Depression in advanced cancer - pitfalls and possible solutions

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Challenges – clinical- and research-wise

- Depression disorders not very common *(Mitchell et al., 2011)*
  - 15% MDD, Adjustment disorder 15%
- Depression: under-detected & under-treated
  - Stable over years & across countries
  - A huge literature; PubMed Sept 2016:
    - ✓ Depression + Cancer=18762 hits 2016
- Has research contributed to suboptimal practice?
  - What can we learn from our mistakes?

Outline

- Ambitious title for 30 min!
  - Share some experiences & reflections
- Background - general aspects
- Conceptual issues
  - The HADS–era and anhedonia
- Assessment and classification
- Materials
- Conclusions

Background – some general aspects

Why interested in the theme?

- Trained as a psychiatrist
- Researcher in oncology and palliative care since 1993
- Studied "depression" from 1993
  - Methodological flaws:
    - ✓Not defined the concept
    - ✓Not assessed relevant variables for studying depression
    - ✓Used suboptimal questionnaires – based upon tradition
- Studies on depression in pall. care since 2006
  - Methodological and empirical

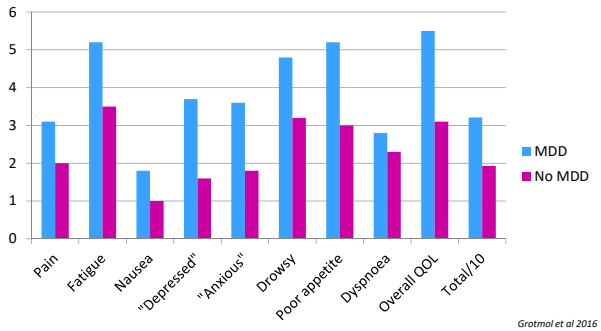
Why is depression of any interest?

- Often not addressed
  - Depression:
    - ✓"Difficult" for non-mental HCPs?
    - ✓Stigmatized
- Depression disorder impacts upon:
  - **QOL & symptoms – few studies**
  - Adherence to oncological treatment
  - Health care consumption
    - ✓Costs
  - Families
  - Wish for hastened death
  - ……..

Depression impacts negatively – QOL

- **QOL – the main goal of palliative care**
  - Determinants?
- EPCRC-CSA data – a possibility to explore QOL predictors
  - 572 pts. – data on disease, social factors and subjective health
  - Limitation – cross-sectional study
- Poor QOL – "predictors":
  - CRP ↑
  - Short survival-time
  - Poor functional status
  - Pain ↑
  - **Depression severity (5 psychological items PHQ9)**
    - ✓Depression severity: 6.7% of observed variance (30%) *Grotmol /Lie et al 2016*

Depression impacts negatively - symptoms – ERCRC CSA-data



Grotmol et al 2016

Depression – some general aspects

- Symptoms – continuous
- Syndromes – categorical
  - Psychiatric disorders – diagnostic systems (ICD10 / DSMV)
    - ✓ Depression Disorders
    - ✓ Adjustment disorders
- Depression used as a term for both
  - Without clearly distinguishing between them

Depression – some general aspects (2)

- Depression and anxiety symptoms co-occur
  - In "normal" emotional reactions
  - In adjustment disorders – "more than anticipated"
  - Anxiety – a common symptom among depressed *(Brenne 2013)*
- **Symptoms vs. syndromes**
  - Not separated in literature & clinics
  - Depression-item in ESAS – what does it measure? *(Brenne 2016)*
    - ✓ Translation or concept?

Symptom vs. disorder

- Symptoms – common and normal
- When do symptoms constitute a disorder?
  - Discussed - cultural perceptions of disease
    - ✓ Statistical modelling - DSM
- Incorporated in psychiatric diagnostic systems
  - **Rules or norms** – varying through-out history
- Fairly agreed-upon criteria in psychiatry/psychology
  - Defined symptoms
    - ✓ Intensity – above a certain level
  - Duration – more than… (two weeks)
  - Functional consequences

What is depression disorder?
DSMV-criteria depression disorder:
-symptom-threshold + duration + functional decline

- **Symptom overlap – a special challenge in pall care**
- **Will be addressed**

Criterion [1]	Symptom type
1. Lowered mood [2]	Psycological
2. Anhedonia [2]	Psychological (?)
3. Anorexia / weight loss	**Somatic**
4. Insomnia / hypersomnia	**Somatic**
5. Psychomotor agitation / retardation	Psychological - Somatic
6. Fatigue	**Somatic**
7. Selfblame	Psychological
8. Lowered concentration	Psychological - Somatic
9. Thoughts dead / suicide	Psychological

[1]: Five or more present for more than 14 days and a change from previously
[2]: One must be present

Conceptual issues – Anhedonia and the HADS-era from 1990

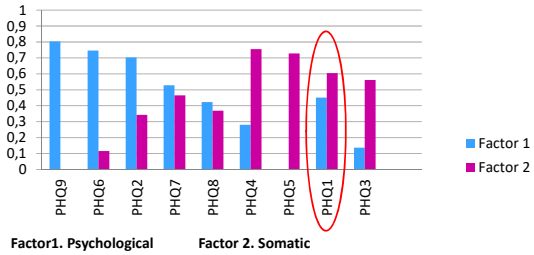
Hospital Anxiety and Depression Scale - *HADS*

- Constructed in 1983 (*Zigmond and Snaith 1983*)
  - Origin: Zung's self-rating depression scale (*1965*)
- 7 items on anxiety, 7 items on depression
  - **Postulated: Unaffected by somatic status**
  - Time window= 1 week, not functional consequences
- Recommended for use in:
  - Oncology (*Maguire, Br J Canc 1989*)
  - Palliative care (*Barraclough, BMJ 1997*)
- Widely used – first in Europe, later N-America:
  - A measure of distress
  - But often referred to / used a diagnostic tool

Anhedonia – a major depression criterion

- Anhedonia + mood + (fatigue -ICD)) = major depression criteria
- Anhedonia - the major content in HADS *(Zigmond and Snaith, 1983)*
  - *Inability to feel pleasure from stimuli that usually give pleasure*
  - 5 items measures anhedonia in HADS-depression scale
    - ✓2 other items: Mood & retardation (=fatigue)
- HADS-depression:
  - Poor predictor of dep. disorder in adv. cancer
    - ✓Le Fevre (1999), Lloyd Williams (2001)…
  - Hypothesis: because primarily measures anhedonia?

PHQ-9 Factor structure rotated – CSA-data



Factor1. Psychological
PHQ9=Self-harm
PHQ6=Self-blame
PHQ2=Mood
PHQ7=Concentration
PHQ8=Retardation

Factor 2. Somatic
PHQ4=Fatigue
PHQ5=Appetite
PHQ1=Anhedonia
PHQ3=Sleep

Possible solutions

- Beware of terminology
  - Symptom - distress – disorder = different constructs
  - Not choose instruments based upon name
- Not use instruments based upon tradition
- Beware of effects of sample's characteristics
- Anhedonia – "more somatic" than psychological
  - Of special relevance in advanced cancer
- HADS – a measure of distress
  - Poor predictor of depression disorder in advanced ca.

Methodological aspects
-assessment and classification

Original Article — MEDICINE

Depression assessment and classification in palliative cancer patients: a systematic literature review

SAGE

- Part of EU-funded project (EPCRC-project)
- Systematic review on depression assessment
  - 202 papers 1966-2007
  - 106 different assessment methods
  - **76 used HADS**
  - 65 used methods unique to one study
  - 27 used structured interviews – gold standard
- Stable pattern over time-periods
- Makes comparisons impossible

Palliative and Supportive Care (2013), **11**, 491–501.
© Cambridge University Press, 2013 1478-9515/13 $20.00
doi:10.1017/S1478951512000909

Depressed patients with incurable cancer: Which depressive symptoms do they experience?

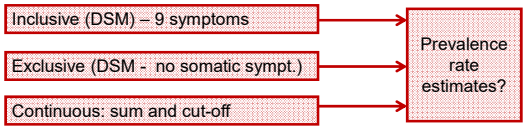
What do the patients tell us?

Also part of EPCRC-project

30 pts. on antidepressants – semi-qualitative study

- Lowered mood & anhedonia
- Restless, constantly focused on disease, sleep disturbance, guilt & thoughts of death as a solution
- **Appetite & weight, fatigue & concentration inseparable from disease – the symptom overlap**
- "New" symptoms: despair, anxiety & withdrawal
- Confirms the symptom overlap

Diagnostics: Does scoring method matter?



Inclusive and exclusive: followed DSM algorithm;
- At least 1 major criteria + 4 other (9 total)
- At least 1 major criteria + 2 other (5 total)

Depression in advanced cancer – Assessment challenges and associations with disease load

H.C. Lie [a,b,*], M.J. Hjermstad [c,d], P. Fayers [c,e], A. Finset [a], S. Kaasa [c,f], J.H. Loge [a,d], on behalf of the European Palliative Care Research Collaborative (EPCRC)

Effect of scoring method (EPCRC, N=969)

- Prevalence rates by scoring method
  - Exclusive: **14.9%**, inclusive: **13.7%**, sum-score: **45.3%**
    - ✓Kappa=.81 for algorithm-scored
    - ✓Two different populations by algorithm & sum-score; Kappa=.32
  - All depressed: higher scores on somatic symptoms
- Limitations
  - Cross-sectional
  - PHQ-9 – screening tool - mode of administration effect?
  - No external criterion

The Edmonton Symptom Assessment System: Poor performance as screener for major depression in patients with incurable cancer

SAGE

- PHQ-9 MDD as the standard
  - EPCRC-data (N=969)
- ESAS-depression item = poor screener
  - Cut-off ≥2: sensitivity=.69, specificity=.60
  - Cut-off ≥4: sensitivity=.51, specificity=.82
  - Wording/translation? **50% Norwegians**
- Performance not improved by adding anxiety-item
- PHQ-9 – a disputable criterion
- **Should have explored the QOL-item**

Assessment & classification – possible solutions

- Structured interview = gold standard
  - PHQ-9 – optimized content validity
  - Can replace interview?
    - ✓Mode of administration effect or?
- Recommendations for use of instruments:
  - Carefully examine population studied
- Beware of symptom overlap
  - Has been known for < 30 yrs.
  - DSM-algorithm makes overcome?
    - ✓Need replication
- Do not rely on ESAS for depression screening

Materials – some aspects

Review Article

How Are Patient Populations Characterized in Studies Investigating Depression in Advanced Cancer? Results From a Systematic Literature Review

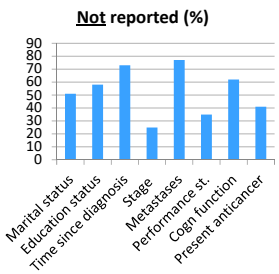
Ekene Janberidze, MD, Marianne Jensen Hjermstad, PhD, Dagny Faksvåg Haugen, MD, PhD, Katrin Barth Sigurdardottir, MD, Erik Torbjørn Lohre, MD, Hanne Catherine Lie, PhD, Jon Håvard Loge, MD, PhD, Stein Kaasa, MD, PhD, and Anne Kari Knudsen, MD, PhD, on behalf of EURO IMPACT

"Depression variables" – seldom assessed *(Janberidze et al,2014)*

- 59 studies on depression & pall.care / advanced cancer (2007-2011)
- Core depression variables not reported
- 50% used HADS
- I.e. studies on symptoms / distress
- **Similar practice for cancer diseases?**

"Basic data" – infrequent/inconsistent reporting

- Core social variables reported in 50%
- Core disease / treatment variables possibly affecting depression invariably reported (20%-70%)
- Consequences for
  - Internal validity of depression measured
  - External validity – i.e. comparisons



Possible solutions

- Beware of the impact of disease status
  - Assess disease and treatment status according to best available recommendations
- Assess relevant "depression variables"
  - Particularly those that might affect upon your study aims / outcome measure
- A need for "standards"
  - Of core palliative variables – **EAPC basic data set**
  - Of "depression-related" variables
  - CONSORT-like aproach?

Conclusions

- Depression; syndrome and symptom
  - Need for consistence in use of concepts
- Lack of definitions / heterogeneous methods
  - Hinders progression in research – hinders clinical impact
  - Anhedonia not a "pure" psychological criterion
- PHQ-9 functions / recommended for screening
  - But still subordinate to str. interviews
    - ✓ Need for studies
- Consider the assessment of the study population carefully

Thank you for your attention