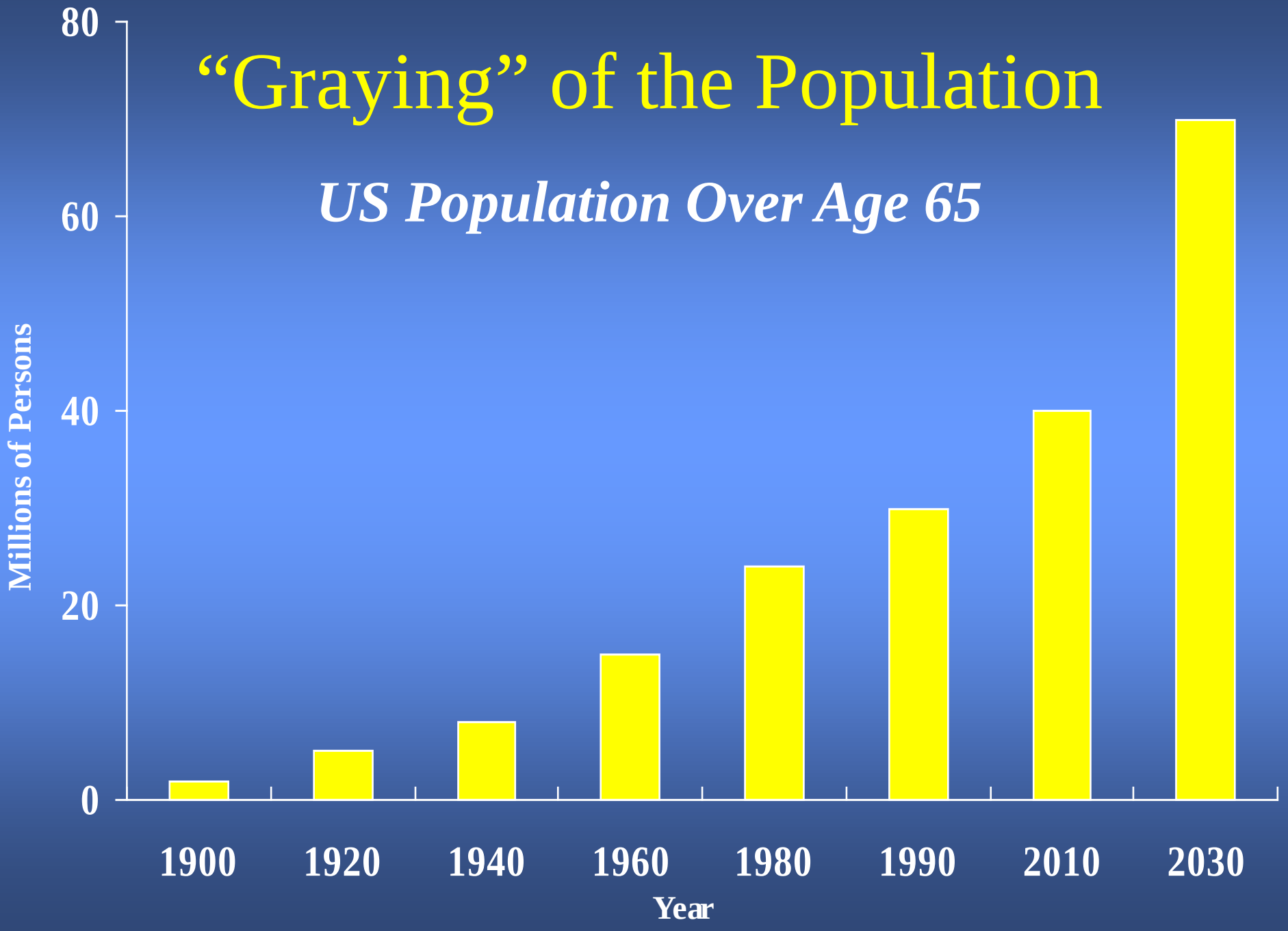
Management of the Acutely Agitated Long Term Care Patient

“Graying” of the Population



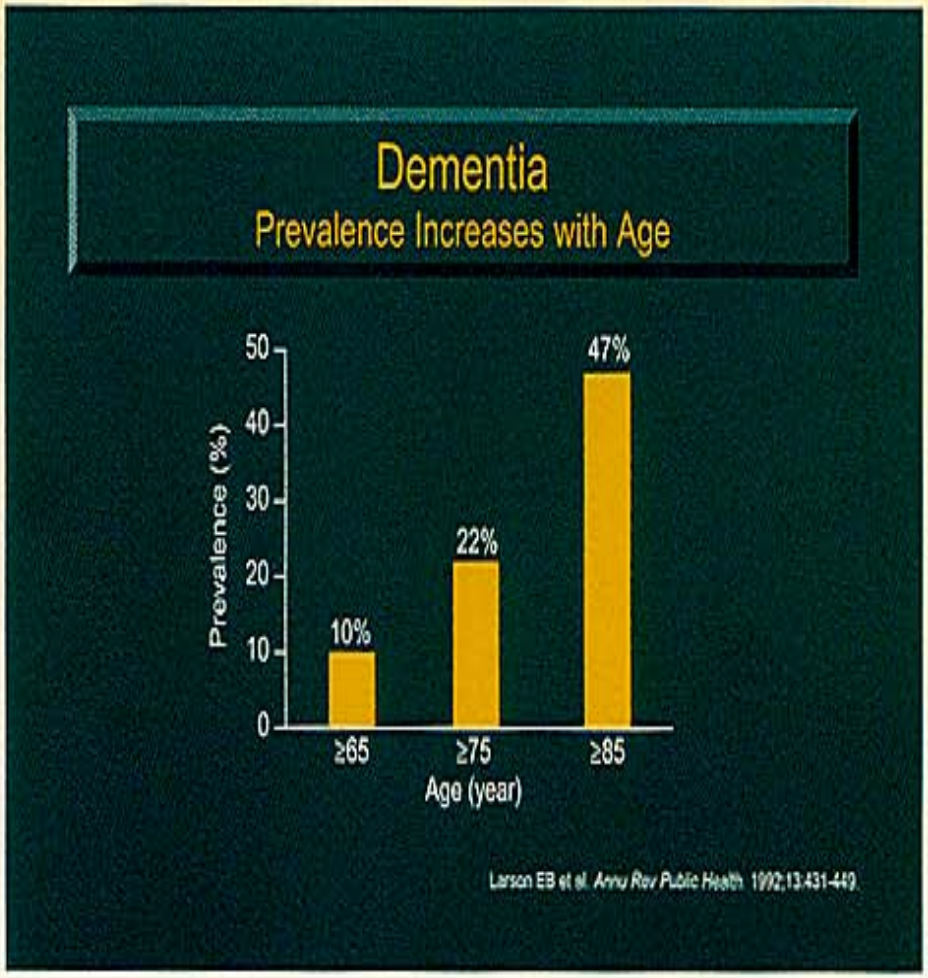
Defining Dementia

- Clinical state characterized by loss of function in multiple cognitive domains.
- Decline must represent a decline from a previously higher level of functioning.
- Diagnosis of dementia should NOT be made if the cognitive deficits occur exclusively during the course of a delirium.
- Alzheimer disease most prevalent.

American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition. Washington, D.C, Amer. Psychiatric Assoc., 1994.

Dementia – Prevalence Increases with Age

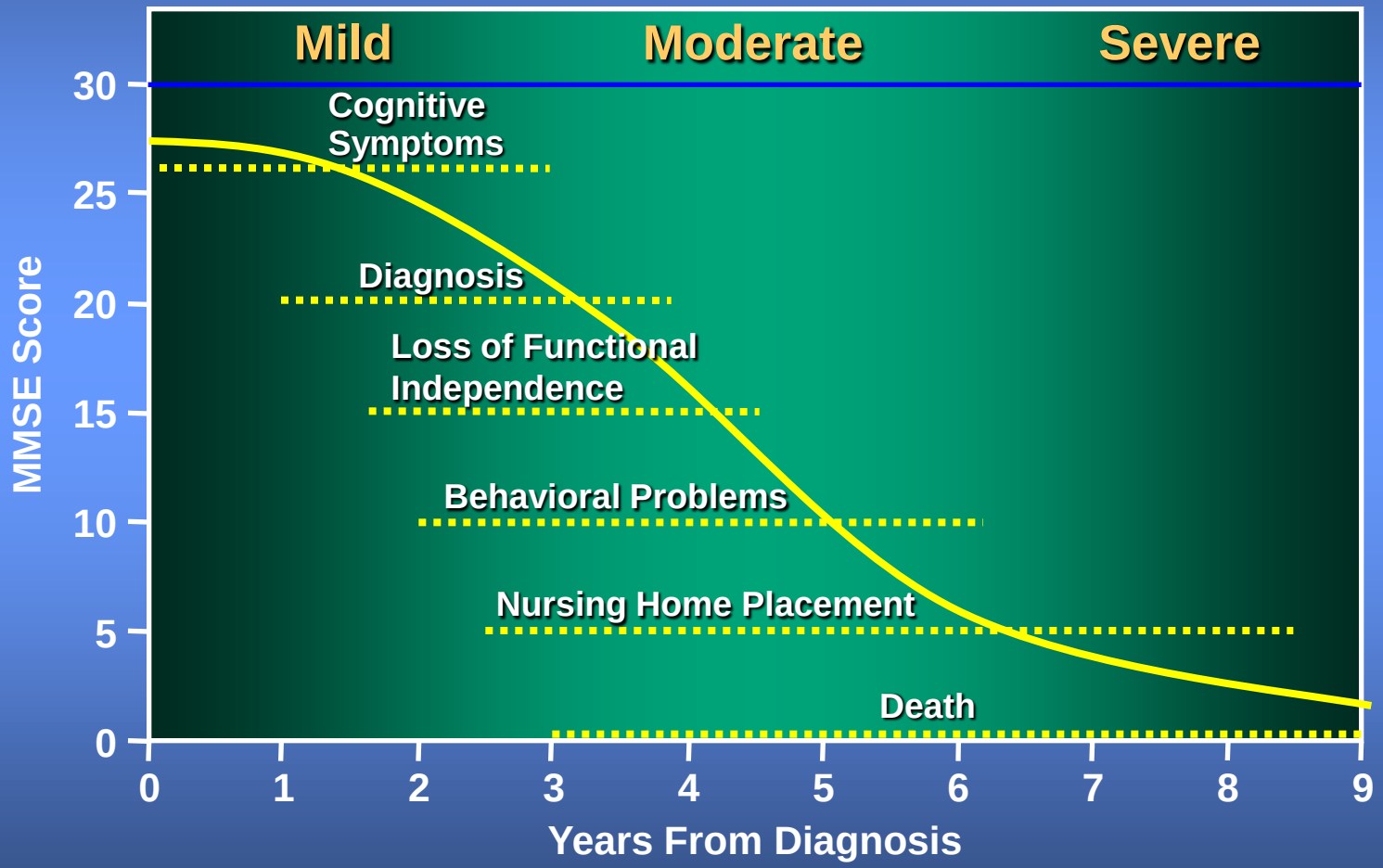
The prevalence of dementia increases with age so that 10% of those older than 65 years suffer from dementia. This increases dramatically to 47% in those older than 85 years. It has been suggested that dementia will be the epidemic of the 21st century.



References

Larson EB, Kukull WA, Katzman RL. Cognitive impairment: dementia and Alzheimer's disease. *Annu Rev Public Health.* 1992;13:431-449.

Clinical Disease Progression



Reprinted from *Clinical Diagnosis and Management of Alzheimer's Disease*, H Feldman and S Gracon; Alzheimer's Disease: symptomatic drugs under development, pages 239-259, copyright 1996, with permission from Elsevier.

Assessment Methods: Staging (cont)

Functional Assessment Staging

Stage 1	**No objective or subjective functional deficit**
Stage 2	**Subjective functional deficit**
Stage 3	**Objective functional deficit and interference with complex social tasks**
Stage 4	**Deficient performance of complex ADL**
Stage 5	**Deficient performance of basic ADL**
Stage 6	**Decreased ability to dress, bathe, and toilet independently**
Stage 7	**Loss of speech, locomotion, and consciousness**

Source: Reisberg B, et al. *Psychopharmacol Bull*. 1988;24:653-659.

What Is "Agitation"?

- Any inappropriate verbal, vocal or motor activity that is not an obvious expression of need
- It is not a diagnostic term but rather a syndromal term (group of symptoms) that describes the clustering of behaviors
- Agitation can result from a variety of underlying general medical, or neuro-psychiatric or psychosocial conditions

Adapted from: Mansfield C et al. (Various references)

Phenomenology of Agitation and Aggression

- **Physically nonaggressive**
  - **Pacing**
  - **Restlessness**
  - **Inappropriate robing/disrobing**
  - **Inappropriate handling of objects (executive dysfunction)**
- **Physically aggressive**
  - **Hitting**
  - **Kicking**
  - **Biting**
  - **Scratching**
  - **Pushing**
  - **Spitting**
  - **Pinching**

Cohen-Mansfield J, Deutsch LH. *Semin Clin Neuropsychiatry.* 1996;1:325-339.

Tariot P. *J Clin Psychiatry.* 1999;60(suppl 8):11-20.

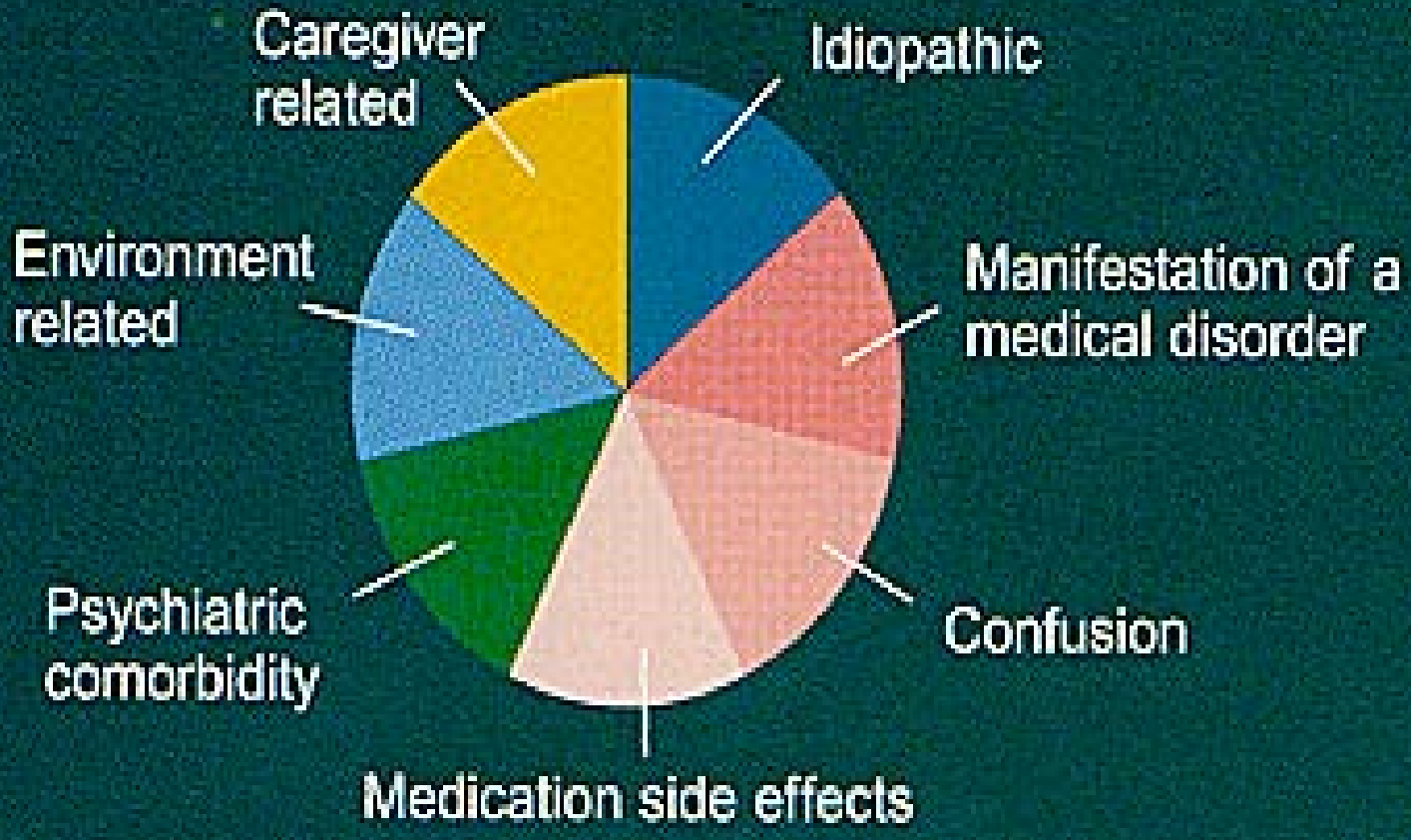
Phenomenology of Agitation and Aggression

- **Verbally nonaggressive**
  - –Complaining
  - –Attention seeking
  - –Repeated questions/phrases
  - –Screaming
- **Verbally aggressive**
  - –Threats
  - –Obscenities
  - –Accusations
  - –Name calling

Cohen-Mansfield J, Deutsch LH. *Semin Clin Neuropsychiatry.* 1996;1:325-339.

Cohen-Mansfield J, Werner P. *Int J Geriatr Psychiatry.* 1997;12:1079-1091.

Possible Etiologies
Agitation "Pie" Chart



Cohen-Mansfield J et al. *Int Psychogeriatr.* 1992;4(2):221-240.
Mintzer JE, Brawman-Mintzer O. *J Clin Psychiatry.* 1996;57(7):55-63.

Medical Causes

- Recent onset of illness/surgery
- Recent change in medication/polypharmacy
- Sleep disturbances: primary, secondary
- Chronic/acute pain
- Cardiovascular disease
- Visual impairment
- Poor nutrition
- Respiratory infection
- **Urinary tract infection**

Management of Acute Episodic Agitation in the Absence of Psychosis or Mood Disturbance

Nonpharmacologic Management

- Evaluate: Reassurance/Redirection alone
- Evaluate: Environmental Triggers Adjustment
- Set-up routines that are patient-specific
- Remove offending pharmacologic agents (such as adjunct anticholinergics, benzodiazepines, etc.)
- Ensure support and patient specific education for the caregiver and/or staff

General Principles of Management of Agitation (cont'd)

- For acute episodic non-persistent agitation that occurs in the absence of mood or psychotic disturbances
  - The *first line approach* requires assessment and a trial of non-pharmacologic management
- For the patient with agitation and concurrent psychosis and/or mood disturbance, the general principles support combining pharmacologic and non-pharmacologic interventions

What Are the Most Common Psychiatric Disorders in the Elderly?

Outpatient Care		Long-Term Care	
Dementia	**10% > age 65 45% > age 85**	**Dementia**	**50-70%**
Depression	**4-5%**	**Affective disorders**	**50-85%**
Substance abuse	**1-5%**	**Schizophrenia**	**0-4%**
Psychosis	**0.1-4%**	**MR/DD**	**1-5%**

Prevalence of Symptoms of Psychosis and Agitation in Dementia

Cache County Study of Memory in Aging (CCSMA)

- First US population study of behavioral disturbances in dementia
- Evaluated the prevalence and severity of mental and behavioral disturbances in the elderly
- 5092 individuals were screened
- Participants with dementia (n=329) were compared to control group without dementia (n=673)

Source: Lyketsos CG et al. *Am J Psychiatry*. 2000;157:708-714.

Prevalence of Symptoms of Psychosis and Agitation in Dementia

NPI Item	Dementia (n=329) %	No Dementia (n=673) %
Apathy	27.4	3.1
Depression	23.7	7.0
Agitation/aggression	23.7	2.8
Irritability	20.4	4.5
Delusions	18.5	2.4
Anxiety	17.0	5.6
Aberrant motor behavior	14.3	0.4
Hallucinations	13.7	0.6
Disinhibition	9.1	0.9
Elation	0.9	0.3

Source: Adapted with permission from Lyketsos CG et al. *Am J Psychiatry*. 2000;157:708-714. American Psychiatric Association.

New Admissions to Nursing Homes

454 new admissions were followed for 1 month

- 79 patients (17%) had behavioral problems that required intervention
- Most frequent diagnoses were dementia complicated by delusions, depression, and/or delirium

Source: Rovner BW et al. *J Geriatr Psychiatry Neurol.* 1992;5:102-105.

Behavioral Problems in Nursing Home Residents

•Restlessness	38%
•Passive aggression	38%
•Active aggression	26%
•Verbal aggression	26%
•Wandering	24%

Rovner BW, et al. *Am J Psychiatry.* 1986;143:1446-1149.

Psychobehavioral Metaphors

- Identify most salient symptom cluster
- Is there a pattern analogous to a drug-responsive syndrome?
- Use as a rational guide to therapy

Tariot P. *J Clin Psychiatry.* 1996;57(suppl 14):21-29.

Behavioral Clusters Matched to Potentially Relevant Medication Classes

- **Disturbed affect/mood**
  - **Anticonvulsants**
  - **Antidepressants**
  - **Atypical Antipsychotics**
- **Anxiety**
  - **Antidepressants**
  - **Anxiolytics-avoid**
  - **Anticonvulsants**
  - **Atypical Antipsychotics?**
- **Psychosis**
  - **Atypical antipsychotics**
  - **High-potency typical antipsychotics-avoid**
- **Agitation/aggression**
  - **Anticonvulsants**
  - **Antidepressants**
  - **Anxiolytics-avoid**
  - **Atypical Antipsychotics**
  - **Cholinergic agents?**

Tariot P. *J Clin Psychiatry.* 1999;60(suppl 8):11-20

McDougle et al. Arch. Gen. Psychiatry, 2000, 57: 794-801

Shapira NA et al. ACNP 2002

Atmarca M et al. Int. Clin. Psychopharmacol. 2002; 17: 115-119

Barnett SD et al. J. Pschopharmacol. 2002: 365-368

Stein et al. Am. J. Psychiatry. 2002

General Principles of Geriatric Pharmacotherapy (cont'd)

- Know the cautions, warnings and physician liability in the medicine's current FDA approved package insert
- With risk for tolerability or safety problems "start low, increase slowly, but obtain meaningful efficacy"
- Different conditions often necessitate different dosages to obtain efficacy
- Tolerability and safety profiles are also often different depending on age, body mass, gender, ethnicity, culture of origin and diagnosis

Pharmacological Approach

- There is no US FDA-approved treatment for agitation associated with dementia
- Dementia with agitation is not viewed as a disease
- Proper documentation and diagnosis leads to better choice of class of medications and increases probability of success

Atypical Antipsychotics and the News

- Multicenter Trial of Atypicals in Dementia patients (first non Industry Sponsored) reported in the10/12/06 issue of USAToday
- Placebo vs Risperidone, Olanzapine and Quetiapine showed no significant clinical difference in 421 randomized patients with DAT for 8 weeks
- Side effects included worsening confusion, sleepiness, tremors and muscle stiffness
- Conclusion: these drugs should be given to patients who are carefully monitored for improvements and adverse events, they are the last line of therapy & they should be used only in the short term

- New England Journal of Medicine, Lon Schneider et. al., 10/06

ADA Consensus on Antipsychotic Drugs and Obesity and Diabetes

Drug	Weight Gain	Diabetes Risk	Dyslipidemia
Clozapine	+ + +	+	+
Olanzapine	+ + +	+	+
Risperidone	+ +	D	D
Quetiapine	+ +	D	D
Aripiprazole*	+/–	–	–
Ziprasidone*	+/–	–	–

*Newer drugs with limited long-term data.
+=increased effect; –=no effect; D=discrepant results.

American Diabetes Association. *Diabetes Care*. 2004;27:596-601.

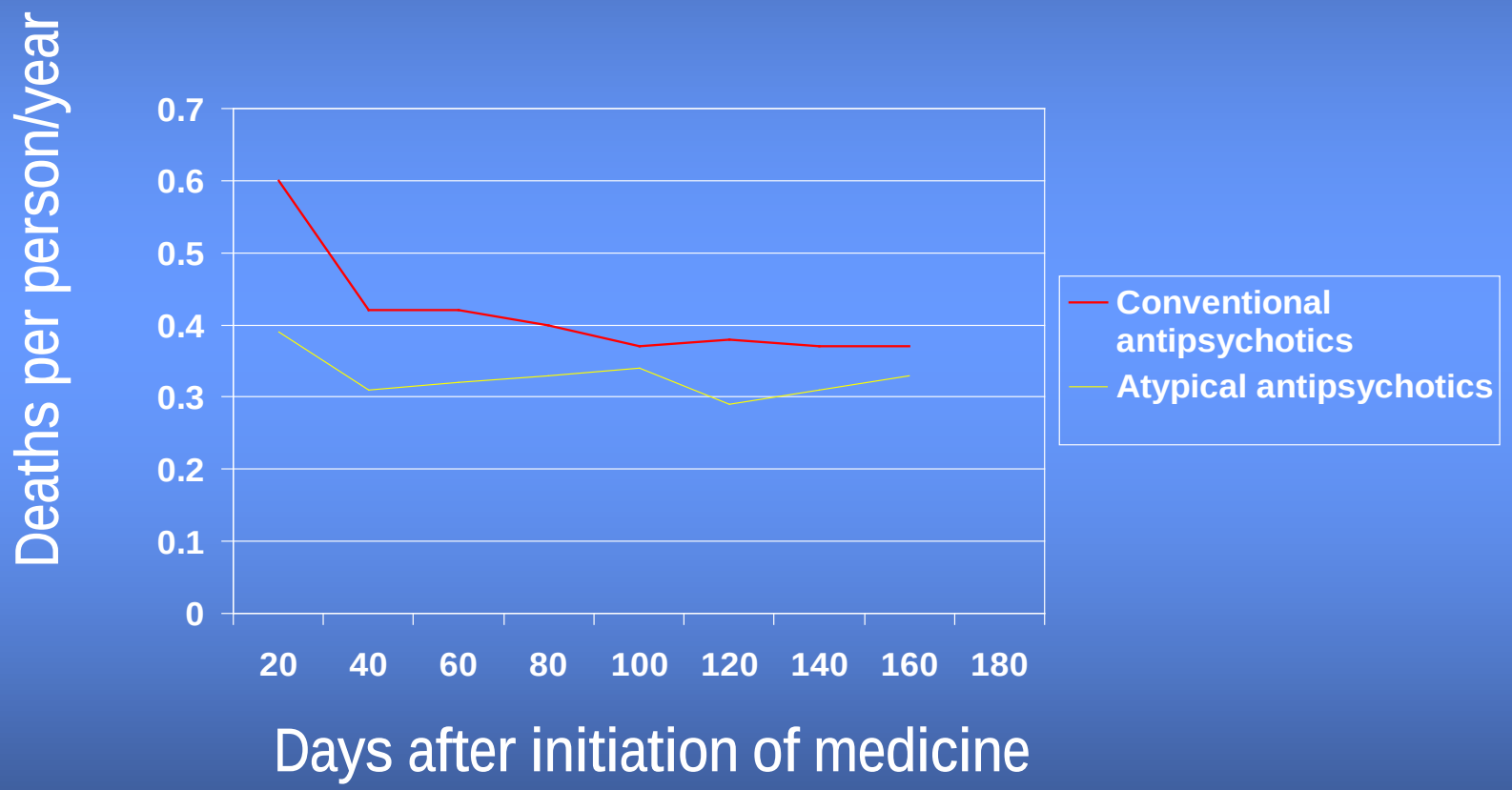
Risk of Cerebrovascular Adverse Events in Elderly Patients With Dementia

	Number of Trials	CVAEs		Numbers Needed to Harm
		Active Drug	Placebo	
Risperidone[1]	4	3.8% (29/764)	1.5% (7/466)	44
Olanzapine[2]	5	1.3% (15/1178)	0.4% (2/478)	117

- In US, letters to health care professionals were sent and warning added in prescribing information
- UK Committee on Safety of Medicines guideline:
  - Avoid use in behavioral and psychological symptoms associated with dementia
  - Limited to short-term and under-specialist advice for the management of acute psychotic conditions with risperidone
  - Consider risk in treating patients with previous history of stroke or transient ischemic attack and assess cerebrovascular disease risk factors including hypertension, diabetes, smoking, and atrial fibrillation

1. Health Canada Advisory for Health Professionals. October 11, 2002. Available at: http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/risperdal1_e.html. Accessed: January 3, 2006; 2. Health Canada Advisory for Health Professionals. March 10, 2004. Available at: http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/zyprexa_hpc_e.html. Accessed: January 3, 2006.

Risk of Death in Elderly Patients: Atypical vs Conventional Antipsychotics



Wang P, et al. *N Engl J Med*. 2005;353:2335-2341

CATIE Trial of Atypical Antipsychotics in AD

- Modest benefits
- Risks of increased mortality and morbidity are not sufficient to justify therapy

Schenider LS, Tariot PN, Dagerman KS, et al. CATIE-AD study group. Effectiveness of aytypical antipsychotic drugs in patients with Alheimer's disease. N Engl J Med 2006; 355:1525-38.

Dementia Antipsychotic Withdrawal Trial (DART-AD): long term follow-up

- 128 patients randomized to 12 months of antipsychotic vs placebo though followed up to 54 months
- Risperidone 67%, haloperidol 26% and other first generation antipsychotics 7%

Ballard C, Hanney M, Theodoulou M, Douglas S, McShane R, Kossakowski K, Gill R, Juszczak E, Yu L, Jacoby R for the DART-AD investigators. The dementia antipsychotic withdrawal trial (DART-AD): long-term follow-up of a randomised placebo-controlled trial. The Lancet, vol 8, February 2009.

DART-AD Trial Results

- 76.6% cumulative probability survival in placebo treated patients vs a 70.3 % survival in patients treated with antipsychotics at 12 months
- 71% cumulative probability of survival vs 46 % survival at 24 months
- 59 % cumulative probability of survival vs 30 % at 36 months
- 53 % cumulative probability of survival vs 26 % at 42 months
- Effect of this study has been a 50% decrease in antipsychotics since 2004!!

Atypical Antipsychotics Do Have a Place

- Where there is a medical need for the drugs
- Where comorbidity permits
- Where the risk/benefit of alternatives is equally high
- Remembering, though, that symptom control does not always equate to quality of life for the person being treated
- Should not use in the following: wandering, restlessness, mild agitation, unsociability, fidgeting, nervousness, poor self care, indifference or uncooperativeness
- Must rule out a physical cause first
- Do not use for an excessive duration or without adequate monitoring
- Do not use in excessive does or in combination with another antipsychotic

Summary

- People 65 years and older are increasing rapidly, thus those with cognitive impairment are growing as well
- Behavioral metaphors help determine the medications we choose to treat cognitively impaired seniors who exhibit agitation or aggression
- Avoid older antipsychotic class, as these are ineffective in chronic use and have marked toxicity
- Atypical antipsychotic agents are effective and safer than the older agents in the acute/chronic rx of agitation/aggression in dementia/delirium
- Antidementing agents, anticonvulsants, antidepressants may be effective and safer alternatives to antipsychotic agents