Depression in the medically ill
The plan

Overview

• Concept of depression in the medically ill
• Epidemiology
• Aetiology
• Impact
• Treatment

Approaches to diagnosis

Depression in HIV/AIDS
What are we dealing with?

• “Depression”-conceptual and diagnostic muddle
  • A synonym for the affect of sadness
  • An expression of dissatisfaction with one’s life situation
  • A symptom of an illness
  • One of several disease syndromes
What are we dealing with?

- The confusion is frequently evident in C-L settings......”Mrs Jones is depressed, but she has good reasons to be depressed”
  - Does this mean Mrs Jones suffers from a depressive disorder (MDE)?
  - Does this mean Mrs Jones has normal and expected sadness asstd with her physical illness?
  - Often it means diagnostic uncertainty-*depression* has many overlapping meanings
  - Does this imply everyone with a physical illness like Mrs Jones will develop MDE

- And it can be dangerous- statements about the “understandability” of depression tend to explain away a serious psychiatric disorder that is eminently treatable
Depression in the medically ill

- So we need to
  - Distinguish distinct psychiatric syndromes from more non-specific affects
    - DSM-5: Major depressive disorder; Persistent depressive disorder (dysthymia); Depressive disorder due to another medical condition
  - Not confuse understandability and normality
  - Use the words sad, or demoralised when we mean the affect sometimes associated with physical illness
  - Develop appropriate treatment plans for particular depressive disorders
Epidemiology of depression in the medically ill

- Problematic
  - Lack of clarity regarding definition of a case
  - Many studies report symptoms: BDI, CES-D, HADS
  - Clinical diagnoses vs structured diagnostic instruments: PSE, DIS, SCID
  - Population studied: inpatient, outpatient, general practice
  - Type and severity of medical illness
  - Sample size
Epidemiology of depression in the medically ill

• “Depression” measured by self-report measures
  • Researchers vary cut-off points to dichotomise patients to ‘depressed’ and ‘not depressed’
    • e.g. CES-D≥16; BDI≥14; HADS ≥ 7 (11)
  • Researchers can also look at subscales e.g. somatic and cognitive items
  • But, these are only measures of level of symptoms
  • Should only be used as screening instruments- may or may not give reliable information re prevalence of specific disorders
    • Symptoms (e.g. insomnia) have various causes
    • Depressive symptoms may be quite transient
  • Reported in up to 50% of medically ill patients
Aetiology of depression in the medically ill

- Unrelated to the medical illness or its treatment
  - Depressive disorders are common-2007, NSMHW, 12 month prevalence = 6.2%
  - PH, FH, recent losses etc

- “Psychological reaction” to the physical illness
  - Illness-severity, time course, disabling/disfiguring
  - Treatment- side-effects, lifestyle changes, dependence on treating staff
  - Situational- family reaction, social/occupational sequelae, supports, other stressors

- “Biological factors”
  - CNS involvement, paraneoplastic syndromes, endocrine disturbance, steroids, chemotherapy, interferon, other medications
Impact of depression in the medically ill?

- Depressive disorders are associated with significant morbidity and mortality
- And in the medically ill
  - Increased functional disability
  - Increased somatic symptom reporting
  - Worse self care and management of illness
  - Poorer adherence to treatment regimens – depressed patients are 3x more likely to be non-compliant with medications than non-depressed patients (Di Matteo et al 2000)
- Increased mortality
  - Self care, medication adherence
  - And other mechanisms e.g. increased mortality in patients with CVD
Treatment of depression in medically ill

- Follows the principles we use in non-medically ill- thorough assessment- diagnosis, contributing aetiological factors, severity, risk, available supports
- And in addition, any special considerations b/c the medical illness
  - Can ‘contributing’ medications be reduced/ceased
  - Could prescribed psychotropics cause problematic drug interactions
    - Pharmacodynamic e.g. serotonin syndrome with SSRI and tramadol
    - Pharmacokinetic e.g paroxetine and (CYP2D6 metabolism) tamoxifen
  - Should drug dose be modified b/c hepatic or renal problems
- Bio-psycho-social approach
Diagnosis of depression in the medically ill

- All the problems of diagnosis of depression *i.e. disorder*, that we encounter in every patient
- Plus
  - Many of the symptoms of physical illness such as anorexia, fatigue, are also symptoms we use when making a diagnosis of depressive disorder
  - Research which led to criteria for MDE and Dysthymic disorder in DSM-111 etc was conducted on patients without significant medical illness
- Four major approaches to diagnosis of major depression in the medically ill- Inclusive, Aetiologic, Substitutive, Exclusive approach
- Overall prevalence rates reported 20-30%
Inclusive approach to diagnosis

- Rifkin and colleagues 1985;
- Simplest approach
- Uses the symptoms of depression whether or not they might be attributable to a primary physical problem
- Is reflected in interviews such as Schedule for Affective Disorders and Schizophrenia (SADS) and the RDC
- Regarded as conceptually clear and ‘clean’
- It is phenomenologic – consistent with DSM-111 atheoretical approach-no aetiologic inferences
- Maximises interrater reliability in diagnosis
- BUT, likely to overdiagnose b/c no discrimination regarding the cause of symptoms
Aetiologic approach to diagnosis

• Spitzer, Williams and Gibbon 1984
• Count a symptom towards the diagnosis of depression only if it is not clearly due to a physical illness (same as decision rule for SCID)
• DSM-111-R (1987) Criteria A .......‘do not include symptoms that are clearly due to a physical condition)
• But, not clear how these distinctions are to be made clinically-the approach requires inference of causality from unclear criteria-likely that its reliability might be low
• However, suggested physicians working in specific settings might become familiar enough with one disease process to be able to reliable differentiate between ‘normal’ symptoms of the illness (e.g. fatigue) and ‘excessive’ symptoms
Substitutive approach to diagnosis

- Endicott 1984; Cavanaugh, Clark& Gibbons 1983, 1991
- Designed to overcome confusion over the symptoms’ cause
- Change the criteria for depression in the medically ill- substitute other symptoms of depression when the DSM criteria are problematic
- How do you choose what to substitute?
  - Replace symptoms which may relate to physical illness with additional cognitive symptoms
  - Cavanaugh et al –factor analytic study using BDI found decreased energy was a poor discriminator of depression and indecisiveness was a relatively good one
  - Endicott-identified 4 criteria for possible substitution
- Not clear whether substitution leads to over or under diagnosis
  - Lower rates when compared with aetiologic approach
Endicott’s substitutive criteria (1984)

Possibly problematic DSM-111 criteria
- Poor appetite or weight loss
- Insomnia or hypersomnia
- Loss of energy or fatigue
- Difficulty thinking or concentrating

Substitution items
- Fearful or depressed appearance
- Social withdrawal or decreased talkativeness
- Brooding, self-pity or pessimism
- Mood not reactive (cannot be cheered up, does not smile, no reaction to good news)
Cavanaugh’s substitutive DSM-111-R criteria

- Added an additional symptom... Patient is not participating in medical care in spite of ability to do so, is not progressing despite improving medical condition and/or is functioning at a lower level than the medical condition warrants.

- And, for 3 symptoms said they must be temporally related to affective/cognitive symptoms of depression:
  - Weight loss or weight gain or increase or decrease of appetite
  - Insomnia or hypersomnia
  - Fatigue or loss of energy
Exclusive approach to diagnosis

- Derived from research on depression in cancer patients by Holland and colleagues at Sloan-Kettering Cancer Institute.
- Simply eliminated anorexia/weight loss and fatigue from the list of 9 depressive criteria and required 4 of the remaining 7 symptoms for a diagnosis of major depression (v 5 of 9 DSM-111-R).
- Like the inclusive approach this is relatively ‘clean’ as it specifies how to apply the criteria.
- BUT it makes it harder for a person to meet diagnosis—some patients with primarily vegetative symptoms will be missed.
Clinical practice-making a diagnosis

• All 4 approaches have specific advantages and disadvantages
• For research- can be argued the Sloane-Kettering group approach is best-maximises specificity i.e greatest confidence the true disorder is really present when diagnosed
• But, for the clinician-the need is to maximise sensitivity so to detect all possible disorders (minimise false negatives)- *depression is generally underdiagnosed* -so best approach is perhaps the inclusive one in the medically ill
  • And when in right situation substitutive approach may assist?
  • And suggest pay greater attention to psychological symptoms and anhedonia
Most physically ill patients retain variable affective responses to their environment, some of them pleasurable.

Unless in continuous pain, physically ill patients can usually respond to humour, to intimacy from family and friends, and to support from staff—so, report they get some pleasure from or have some interest in activities around them. They may be able to smile and laugh at jokes.

For those with pervasive and sustained loss of interest or pleasure a diagnosis of major depression should be considered—leading to review of what other symptoms are present and features on MSE including concentration and ST memory.
Depression in HIV/AIDS

In 1981, the June 5 edition of the US Communicable Disease Centre’s epidemiology newsletter, Morbidity Mortality Weekly Report (MMWR) featured a front page article describing a mysterious series of homosexual men from Los Angeles and New York with acquired immunodeficiency, pneumocystis carinii pneumonia and Kaposi’s sarcoma.
HIV/AIDS

1st recorded case in Australia - Sydney October 1982

1st Australian death in Melbourne in July 1983

Mid 1983, AIDS declared a notifiable disease in Australia
HIV/AIDS- the first decade

• 1987-1\textsuperscript{st} drug approved for treatment of HIV infection
  • Zidovudine (AZT) nucleoside analogue reverse transcriptase inhibitor
  • Did not provide LT benefits
  • Significant SE incl nausea, headaches, myopathy, anaemia

• Then followed
  • other nucleoside RTI
    • Didanosine (ddi), lamivudine (3TC), stavudine (d4T), zalcitabine (ddc)
    • Dual therapy had greater efficacy than monotherapy
  • Advances in prophylaxis against opportunistic infections esp PCP
HIV/AIDS- the second decade

• 1996
  • better understanding of the dynamics and pathophysiology of HIV
  • Viral load testing to assess response to treatment and prognosis
  • Introduction of new and more potent antiretroviral drugs
  • Drugs from 3 different classes used in combination –HAART

• HAART changed things
  • Sharp decline in incidence of AIDS-defining illnesses and hospitalisations and deaths
  • Estimated number of AIDS related deaths in USA fell by around 70% from 1995-1999
  • But, lots of SE, and complex medication regimens make adherence difficult
HIV/AIDS today

• Over the years a range of agents and distinct classes of antiretroviral drugs have been developed/are being developed
• Now 5 classes of antiretroviral drug-each of which inhibits a specific stage of the HIV lifecycle
• With proper adherence HAART can suppress viral replication for decades, dramatically increasing the life expectancy of the HIV infected individual
Fairfield group studies of Depression in patients with HIV/AIDS

- Established a C-L Psychiatry service at Fairfield Infectious Diseases Hospital in Melbourne in 1993
  - Formerly the Queen’s Memorial Infectious Diseases Hospital, estab 1904
  - 138 beds for treatment of infectious diseases in Melbourne
  - 40 beds for inpatient treatment of people with HIV/AIDS
HIV/AIDS in 1993

• Highly stigmatised disease
• Commonly debilitating opportunistic infections
  • Pneumocystis pneumonia
  • Cryptococcosis- meningitis, diarrhoea
  • Cerebral toxoplasmosis
• Awful prognosis
• Treatment had bad side-effects
• Psychiatric sequelae
  • HIV dementia
  • HIV mania
  • Depression?
Study 1- BDI in 100 outpatients

- Physician’s understanding about depression
- 100 consecutive patients completed BDI at physician review
  - 7 women, 93 men
  - Age range 24-64 (mean 36.48±8.86 years)
  - 72 homosexual/bisexual; 13 H/B and IDU
  - 6 heterosexual; 6 Hetero and IDU
  - 3 infected following blood transfusion
  - 59 asymptomatic, 41 symptomatic (AIDS)
  - 77 on antiretroviral therapy (34 on combination)
  - 57 taking prophylactic therapy against PCP
  - CD4 count 0-1220 (mean 270±249)
Study 1

- BDI scores range 0-42 (mean 14.38 ± 19.01)
  - 40 scored 0-10 (not depressed)
  - 40 scored 11-20 (mild depression)
  - 14 scored 21-30 (moderate depression)
  - 6 scored ≥ 31 (severe depression)

- Split to those scoring BDI ≥ 14 (n=44) and those scoring <14 (n=56)
  - 7 somatic items of BDI reported frequently irrespective of BDI score
  - Cognitive/affective items reported more frequently by those with score ≥ 14
    - Esp sadness, discouraged about the future, feeling like a failure, dissatisfaction, feeling guilty, feeling disappointed in self, feeling critical of self and suicidal ideation
Study 1- those with BDI ≥14 and those with BDI < 14

- Comparing sociodemographic and illness related variables
  - No difference in age or relationship status
  - More of those in ≥ 14 group were retired or on sickness benefits/disability pension
  - History of IDU more common in the ≥ 14 group
  - No association between CDC stage of disease, current CD4 count, months known to be seropositive, treatment with antiretroviral medications and high or low BDI score
Study 2-depressive disorder in 192 patients

- 192 patients recruited by RA during 1995/1996, completed BDI and various other questionnaires
  - Those scoring ≥ 14 on BDI seen by psychiatrist/registrar for assessment-diagnoses made using DSM-111-R
  - A random sample of patients scoring< 14 were seen (blind) for assessment
- BDI scores ranged 0-41 (mean 14.62 ±9.6)
Study 2-depressive disorder in 192 patients

- 95 patients scored ≥14 on BDI
  - Predictors of elevated BDI score were:
    - higher Life Event Inventory score;
    - being on sickness benefits/pension;
    - having diagnosis of AIDS;
    - no current relationship;
    - PH of depression
  - Cognitive/affective items more often endorsed by those with higher BDI scores: sadness, discouraged about the future, dissatisfaction, irritability, loss of interest in people, difficulty with decisions, feeling unattractive
Study 2 - psychiatric assessment

• Completed for 84 patients who scored $\geq 14$ on BDI (11 patients refused)
• Diagnoses made
  • Major depression n=21
  • Dysthymia n=1
  • Adjustment disorder with depressed mood n=7
  • Adjustment disorder anxious mood n=1
  • Adjustment disorder mixed n=1
  • Bipolar disorder (in remission) n=1
  • V code n=1
  • No diagnosis n=50
Study 2 - comparing those with depressive disorder (MD/dysthymia/adj dis with depressed mood) (n=29) and those without (n=55)

• Those with depressive disorder
  • Had greater mean ± sd BDI score 24.5±7.1 vs 19.7±8.4; p=0.08
  • Statistically signif different rate of reporting of 5 BDI items: discouraged about the future (p=0.02); irritability (p=0.02); loss of interest in people (p=0.02); sleep disturbance (p=0.03) and loss of interest in sex (p=0.06)

• Those without depressive disorder were more often on sickness benefits/pension (p=0.041) and were more often not in a current relationship (p=0.014)

• No differences in age, sex, living alone, excess alcohol or drug use, family or past history of depression, number (%) with AIDS
Study 3- utility of 4 approaches to diagnosis

• Aim- compare the utility of four approaches to the diagnosis of depression in patients with HIV/AIDS
  • Study subjects-male, IP, referred for assessment and/or management of depression and diagnosed with MD using DSM-111-R criteria (aetiological approach)
  • Controls- male, IP, referred to C-L and diagnosis of MD (DSM-111-R) not made
• Modifications to criteria sets
  • Substitutive- took out appetite/weight disturbance, psychomotor agitation/retardation, loss of energy and substituted sense of failure, sense of punishment, frequent crying
  • Exclusive- took out fatigue and appetite/weight disturbance (need 5 of 7 criteria)
Study 3

• ‘patients’ with MD according to DSM-111-R n=17
  • Substitutive criteria n=17
  • Inclusive criteria n=17
  • Exclusive criteria n=15 – when fatigue and weight loss omitted could not meet 5 of the remaining symptom groups

• ‘controls’ – nil of 17 met DSM-111-R criteria
  • Substitutive criteria n=2
  • Inclusive criteria n=5
  • Exclusive criteria n=1
Study 3- control #1

• Did not meet aetiologic criteria- DSM-111-R but did meet substitutive, inclusive and exclusive approaches

• Why........
  • Advanced HIV disease, CD4 35, moderate physical disability, met 8 of 9 criteria for depression in DSM-111-R but a number of symptoms were ‘excluded’ as weight loss, insomnia, loss of energy, apathy, decreased interest and poor concentration were all judged to be due to his physical illness- so could not meet DSM-111-R
  • In the exclusive approach only weight loss and fatigue were excluded, and patient had 6 of remaining 7 criteria
  • Judged to be depressed with inclusive and substitutive criteria
Study 3- control #2

• Did not meet aetiologic DSM-111-R criteria but did meet substitutive and inclusive criteria

• Why........
  • Multiple severe symptoms related to advanced disease and marked physical disability so not able to be counted towards a aetiologic DSM-111-R diagnosis
  • Patient had markedly depressed affect, feelings of hopelessness, sense of failure and fearfulness
Study 3- controls #3, #4, #5

• All met inclusive criteria but not aetiological, exclusive or substitutive criteria

• Why.....
  • All had physical symptoms thought to be due to the physical illness not due to depression-included symptoms of fatigue, weight loss, poor concentration, apathy and loss of illness.
Study 3

• We used aetiological DSM-111-R clinically and felt we had good understanding of when to apportion causation to physical v psychological illness

• Using different criteria sets and rules, up to 5 additional ‘depressed’ patients were identified from the control group but on follow-up and review did not feel any of these ‘false positive’ diagnoses made by other criteria sets were suffering from depression

• So……
  • Inclusive approach maximises sensitivity- but may mean some patients receive unnecessary treatment
  • Exclusive approach is ‘cleanest’-but may miss true cases of depression
  • Substitutive approach, less false positives; does depend on choosing appropriate substitute items
  • Aetiological approach which we favoured- does rely on inference-a method which is typically unreliable
Study 4 – exploring depression in a larger group

- 322 PLWHA (13 female, 309 male) attending GP clinics or ID outpatient clinic
- Used the Inventory to Diagnose Depression (IDD)-self report measure designed to detect MDD based on DSM-111 criteria (Zimmerman et al 1986)
- Mean age 41.4 years, 54.3% in paid employment, most were medically well, median CD4 count 476 cells/µL, median viral load 235 copies/mL, <20% had AIDS, 2/3 on HAART
- 37% using illicit drugs, mostly cannabis
Study 4

- 70 of 322 (21.7%) participants met criteria for syndromal depression (IDD)
- No difference between depressed v non-depressed –CD4 count, viral load, on/not taking antiretroviral therapy, duration known seropositivity, stage of disease
- Depressed group were
  - More likely to have a history of psychiatric illness
  - More likely to have a history of illicit drug use
  - Less likely to be in paid FT employment
  - Less likely to be involved in intimate relationship and to be living with partner
What did we learn from our studies?

• How useful is the BDI as ‘screen’ for depression in medically ill (study 1&2)
  • Significant number scored ≥ 14 on BDI- 44% study 1 and 49% study 2
  • In both studies those scoring BDI ≥ 14 were more likely to report cognitive/affective symptoms
  • In study 2, those with depressive disorder reported diff rates of 4 cognitive/affective BDI items: discouraged about the future, irritability, loss of interest in people, loss of interest in sex; as well as sleep disturbance.
  • In study 2, 49% scored BDI ≥ 14 but only 1/3 of that group had a depressive disorder- prevalence of depressive disorder around 16% of total study population
What did we learn from our studies?

• How did very different illness course/prognosis affect findings re depression (study 4)
  • Prevalence of depression 21.7% (IDD not clinical interview)
  • Comparing depressed and non-depressed
    • No difference in disease stage/treatment etc
    • Depressed more likely to have
      • PH psychiatric illness
      • History of illicit drug use
    • Depressed less likely
      • FT employment
      • Intimate relationship/living with partner
What did we learn from our studies?

• What is the best approach to diagnosis (study 3)?
• No easy answer!
• If the clinician is familiar with the physical illness, then aetiologic does seem a good approach
• The inclusive approach does not seem useful/appropriate b/c overdiagnosis (and no clinical skill!!) and the exclusive underdiagnosis
• The substitutive approach has face validity, but......
• So, the answer is being a good clinician- looking beyond a checklist of DSM symptoms, understanding the various manifestations of depression, longitudinal history, repeat assessment, corroborative information
<table>
<thead>
<tr>
<th>Contributor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Anne Mijch</td>
</tr>
<tr>
<td>De Jennifer Hoy</td>
</tr>
<tr>
<td>Dr Alan Street</td>
</tr>
<tr>
<td>Dr Alex Cockram</td>
</tr>
<tr>
<td>Dr Angela komiti</td>
</tr>
<tr>
<td>A/Prof Trevor Norman</td>
</tr>
<tr>
<td>Dr John Lloyd</td>
</tr>
<tr>
<td>Mr Paul Gretch</td>
</tr>
<tr>
<td>Ms Jean McCausland</td>
</tr>
</tbody>
</table>