Targeting depression after ARDS

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Sunnybrook Health Sciences and University of Toronto
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Conflicts of interest

• None
Objectives

- Review epidemiology of depression after ARDS
- Review interventions
- Highlight considerations for future research
The post ICU survivorship glass is well over 1/2 full for patients discharged home
Complex causal pathways to post ARDS morbidity

- Pre-ICU factors
  - Quality of life
  - Coping skills
  - Socioeconomic status

- Risk factor for critical illness
  - Trauma
  - Burn
  - Stroke

- Critical illness
  - ARDS
  - Sepsis
  - Nosocomial complications

- Critical care
  - Sedation
  - Pharmacologic paralysis
  - Immobility
  - Corticosteroids

- Mediating conditions
  - Musculoskeletal
  - Cognitive
  - Psychiatric
  - Risk factor related impairment
  - Response to post-ICU therapy

- Post-ICU factors
  - Family support
  - Rehabilitation

Post-ICU quality of life

Curr Opin Crit Care 2007;13:476–481
Psychiatric morbidity

- Delirium
- Cognitive impairment
- **Depression**
- Post-traumatic stress disorder
- Anxiety
Depression: important cause of lost DALYs

<table>
<thead>
<tr>
<th>Category</th>
<th>Disease or Injury</th>
<th>2002 Rank</th>
<th>2030 Ranks</th>
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<td>Within top 15</td>
<td>Perinatal conditions</td>
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<td></td>
<td><strong>Unipolar depressive disorders</strong></td>
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<tr>
<td></td>
<td>Diarrhoeal diseases</td>
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<td>Road traffic accidents</td>
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<td>Congenital anomalies</td>
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<td>Hearing loss, adult onset</td>
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<td>Violence</td>
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<td>13</td>
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<td>Self-inflicted injuries</td>
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<td>Diabetes mellitus</td>
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10-30% of depression DALYs avoidable using current Rx, assuming 50% coverage

‘Incidence’ after ARDS

• Questionnaires, variable cutpoints
  – None at 1 yr in 1st study
  – Median 34% (17%-43%) in 3 cohorts (n=169)
  – 41% at 5 yr
  – 28% 1 yr after H1N1 (1/3 received ECLS)

• Structured clinical interviews
  – 25% at 2 mo; 4% at 8 yr

• 22% of antidepressant-naive survivors prescribed antidepressants at 2 mo

Questionnaire vs. SCID

- Sens, Spec ~80%
- PPV 68% for score ≥16
- Imperfect for screening and for definitive dx

Psychosomatics 2006; 47:399–407
Comparison to other populations

• Post MI: 9% depression at 1 yr
• Post CABG: 38% at 5 yr

• General population: 9.5%
  – Using SCID over 1 year period

Risk factors for depression

• Premorbid status
  – Age, gender, education, SES
  – Alcohol and substance abuse

• Critical illness variables
  – Severity of illness, underlying diagnosis

• ICU variables
  – Sedation
  – Hypoglycemia
  – Length of ICU stay and MV

• Post-ICU variables
  – Physical recovery
  – Time since ICU discharge
Intensive care unit hypoglycemia predicts depression during early recovery from acute lung injury*

David W. Dowdy, ScM; Victoriano Dinglas, BS; Pedro A. Mendez-Tellez, MD; O. Joseph Bienvenu, MD, PhD; Jonathan Sevransky, MD; Cheryl R. Dennison, PhD; Carl Shanholtz, MD; Dale M. Needham, MD, PhD

• Prospective cohort study
• 12 ICUs, 4 hospitals, Baltimore, MD
• 104 consecutive ALI survivors
• Monitored during 1717 ICU patient-days
• Screened for depression at 3 months after ARDS

CCM 2008; 36: 2726-2733.
Depressive Symptoms and Impaired Physical Function after Acute Lung Injury
A 2-Year Longitudinal Study

- 40% cumulative incidence of depressive symptoms
- Greatest incidence at 3 months FU
- Risk factor:
  - Education < 12 yr; OR 3.14 (1.49–6.58)
- Others dropped out in regression
  - Disability or unemployment
  - Comorbidity burden
  - Hypoglycemia
- BDZ exposure not significant
Depressive Symptoms and Impaired Physical Function after Acute Lung Injury

Trajectory in patients who remit in 24 mo
- 39% depr.
- 54% phys.

Trajectory in patients who do not remit

Self-reported Depressive Symptoms and Memory Complaints in Survivors Five Years After ARDS

Neill K. J. Adhikari, MDCM; Catherine M. Tansey, PhD; Mary Pat McAndrews, PhD; Andrea Matte, BSc; Ruxandra Pinto, PhD; Angela M. Cheung, MD, PhD; Natalia Diaz-Granados, MSc; and Margaret S. Herridoe, MD, MPH

• Depressive symptoms were similar at ~2 and 5 years after ICU discharge
Implications: memory

• ↑ depression symptoms associated with ↑ memory complaints

• Other studies show relationship between major depression and objective memory deficits
  – ? reduced hippocampal neurogenesis

## Implications: HRQL

<table>
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<th>Study</th>
<th>Measure of Association</th>
<th>Instrument</th>
<th>PF</th>
<th>PR</th>
<th>BP</th>
<th>GH</th>
<th>V</th>
<th>SF</th>
<th>ER</th>
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- Symptoms of depression associated with a significantly lower HRQL
- Depressive symptoms were strongly associated with a diminished mental component score

Psychosomatic Medicine 2008; 70: 512--519.
Implications: mind-body connection

Adjusted OR 2.66 (1.17–6.01) for association
Implications: return to work

• At 2 yr: moderate-severe depression sxs ➔ less likely to return to work
  – OR 0.21, 95% CI 0.07-0.62
• At 5 yr: most patients had returned to work
  – Weaker and non-sig association with depression symptoms

CHEST 2009; 135;678-687; CHEST 2011; 140; 1484-1493.
What can be done?

• Routine ICU care:
  – Modification of sedation practices?
  – Avoidance of hypoglycemia?
The Long-term Psychological Effects of Daily Sedative Interruption on Critically Ill Patients

John P. Kress, Brian Gehlbach, Maureen Lacy, Neill Pliskin, Anne S. Pohlman, and Jesse B. Hall

- Patients from RCT and cohort
- No effect on BDI-II defined depression (small n)
- Trend to less PTSD (0% vs. 32%, p = 0.06)
What can be done?

• Don’t ignore prevalent cases:
  – Continue antidepressants the patient is already taking, or restart on ward transfer

• Treatment of incident cases:
  – Case-finding in ward and post-hospital settings
  – Challenges:
    • When?
    • Who treats?
    • How is treatment related to other priorities in rehabilitation?
The PRaCTICaL study of nurse led, intensive care follow-up programmes for improving long term outcomes from critical illness: a pragmatic randomised controlled trial

- structured case review including screening for psychological morbidity and referral if needed
- referred for psychological review
  - 24% at 3 mo, 6% at 9 mo
- No effect on depression or anxiety at 12 mo or less
- Reasons:
  - Population?
  - Timing of intervention?
  - Availability of specialist services?

BMJ 2009;339:b3723
The mental health bundle: bringing the couch to the bedside?
The ICU diary

• Data: patient’s appearance and condition, other ICU events, treatments, names of visitors

• Kept at bedside and completed by any staff
Clinical psychologist in the ICU

– educational interventions, counseling, stress management, psychological support and coping strategies

– 3 psychologists, €30,000/yr

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<tr>
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<th>Pre (n=86)</th>
<th>Post (n=123)</th>
<th>P</th>
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<tbody>
<tr>
<td>Anxiety</td>
<td>17.4%</td>
<td>8.9%</td>
<td>0.08</td>
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<tr>
<td>Depression</td>
<td>12.8%</td>
<td>6.5%</td>
<td>0.14</td>
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<tr>
<td>PTSD</td>
<td>57%</td>
<td>21.1%</td>
<td>&lt;0.0001</td>
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<tr>
<td>Psych meds</td>
<td>41.7%</td>
<td>8.1%</td>
<td>&lt;0.0001</td>
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Considerations for the future

• Importance of the correct instrument:
  – SF-36 mental health domains correlated with BDI-II
    • But insensitive to temporal changes detected by BDI-II
  – Measure affective state rather than somatic/neurovegetative symptoms

• Focus on modifiable risk factors in the ICU
  – Longer-term follow-up of ICU sedation trials
Considerations for the future

• Prevalence, incidence, and attributable risk
  – How much post-ARDS depression was present (even if untreated) before critical illness?
  – What is the attributable risk?
    • Relative effect of ARDS on risk of new depression may be high even if absolute risk is not
  – Is the ICU (vs hospital, surgery) even a risk factor?

• Population-based cohort with long time horizon pre-ICU and control group not admitted to ICU
Considerations for the future

• Candidate interventions are complex
  – Timing
  – Personnel
  – Duration of follow-up
  – Availability of specialist referral
  – Need to be informed by pilot data

• Statistically indeterminate trial of a complex intervention may inspire unwarranted nihilism
Conclusions

• The apparent incidence of depression post ARDS is high
• Even if uncovered by ICU care and not caused by ICU care, these symptoms interfere with physical function, QoL, and may delay return to work
• Early psychological support in the ICU may prevent some of this
• Tailored post-ICU follow-up needs further study