
Awareness of diabetes in association with antipsychotics

**France/Germany/Italy/Spain/UK
Australia/Canada/USA**

September 2000

prepared for: Eli Lilly & Co.

prepared by: Phoenix International Research

Method & sample

- total of 544 psychiatrists interviewed - divided by type of practice

	TOTAL	AUS	CAN	FR	GER	IT	SP	UK	USA
Base: all	544	60	60	61	60	60	60	60	123
office	156	16	11	20	23	11	13	-	62
hospital	218	6	19	21	30	6	15	60	61
both	170	38	30	20	7	43	32	-	-

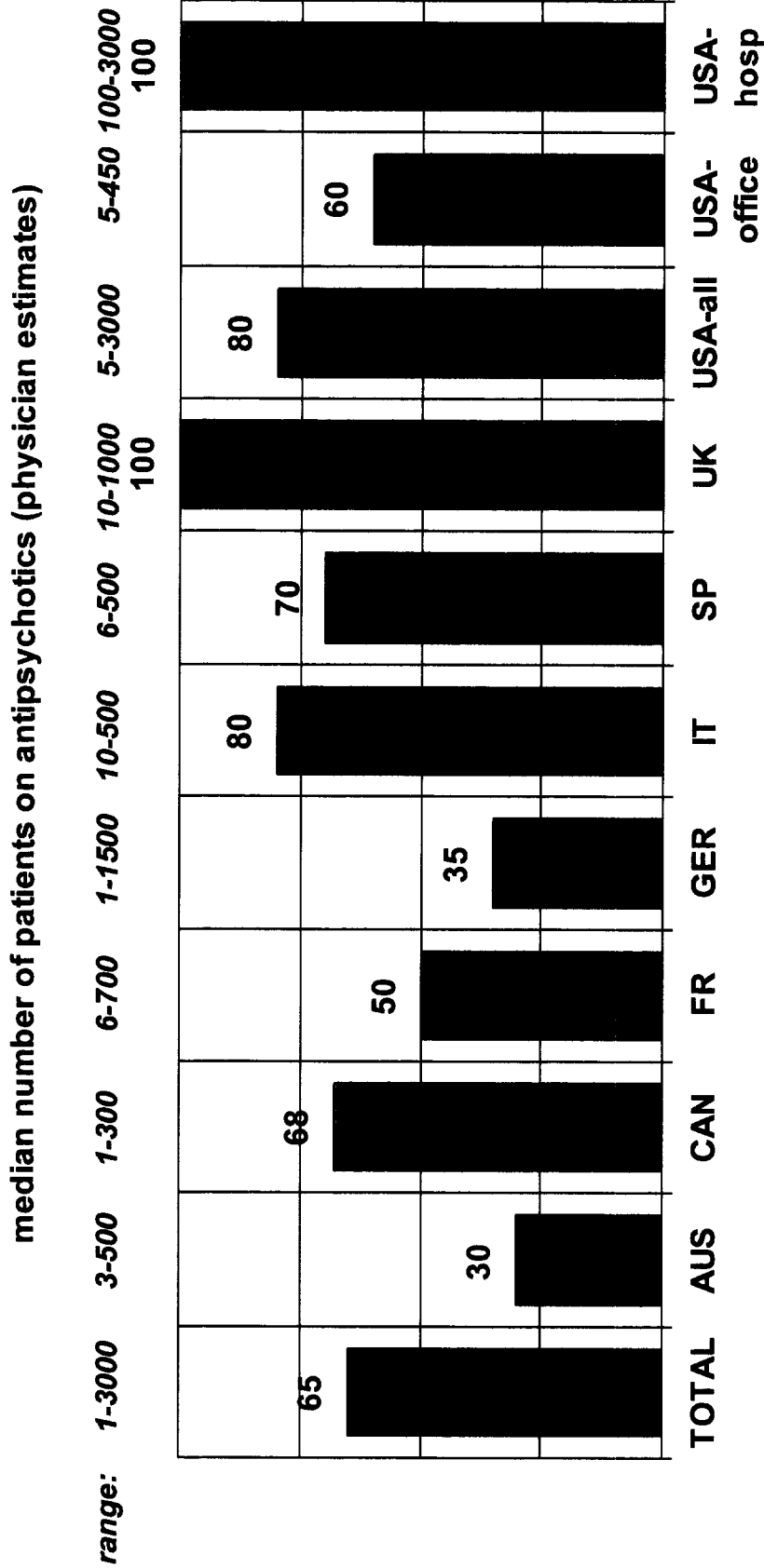
- fieldwork conducted by telephone, during September/October 2000 by:

- Australia: Status Quo, Sidney
- Canada: Mark Lovell & Associates, Montreal
- France: Harris Medical, Paris
- Germany: Searchlight Pharma Partner, Hamburg
- Italy: ISI Research, Milan
- Spain: Ergo Advanced Research, Barcelona
- UK: Fieldwork International, London
- USA: Able Astor, Chatsworth CA

- coding, editing and data processing conducted by Phoenix International Research, London

**Caseloads:
number of patients on antipsychotic treatment is
highly variable - within and between markets**

Q13

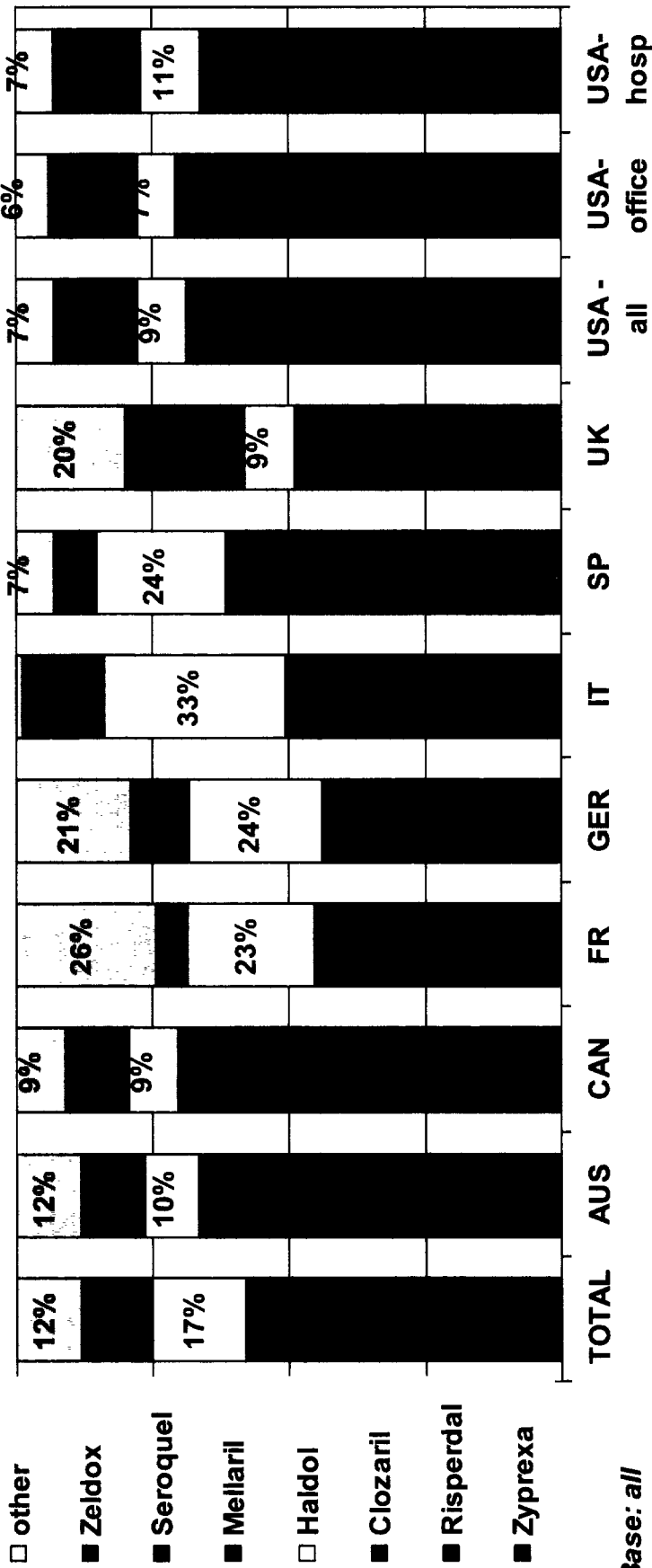


Base: all

Q14

Zyprexa and Risperdal are the two main agents used in English speaking countries - but still widespread use of traditional neuroleptics in Europe

mean % of patients on each antipsychotic

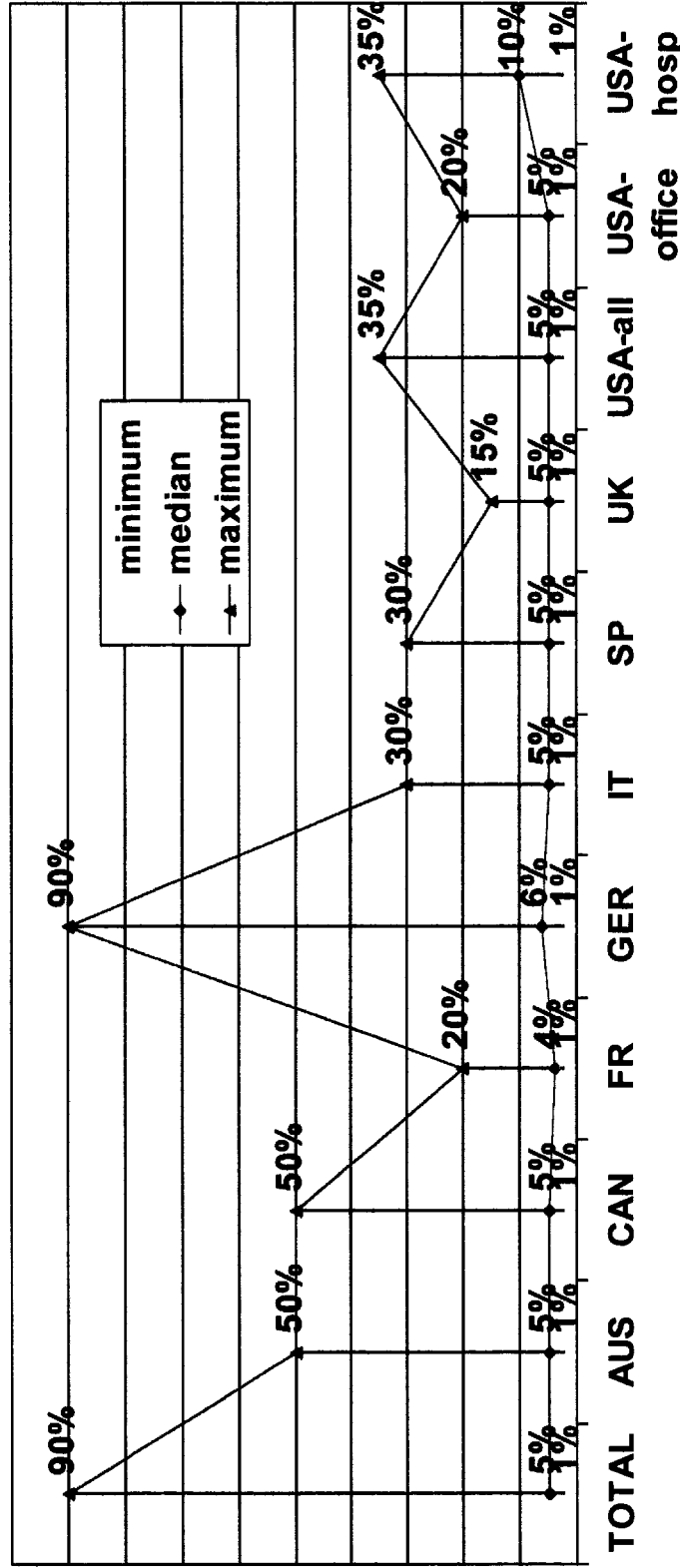


Base: all

Q1

About 5% of patients on antipsychotics estimated to suffer with diabetes

median % of patients on antipsychotics suffering with diabetes
(physician estimates)



Base: all

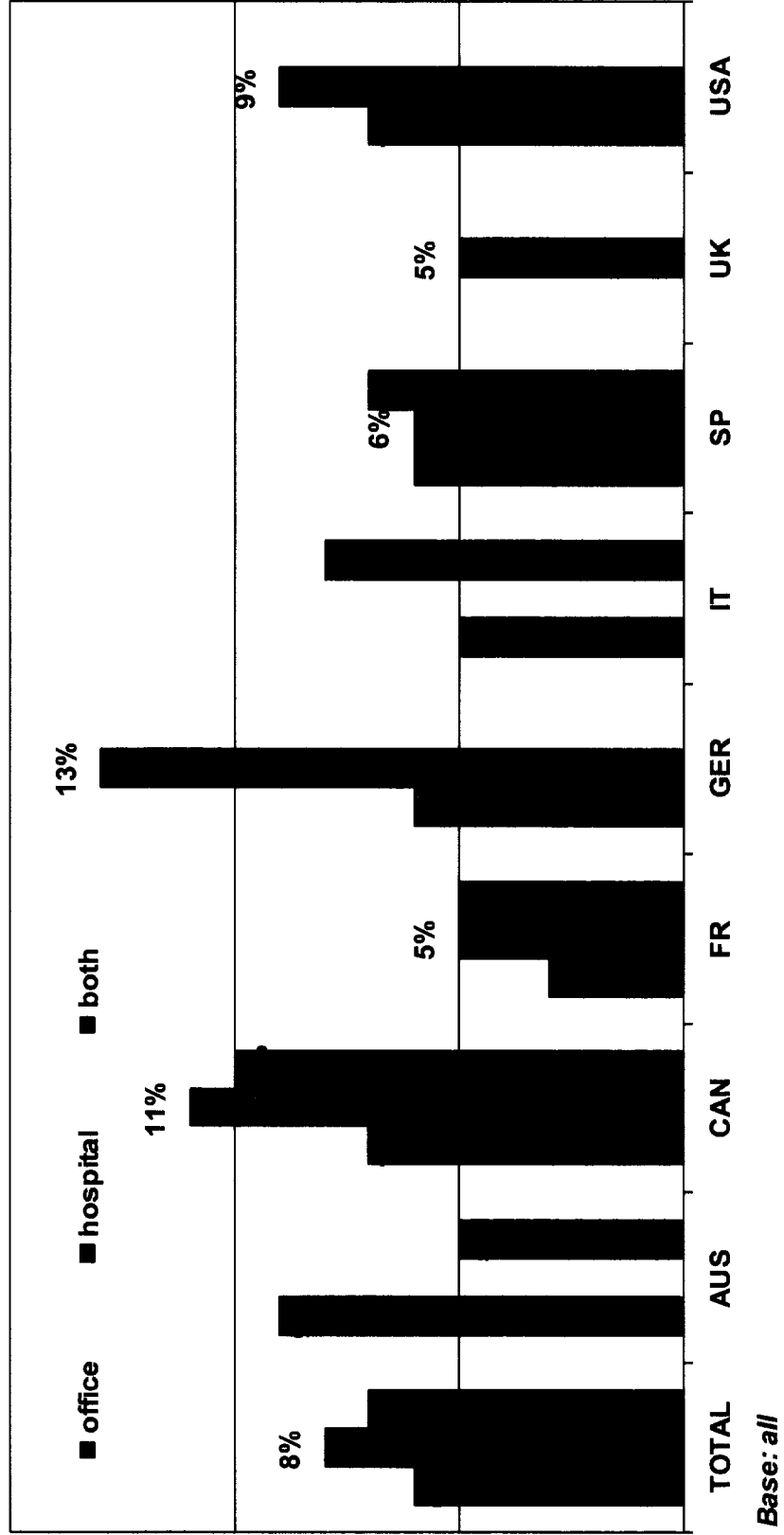
most cite figures between 1-5%; virtually all between 1-10%

just a few individuals (more so in Germany) cite higher figures ... up to 90%

Q1

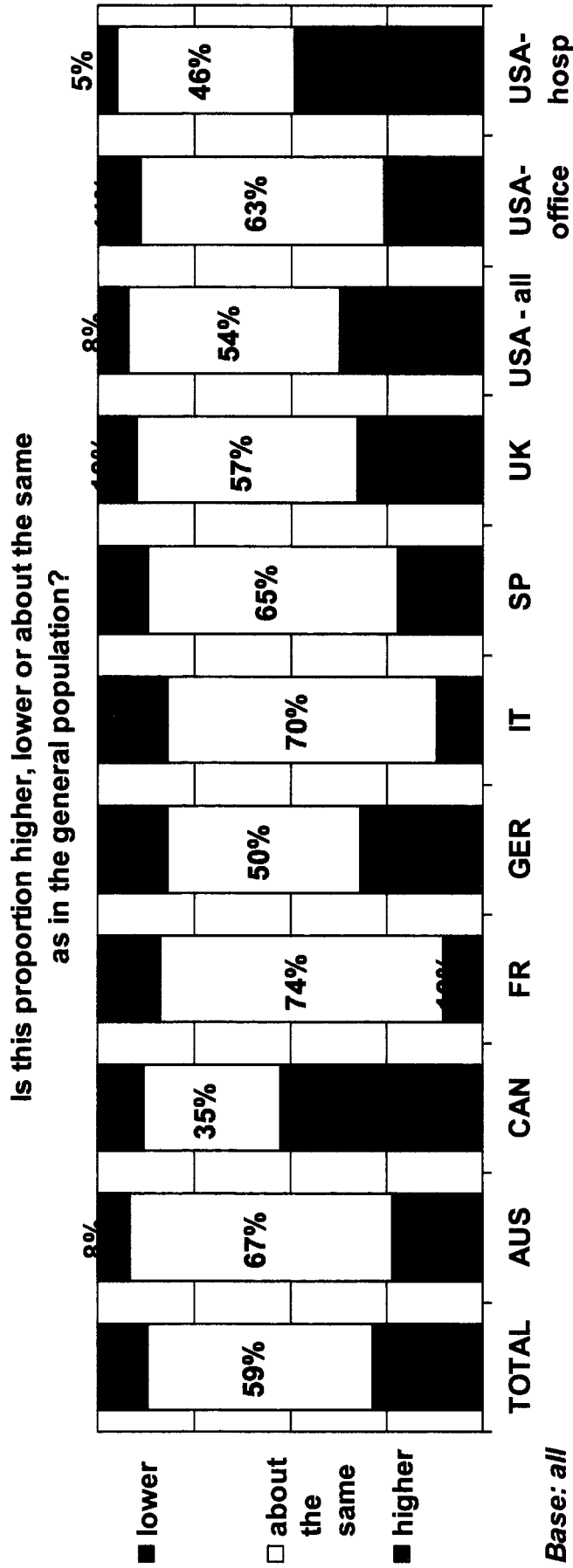
Those with hospital practice tend to give higher estimates for % of patients on antipsychotics suffering with diabetes than office practice psychs.

mean % of patients on antipsychotics suffering with diabetes
(physician estimates)



Q2

About 1 in 3 overall say more patients on antipsychotics suffer with diabetes than in the general population - but national views differ substantially



- about half of Canadian, US hospital psychs. consider proportion higher vs
 - just 10-12% in France, Italy
 - 20-25% in Australia, Spain - and US office psychs.
 - apx. 1/3 in Germany, UK

Q2a

About 1/3 of those who consider prevalence of diabetes to be higher attribute this to specific antipsychotic drugs - more so in USA

What do you attribute this higher level of diabetes among patients on antipsychotic treatment to?

	TOTAL	AUS	CAN	FR	GER	IT	SP	UK	all	USA office	hosp
Base:*	157	14	32	6	19	7	13	20	46	16	30
related to the conditions being treated with antipsychotics	50%	79%	19%	3	63%	2	23%	75%	59%	31%	73%
a side effect of antipsychotics generally	39%	43%	59%	2	21%	4	46%	25%	33%	25%	37%
a side effect of specific antipsychotic drugs	36%	36%	34%	3	16%	1	38%	25%	50%	50%	50%

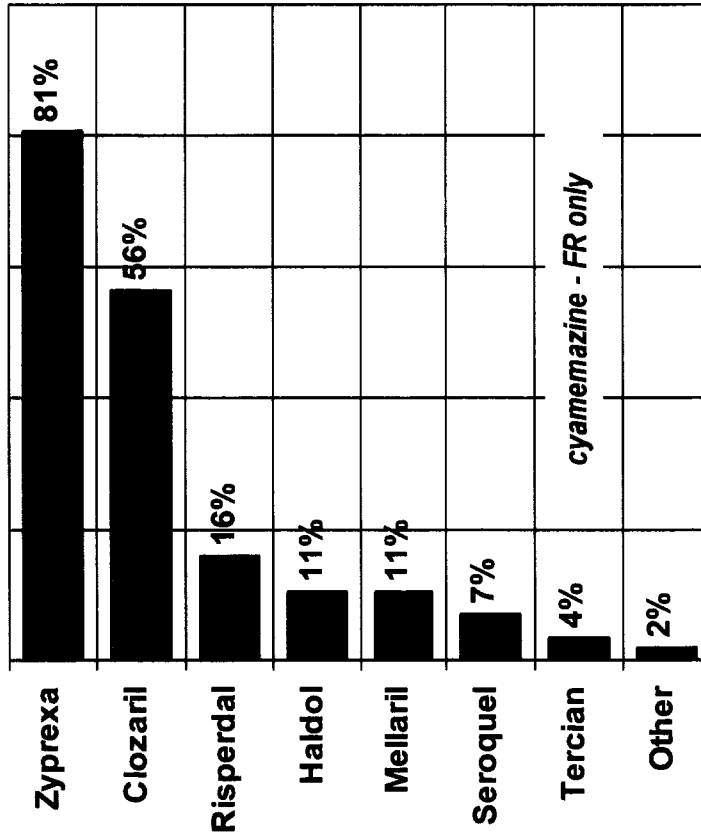
raw data raw data

Base: *those who consider proportion of patients on antipsychotics suffering with diabetes to be higher than in the general population

Q2b

Those who associate increased risk of diabetes with specific agents mainly mention Zyprexa

antipsychotics associated with increased risk of diabetes



Base: those who attribute increased risk of diabetes to specific antipsychotics (57)

- about 10% of the sample associate increased risk of diabetes with specific antipsychotics -
 - almost half this group are in the USA (23/57) ... 11 in Canada
- most (of this small group) mention Zyprexa in this context - about half also Clozaril
- other agents mentioned by just 1 or 2 in each market

Q3

Obese patients/those with weight gain problems on antipsychotics thought most likely to develop diabetes

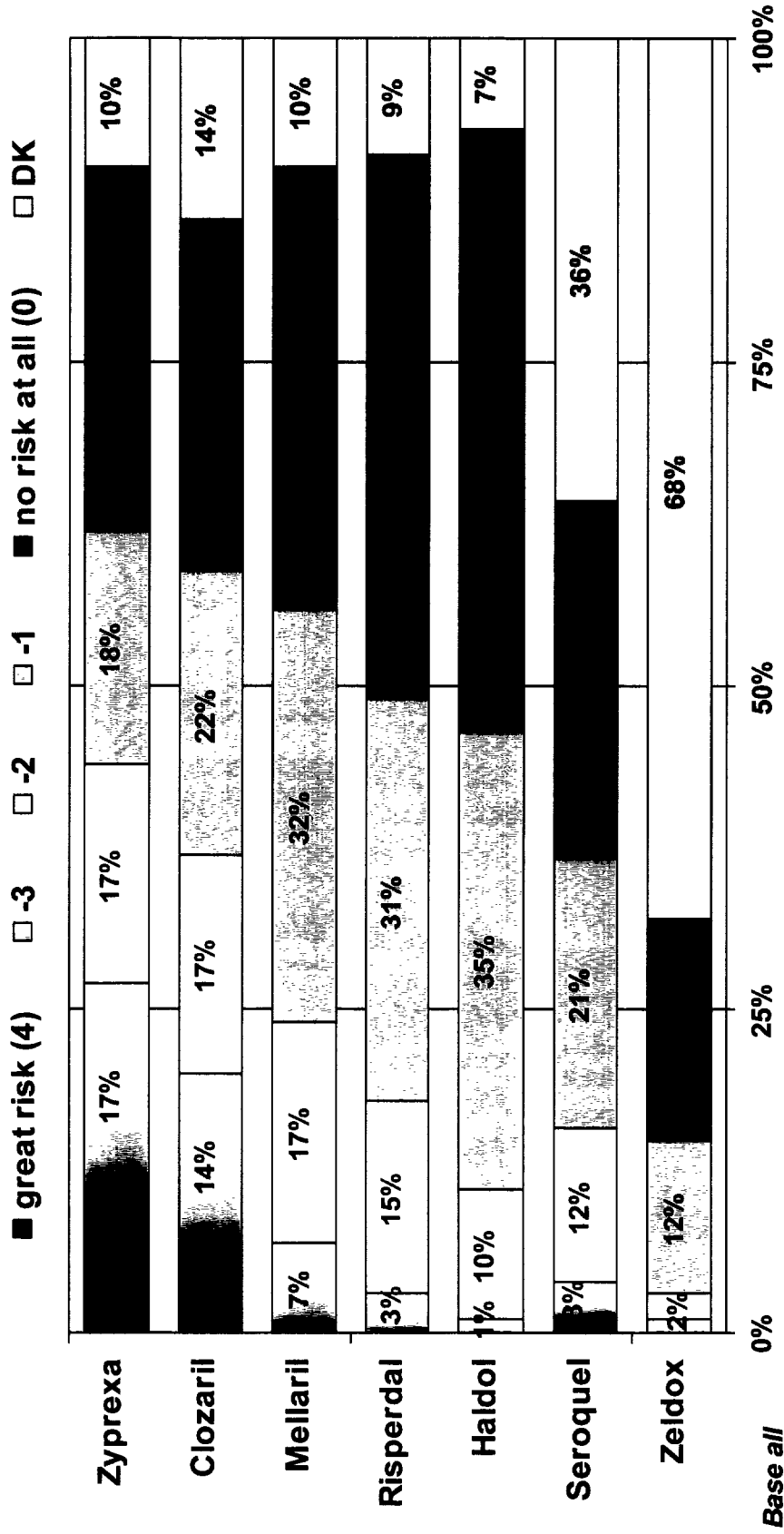
	What types of patient on antipsychotic treatment are most likely to develop diabetes? USA										
	Total	AUS	CAN	FR	GER	IT	SP	UK	all	office	hosp
Base: all	544	60	60	61	60	60	60	60	123	62	61
obese patients/those who have weight gain/ weight problems/are overweight	62%	75%	78%	36%	57%	30%	73%	37%	85%	89%	80%
elderly patients	26%	28%	27%	11%	55%	13%	47%	17%	16%	16%	16%
those with a family history of diabetes/genetically predisposed/hereditary	13%	8%	23%	10%	-	7%	2%	10%	27%	24%	30%
young-middle aged patients	5%	8%	10%	5%	-	8%	3%	2%	5%	6%	3%
(chronic) schizophrenics	4%	-	3%	8%	-	7%	-	2%	7%	2%	13%
those with poor diets/ bad eating habits	3%	8%	-	5%	-	3%	2%	2%	2%	2%	2%
women	2%	-	5%	3%	-	2%	2%	-	4%	2%	7%
sedentary/inactive patients/ lack of exercise	2%	5%	2%	2%	-	-	2%	-	3%	5%	2%
none	16%	8%	5%	25%	12%	32%	12%	35%	7%	8%	5%

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Q4b

On prompting, between one-third and half associate some risk of developing diabetes while on long-term treatment with Zyprexa - or Clozaril

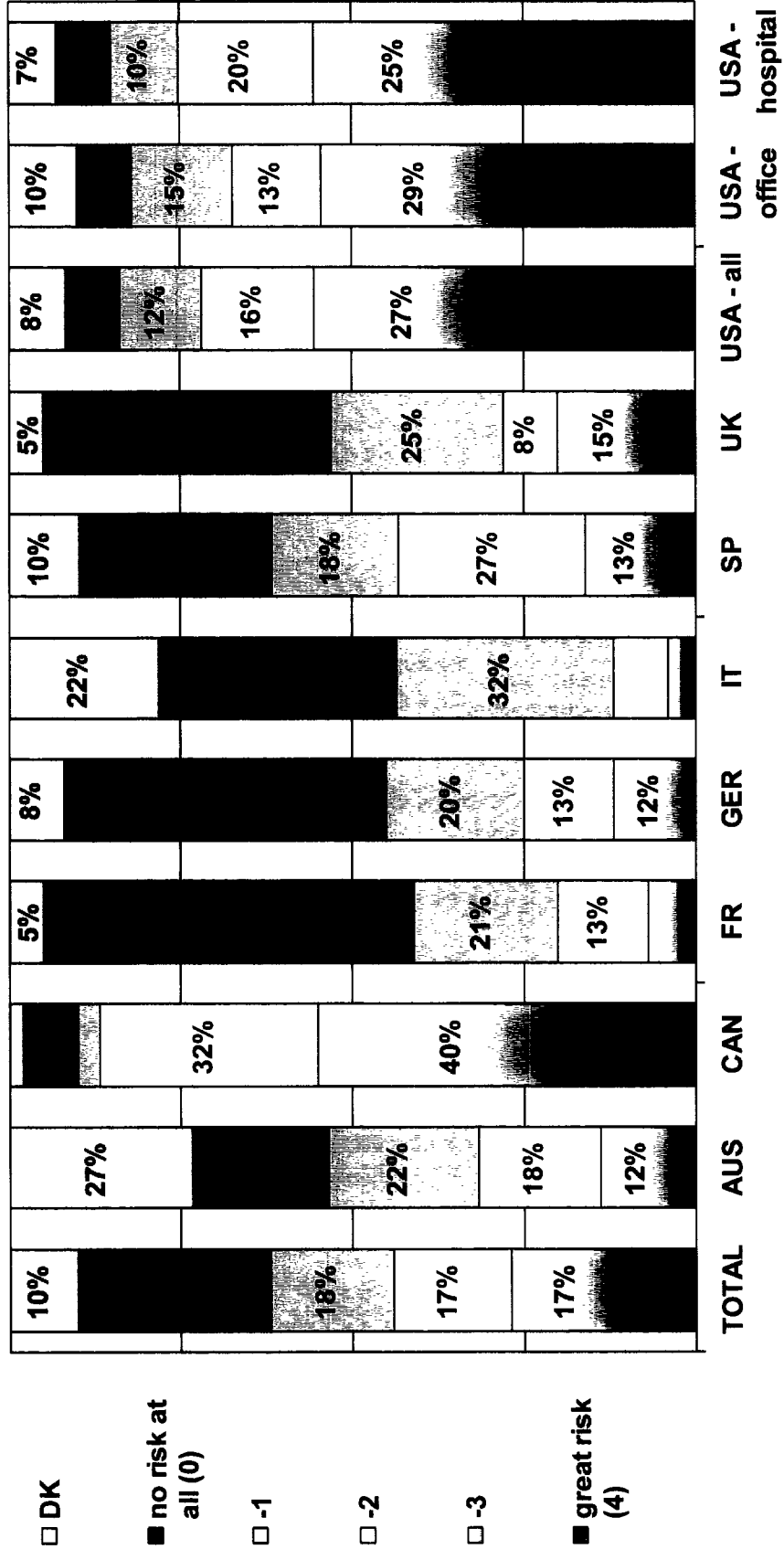
Risk of diabetes associated with specific antipsychotics (prompted)



Q4b

Strength of association of diabetes with Zyprexa varies considerably by country - strongest in USA, Canada - least in continental Europe

Risk of diabetes associated with Zyprexa (prompted)

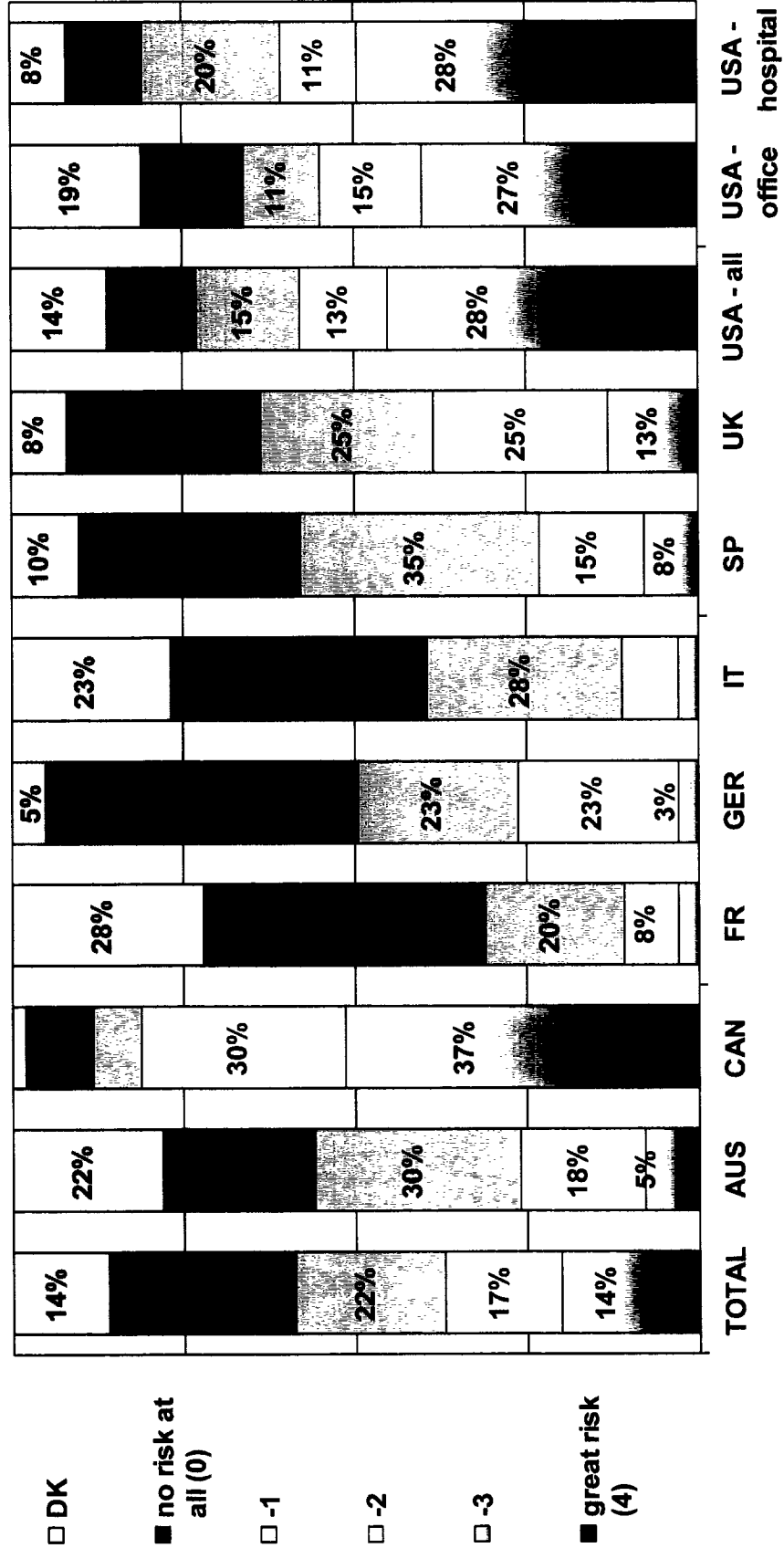


Base all

Q4b

Association of diabetes with Clozaril is less strong - but follows same national patterns

Risk of diabetes associated with Clozaril (prompted)



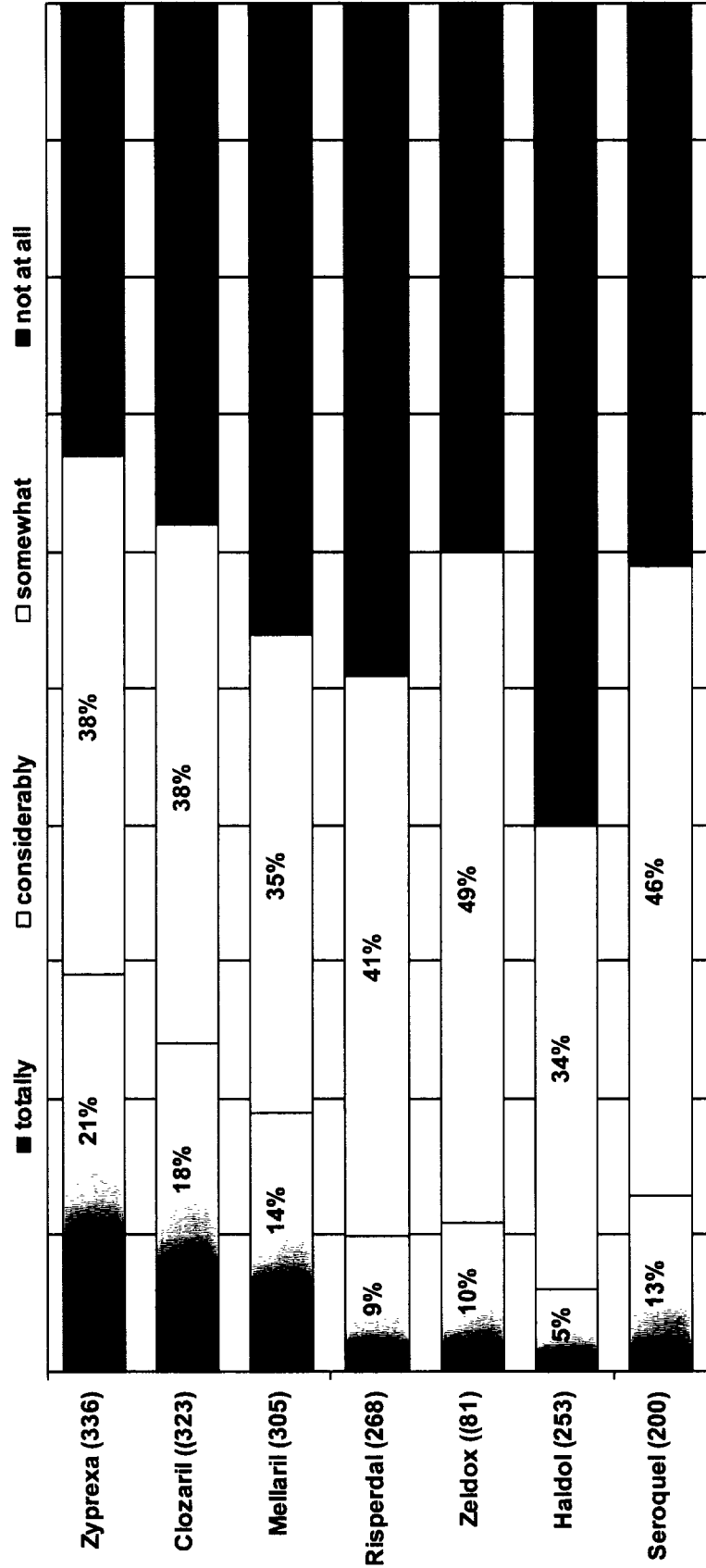
Base all

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Q5

Most restrict their use of products associated with increased risk of diabetes at least 'somewhat'

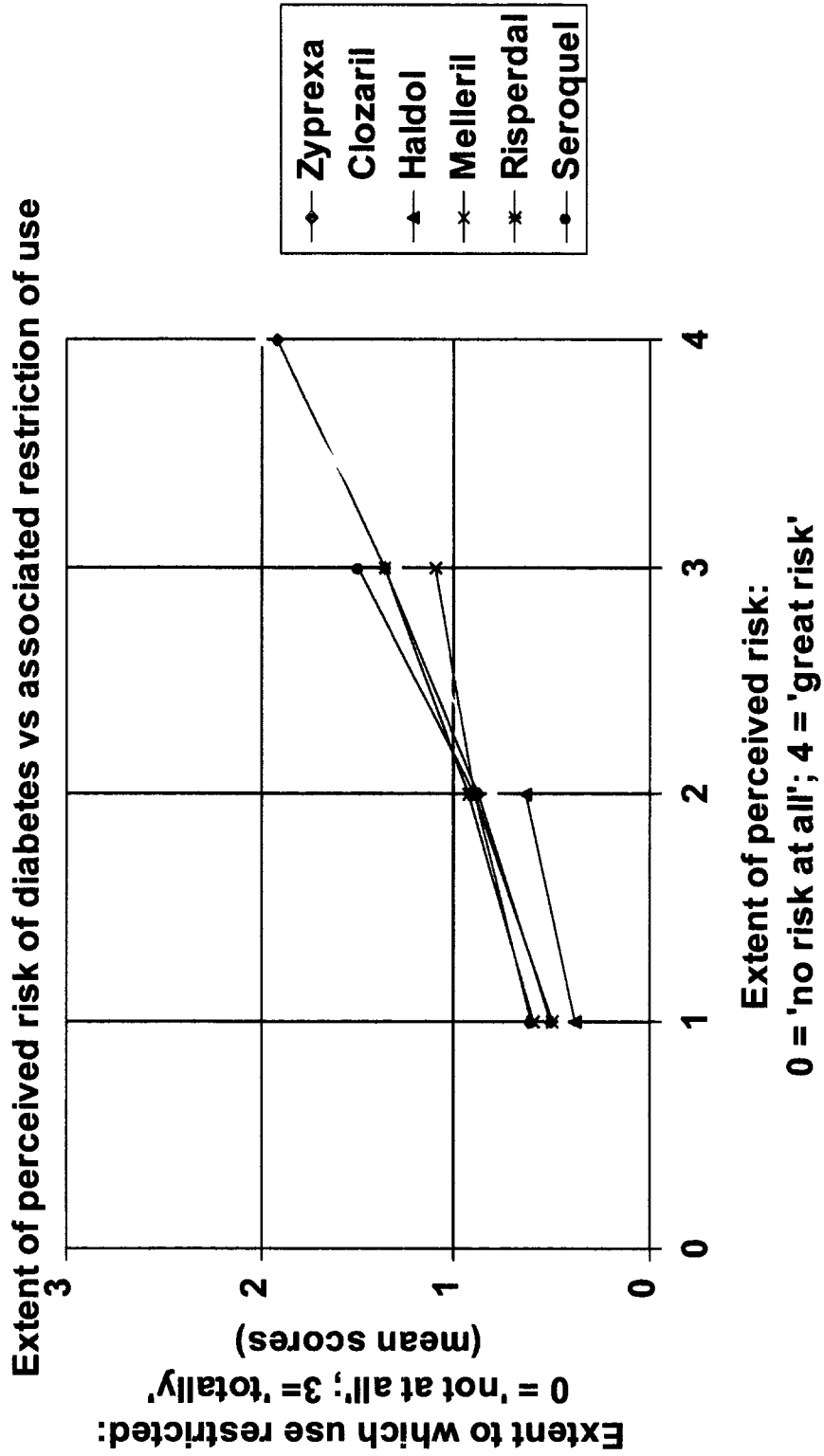
Extent to which concern about risk of diabetes restricts use of specified agents



Base: those who associate specified drugs with increased risk of diabetes

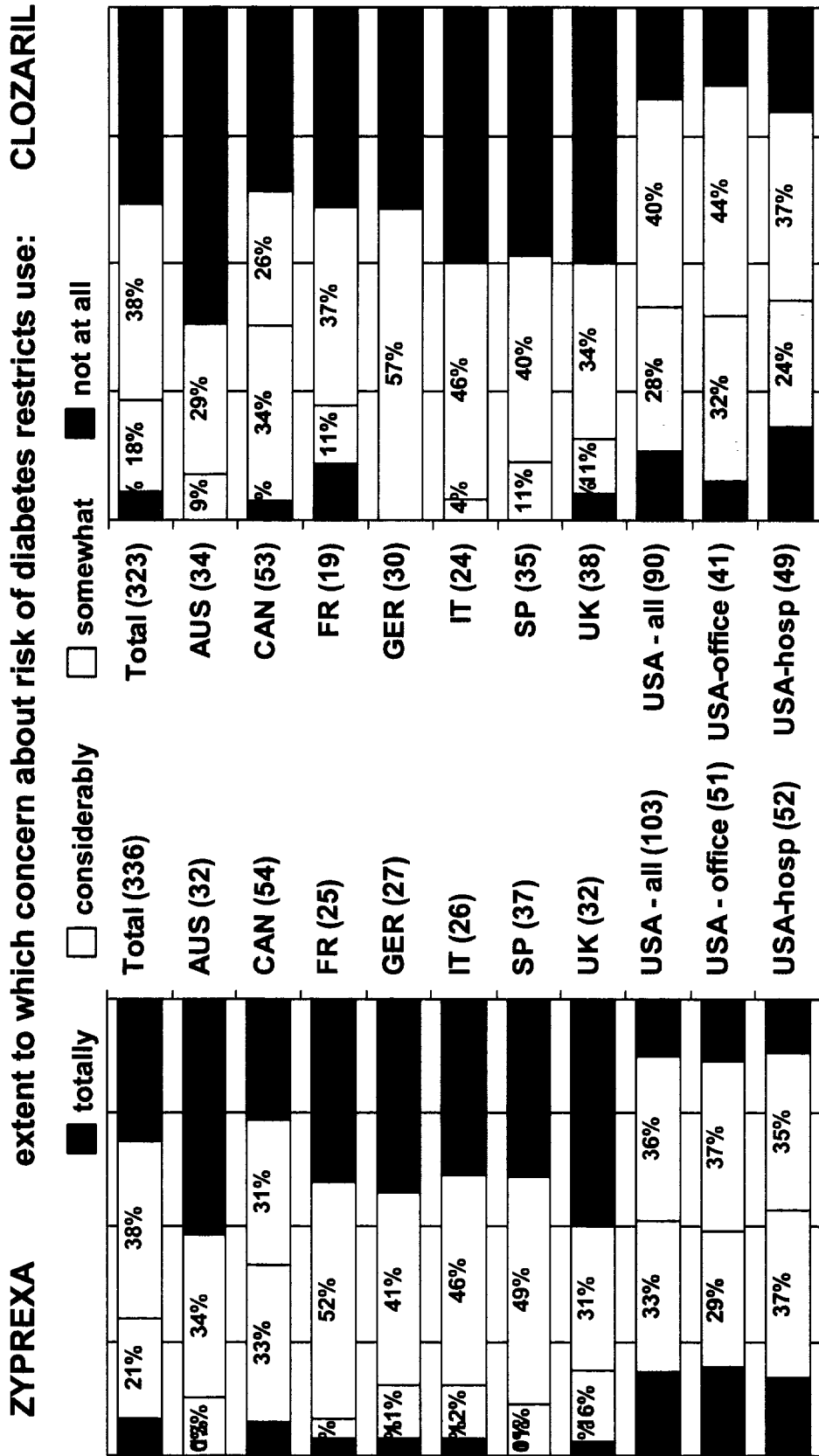
Q.4/5

Impact correlates with extent of concern about diabetes



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Perceived risk therefore restricts use most in Canada, USA - for both Zyprexa and Clozaril (Q5)



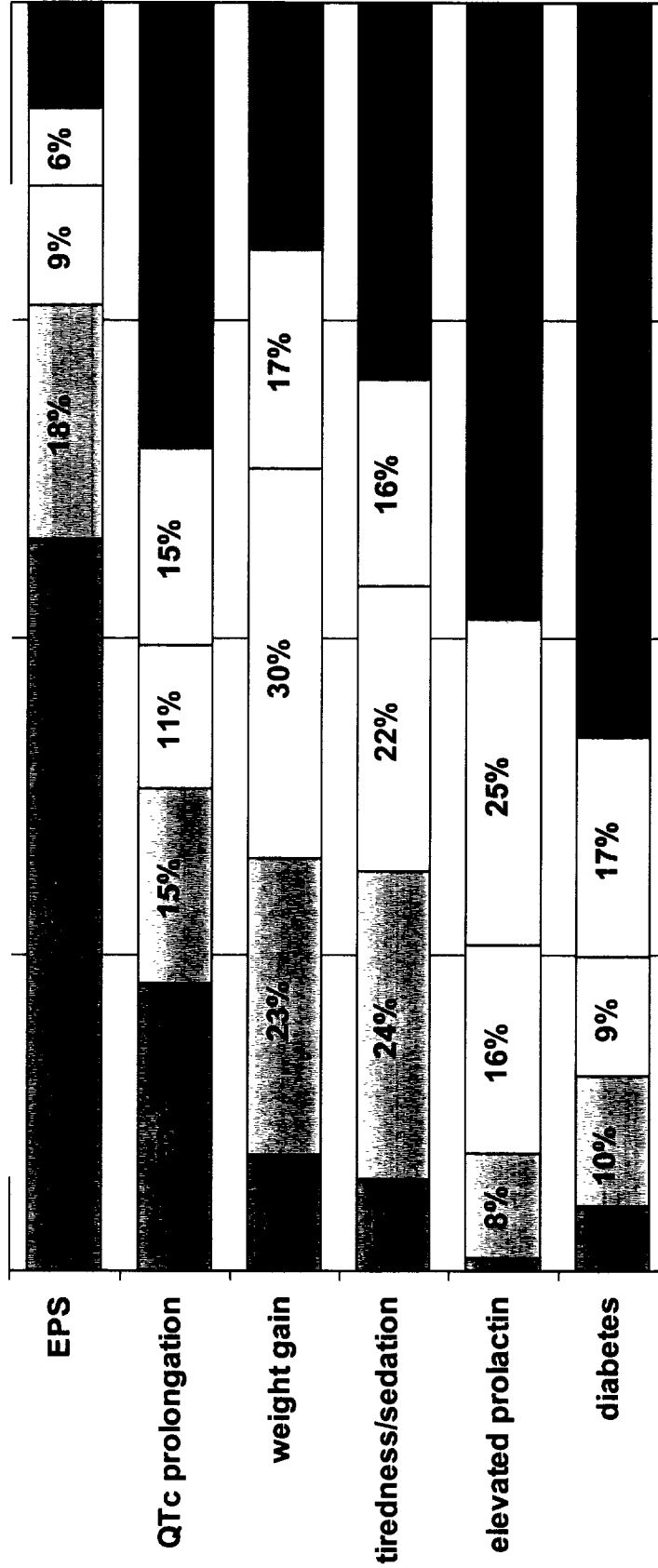
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Q9

Increased risk of diabetes of least concern of all problems assessed

% sample giving each problem specified rank

■ most □ 2nd most □ 3rd most □ 4th most ■ 5th most ■ 6th most



Base: all

Base: all

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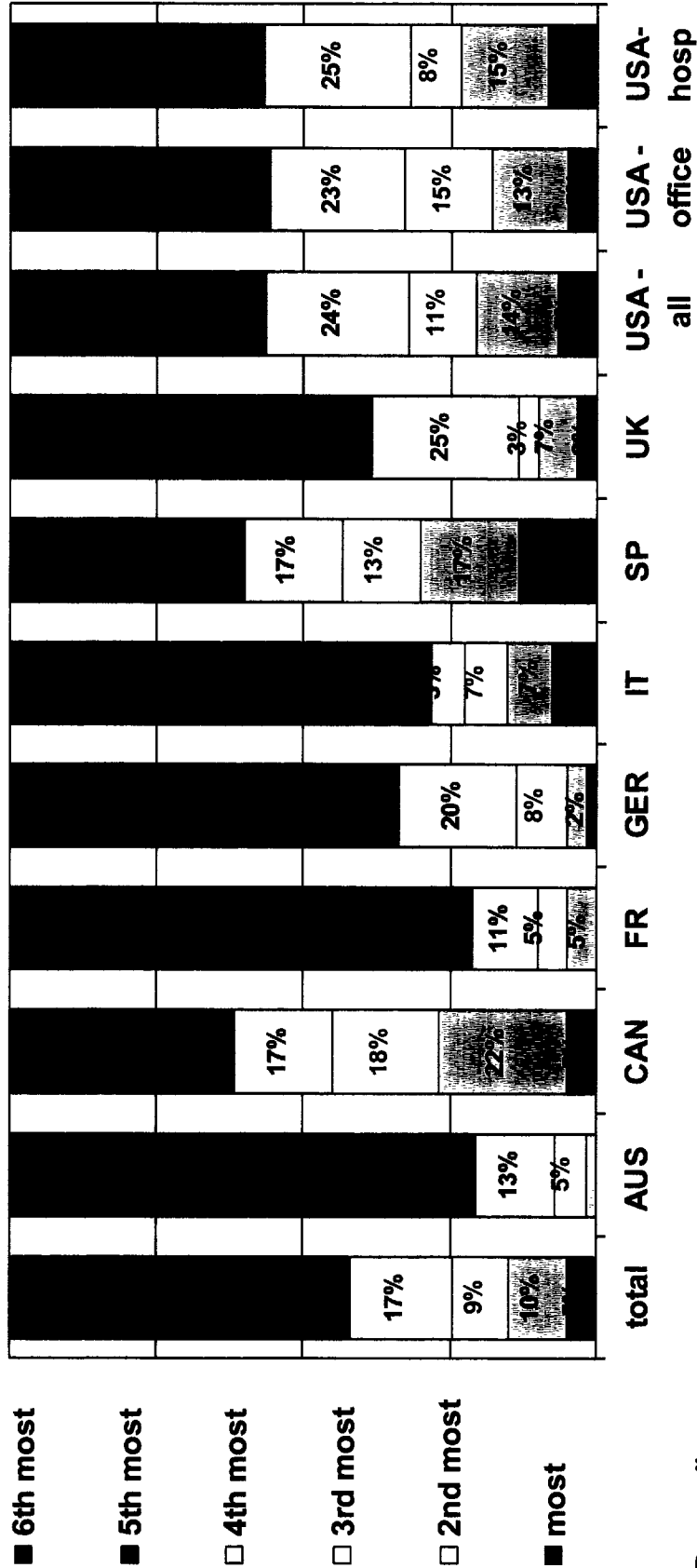
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Q9

Increased risk of diabetes accorded more importance in Canada, Spain - also USA, but a minor issue in Australia, rest of Europe - including UK

relative importance of diabetes: % sample giving each



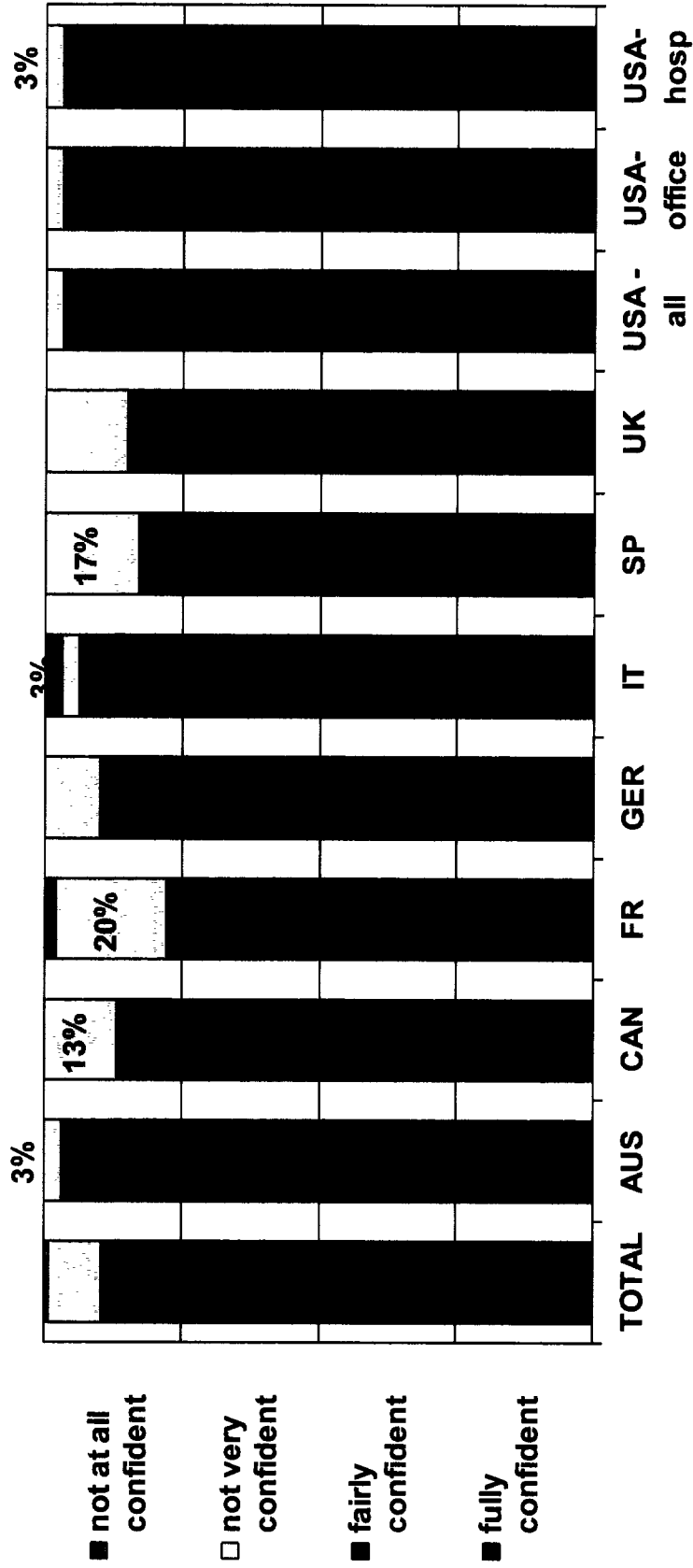
Base: all

Base: all

Q7

Most psychiatrists feel (fairly) confident about recognising the signs and symptoms of diabetes

How confident do you feel about recognising the signs & symptoms of diabetes?

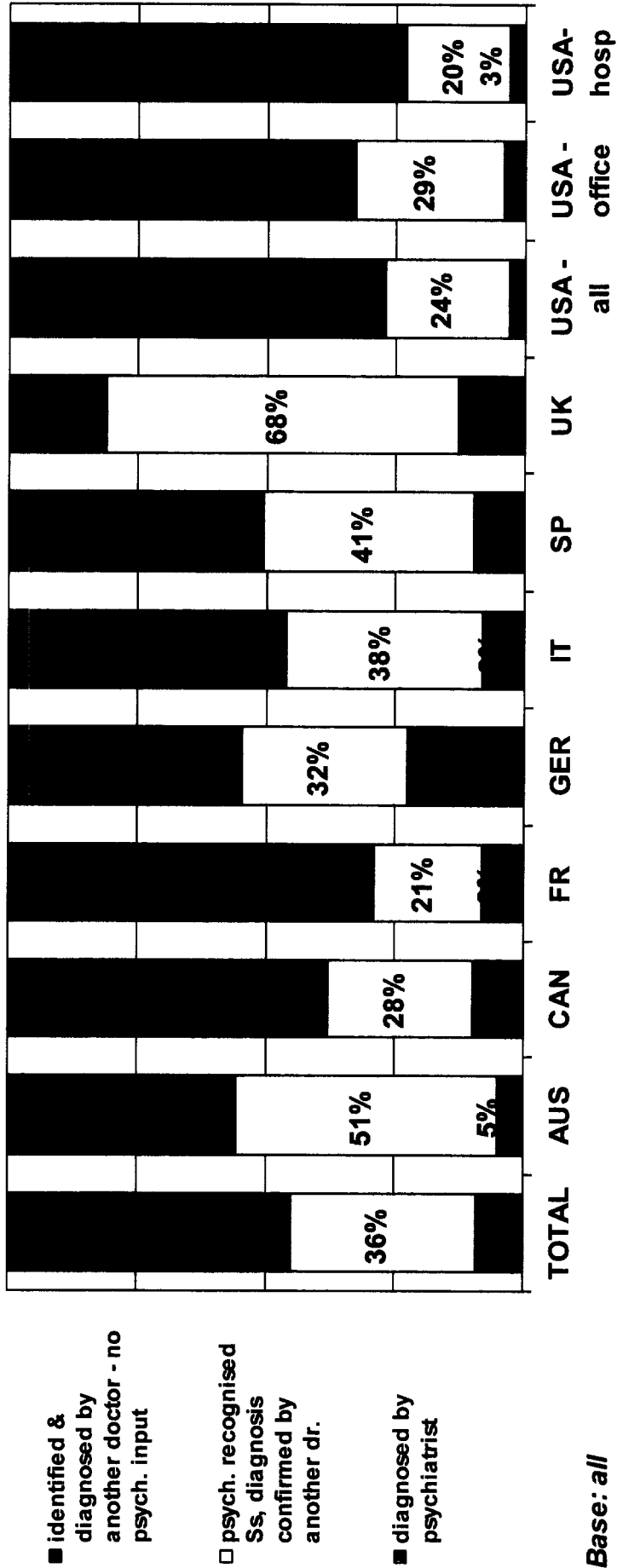


Base: all

Q6

Despite stated confidence, most diabetes cases were recognised and diagnosed by another physician

extent of involvement in diagnosis of diabetes developing in patients under their care: mean % of patients



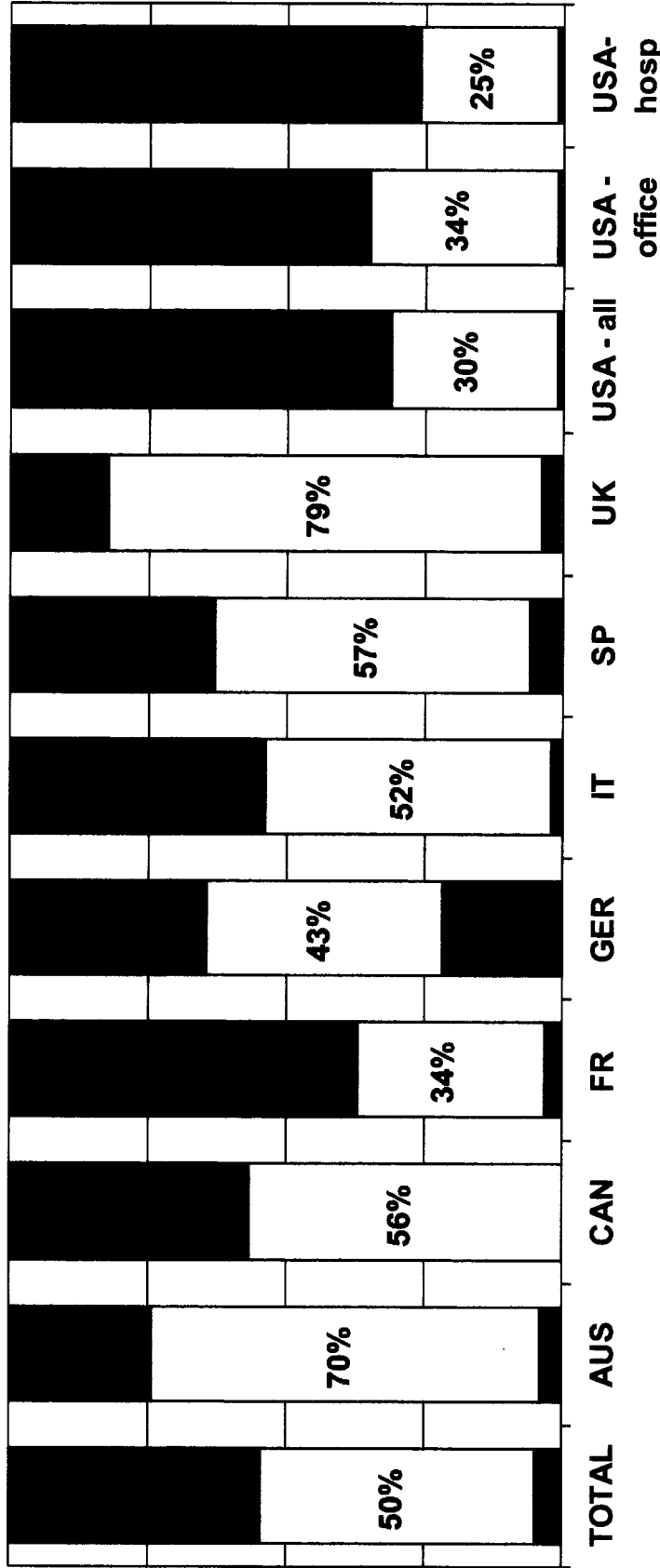
Base: all

majority - particularly in USA, FR, CAN - had no involvement in diagnosis at all

Q8

Psychiatrists report virtually no involvement in initiation of antidiabetic treatment (except in Germany)

Extent of involvement in initiation of treatment for diabetes: mean % of cases



Base: all

- initiated by another doctor - no psych. involvement
- referred for initiation of Rx
- initiated by psych.

Q8a/b

Antidiabetic treatment initiated by PCPs and/or internists and/or diabetologists - varies by market

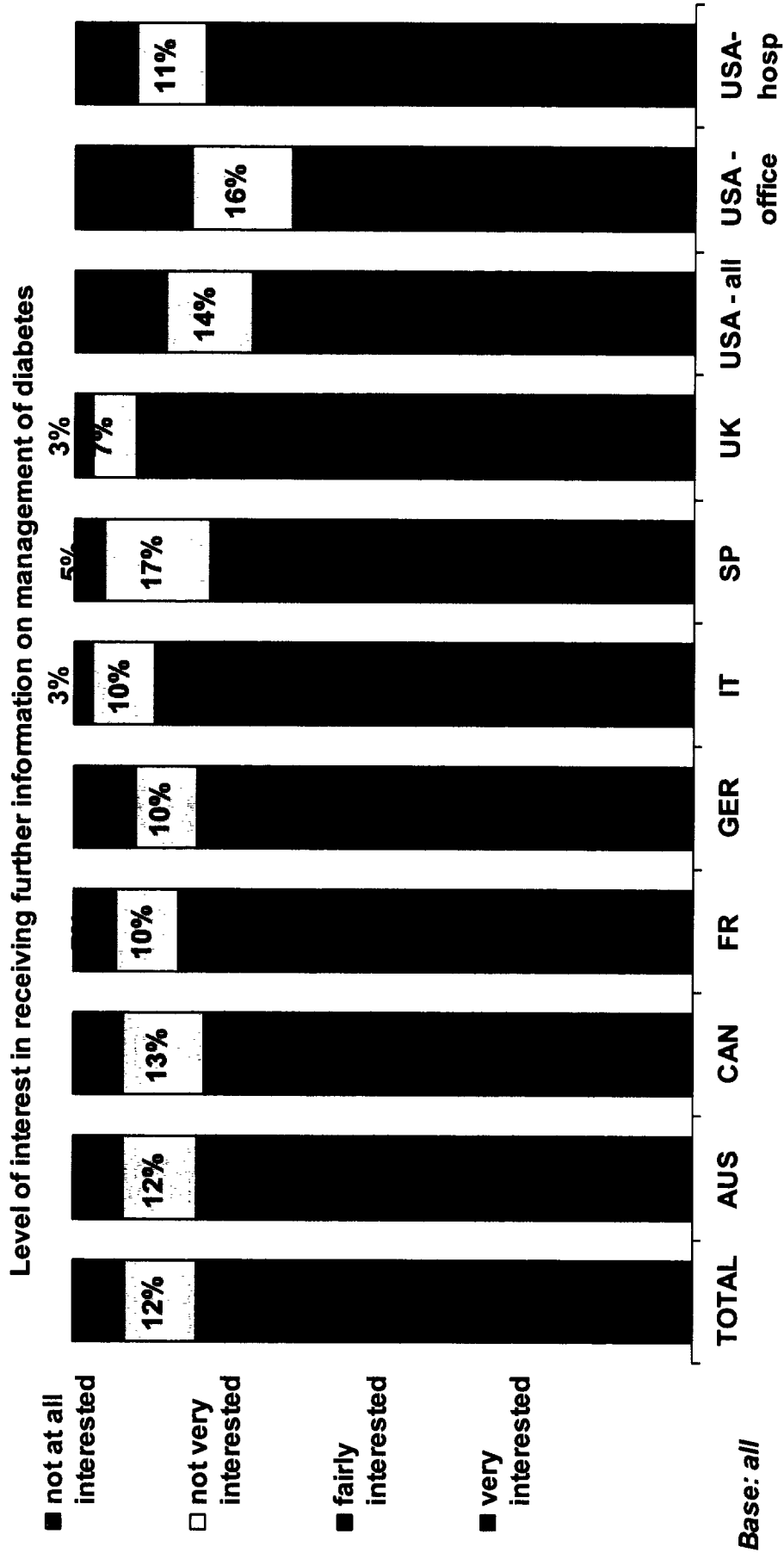
	Total	AUS	CAN	FR	GER	IT	SP	UK	total	USA office	hosp
Base: those who referred pts for initiation of Rx	376	46	41	33	33	38	43	59	83	43	40
GP/FP	56%	70%	83%	61%	33%	29%	53%	56%	55%	56%	55%
diabetologist/endocrinologist	51%	59%	37%	73%	18%	74%	77%	66%	24%	35%	13%
internist/general physician	36%	2%	10%	6%	88%	13%	26%	34%	77%	79%	75%
geriatrician	2%	-	-	-	-	-	-	12%	-	-	-
<hr/>											
Base: physicians who had no involvement in initiation of Rx	310	18	29	46	28	31	34	24	100	49	51
GP/FP	63%	22%	76%	74%	61%	48%	56%	79%	66%	63%	69%
internist/general physician	48%	-	21%	7%	64%	26%	29%	38%	94%	98%	90%
diabetologist/endocrinologist	47%	22%	52%	59%	14%	65%	56%	46%	47%	49%	45%
geriatrician	1%	-	3%	-	-	-	-	13%	-	-	-
not answered	6%	67%	-	-	4%	-	18%	4%	-	-	-

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Vast majority are interested in receiving further information on management of diabetes - less so in the USA



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Q.11

Primary informational needs are recognising the signs and symptoms and understanding the relationship between diabetes and antipsychotics

	What subjects should this information address?							USA			
	Total	AUS	CAN	FR	GER	IT	SP	UK	all	office hosp	
Base: those interested in receiving info. on management of diabetes	499	55	55	57	54	58	57	58	105	50	55
recognising signs & symptoms	25%	18%	35%	7%	15%	7%	49%	29%	32%	28%	36%
association/relationship/link between diabetes and antipsychotics	23%	47%	9%	21%	17%	43%	4%	29%	18%	16%	20%
making diagnosis	17%	5%	20%	4%	20%	3%	44%	22%	15%	8%	22%
treatment with oral antidiabetics	16%	16%	13%	5%	30%	5%	25%	41%	6%	6%	5%
pathophysiology of diabetes	16%	20%	16%	12%	13%	16%	18%	36%	6%	6%	5%
Initiating treatment	16%	15%	11%	11%	26%	9%	33%	26%	6%	6%	5%
Insulin treatment	12%	16%	9%	-	17%	5%	21%	21%	9%	10%	7%
(patient) info. about a balanced diet/prevention of weight gain	8%	7%	16%	11%	4%	-	2%	2%	17%	18%	16%

Q12

Main sources of information on diabetes are journals; Canadian physicians have most information- those in France, UK least

	Sources of information regarding diabetes in patients on antipsychotics										
	Total	AUS	CAN	FR	GER	IT	SP	UK	all	office	hosp
Base: all	544	60	60	61	60	60	60	60	123	62	61
journals	56%	68%	70%	28%	52%	53%	67%	37%	63%	56%	69%
sales rep.	20%	27%	47%	5%	3%	18%	23%	-	30%	37%	23%
conferences	20%	15%	42%	2%	22%	7%	13%	22%	28%	24%	31%
peers/colleagues	19%	23%	30%	11%	33%	22%	30%	10%	8%	10%	7%
Internet - company web sites	5%	7%	13%	2%	10%	2%	2%	3%	3%	3%	3%
(clinical) literature/text books	5%	-	5%	2%	17%	8%	8%	-	1%	2%	-
professional Internet forums	3%	2%	7%	2%	5%	3%	3%	-	3%	5%	2%
other	11%	3%	13%	18%	18%	17%	13%	7%	4%	6%	2%
none	21%	20%	7%	46%	22%	8%	5%	47%	17%	19%	15%

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Summary & conclusions

- **views on prevalence of diabetes in patients on antipsychotics and the underlying causes vary substantially internationally**
 - **mainly associated with obesity/weight gain**
 - **link with antipsychotics, particularly Zyprexa, is mainly a North American phenomenon - little comment elsewhere**
- **associated risk of diabetes restricts product usage 'somewhat' - irrespective of the brand**
- **however, diabetes is not a major problem**
 - **most rank it 5th or 6th among problems commonly associated with antipsychotics**
 - **even in North America, less than 1 in 3 include this among the top 3 problems**
 - **EPS, weight gain, tiredness are accorded far more importance**
- **most psychiatrists CLAIM to feel 'fairly confident' about recognising the signs & symptoms of diabetes**
 - **however, most cases were identified and first treated without their input**
 - **psychiatrists have virtually no involvement in drug treatment**
- **most would nevertheless welcome further information on management of diabetes in their patients - to cover**
 - **diagnosis/recognition of the symptoms**
 - **the link between diabetes and antipsychotics**

Walter Deberdt

11/06/00 05:09 AM

To: Tricia M Timpe/AM/LLY@Lilly
cc: Elyse Breeden/AM/LLY@Lilly, Patrizia Cavazzoni/AM/LLY@Lilly, Barry Jones/AM/LLY@Lilly
Subject: Re: amantadine data

Tricia,

Up to now the only data I have are coming from the case observation series (n=12). I'm sending you herewith an Excell sheet with the **individual data** and also the Powerpoint version of the poster that contains a graph of these individual data. What is striking in these data is their consistency, although I verified that there is no reporting bias from the side of the investigators: they really reported everybody they knew of.



summary table.xls Poster amantadine cases.ppt

In these data you will also see that at one center everybody received only 100 mg amantadine once a day, while in the other 3 pts. received 200 mg and 3 received 300 mg, in most cases divided over 2 or 3 intakes. In this small sample **there was no indication of any dose-effect relationship.**

Meanwhile other centers here in Belgium are using amantadine. They confirm the efficacy at this low dose. **There seems also to be a clinically relevant extra effect on depressive symptoms.**

Recruitment in the local study should start from now on. An interim analysis is foreseen when all patients reach Visit 2, i.e. 4 weeks of treatment with 100 mg/d. You can expect these data in April next year.

Kind regards,

Walter
Tricia M Timpe

Tricia M Timpe
10/31/2000 08:41 PM

To: Walter Deberdt cc: Elyse Breeden, Patrizia Cavazzoni, Barry Jones

Hi Walter!

I have a question for you. What would the possibility of obtaining data from the amantadine study that you performed. Specifically what is the baseline and endpoint weight per patient **and** what was the dose of amantadine they were on (ie was there a dose response seen for amantadine)?

We have some final details we need to pass by an endocrinology expert to prove the viability of using amantadine for olanzapine associated weight gain.

Thanks!!
tricia

ZY 2220 863

Juan R. Bustillo, MD
John Lauriello, M.D.

Dennis West

Dear Dennis

Below is the abstract we have submitted for International Congress on Schizophrenia Research and will submit for ACNP. As you will note the study is completed but results are forthcoming. We will send you the proposed poster with results prior to each meeting.

J Lauriello
J Bustillo

TREATMENT OF WEIGHT-GAIN WITH FLUOXETINE IN OLANZAPINE-TREATED SCHIZOPHRENIC OUTPATIENTS

Olanzapine (OLZ) has become a first line treatment for schizophrenia. Although its side-effect profile is quite favorable it can induce significantly more weight-gain than many other antipsychotics. Fluoxetine (FLX), a serotonin reuptake inhibitor, is an effective anorectic agent during the first few months of its use. Since OLZ-induced weight-gain may be mediated by its serotonergic blockade; FLX may be an effective anorectic agent in OLZ-treated patients. As the maximum weight-gain with OLZ and weight-loss with FLX occur between 8 and 12 weeks with both treatments, early addition of FLX may prevent OLZ-induced weight gain. The primary goal of this study evaluated the efficacy of high-dose FLX (60mg) as a weight reducing agent for patients with early weight-gain with OLZ. Persons with schizophrenia (N=53) initiated open-label OLZ and weighed weekly. N=31 met predetermined criteria of sustained 3% weight-gain during the initial 1-2 mos of OLZ treatment and were randomized to double-blind FLX or placebo for 4 mos. N=10 did not gain the weight and N=12 terminated prior to randomization. Outcome measures to be presented are weight, appetite and body-fat composition. We also explore the effects of OLZ treatment and addition of FLX on cigarette smoking parameters.

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