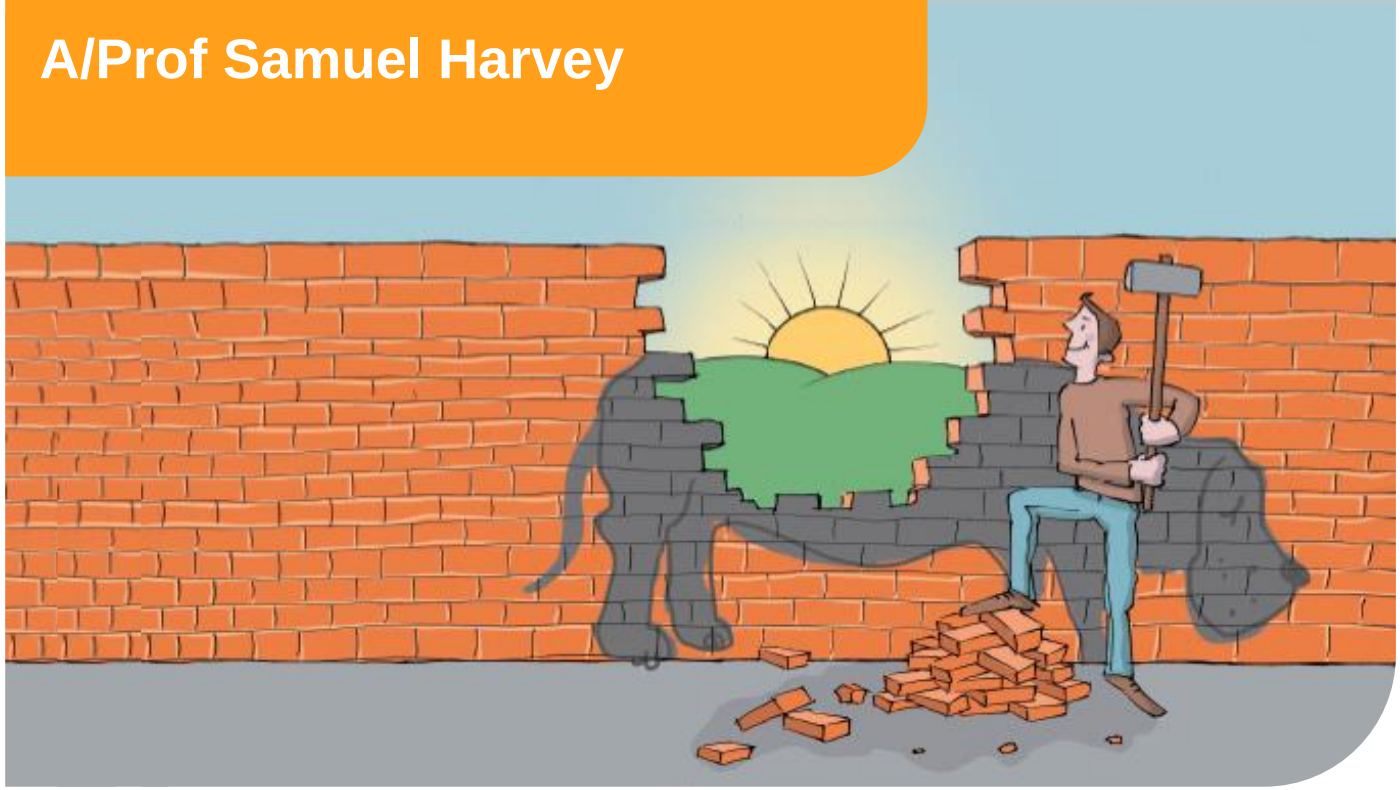
Depression and anxiety in chronic kidney disease

A/Prof Samuel Harvey



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Key questions

1. What do we mean by ‘depression’ and ‘anxiety’?
2. How common are these problems?
3. How can they be detected and treated?
4. New and emerging developments

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Spectrum of mood

Depressed | Sad | Euthymic | Happy | Manic

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ICD-10 Depressive Episode:
Core Symptoms

At LEAST two of the following

- Depressed mood
- Loss of interest and enjoyment
- Reduced energy

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ICD-10 Depressive Episode: Other symptoms

Plus at LEAST two of the following:

- Reduced concentration
- Reduced self esteem
- Ideas of guilt and unworthiness
- Bleak, pessimistic views of future
- Ideas or acts of self harm
- Disturbed sleep
- Diminished appetite

Whole episode lasting at least 2 weeks

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Influence of Life Stress on Depression: Moderation by a Polymorphism in the 5-HTT Gene

Avshalom Caspi,[1,2] Karen Sugden,[1] Terrie E. Moffitt,[1,2]*
Alan Taylor,[1] Ian W. Craig,[1] HonaLee Harrington,[2]
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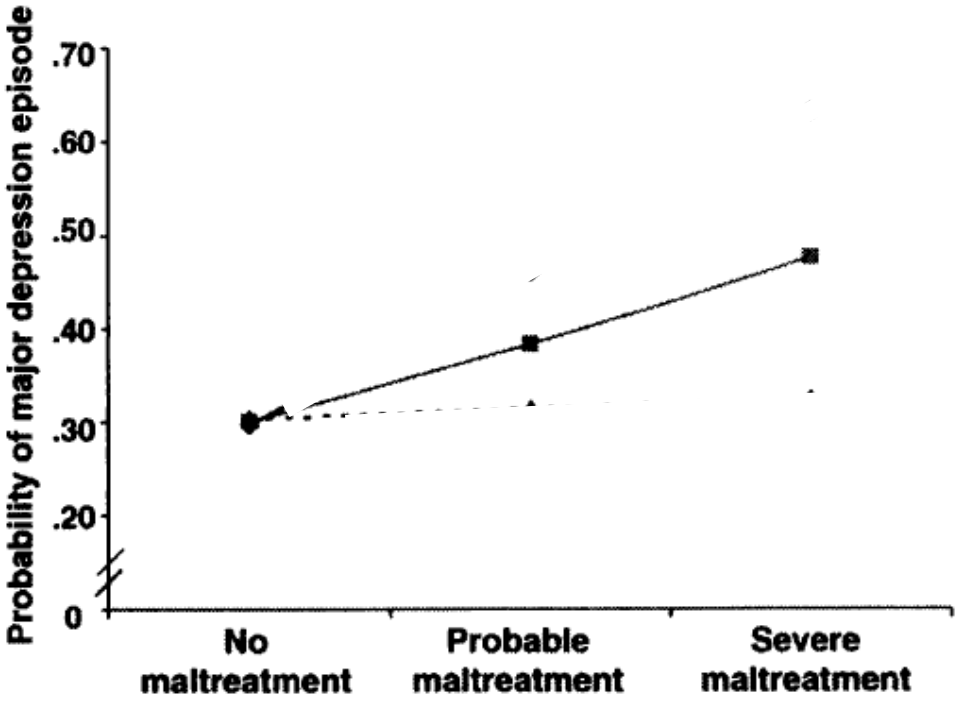

Science
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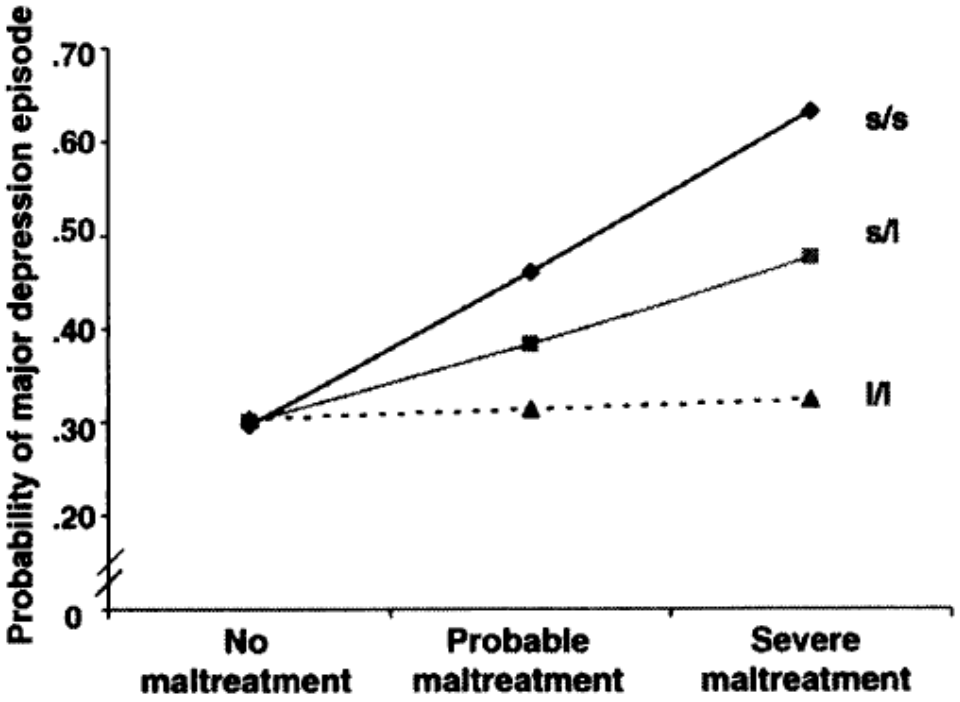

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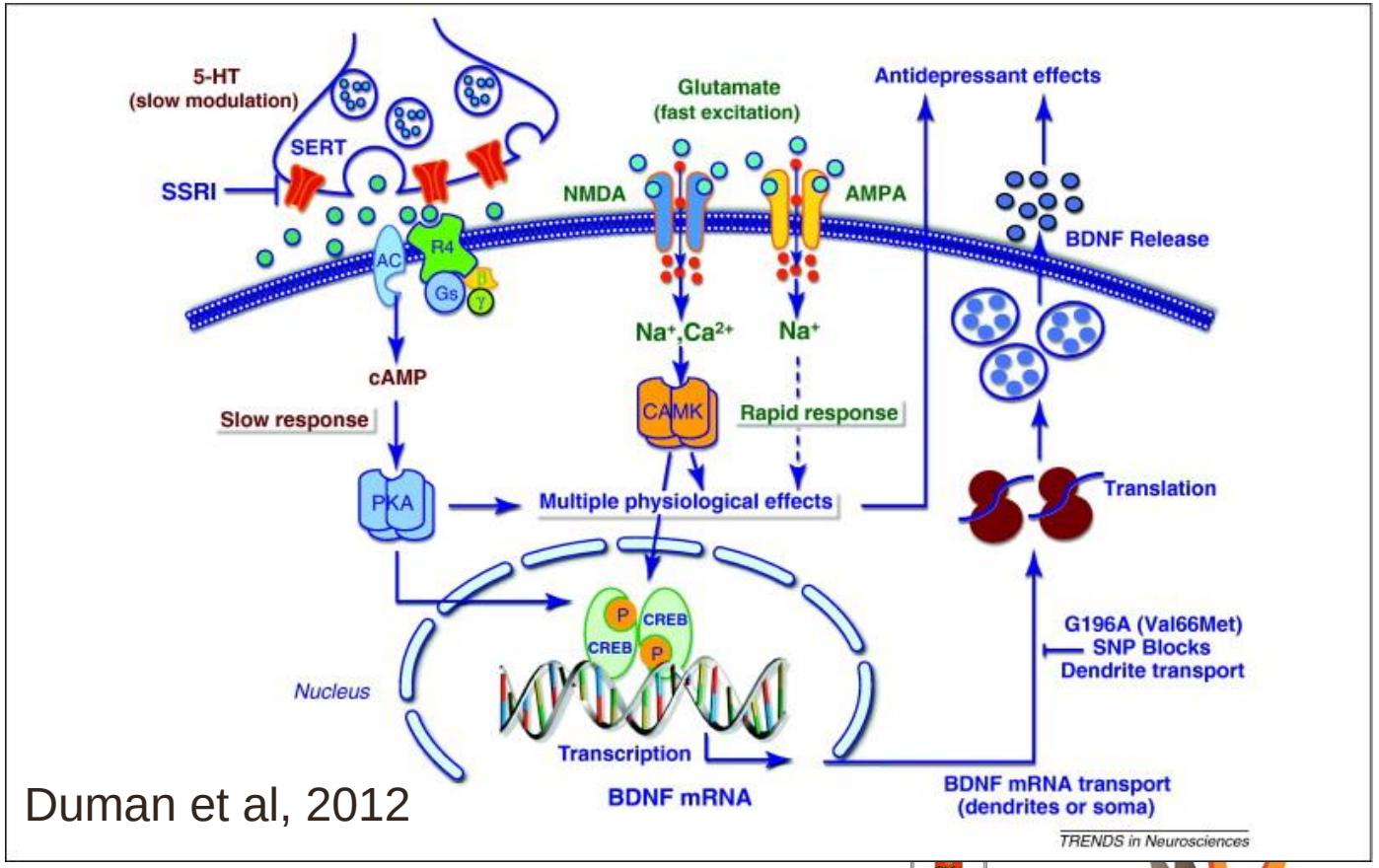
Beyond the monoamine Hypothesis



Duman et al, 2012

How common is depression in CKD?

http://www.kidney-international.org

clinical investigation

Prevalence of depression in chronic kidney disease: systematic review and meta-analysis of observational studies

Suetonia Palmer[1], Mariacristina Vecchio[2], Jonathan C. Craig[3], Marcello Tonelli[4], David W. Johnson[5], Antonio Nicolucci[2], Fabio Pellegrini[2,6], Valeria Saglimbene[2], Giancarlo Logroscino[7], Steven Fishbane[8] and Giovanni F.M. Strippoli[2,3,9,10]

[1]Department of Medicine, University of Otago, Christchurch, Christchurch, New Zealand; [2]Department of Clinical Pharmacology and Epidemiology, Consorzio Mario Negri Sud, S. Maria Imbaro, Italy; [3]School of Public Health, The University of Sydney, Sydney, New South Wales, Australia; [4]Department of Medicine, University of Alberta, Edmonton, Alberta, Canada; [5]Department of Nephrology, University of Queensland at Princess Alexandra Hospital, Brisbane, Queensland, Australia; [6]'Casa Sollievo della Sofferenza' Hospital, IRCCS, San Giovanni Rotondo (Foggia), Italy; [7]Department of Neurology and Psychiatry, University of Bari, Bari, Italy; [8]Department of Medicine, Hofstra North Shore LIJ School of Medicine, Great Neck, New York, USA; [9]Diaverum Scientific Office, Lund, Sweden and [10]Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy

Kidney International (2013) **84**; 179–191

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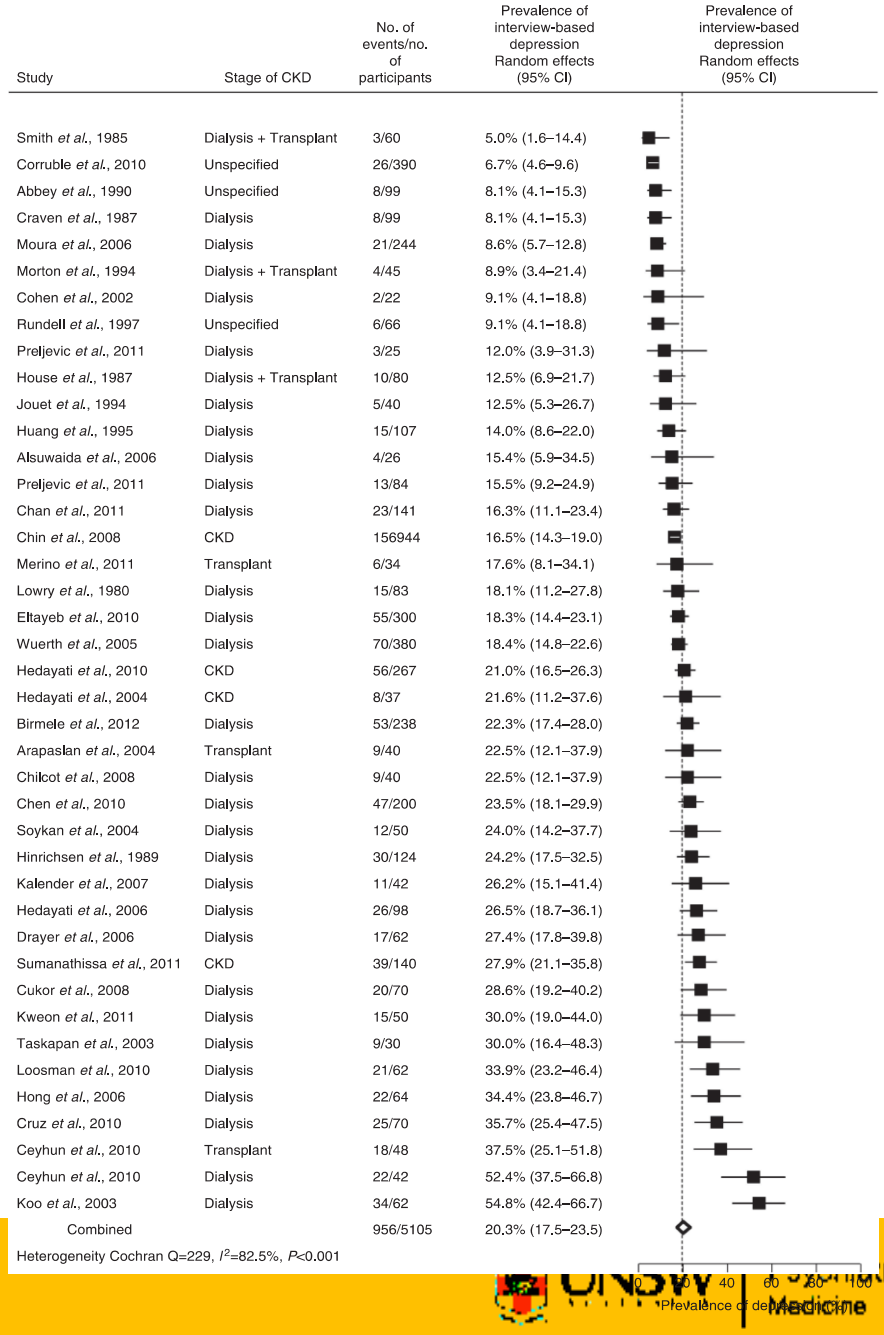
Meta-analysis

Palmer et al *Kid International* Jan 2013

- 249 populations (55982 participants) in 228 separate studies
- Looked at self reported symptom scales separately to clinical interviews
- Focused on point prevalence, not prevalence over a period of time
- Methodologically very sound

Depression in CKD

- Community prevalence estimates usually around 7%
- Prevalence for interview based depression 22.8%
- Suggestion that self report scales over-estimate prevalence (up to 39% in dialysis populations)
- Prevalence remained high amongst transplant recipients (25.7%)



Why is depression so common amongst CKD patients?

- Complex
- Many bidirectional factors
- Clearly not just because of dialysis, but CKD's impact on independence, self image, control, etc very important
- Shared risk factors (eg lifestyle)
- Shared pathological processes (eg inflammation)

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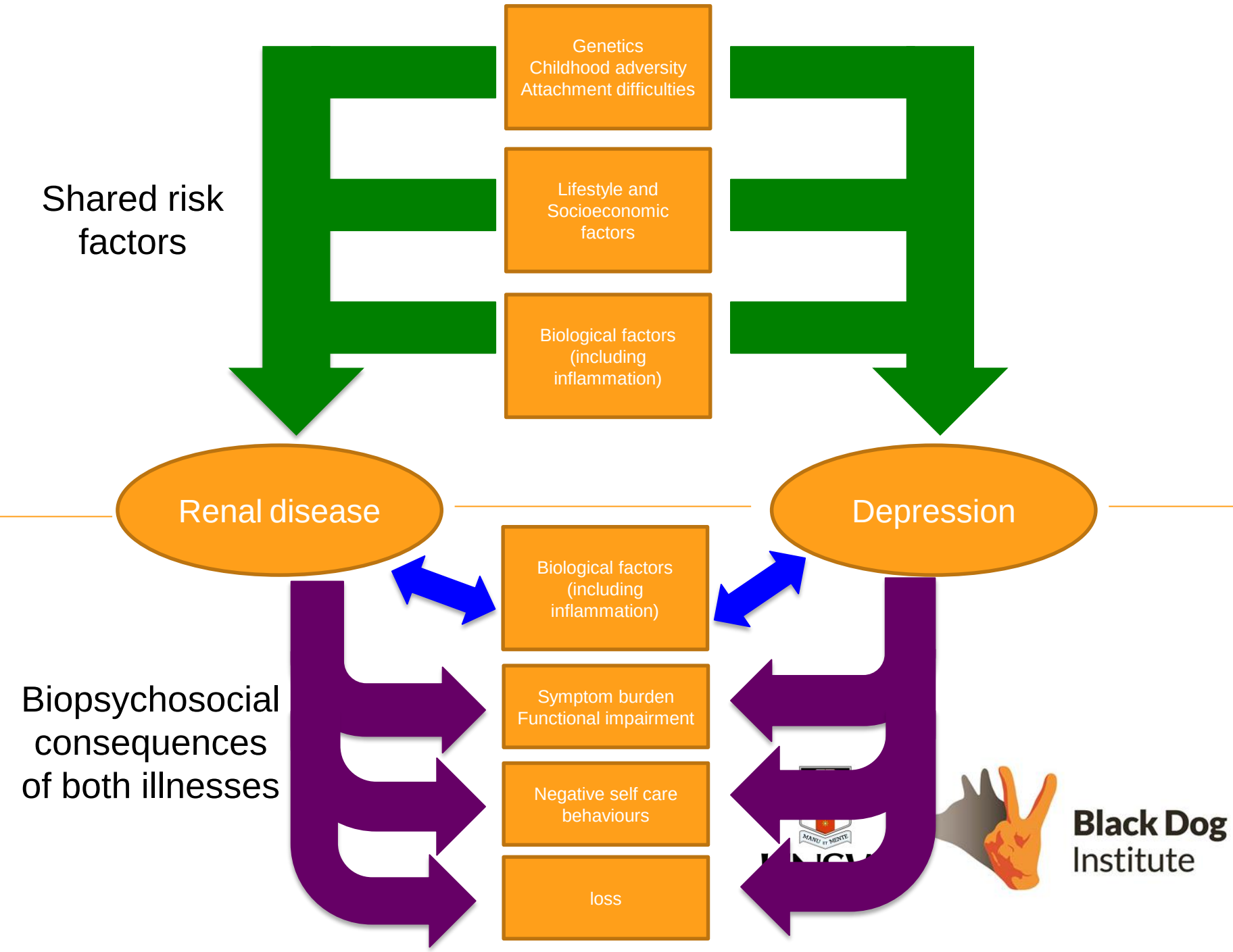
Shared risk factors
Genetics
Childhood adversity
Attachment difficulties
Lifestyle and Socioeconomic factors
Biological factors (including inflammation)
Renal disease
Depression
Biopsychosocial consequences of both illnesses
Biological factors (including inflammation)
Symptom burden
Functional impairment
Negative self care behaviours
loss
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Why does all this matter?

ARTICLE IN PRESS

AJKD

Original Investigation

Association Between Depression and Death in People With CKD: A Meta-analysis of Cohort Studies

Suetonia C. Palmer, MBChB, PhD,[1] Mariacristina Vecchio, MSc,[2] Jonathan C. Craig, MBChB, PhD,[3] Marcello Tonelli, MD,[4] David W. Johnson, MBBS (Hons), PhD,[5] Antonio Nicolucci, MD,[2] Fabio Pellegrini, MSc,[2,6] Valeria Saglimbene, MSc,[2] Giancarlo Logroscino, PhD,[7] S. Susan Hedayati, MD,[8] and Giovanni F.M. Strippoli, MD, MM, MPH, PhD[2,3,9,10]

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Mortality meta-analysis

- 22 cohort studies (83381 participants) following adults with CKD for between 3 months and 6.5 years
- Co-morbid depression associated with an increased risk of death from any cause **RR 1.59** (CI: 1.35-1.87)
- Similar to the level of risk associated with smoking (**HR 1.59**)

Not just death……

Online article and related content current as of June 29, 2010.

Association Between Major Depressive Episodes in Patients With Chronic Kidney Disease and Initiation of Dialysis, Hospitalization, or Death

S. Susan Hedayati; Abu T. Minhajuddin; Masoud Afshar; et al.

JAMA. 2010;303(19):1946-1953 (doi:10.1001/jama.2010.619)

- 267 patients with chronic kidney disease (stages 2-5 not receiving dialysis)
- Followed up to one year
- Primary outcome was “event-free survival” (not dead, hospitalised or begun on maintenance dialysis)

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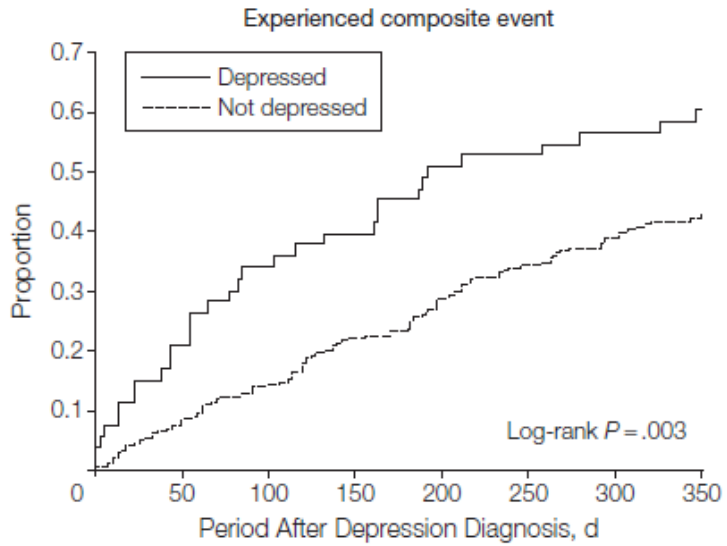
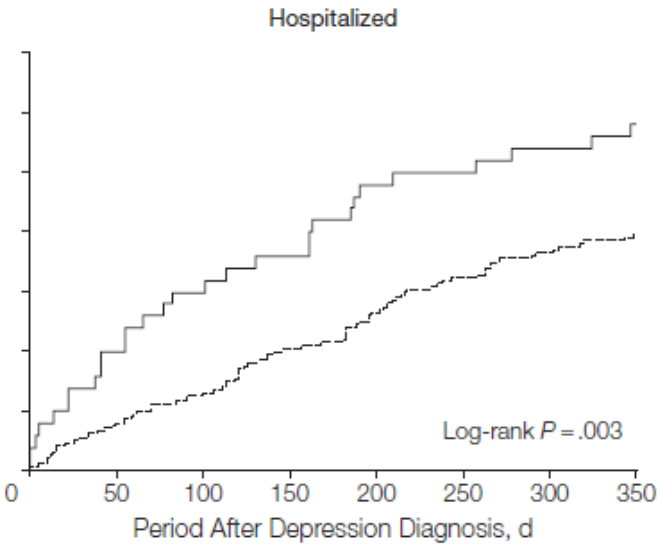
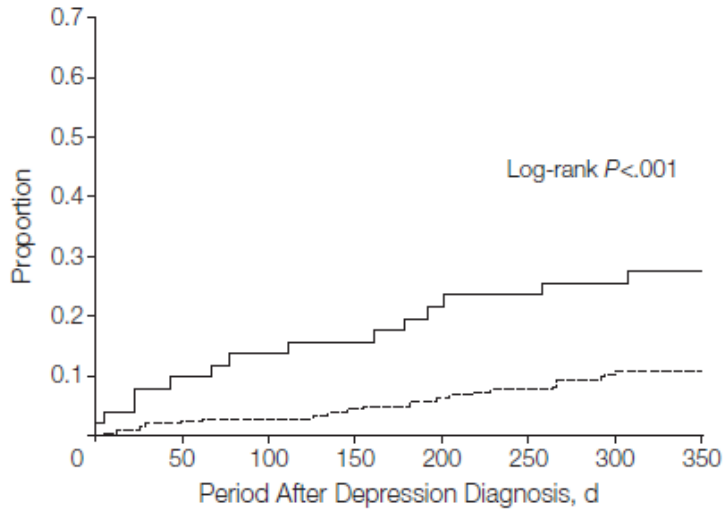


No. at risk

Depressed	55	42	35	32	26	25	23	21
Not depressed	208	187	175	159	146	134	125	116

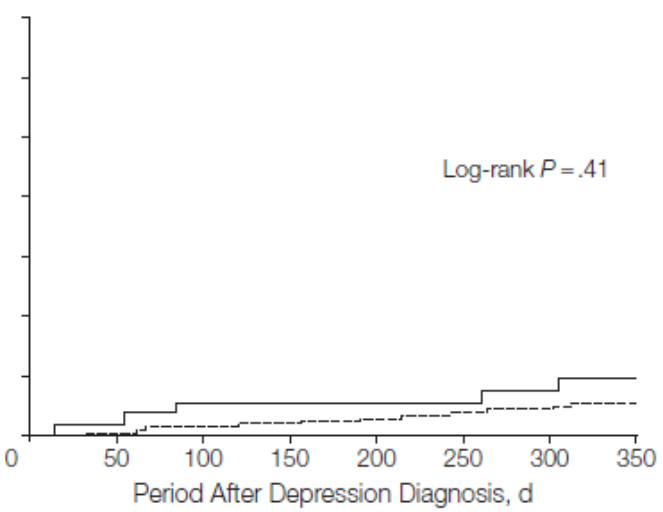


	55	40	35	32	26	25	23	21
	208	186	175	160	148	135	126	119



No. at risk

Depressed	56	46	44	40	38	36	35	35
Not depressed	210	201	198	195	191	185	178	170



	56	52	50	50	50	50	49	47
	211	204	202	201	199	197	196	191

If you were going to screen…..

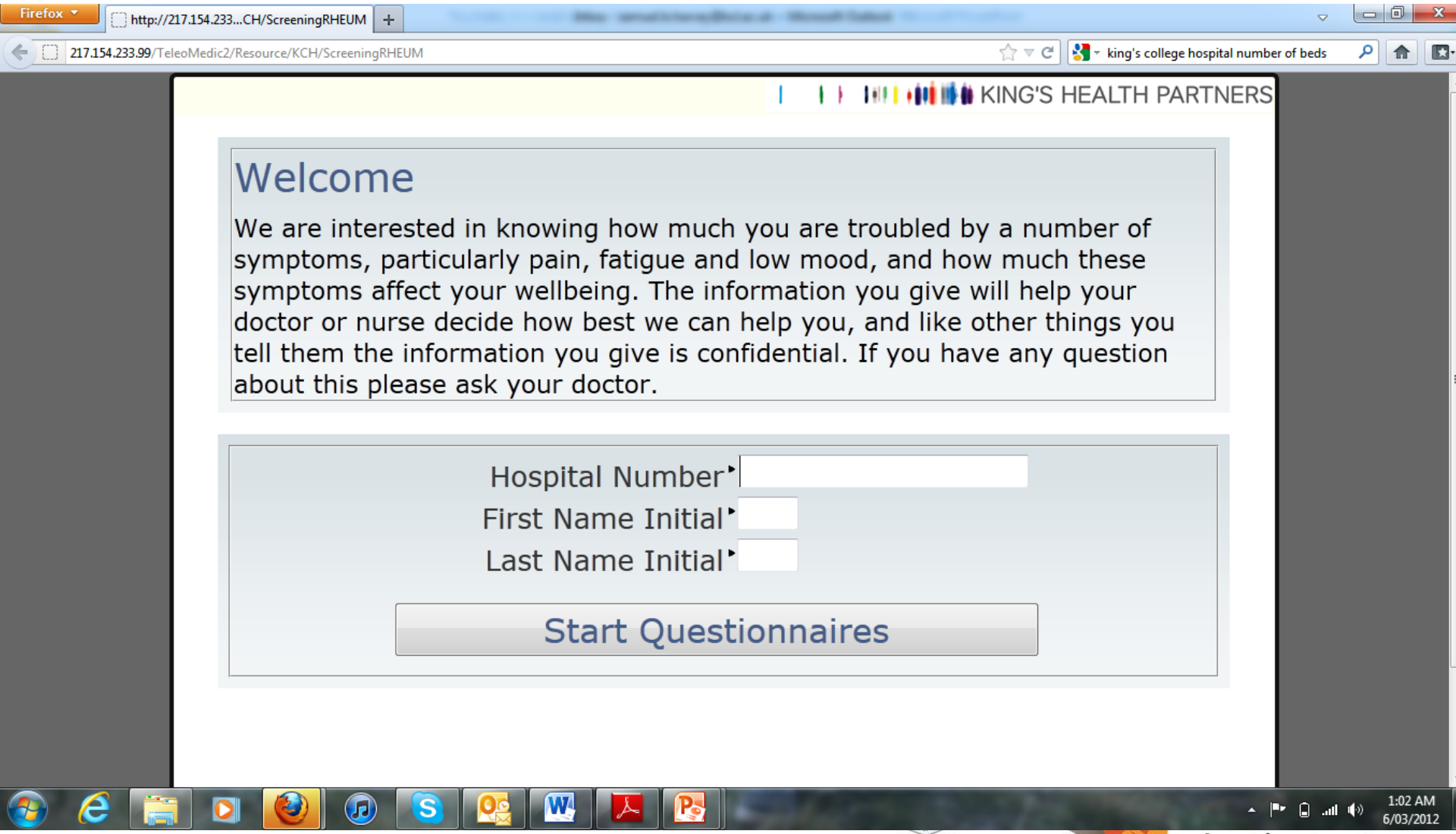
- Need to be aware of overlap in some symptoms – either use screening tools designed to avoid these (eg HADS) or modified threshold of standard screening tool
- Need a system in place to deal with positive results without causing too much anxiety

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME: _____ **DATE:** _____

Over the *last 2 weeks,* how often have you been bothered by any of the following problems?
(use "✓" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3
add columns:		+	+	
(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card.)			**TOTAL:**	



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PCS

Clinical Information System

Patient Name: **EPR, TESTFIVE** DOB: **12/12/1978** Hospital No.: **EPR5**

Address: **test, tesat, test** NHS No.:

Search

List

DAS-28 Baseline | Exam Date | (Select new Baseline...)

EULAR Response

Physician Global VAS mm

CRP mg/l Date dd/mm/yyyy No Data

Patient Assessment

Latest HAQ 2 Date 11/03/2011 dd/mm/yyyy Patient Measures

Modified HAQ 2

Fatigue 58 mm

Pain VAS 70 mm

EMS mins

PHQ-9 Score PHQ-9 Category Depression screen negative

GAD-7 Score 11 GAD-7 Category This indicates the patient has significant levels of anxiety which would be worth exploring further

Additional Notes

Cancel Save Close Letter

Done Local intranet

What about anxiety?

- Very common and often missed
- Generalised anxiety disorder vs specific phobias
- Can be very disabling….but often quite treatable
- Possible clues include difficult behaviour, avoidance and alcohol use

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Treating co-morbid depression

Antidepressants for depression in physically ill people (Review)

Rayner L, Price A, Evans A, Valsraj K, Higginson IJ, Hotopf M

THE COCHRANE COLLABORATION®

- Antidepressants were more efficient than placebo
- Suggests depression should be treated even if part of an "understandable" reaction to physical ill health

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ANZJP

Australian & New Zealand Journal of Psychiatry
2014, Vol. 48(6) 530–541
DOI: 10.1177/0004867414528589

Depression and chronic kidney disease: A review for clinicians

Alison Bautovich[1,2,3], Ivor Katz[3,4], Michelle Smith[1,5], Colleen K Loo[1,3,6] and Samuel B Harvey[1,3,6]

Drug	Comments	Potential class adverse events	Recommendation for use in CKD
SSRIs (Hedayati et al., 2012; Taylor et al., 2012)		Nausea, dyspepsia and diarrhoea Headache and insomnia	
Citalopram (Cohen et al., 2004; Hosseini et al., 2012; Kelly et al., 2003)	• Less than 15% excreted in urine • Has been shown to treat depression in CKD and improve QOL • Manufacturer does not recommend use if GFR<20 ml/min • Dose adjustment normally not required in renal impairment, but use with caution when GFR <10 ml/min	Increased risk of bleeding Agitation and anxiety in early stages of treatment Sexual dysfunction Hyponatraemia Some (not all) SSRIs are potent inhibitors of cytochrome enzymes which may lead to drug interactions	✓✓
Fluoxetine (Baghdady et al., 2009; Blumenfield et al., 1997; Levy et al., 1996)	• 5–10% excreted in urine • Long half-life • If GFR <20 ml/min, consider using on alternate days or low dose • Small study suggested relative safety and efficacy in ESKD		✓✓
Sertraline (Brewster et al., 2003; DeVane et al., 2002)	• Less than 1% excreted unchanged in urine • Pharmacokinetics in renal impairment are unchanged in single dose studies, but no published data on multiple dosing • No dose adjustment required • Acute renal failure has been reported, so use with caution		✓
Paroxetine (Doyle et al., 1989; Koo et al., 2005)	• Less than 2% excreted in urine • Increased plasma concentration found when GFR <30 ml/min • If GFR <30 ml/min start at 10–20 mg/day and increase slowly • Has been shown to reduce depressive symptoms in ESKD • Rarely associated with Fanconi's syndrome (acute renal failure)		✓

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Non-pharmacological

- CBT or mindfulness-based CBT
  - benefits beyond depression e.g. medication adherence, reducing pain, anxiety symptoms
  - modify negative attitudes to illness
  - group, individual or e-format
  - observational studies are promising
  - may not have to be delivered by a psychologist

Non-pharmacological

- Exercise therapy

 - shown to have benefit on depression, but also CV risk, efficacy of dialysis, weight loss and QOL

 - major challenge is completion of programs

- Change in dialysis regimen
- Dealing with problematic symptoms
- Dealing with social issues
- Etc

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New developments

- New treatments for depression: new types of brain stimulation, ketamine, anti-inflammatories, etc
- Prevention and risk algorithms
- E-health initiatives (eg MyCompass, This Way Up, HeadGear, others)

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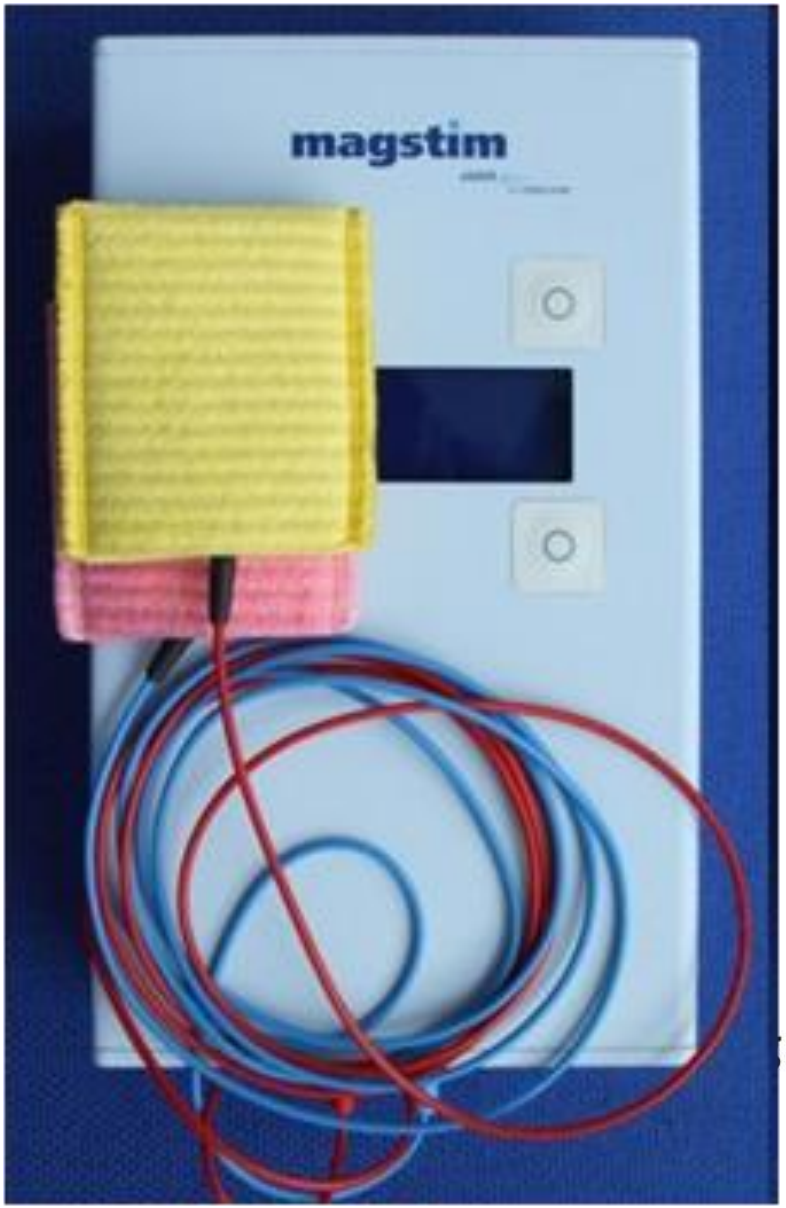
tDCS – transcranial direct current stimulation

- Non-invasive form of brain stimulation
- Low amplitude current (2-3mA vs 800-900mA with ECT)
- Pooled estimate of effect size (hedges' g) 0.74 (CI 0.21-1.27) ie similar to that found for anti depressants

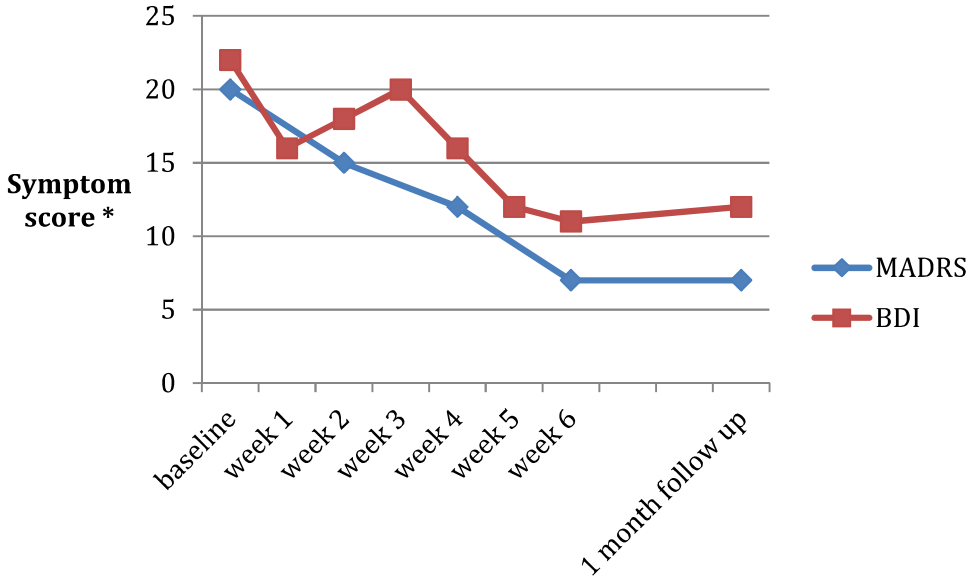


Psychosomatics 2016:57:305–309

Case Reports

Transcranial Direct Current Stimulation as a Treatment for Depression in the Hemodialysis Setting

Alison Bautovich, M.B.B.S., B.Sc. (Med), Colleen Loo, M.D., Ivor Katz, Ph.D., Donel Martin, Ph.D., Samuel Harvey, Ph.D.



Thank you

- Collaborators: Dr Alison Bautovich
  A/Prof Ivor Katz
  Prof Mark Brown
  Prof Colleen Loo
- s.harvey@unsw.edu.au

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