South West London and St George's NHS
Mental Health NHS Trust

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

Johnson et al. BMJ 2005, 559-564
North Islington Study

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

Cite this article as: BMJ, doi:10.1136/bmj.38519.678148.8F (published 15 August 2005)

Papers

Randomised controlled trial of acute mental health care by a crisis resolution team: the north Islington crisis study

Sonia Johnson, Fiona Nolan, Stephen Pilling, Andrew Sandor, John Hoult, Nigel McKenzie, Ian R White, Marie Thompson, Paul Bebbington

Abstract

Objective To evaluate the effectiveness of a crisis resolution team.
Design Randomised controlled trial.
Participants 260 residents of the inner London Borough of Islington who were experiencing crises severe enough for

previous randomised trial has evaluated crisis resolution teams in the context of a modern community mental health system, although our recent naturalistic study suggested reduced admission rates and better patient satisfaction after their introduction.[10]

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

Controlled comparison of two crisis resolution and home treatment teams

P. Tyrer,[1] F. Gordon,[1] S. Nourmand,[1] M. Lawrence,[2] C. Curran,[2] D. Southgate,[3] B. Oruganti,[4] M. Tyler,[5] S. Tottle,[5] B. North,[1] E. Kulinskaya,[1] J. T. Kaleekal,[4] J. Morgan[2]

The Psychiatrist (2010), **34**, 50–54, doi: 10.1192/pb.bp.108.023077

[1]Imperial College London; [2]Pendine Centre, Cardiff; [3]Whitchurch Hospital, Cardiff; [4]South Cardiff Crisis Resolution and Home Treatment Team; [5]Cardiff and Vale NHS Trust
Correspondence to Peter Tyrer

Aims and method To compare an existing crisis resolution service with a new crisis resolution team (CRT) in Wales. The impact of the new team was measured by changes in bed days and admissions. A random sample of patients from each service was assessed for service satisfaction, social functioning and quality of life after first presentation.

BRITISH JOURNAL OF PSYCHIATRY (2000), 177, 43–46

Outcomes of crises before and after introduction of a crisis resolution team

SONIA JOHNSON, FIONA NOLAN, JOHN HOULT, IAN R. WHITE, PAUL BEBBINGTON, ANDREW SANDOR, NIGEL McKENZIE, SEJAL N. PATEL and STEPHEN PILLING

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

Johnson et al. BMJ 2005, 559-564
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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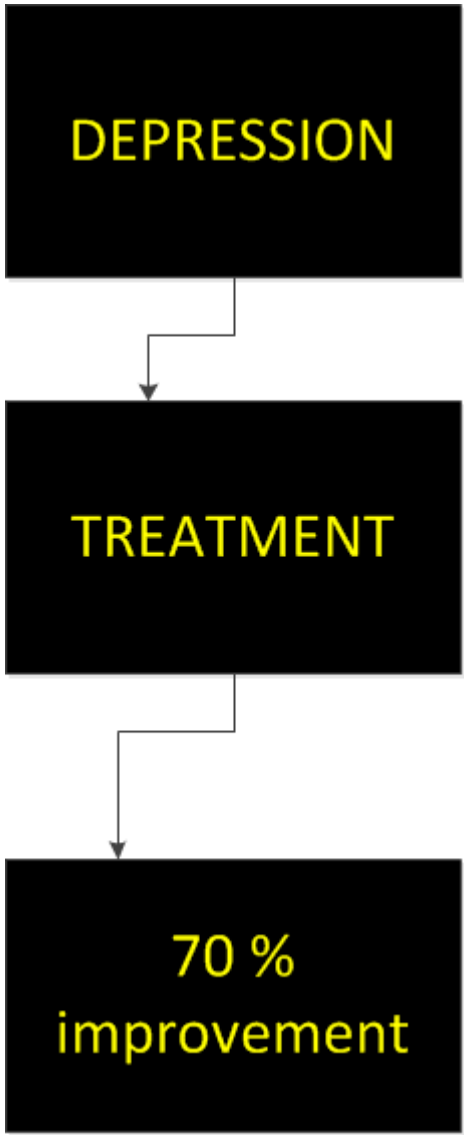
Different results

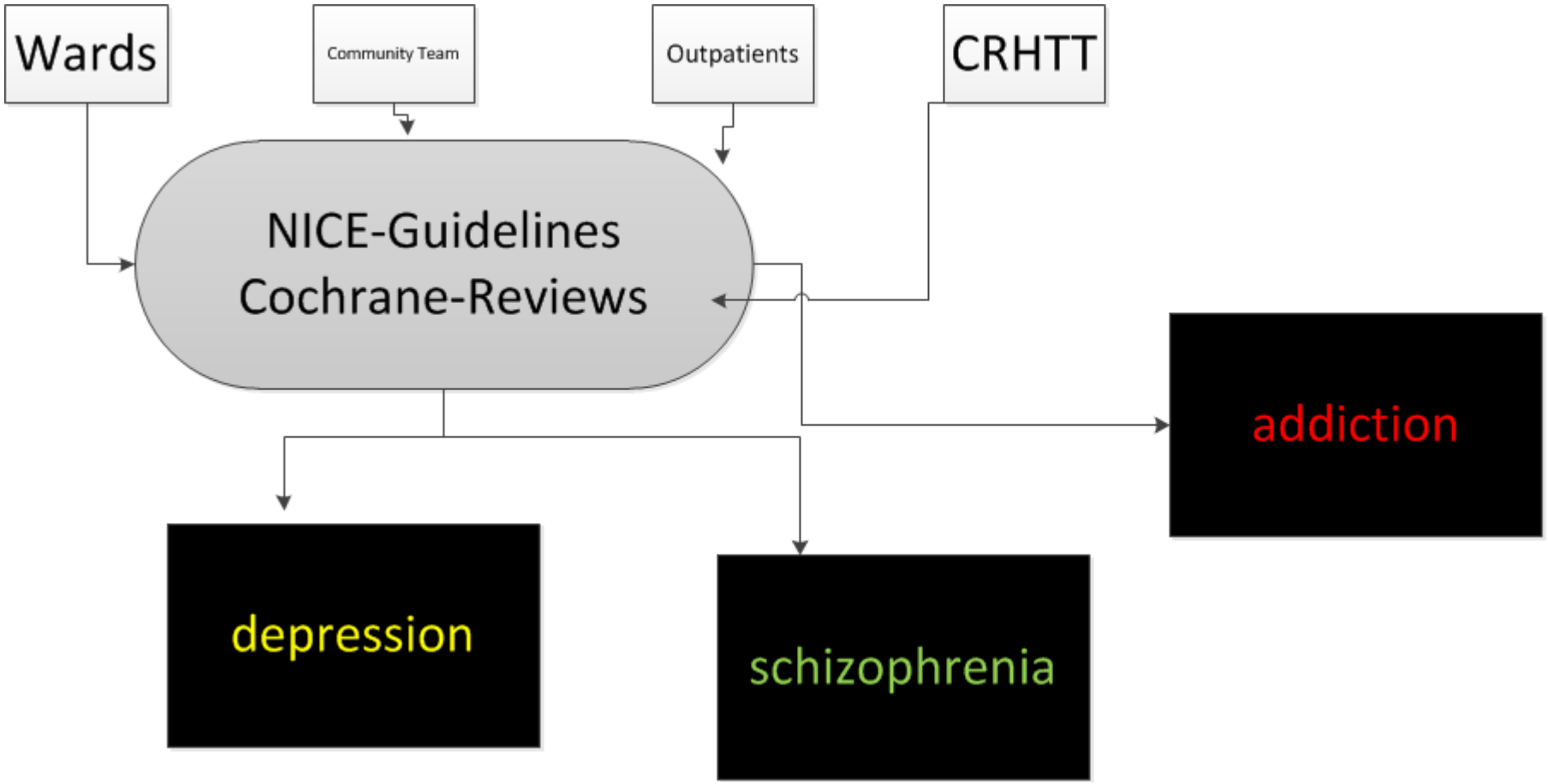
- Limited evidence and contradictory results
- ‘Effectiveness predictions are always dicey’
  (Cartwright, Lancet, 2011)
- From does it work somewhere to will it work for us *(Cartwright and Munro, JECP, 2010)*



- 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


Wards
Community Team
Outpatients
CRHTT
NICE-Guidelines
Cochrane-Reviews
addiction
depression
schizophrenia

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)

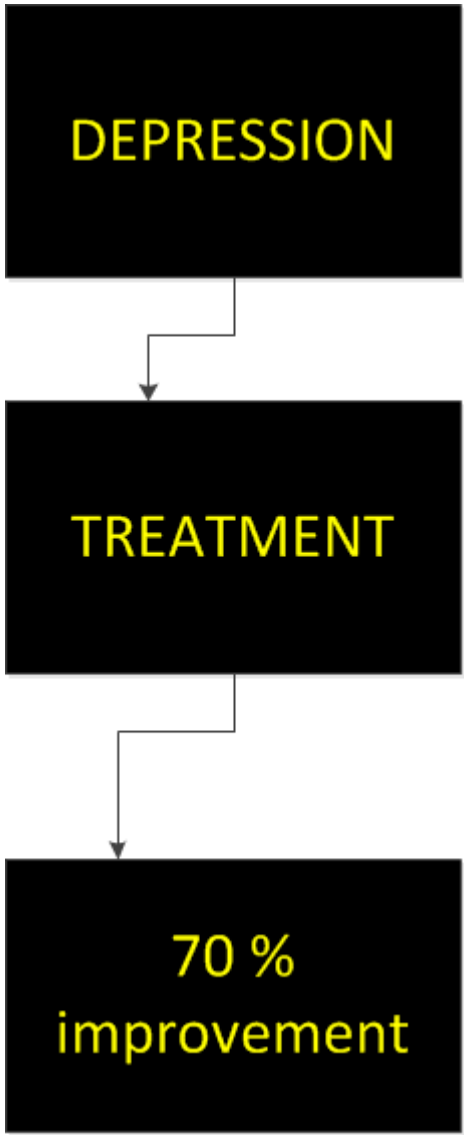
- But almost all empirical studies refer to diagnosis (some like the CRHTT to the intervention)


10

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



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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 the difference
- Example Depression

OPEN ACCESS Freely available online PLoS Medicine

Initial Severity and Antidepressant Benefits: A Meta-Analysis of Data Submitted to the Food and Drug Administration

Irving Kirsch[1]*, Brett J. Deacon[2], Tania B. Huedo-Medina[3], Alan Scoboria[4], Thomas J. Moore[5], Blair T. Johnson[3]

1 Department of Psychology, University of Hull, Hull, United Kingdom, 2 University of Wyoming, Laramie, Wyoming, United States of America, 3 Center for Health, Intervention, and Prevention, University of Connecticut, Storrs, Connecticut, United States of America, 4 Department of Psychology, University of Windsor, Windsor, Ontario, Canada, 5 Institute for Safe Medication Practices, Huntingdon Valley, Pennsylvania, United States of America

BJPsych The British Journal of Psychiatry (2011) 199, 501–507. doi: 10.1192/bjp.bp.111.093336

Assessing the 'true' effect of active antidepressant therapy v. placebo in major depressive disorder: use of a mixture model

Michael E. Thase, Klaus G. Larsen and Sidney H. Kennedy

Articles

Selective serotonin reuptake inhibitors in childhood depression: systematic review of published versus unpublished data

Craig J Whittington, Tim Kendall, Peter Fonagy, David Cottrell, Andrew Cotgrove, Ellen Boddington

Summary

Introduction

RC PSYCH

BJPsych The British Journal of Psychiatry

Effects of anxiety on the long-term course of depressive disorders

William Coryell, Jess G. Fiedorowicz, David Solomon, Andrew C. Leon, John P. Rice and Martin B. Keller

BJP published online October 7, 2011 Access the most recent version at doi: 10.1192/bjp.bp.110.081992

RC PSYCH

BJPsych The British Journal of Psychiatry

Antidepressant medications *v.* cognitive therapy in people with depression with or without personality disorder

Jay C. Fournier, Robert J. DeRubeis, Richard C. Shelton, Robert Gallop, Jay D. Amsterdam and Steven D. Hollon

BJP 2008, 192:124-129.

Access the most recent version at doi: 10.1192/bjp.bp.107.037234

Differential responses to psychotherapy versus pharmacotherapy in patients with chronic forms of major depression and childhood trauma

Charles B. Nemeroff*†‡, Christine M. Heim*†, Michael E. Thase‖, Daniel N. Klein§, A. John Rush¶‖, Alan F. Schatzberg¶‖, Philip T. Ninan*†, James P. McCullough, Jr.*^^, Paul M. Weiss*†, David L. Dunner*‡‡, Barbara O. Rothbaum*†, Susan Kornstein**§§, Gabor Kelemen*¶¶, and Martin B. Keller*¶¶

- Nemeroff et al. (2003) depression + childhood trauma better outcome with psychotherapy)
- Fournier et al. (2008) depression + personality disorder better outcome pharmacotherapy
- Kirsch et al. (2008) antidepressants do no work for mild to moderate depression
- Thase et al. (2011) antidepressants do work with mild to moderate depression
- Whittington et al. (2004) SSRI's 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.

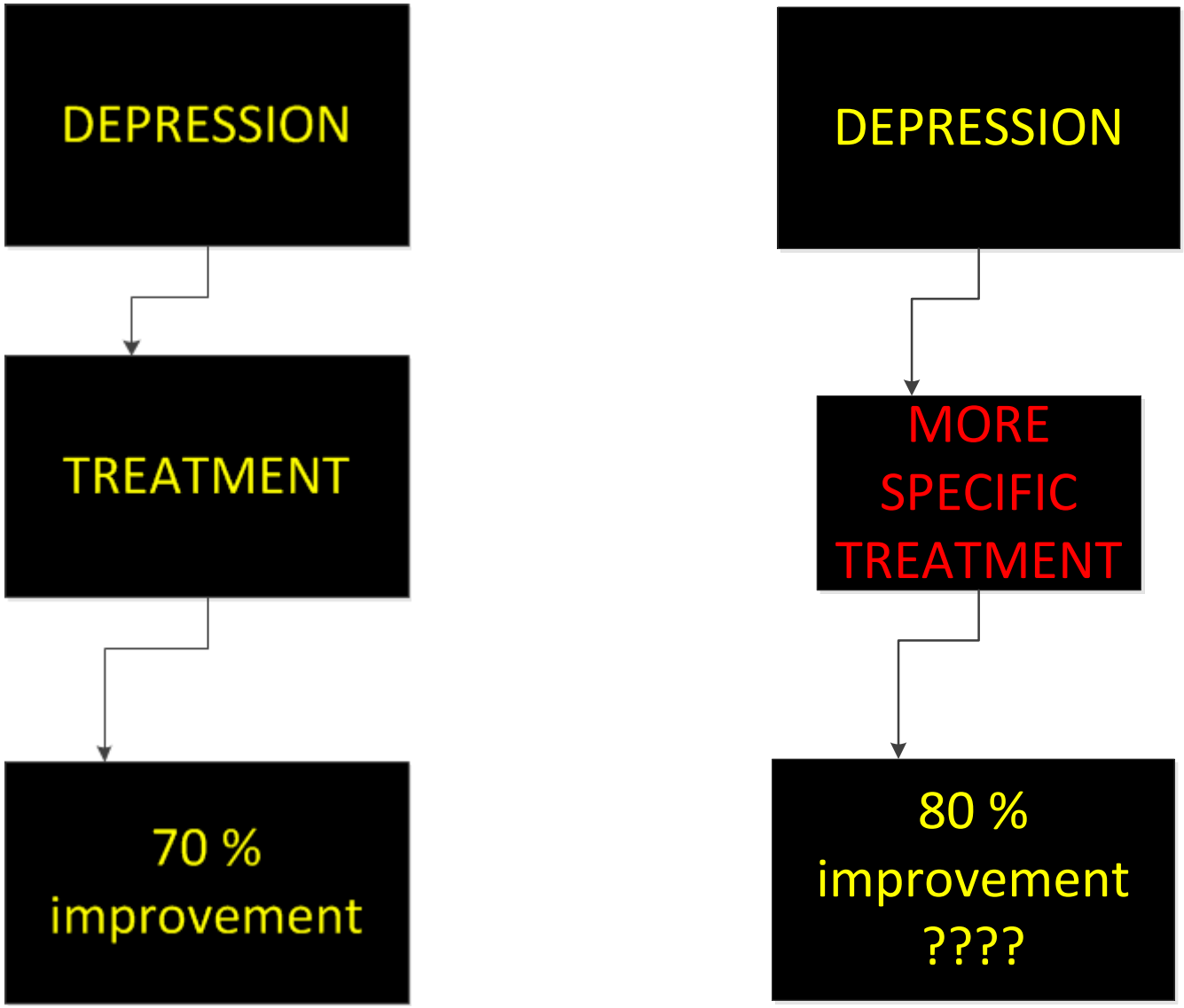
Jill I. Mattia, Ph.D.

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


DEPRESSION
TREATMENT
70 %
improvement
DEPRESSION
MORE
SPECIFIC
TREATMENT
80 %
improvement
????

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

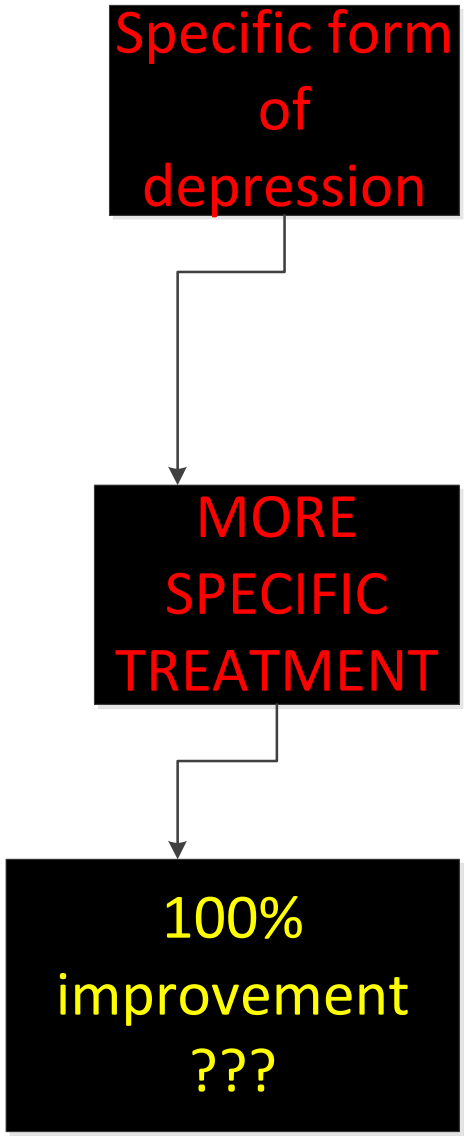
Gregory E. Simon, M.D., M.P.H.; Roy H. Perlis, M.D., M.Sc.

Am J Psychiatry 2010;167:1445-1455.

‘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 Hydrochloride

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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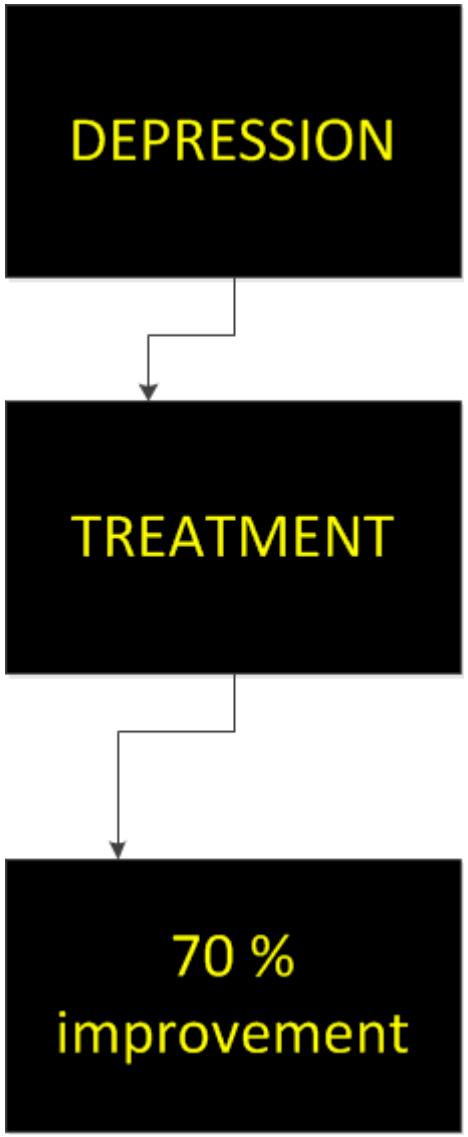

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- A kind of research program check whether results are the same and if not why not?
- Could be diagnosis and/or treatment needs to be adjusted

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 a capacities or mechanisms but some approximation

- Thank you
- Questions?
- Comments?

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