Camden and Islington NHS
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# Depression: an update for General Practitioners

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April 20, 2017

CamED: Mental Health Update

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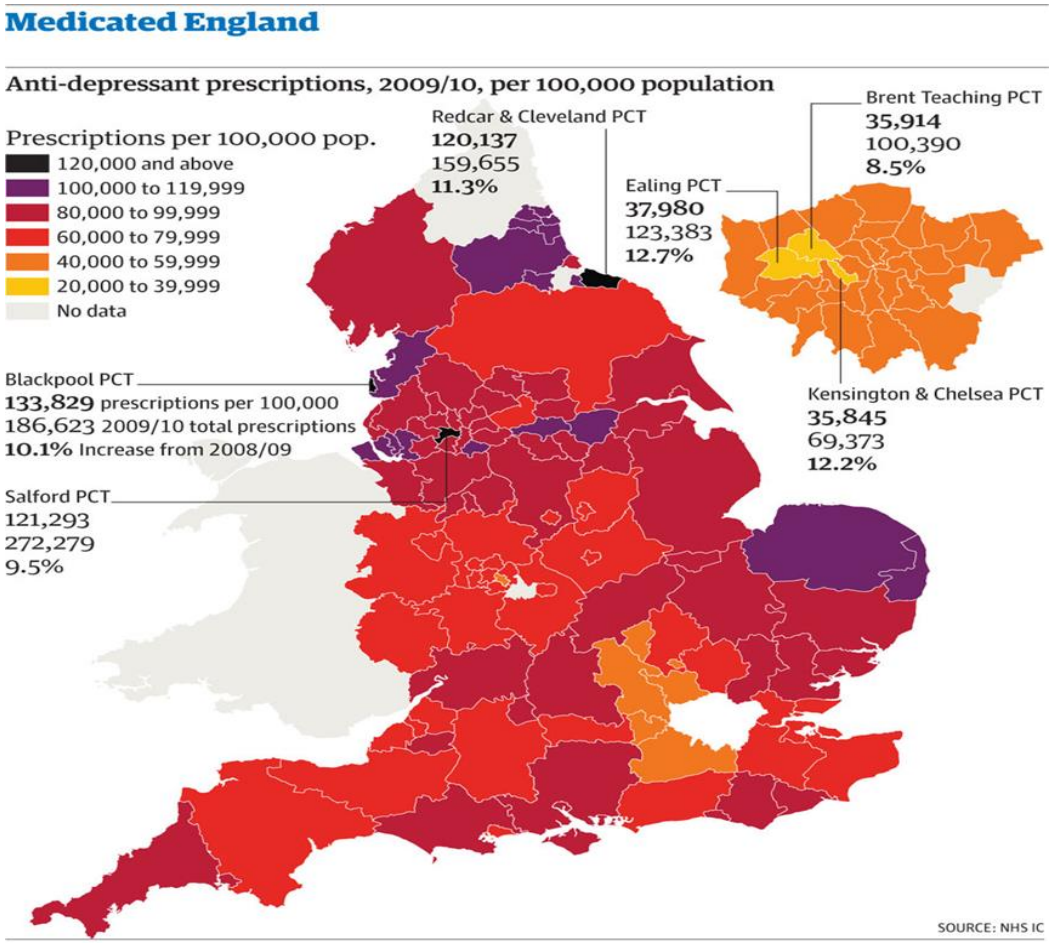
# 64 million antidepressant prescriptions in England in 2016



# Diagnosis (ICD-10 Criteria)

Key symptoms (at least one of these, most days, most of the time for at least 2 weeks):

- persistent sadness or low mood; and/or
- loss of interests/pleasure
- fatigue/low energy

Associated symptoms:

- disturbed sleep
- poor concentration or indecisiveness
- low self-confidence
- poor or increased appetite
- suicidal thoughts or acts
- agitation or slowing of movements
- guilt or self-blame

# Categorizing severity

The 10 symptoms define the degree of depression and management is based on the particular degree:

- not depressed (fewer than four symptoms)
- mild depression (four symptoms)
- moderate depression (five to six symptoms)
- severe depression (seven or more symptoms, with or without psychotic symptoms)

- symptoms should be present for a month or more and every symptom should be present for most of every day

# Management: Mild Depression

- Individual guided self-help based on the principles of cognitive behavioural therapy (CBT)
- Computerised CBT
- Structured group physical activity programme
- Group CBT
- Antidepressants: Not recommended unless past history of moderate/severe episodes and/or failure to respond to psycho-social interventions

Ref: NICE guidance, April 2016

# Management: Moderate/Severe Depression

- Antidepressant (normally a selective serotonin reuptake inhibitor [SSRI]) or
- A high-intensity psychological intervention, normally one of the following:
- CBT
- Interpersonal therapy (IPT)
- Behavioural activation (evidence less robust than for CBT or IPT)
- Behavioural couples therapy
- Moderate/severe depression: combination of medication and a high-intensity psychological intervention (CBT or IPT).

Ref: NICE guidance, April 2016

# How to choose treatments?

- Duration of the episode of depression and the trajectory of symptoms
- Previous course of depression and response to treatment
- Likelihood of adherence to treatment and any potential adverse effects
- Patient's treatment preference and priorities.

- Remember - goal of treatment is remission! (HAM-D17 ≤ 7, MADRS < 10, QIDS-SR≤ 5)

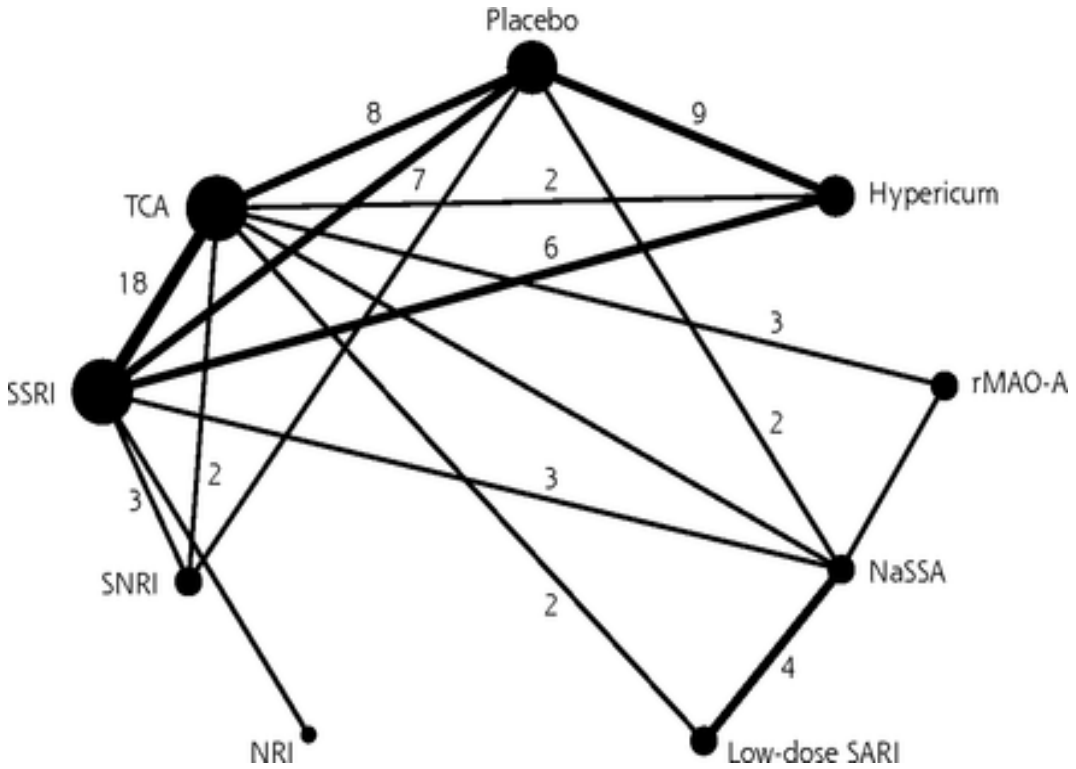
# Antidepressants: the basics

- Discuss with patient – choice of drug and use of other non-drug treatments
- Inform patient of timeframe for expected response (2-4 weeks)
- Prescribe an effective dose
- For single episode, continue treatment for at least 6-9 months,
- For patients with ≥2 episodes and functional impairment, continue for at least 2 years
- Withdraw gradually; inform patients of discontinuation symptoms

# Do they work?

- For patients with moderate depression 20% recover with no treatment, 30% respond to placebo, 50% respond to antidepressants (Anderson et al, 2008).
- Meta-analyses of RCTs of SSRIs show they are superior to placebo in terms of efficacy (OR = 1.62, 95% CI 1.51-1.72) (Cipriani et al 2016).
- Placebo response has diminished due to methodological improvements in trials.
- Sub-syndromal depression – little difference between placebo and antidepressant.
- Dysthymia (duration of $\geq$ 2 years) benefits from antidepressant treatment.

# Are all antidepressants the same?




Linde et al (2015). Efficacy and Acceptability of Pharmacological Treatments for Depressive Disorders in Primary Care: Systematic Review and Network Meta-Analysis. Ann Fam Med January/February 2015 vol. 13 no. 1 69-79

# Are all antidepressants the same?

- Meta-analyses show that efficacy for all antidepressants are equivalent.
- SSRIs - most evidence base for being effective in primary care.
- Side effects, discontinuation symptoms, and potential interactions with other drugs or physical health problems vary between drugs.
- TCAs – higher risk of QTc prolongation (SSRIs, Mirtazapine recommended in cardiac disease)
- SSRIs – high risk of sexual dysfunction (Mirtazapine, Agomelatine, Bupropion much lower)
- Fluoxetine, fluvoxamine and paroxetine - higher propensity for drug interactions.
- Paroxetine and Venlafaxine - higher incidence of discontinuation symptoms.

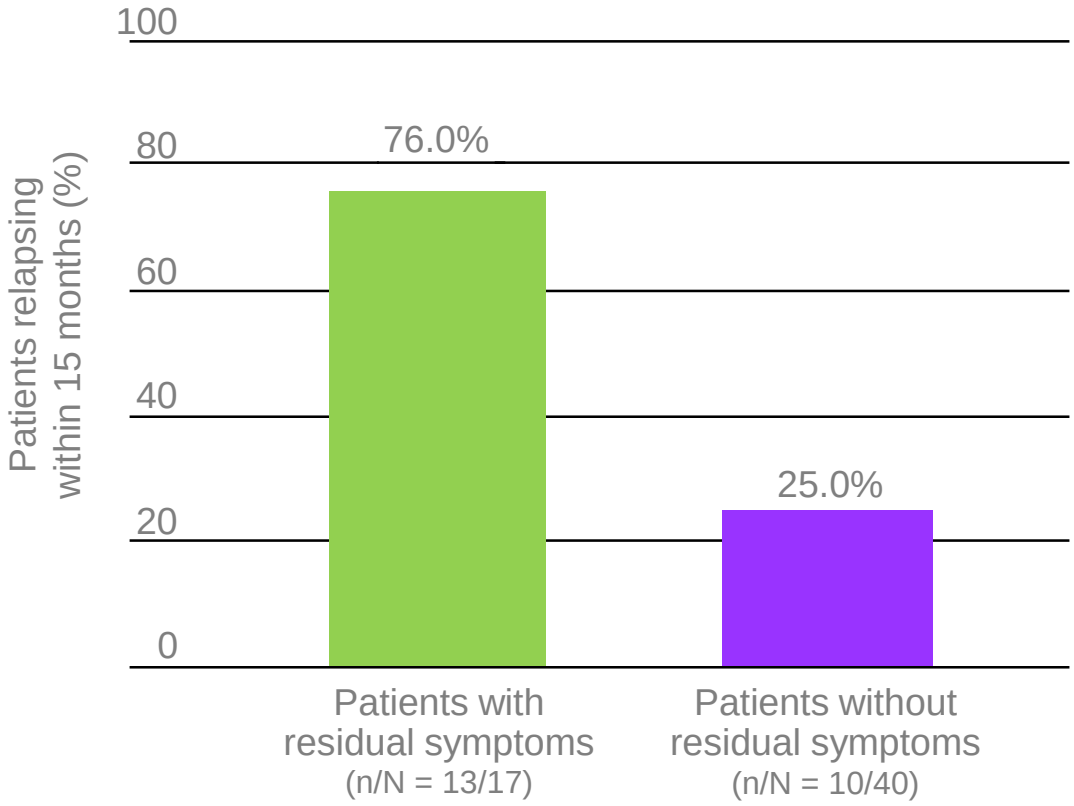
# Comparing SSRIs

- Sertraline tends to be superior than others in terms of acceptability.
- SSRIs also licensed for anxiety disorders and efficacy is roughly equivalent for all.

# Challenges in treating depression

- The majority of patients with depression do not respond to or do not achieve remission through the first treatment
- The chance of achieving remission reduces with each new treatment attempt
- The risk of relapse increases with each new treatment attempt
- Lack of improvement during the first two weeks of treatment may indicate that changes in depression management should be considered earlier than conventionally thought

# Residual symptoms predict relapse




Paykel ES et al. *Psychol Med* 1995;25:1171–80

# Non-response to treatment

- What should be done if the patient does not achieve remission?

- Reconsider the diagnosis?
- Has the patient been adherent to the treatment?
- Increase dosage?
- Change treatment?
- Augment treatment?

# Next step treatments

- Dose Increase

The evidence supporting the efficacy of dose increase is limited, but it could be considered in individual patients especially if:

- there are minimal side-effects and/or,

- there has been some improvement on the antidepressant and/or,

- the current antidepressant has a possible dose response (e.g. venlafaxine, escitalopram, TCAs)

# Switching antidepressants

Consider especially if:

- troublesome or dose-limiting side effects and/or,
- no improvement
- switching abruptly is generally preferable unless there is a potential drug interaction in which case follow the recommended taper/washout period
- switch either within- or between-antidepressant class initially
- consider a different antidepressant class after more than one failure with a specific class

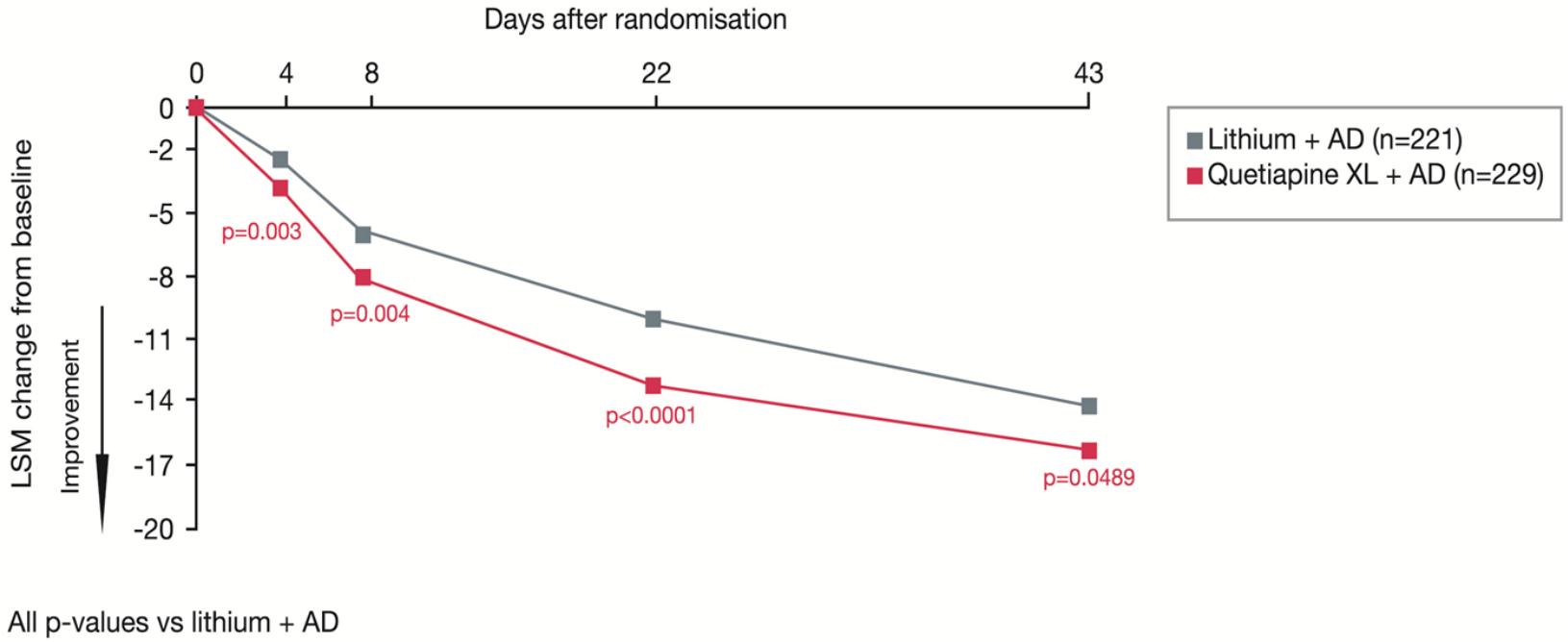
# Augmentation/combination treatment

- If a patient has failed 2 antidepressant trials, best to seek specialist opinion.

Consider adding a second agent especially if:

- there is partial/insufficient response on the current antidepressant and there is good tolerability of current antidepressant
- switching antidepressant has been unsuccessful
- establish the safety of the proposed combination
- choose the combinations with the best evidence base first

# Lithium vs atypical antipsychotic augmentation




All p-values vs lithium + AD

Montgomery, et al. *Journal of Psychopharmacology*. 2010;24(Suppl 3): A10.

# Other next-step treatment options

- CBT + medication
- Other psychological or behavioural treatments that have established acute treatment efficacy
- Neurostimulatory treatments:

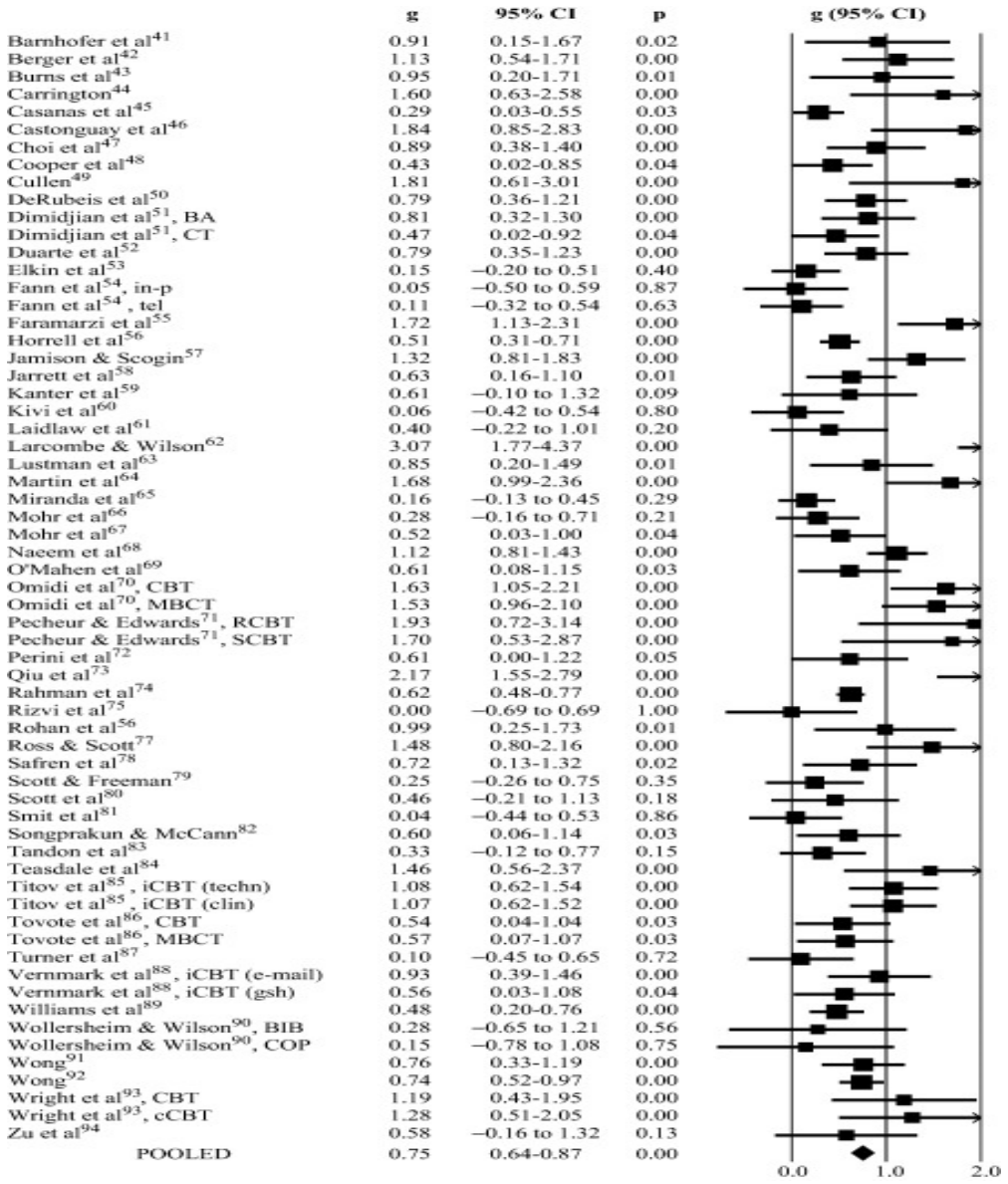
-ECT

-rTMS (used with promising results in CDAT)

-TDCS

- VNS, DBS, Neurosurgery

# CBT




Cuijpers et al. World Psychiatry. 2016 Oct; 15(3): 245–258.

# COBALT Study

- CBT as an adjunct to pharmacotherapy for primary care based patients with treatment resistant depression (n=469).
- Multi-centre trial in UK primary care.
- 46% in the intervention group met criteria for response at 6 months compared with 22% in the usual care group (odds ratio 3·26, 95% CI 2·10–5·06, p<0·001).

Wiles et al. Lancet. 2013 Feb 2;381(9864):375-84.

# Summary

- The goal of depression treatment is complete freedom from symptoms (remission)
- Approximately 1/3 of MDD patients achieve remission during the first treatment attempt with antidepressants
- For each added treatment step, the number of patients achieving remission decreases and the risk of relapse increases
- Failure to achieve a 20% reduction in HAM-D17 after 2 weeks of treatment is a good predictor that the patient will not achieve remission through continued treatment with that agent

# Summary

- Increasing dose of the SSRI seems unlikely to produce much extra benefit
- Augmentation strategies (another AD, AAP, or lithium have been investigated) have been discussed
- MDEs occur in Bipolar Disorder as well as MDD so always ask about manic/hypomanic symptoms
- Lots of uncertainty about the risk/benefits of antidepressants in Bipolar Disorder.

# Questions?