



National Prescribing Service Limited

Case Study 5:

New Drugs

December 1999

Scenario

You are visited by Mrs Parker an overweight 50 year old woman with mild hypertension and mildly elevated cholesterol levels but no other risk factors. Her only symptoms are insomnia and crying as she thinks her life is worthless now that her children have left home. She is also anxious about her son's wedding in 6 months because she has always felt overwhelmed by big parties.

Inside

Expert Commentary

by Dr Peter Mansfield and Associate Professor Joel Lexchin

Introduction	page 3
Discussion of various drug therapies	page 5
Appetite suppressant	
Thiazide diuretic	
Calcium channel blocker (CCB)	
Angiotensin II receptor antagonist (A2 antagonist)	
Hormone Replacement Therapy (HRT)	
HMG – CoA reductase inhibitor (“statin”)	
Benzodiazepine	
Tricyclic antidepressant (TCA)	
SSRI for depression	
SSRI for social phobia	

References	page 15
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Expert Commentary

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Introduction

The case scenario was designed to reflect the uncertainty seen in real life in general practice so the information was complex, ambiguous and incomplete. Consequently, different GPs may have good reasons for interpreting the scenario and the questions differently. For that reason there are no right answers. However we have provided our “recommended answers” with very brief comments based on a sceptical analysis of the best available evidence in the light of our clinical experience.

It is common in general practice to have to jump to quick decisions about diagnosis and therapy with incomplete information. Some GPs jump more quickly than others to more severe diagnoses and then to prescribing more drugs. The aim of the case study was to see which way you would go and then give you the opportunity to reflect on what may have influenced you to respond the way you did.

The recommended diagnoses for Mrs Parker are: mild hypertension with mildly elevated cardiovascular disease (CVD) risk (not severe risk), life stage transition distress (not major depression) and normal introversion (not social phobia).

You were asked to rate the appropriateness for Mrs Parker of 15 therapies on a 1 to 5 scale where 1 = very inappropriate vs 5 = very appropriate.

You were also asked questions designed to indicate your level of exposure to information from drug companies, e.g. “How often do you see drug reps?” Then you were asked questions designed to indicate your level of trust in information from drug companies, e.g. “What percentage of drug advertisements contain potentially misleading claims?”

The results for 10 drug therapies are provided in this report. A more complete report will be published later.

The results show that the GPs who were more exposed to information from drug companies and/or more accepting of information from drug companies were more likely to believe that new drugs were appropriate for Mrs Parker. To demonstrate the

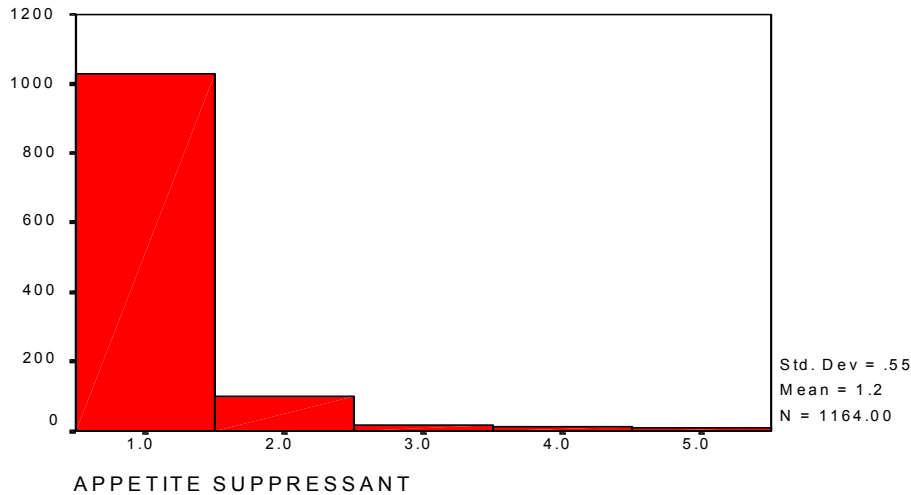
importance of that finding two groups of doctors are compared in this report: “More accepting” GPs vs “Less accepting” GPs. “More accepting” GPs are those who indicated that less than 50% of drug advertisements were potentially misleading and that their prescribing was improved by information from drug companies often or always. “Less accepting” GPs are those who indicated that more than 50% of drug advertisements were potentially misleading and that their prescribing was improved by information from drug companies rarely or never.

Many GPs did not answer every question. Please find enclosed your response sheet so that if you want to you can compare your responses with responses from 1,181 GPs and with our recommended answers.

Appetite Suppressant

Results:

97% of 1164 respondents indicated that appetite suppressants would be inappropriate or very inappropriate (rating 1 or 2).



Comment:

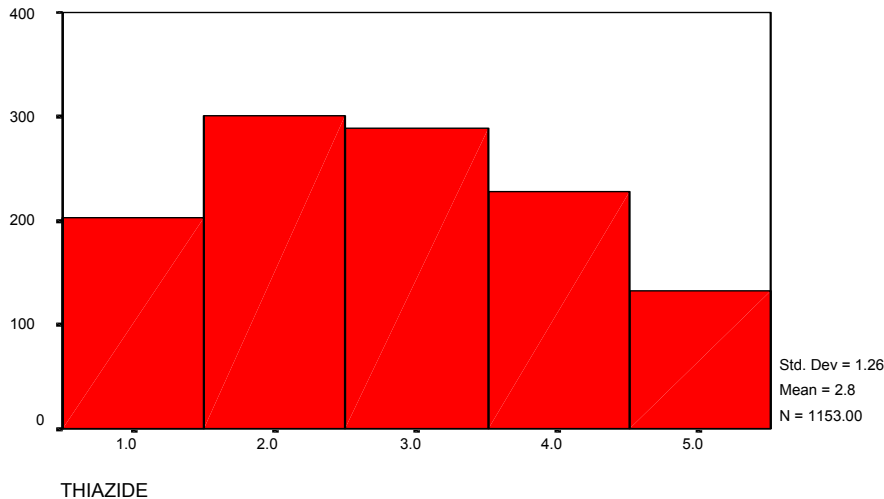
Our recommended answer: 1 = very inappropriate.

There is no good evidence to support the use of appetite suppressants. Promotion of orlistat (Xenical ®) started recently. Orlistat is not appropriate for Mrs Parker who is overweight but not obese (obese = BMI >30). Orlistat is an expensive way to lose a small amount of weight. There is no evidence yet on whether the loss is maintained long-term nor whether it leads to clinically important benefits. See: Therapeutics Letter 34 www.ti.ubc.ca/pages/letter34.htm#Orlistat It would be better for Mrs Parker to develop a taste for physical activity such as walking and a Mediterranean-like-diet such as the CSIRO / ACF 12345+ diet.

Thiazide

Results:

44% of 1150 respondents indicated that a thiazide would be inappropriate or very inappropriate (rating 1 or 2). However, there was more support for thiazides than the other antihypertensive drug options.



Comment:

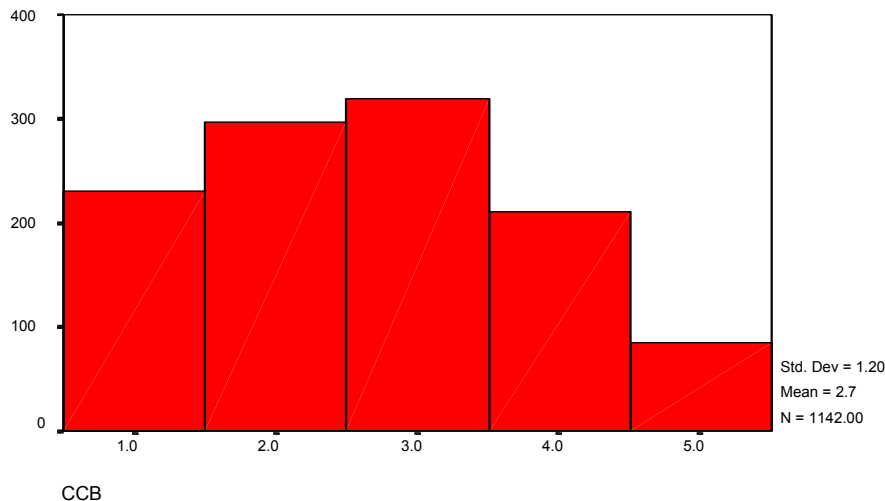
Our recommended answer: 5 = very appropriate. However we assumed that non-drug therapy including walking and reduction of excessive salt had already commenced during the repeat visits required to make the diagnosis of hypertension. If you assumed that non-drug therapies had not been tried yet and consequently gave a lower rating for all antihypertensive drugs then we agree with you.

Thiazides and thiazide like drugs (eg chlorthalidone) are old but using them in very low doses (eg hydrochlorthiazide 25mg ½ tablet daily or chlorthalidone 25mg ½ tablet daily) is new. These drugs have been shown to delay cardiovascular disease and death for people like Mrs Parker. They are better supported by evidence than other antihypertensives. The best study comparing drugs for hypertension is the TOMHS study. It compared chlorthalidone 15mg with an ACE inhibitor (enalapril), a calcium channel blocker (amlodipine), a beta-blocker (acebutolol, not available in Australia) and an alpha-blocker (doxazosin, not available in Australia). The TOMHS study found that chlorthalidone and acebutolol were best for improving quality of life. In our clinical experience, patients appreciate being able to pay less for a better drug.

Calcium channel blocker (CCB)

Results:

46% of 1142 respondents indicated that a calcium channel blocker (CCB) would be inappropriate or very inappropriate (rating 1 or 2).



Amongst GPs who were less accepting of drug company information than average, the percent who indicated that a CCB was appropriate (rating 4 or 5) was 12%. By contrast, amongst GPs who were more accepting than average, the percentage who indicated that a CCB was appropriate was 35%.

Comment:

Our recommended answer: 1 = very inappropriate.

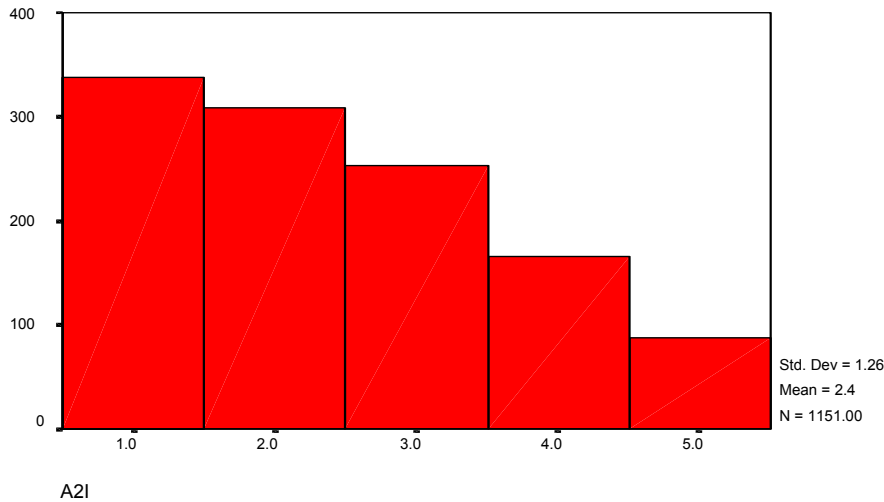
There are two groups of CCBs. The dihydropyridine CCB group includes amlodipine and felodipine. Most published trials comparing dihydropyridine CCBs with other antihypertensives have suggested that dihydropyridine CCBs may be associated with higher rates of cardiovascular events than thiazides and ACE inhibitors. Consequently, we do not recommend dihydropyridine CCBs for hypertension. See: Healthy Scepticism Jan 1999, Vol 2 (1) www.camtech.net.au/malam/nz/healthy.htm

One small trial has suggested that the non-dihydropyridine CCB verapamil may be as effective at reducing CVD events as the thiazides. Because there is little evidence to support non-dihydropyridine CCBs we do not recommend them.

Angiotensin II receptor antagonists (A2 antagonist)

Results:

56% of 1151 respondents indicated that an A2 antagonist would be inappropriate or very inappropriate (rating 1 or 2).



Amongst GPs who were less accepting of drug company information than average, the percent who indicated that an A2 antagonist was appropriate (rating 4 or 5) was 12%. By contrast, amongst GPs who were more accepting than average, the percentage who indicated that an A2 antagonist was appropriate was 34%.

Comment:

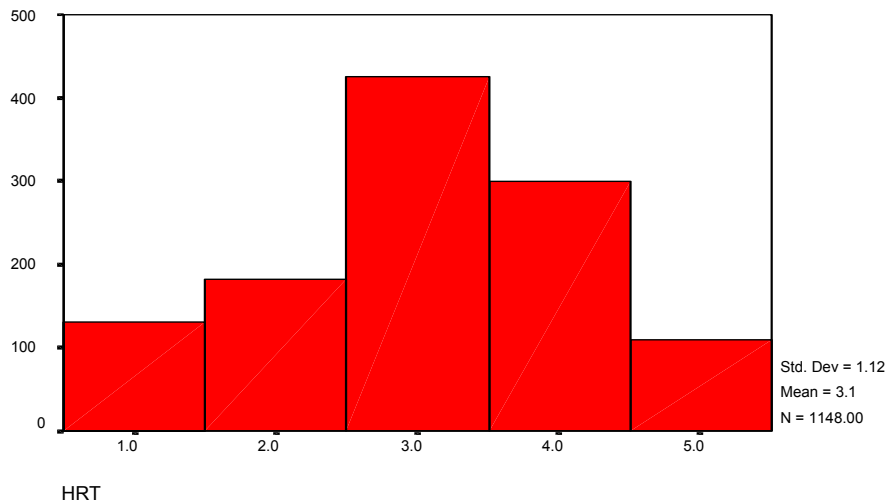
Our recommended answer: 1 = very inappropriate.

A2 antagonists are very new drugs. They do reduce blood pressure. However, as yet there is no evidence of any clinically important benefit from lowering blood pressure with A2 antagonists so we do not recommend them. A2 antagonists may provide an alternative for those who require an ACE inhibitor, but who cannot tolerate it due to a drug-induced cough.

Hormone Replacement Therapy (HRT)

Results:

27% of 1148 respondents indicated that HRT was inappropriate or very inappropriate (rating 1 or 2).



Amongst GPs who were less accepting of drug company information than average, the percent who indicated that HRT was appropriate (rating 4 or 5) was 31%. By contrast, amongst GPs who were more accepting than average, the percentage who indicated that HRT was appropriate was 41%.

Comment:

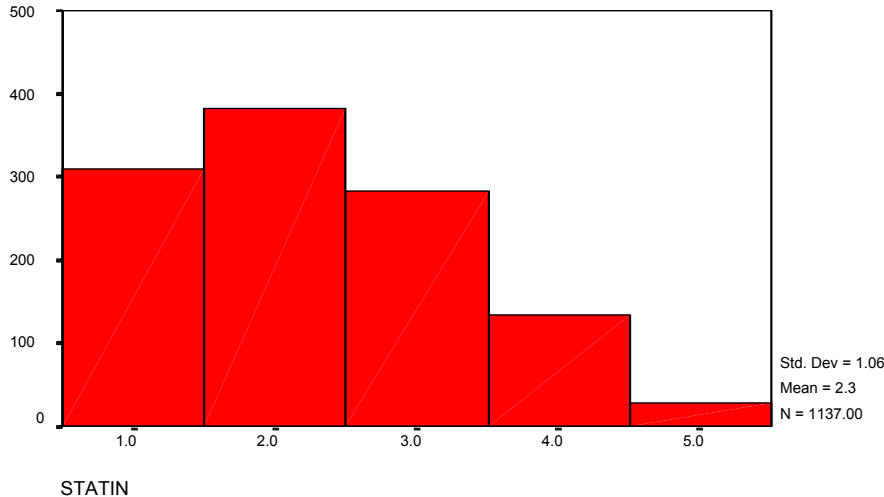
Our recommended answer: 1 = very inappropriate.

Mrs Parker does not have peri-menopausal symptoms so the issue here is the use of HRT for “prevention”. This is a difficult topic. Australian doctors have received conflicting messages about HRT. Most of these messages have been based on observational studies. Observational studies are less reliable than randomised controlled trials (RCTs). The best RCT done so far is the HERS study of secondary prevention for women with established cardiovascular disease. The HERS study found that HRT increases the rate of non-fatal infarcts and CVD deaths in the first year without providing any benefit over 5 years. In the absence of evidence of any benefit sufficient to compensate for short-term harm the use of HRT for secondary prevention is not justified. There is no RCT evidence to support the use of HRT in primary prevention. The harm to benefit ratios of drugs are usually worse for primary than for secondary prevention so it is difficult to justify use of HRT for Mrs Parker. See: Therapeutics Letter 30 www.ti.ubc.ca/pages/letter30.htm

Statin

Results:

61% of 1137 respondents indicated that a statin would be inappropriate or very inappropriate (rating 1 or 2).



Amongst GPs who were less accepting of drug company information than average, the percent who indicated that a statin was appropriate (rating 4 or 5) was 10%. By contrast, amongst GPs who were more accepting than average, the percentage who indicated that a statin was appropriate was 23%.

Comment:

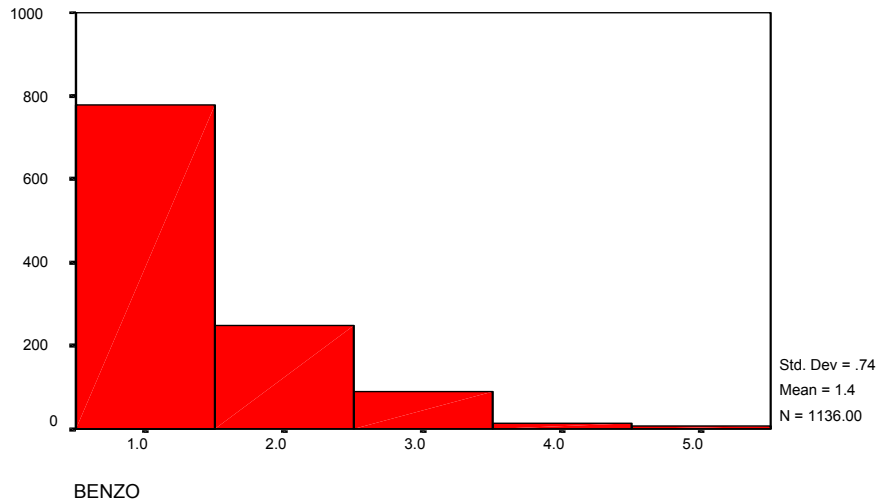
Our recommended answer: 1 = very inappropriate.

We recommend the New Zealand CVD risk calculator distributed by NPS or see: www.bmj.com/cgi/content/full/320/7236/709 This calculator makes it easy to estimate that once her BP is addressed, Mrs Parker's absolute risk of having any cardiovascular problems in the next 5 years is likely to be less than 5%. Because Mrs Parker has such a low risk her chances of getting a worthwhile benefit from a statin are tiny. The benefit that could be gained from a statin is very likely to be so small that the risks of adverse effects are not justified, let alone the cost. Use of drugs in situations where they are not cost effective diverts resources from people who need those resources more. Improvements in diet and physical activity would be more appropriate.

Benzodiazepine

Results:

90% of 1136 respondents indicated that a benzodiazepine would be inappropriate or very inappropriate (rating 1 or 2).



Comment:

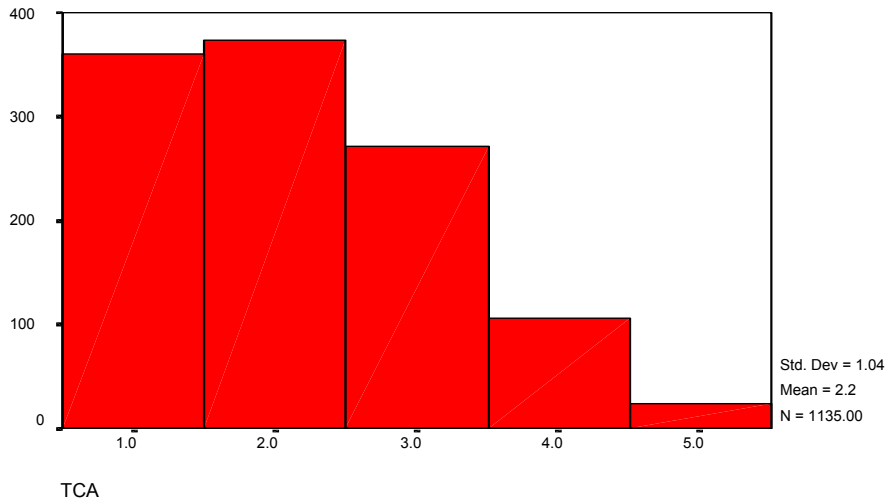
Our recommended answer: 1 = very inappropriate.

A recent meta-analysis has found that whilst benzodiazepine users think that they get to sleep 10 to 20 minutes quicker than with placebo the objective difference in getting to sleep is not significant. The average decrease in sleep latency was only 4.2 minutes (95% confidence intervals -0.7 to 9.2 minutes). It is difficult to justify the initiation of benzodiazepines because the benefits are so small, there are non-drug therapies for insomnia that work better and there are risks of cognitive dysfunction and addiction. It would be better to address the causes of Mrs Parker's insomnia. See the meta-analysis: www.cma.ca/cmaj/vol-162/issue-2/0225.htm

Tricyclic antidepressant (TCA)

Results:

65% of 1135 respondents indicated that tricyclic antidepressant would be inappropriate or very inappropriate (rating 1 or 2).



Comment:

Our recommended answer: 1 = very inappropriate.

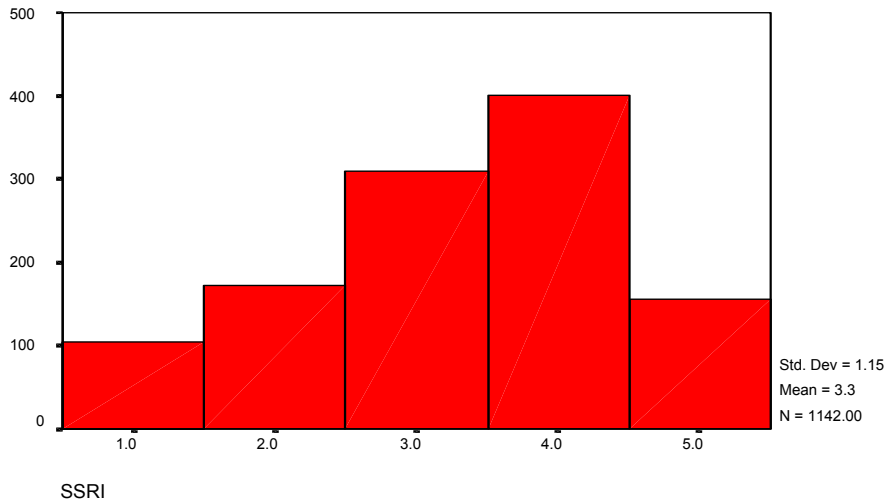
Mrs Parker has life stage transition distress. She does not meet the diagnostic criteria for major depression. If she did have major depression severe enough to require hospitalisation then a TCA would have been better than an SSRI because there is some evidence TCAs are more effective. For less severe depression there is no clear difference in the effectiveness of TCAs and SSRIs. This may be because most people get better anyway or because of the placebo effect. The rate of discontinuations because of side effects for SSRIs and secondary amine TCAs such as desipramine (Pertofran®) are not different. When considering what to prescribe, when there is no clear evidence of a difference in effectiveness, it may be useful to mention the adverse effects of the alternatives and ask patients about their preferences (eg dry mouth vs sexual dysfunction). TCAs are more dangerous in overdose. Unfortunately there is no good evidence that the increased use of SSRIs has reduced the rate of fatal suicides from all causes.

Cognitive Behaviour Therapy (CBT) is as effective as drugs for major depression in the short term and leads to a lower relapse rate. CBT is more appropriate, compared to drugs, for less severe depression and distress. For more on depression see the next section.

SSRI for depression

Results:

24% of 1142 respondents indicated that a SSRI for depression would be inappropriate or very inappropriate (rating 1 or 2).



Amongst GPs who were less accepting of drug company information than average, the percent who indicated that a SSRI for depression was appropriate (rating 4 or 5) was 37%. By contrast, amongst GPs who were more accepting than average, the percentage who indicated that a SSRI for depression was appropriate was 49%.

Comment:

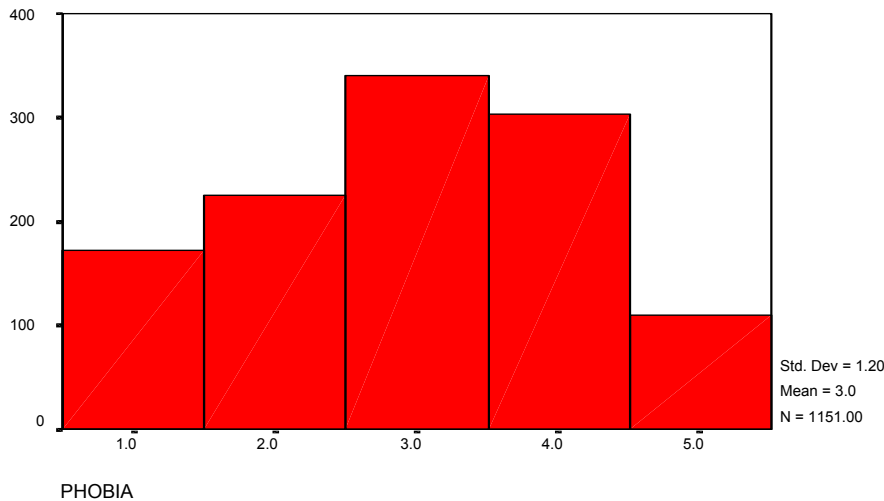
Our recommended answer: 1 = very inappropriate.

Mrs Parker is distressed. That is different from depression. However, we accept that some GPs may have interpreted the question as indicating that the diagnosis of depression had been made. Mrs Parker is likely to find new meaning in life by herself. However a few half hour sessions of simplified cognitive therapy could be dramatically helpful. Clinical experience suggests that use of any antidepressant risks masking her symptoms and undermining her ability to achieve mastery over the cause of her distress. One way to learn about simplified cognitive therapy is to read Greenberger D, Padesky C. Mind over mood. Guilford Press, New York 1995. Clinical experience suggests that it is easier to learn how to provide simplified cognitive therapy than many GPs realise.

SSRI for social phobia

Results:

34% of 1151 respondents indicated that a SSRI for social phobia would be inappropriate or very inappropriate (rating 1 or 2).



Amongst GPs who were less accepting of drug company information than average, the percent who indicated that a SSRI for social phobia was appropriate (rating 4 or 5) was 25%. By contrast, amongst GPs who were more accepting than average, the percentage who indicated that a SSRI for social phobia was appropriate was 43%.

Comment:

Our recommended answer: 1 = very inappropriate.

Mrs Parker does not meet the diagnostic criteria for social phobia. However, we accept that some GPs may have interpreted that question as indicating that the diagnosis of social phobia had been made. She is one of 40% of the Australian population who are introverts. Introversion is a normal personality variant. It would be appropriate to tell her that her anxiety about parties is normal and arises from a personality variation which also brings many advantages both for her and for those she cares about (eg capacity for depth of focus). It would also be appropriate to tell her that mild anxiety improves performance and so whilst it is often unpleasant it can be beneficial. It would not be appropriate to medicalize 40% of the Australian population.

References

Grimm RH. *Relationships of quality-of-life measures to long-term lifestyle and drug treatment in the Treatment of Mild Hypertension Study*. Arch Intern Med. 1997;157(6):638-48