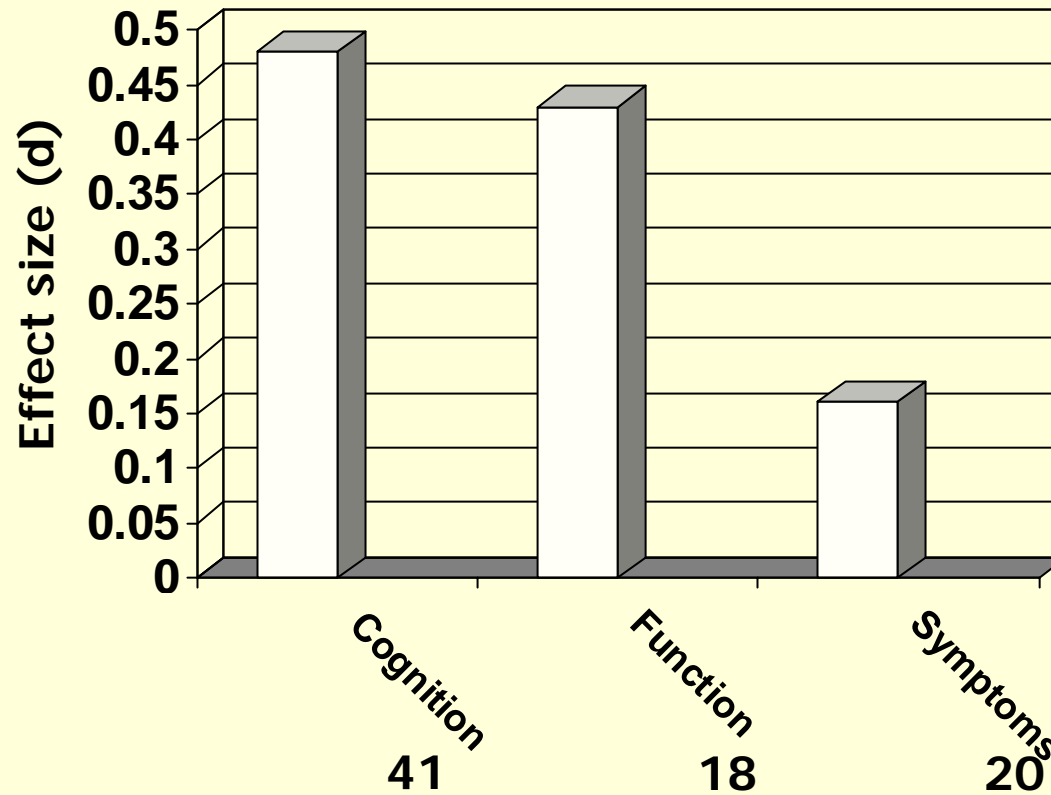


## Is methodology important?

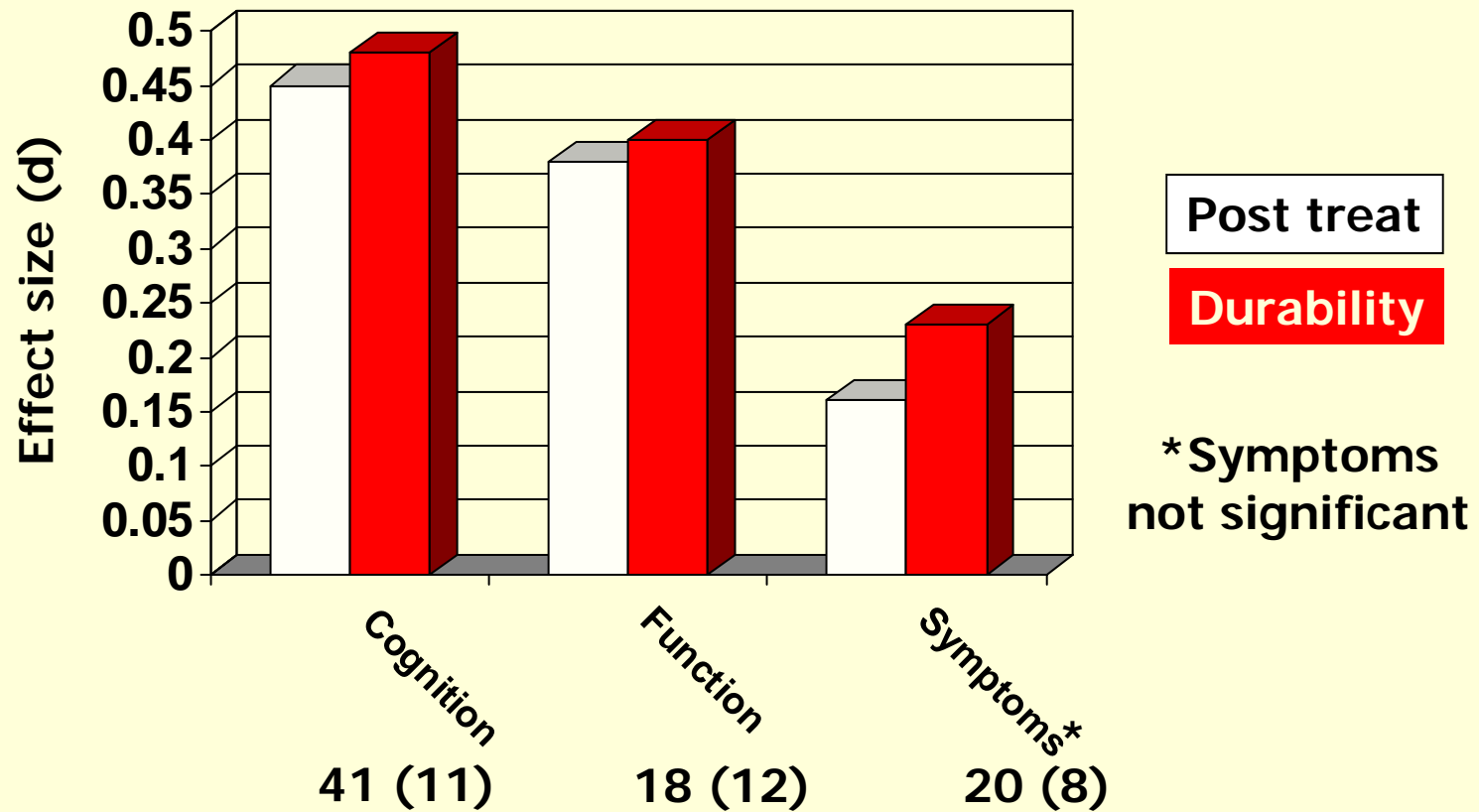


## Is it durable?

Data at 6 months (average)



## Is it durable? Data at 6 months (average)



## Is CRT acceptable to service users?

- 85% of trials have a drop out rate of less than 20%.
- Average 5 % therapy drop out overall.
- Rose et al. (2008) participatory study:
  - CRT is acceptable and valued.
  - **But** side effect.. benefits of CRT on self esteem were linked with improvement on tasks...if clients felt they hadn't improved self esteem scores were lower.

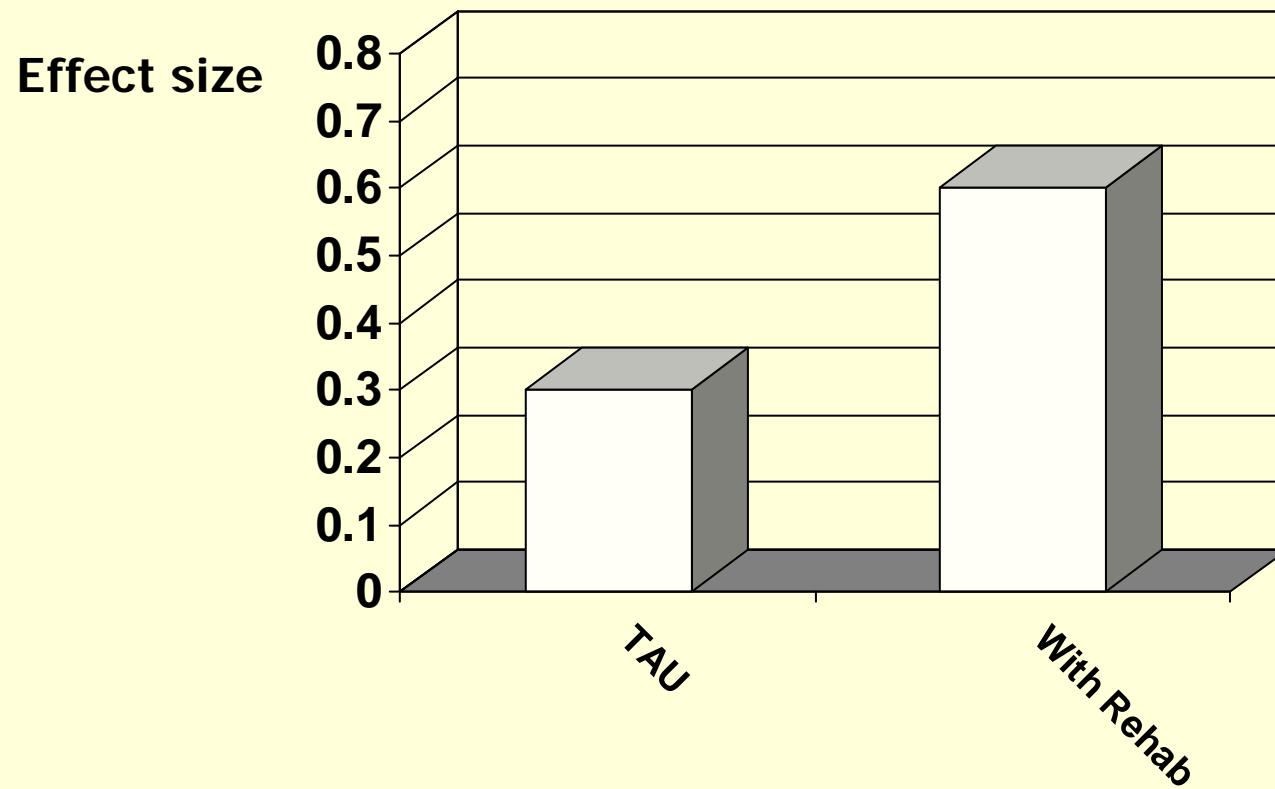
# Do *client characteristics* influence improvement?

- Higher symptoms associated with small cognitive improvement.
- Trials that included only impaired participants showed higher effect size (0.53 versus 0.35)
- Age not significant in meta analysis (but narrow age range?)
- ....two trials suggest younger people do better (McGurk, 2008, Wykes et al. 2009).

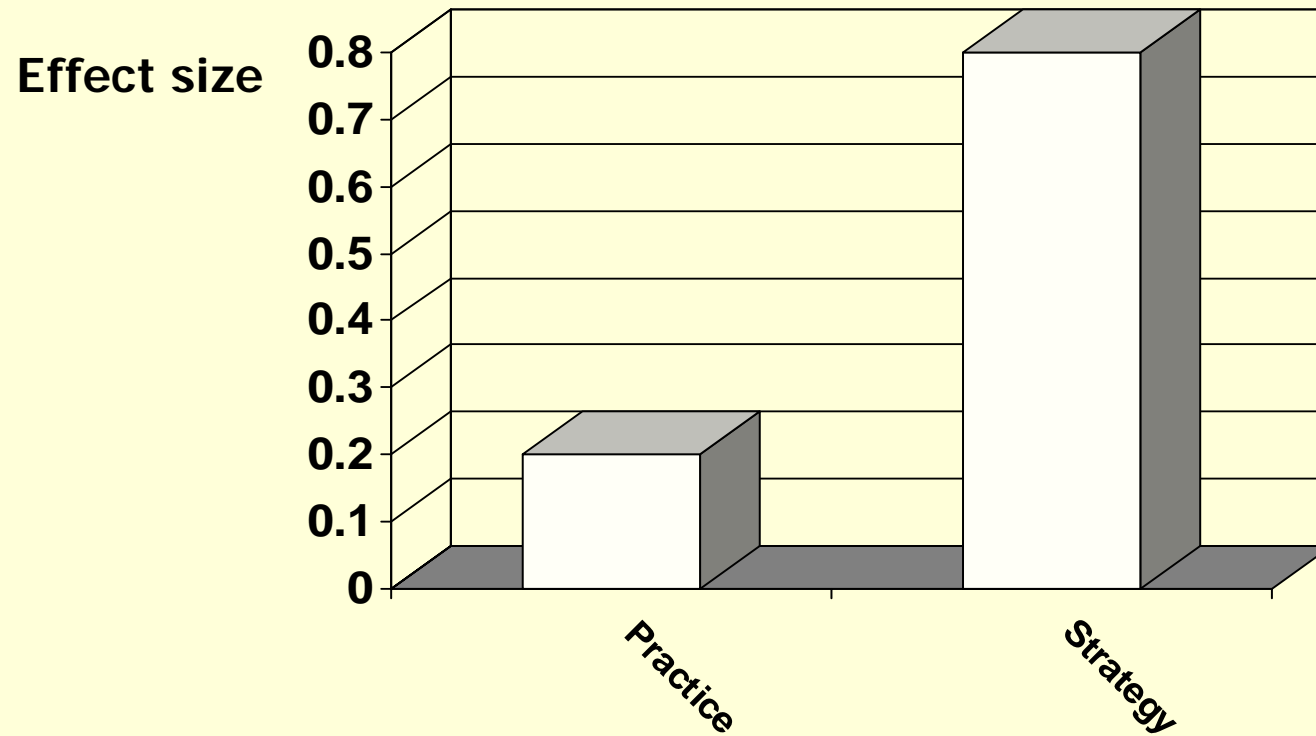
# *And therapy characteristics?*

- Little evidence of effects on **cognition outcome** with:
  - comparison against active control treatment
  - Variable dose (intensity or length of therapy)
  - Approach (strategy based or drill / practice)
  - When adjunctive rehabilitation included in the package of care
- But for the functioning outcomes >

But therapy effects on functioning....



But therapy effects on functioning....



Those with psychiatric rehabilitation (N = 4)

# CRT: summary

- Moderate - and durable effect - on cognitive skills
- Cognitive improvement *generalises* to moderate effects on functioning
- Larger effect on functioning outcomes when
  - a strategy training approach was used and
  - in particular when combination with a rehabilitation package
- Negligible effect on symptoms

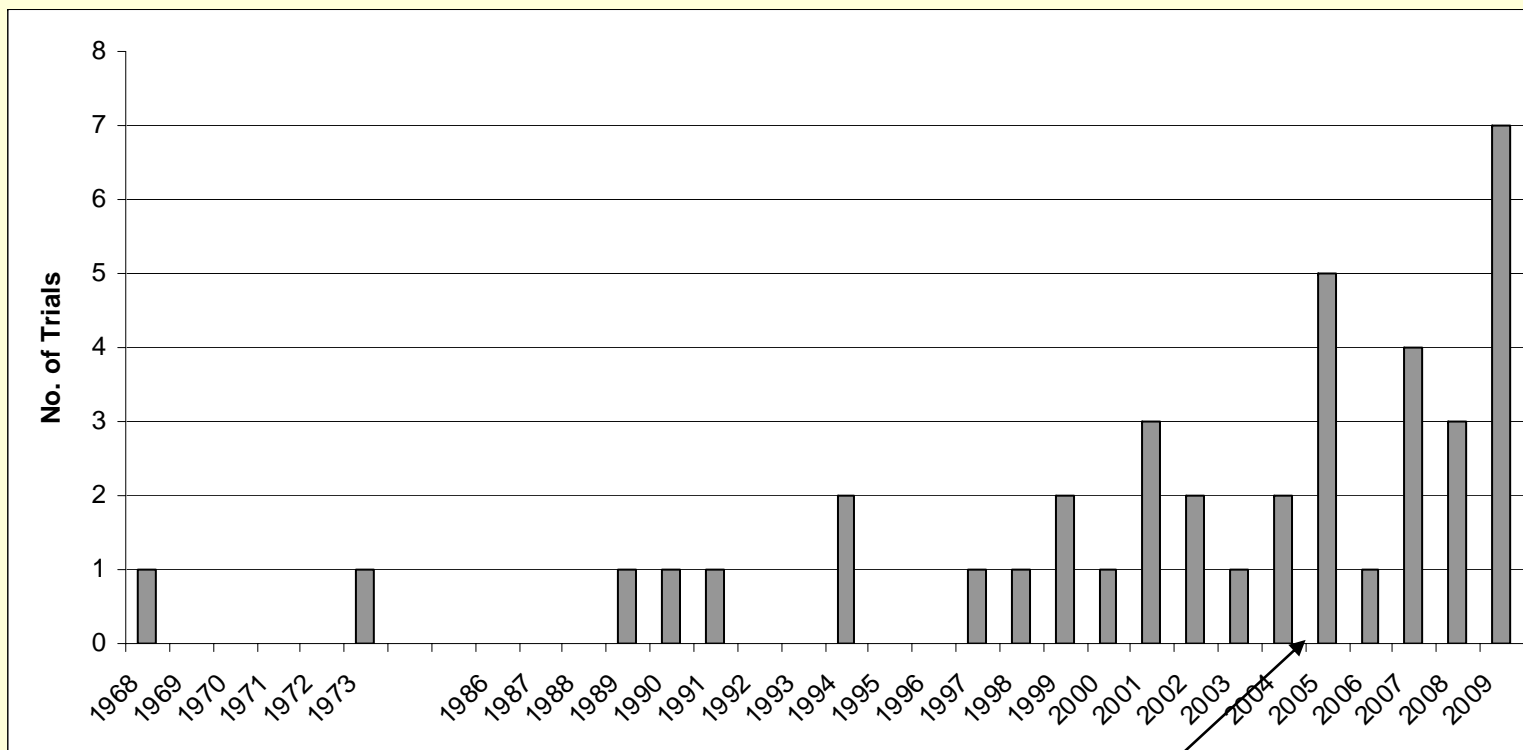
# NICE (2009)

**“there was little consistent advantage of cognitive remediation over standard care and attentional controls.....**

**.....given this finding and the variability in both the methodological rigour and effectiveness of cognitive remediation studies, it was the opinion of the GDG that further UK-based research is required”.**

# Progress since NICE (2009)

- NICE review included 17 trials
- Included trials of cognitive **adaptation**
- Excluded trials
  1. with concurrent vocational rehabilitation
  2. without a functioning outcome
  3. durability data for cognition
- 20 trials published since 2004 - only 4 which included in NICE review



**Half the total trials published 2005 - 2010**

# PORT

(US: Patient Outcomes Research Team)

“rigorous clinical trials are still a minority of studies”

# PORT

(US: Patient Outcomes Research Team)

“rigorous clinical trials are still a minority of studies”

	Methodology score (out of 100)*
CBTp	61.2 (18.0)
CRT	57.0 (12.5)

Not significantly different:  $t(72) = 1.2$   $p > 0.05$

\*Clinical Trials Assessment Measure (Tarrrier and Wykes, 2004)

# PORT

(US: Patient Outcomes Research Team)

“variation among cognitive remediation models and programs is too great to allow identification of key elements of the intervention”

# PORT

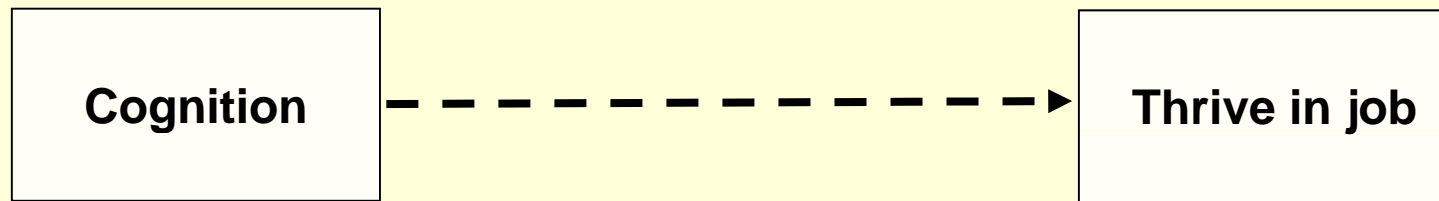
(US: Patient Outcomes Research Team)

“variation among cognitive remediation models and programs is too great to allow identification of key elements of the intervention”

Message: there is a Need for a coherent model!

1. Why is cognition important?
2. What is cognitive remediation therapy (CRT)?
3. What is the evidence that CRT benefits cognition?
4. Do benefits generalise to community functioning?
5. **What about mechanisms for transferring therapy gains to community outcomes?**

# Too simple?



# CRT: summary

- Moderate - and durable effect - on cognitive skills
- Cognitive improvement *generalises* to moderate effects on functioning
- Larger effect on functioning outcomes when
  - a strategy training approach was used and
  - in particular when combination with a rehabilitation package
- Negligible effect on symptoms

# CRT: summary

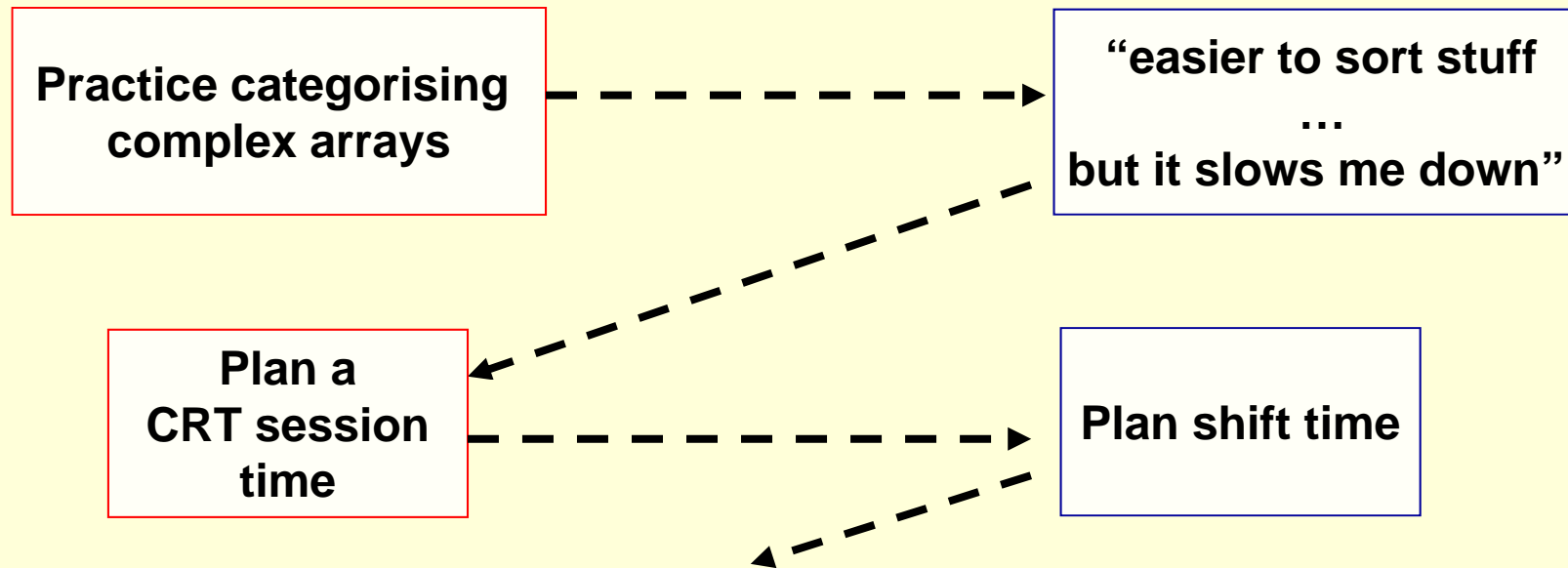
- Moderate - and durable effect - on cognitive skills
- Cognitive improvement *generalises* to moderate effects on functioning
- Larger effect on functioning outcomes when
  - a strategy training approach was used and
  - in particular when combination with a rehabilitation package
- Negligible effect on symptoms

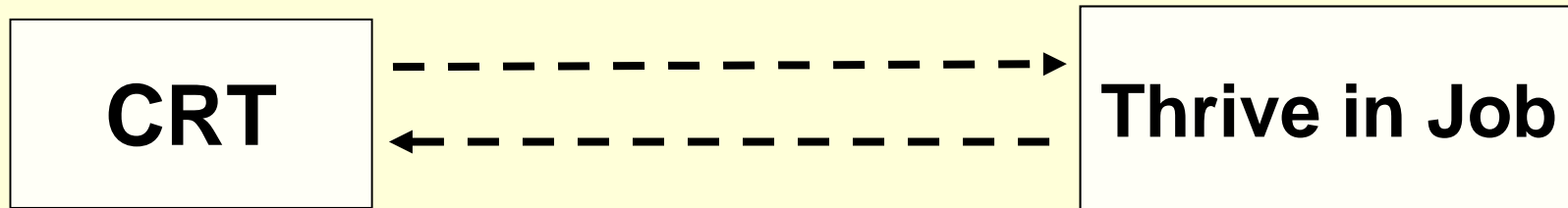
**CRT**

**Work**  
**(e.g. sorting items in a**  
**clothes shop)**

# CRT

# Work (e.g. sorting items in a clothes shop)





Ability to monitor / regulate: (e.g. monitor performance; e.g. notice errors and respond)

Develop Knowledge about thinking ("**I'm impulsive at times**")  
and strategies ("**its useful to stop and plan**")

Notice similarities and draw analogies between CRT tasks and real world tasks and vice versa.

**Meta cognitive skills**

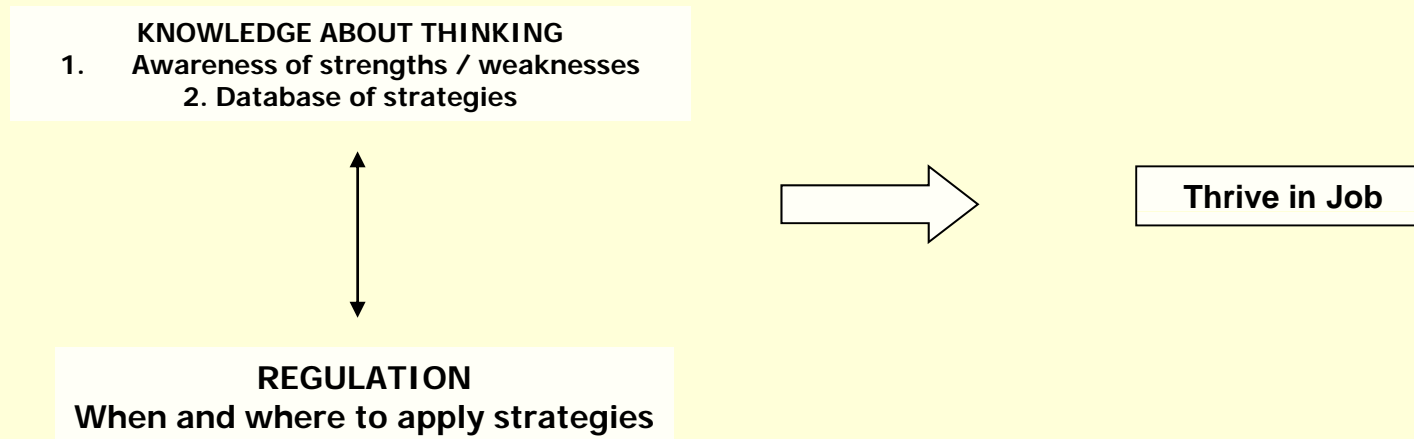
# Meta cognitive skills on WCST

(Koren et al. 2005; Stratta et al. 2008)

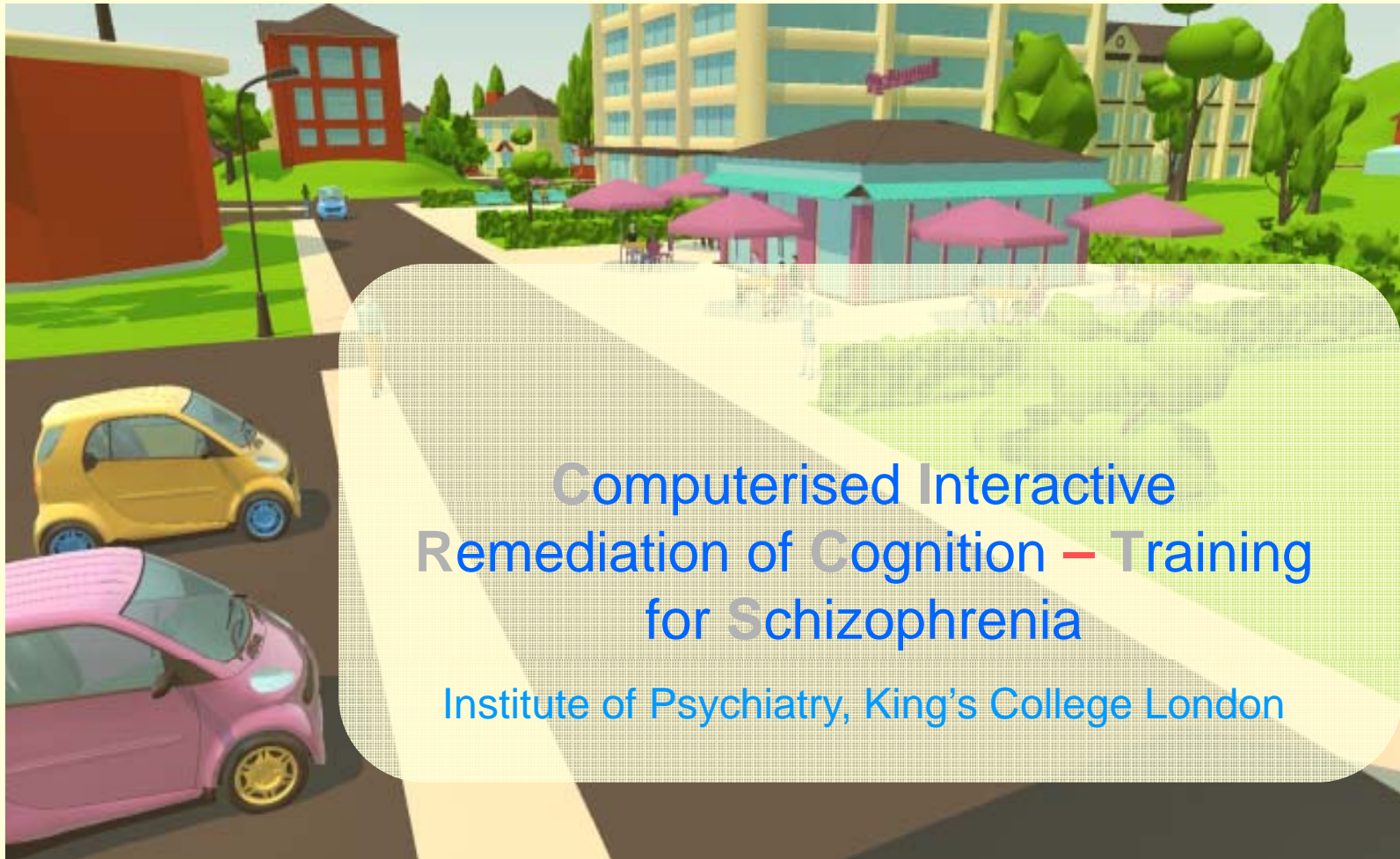
The image shows a screenshot of the Wisconsin Card Sorting Test (WCST) interface. At the top, there are four stimulus cards: a red triangle, two green stars, three yellow plus signs, and four blue circles. Below these is a single green triangle card. The interface is divided into two sections: 'Self monitoring' and 'Self regulation'. The 'Self monitoring' section features a 'Level of Confidence' slider ranging from 0 (Just guessing) to 100 (Completely confident), with a 'Monitoring' button below it. The 'Self regulation' section features a question 'Include sort in final overall score?' with radio buttons for 'yes' and 'no', and a 'Control' button below it. A central green triangle card is positioned between the two sections.

Meta cognitive skills more closely associated **clinical insight** (Koren et al. 2005) and **social functioning** (Stratta et al. (2008) than conventional measures.

# CRT aimed at meta cognitive skills should...



# What about meta cognitive skills in CRT?



Key

Clear

从点化本文格只中电将来用业向即三内脑在说户级

a b c d e f g h i j k l m n o p q r s t u v

企面种片

w x y z

Message

种电三三文文

Type Your Answer Here:

Key

从点化本文格只中由将去用业向即三内脑在说户级  
a b c d e f g p q r s t u v

企面种片  
w x y z

Message

种电三三文文

Type Your Answer Here:

**Before you start...**

**Task Difficulty**

How difficult do you think this task will be? (1=easy to 5=difficult)

1 2 3 4 5

**Task Length**

How many minutes do you think this task will take?

0-1 1-3 3-9 9-15 15+

OK

Key

从点化本文格只中由将要用业向即三内脑在说户级

a b c d e

p q r s t u v

企面种片

w x y z






Message

种电三三文

Type Your Answer Here:

### Strategy Selector

Choose from the available strategies below:

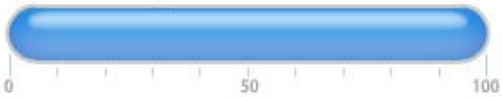
-  Highlight the code
-  Guess the rest of the word when you've seen enough
-  Use your mouse to scan the code grid
-  Check that your message makes sense
-  Cross off each symbol as you translate it

OK

## Codes

### Score

Well done, you've finished the task!



You used the hint 0 times.

### Task Difficulty

How difficult did you find this task?

EASY-----HARD



It took you 0 minutes.  
Your initial estimation was 2 minutes.

### Strategies

How useful were the strategies?

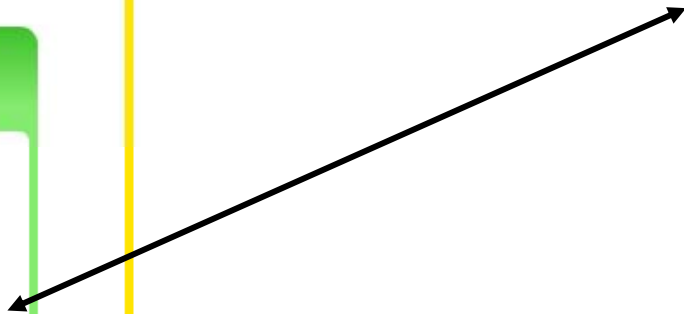
USELESS-----USEFUL



Highlight the code



Other



C I R C U I T S

00:08

T

Your Journey



Your Location



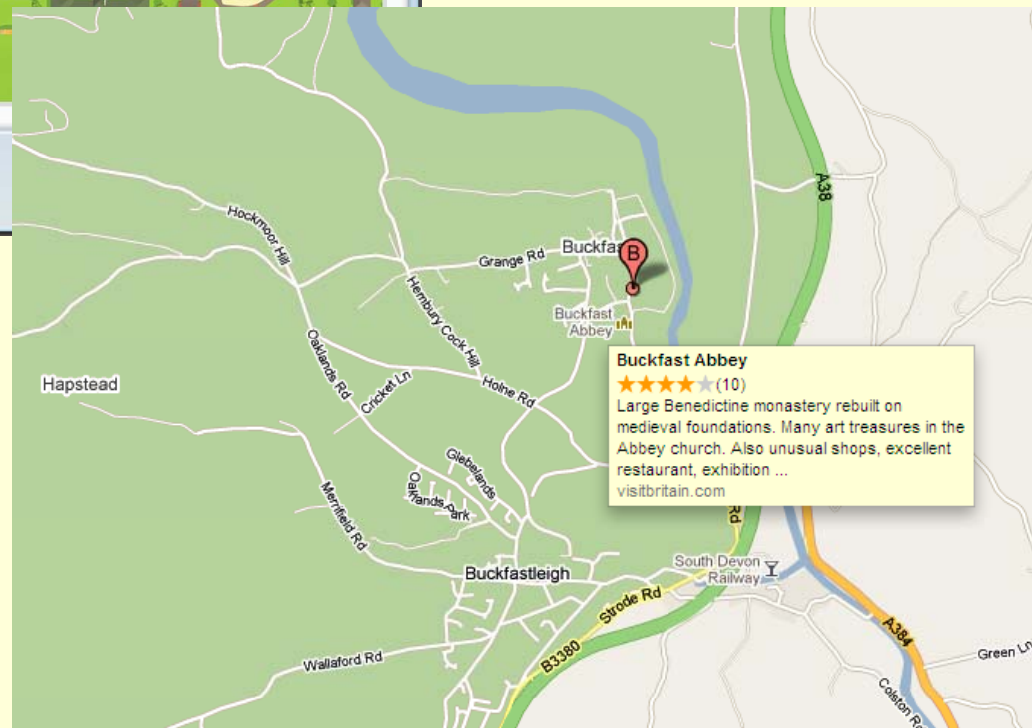
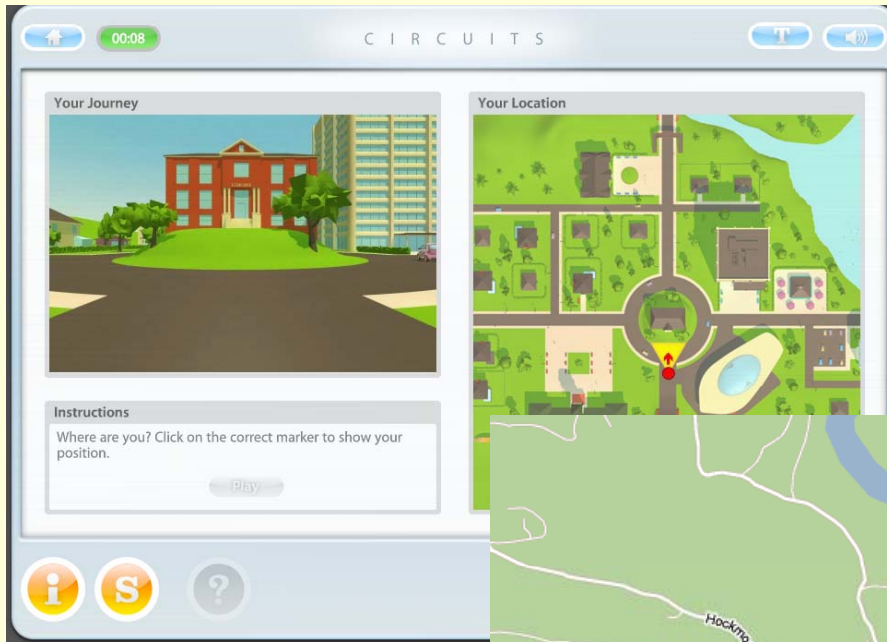
Instructions

Where are you? Click on the correct marker to show your position.

Play

i S ?

Done



# Feasibility study

- Clients (N = 5) rated circuits as:
  1. Attractive
  2. Culturally appropriate
  3. Age appropriate
  4. Clear and understandable
- The same participants also bug tested and suggested numerous design changes.

# Circuits

- Provides additional measures of the “process” of change in response to CRT
- Easily transportable – can operate without an internet connection.
- Potentially less therapist (and client) fatigue
- Administering a computerised therapy requires less specific training for therapists.....however.....

# Circuits

## Therapists have a key role in CRT

- Facilitate training > promote metacognition
- Facilitate goal setting and monitoring.
- Develop and use *working alliances* with people who have either frequently suffered stigma in educational contexts or have been socially excluded, or both.
- Trust, mutual confidence and acceptance are important for engagement.

1. Is cognition important? ✓
2. Does CRT benefit cognition? ✓
3. Do benefits generalise to community outcomes? ✓
4. Do we know how generalisation takes place? ?