Predicting the effect of interventions in psychiatry

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Acknowledgements:
Robert Bertram
Anonymous referee for JECP
Prediction: Will it work?

• EBM for CRHTT for junior doctors
  – Mill’s method of difference
  – Interpretation RCTs, if possible, otherwise pre-post studies, or area comparison

• Problems-Role of diagnosis/classification

• Capacities (approximation)/Mechanisms?
• Empirical Evidence?
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UK-style home treatment teams

• Treating people at home instead of hospital admission
• Complex intervention
• Complex environment

• One RCT (published 5 years after UK wide roll out)
• Observational studies contradictory results
Main findings: reduction in bed days and admissions

6 months
CRHTT 29% admitted, TAU 67% admitted, \( p<0.001 \)

Beddays in hospital
CRHTT 16.1 TAU 35.0, \( p<0.001 \)
Tyrer et al. 2010
The Psychiatrist, 34, 50-54

Complicated design, 9 months period
Pre-post comparison and catchment area comparison

Pre-CRHTT  222 admissions per 1000
Post-CRHTT  205 admissions per 1000, n.s.

Control area  598 admissions per 1000
552 admissions per 1000, n.s.

Total beddays $p=0.041$ for CRHTT, $p=0.073$ Control area
Pre-post comparisons

• Johnson et al (2005) pre-post 6 months difference in adm $p<0.01$, difference in bed days n.s.
• Forbes et al. (2010) n.s.
• Barker et al. (2011) $p<0.001$ (average length of stay)
• Jacobs and Barrenho (2011) n.s.
• Etc. Hubbeling and Bertram, Journal of Mental Health 2012
Different results

- Limited evidence and contradictory results
- Applying hierarchy not appropriate, although this is what the RCPsych exam committee wants
North Islington study

Complicated consent procedure
- reason only 1 RCT done
- bias introduced

1. Patients with decisional capacity consented

2. Patients known to services who were informed about study and who did not opt out

3. Patient's whose carer consented

For 2. and 3. consent was obtained later in the study

Probably less ill patients
survey 2005-2006
243 teams 177 responses

1. alternative to hospital admission for acute mental health difficulties 98%
2. intense involvement until crisis is resolved 97%
3. gatekeeper to acute in-patients beds 72%
4. on call or on duty between 10 p.m. and 8 a.m. 67%
5. 7 days a week 24 hrs telephone support service 63%
6. 7 days a week 24 hrs home visiting service 55%

(Onyett et al. Psychiatric Bulletin 2008)
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• ‘Effectiveness predictions are always dicey’
  *(Cartwright, Lancet, 2011)*

• From does it work somewhere to will it work for us
  *(Cartwright and Munro, JECP, 2010)*
• Also in specific CRHTT there must be 70% improvement in patients with depression
Tentative Solution

• More RCTs probably not useful, how can you compare results?
• Tentative approximate solution: Different patients different diagnoses
• Check appropriate treatment each diagnosis
• Guidelines/Empirical data
  – Somebody with depression recommended treatment
Diagnosis in psychiatry

• Debate about homosexuality in -70.
• Diagnosis in psychiatry is to a large extent classification by consensus, not cutting nature at its joints
  (Cooper, HoP, 2004)

• But almost all empirical studies refer to diagnosis (some like the CRHTT to the intervention)
Improving diagnosis

- DSM-V/ICD-11
- Endophenotype \(^{(Gottesman \ and \ Gould \ et \ al. \ AJP, \ 2003)}\)
- Latent class analysis \(^{(Cramer \ et \ al., \ BBS, \ 2010)}\)
  - Based on self-reports psychological states
  - Post-hoc rationalisations/Multiple realisability problem

- Limited data available
Also in specific CRHTT there must be 70% improvement in patients with depression
Solution?

- Within home treatment only type of subgroups for which there are empirical data available are different diagnostic categories.
- Look at patients with particular diagnoses and see whether guidelines are implemented.
- Look at outcomes for different patients.
- If not the same as in RCTs try to explain the difference.
- Example Depression.
• Nemeroff et al. (2003) depression + childhood trauma better outcome with psychotherapy.
• Fournier et al. (2008) depression + personality disorder better outcome with pharmacotherapy.
• Kirsch et al. (2008) antidepressants do not work for mild to moderate depression.
• Thase et al. (2011) antidepressants do work with mild to moderate depression.
• Whittington et al. (2004) SSRIs with in children.
• Coryell et al. (2012) worse outcome if also anxiety disorder.
Representativeness

- 346 ‘depressed’ patients
- 29 suitable for inclusion

Article

Are Subjects in Pharmacological Treatment Trials of Depression Representative of Patients in Routine Clinical Practice?

Mark Zimmerman, M.D.
Jill I. Mattia, Ph.D.
Michael A. Posternak, M.D.

Objective: The methods used to evaluate the efficacy of antidepressants differ from treatment for depression in routine clinical practice. The rigorous inclusion/exclusion criteria used to select subjects for participation in efficacy studies potentially limit to the depressed patients to determine how many would have qualified for an efficacy trial.

Results: Approximately one-sixth of the 346 depressed patients would have been excluded from an efficacy trial because
DEPRESSION

MORE SPECIFIC TREATMENT

70% improvement

80% improvement ????
Personalized Medicine for Depression: Can We Match Patients With Treatments?

‘While individuals vary widely in response to specific depression treatments, the variability remains largely unpredictable’.

In other words: **no subgroup of patients can be identified before starting treatment** for whom this particular treatment will be effective.

Question whether past history for individual patients would be predictive
Specific form of depression

MORE SPECIFIC TREATMENT

100% improvement ???
DULOXETINE
Additional information interactions (Duloxetine).

Indications
major depressive disorder; generalised anxiety disorder; diabetic neuropathy (section 6.1.5); stress urinary incontinence (section 7.4.2)

Dose
Major depression, adult over 18 years, 60 mg once daily
Generalised anxiety disorder, adult over 18 years, initially 30 mg daily, increased if necessary to 60 mg once daily; max. 120 mg daily
Diabetic neuropathy, adult over 18 years, 60 mg once daily; max. 120 mg daily in divided doses

Note
In diabetic neuropathy, discontinue if inadequate response after 2 months; review treatment at least every 3 months

For incontinence
Dose
adult over 18 years, 40 mg twice daily, assess for benefit and tolerability after 2–4 weeks

Note
Initial dose of 20 mg twice daily for 2 weeks can minimise side-effects
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• A kind of research program check whether results are the same and if not why not?

• Could be diagnosis and/or treatment needs to be adjusted
Prediction: Will it work?

• For Home Treatment Teams look for evidence for each condition, pragmatic choice because some data available

• But is this looking for mechanisms or capacities?

• Certainly not fixed causal contributions, only certain percentage will improve
No fixed causal contributions

• But causal claims are made
• It also seems reasonable to tell patients with depression that most people with that condition improve with treatment
• Knowledge of treatment for depression is limited, patients might change and treatment might change
• Approximate capacities
What to do?

• Looking at treatment for depression in CRHTTs
  – Same effect
  – If not why not?

• Kind of provisional endpoint
• Fixed causal contribution impossible
• This is not looking at capacities or mechanisms but some approximation
• Thank you
• Questions?
• Comments?
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