
Phenomenology of and Risk Factors for New-Onset Diabetes Mellitus and Diabetic Ketoacidosis Associated with Atypical Antipsychotics: An Analysis of 45 Published Cases

Jin H, Meyer JM, Jeste DV ANN Clin Psych 14;Mar 2002: 59-64

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Answers That Matter.

Phenomenology of and Risk Factors for New-Onset Diabetes Mellitus

- 45 cases of new-onset DM or DKA
 - Clozapine – 20
 - Olanzapine – 19
 - Risperidone - 3
 - Quetiapine – 3

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Phenomenology of and Risk Factors for New-Onset Diabetes Mellitus

- 87% male
- 47% African American
- 42% presented with DKA
- Blood Glucose at time of diagnosis
 - 89% > 300mg/dL
 - 63% > 500mg/dL

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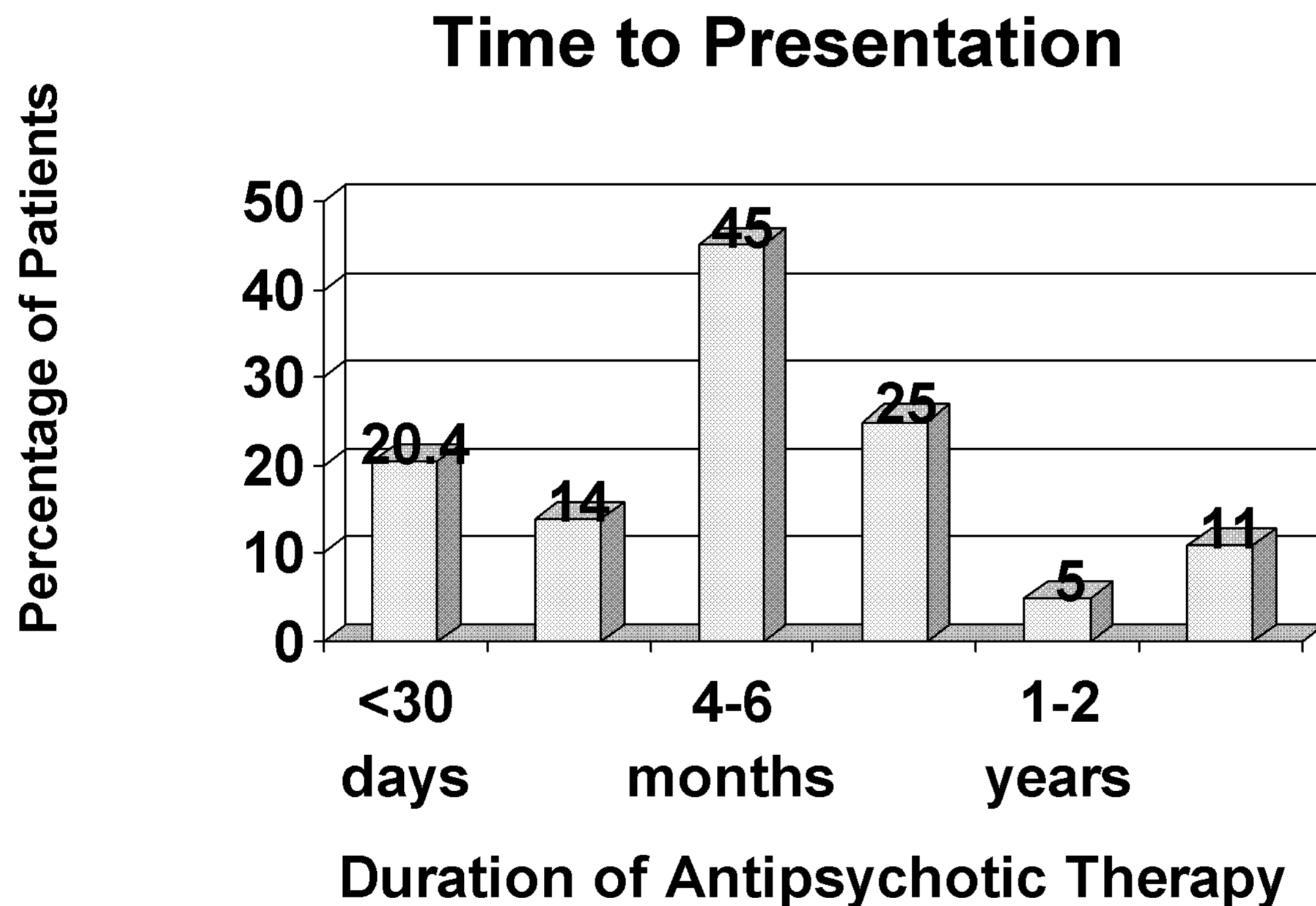
Phenomenology of and Risk Factors for New-Onset Diabetes Mellitus

- 32 (71%) patients had weight measurement
 - 50 % (16) manifested no weight gain at time of presentation with DM
 - 84% were overweight (>5% over ideal weight) at baseline
- 77% received adjunctive medications

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Phenomenology of and Risk Factors for New-Onset Diabetes Mellitus

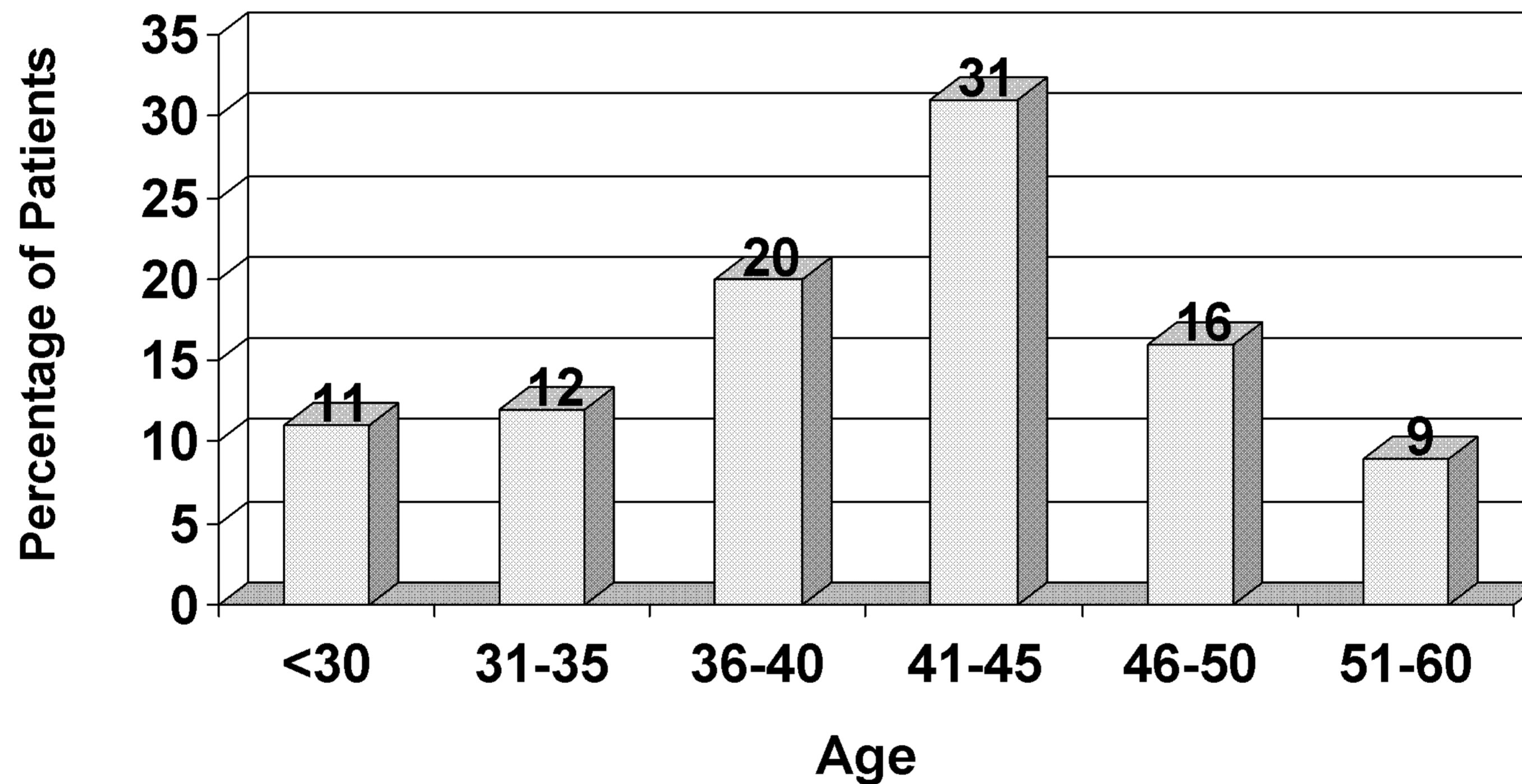
Mean duration of antipsychotic prior to DM was 19 weeks.



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Phenomenology of and Risk Factors for New-Onset Diabetes Mellitus

Age at Time of Diagnosis



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File name/location

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Phenomenology of and Risk Factors for New-Onset Diabetes Mellitus

- Patients with DKA vs those with DM
 - Women
 - Younger
 - Less overweight at baseline
 - Presented with higher blood glucose

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Olanzapine-Associated Diabetes Mellitus

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852

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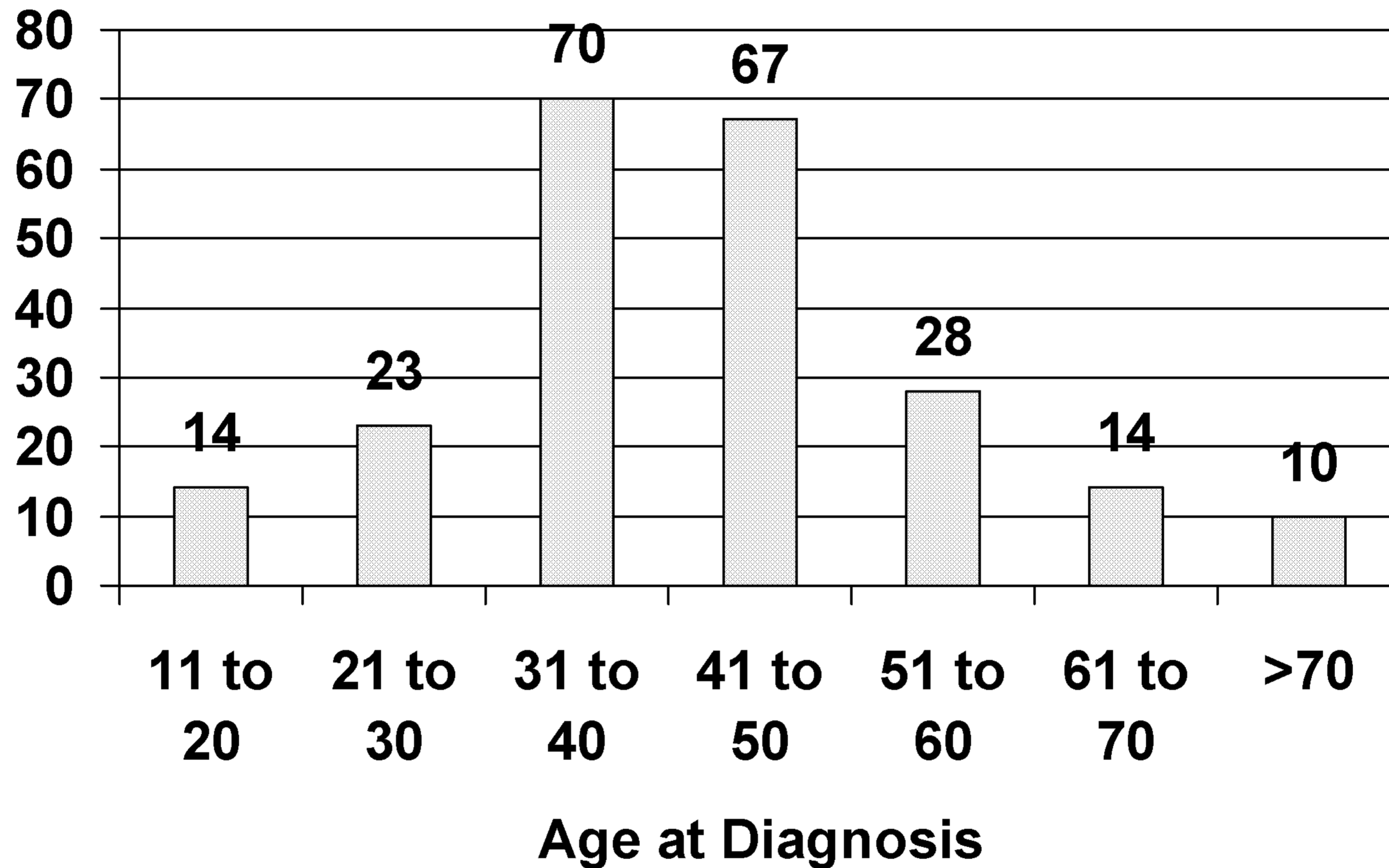
Answers That Matter.

Olanzapine-Associated Diabetes Mellitus

- 237 cases of olanzapine associated DM or hyperglycemia
 - 41 cases in 22 publications
 - 215 from the United States
 - 22 from outside the US
- 188 (79%) newly diagnosed
 - 153 met criteria for diagnosis of DM (mean age 40 years)
 - 35 contained insufficient information for diagnosis of DM
 - 19 treated with anti-diabetic therapy
- 44 (19%) exacerbation of preexisting DM (mean age 52 years)
- 5 (2%) could not be classified

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852

Olanzapine-Associated Diabetes Mellitus



Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852

Olanzapine-Associated Diabetes Mellitus

- 150 patients had race information
 - 56% caucasian
 - 39% African American
 - 3% Hispanic
 - 3% Asian

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852

Olanzapine-Associated Diabetes Mellitus

- Time to Onset
 - All patients
 - 2-45 days
 - ≤ 6 months for 73%
 - Among newly diagnosed DM
 - ≤ 1 month for 13%
 - ≤ 3 months for 47%
 - ≤ 6 months for 70%
 - Among those with exacerbation of preexisting DM
 - ≤ 1 month for 55%
 - ≤ 3 months for 84%
 - ≤ 6 months for 97%

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852

Olanzapine-Associated Diabetes Mellitus

- Dose

- All patients – 15.6mg
- Newly diagnosed patients - 16.1mg
- Exacerbation of preexisting DM – 13.2mg
- Those with ketosis or acidosis – 16.6mg
- Those without ketosis or acidosis –15.0mg

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852

Olanzapine-Associated Diabetes Mellitus

- Metabolic Acidosis
 - Among all patients 80 (34%)
 - Among newly diagnoses patients 74 (39%)
 - Among patients with exacerbation of preexisting DM 3 (7%)

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852

Olanzapine-Associated Diabetes Mellitus

- Deaths
 - 15 total
 - 8 male, 7 female
 - 14 occurred in newly diagnosed patients
 - Time to onset <3 months for 8 patients
 - Mean daily dose = 17.9 mg
 - 13 occurred during or soon after the hyperglycemic episode
 - 1 died of necrotizing pancreatitis 1 month after hyperglycemic episode

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852

Olanzapine-Associated Diabetes Mellitus

- Other Risk Factors

- 76% were either overweight at baseline or gained a significant amount of weight
- 43% of newly diagnosed patients had a family history of DM
- 6 patients had hepatitis
- 8 patients had been taking another atypical antipsychotic
- 31% received valproate

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852

Olanzapine-Associated Diabetes Mellitus

- Authors' discussion and conclusions
 - Gravity of outcomes highlights need to further investigate the potential association
 - Relationship between olanzapine and DM established by;
 - Number of cases reported
 - Prompt reversibility when drug is withdrawn
 - Mean age at diagnosis is considerably less than that seen in general population
 - Frequency of newly diagnosed DM in people < 44 in the olanzapine-treated patients (66%) is twice that seen in the general population (33%)
 - Gender distribution is different than that of the general population (M:F 1.8 vs 0.8)

Koller EA, Doraiswamy PM. Pharmacotherapy 2002,(7).841-852

Olanzapine-Associated Diabetes Mellitus

- Authors' discussion of limitations
 - Underreporting characteristic of this system
 - Distortions in reporting due to clinician awareness
 - Clinician awareness of weight gain may contribute to more frequent monitoring and detection of DM
 - Rate cannot be determined
 - Causality cannot be established
 - Contribution of other risk factors cannot be ruled out
- However, the authors conclude that their results suggest a causal relationship

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852