UNIVERSITEIT GENT

Appropriate Use of Psychotropic Drugs in Frail Older People

Prof. dr. Mirko Petrovic

Department of Geriatrics
Ghent University Hospital

BVGG-SBGG Interuniversity Course, 16th March 2018

Appropriate Use of Psychotropic Drugs in Frail Older People

- Antipsychotics
- Benzodiazepines
- Antidepressants
  - Prevalence
  - Particular aspects in older adults
  - Recommendations for appropriate use/ withdrawal

Geriatric drug utilisation of psychotropics in Belgian nursing homes

- Objective: to determine the prevalence of psychotropic drug use in Belgian nursing homes, in relation to residents' and institutional characteristics.

- Methods: the PHEBE project (Prescribing in Homes for the Elderly in Belgium, 2005) was a cross-sectional study, investigating drug use in 76 nursing homes.
  - Psychotropics were categorised into antipsychotics, benzodiazepines, antidepressants and anti-dementia drugs using the ATC classification.

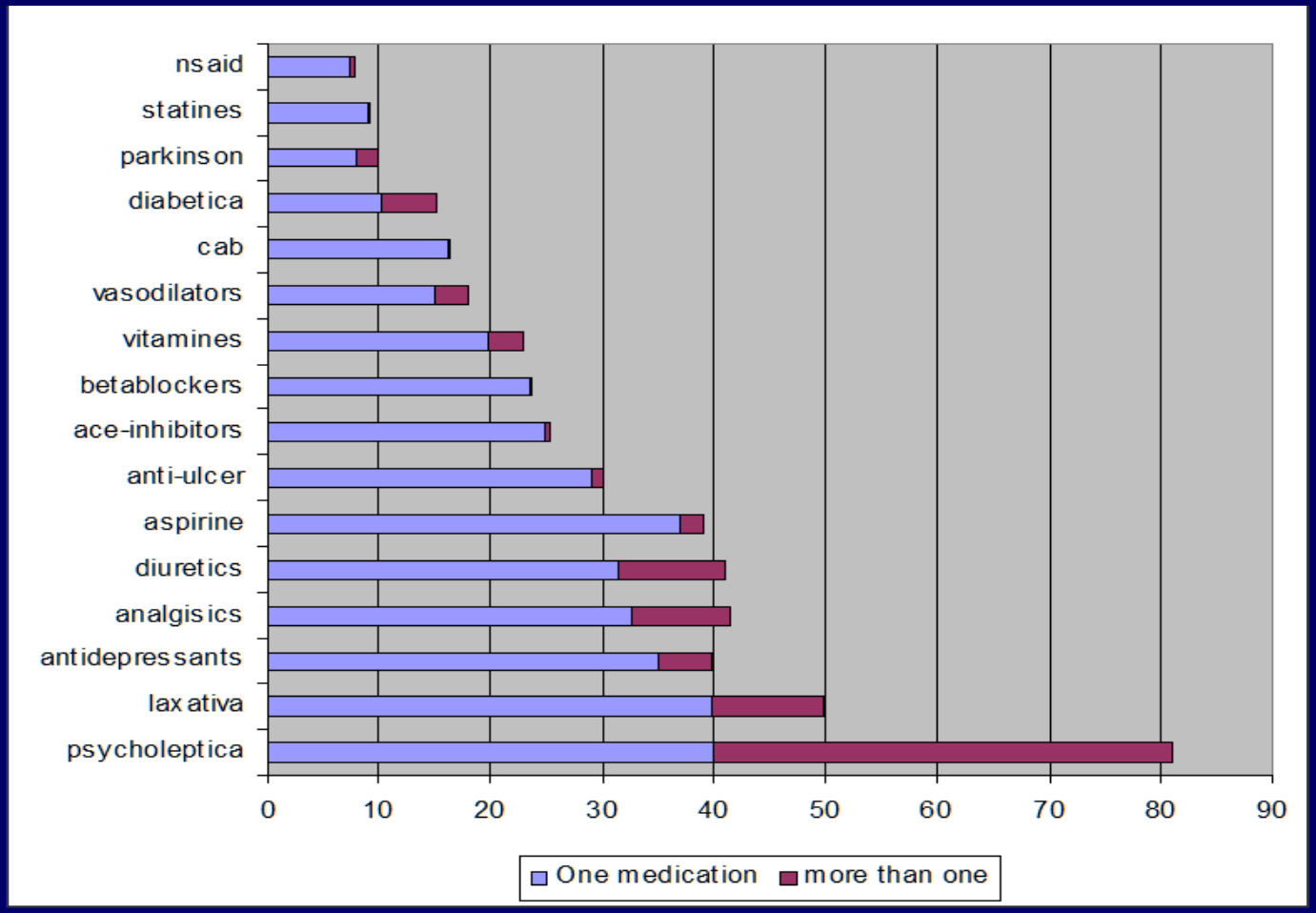
Azermai, Elseviers M, Petrovic M et al.
Hum. Psychopharmacol Clin Exp 2011; 26: 12–20.

Geriatric drug utilisation of psychotropics in Belgian nursing homes

- Results:
  - Residents' mean age (n=1730) was 85 (SD: 8) years and 78% were female.
  - The overall prevalence of psychotropic drug use among nursing home residents was 81%.
    - Benzodiazepines were used by 54% and antipsychotics by 33% of all residents.
    - Antidepressants were prescribed in 40%.
      - Residents received a higher number of antipsychotics ($p<0.001$) but fewer antidepressants with increasing severity of dementia.
    - Anti-dementia drugs were used by 8%.
  - Institutional characteristics showed no relationship with psychotropic drug use, except for a lower use when medication was dispensed by a pharmacist ($p=0.001$).

Azermai M, Elseviers M, Petrovic M et al.
Hum. Psychopharmacol Clin Exp 2011; 26: 12–20.

Prevalence of medication use per therapeutic group in Belgian nursing homes



Vander Stichele R et al.
Belgian Health Care Knowledge Centre, 2006

Geriatric drug utilisation of psychotropics in Belgian nursing homes

- Conclusion:
  - As in other European countries
    - the Netherlands 83%, van Dijk K. et al., 2000
    - Austria 75%, Mann E. et al., 2009
    - Sweden 73%, Holmquist I. et al., 2003
  - the prevalence of psychotropic utilisation in Belgian nursing homes is exceedingly high (81%), with excessive duplicate use.

Azermai M, Elseviers M, Petrovic M et al. Hum. Psychopharmacol Clin Exp 2011; 26: 12–20.

Psychotropic drugs in frail older people

- Mainly used to treat behavioural and psychological symptoms of dementia (BPSD)
  - an umbrella term that embraces a heterogeneous group of non-cognitive symptoms and behaviours

Psychotropic drugs in frail older people

Medication Sensitive Symptoms:

- Agitation
- Physical aggression
- Irritability
- Psychotic symptoms
- Depression
- Anxiety

Psychotropic drugs in frail older people

Pharmacotherapy Spectrum:

- Antipsychotics
  - typical vs. atypical
- Benzodiazepines
- Antidepressants
- Anti-epileptics
- Cholinesterase-inhibitors

Antipsychotics

Antipsychotics

- Broadly used
- A Canadian study of 15 317 NH-residents
- Antipsychotics prescribed in 32.4%
- A great variation betweens NHs
  - Not explained only by demographic or clinical factors (dementia, psychosis)

Graham I et al. Healthc Q. 2007;10: 20-2.

Antipsychotics

- The most important indications:
  - Physical agression
  - Psychosis (hallucinations and delusions)

Typical antipsychotics

- Limitted evidence concerning efficacy in treatmant of BPSD
- No difference between different products in efficacy and adverse effects (extrapyramidal symptoms, sedation)
  - 2 RCT's
  - 2 meta-analyses (12 studies)
  - Study duration 17 d – 16 w

Sink K et al. JAMA 2005; 293: 596-608.

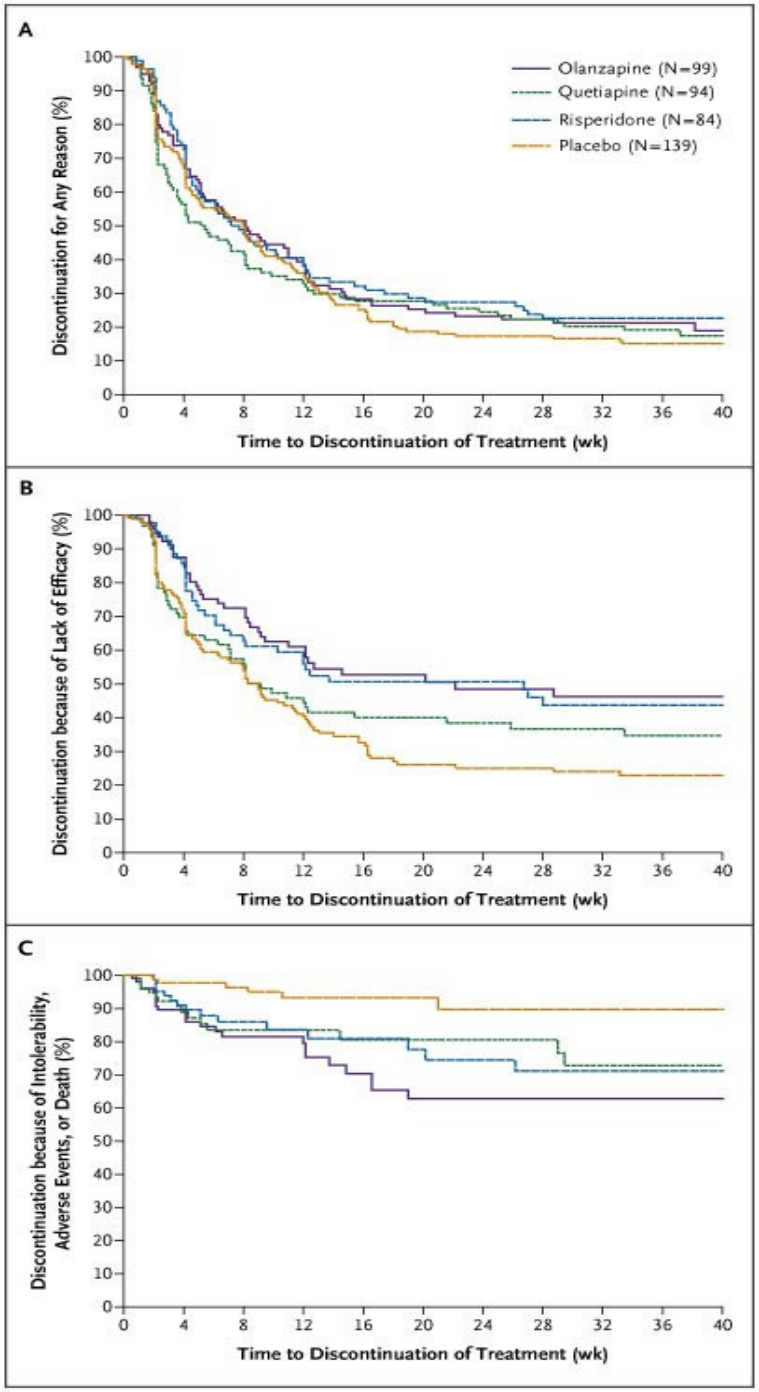
Atypical antipsychotics

- Olanzapine (5-10 mg/d) en risperidone (1 mg/d) seem moderately effective in the treatment of BPSD in patients with Alzheimer- or vascular dementia
- The incidence of extrapyramidal symptoms is low, but sedation remains a problem
- A higher risk of ischaemic CVA has been shown
  - 6 RCT's
  - Studieduur 1 d – 12 w

Sink K et al. JAMA 2005; 293: 596-608.

Risperidone for BPSD (< 3 months): Efficacy

Ballard C, Howard R. Nature Neuroscience Reviews, 2006	Target symptom	Outcome measure	Mean Difference from Placebo
Risperidone 1mg	Psychosis	BEHAV-AD	MD -0.79, 95% CI -1.31 to -0.27, p=0.03
Risperidone 1mg	Aggression	BEHAV-AD	MD -0.84, 95% CI -1.28 to -0.40, p=0.0002
Risperidone 2mg	Aggression	BEHAV-AD	MD -1.50, 95% CI -2.05 to -0.95, p<0.0001



CGIC improvement at 12 weeks

32% olanzapine
26% quetiapine group,
29% risperidone group,
21% placebo group

(P=0.22).

Schneider L et al. NEJM 2006; 355:1533-1538

Risperidone for BPSD (< 3 months): Adverse effects

Ballard C, Howard R. Nature Neuroscience Reviews, 2006	Adverse Outcome	Odds Ratio
Risperidone	Stroke/CVAE	3-4
Atypical antipsychotics	Mortality	1.5-1.8
Atypical Antipsychotics	Accelerated cognitive decline	1.5-4
Risperidone (1-2mg)	Ankle oedema	2.4-3.3
Ripseridone (1-2mg)	Chest infections	2.9
Risperidone (1-2mg	Extra-pyramidal symptoms	1.8-3.4
Risperidone (1-2mg)	Sedation	2.4-4.5

Antipsychotics and hip fracture risk in HN residents

Medication	Adj. OR	95% CI
Atypicals	1.37	1.11-1.69
Olanzapine	1.34	0.87–2.07
Risperidone	1.42	1.12–1.80
Conv. antipsychotics	1.35	1.06–1.71
Haloperidol	1.53	1.18–2.26

Liperoti R et al. J Clin Psych 2007;68: 929-34.

Increased mortality risk due to antipsychotics in NH residents

- FDA 2005: meta-analysis of 17 placebo controlled trials with atypical antipsychotics in AD: a significant increase of mortality risk associated with use of antipsychotics (OR 1.7)

- Schneider et al, JAMA 2005 : meta-analysis of 15 trials, with a significant increase of mortality risk (OR 1.54)

- Mortality risk less increased in observational studies

Antipsychotics
Recommended daily dose

- Haloperidol: 0.25 – 2 mg
- Risperidone: 0.25 – 2 mg
- Olanzapine: 2.5 – 10 mg
- Quetiapine: 12.5 – 100 mg

Antipsychotics for Dementia website:
www.bpac.org.nz/a4d

Guidelines for rational use of antipsychotics in older people with dementia

- Therapeutic response with antipsychotics is usually expected within 1 to 2 weeks and clinical improvement within 12 weeks. The treatment should be ceased in case of no response and the patient should be re-evaluated.

- After a period of stabilisation, cessation of antipsychotics only occasionally leads to a relapse of BPSD.

- Re-evaluate use of antipsychotics within 3 months and if the symptoms are under control undertake a withdrawal.

- Reduce the dose with 50% every 2 weeks and stop 2 weeks after the use of the lowest dose.

NICE Clinical Guideline 42: Dementia. 2006.

Guidelines for rational use of antipsychotics in older people with dementia

- Antipsychotics are not recommended in case of mild or moderate symptoms
- Antipsychotics could be considered for the treatment of severe symptoms
  - After evaluation of pros and cons
  - Attention for adverse effects and consciousness
- The treatment should be targeted and limited in time

NICE Clinical Guideline 42: Dementia. 2006

Therapy
3T' (target, titration, time)

- Non-pharmacologic: first choice in mild forms
- Pharmacologic : in case of severe distress
- The use of antipsychotics should have a specific target symptom.
- The initial dose should be low and has to be slowly up-titrated.
- Use of antipsychotics should be limited in time.
- Avoid mutual combinations and combinations with other psychotropics.

Withdrawal versus continuation of chronic antipsychotic drugs for BPSD

- 9 randomised trials (606 participants)
  7 in Nursing Homes, one in an outpatient setting

  and one in both settings

- Different types of antipsychotics, prescribed at different doses - were withdrawn

- Both abrupt and gradual withdrawal schedules were used

Declercq T, Petrovic M et al. Cochrane Database of Systematic Reviews 2013, Issue 3. Art. No.: CD007726. DOI: 10.1002/14651858.CD007726.pub2.

Withdrawal versus continuation of chronic antipsychotic drugs for BPSD

- 9 different trials from 11 papers:

- Devenand D et al. NEJM 2012; 367:1497–507.
- Devanand D. et al. Int J Geriatr Psychiatry 2011; 26:937–43.
- Ballard C. et al. PLoS Med. 2008; 5:e76.
- Ballard C. et al. J Clin Psychiatry. 2004; 65:114-9.
- Ruths S. et al. J Am Geriatr Soc. 2004; 52:1737-43.

Withdrawal versus continuation of chronic antipsychotic drugs for BPSD

- van Reekum R et al. Int Psychogeriatr. 2002; 14:197-210.
- Cohen-Mansfield J et al. Arch Intern Med 1999;159:1733-40.
- Bridges-Parlet S et al. J Geriatr Psychiatry Neurol 1997;10:119-26.
- Findlay D et al. Int J Geriatr Psychiatry 1989, 4: 115-120.

Withdrawal versus Continuation of chronic antipsychotic drugs for BPSD

- Primary efficacy outcomes were success of withdrawal and BPSD relapse.
  - In 7/9 trials, no overall significant difference regarding primary outcomes was reported between groups.
  - In one pilot study of patients who had responded to haloperidol, time to relapse was significantly shorter in the discontinuation group ($P = 0.04$).

Withdrawal versus Continuation of chronic antipsychotic drugs for BPSD

In one trial in patients who had responded well to risperidone for 4 - 8 months discontinuation led to an increase in the Neuropsychiatric Inventory score of 30% or greater (P = 0.004, hazard ratio 1.94, 95% CI 1.09 to 3.45 at four months).

Withdrawal versus Continuation of chronic antipsychotic drugs for BPSD

- Our findings suggest that in many patients with Alzheimer's dementia and BPSD, chronic antipsychotics can be safely withdrawn chronic antipsychotics can be without detrimental effects on their behaviour.

- The question whether withdrawal is associated with any change in cognition or function has not been examined.

- The results of this review suggest that discontinuation programmes could be incorporated into routine practice.

Withdrawal versus continuation of chronic antipsychotic drugs for BPSD

- However, 2 studies of people whose agitation or psychosis had previously responded well to antipsychotic treatment found an increased risk of relapse or shorter time to relapse after discontinuation.

- Two other studies suggest that people with more severe NPS at baseline could benefit from continuing their antipsychotic medication. In these people, withdrawal might not be recommended.

Benzodiazepines

Benzodiazepines

- The most important indications:
  - Insomnia
  - Anxiety/ Unrest

Prevelance of BZDs use in older adults

- Individuals over 65 years receive 30% of all prescriptions for benzodiazepines.
- One-year exposure to BZD use for older adults averages 32% (range 9-54%).
- Prevalence of BZD use in the community setting among older people varies between 10 and 37%.
- Prevalence in the institutional setting is very high (acute care up to 45%, long-term care up to 72% and terminal care up to 59%).

Svarstad B et al. JAGS 2001; 49: 1673-1678.
Fourrier A et al. Eur J Clin Pharmacol 2001; 57: 419-425.
Petrovic M. et al. Acta Clinica Belgica 2006; 61:119-126.

Side effects

- Tolerance
- Rebound insomnia
- Subjective hangover
- Residual effects
- Dependence
- Paradoxical stimulation

Particular aspects in older adults

- Decreased consciousness, confusion, motoric disorders with higher risk of falls and fractures
- Memory and coordination disorders, slowed learning process
- Respiratory depression and hypercapnia

Morgan K, Drugs 1990; 40: 688-96.

Modifications in pharmacokinetics

- Due to decreased lever blood flow, plasma albumin and lean body mass:
  - a prolongation of the half-life of the oxidized drugs
  - increased elimination half-time
  - prolonged effects on the days after administration and accumulation of active metabolites

McLean AJ. Pharmacol Rev 2004;56:163-84

Modifications in pharmacodynamics

- May occur as consequence of increased sensitivity of receptors.
- Older people are more sensitive to the influence of benzodiazepines on cognitive function.
- Older adults require both a lower dose and a lower plasma concentration to cause a constant level of sedation.
- Dosing: >65 year: < 50%

Hilmer SN. Fund Clin Pharm 2007; 21:217-30
Cusack BJ. Am J Ger Pharmacother 2004; 2:274-302

Withdrawal from benzodiazepines

- No uniform recommendations with regard to optimal duration of a withdrawal programme
  - a variable withdrawal period ranging from 2 to 12 weeks may be allowed
- The motivation should be evaluated
- Stabilisation period
- Withdrawal period

Withdrawal from benzodiazepines

- Review BZD medication
  - initial reasons for use
  - type of BZD, response to, and patterns of use
  - side-effects reported or observed
  - current / past withdrawal history and symptoms
- Obtain physical history (concurrent medical problems)
- Mental health history (e.g. depression)
- Other drug (and alcohol / prescription drug) use
- Discuss options
  - risks of continued and prolonged use
  - withdrawal potential / risks, management options

Withdrawal from benzodiazepines

- Progressive withdrawal
  - A fixed withdrawal schema (dose, time interval)
  - An individually tailored withdrawal schema
- Intermittent prescribing
  - Periods of use exchanged with drug free periods
- Fast withdrawal

Petrovic M et al. Eur J Clin Pharmacol 2002; 57: 759-764

Withdrawal from benzodiazepines

- Transformation to an equivalent diazepam dose (1 week)
- 20% reduction per week (until week 4)
- Eventually spread last 20% in 2 weeks of 10%
- Eventually prologue every step by 1 week

Salzman C. J Clin Psychopharmacol. 2000; 20: 99.

Withdrawal

- A short-term BZD withdrawal program is possible in the hospital setting.
- Two-thirds of chronic older users can successfully be withdrawn from BZDs by a single step of dose reduction, maintained during 1 week if psychological support is included in the withdrawal programme.
- A faster taper should be encouraged, as it may fit in a short-term admission to the ward. Withdrawal symptoms, if any, will not pass unrecognised and may be sufficiently treated.
- Although abrupt cessation of benzodiazepine treatment is uneventful in a substantial number of patients, it is not recommended because of potential delirious withdrawal effects.

Petrovic M et al. Int J Geriatr Psychiatry 1999; 14: 754-760
Petrovic M et al. Eur J Clin Phharmacol 2002; 57: 759-764.

Benzodiazepines

- Preference for intermediate acting BZD
  - Lormetazepam, lorazepam, oxazepam
- Limited in time
  - For insomnia not longer then 2 weeks
  - For anxiety disorders max. 2 months
- Never combine 2 or more BZD at the same time
- Attention for combination with other psychotropics
- recommended daily dose:

á ✱ Equivalent of 5 – 10 mg diazepam

Morin C. et al. JAMA 1999; 281: 991-999.

Antidepressants

Antidepressants

- Community studies have shown that 25% of older persons report having depressive symptoms, but only 1% to 9% meets the criteria for major depression.

- Higher prevalence rates are reported in the hospitalised older people (36% to 46%) and patients in long-term care facilities (10% to 22%).

- Antidepressants are more hazardous in old age due to age-related pharmacokinetic and pharmacodynamic changes, concomitant diseases and polypharmacy.

Lebowitz B et al. JAMA 1997; 278: 1186-90.

Teresi J et al. Soc Psychiatr Epidemiol 2001; 36: 613-620.

Antidepressants

- Older patients are at an increased risk for adverse drug effects, which may be exacerbated by concurrent medical illnesses.
- Moreover, the same side effects may be more dangerous in older compared to younger adults. Drug interactions are also more likely in older patients, as they often take several medications.
- Because of these risks, it is advisable to “start low and go slow” when starting antidepressants in older patients.
- In general, it is recommended that initial antidepressant doses should be one-third to one-half of the usual adult dose and should be titrated appropriately to minimise adverse reactions.

Antidepressant use in Belgian nursing homes

- The prevalence of AD use in Belgian nursing homes was 39.5% (684/1730)
  - Depression 66.2%
  - Insomnia 13.4%
  - Anxiety 6.2%
  - Pain 2.5%

Bourgeois J et al. Drugs Aging 2012; 29: 759-769.

Antidepressant use in Belgian nursing homes

- Depression
  - SSRI (citalopram, sertraline, escitalopram) 74.8%; venlafaxine 10.7%; mirtazapine 8.2%
- Insomnia
  - Trazodone 90.5%
- Anxiety
  - SSRI 64.7%, trazodone 14.7%, venlafaxine 8.8%
- Pain
  - TCA 66.6%

Bourgeois J et al. Drugs Aging 2012; 29: 759-769.

Antidepressant use in Belgian nursing homes

- Prescribed daily dose
  - Depression: 1 DDD 58.4%, <1 DDD 32%, >1 DDD 9.5%
  - Insomnia: <1 DDD 98.2%
  - Pain: 87.5% <1 DDD

Particular aspects in older adults

- Fall risk
  - A significant dose-response relationship has been found between antidepressants and falls (HR 1.60, 95% CI 1.20-2.14).
  - Fall risk increases with 29% at 0.25 of DDD of an antidepressant.

Sterke C et al. J Clin Pharmacol 2012; 52: 947-955

Particular aspects in older adults

- Bone loss
  - Use of SSRI has been shown to be associated with an increased rate of bone loss at the hip in a chort of older women participating in the Study of Osteoporotic Fractures (a prospective chort study of community dwelling women).

Diem S et al. Arch Intern Med 2007; 167: 1240-45

Pharmacotherapy of depression in old age

- Systematic review of the literature
- Selection criteria:
  - Controlled clinical trials between 1980 and 2005 in English;
  - (MeSH): elderly, geriatric, senile, older, older age, later life aged, 60-and-over combined (AND) with depression or dysthymia AND pharmacotherapy;
  - Efficacy measures, number of patients, percentage of responders and diagnostic criteria used for diagnosis of depression had to be mentioned.
  - Specific inclusion criteria: randomisation of subjects, placebo or active comparator control arm and study duration of four weeks or greater.
  - Subjects age 60 and over and with diagnosis of major depressive disorder or unipolar depression using defined criteria, such as DSM.

- 36 randomized controlled trials of patients over the age of 60
- in addition to a meta-analysis which included 17 randomised controlled studies.

Petrovic M et al. Acta Clin Belg 2005; 60-3

Pharmacotherapy of depression in old age

- There is a paucity of data on the use of antidepressants in very old individuals, patients with significant comorbidity and patients with dementia.

- Existing clinical evidence suggests that the main antidepressant classes are equally effective in the treatment of older people with depression.

- Although newer antidepressants are not more effective than older ones, they are better tolerated and are safe especially in overdose. The adverse effect data suggest modest superiority of SSRIs over TCAs.

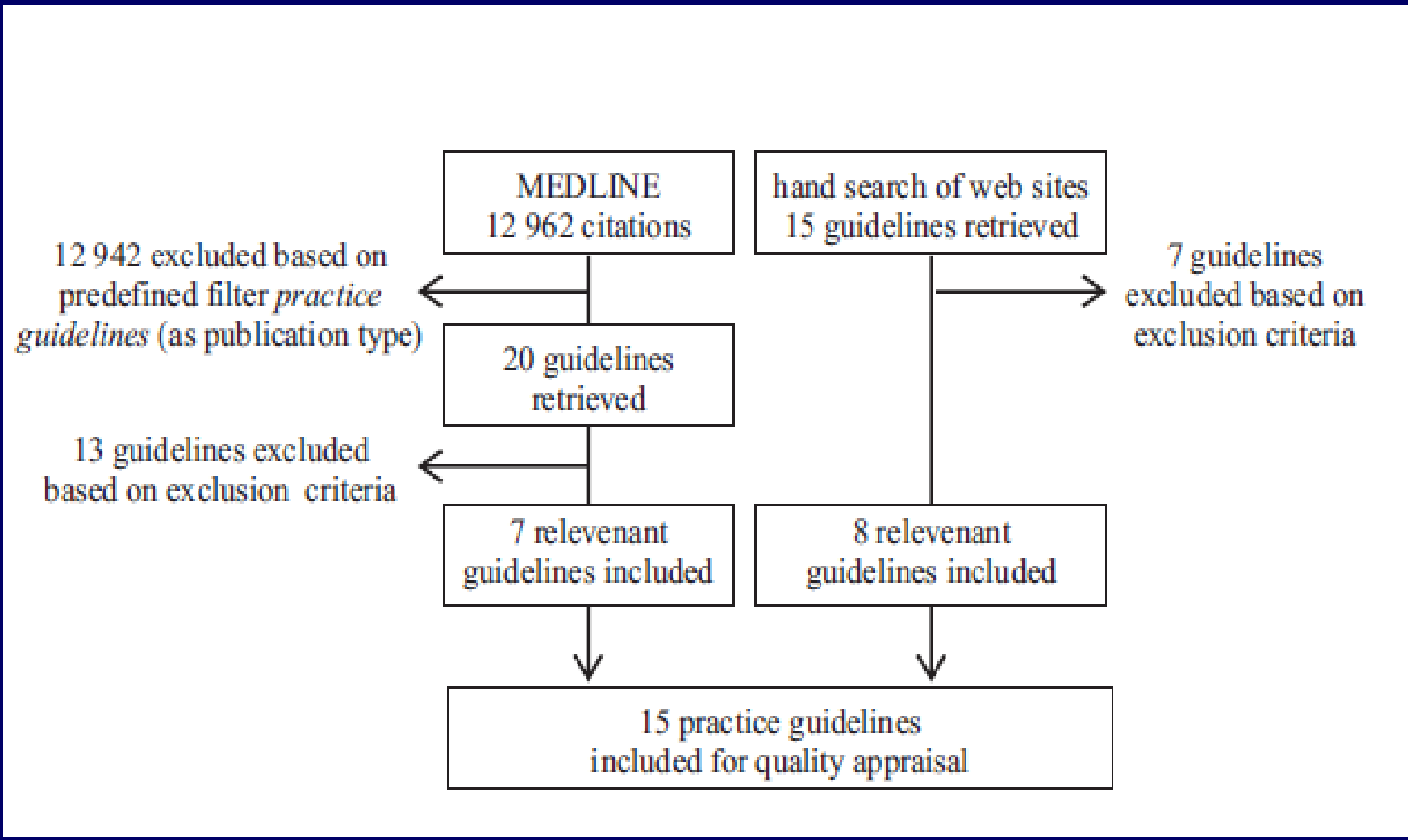
Pharmacotherapy of depression in old age

- Antidepressant treatment of four weeks is likely to have a beneficial effect compared to placebo.

- As to prevention of relapse and recurrence, antidepressants should be continued for at least six months after good initial response. In patients with high risk of relapse, treatment should be continued for at least two years. Long-term efficacy in patients at high risk of relapse has been shown for TCAs dosulepin (dothiepin) and nortriptyline and for the SSRI citalopram.

- In patients with dementia who have persistent and significant symptoms antidepressant treatment may be indicated. At present, the TCA clomipramine and SSRIs citalopram and sertraline have been reported as being superior to placebo in such patients.

Systematic Appraisal of Dementia Guidelines for the Management of Behavioural and Psychological Symptoms



Azermai M, Petrovic M et al., Ageing Res Rev 2012, 11: 78-86.

Description of retrieved dementia guidelines

Guideline Development Group	Abbreviation	Country	Year	diagnosis dementia	management dementia	management BPSD	Nr of references	Grading evidence	Funding
1. Ministry of Health Malaysia	MOH (M)	Malaysia	2009		x	x	333	yes	yes (pharmaceutical)
2. Group Health	GH	America	2009	x	x	x	31	no	not stated
3. British Columbia Medical Association	BMCA	Canada	2008	x	x	x	18	no	not stated
4. American Psychiatric Association	APA	America	2007		x	x	289	yes	yes (pharmaceutical)
5. 3rd Canadian Consensus Conference	CCC	Canada	2007	x	x	x	18	yes	yes (pharmaceutical)
6. Ministery of Health Singapore	MOH (S)	Singapore	2007	x	x	x	162	yes	not stated
7. European Federation of Neurological Societies	EFNS	Europe	2006	x	x	x	253	yes	yes (non-pharmaceutical)
8. National Institute for Health and Clinical Excellence	NICE	United Kingdom	2006	x	x	x	768	yes	yes (non-pharmaceutical)
9. Scottish Intercollegiate Guideline Network	SIGN		2006		x	x	183	yes	not stated
10. Canadian Coalition for Seniors Mental Health	CCSMH	Canada	2006			x	36	yes	yes (non-pharmaceutical)
11. American Academy of Neurology	AAN	America	2005		x	x	175	yes	not stated
12. Italian Association of Psychogeriatrics	IAP	Italy	2005		x	x	276	yes	yes (pharmaceutical)
13. Dutch College of Clinical Geriatrics	DCGP	The Netherlands	2005	x	x	x	265	yes	yes (non-pharmaceutical)
14. American Geriatric Society & American Association for Geriatric Psychiatry	AGS & AAGP	America	2003			x	57	yes	yes (pharmaceutical)
15. Royal Australian College of General Practitioners	RACGP	Australia	2003		x	x	29	no	yes (non-pharmaceutical)

Azermai M, Petrovic M et al., Ageing Res Rev 2012, 11: 78-86.

Quality appraisal by AGREE

Guideline Development Group	Abbreviation	DOMAINS OF APPRAISAL					
		Scope and purpose	Stakeholder involvement	Rigour of development	Clarity and presentation	Applicability	Editorial independence
Included guidelines		%	%	%	%	%	%
Dutch College of Clinical Geriatrics	DCCG	94	79	90	87	33	8
National Institute for Health and Clinical Excellence	NICE	89	88	81	96	72	83
Scottish Intercollegiate Guideline Network	SIGN	61	58	92	92	39	8
3rd Canadian Consensus Conference	CCC	83	58	71	63	8	92
Ministry of Health Malaysia	MOH (M)	100	58	96	92	33	58

Azermai M, Petrovic M et al., Ageing Res Rev 2012, 11: 78-86.

Overview of recommendations

Recommendations (grading)[2]	INCLUDED GUIDELINES[1]					Sufficient agreement?
	DCCG 2005	NICE 2006	SIGN 2006	CCC 2007	MOH(M) 2009	
Non-pharmacological treatment		/	*	*	*	
Use of aroma therapy	.	+ (moderate)	?	+ (C2)	?	No
Use of multisensory stimulation	.	+	? (gpp)	+ (C2)	- (A)	No
Use of music	.	+ (moderate)	?	+ (B1)	+ (A)	Yes
Use of massage and touch interventions	.	+ (moderate)	.	+ (C2)	?	No
Use of bright light therapy	.	.	- (gpp)	+ (C2)	?	No
Use of behaviour management	.	+ (moderate)	+ (B)	+ (B1)	.	Yes
Pharmacological treatment	*	*	/	*	*	
After trial of non-pharmacological interventions or in combination with non-pharmacological interventions or when non-pharmacological interventions have failed	+ (4)	+	.	+ (C1)	+ (C)	Yes
Antipsychotics	*	*	*	*	*	
For (severe) psychosis and/or aggression/agitation	+ (1)	+	.	+ (A1)	+ (A)	Yes
Use of atypical antipsychotics (risperidone, olanzapine)	+ (1)	.	+ (gpp)	+ (A1)	+ (A)	Yes
Use of conventional antipsychotics (haloperidol)	+ (1)	.	+ (A)	.	.	Yes
Choice based on individual risk/benefit analysis	.	+	.	.	+ (C)	Yes
Start at low dose and titrate upwards	.	+	.	+ (B3)	+ (C)	Yes
Time-limited use and regular reassessment (every 3 months or according to clinical need)	+ (4)	+	.	+(B3)	+ (C)	Yes
Withdrawal after behavioural stability	.	.	.	+ (A1)	+ (C)	Yes
Benzodiazepines	*	*	/	*	/	
For acute agitation or agitation based on anxiety (short-term use)	+ (3,4)	+	.	+ (B1)	.	Yes
Antidepressants	*	*	*	*	*	
For comorbid depression use of Selective Serotonine Reuptake Inhibitors)	+ (2)	+ (moderate)	+ (D)	+ (B3)	+ (A)	Yes
Acetylcholinesterase inhibitors (A-Chl)	*	*	*	*	*	
Use of A-Chl	?	+ (moderate)	+ (B)	+ (B3)	+ (B)	No
Memantine	/	*	*	*	*	
Use of memantine	.	?	?	+ (B3)	B	No

Azermai M, Petrovic M et al., Ageing Res Rev 2012, 11: 78-86.

Main findings:
9 key recommendations

Main findings: 9 key recommendations

1. *If* a person with dementia shows distressing behavioural symptoms,
   then → consider non-pharmacological interventions first (music, behaviour management)
2. *If* non-pharmacological interventions have failed,
   then → consider psychotropic medication
3. *If* a person with dementia shows co-morbid depression, *then* →consider antidepressants (SSRI's)
4. *If* a person with dementia shows acute agitation or agitation based on anxiety,
   then →consider the short-term use of benzodiazepines (with caution)
5. *If* a person shows severe agitation/aggression/psychosis,
   then → consider antipsychotic medication

Main findings: 9 key recommendations (cont.)

6. *If* antipsychotic medication is considered,
   then → carefully evaluate the individual risks-benefits to make a choice for typical or atypical agents
7. *If* an antipsychotic is started,
   then→initiate a low starting dose and titrate upwards in function of the resident's response and presence of adverse effects
8. *If* an antipsychotic is started,
   then →treatment should be time-limited and regularly reviewed (every 3 months or according to clinical need)
9. *If* there is a period of behavioural stability,
   then→periodical attempts of antipsychotic discontinuation should be considered