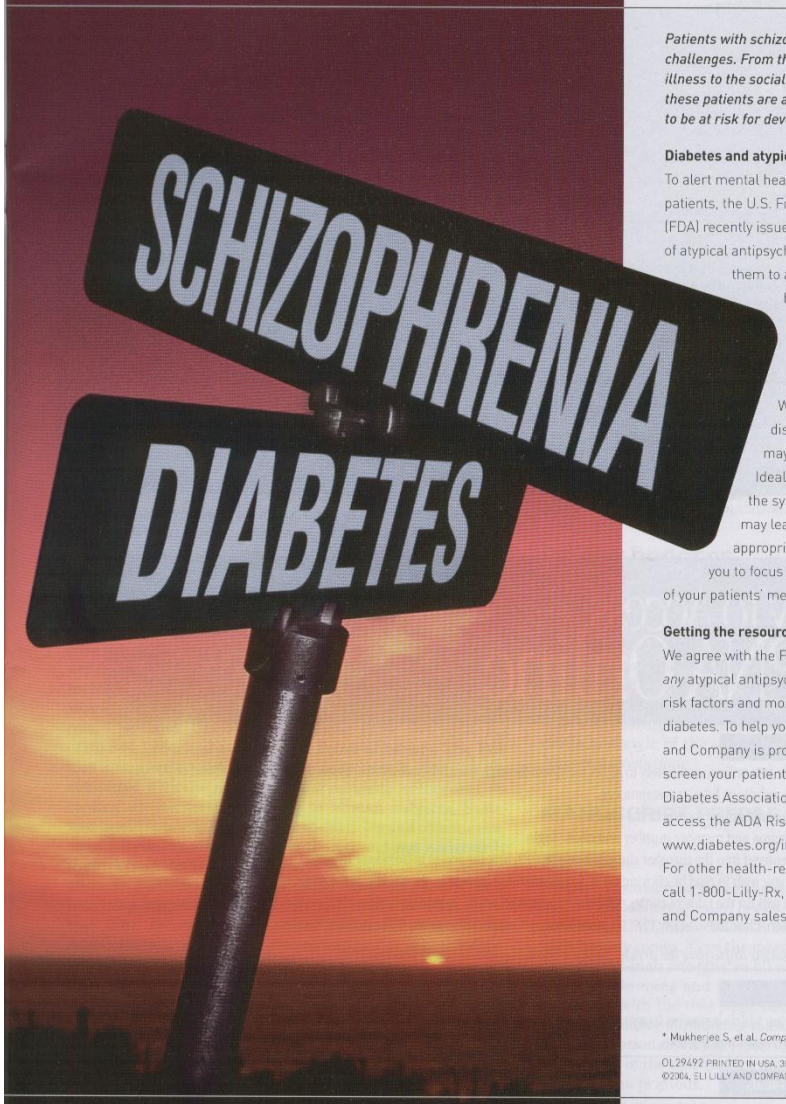
The way through this intersection starts with you.



*Patients with schizophrenia face a host of challenges. From the perplexing nature of their illness to the social stigma that surrounds it, these patients are also 2 to 4 times more likely to be at risk for developing diabetes.**

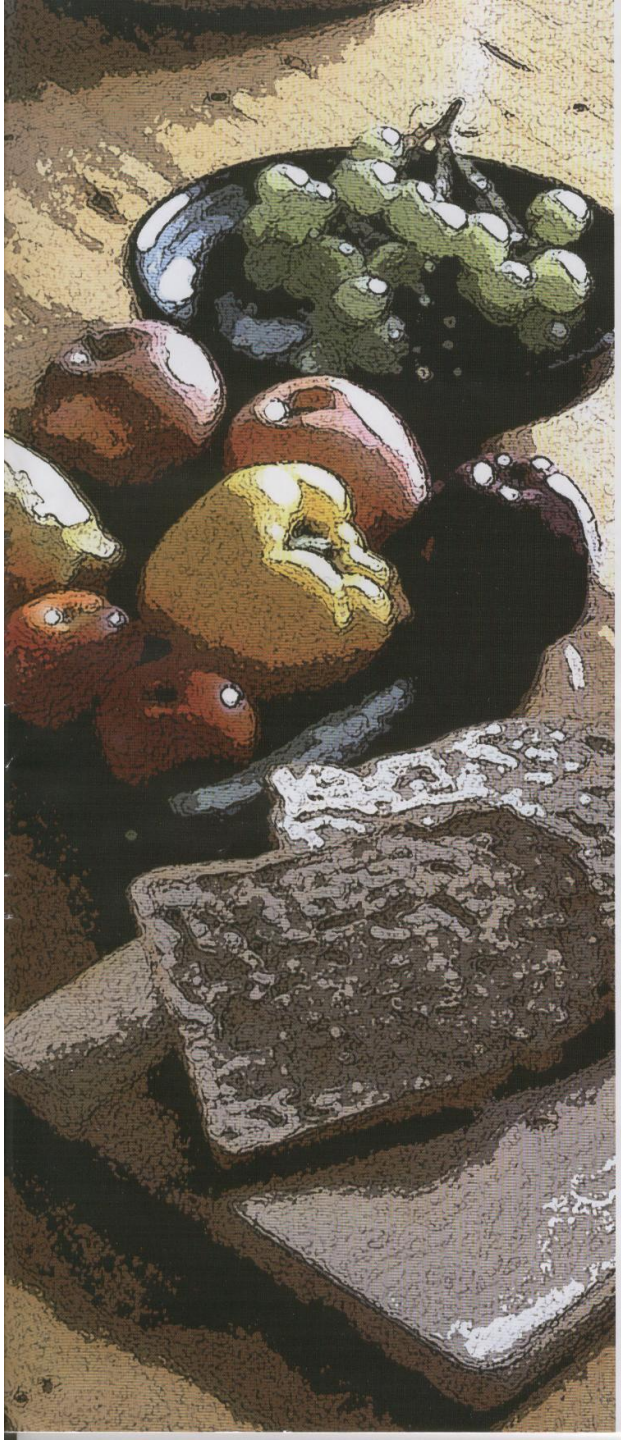
Diabetes and atypical antipsychotics.
To alert mental health professionals and their patients, the U.S. Food and Drug Administration (FDA) recently issued letters to all manufacturers of atypical antipsychotic medications advising them to add warning information on hyperglycemia and diabetes to their prescribing information.

Another counseling opportunity.
When counseling your patients, discuss the diabetes risks that may be related to their illness. Ideally, this increased attention to the symptoms of diabetes mellitus may lead to earlier detection and appropriate treatment — and allow you to focus on treating the core symptoms of your patients' mental illness.

Getting the resources you need.
We agree with the FDA that *every* patient prescribed *any* atypical antipsychotic should be screened for risk factors and monitored for symptoms of diabetes. To help you help your patients, Eli Lilly and Company is providing resources to help you screen your patients, including the American Diabetes Association's Diabetes Risk Test. To access the ADA Risk Test, go to the ADA Web site: www.diabetes.org/info/risk/risktest.jsp.
For other health-related information, please call 1-800-Lilly-Rx, or contact your Eli Lilly and Company sales representative.

* Mukherjee S, et al. *Compr Psychiatry.* 1996;37:68-73.

Lilly
Answers That Matter.



Mental Health Nursing

JULY 2005
VOLUME 25 • NUMBER 4

The Good Life: Meeting the physical needs of those with mental illness

- Glasgow's global health clinic
- Physical health checks for those with SMI

PLUS

- One session treatment for phobia
- Reviews

The Official Journal of

mhna
Mental Health Nurses Association

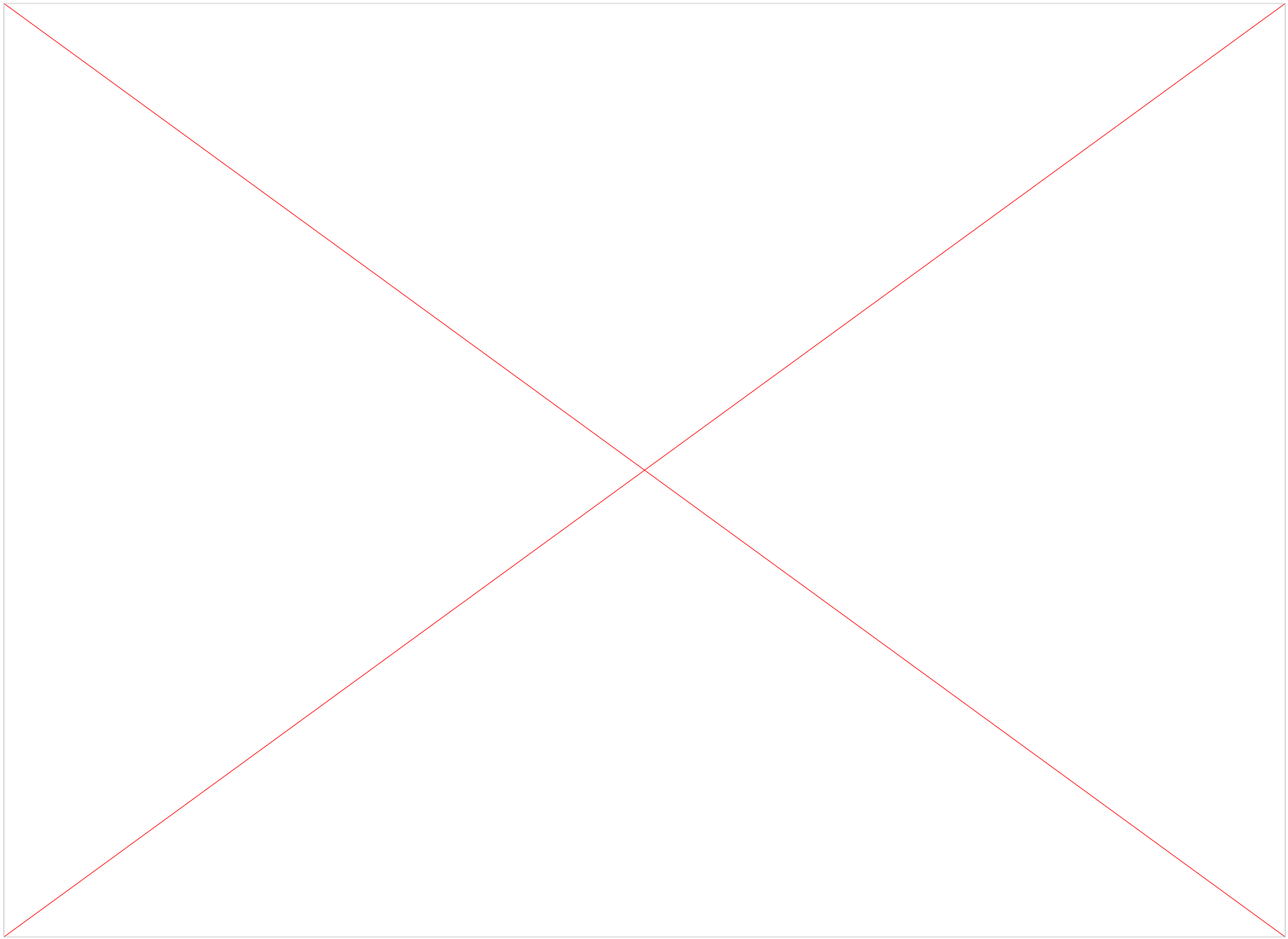
amicus
the union

Health checks for those with SMI

Are patients with severe mental illness getting appropriate physical healthcare? How regularly are they receiving a physical check-up and how often do they get involved in some form of physical exercise? In this study, by Rishi Rahka and Mark McKeown a patient is considered to be suffering from a severe mental illness (SMI) if they either have a diagnosis of schizophrenia, bipolar affective disorder, severe depression or a form of psychotic illness where more than one admission to hospital or secondary care was required and for which they are still receiving anti-psychotic medication or mood stabilisers or anti-depressants. In many cases a combination of these types of medication are being utilised for general efficacy in their condition. This article represents an audit, supported by valid data which has arisen from feedback received from an unfinished project that is being carried out in eight different mental health trust sites across the country. It looks at the levels of physical health checks and physical activity in people suffering from SMI

Full title: Health promotion for people with severe mental illness: are well-being support programmes the way forward?

Rishi Rahka is an RMN who is currently working as a nurse advisor for the Well-Being Support Programme, a project that is being sponsored by Eli Lilly. He is based at Scarborough House Assertive Outreach Team, Birmingham and Solihull Mental Health Trust. Mark McKeown is also a nurse advisor on the same programme. He is working in Coventry Mental Health Trust.



Date: 02/11/2004 10:51:50 PM
From: CN=Gregory T Brophy/OU=AM/O=LLY
Subject: Preparation for After Action Review
Attachments: After Action Review Process.ppt

Bert, here are some of my initial thoughts on the questions posed by David Kinard. Michele, attached are the key questions for the Review meeting on Friday from 10-12 - thanks for filling in for me on this. Robin, I would also like you to feed your thoughts into Michele on these questions.
To a great extent, how these questions are addressed depends on if the group looks at the broad question of ADA influence - from when we first got involved with this (my recommendation), vs. how we ran the drill once we knew the outcome was negative (i.e. we should have had greater influence early on before it was a done deal). So if people take the broader approach, here are some of my preliminary thoughts (for slide 4/5):

Supposed to happen: ADA was to come out with a recommendation similar to FDA's conclusion - comparable risk across atypicals
What happened: Differential risk, limited evaluation of the data, deck stacked against us even before the meeting began, railroaded process
Why did it happen: We underestimated the players, didn't really understand role & approach competition would take, under appreciated ADA backlash to other Lilly actions with it, inadequately influenced key players on decision, thought science and data would win - under appreciated the influence of weight gain on the action (perhaps too busy defending against it), FDA presentation was not as strong as it could have been to influence group (particularly the response to the weight gain question), our "full court press" action in the last few days was good, but came at a point too late to fundamentally influence the outcome

American Diabetes Association.

Cure • Care • Commitment®

Mission ·
to prevent and cure diabetes
and to improve the lives of all
people affected by diabetes.

EMBARGOED
Until 12 a.m., January 27, 2004

Contact: **Kendra Gutschow, ADA**
(703) 549-1500 ext. 2146

Antipsychotic Drugs Raise Obesity, Diabetes and Heart Disease Risks:

Joint Panel Urges Increased Screening, Monitoring of Side Effects

(Alexandria, VA) – People who take antipsychotic drugs for the treatment of a variety of mental illnesses may be at increased risk for obesity, diabetes and high cholesterol – all of which can lead to heart disease. Because of this, a joint panel of the American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, and the North American Association for the Study of Obesity has issued a consensus statement asking doctors to carefully screen and monitor patients on these medications for signs of rapid weight gain or other problems that could lead to diabetes, obesity and heart disease and refer them to specialists if necessary.

The consensus statement, published in the February issue of *Diabetes Care*, outlines guidelines for doctors treating people with a class of drugs known as second-generation antipsychotics (SGAs). These drugs, the use of which has soared in recent years, are used to treat a variety of mental illnesses, including: schizophrenia spectrum disorders; bipolar disorder; dementia; psychotic depression; autism and developmental disorders; and, to a lesser extent, delirium; aggressive behavior; personality disorders; and posttraumatic stress disorder.

The panel also concluded that the SGAs differ in their risk profiles and that some SGAs, such as clozapine and olanzapine, while effective treatment options, raise a greater risk of weight gain, diabetes and lipid disorders than others. The statement notes that "...Even for those medications associated with an increased risk of metabolic side effects, the benefits to specific patients could outweigh the potential risks." Thus, while risks reviewed in this study should influence choice of medication, the need to balance benefits and a wide range of risks underscores the importance of tailoring treatments to individual patients.

Summary of the After Action Review of Zyprexa and ADA (held 2/13/04)

- Close contact was not maintained with the presenters or the writing panel of the consensus panel. **Solution**: a systematic well orchestrated approach is needed with similar events that are likely to happen in the future in order to ensure that the information available is accurate and free of interpretation bias
- Crisis atmosphere on the Zyprexa leadership team during 2-3 weeks around the publication of the ADA consensus. **Solution**: A hand railed team with defined leadership, headcount and clear accountability needs to be created to address similar events. A team has been assembled led by Bert VandenBergh.

22 January 2004

Richard Kahn, PhD
Chief Medical and Scientific Officer
American Diabetes Association
1701 N. Beauregard St.
Alexandria, VA 22311

RE: Consensus Development Conference on
Antipsychotic Drugs and Obesity and Diabetes

Dear Dr. Kahn,

Eli Lilly and Company commends the American Diabetes Association for its initiative in addressing issues concerning metabolic adverse events in patients using atypical antipsychotics. As the sponsor that initially brought these issues to the attention of the ADA, Lilly appreciated the opportunity to partner with ADA, APA, AACE, NAASO, and other sponsors in presenting data at the Consensus Development Conference.

We have reviewed the Consensus Statement forwarded to us by the ADA and commend the working group for bringing focus to the critical issue of increased rates of diabetes in patients with serious mental illness. However, we have significant concerns regarding the conclusion that there are differential rates of treatment-emergent diabetes among second-generation antipsychotics (SGAs). We disagree with the following conclusion as stated on page 600:

> "Clozapine and olanzapine are associated with the greatest weight gain and highest occurrence of diabetes and dyslipidemia. Risperidone and quetiapine appear to have intermediate effects. Aripiprazole and ziprasidone are associated with little or no significant weight gain and no diabetes or dyslipidemia, although they have not been used as extensively as the other agents" (pg. 600).

Why this matters...

The data showed that everyone interviewed, which included not only psychiatrists, PCPs, and nurses, but also Lilly sales directors, DMs, sales reps and Marketing staff, exhibited language that was devoid of emotion around the side effects of Zyprexa. This represents an "emotional gap" that must be bridged before many MDs will feel more in control when treating patients on Zyprexa. Furthermore, if we can communicate to the MD on an emotional level and help them address the psychological impact of weight gain for the patient, we will most likely make significant strides towards resolving this issue in their minds.

Best regards,

Tom Reck
Market Research Associate
Zyprexa - U.S.
w) 317.655.8983
treck@lilly.com

Lingustic Market Research Objectives

- **Understand the perceptions of weight gain internally and externally**
  - Lilly Marketing
  - Lilly Medical
  - Lilly Sales Force
  - Called on Physicians and health care professionals
- **Understand weight gain from a medical versus emotional standpoint**
- **Understand how weight gain and weight gain related health concerns play on the emotions of both MDs and patients in relation to Zyprexa**
  - Pt demands to be taken off of Zypexa b/c they don't want to be fat
  - MD takes pt off Zyprexa due to pt appearance and potential health related issues
- **Understand what language Lilly can implement to help communicate with health care professionals regarding the weight gain issue.**
  - Communication with MDs, Treatment Teams and potentially patients.
- **Understand the marketing mix implications to most effectively communicate our message.**
  - What can we do outside of the sales force.

Critical Observations on this new information

This data is an enhancement to and consistent with our previous message

Remember, handle this objection, like weight gain, in the context of overall efficacy.

- This is all about tone. We must handle the objection in a confident and forthcoming manner, but must only answer the question to the depth required
  - Do not bypass the objection handle it when it happens.
  - Tailor the response to situation, probe, get back to joint discovery

Situational Analysis:

Where we were vs. Where we are going

From

- Weight gain is manageable
- Weight gain is predictable
- Weight gain is not the only predictor of diabetes
- Diabetes risk is a class effect with comparable rates across all products
- Diabetes is mainly a patient population issue
- Handling diabetes and weight gain as an objection

To

- Lilly understands the challenges physicians face in treating this population
- Lilly acknowledges weight gain challenges and potential consequences
- Lilly is providing me with options to address weight gain in some of my patients
- External entities provide me with the facts related to diabetes
- Lilly is providing help regarding how to assess, counsel, and refer patients at risk for diabetes

Big opportunity for the brand: Weight gain

- Weight Gain
  - Perceived as very prevalent
  - Sometimes significant
- Results
  - Patients denied Zyprexa
  - Unhappy customers (Declining Doctors)
  - Loss of $

Root of Problem

Issue cannot be “fixed”, **must** be managed

Relationship issue with the brand.

Proper implementation is key!

Our goal and focus is on creating a market with Donna. The competition wins if we are distracted into talking about diabetes. So, stand strong against their ploys and answer the AOC concisely and with confidence!

Handling the Diabetes AOC:

This is a highly competitive driven issue.

Therefore, we will NOT proactively address the diabetes concern, but rather only when it arises from an MD.

If it does, please do the following:

1. Cushion/Clarify the AOC
2. Handle by providing the verbatim
3. Check for agreement, **if not satisfied then utilize the sell sheet**
4. Restate the verbatim while utilizing the diabetes sell sheet
5. Check for agreement and get back to Donna!

Handling AOC - Other Risk Factors

For customers who ask about Diabetes as it relates to risk factors such as weight, please provide the following verbatim.

1. While there is a relationship between weight (or specifically obesity) and diabetes, it is not exact and constitutes one of **many** risk factors for diabetes. For example, another is hyperprolactinemia (*Inside cover, "A number of factors…" section 4)*
2. Even among the patients that had substantial weight gain with Zyprexa, over 96% had no glycemic abnormalities at all. (*Inside cover, "Weight gain…." section 2)*

Remember correct tone is critical, Confident and informative!

Our customers just want the facts and reassurance

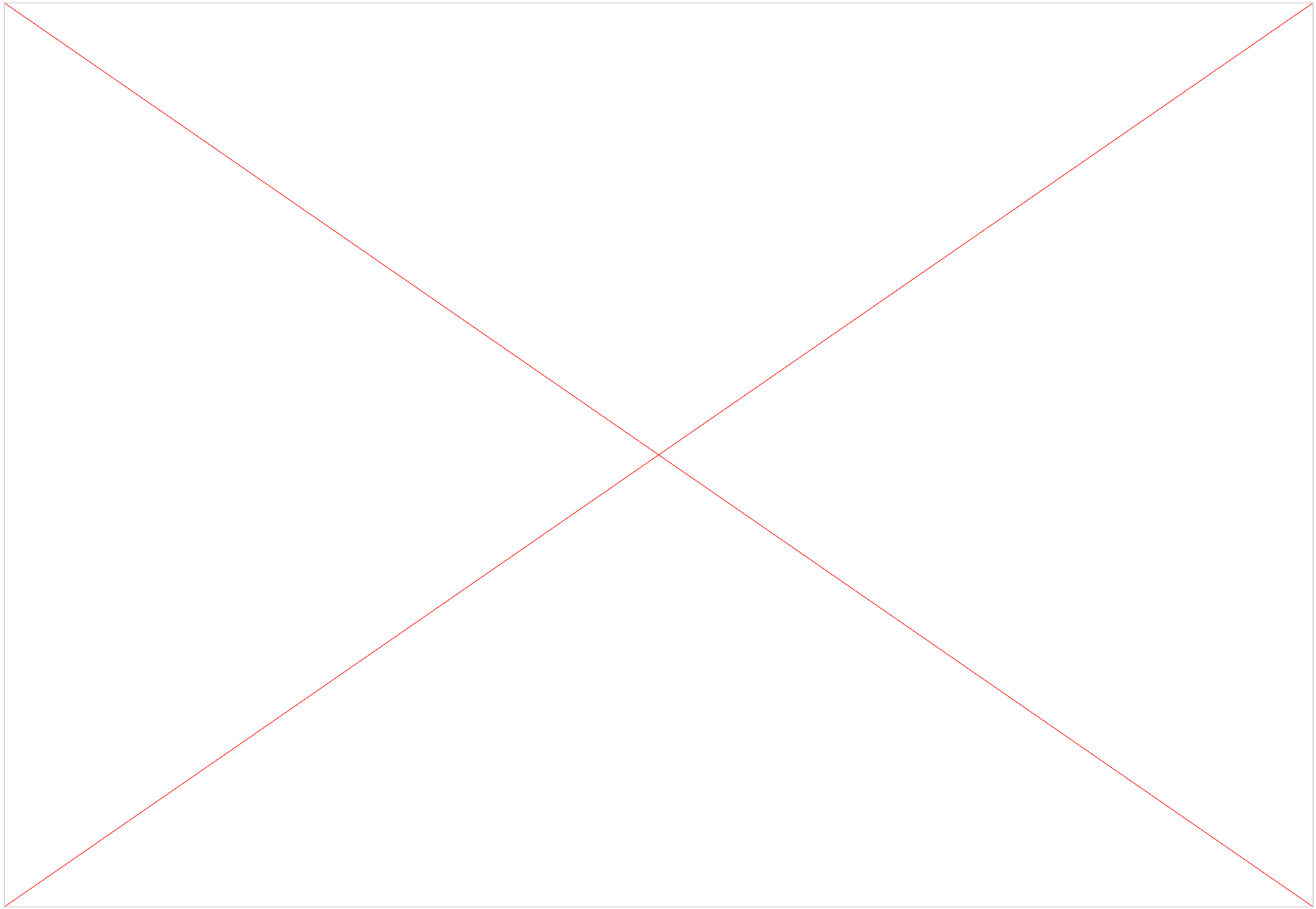
I am concerned about weight gain.
Cushion: *Thanks for letting me know your concern.*
Clarify: *Is this something you have seen in your patients or heard about?*
Address AOC: *Zyprexa may cause an increase in appetite that can lead to weight gain. The increase in appetite can be manageable, and diet and behavioral modifications can help. Many describe this as carb-craving so discussing this up front with your patients is helpful. You can suggest that patients drink diet soda instead of regular soda, or cut back on the amount of carbohydrates they eat. Some patients adopt a "1-plate rule" when they sit down for dinner. Increasing daily activity may also help manage weight*
Check for Agreement *How do you manage weight gain that results from other medications? If the physician has further questions, offer to have a medical letter sent to them.*
Get back to Selling

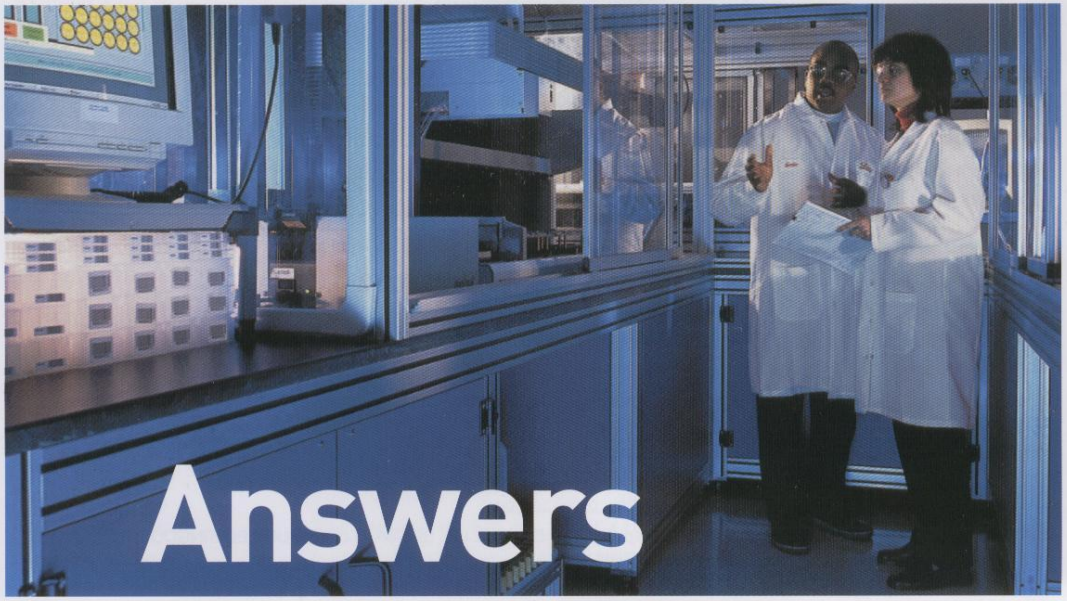
Doubt is our product since it is the best means of competing with the "body of fact" that exists in the mind of the general public. It is also the means of establishing a controversy. Within the business we recognize that a controversy exists. However, with the general public the consensus is that cigarettes are in some way harmful to the health. If we are successful in establishing a controversy at the public level, then there is an opportunity to put across the real facts about smoking and health. Doubt is also the limit of our "product". Unfortunately,

690010954

Brown & Williamson 1969
http://legacy.library.ucsf.edu/tid/rgy93f00

Doubt is also the limit of our product. Unfortunately, we cannot take a position directly opposing the anti-cigarette forces and say that cigarettes are a contributor to good health. No information that we have supports such a claim.





Medicines. Discovering breakthrough treatments. Confronting many of the most challenging diseases facing humanity.

Information. Openly sharing the knowledge you need. Helping you make the best health care decisions possible.

Medicine and information. The answers you're looking for.

We're celebrating 125 years of lifesaving innovation. **www.lilly.com**

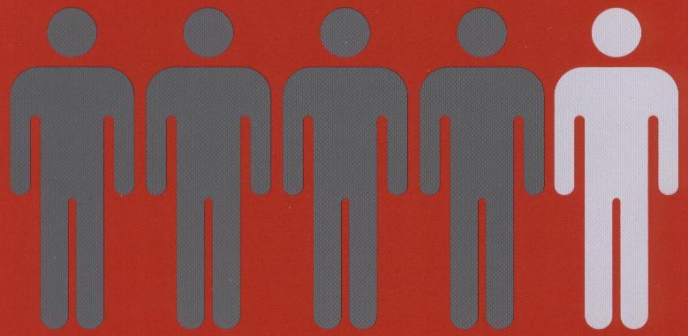
Lilly

Answers That Matter.

When asked a question about weight gain, Dr. Tollefson's response misleadingly turned an adverse event into a therapeutic benefit. He states, "So we went back and analyzed our data and saw that the vast majority of weight gain reported initially as an adverse event, in fact, was weight gain occurring in patients who had baseline before starting treatment, had been below their ideal body weight. **So we really look at this, with the majority of patients, as being part of a therapeutic recovery rather than an adverse event. And that data, I think is fairly compelling, because it was included in our labeling.** (Emphasis added)"

The information on weight gain was indeed included in the approved labeling, but as an adverse event, not a therapeutic benefit. Since the product was approved at the time of this teleconference, Dr. Tollefson knew or should have known what information the approved labeling contained and in what section it appeared. His statements were therefore, false and misleading.

KNOWTHEFACTS

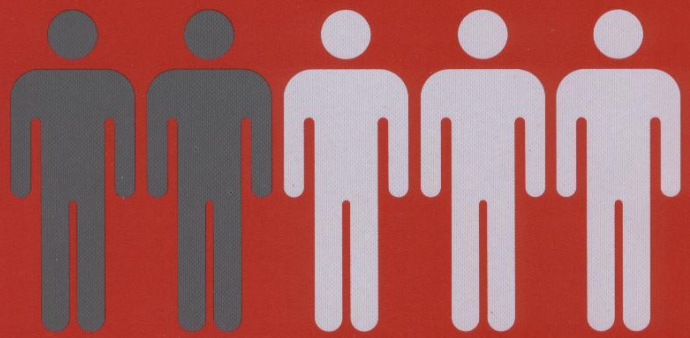


13% of patients had diabetes in the landmark CATIE schizophrenia study at baseline—4 times more common than in the general population.[1]

Be aware.
Screen and monitor your patients.
Make a difference.

Pfizer

KNOW THE FACTS



41% of all patients had the metabolic syndrome at baseline in the landmark CATIE schizophrenia study.[2]

Be aware.
Screen and monitor your patients.
Make a difference.

Pfizer

References: 1. Goff DC, Sullivan LM, McEvoy JP, et al. A comparison of ten-year cardiac risk estimates in schizophrenia patients from the CATIE study and matched controls. *Schizophr Res.* 2005;80:45-53. **2.** McEvoy JP, Meyer JM, Goff DC, et al. Prevalence of the metabolic syndrome in patients with schizophrenia: baseline results from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial and comparison with national estimates from NHANES III. *Schizophr Res.* 2005;80:19-32.

GZ280304A

Printed in USA/December 2006

Lab Chemistry: Change from Baseline to Ave of 2 Highest Values

		O (n=336)	QT (n=337)	R (n=341)	P (n=261)	Z (n=185)
Bl Glucose (mg/dL)	Mean (S.E.) Median Exposure-adj. Mean	15.0 (2.8) 7.0 13.7 (2.5)	6.8 (2.5) 4.3 7.5 (2.5)	6.7 (2.0) 5.5 6.6 (2.5)	5.2 (2.0) 1.5 5.4 (2.8)	2.3 (3.9) 2.5 2.9 (3.4)
Hemoglobin A1C (%)	Mean (S.E.) Median Exposure-adj. Mean	0.41 (0.09) 0.20 0.40 (0.07)	0.05 (0.05) 0.10 0.04 (0.08)	0.08 (0.04) 0.05 0.07 (0.08)	0.10 (0.06) 0.05 0.09 (0.09)	-0.10 (0.14) 0.10 0.11(0.09)
Cholesterol (mg/dL)	Mean (S.E.) Median Exposure-adj. Mean	9.7 (2.1) 8.5 9.4 (2.4)	5.3 (2.1) 3.5 6.6 (2.4)	-2.1 (1.9) -3.0 -1.3 (2.4)	0.5 (2.3) 0.5 1.5 (2.7)	-9.2 (5.2) -1.0 -8.2 (3.2)
Triglycerides (mg/dL)	Mean (S.E.) Median Exposure-adj. Mean	42.9 (8.4) 33.5 40.5 (8.9)	19.2 (10.6) 17.5 21.2 (9.2)	-2.6 (6.3) 3.0 -2.4 (9.1)	8.3 (11.5) 2.0 9.2 (10.1)	-18.1 (9.4) -7.0 -16.5 (12.2)
Prolactin (ng/mL)	Mean (S.E.) Median Exposure-adj. Mean	-6.1 (1.2) -0.9 -8.1 (1.4)	-9.3 (1.4) -2.7 -10.6 (1.4)	15.4 (1.5) 9.2 13.8 (1.4)	0.4 (1.7) 1.4 -1.2 (1.6)	-4.5 (1.6) -2.4 -5.6 (1.9)

THE BRITISH JOURNAL OF PSYCHIATRY

APRIL 2004 VOL. 184
SUPPLEMENT 47

Schizophrenia and diabetes 2003: an expert consensus meeting

EDITED BY T. G. DINAN

PUBLISHED BY THE ROYAL COLLEGE OF PSYCHIATRISTS
ISSN 0007-1250

Diabetes in Asylum History

Maudsley 1897 Diabetes
Kooy 1919, HG
Raphael & Parsons 1921 HG
Drury & Farron-Ridge 1921 HG
Lorenz 1922 HG (Catatonia)
Barrett & Serre 1924 HG
Henry & Magnan 1925 HG
Kasanin 1926 HG

2-4 fold increase in risk

Antipsychotics and Glucose

Courvoisier et al	1953	Glycemia
Giacobini & Lassenius	1954	Glycemia
Merivale & Hunter	1954	Glycemia
Charatan & Bartlett	1955	Glycemia
Hiles	1956	DM & Glycemia
Winkelmayer	1962	DM
Keskiner	1973	DM – 25%

US

1.2% 18-44

6.3% 45-64

Isle of Ely

4.5% undx diabetes

16.7% GTT

Australia

7.4% diabetes

16.4% GTT or HG

Japan & Sngpre

5 – 9% diabetes

10-18% GTT

North Wales Asylum

No. Patients – 3,170 No. Diabetics - ?
No. Psychoses - 1,041 No. Diabetics - ?
No. Mood Dis - 695 No. Diabetics – ?
Other - 1,434 No. Diabetics - ?

North Wales Asylum

No. Patients – 3,170 No. Diabetics - 64
No. Psychoses - 1,041 No. Diabetics - 20
No. Mood Dis - 695 No. Diabetics –12
Other - 1,434 No. Diabetics - 28

North Wales Asylum

No. Patients – 3,170 No. Diabetics - 128
No. Psychoses - 1,041 No. Diabetics - 40
No. Mood Dis - 695 No. Diabetics – 24
Other - 1,434 No. Diabetics - 56

North Wales Asylum

No. Patients – 3,170 Diabetics – 5
Psychoses - 1,041 Diabetics – 0
Mood Disorders - 695 Diabetics – 2
Other - 1,434 Diabetics – 3

No. with pre-existing diabetes – 2 (0.06%)

1994 – 2006

Schizophrenia
Delusional Disorder
Acute and Transient Psychoses
Non-specific Non-Organic Psychosis
Bipolar Disorder
Manic Episodes

N = 395

Hospital Database
Pharmacy Database
General Practitioners

Diabetes & F Codes

1996-2006

1031 Individuals

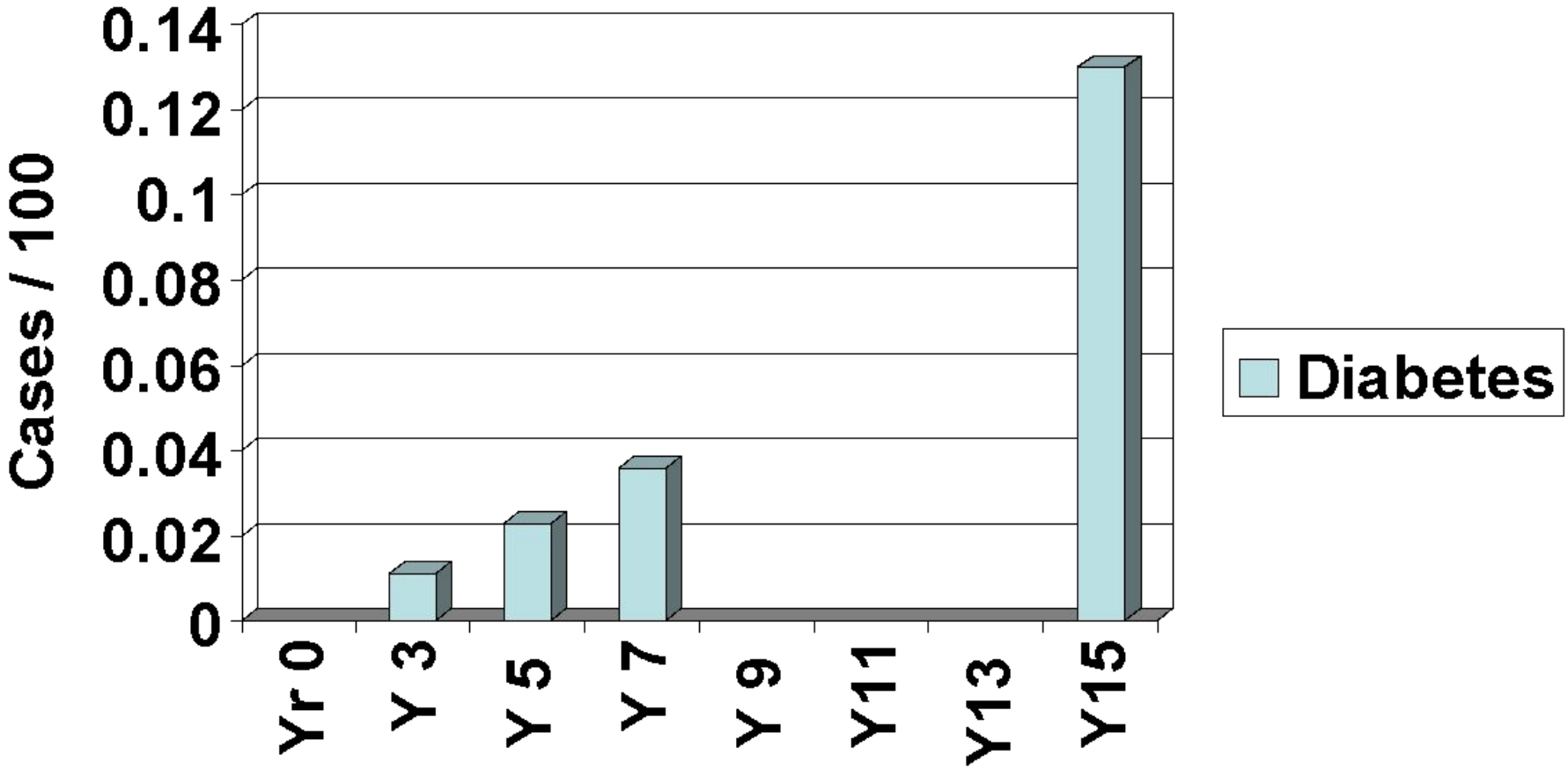
F00-99	368 ***
F10-19	204
F20-29	45
F30-39	230
F40-69	284

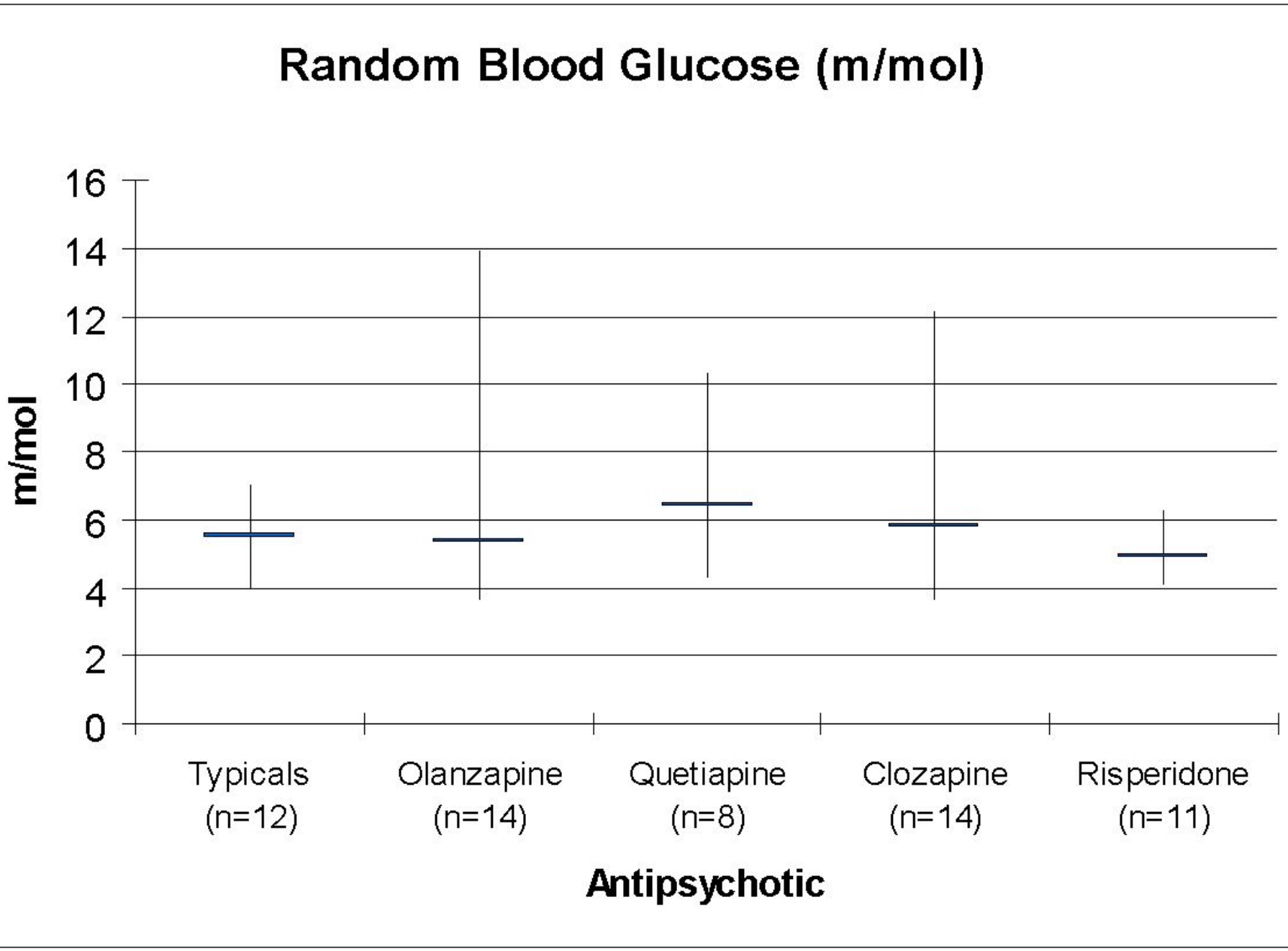
413 now dead –

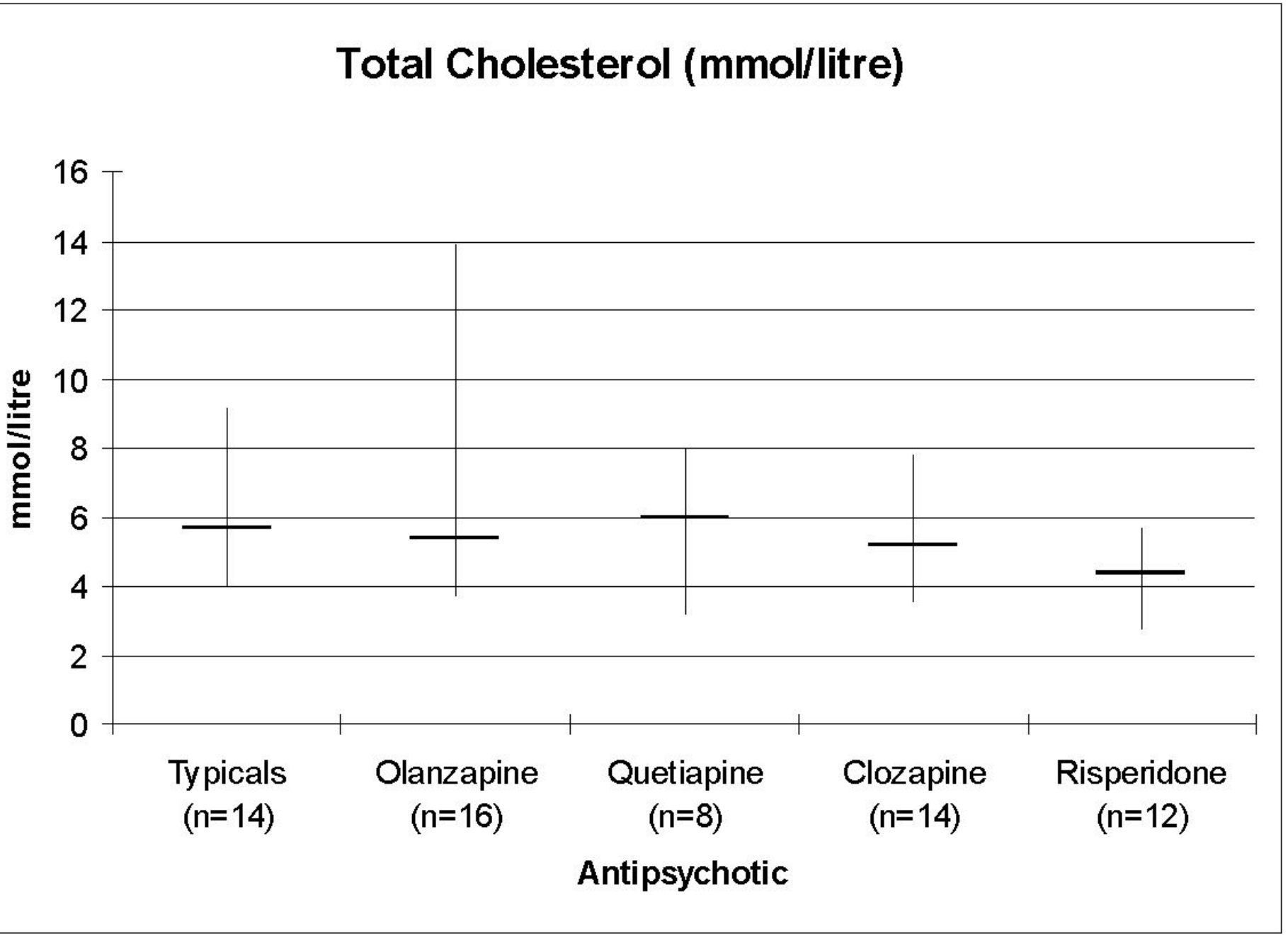
Prevalence 617/200K = 0.3%

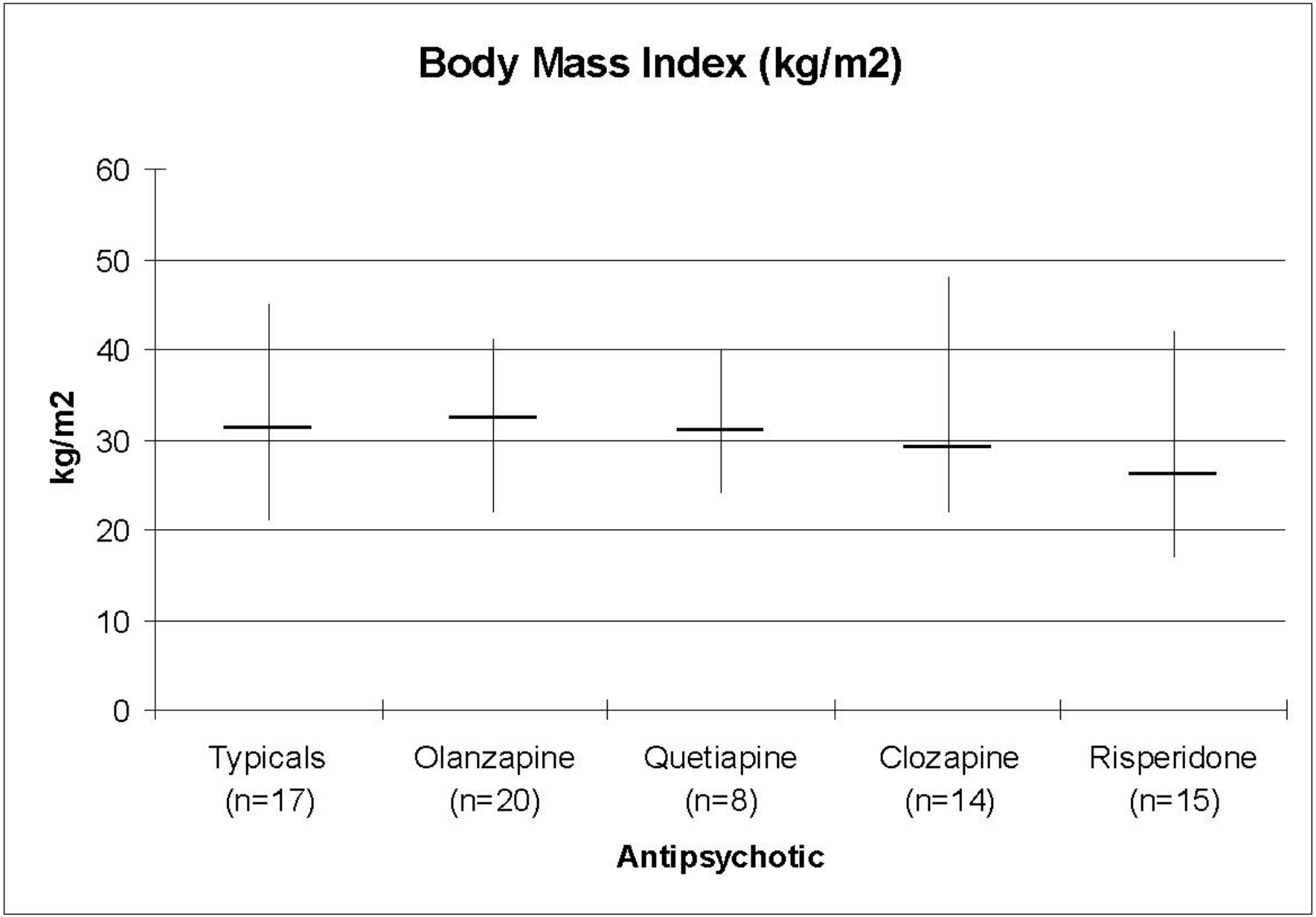
SMI - 66

Prevalence of Diabetes in Serious Mental Illness




Random Blood Glucose (m/mol)
m/mol
16
14
12
10
8
6
4
2
0
Typicals (n=12)
Olanzapine (n=14)
Quetiapine (n=8)
Clozapine (n=14)
Risperidone (n=11)
Antipsychotic

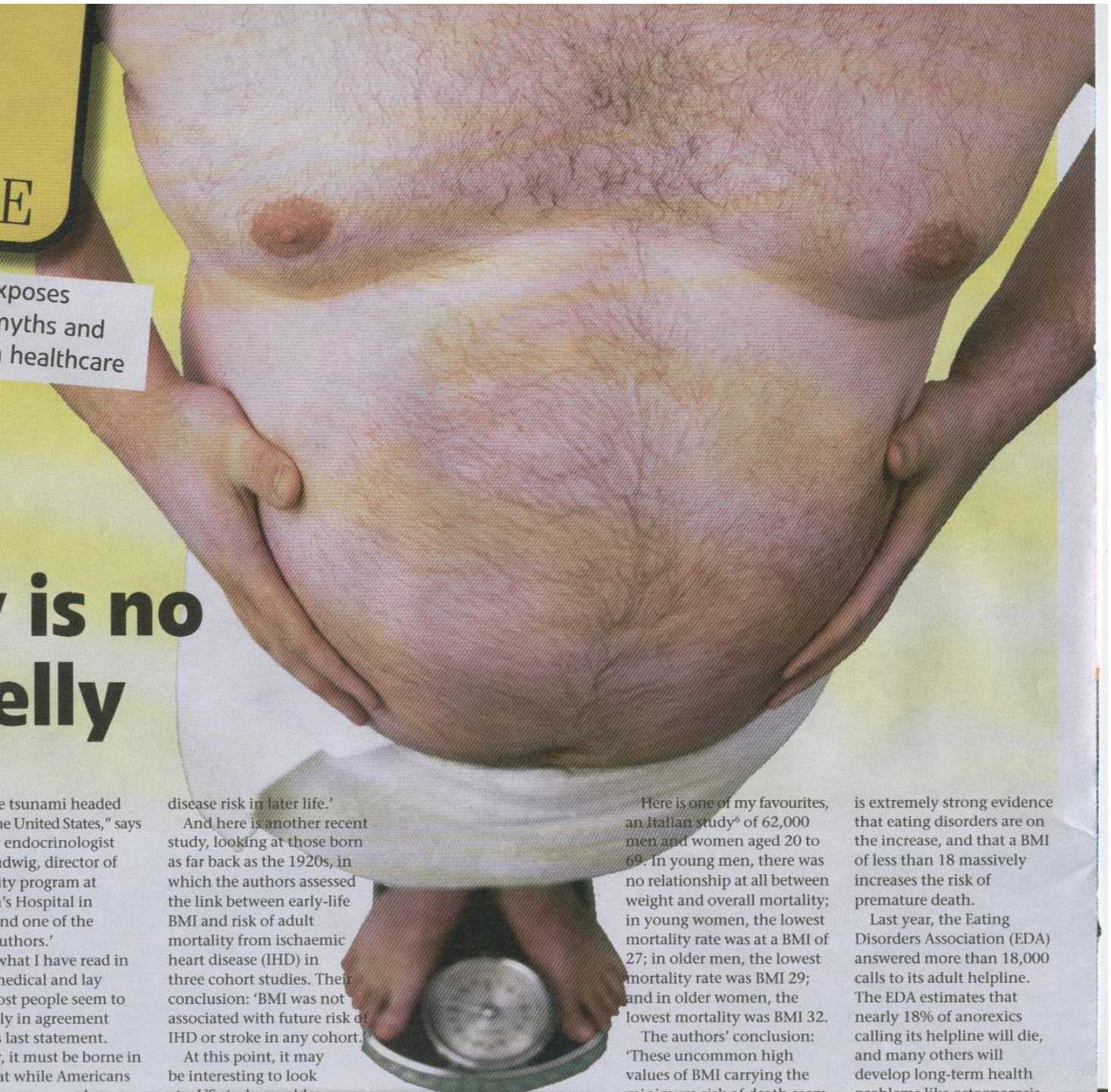

Total Cholesterol (mmol/litre)
16
14
12
10
8
6
4
2
0
mmol/litre
Typicals (n=14)
Olanzapine (n=16)
Quetiapine (n=8)
Clozapine (n=14)
Risperidone (n=12)
Antipsychotic


Body Mass Index (kg/m2)
60
50
40
30
20
10
0
kg/m2
Typicals
(n=17)
Olanzapine
(n=20)
Quetiapine
(n=8)
Clozapine
(n=14)
Risperidone
(n=15)
Antipsychotic

MEDICINE

Dr Malcolm Kendrick exposes sloppy science, medical myths and unhealthy assumptions in healthcare

Obesity is no casus belly



Obesity is being presented as the next massive threat to health – our children may even die before us due to the terrible danger of being fat. Celebrity chef Jamie Oliver has taken to dressing up in a fat suit to make the point.

A couple of years back, a *NEJM* study was reported on a US news website:[1]

'Obesity could shorten the average lifespan of an entire generation – today's children a massive tsunami headed toward the United States," says pediatric endocrinologist David Ludwig, director of the obesity program at Children's Hospital in Boston and one of the study's authors.'

From what I have read in the UK medical and lay press, most people seem to be broadly in agreement with this last statement. However, it must be borne in mind that while Americans

disease risk in later life.'

And here is another recent study, looking at those born as far back as the 1920s, in which the authors assessed the link between early-life BMI and risk of adult mortality from ischaemic heart disease (IHD) in three cohort studies. Their conclusion: 'BMI was not associated with future risk of IHD or stroke in any cohort.'[2]

At this point, it may be interesting to look

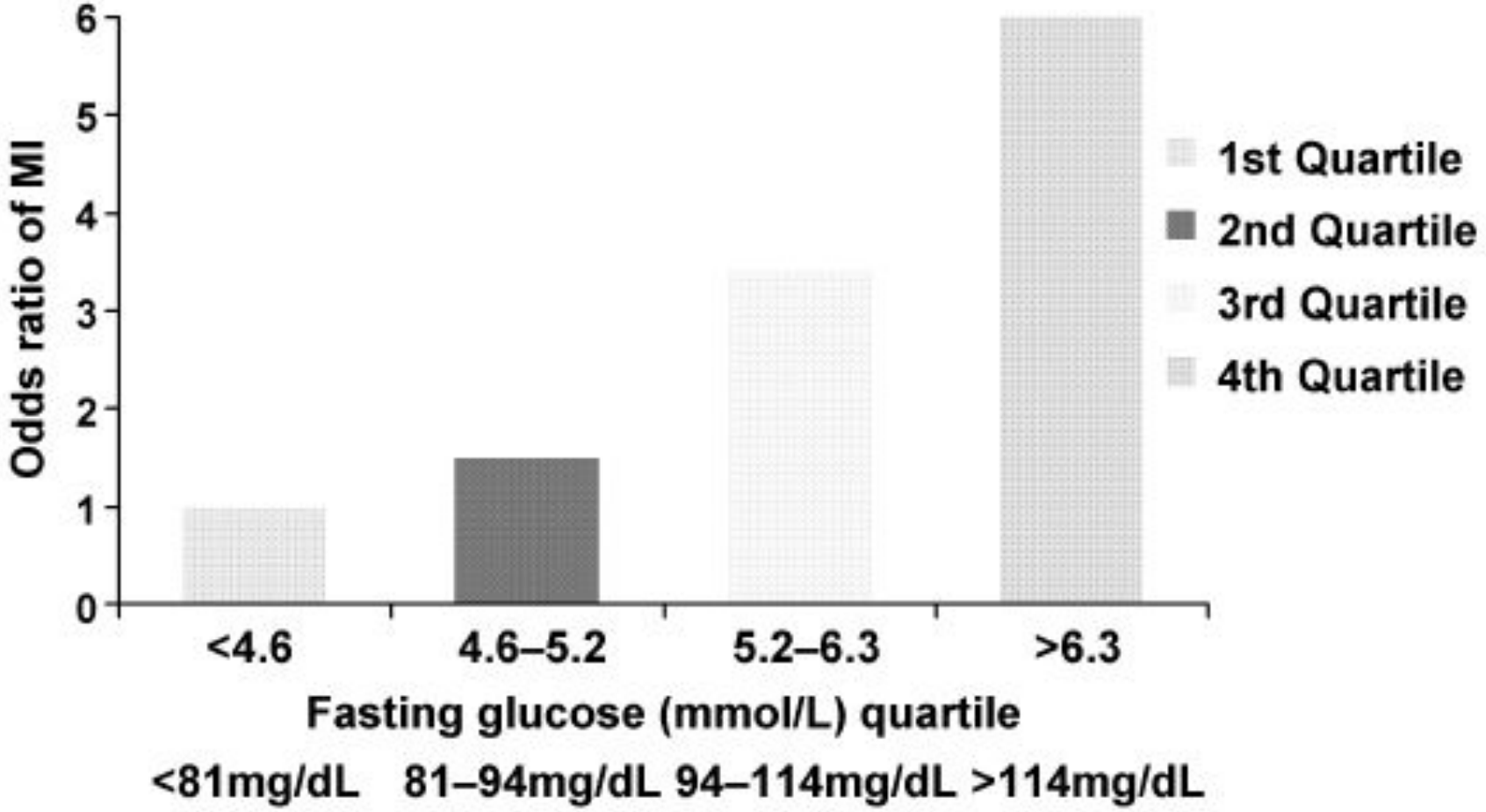
Here is one of my favourites, an Italian study[6] of 62,000 men and women aged 20 to 69. In young men, there was no relationship at all between weight and overall mortality; in young women, the lowest mortality rate was at a BMI of 27; in older men, the lowest mortality rate was BMI 29; and in older women, the lowest mortality was BMI 32.

The authors' conclusion: 'These uncommon high values of BMI carrying the

is extremely strong evidence that eating disorders are on the increase, and that a BMI of less than 18 massively increases the risk of premature death.

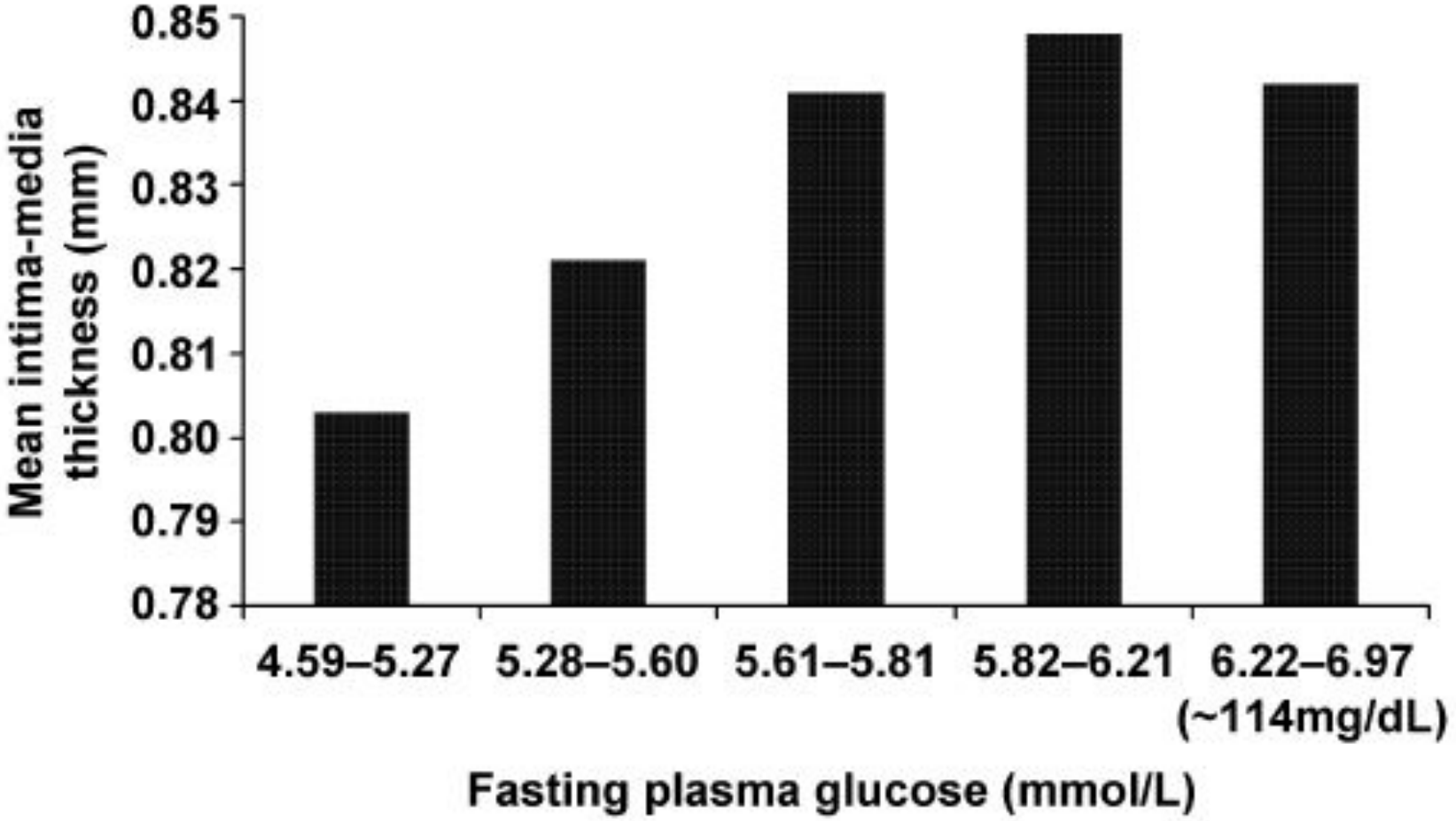
Last year, the Eating Disorders Association (EDA) answered more than 18,000 calls to its adult helpline. The EDA estimates that nearly 18% of anorexics calling its helpline will die, and many others will develop long-term health

Odds ratio of MI as a function of fasting blood glucose



Gerstein HC et al. J Am Coll Cardiol 1999;33:612–19.

Carotid intima-media thickness as a function of FPG



Hanefeld M et al. Atherosclerosis 1999;144:222–35.

- The ADA "Table 2" is somewhat misleading because makes the drugs look linear in their side effects with its use of plusses and minuses. It should list Clozaril & Zyprexa first with 22 lbs weight gain in 14 months, then Seroquel & Risperdal second (7 lbs.), and then Abilify and Geodon (2.2 lbs).

    - *"The efficacy 'improvement' of Zyprexa, even if it existed, would not justify its much higher weight gain."*

    - *"Even if Zyprexa was a bit better, which is not shown, as a doctor, you err on the side of caution—you should start with a treatment that has low side effects and work your way up if you don't get the benefits you want—but don't risk the weight gain first".*

- Lilly is "burning credibility" by denying the metabolic side effects of Zyprexa through semantics.

- Many practitioners are aware of the different metabolic profile of Zyprexa, and many would prefer straight answers from the company.

    - *"Lilly is playing a language game with the FDA pronouncements. Because the FDA class warning is about diabetes, Lilly can claim that there is no direct link with diabetes—which is true in one sense. But there is a direct link with weight gain, visceral fat, insulin sensitivity, and thus diabetes, stroke, and myocardial infarction. So while Lilly is technically correct, this is whitewash. They are, however, doing an outstanding job of politicizing and language games."*

ZYPREXA - LEGAL

Dec 2006 - $1.2 billion in plaintiffs' settlements
& more unsettled

Pennsylvania,
Louisiana,
West Virginia,
Alaska,
New Mexico,
Mississippi
Montana – "all funds spent by Montana or its citizens on Zyprexa since its launch in 1996, treble damages and attorneys' fees".

+ 20 States

Causality isn't established

Scientifically, causation is never "established"
except as the best (most consistent)
theoretical explanation for an empirical association.

Has anyone in industry or law
ever read anything about causation?

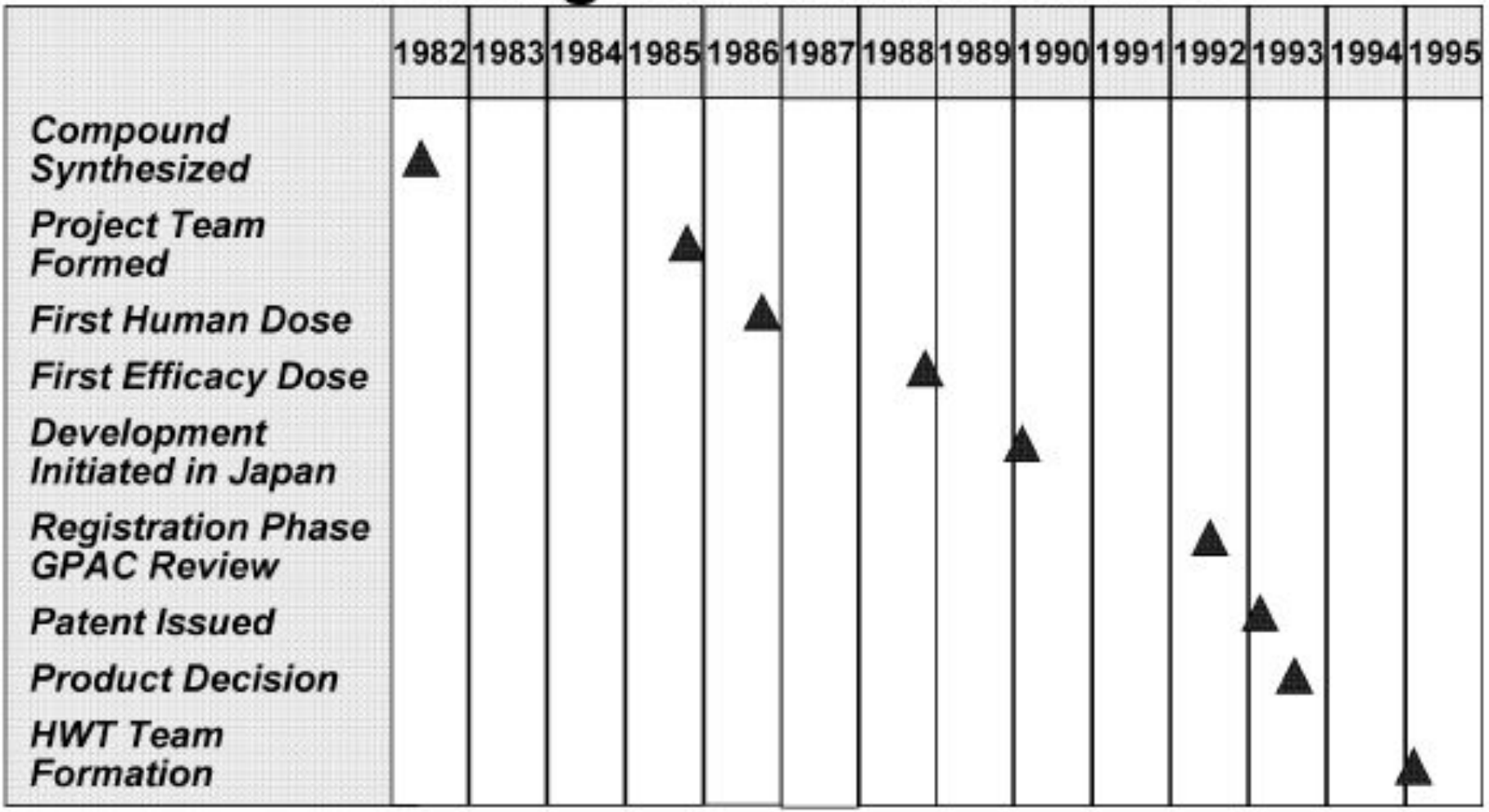
Diabetes is a disease which often shows itself in families in which insanity prevails

Henry Maudsley

The Pathology of Mind

ZYPREX
Olanzapine

Background Milestones



GDT/dle

July 20, 1995

ZYPREX Olanzapine

Clinical Studies Stages II and III

Examples - 1996 Plan

Objective	Locale	PI
• Emerging market registration	Hong Kong/China Mexico	Lieh-Mak
• New indication	global	many
– mania		
– psychosis in Alzheimer's	global	many
• Expand the package insert wording	U.S.	Lieberman, et al,
– relapse prevention	Neth	Kahn
– refractory	U.S.	Tamminga
• Commercialization -	multistate	many
• Local opinion leader involvement - templates	global	many

Pike/AM/LLY@Lilly, Francine K Maas/AM/LLY@Lilly

cc:

Subject: Zyprexa Side Effects Linguistic Research Results

All,

Attached you will find the executive summary from our recent linguistic research study. Please let me know if you would like the final PowerPoint presentation.

Why this matters...

The data showed that everyone interviewed, which included not only psychiatrists, PCPs, and nurses, but also Lilly sales directors, DMs, sales reps and Marketing staff, exhibited language that was devoid of emotion around the side effects of Zyprexa. This represents an "emotional gap" that must be bridged before many MDs will feel more in control when treating patients on Zyprexa. Furthermore, if we can communicate to the MD on an emotional level and help them address the psychological impact of weight gain for the patient, we will most likely make significant strides towards resolving this issue in their minds.

Best regards,

Tom Reck
Market Research Associate
Zyprexa - U.S.
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Section 3.2.1.1: John, here is how I rewrote the HGHL disposition section to try to soften the "only 66 completers" language. New or revised text is shown in green:

Table WS.2.2 (Section 2.3.2) summarizes patient disposition and reasons patients discontinued from the double-blind maintenance period. Three hundred sixty-one patients began double-blind treatment (225 olanzapine, 136 placebo). Patients who experienced recurrence were discontinued from the double-blind maintenance period (and entered into the open-label rescue period), but "recurrence" was not formally captured as a reason for discontinuation for these patients. At the end of the double-blind maintenance period, 66 patients had completed all 12 months of treatment without recurrence of a manic, mixed, or depressive episode or discontinuing for any other reason. A statistically significantly greater percentage of olanzapine-treated patients completed double-blind treatment compared with placebo-treated patients (23.6% vs. 9.6%). The most common

period. John and I discussed Mauricio's comment (below, purple) and the resulting text (below, blue), based on analyses in HGHL study report. John is ok with this explanation BUT has reservations about including it, because it operates on the assumption that olz automatically increases glucose. This may be a true assumption, but do we want to present this this way? Does inclusion of this explanation open us up to questions on glucose that we'd rather not bring up? John suggests that if we include it, we need to pass it by Patrizia to check it against the company line on this topic. Mauricio--how strongly do you feel about including an explanation here? (Discussion at ISS online resulted in