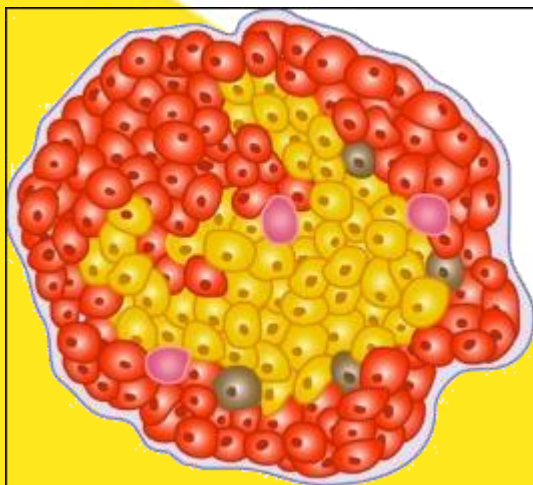


Cardiology Update 2011
Davos, February 14, 2011



Management of Diabetes in 2011: Cases



University Hospital
Zurich

Roger Lehmann
Department of Endocrinology and Diabetes

38 year-old patient

Emergency consultation 10.2.2011

- History: Thirst, 5 l of water consumption per day for last few days
(after asking for first occurrence of symptoms: since fall)
- Weight loss? For 6 months no use of scale. In pharmacy blood glucose measurement: 20 mmol/l
- Concerned father is retired professor of medicine and asks for emergency consultation.

What are the most important points, which you need to know, to start the correct treatment?



38 year-old patient

Emergency consultation 10.2.2011

- Family history?
- Grandfather (father's side) diabetes with the age of 60 yrs. Father diabetes at the age of 58 years (insulin treatment from the start), father's brother diabetes as well. Brother obese and he got a kidney transplantation due to hypertensive nephropathy
- Weight? Metabolic Syndrome?
- Personal History?
- Up to the age of 17 competitive rowing and normal weight, then no sport anymore and weight gain of 10 kg. Lost weight again. At age 20: hotel management school, weight gain of 22 kg in first year, then loss and regaining of weight.
- Year 2000: Stop smoking, weight 73 kg, then weight gain up to 120 kg
- Profession?
- IT Consulting



38 year-old patient

Emergency consultation 10.2.2011

- Physical exam
- 178 cm, 155 kg (BMI 48.9), BD 169/110 mm Hg, P 104, AF 18
- Lab?
- HbA1c: 8.5%, Glucose 12.2 mM, MAU 30.2 mg/l, Alb/Kreat 2.6

Diabetes Type?

- Type 1 Diabetes?
- Type 2 Diabetes?
- Classical Case of MODY Diabetes?
- Unclear, could be all.
- Referral to diabetologist



38 year-old patient

Emergency consultation 10.2.2011

- Lab?
- Cholesterol 7.1mM, Triglycerides 9.0 mM, (HDL not measurable)
- TSH: 1.99 mU/l
- C-Peptide with a glucose of 14.8 mM: 1650 pmol/l
- Antibodies: Anti-GAD 65 IE/ml (N <10) and IA-2: negativ

Diabetes mellitus Type 2



Your initial treatment? (M)

- Nutritional counseling and increased physical activity
- Metformin
- Glitazone (Actos)
- DPP-4 Inhibitor
- GLP-1 Analog (Byetta or Victoza)
- Combination therapy
 - Metformin and Sulfonylurea
 - Metformin and DPP-4 inhibitor
 - Metformin and GLP-1 Analog
- Basal-bolus insulin therapy



38 year-old patient

Emergency consultation 10.2.2011

- Suggestions for therapy?

	Intervention	↓ HbA1c (%)	Weight (kg/yr) per ↓1% HbA1c	Hypoglycemia Monotherapy
Schritt 1	Lifestyle (Nutrition, Physical Activity)	1-2	-4.0	No
	Metformin	1.5	-1.0-1.5	No
Schritt 2a or 2b	GLP-1 Analogue (Byetta, Victoza)	1.0-1.5	-3.0	No
Schritt 2 a or 2b	DPP-4 Inhibitor (Januvia, Galvus) Combination: Janumet, Galvumet	0.8 2.0	0.0 - -1.0	No
Schritt 2a or 2b	Sulfonylurea, Glinide	1.0-1.5	3.0	Yes
Schritt 2b	Glitazone	1.0	4.0	No
Schritt 3	Insulin (bedtime or prandial)	1.0-1.5	3.0	Yes
Schritt 4	Intensified insulin therapy	1.5-5.0	3.0	Yes

56 year old manager

- 2 years consultation in your medical office
- 92 kg, 178cm, BMI 30
- You diagnosed diabetes type 2 and gave thorough nutritional advice and recommended weight loss of 5kg
- Weight reduction of 6 kg
- After one year treatment with metformin 850 mg 1-0-1
- No further consults up to now



56 year old manager

- Physical findings and Lab:
- Weight 88kg (+4kg), height 1.78m, BMI 29kg/m²
- HbA1c 8.9% (8 months ago: 7.5%),
- Glucose profile: 10.7 / 13.2 / 8.6/ 9.1 mmol/l



56 year old manager

Lab results:

Kreatinin: 90 $\mu\text{mol/l}$,

Total Cholesterol: 7.4mmol/l

HDL: 0.8mmol/l

LDL: 3.4mmol/l

Triglycerides: 2.9mmol/l

Microalbuminuria: positiv (55 mg/l)

Other findings:

Erectile dysfunction

Blood pressure: 152/95mmHg

Smoker: 30 pack years

Treatment:

Metformin 850 mg 1-0-1



56 year old manager

- Do you need more lab results or examinations?
- Which is the most important treatment goal?
- Which targets do you try to achieve?
 - HbA1c
 - Lipids
 - Blood pressure
 - Aspirin?
- With which treatment?
- Where do you expect the greatest success or complications?



56 year old manager

- Which targets do you try to achieve?
 - HbA1c
 - Lipids
 - Blood pressure
 - Aspirin?
- With which treatment?



Take home message 2011: Therapeutic targets in type 2 diabetes mellitus

- **Multifactorial therapy with:**
 - Stop Smoking
 - Statin treatment independent of cholesterol level
 - Blood pressure < 130 / 80 mm Hg or <140 and >70 mm Hg (ACCORD)
 - Anti-Platelet Treatment
- **HbA1c Target?**
 - HbA1c = 7.0 % or HbA1c < 7% or >7%?

Where do you expect the greatest success or complications?

Flexible HbA1c Targets

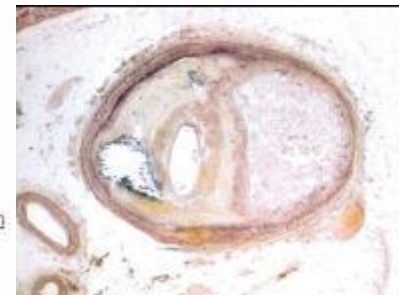
- 3 Studies of ACCORD lead to one message:
- Not: the lower, the better, but flexible targets for glucose, lipids, and blood pressure

HbA1c-Target: 7.0% (avoid Hypoglycemia)

- **Important Factors:**
- Short Diabetes Duration
- Short life expectancy
- Risk Hypoglycemia
- Coronary Heart Disease

⇒ more intensive Therapy

⇒ less intensive Therapy





Modern therapeutical algorithm

⇒ ø hypglycemia and ø weight gain:



National Institute for Health and Clinical Excellence (NICE): Guideline on newer drugs 6/2009

	Intervention	↓ HbA1c (%)	Weight (kg/yr) per ↓1% HbA1c	Hypoglycemia Monotherapy
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Schritt 4	Intensified insulin therapy	1.5-5.0	3.0	Yes

46 year-old man with bipolar psychosis

- Obesity 135 kg, 185 cm (BMI 39.4kg/m²)
- 2007 Bipolar Psychosis
 - Recurrent hospitalizations in psychiatry
Hospitalisationen
 - Treatment with: Lithium and atypical neuroleptic
(Lithiofor, Risperdal)
- Diabetes Type 2 diagnosed 2009
 - untreated

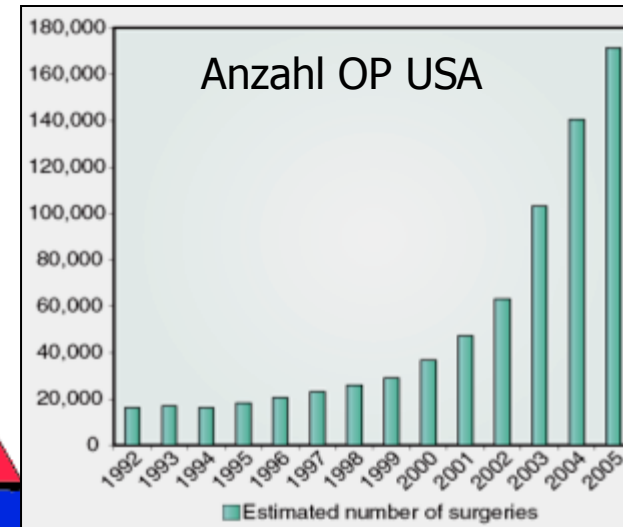
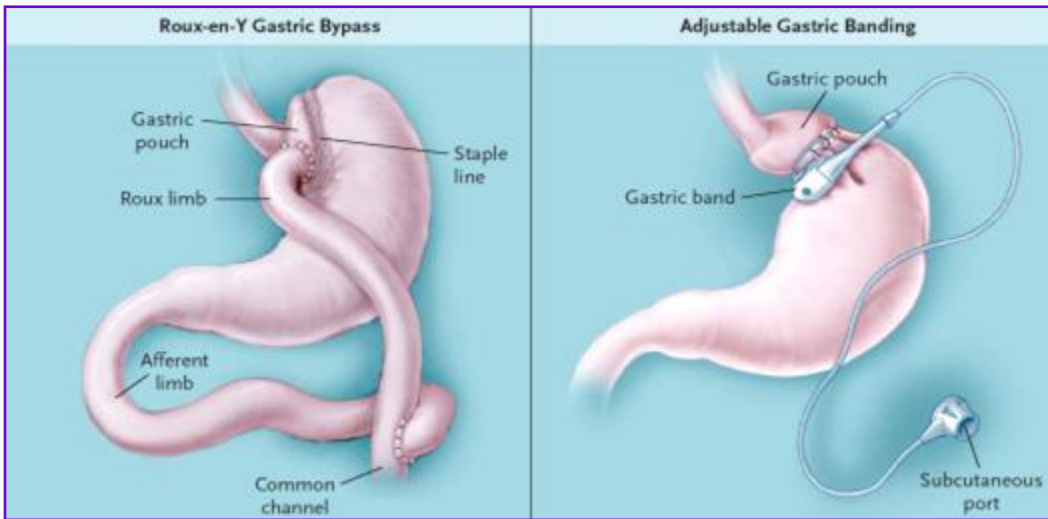


46 year-old man with bipolar psychosis

- 2010 Hospitalization because of high HbA1c > 10%
- Actual findings: 110 kg (BMI 32.2)
- Cause of weight loss?
- Therapeutic options ?



Treatment of obesity



Bariatric Surgery
BMI > 40 kg/m²



Medications
BMI 30-40 kg/m²



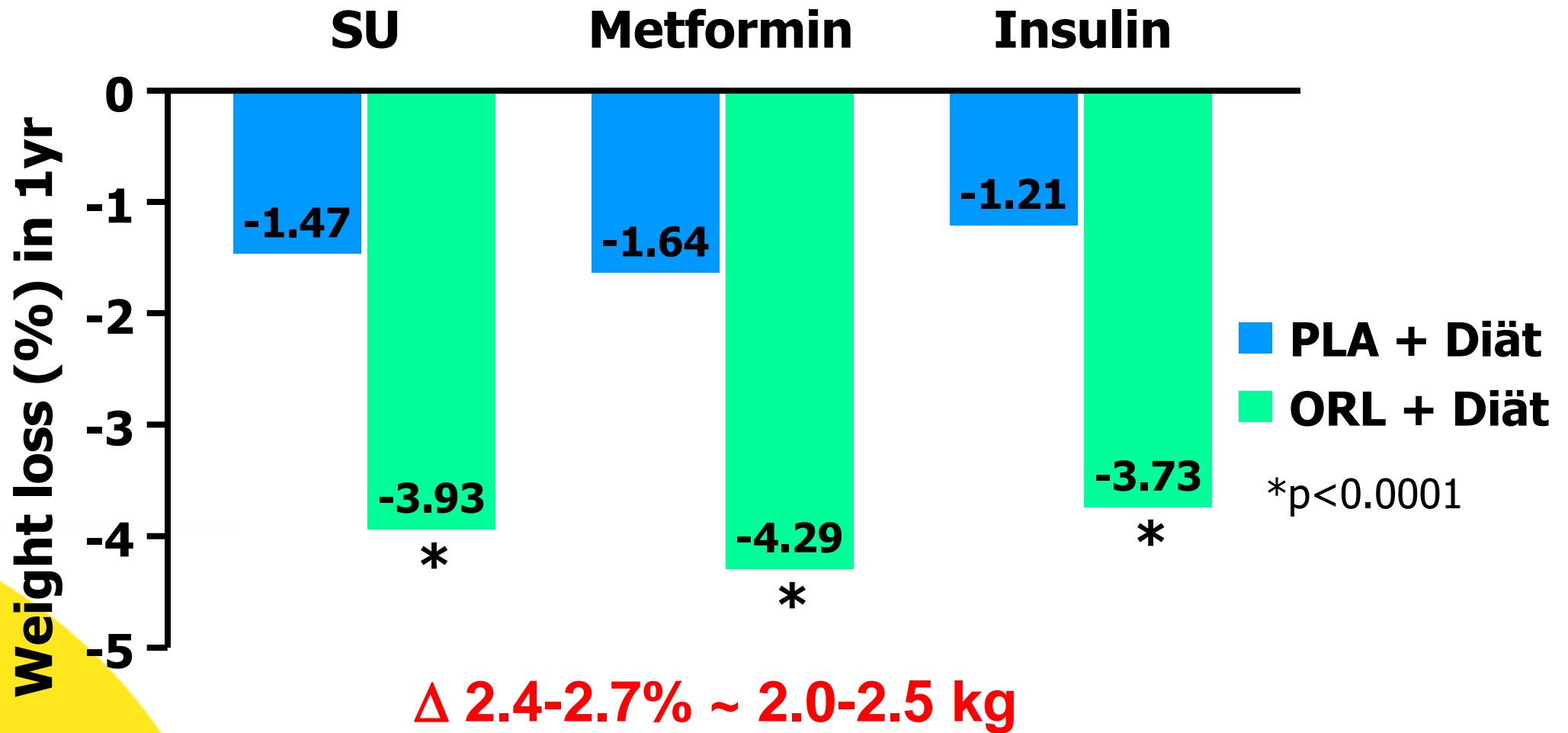
Lifestyle-Changes
Nutrition-Physical Activity-Behavior
BMI < 30 kg/m²

Medication for weight loss?

- Rimonabant: Endocannabinoid-Receptor Blocker
 - Withdrawn
- Sibutramin (Reductil): withdrawn
- Orlistat (Xenical 120 mg; daily cost 2.91 Fr)
- new: Alli 60 mg (daily cost 2.50 Fr.)
- GLP-1 Analog
- DPP-4 Inhibitor



Weight loss with Orlistat (Xenical®) in 2400 obese patients with type 2 diabetes Metaanalysis of 7 studies



Weight Increase with Antidiabetic Therapy

- Renal glucose threshold: 10 mM (~7.3% HbA1c)

- **Per 1% HbA1c ↓: Weight ↑ 3 kg pro Jahr (57 kcal/d = 8 g/Tag)**



15 g glucose = 60 kcal

46 year-old man with bipolar psychosis

- 2010 Hospitalization because of high HbA1c > 10%
- Actual findings: 110 kg (BMI 32.2)
- **Best Treatment?**
- Metformin
- Sulfonylurea/Glinide
- DPP-4 Inhibitor
- GLP-1 Analog
- Insulin
 - Which treatment form?



Depression + Diabetes mellitus



**Rate of Depression
= double normal rate in
Patients with diabetes**

- **more complications**

Anderson et al., 2001 Diabetes Care; 24:1069-78



Schizophrenia + Diabetes mellitus



Leo Navratil, 2001
Schizophrenie-Fondation
Schweiz

Higher prevalence of diabetes even before treatment with atypical neuroleptica

Up to 50% of patients treated with neurleptica = overweight

Dixon L 2000, Schizophr Bull, 26: 903-912
Baptista T 1999, Acta Psychiatr. Scand 100: 3-16



Schizophrenia + Diabetes/metabolic syndrome

Prevalence of impaired glucose tolerance and type 2 diabetes ↑

Patients with Schizophrenia

Normal

7 % impaired glucose tolerance

**14.5 % Diabetes mellitus
(6.5 % newly diagnosed)**

5 %

21.5 % metabolic syndrome

Metabolic Syndrome + Schizophrenia

..... Why the metabolic syndrom occurs in Schizophrenia is as yet unclear, but

unhealthy life style

- **poor diet**
- **smoking**
- **↓exercice**



**Ryan MC et al., Life Science 2002
Kahl , MMW Fortschr Med., 2005**



Atypical Neuroleptica

Obesity
(Zytokines ↑)

Dyslipidemia

D. mellitus

„Atypica Rx“
In Schizophrenia



Sussman N 2001, J. Clin Psychiatry, 62 :5-12

Sernyak MJ et al. 2002, Am J Psychiatry, 159:561-66

Henderson DC et al. 2001, J Clin Psychiatry 62:39-44



Psychopharmacological drugs + Zytokines

- Clozapin*
- Olanzapin**
- Tricyclica***



TNF- α ↑

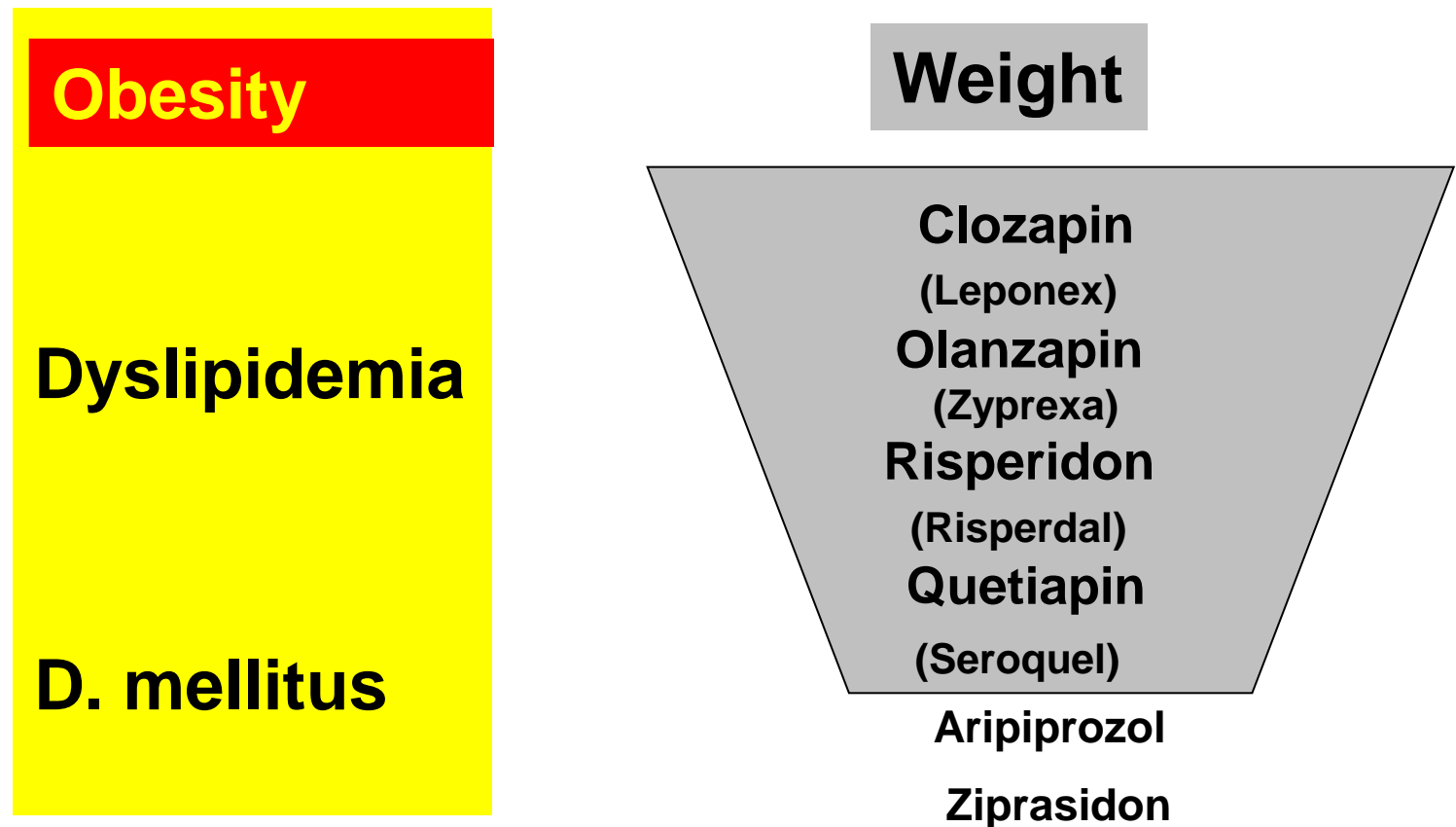


Sleep, affection, cognition, sexuality

Pollmächer et al 1997*
Schuld 2000 et al,**
Kraus et al. 2001***



Atypical Neuroleptica



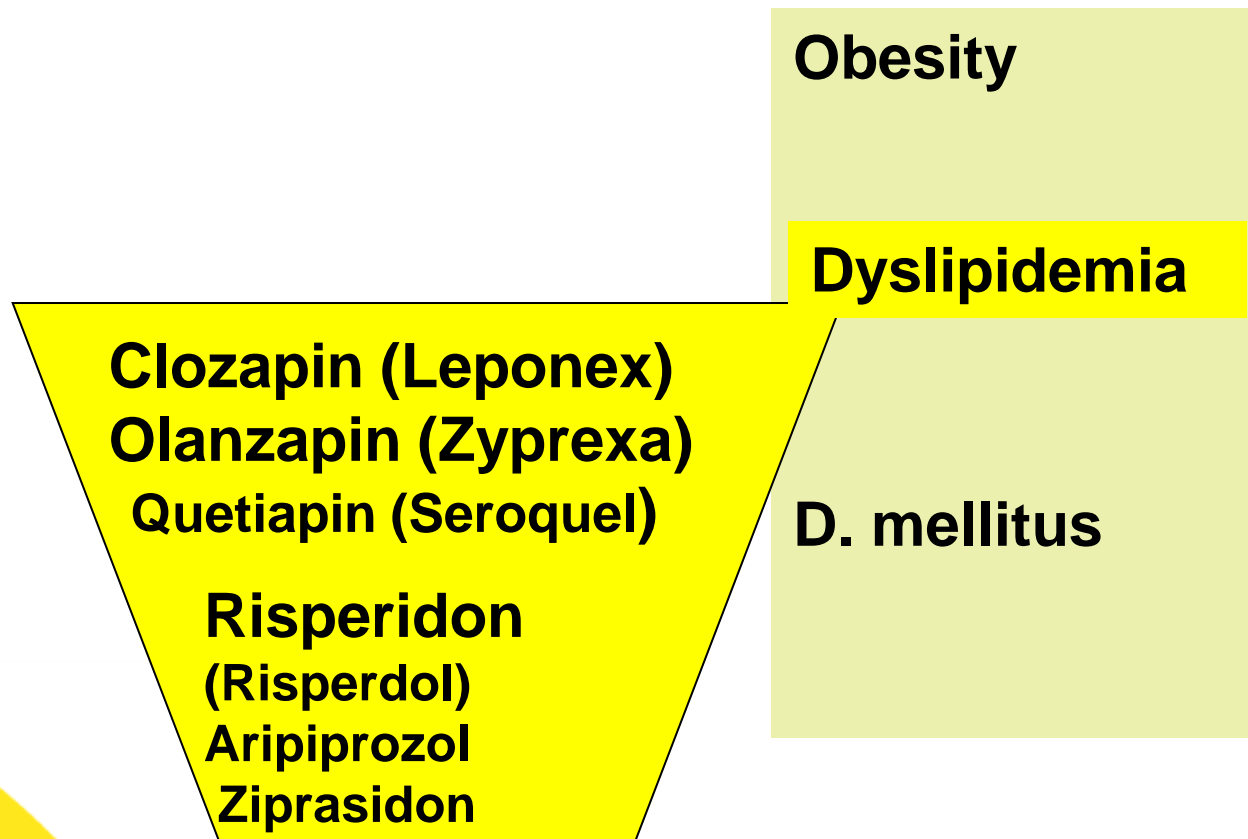
American Diabetes Association for Study of Obesity

J. Clin. Psychiatry 2004;65: 267-272

Annual Meeting of the American Psych. Association, 2005



Atypical Neuroleptica



Thank you for your attention

