Depression and anxiety in chronic kidney disease

A/Prof Samuel Harvey
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
Spectrum of mood

MOOD

Depressed  Sad  Euthymic  Happy  Manic
ICD-10 Depressive Episode: Core Symptoms

At LEAST two of the following

- Depressed mood
- Loss of interest and enjoyment
- Reduced energy
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.
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 Joseph McClay,1 Jonathan Mill,1 Judy Martin,3 Antony Braithwaite,4 Richie Poulton3
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![Graph showing the probability of major depression episodes with and without maltreatment for different genetic polymorphisms.](image-url)
Beyond the monoamine Hypothesis

Duman et al, 2012
How common is depression in CKD?

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

Suetonia Palmer¹, Mariacristina Vecchio², Jonathan C. Craig³, Marcello Tonelli⁴, David W. Johnson⁵, Antonio Nicolucci², Fabio Pellegrini²,⁶, Valeria Saglimbene², Giancarlo Logroscino⁷, Steven Fishbane⁸ and Giovanni F.M. Strippoli²,³,⁹,¹⁰

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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 overestimate 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)
Shared risk factors

Genetics
Childhood adversity
Attachment difficulties

Lifestyle and
Socioeconomic factors

Biological factors
(including inflammation)

Biopsychosocial consequences of both illnesses

Biological factors
(including inflammation)

Symptom burden
Functional impairment

Negative self carebehaviours

Loss

Renal disease

Depression
Why does all this matter?

Article in Press

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, PhD²,³,⁹,¹⁰
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)**
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)
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: ___________________________**

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

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>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</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead, or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

(add columns: 0  + 0  + 0  = **TOTAL:**)

*(Healthcare professional: For interpretation of TOTAL, please refer to American Psychiatric Association)*
Welcome

We are interested in knowing how much you are troubled by a number of symptoms, particularly pain, fatigue and low mood, and how much these symptoms affect your wellbeing. The information you give will help your doctor or nurse decide how best we can help you, and like other things you tell them the information you give is confidential. If you have any question about this please ask your doctor.

Hospital Number
First Name Initial
Last Name Initial

Start Questionnaires
Patient Name: EPR, TESTFIVE
DOB: 12/12/1978
Hospital No.: EPR5
NHS No.:

Clinical Information System

PCS

EULAR Response
Physician Global VAS mm

CRP mg/dl Date dd/mm/yyyy

Patient Assessment

Latest HAQ 2 Date 11/03/2011 dd/mm/yyyy
Modified HAQ 2
Fatigue 58 mm
Pain VAS 70 mm
EMS mins

PHQ-9 Score 11 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
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
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
Treating co-morbid depression

Antidepressants for depression in physically ill people (Review)

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

- Antidepressants were more efficient than placebo
- Suggests depression should be treated even if part of an “understandable” reaction to physical ill health
## Depression and chronic kidney disease: A review for clinicians

Alison Bautovich\(^1,2,3\), Ivor Katz\(^1,4\), Michelle Smith\(^1,5\), Colleen K Loo\(^1,3,6\) and Samuel B Harvey\(^1,3,6\)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Comments</th>
<th>Potential class adverse events</th>
<th>Recommendation for use in CKD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SSRIs</strong></td>
<td>(Hedayati et al., 2012; Taylor et al., 2012)</td>
<td>Nausea, dyspepsia and diarrhoea Headache and insomnia</td>
<td></td>
</tr>
<tr>
<td><strong>Citalopram</strong></td>
<td>(Cohen et al., 2004; Hosseini et al., 2012; Kelly et al., 2003)</td>
<td>Less than 15% excreted in urine Has been shown to treat depression in CKD and improve QOL Manufacturer does not recommend use if GFR&lt;20 ml/min Dose adjustment normally not required in renal impairment, but use with caution when GFR &lt;10 ml/min</td>
<td>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</td>
</tr>
<tr>
<td><strong>Fluoxetine</strong></td>
<td>(Baghdady et al., 2009; Blumenfield et al., 1997; Levy et al., 1996)</td>
<td>5–10% excreted in urine Long half-life If GFR &lt;20 ml/min, consider using on alternate days or low dose Small study suggested relative safety and efficacy in ESKD</td>
<td></td>
</tr>
<tr>
<td><strong>Sertraline</strong></td>
<td>(Brewster et al., 2003; DeVane et al., 2002)</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td><strong>Paroxetine</strong></td>
<td>(Doyle et al., 1989; Koo et al., 2005)</td>
<td>Less than 2% excreted in urine Increased plasma concentration found when GFR &lt;30 ml/min If GFR &lt;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)</td>
<td></td>
</tr>
</tbody>
</table>
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
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
New developments

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

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