Trials and tribulations:
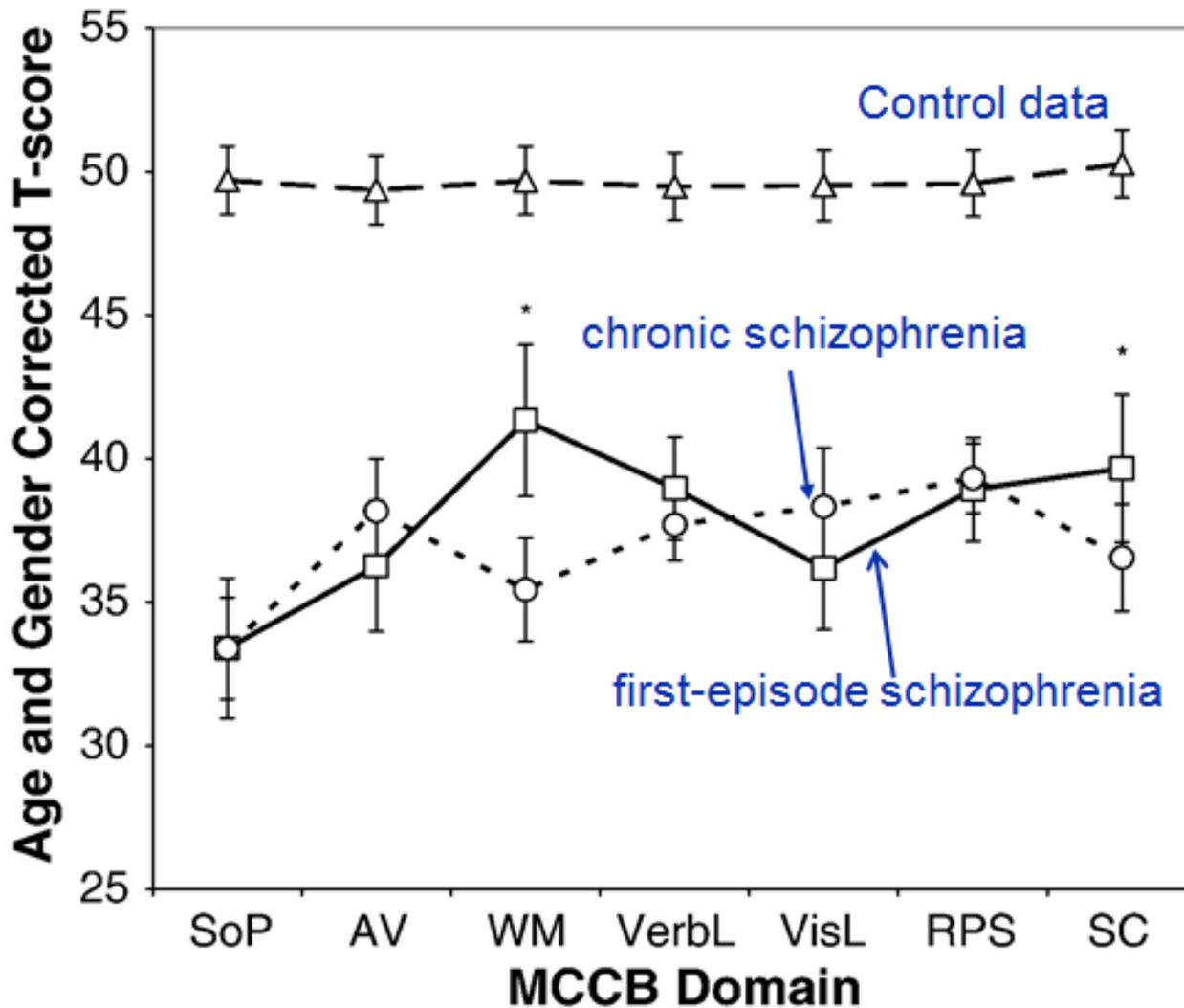## Personalising cognitive treatment in schizophrenia
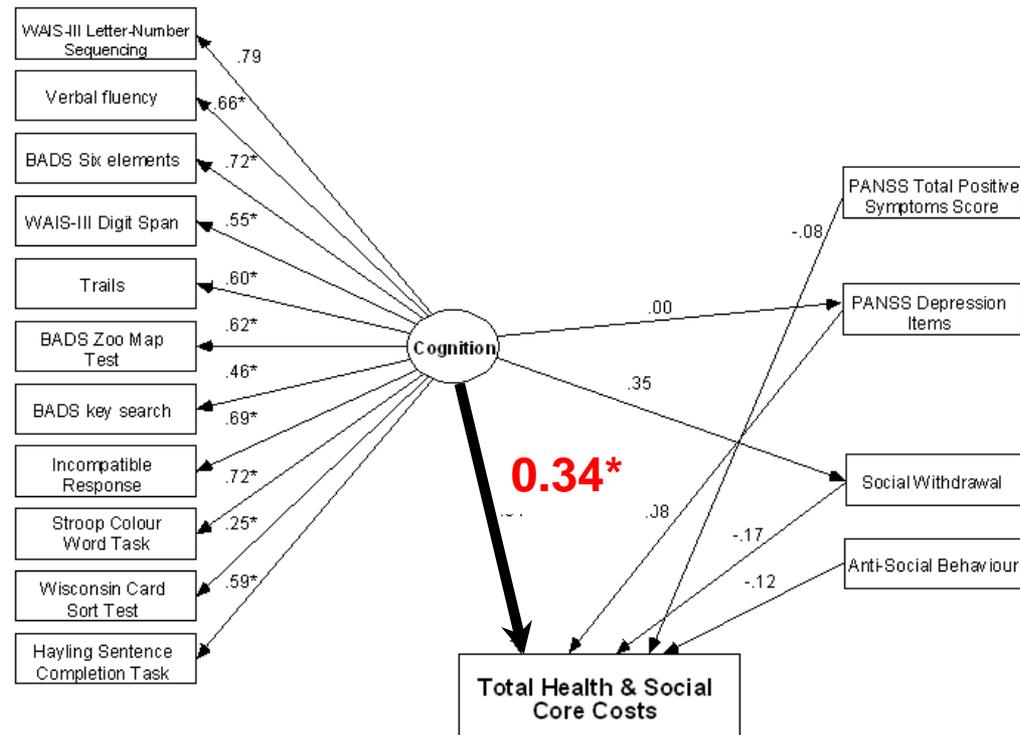
Til Wykes

Institute of Psychiatry, Psychology and Neuroscience

King's College London

ISCTM Feb 2015

SoP: Speed of Processing, AV: Attention/Vigilance, **WM: Working Memory**, VerbL: Verbal Learning,
VisL: Visual Learning, RPS: Reasoning and Problem Solving, **SC: Social Cognition**,

McCleery et al., 2014; Sz.Res.

Structural Equation model with only one cognitive variable

Cognition difficulties predict cost

*Significant at the 0.05 level

First episode

"I was looking at A or B for some subjects now I'm looking at C or D if I'm lucky."

"Memory loss is the new thing that's bothering me."

"I have low concentration"

"I'm coming to terms with the fact that I have got a learning difficulty."
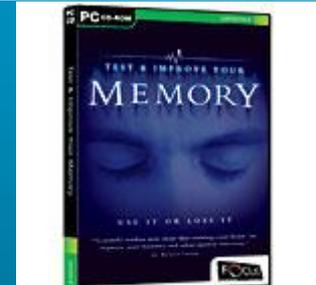
Michael, Aged 16 years

What should we do about it?

Cognitive remediation

CRT is not …….
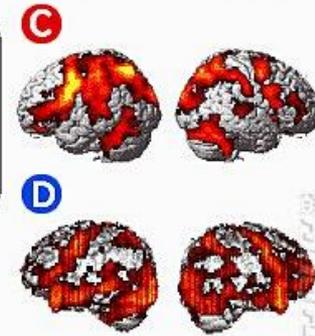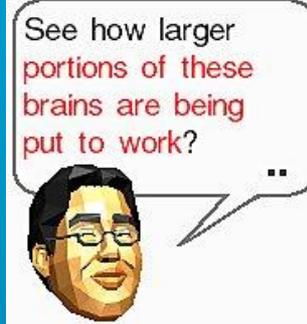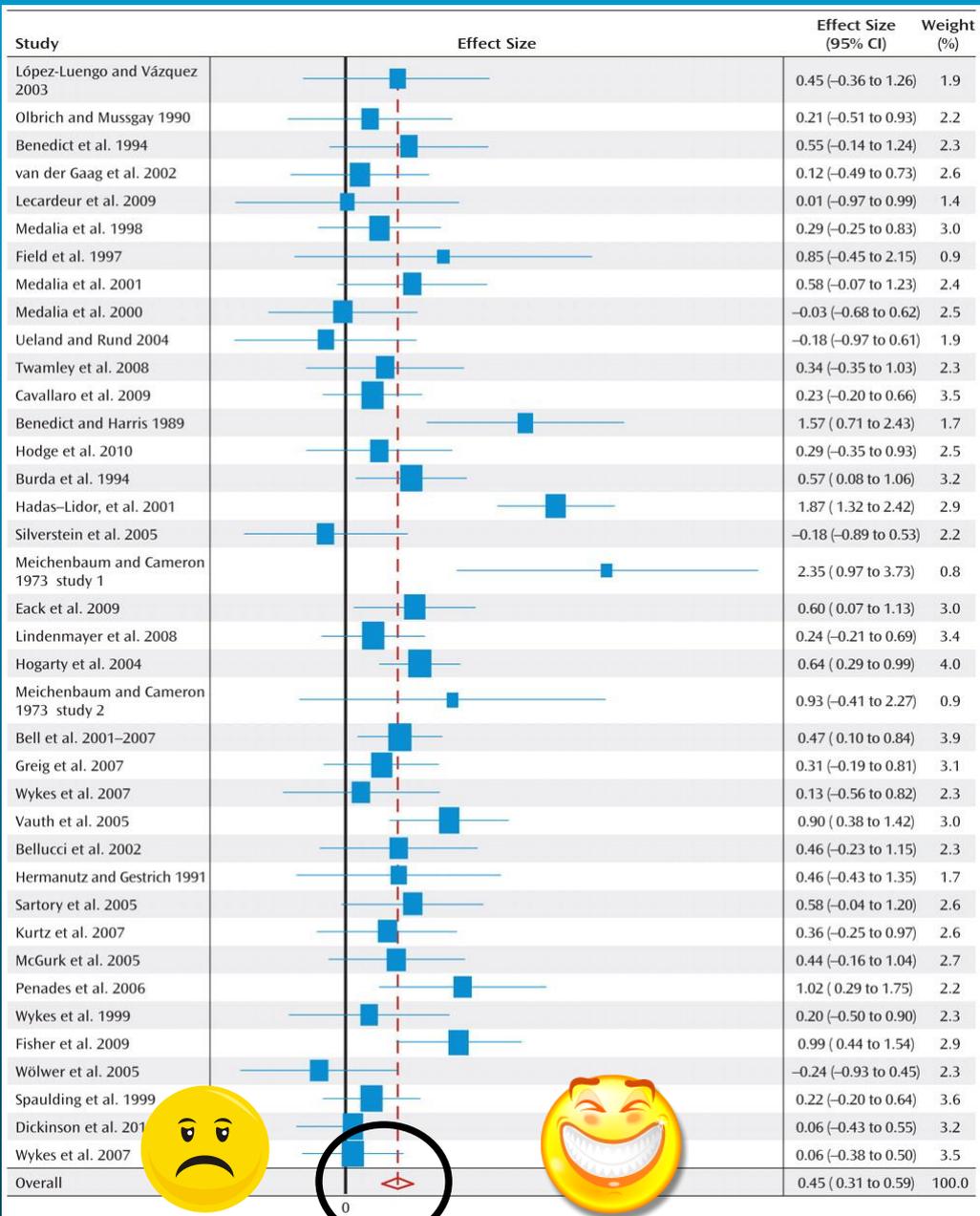
Is cognitive remediation effective?

Meta-analysis 1982 participants Effect size 0.45

Wykes et al., 2011

Transfer: How is cognition related to outcome?

Too simple?

How do they work?

Wykes, Reeder, Huddy, Rice, Taylor, Wood, Ghirasim, Kontis & Landau, 2012
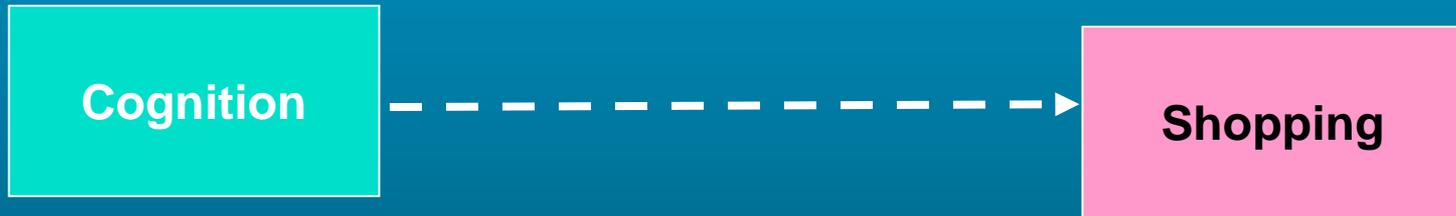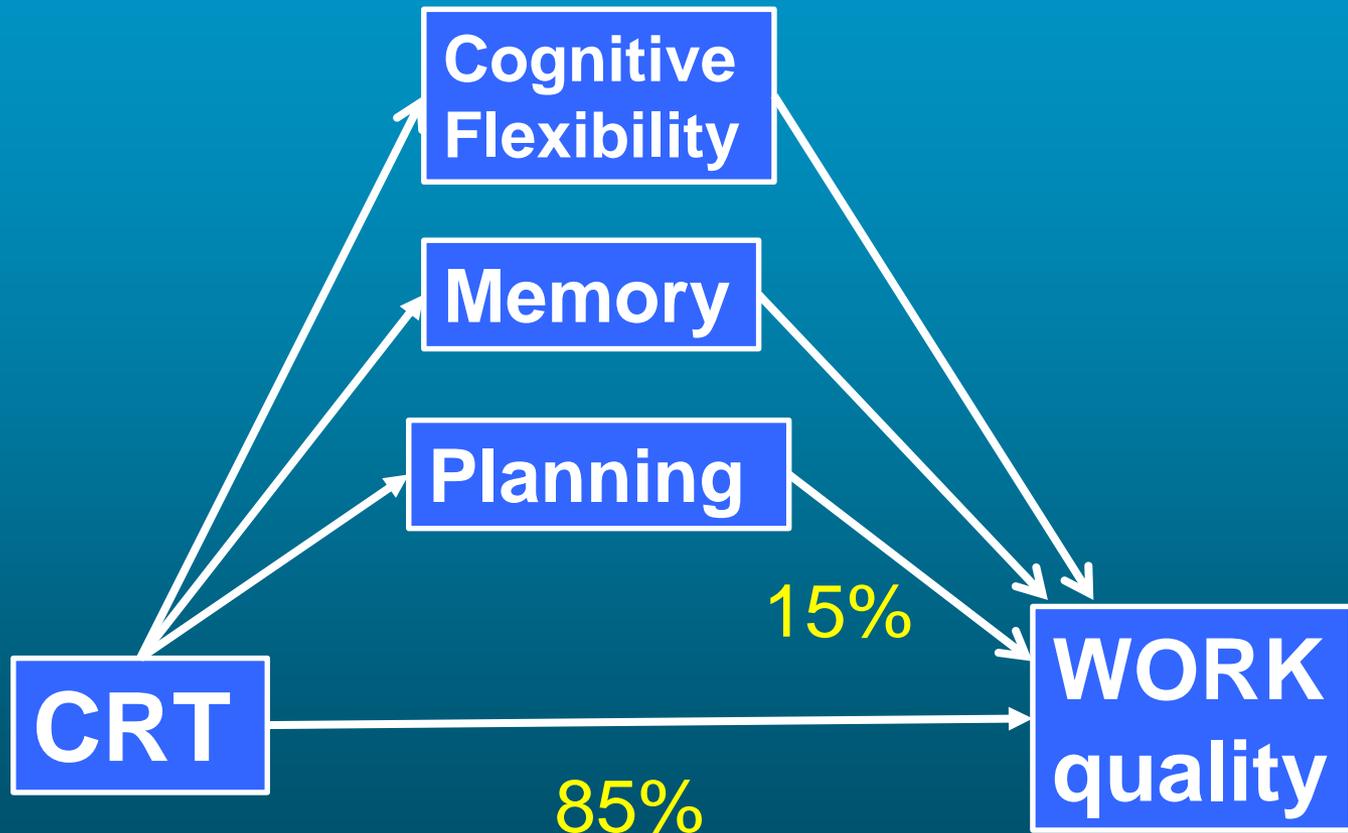
Optimising transfer to valued recovery outcomes

Models are not mutually exclusive or exhaustive…

Figure 2: Effects of mediator or moderators on behaviour change
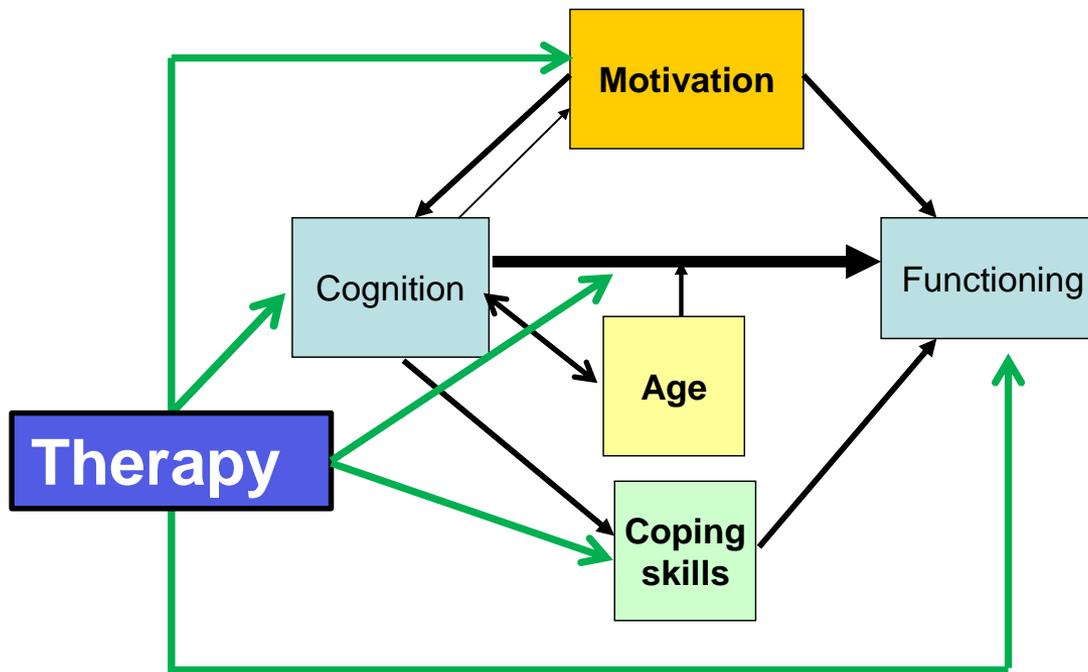
The personalisation agenda
not all improve hence the modest effects

- **For whom**
  - For older or younger people?

- **When**
  - When symptoms are stable or functioning is poor?

- How
  - Which therapies?

Limits of meta-analyses ...

- Age suggested as affecting outcome
  - McGurk and Mueser 2008, Wykes et al 2009, Kontis et al, 2013

- Average age in studies is 35.8 years

- 65% studies had an average age between 30 and 40 years

Where to next?

1. Improving transfer to functional recovery
2. Cost effectiveness, utility, benefit
3. Mechanisms of action
4. New targets for CRT
5. Augmenting CRT

For large scale roll out to services

Where to next?

A large scale database of participant level data would help

DoCTRS

Database of Cognitive Training and Remediation Studies

DoCTRS

Currently 7 studies, 430 participants,
(143 female; 287 male; Mean age: 34.5)

Messy data

- Mainly small studies
- Unbalanced groups
- Population sub-structure
- Missing data
- Multicollinearity
- Validating predictive models

Study 1: Make the database useful

- **Calibration** to relate different measures of the same underlying construct (e.g. 99 measure of cognition) using latent class modelling

- Employ **missing data** methods using multiple observations of a similar construct to improve current imputation methods

- Create **user-friendly software code** which can be used by mental health researchers and clinicians

Study 2: Identify mediators and moderators

- Identify moderators and composite scores of moderators of therapy treatment heterogeneity

- Use innovative statistical and machine learning algorithms to identify those that predict successful (and unsuccessful) outcomes

- Inform strategies for carrying out pooled mediation analyses to understand pathways leading to outcome improvements under therapy (meta-mediation analysis)

Trials and tribulations

- **Building the database**
  - To submit that is the question - PIs have the option of submitting data to the database

- **Attributing authorship?**
  - Career prospects
  - Guaranteeing database credit - if a database is publicly available e.g. ONS - credit data source

- **Wasting time**
  - Poor science through invalid questions
  - Fishing exercises
  - Duplication of effort – the problem of competition

But it can happen

- Public grant funders demand we provide publically accessible databases - but we need to consider international collaboration

    - **ALSPAC** – a national UK birth cohort
    - **ATLAS** – studies at CERN - Higgs Boson etc
    - **ONS** – UK population statistics
    - **GWAS consortia** e.g. Wellcome Consortium

ATLAS organisation

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Deputy: K. Tokushuku)

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Just the "A"s

Conclusion

1. Improving transfer to functional recovery
   - Need mediation and moderation analyses

2. Cost effectiveness, utility, benefit
   - Comparison between studies provides indicators of costs and level of benefits

3. Mechanisms of action
   - Test different models across data sets

4. New targets for CRT
   - Already identified one potential target

5. Augmenting CRT
   - Testing different augmentation strategies against each other to find signals

Then we can have large scale roll out to health services