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Understanding the non-pharmacological correlates of self-reported efficacy of antidepressants

Read J, Gibson K, Cartwright C, Shiels C, Dowrick C, Gabbay M. Understanding the non-pharmacological correlates of self-reported efficacy of antidepressants.

Objective: To explore the non-pharmacological correlates of the perceived effectiveness of antidepressants (ADs), thereby enhancing understanding of the mechanisms involved in recovery from depression while taking ADs.
Method: An online survey was completed by 1781 New Zealand adults who had taken ADs in the previous 5 years.
Results: All 18 psychosocial variables measured were associated with depression reduction, and 16 with improved quality of life (QoL). Logistic regression models revealed that the quality of the relationship with the prescriber was related to both depression reduction and improved QoL. In addition, depression reduction was related to younger age, higher income, being fully informed about ADs by the prescriber, fewer social causal beliefs for depression and not having lost a loved one in the 2 months prior to prescription. Furthermore, both outcome measures were positively related to belief in 'chemical' rather than 'placebo' effects.
Conclusion: There are multiple non-pharmacological processes involved in recovery while taking ADs. Enhancing them, for example focusing on the prescriber–patient relationship and giving more information, may enhance recovery rates, with or without ADs.

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Key words: depression; antidepressants; therapeutic relationship; causal beliefs; non-specific effects

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Significant outcomes

- Self-reported positive outcomes while taking antidepressants are related to multiple psychosocial variables.
- Patient characteristics, including demographics and causal beliefs, are related to whether antidepressants are perceived to have worked.
- The patient–prescriber relationship, including amount of information imparted, is an important predictor of outcome when taking antidepressants.

Limitations

- Older people, poorer people and ethnic minorities were under-represented in the convenience sample.
- The data relied on self-report.
- The causal direction of some of the correlational findings is ambiguous.

Introduction

By 2005, one in 10 people over the age of six in the USA were being prescribed antidepressants (ADs) annually (1). In England, prescriptions for ADs increased 10% per year between 1998 and 2010 (2). In New Zealand, where the current study was conducted, the number of annual prescriptions rose by

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37% between 2006/07 and 2011/12, from 1 007 109 to 1 385 133; while the number of recipients per year increased by 35% from 304 530 to 412 631 (PHARMAC, personal communication, 2012), in a population of 4.4 million, of whom 3.7 million are aged 16 or older. Thus, one in nine of the adult population (and approximately one in six women) are now prescribed ADs every year. These dramatic increases in prescribing rates are occurring in the context of stable prevalence rates of depression and high rates of prescribing to people who do not meet diagnostic criteria for a depressive 'disorder' (3). Another contextual factor is the pervasive influence of the pharmaceutical industry, not least in terms of their funding of mental health internet websites which espouse simplistic biogenetic causal explanations and promote their products (4, 5).

Recent research has raised concerns about the efficacy of ADs, compared with psychological treatments or placebo; with placebo response rates of around 50% being found (6–8). Less than half of drug trials find ADs superior to placebo (8). A meta-analysis (9), which included previously unpublished drug company studies, found that 'the overall effect of new-generation AD medications is below recommended criteria for clinical significance' (p. 265) with no significant benefit compared with placebo for all but 'patients at the upper end of the very severely depressed category' (p. 260).

The non-specific effects of a treatment are clearly an important ingredient of why ADs, and other treatments, work. Depression has been found to be highly sensitive to such effects (10). These effects are persistent not transient (11) and have demonstrable neural correlates (12). A recent review of AD drug trials categorised the factors that can influence non-specific, or non-pharmacological effects into five domains: healthcare environment, practitioner characteristics, patient characteristics, practitioner–patient interaction and non-pharmaceutical drug characteristics (7). The focus of this particular review was the infrequency with which most of these factors are recorded in drug trials, thereby limiting the ability of the trials to accurately assess the pharmacological effect of ADs. For example, none of the 82 studies recorded either the beliefs or expectations of the patients, and – in the practitioner–patient domain – only 2% recorded levels of empathy or congruence. Besides enhancing the validity of drug trials, an equally compelling reason for studying these variables is that by understanding the psychosocial factors that are related to perceived positive outcomes while taking ADs we may be better able to identify and enhance those factors which lead to better outcomes, with or without ADs.

Aims of the study

The current study, therefore, reports the findings from an online questionnaire completed by antidepressant users, with a primary focus on patient characteristics (demographics and beliefs) and practitioner–patient interactions (quality of relationship and information conveyed). The associations between these various factors and two measures of perceived effectiveness, reduced depression and improved quality of life, are reported.

Material and methods

Instrument

The questionnaire had 47 questions (in either yes/no, likert scale, or open-ended formats), in eight sections: demographics; the prescribing process; information about AD usage and perceptions of their effectiveness; side-effects; benefits; experiences of alternative treatment options; and beliefs about the causes of depression. The criteria for participation included having been prescribed ADs in the last 5 years and being 18 years of age or over.

Recruitment

The study was approved by the University of Auckland Human Participants Ethics Committee. The anonymous questionnaire was placed online using a survey website that guarantees the protection of data. A Google web page advertising the study (www.viewsonantidepressants.co.nz) provided the participant information for the study and a link to the online questionnaire. The study was further publicised in the New Zealand media via media releases, interviews with the researchers and advertisements.

Participants

Of the 2171 people who started the survey, 295 stopped before the end of the second section (question 19 of 47) and their responses were not analysed. Of the remaining 1876, 45 cited medications other than ADs in response to questions about which AD they had been prescribed. The Internet Protocol address (IP) of 168 of the remaining 1831, was the same as at least one other respondent, indicating possible use of the same computer (although several devices can share IP addresses). The responses of these 168 were checked, and two

respondents whose scores were nearly identical to those of someone else with the same IP were excluded. This left 1829. A further 48 who had been prescribed ADs but had not taken them were excluded, leaving 1781 for analysis. The number of responses to each question varied as not all participants responded to all questions.

Data analysis

Two outcomes were measured in the study:

i) Perceived reduction in depression – ('Yes' or 'No' in response to 'Did the antidepressant reduce your depression?')

ii) Perceived improvement in quality of life (QoL) – ('greatly improved', 'slightly improved', 'unchanged', 'slightly worse' or 'a lot worse' – in response to 'While taking antidepressants my quality of life was . . .').

It was hypothesised that a range of 18 psychosocial factors may be associated with these two outcomes. These potential explanatory factors (see Table 1) included sociodemographic attributes, information received from the prescribing doctor, perceived relationship with the doctor and beliefs about the causes of their own depression, about the efficacy of ADs and about 'chemical' vs.

Table 1. Descriptive data for the 20 variables used in the analyses

	N	%
Gender		
Male	425	23.4
Female	1397	76.6
Age		
35 and under	690	37.8
36–55	846	46.4
Over 55	289	15.8
Annual personal income		
Under $20 000	534	29.5
$20 000–60 000	737	40.7
Over $60 000	541	29.9
Educational level		
Not finished high school	129	7.1
Finished high school	314	17.2
Certificate/diploma	477	26.1
University degree	545	29.8
University postgrad degree	362	19.8
'Please rate your level of depression in the year before taking antidepressants'		
Mild/none	333	19.4
Moderate	649	37.8
Severe	733	42.7
'Who first suggested the idea of taking an antidepressant?'		
GP/Psychiatrist	1343	79.4
Informal (patient, relative, friend)	349	20.6
'In the 2 months before you were first prescribed antidepressants, had a loved one died?'		
No	1683	92.7
Yes	133	7.3
'Were you told what benefits to expect from taking the antidepressants?'		
No	395	22.2
Yes	1386	77.8
'Did the prescribing doctor tell you how antidepressants work?'		
No	731	41.3
Yes	1039	58.7
'Did the doctor tell you how long you should take the antidepressants for?'		
No	807	45.1
Yes	982	54.9
'Did the doctor inform you about possible side-effects?'		
No	630	35.8
Yes	1130	64.2
'Did the prescribing doctor say what problem(s) s/he thought you had that would be helped by taking antidepressants?'		
No	253	14.1
Yes	1538	85.9
'Could you estimate approximately how long the doctor spent with you on the day they prescribed antidepressants?'		
15 min or less	758	41.9
15–30 min	607	33.6
Over 30 min	443	24.5
'How would you describe your relationship with the doctor?'		
Not good/Not at all good	137	7.6
Not sure	296	16.3
Very good/Good	1379	76.1
'How well do you think your doctor understood your problem(s)?'		
Not a lot/Not at all	323	17.9
OK	387	21.4
A lot/Quite a lot	1099	60.8
No of social causes indicated		
>5	499	29.8
3–5	771	46.1
<3	402	24.0
No of biological causes identified		
None/one	816	49.8
Two/three	823	50.2
Adverse effect severity score		
Score >20	291	26.1
Score 11–20	330	29.6
Score 0–10	495	44.4
'Antidepressants are the best treatment'		
Disagree/strongly disagree	654	39.4
Not sure	675	40.7
Agree/strongly agree	331	19.9
'If you benefitted from antidepressants, to what extent do you think it was because of the chemical effect of the antidepressants vs. the placebo effects of hope and expectation?'		
>50% placebo	77	5.2
50% chemical/50% placebo	195	13.2
>50% chemical	1203	81.6

'placebo' effects. Two additional factors, adverse drug effects reported by the participants and level of depression in the year prior to prescription, were also included in the analyses, because it was assumed that they might also be predictors of perceived efficacy and, therefore, potential confounders of relationships between the psychosocial variables and the two outcome measures.

In the univariate analyses for the two outcomes, the chi-squared test and the Cochran–Armitage test-for-trend were used to estimate the statistical significance of association between each of the potential explanatory variables and the two outcome measures.

For both reduction in depression and improvement in QoL, logistic regression models were constructed to estimate *independent* effects associated with positive outcome. The improvement in QoL measure was rendered dichotomous by counting 'greatly improved' and 'slightly improved' as a positive response and 'unchanged', 'slightly worse' and 'a lot worse' as a negative response. Only variables significantly associated with outcome at the univariate level for each of the two outcome measures were entered as covariates in the regression models. For each covariate, Odds Ratios, 95% Confidence Intervals and the *P*-value are reported.

To optimise the efficiency of the two multivariate analyses, the number of independent variables was reduced by computing 'scores' based on an aggregation of responses to related questionnaire items or by transforming multiple items into a single variable (see Tables 2 and 3).

A 'social causes' variable was created on the basis of a respondent agreeing with a number of potential causes of their depression that were social or personal in nature. There were 10 of these potential causes included in the questionnaire: 'work stress', 'family stress', 'childhood neglect or abuse', 'other distressing childhood experience', 'loss of loved one', 'pace of modern life', 'financial problems', 'relationship problems', 'social isolation' and 'unemployment'. In the same section of the questionnaire, three biological causes were included as options: 'heredity/genes', 'chemical imbalance' and 'disorder of the brain'.

An adverse effects score was computed using 20 side-effects known to be potentially associated with AD use, which were included as a list in the questionnaire. Respondents were asked to rate their experience of each, from 'not at all' (=0) to 'severe' (=3). An overall severity score was computed for each respondent by aggregating responses to the 20 items, to give a maximum severity score of 60. The adverse effects experienced have been published in detail elsewhere (13).

The five items relating to information provided to the patient at the outset of AD use (pertaining to expected benefits of taking AD, how the AD works, an estimate of duration, potential side-effects and the nature of the problem being addressed by the AD) were collapsed into one overall dichotomous measure of whether the respondent reported they had received *all* this information or not.

Finally, the two items requesting the respondent to describe their relationship with the prescribing doctor and to report how well s/he had understood the patient's problem were collapsed into one dichotomous variable: Whether the respondent felt that their relationship with the doctor was both 'good' (or 'very good') *and* that their problem was understood 'a lot' (or 'quite a lot').

For both univariate and multivariate analyses, a conventional criterion of statistical significance ($P < 0.05$) was assumed. SPSS (IBM, Armonk, NY, USA) was used for analyses.

Results

Sample characteristics and descriptive data

Females constituted 76.6% of the sample. The modal age group was 36–45 (24.2%); 16.3% were 18–25, and 15.9% were 56 or older. The men were significantly older than the women ($P < 0.001$). A large majority, 92.1%, identified as 'New Zealand/European'; 2.9% as Maori, 1.2% as Asian, 0.4% as Pacific Islander and 3.5% as 'Other'. The majority, 89.1%, identified as heterosexual; 2.2% as gay, 2.9% as lesbian and 5.7% as bisexual. (Neither ethnicity nor sexual orientation were included in analyses, because of the low numbers in the smaller groups).

In terms of education, 49.6% had a university degree; 26.1% had gained a diploma or certificate after high school, 17.2% had completed high school, and 7.1% had not completed high school. (In 2006, 14.2% of adult New Zealanders had an undergraduate degree or higher and 22.4 per cent had no formal qualification (14)]. Education was not significantly related to age or gender. Annual personal income (in New Zealand dollars) ranged from 'less than $10 000' (15.0%) to 'more than $100 000' (7.7%). The modal income was '$40 000 to $59 999' (22.1%). [The median income of the NZ population in 2012 was $29 000 (15)]. Income was significantly related to older age and being male.

Table 2. Variables associated with perceived reduction in depression

	% (*n*/*N*)	*P*	Adjusted* Odds Ratio(95% CI)	*P*
Gender				
Male	78.4 (313/399)	0.009	1.0	
Female	84.1 (1095/1302)		1.41 (0.64–3.09)	0.39
Age				
Over 55	84.1 (228/271)	0.03	1.0	
36–55	84.8 (668/788)		3.18 (1.03–9.83)	0.04
35 and under	79.8 (517/648)		4.16 (1.24–13.9)	0.02
Annual personal income				
Under $20 000	75.8 (382/504)	<0.001	1.0	
$20 000–60 000	83.6 (572/684)		2.01 (0.96–4.21)	0.06
Over $60 000	88.5 (448/506)		5.56 (1.86–16.6)	0.002
Educational level				
Not finished high school	76.1 (89/117)	0.003	1.0	
Finished high school	77.6 (229/295)		0.39 (0.09–1.72)	0.21
Certificate/diploma	82.1 (368/448)		0.70 (0.17–2.97)	0.63
University degree	85.0 (431/507)		0.78 (0.19–3.16)	0.72
University postgrad degree	87.4 (298/341)		1.33 (0.27–6.62)	0.73
Loss in 2 months before antidepressants (AD) use				
No	83.4 (1316/1578)	0.04	1.0	
Yes	76.2 (93/122)		0.32 (0.11–0.88)	0.03
Received all key information† from doctor about AD				
No	78.4 (845/1078)	<0.001	1.0	
Yes	91.3 (431/472)		2.73 (1.02–7.72)	0.04
Relationship with doctor 'good' and felt he/she understood the problem				
No	69.8 (474/679)	<0.001	1.0	
Yes	91.6 (918/1002)		2.11 (1.01–4.49)	0.04
Time spent with doctor				
15 min or less	76.4 (528/691)	<0.001	1.0	
15–30 min	86.5 (501/579)		0.82 (0.36–1.85)	0.63
Over 30 min	88.1 (370/420)		1.88 (0.70–5.07)	0.21
Who first suggested AD use				
GP/Psychiatrist	81.5 (1023/1255)	0.002	1.0	
Informal (patient, relative, friend)	88.6 (288/325)		1.37 (0.63–3.02)	0.43
Depression severity in year before AD use				
Mild/none	66.5 (216/325)	<0.001	1.0	
Moderate	86.0 (551/641)		1.70 (0.73–3.91)	0.22
Severe	87.7 (641/731)		2.69 (1.13–6.39)	0.02
No of social causes indicated				
>5	77.4 (384/496)	<0.001	1.0	
3–5	85.3 (654/762)		2.32 (1.12–4.80)	0.02
<3	86.3 (340/394)		4.19 (1.40–12.6)	0.01
No of biological causes indicated				
None/one	79.6 (641/805)	<0.001	1.0	
Two/three	88.9 (724/814)		2.03 (0.99–4.16)	0.05
'Antidepressants are the best treatment'				
Disagree/strongly disagree	90.7 (606/668)	<0.001	1.0	
Not sure	70.0 (452/646)		1.76 (0.60–5.14)	0.30
Agree/strongly agree	95.1 (310/326)		1.93 (0.89–4.20)	0.10
Adverse effect severity score				
Score >20	61.9 (180/291)	<0.001	1.0	
Score 11–20	86.2 (281/326)		3.09 (1.35–7.07)	0.008
Score 0–10	92.2 (450/488)		4.78 (2.02–11.3)	<0.001
Chemical/placebo belief				
>50% placebo	61.0 (47/77)	<0.001	1.0	
50% chemical/50% placebo	89.2 (174/195)		4.28 (1.41–13.1)	0.01
>50% chemical	94.8 (1125/1187)		6.88 (2.57–18.4)	<0.001

*Adjusted for covariates that were significant in the univariate analysis.

†Information relating to expected benefits of taking AD, how the AD works, an estimate of duration, potential side-effects and the nature of the problem being addressed by the AD.

About half (52.6%) reported first being prescribed ADs between 2000 and 2009; with 25.9% reporting 2010–2013; 16.1% 1990–1999, and 5.4% prior to 1990; and 69.1% were still taking ADs. Just over half (51.7%) had taken them for more than 3 years, and 7.8% for less than 3 months. In 83.6% of cases, the prescriber was a GP, and in 16.4% a psychiatrist. Of the 1715 (93.8%) who

Table 3. Variables associated with perceived improvement in quality of life

	% (*n*/*N*)	*P*	Adjusted* Odds Ratio(95% CI)	*P*
Gender				
Male	78.4 (313/399)	<0.001	1.0	
Female	87.5 (1147/1311)		1.70 (0.81–3.57)	0.16
Age				
Over 55	86.9 (239/275)	0.002	1.0	
36–55	87.9 (695/791)		2.64 (0.75–9.35)	0.13
35 and under	81.5 (529/649)		2.84 (0.83–9.71)	0.10
Annual personal income				
Under $20 000	80.8 (407/504)	<0.001	1.0	
$20 000–60 000	85.1 (587/690)		1.02 (0.45–2.31)	0.97
Over $60 000	90.2 (458/508)		1.94 (0.68–5.55)	0.22
Educational level				
Not finished high school	81.9 (95/116)	0.19	–	–
Finished high school	82.9 (247/298)		–	–
Certificate/diploma	85.1 (383/450)		–	–
University degree	85.5 (435/509)		–	–
University postgrad degree	89.0 (306/344)		–	–
Loss in 2 months before antidepressants (AD) use				
No	85.7 (1358/1584)	0.19	–	–
Yes	81.5 (101/124)		–	–
Received all key information† from doctor about AD				
No	81.9 (887/1083)	<0.001	1.0	
Yes	92.6 (439/474)		1.36 (0.51–3.67)	0.54
Relationship with doctor 'good' and felt he/she understood the problem				
No	72.5 (494/681)	<0.001	1.0	
Yes	94.0 (948/1009)		2.93 (1.29–6.66)	0.01
Time spent with doctor				
15 min or less	78.3 (545/696)	<0.001	1.0	
15–30 min	90.5 (523/578)		1.42 (0.55–3.68)	0.46
Over 30 min	89.6 (381/425)		2.04 (0.80–5.21)	0.14
Who first suggested AD use				
GP/Psychiatrist	84.5 (1066/1261)	0.04	1.0	
Informal (patient, relative, friend)	89.0 (292/328)		1.73 (0.78–3.79)	0.17
Depression severity in year before AD use				
Mild/none	70.1 (232/331)	<0.001	1.0	
Moderate	88.1 (571/648)		1.26 (0.52–3.09)	0.61
Severe	90.1 (656/728)		2.06 (0.83–5.11)	0.12
No of social causes indicated				
>5	80.5 (400/497)	<0.001	1.0	
3–5	88.4 (680/769)		1.38 (0.65–2.99)	0.40
<3	87.8 (347/395)		1.65 (0.58–4.73)	0.40
No of biological causes indicated				
None/one	81.9 (663/810)	<0.001	1.0	
Two/three	90.6 (742/819)		1.51 (0.73–3.11)	0.27
'Antidepressants are the best treatment'				
Disagree/strongly disagree	73.1 (474/648)	<0.001	1.0	
Not sure	92.4 (620/671)		2.10 (0.70–6.31)	0.19
Agree/strongly agree	96.7 (319/330)		2.65 (1.17–6.03)	0.02
Adverse effect severity score				
Score >20	73.1 (474/648)	<0.001	1.0	
Score 11–20	92.4 (620/671)		2.63 (1.21–5.73)	0.02
Score 0–10	96.7 (319/330)		12.1 (3.84–28.4)	<0.001
Chemical/placebo belief				
>50% placebo	70.7 (53/75)	<0.001	1.0	
50% chemical/50% placebo	88.7 (173/195)		2.49 (0.78–7.97)	0.12
>50% chemical	96.3 (1152/1196)		3.06 (1.10–8.53)	0.03

*Adjusted for covariates that were significant in the univariate analysis.

†Information relating to expected benefits of taking AD, how the AD works, an estimate of duration, potential side-effects and the nature of the problem being addressed by the AD.

reported which AD they had been prescribed, the most common was fluoxetine (22.4%), followed by citalopram (20.3%), paroxetine (8.7%), tricyclics (4.5%) and venlafaxine (2.2%). Thirty-nine percent reported that they had been prescribed multiple ADs. Participants reported the following levels

of depression in the year before taking ADs: 'severe' – 42.7%, 'moderate' – 37.8%, 'mild' – 11.8% and 'not at all' – 7.6%.

Association between psychosocial variables and perceived depression reduction

Nearly 83% (1416/1710) of respondents perceived a reduction in their depression as a result of taking ADs. Of those who experienced a reduction, 1.3% thought this happened the same day, 1.6% the next day, 13.0% within 2–7 days, 17.3% in the second week, 23.0% in the third week, 13.6% in the fourth week and 30.2% in the next month.

All variables analysed were associated with perceived depression reduction at the univariate level (see Table 2).

Demographics. Compared with male respondents, a significantly higher proportion of females perceived a reduction in their depression (84% vs. 78%, $P = 0.009$). Older participants (over 35) were more likely to report a positive outcome (85% vs. 80% of younger respondents, $P = 0.01$). Higher personal income was associated with perceived reduction in depression (86% of those with income >$20 000 a year compared to 76% of respondents with a lower annual income, $P < 0.001$). Higher proportions of those with a university degree reported reduction in depression (86%, compared to 80% of those without one, $P < 0.001$).

Patient–prescriber interactions. People receiving relevant information when prescribed ADs were more likely to report depression reduction. Over 85% of those who were told about potential benefits of taking the medication reported subsequent improvement in depression, compared with 73% of those who received no such information ($P < 0.001$). Similar differences were found for those receiving information about how the AD works (88% vs. 74%, $P < 0.001$), how long they should take it (85% vs. 79%, $P < 0.001$), possible side-effects (88% vs. 72%, $P < 0.001$) and the problems for which the ADs would be helpful (84% vs. 74%, $P < 0.001$).

The length of the initial consultation with the doctor was associated with perceiving a reduction in depression; 87% of respondents having a >15 min consultation compared to 76% of those with a shorter one ($P < 0.001$). Compared with participants who reported that their relationship with the doctor was 'not good' 'not at all good' or were 'not sure', those reporting a 'good' or 'very good' relationship had a higher rate of reduction in depression (67% vs. 87%, $P < 0.001$). A higher proportion of respondents who felt that the doctor understood their problem 'a lot' or 'quite a lot' experienced a reduction in their depression (91% vs. 69%, $P < 0.001$).

Beliefs. Fewer (77%) respondents identifying more than five social causes reported a reduction in depression than those indicating five or less (86%) ($P < 0.001$). Conversely, 89% of respondents indicating more than one biological cause reported a reduction in depression, compared with 80% of those reporting only one or no biological cause ($P < 0.001$).

A belief that 'antidepressants are the best treatment for depression' increased the likelihood of perceived depression reduction (95% of those who agreed with the statement, compared with 81% of those who disagreed or were 'not sure', $P < 0.001$). Nearly 95% of respondents who believed the effect of ADs is over 50% 'chemical' in nature reported a reduction in depression, compared with 61% of those who believed it was largely 'placebo' ($P < 0.001$).

Other. People receiving initial advice to take ADs from an informal source (e.g. friend or family) were more likely to have a subsequent positive outcome (89%, compared with 82% receiving such advice from a GP or psychiatrist, $P = 0.002$).

Within the small group (133) of respondents who reported 'loss of a loved one' in the 2 months before first receiving an AD, the proportion of those reporting depression reduction was lower (76%, compared with 83% of those with no such bereavement, $P = 0.04$)

Besides the 18 psychosocial variables, a higher proportion of respondents reporting that their depression was 'moderate or severe' in the year before the first AD prescription went on to perceive a reduction in their depression (87%, compared with 66% of those reporting 'no or mild depression', $P < 0.001$). Finally, a higher score on the adverse effects scale was negatively associated with reported reduction in depression. Sixty-two percent of respondents scoring over 20 on the scale reported depression reduction during the period of AD use, compared with 92% of those with a score of 10 or under ($P < 0.001$).

Regression analysis. Of the 12 non-pharmacological items entered as covariates in a logistic regression model to estimate their *independent* effect on perceived depression reduction, seven retained their statistically significant effect in the multivariate model (see Table 2).

Age was independently associated with depression reduction; but the direction of the association

was the reverse of that found at univariate level. Respondents aged 35 and under were *more* likely to report depression reduction than those aged over 55 (Odds Ratio 4.2; $P = 0.02$). Respondents with a personal annual income over $60 000 were more likely than those with an income under $20 000 to report reduction in depression (OR 5.6; $P = 0.002$).

Respondents who described their relationship with the prescribing doctor as 'good' *and* felt s/he understood their problems were more likely to report depression reduction than other participants (OR 2.1; $P = 0.04$). People who were given full information about ADs were more likely to experience a reduction in depression than those who were not (OR 2.7; $P = 0.04$).

Respondents who responded 'yes' to 'In the two months before you were first prescribed antidepressants, had a loved one died?' were less likely to report depression reduction than those responding 'no' OR 0.3; $P = 0.03$).

Two belief variables were independently predictive of depression reduction. Respondents who believed that the effect of the AD was over 50% chemical were more likely to report depression reduction than those who believed it was largely placebo (OR 6.9; $P < 0.001$). Respondents who identified less than three social causes were more likely to report reduced depression than those who identified more than five (OR 4.2; $P = 0.01$). [People who selected two or three of the three biological causes were more likely to report reduced depression than those who selected one or none, but this was not quite statistically significant (OR 2.0; $P = 0.05$)].

In addition, participants who rated their depression in the year before the AD prescription as 'severe' were more likely to perceive depression reduction than those who rated it as 'mild' or as 'not at all' (OR 2.7; $P = 0.02$). In terms of adverse drug effects, compared with the reference category (>20), respondents scoring $\leq$10 or less were more likely to report depression reduction (OR 4.8; $P < 0.001$).

Association between psychosocial variables and perceived improvement in quality of life

Responses to the item 'While taking antidepressants my QoL was …' were as follows: 'greatly improved' 49.2%, 'slightly improved 36.1%, 'unchanged' 5.4%, 'slightly worse' 4.4% and 'a lot worse' 4.5%. Sixteen of the 18 psychosocial variables were significantly associated with this outcome at the univariate level (the exceptions being education level and loss of a loved one).

Demographics. A significantly higher proportion of females perceived an improvement in QoL (88% vs. 78% of males, $P < 0.001$). Compared with the younger group, older respondents (>35) were more likely to report improvement in QoL (88% vs. 82%, $P = 0.002$). A higher personal income was associated with a positive outcome (87% of those with income >$20 000 a year reporting a QoL improvement, compared with 81% of respondents with a lower annual income, $P = 0.001$).

Patient–prescriber interactions. Over 88% of those who were told about potential benefits of taking ADs reported improvement in QoL, compared with 76% of those who received no such information ($P < 0.001$). Similar differences in reported QoL improvement were found for those receiving information about how the AD works (90% vs. 78%, $P < 0.001$), how long they should take it (87% vs. 83%, $P = 0.02$), possible side-effects (90% vs. 76%, $P < 0.001$) and the problems that the AD would treat (87% vs. 75%, $P < 0.001$).

The length of the initial consultation was associated with improved QoL [90% of respondents having a >15 min consultation compared with 78% of those with a shorter one ($P < 0.001$)]. Those reporting a 'good' relationship with their doctor had a higher rate of reporting QoL improvement (90% vs. 69% of those rating relationship as 'not good' or 'not sure', $P < 0.001$). A higher proportion of respondents who felt that the doctor understood their problem 'a lot' experienced an improvement in their QoL (94% vs. 72%, $P < 0.001$).

Beliefs. Respondents seeing social causes as the basis of their depression were less likely to report improvement in QoL Eighty-one percent of those indicating more than five social causes in the survey reported QoL improvement, compared with 88% of those indicating five or less ($P < 0.001$). Conversely, 91% of respondents who indicated two or three biological causes reported an improvement in QoL, compared with only 82% of those reporting one or no biological cause ($P < 0.001$).

When the respondent agreed that 'antidepressants are the best treatment for depression', the likelihood of a reported QoL improvement increased (97% of those who agreed with the statement compared to only 73% of those who disagreed, $P < 0.001$). Nearly 96% of respondents who believed that the effect of the AD was 'over 50% chemical' reported a QoL improvement, compared with 71% of those who believed it was largely placebo ($P < 0.001$).

Other. People who had initially been advised to take ADs from an informal source (e.g. friend or family) were more likely to perceive QoL improvement (89%, compared to 85% receiving such advice from a GP or psychiatrist, $P = 0.04$).

Higher proportions of respondents reporting that their depression was 'moderate or severe' in the year before the first AD prescription went on to perceive some improvement in QoL (89%, compared to 70% of those reporting 'no or mild depression', $P < 0.001$).

A perceived improvement in QoL was more likely for those respondents with lower adverse effect severity scores. Nearly 95% of those scoring 10 or under on the severity scale reported QoL improvement, compared with only 71% of those with a score higher than 20 ($P < 0.001$).

Regression analysis. Only three of the psychosocial variables entered as covariates in the logistic regression model for perceived improvement in QoL retained their statistically significant effect in the multivariate model (Table 3). (Two of these were in common with the variables independently predicting depression reduction: relationship with doctor and belief in 'chemical' vs. 'placebo' effects).

Respondents who described their relationship with the prescribing doctor as 'good' *and* felt s/he understood their problems were more likely to report improved QoL (OR 2.9; $P = 0.01$). Compared with respondents who believed that the effect of the AD was largely placebo, those who reported that it was over 50% chemical were more likely to report QoL improvement (OR 3.1; $P = 0.03$). Unlike depression reduction, improved QoL was related to believing that 'antidepressants are the best treatment' ($P = 0.02$).

In terms of adverse effects, compared with the reference category (score of over 20), respondents scoring 10 or less were more likely to report improvement in QoL (OR 12.1; $P < .001$). Severity of depression was not significantly related to improved QoL in the regression analysis.

Discussion

The overall pattern of results indicates that the perceived efficacy of ADs is strongly related to a large range of psychosocial variables, including age, income, beliefs and attitudes, and the relationship with, and information imparted by, the prescriber. Ten of these effects (seven for depression reduction and three for improved QoL) were independent of each other and of self-reported adverse effects and depression severity. While some of these relationships have been identified before, others, such as the amount of information imparted, and beliefs about placebo vs. chemical effects, have not.

Positive findings on the two outcome measures can result from either the therapeutic effect chemically induced by AD drugs or non-specific, non-pharmacological effects or both. Our findings, therefore, are informative whether understood as identifying which factors might be enhancing the pharmacological effects of ADs or seen from the perspective of identifying purely non-pharmacological, psychosocial factors. Some psychosocial variables, such as gender and age, may influence the chemical effects of ADs (see Demographics below). It is harder to see how beliefs, about causes, ADs and placebo effects, or how well one felt understood by the prescriber and how much information was received, might enhance the chemical effects.

The prescriber–patient relationship

In psychotherapy research, including for depression (16), the therapeutic alliance is well established as a strong predictor of positive outcome. This is rarely assessed, however, in drug trials (7). In the current study, the patient–prescriber relationship was a powerful, independent predictor of the perceived efficacy of ADs. Related factors, such as the amount of information conveyed, were also related to a positive outcome. The few studies that have reported on interactions with patients in the process of prescribing ADs tend to adopt a rather narrow medical framework, assuming that the relationship and information are important primarily because they increase adherence to medication [which can be as low as 32% after 3 months (17)], rather than because they can have a direct effect on depression (17–19). A recent study of 43 psychiatrists found that the consultations in which ADs were prescribed lasted an average of 17.5 min, that the most commonly discussed topic was 'medication adherence' and that in none of the 200 meetings was the patient 'given an opportunity to talk' (20).

Beliefs and attitudes

Previous studies in the domain of patients' beliefs – for a range of treatments and problems – have often, understandably, focussed on receiving one's preferred treatment (21) and having positive treatment expectations (22), both of which, perhaps unsurprisingly, are highly predictive of positive outcome with ADs. In the current study, causal

beliefs and low belief in the placebo effect were related to perceived positive outcomes. It should be noted, however, that assessing beliefs or attitudes *after* a view on efficacy has been formed means that the former could have been determined by the latter, rather than vice versa. For example, belief in biogenetic (vs. social) causes and in chemical effects (vs. placebo effects) may operate to enhance perceived efficacy, but may also be increased by a positive outcome, via either pharmacological and/or non-pharmacological effects.

Demographics

The worse depression outcomes for poorer people in the current study have been found fairly consistently (23, 24), with some exceptions (21). The most parsimonious explanation seems to be that the adverse social factors which often precipitate depression, and which are experienced more often by poorer people, also inhibit the effectiveness of ADs because they do not disappear with an AD prescription (23).

Future research might address differential outcomes by gender and age, with a focus on measuring both pharmacological and non-pharmacological effects influencing any differences. For example, in the current study, women were significantly more likely to report both depression reduction and improved QoL (although in the regression analyses the odds ratios – 1.41 and 1.70 respectively – were not statistically significant). Possible biological explanations for gender differences might include ovarian hormones, and menopausal status (25) and body mass at same dosage (which, along with metabolic rate differences, might also partially explain differential response by age). Possible psychosocial variables that could potentially enhance perceived efficacy in women might include better therapeutic relationships. Women in the current study reported a slightly better relationship with the prescriber (1.96 vs. 1.85; $P = 0.03$), but there was no difference in how understood they felt. Women were also more likely to be told about the benefits of ADs (79.0 vs. 73.7%; $P = 0.02$) and more likely to be told what problems they had that would be helped (87.4% vs. 80.8%; $P = 0.001$).

Clinical implications

This is by no means the first study of ADs to suggest that clinicians can influence treatment outcomes via the nature of their interactions with patients (26, 27). A recent systematic review of a wide range of treatments for depression concluded:

> Although the surface features of psychotherapy, antidepressants, exercise and acupuncture are very different, they do result in similar reduction of depressive symptoms and may have the same mechanisms of action. The lack of significant differences between very diverse active treatments suggests that non-specific therapeutic factors may account for a large part of the effectiveness of these depression treatments (6, p. 9).

What are the ramifications of finding so many psychological and social predictors of effectiveness, as experienced by AD recipients, in this and previous studies? Perhaps the most obvious clinical implications, beyond trying to ameliorate the social circumstances driving the depression – such as poverty, emanate from the findings about the relationship with the prescriber and the amount of information provided (which no doubt helps build the relationship). Rather than regarding placebo or 'non-specific' effects as merely an irritating threat to efforts to prove the efficacy of one's favoured treatment, it can be useful to understand them and then enhance them. Making the time (which is not always easy) to explore the patient's view of their problems, including their thoughts about ADs [which are often complex and ambivalent (28)], and about alternative treatments, and their causal beliefs (which may differ from our own) is also important. Another New Zealand study found that GPs often do explore psychosocial causes and consider non-medical treatments but are constrained from making appropriate referrals by the lack of accessible, affordable services (29).

The interpersonal factors in a professional encounter in which a decision about ADs, or any other treatment is being considered, may, for some patients, be more important than the decision itself or the treatment itself. Listening carefully to someone's story, rather than being too concerned about adherence to a single treatment modality, can, it seems, be curative all by itself. Indeed, a recent *British Medical Journal* review of issues relating to diagnosis of, and treatment for, depression (3), concluded:

> High rates of placebo response account for much of the seeming beneficial effects of medication and this should be discussed sensitively with patients, who also need to be made aware of the side-effects, risks and costs associated with ADs. Informing them of the way that drug companies have acted to boost sales of their drugs may also be appropriate. There is still a widely held belief that all depression is "brain disease" caused by chemical

imbalance which can be "corrected" by pills, and countering it is important by noting the relevance of life circumstances.

This focus on social factors is consistent with a recent call for the adoption of a public health approach to the prevention and alleviation of depression (30).

Limitations

This self-selected, convenience sample, despite being the largest ever surveyed, was not, in some regards, representative of the New Zealand population. Maori, Pacific Islanders, men, older people, and poorer and less educated people were all under-represented. The over-representation of women (77%) is not of great concern because women are prescribed ADs at approximately twice the rate as men internationally. Although an internet sample may be biased towards the more wealthy and better educated, 80% of New Zealand households have internet access. The use of the internet does, however, introduce the possibility that people who are disgruntled with their treatment may be over-represented. This seems unlikely, however, given that the majority (83%) reported that they believed the drugs had reduced their depression, a rate far higher than most conventional efficacy studies of ADs.

The study relied on self-report. Conventional studies, however, also rely, to varying degree, on self-report. One concern is that some of the data are retrospective and therefore subject to the fallibilities of memory of experiences from weeks to several years in the past. The majority (69%), however, were still taking the ADs at the time of completing the questionnaire.

It is difficult to draw firm conclusions about the meaning of some of the findings, including about causality, or the direction thereof. For example, the relationship between positive attitudes to ADs and positive outcome, if causal, could have been in either direction, or both. Therefore, prospective studies are essential.

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