PATIENT-CENTREDNESS IN A BLACK TOWNSHIP

A prospective study amongst the private general practitioners in Ga-Rankuwa, South Africa

ABSTRACT/SUMMARY

Purpose: The purposes of this study were to assess the degree to which a patient-centred approach is used by the private general practitioners in the black township where we practise and to test both its short and long term effectiveness. We postulated that patient-centredness would be positively associated with:

- (i) patients feeling understood;
- (ii) patient satisfaction;
- (iii) symptom resolution;
- (iv) concern resolution; and
- (v) the long term control of hypertension, diabetes mellitus and asthma.

Method: The study was conducted in Ga-Rankuwa. South Africa, a large black township, northwest of Pretoria. A random sample of 10 private general practitioners was chosen. Eligible patients were all those over 16 years who presented with a symptom or one of the three target conditions. Patient-centredness was scored in terms of the doctor's facilitation of the patient's reasons for coming, including symptoms, thoughts, feelings and expectations, from an audio-tape of the entire consultation. Post-consultation interviews were conducted to assess the immediate patient outcomes. Follow-up during the next 12 months was planned in order to assess the long-term outcomes, but this was circumvented by failure to obtain sufficient patients with the targeted chronic conditions.

Results: Seven general practitioners conducted 167 consultations for a patient response rate of 94%, of which 154 of the audio-tapes were of sufficient sound quality to be scored. The mode, median and mean of the patient-centred scores were 1.00, 1.25 and 1.40 respectively out of a total possible of 3.00. Only four of the consultations scored high enough to be considered patient-centred. None of the immediate patient outcomes was found to be associated with the level of patient-centredness present in the consultations studied. Only six patients had hypertension, diabetes mellitus or asthma.

Conclusion: The degree to which a patientcentred approach is practised by the private general practitioners in Ga-Rankuwa township is low. Half measures with

Henbest RJ, Dept of Family Medicine, PO Box 222, MEDUNSA 0204 (Research Team: Henbest R, Malete N, McLeod E, Pitse E, Lepule R) respect to patient-centredness would seem not to be of value; rather, it would seem that patient-centredness is only effective once a reasonably high level of skill has been reached. Further research into the long term effectiveness of a patient-centred approach is required.

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"Patient-centredness in the consultation has been shown to be associated with a variety of improved patient outcomes, including increased patient satisfaction, compliance, patients feeling understood and symptom and concern resolution..."

The importance of the doctor-patient relationship has been increasingly recognized during the latter half of this century and the need to demonstrate a relationship between the process of care and patient outcomes has been emphasized^{4,5}. One of the key concepts to emerge has been that of patient-centred care^{6,7,8}.

Patient-centredness in the consultation has been shown to be associated with a variety of improved patient outcomes, including increased patient satisfaction^{9,10}, compliance^{9,10}, patients feeling understood¹¹, symptom and concern resolution¹¹, blood pressure control^{12,13}, diabetes control^{12,13}, peptic ulcer resolution¹³ and headache resolution¹⁴ in the relatively affluent West. One study has also demonstrated the effectiveness of a patient-centred approach with respect to short-term patient outcomes amongst non-Western poor attending state health services¹⁵.

The purposes of this study were to assess the degree to which a patient-centred approach was used by the private general practitioners in the black township where we practise and to test both its short and long term effectiveness. We postulated that patient-centredness would be positively associated with:

- (i) patients feeling understood;
- (ii) patient satisfaction;
- (iii) symptom resolution;
- (iv) concern resolution; and
- (v) the long term control of hypertension, diabetes mellitus and asthma.

METHOD

Background and setting

Originally, we had planned to start this research in 1993 in Soshanguve, a large black township 30 kilometres north of Pretoria, with a three-year grant from the Medical Research Council (MRC) of South Africa. Soshanguve had been chosen because we were familiar with the township. The Department of Family Medicine of Medunsa/Ga-Rankuwa Hospital had been involved in patient care in Soshanguve for about 15 years, had a fulltime community-based teaching practice there since 1986 and a number of our nursing staff lived there. However, 1993 and 1994 saw a lot of changes in South Africa. One that affected this research was that it was decided by Government that Soshanguve would not be part of the Medunsa Academic Complex. This meant that the posts required to continue to provide a service in Soshanguve would not be forthcoming. By 1994 it seemed likely that we would have the opportunity to become community-based in Ga-Rankuwa, a large black township, 32 kilometres northwest of Pretoria, where most of our hospital patients came from. Although we would cross provincial borders, at least they would not be as formidable as the previous international ones, when Ga-Rankuwa township was part of the former independent homeland of Bophuthatswana (which means the lands which bind the Tswana speaking people together). The MRC gave us a three-year extension to do the project in Ga-Rankuwa.

Study design and data collection

The design was that of a prospective follow-up study. The entire consultation was audio-taped and later scored for patientcentredness by an independent rater. Immediately following the consultation, patients were interviewed in their language of choice, using a structured questionnaire by one of three interviewers, in order to provide demographic data and to determine the immediate patient outcomes. At the same time, the entire patient's chart was reviewed by an independent member of the research team, using forms specifically designed for recording the patient's history and management of hypertension, diabetes mellitus and asthma, in order to assess the long term outcomes. Patients and their families were then to be followed up four times during the next 12 months to further determine the long term patient outcomes, but this was not done, as described below under *Sample*.

An attempt was made to reduce possible bias by ensuring that the interviewers and the chart reviewer did not observe or listen to the tapes of the consultations and were blind to the scoring of the tapes for patientcentredness and by having the doctors unaware of the hypotheses of the study so that they were not influenced to direct their behaviour in any particular way.

Patient-centredness:

Definition and measurement

Patient-centred care was defined operationally as care in which the doctor responds to the patient in such a way as to facilitate the patient's expression of all of his or her reasons for coming, including symptoms, thoughts, feelings and expectations.

A patient-centred score ranging from 0.00 to 3.00 was determined from the audio-tape of each consultation in terms of the doctor's responses to the patient's offers. The doctor's response was scored as 0 if the offer was ignored, as 1 if only closed responses were used, as 2 if openended responses were given and as 3 if expression of the patient's thoughts, feelings or expectations was specifically facilitated. The final score for the consultation was calculated by taking the highest score achieved for each offer, summing them and then dividing by the number of offers. This method has been shown to be valid, reliable, sensitive and practical¹⁶. A single scorer scored each consultation in its entirety.

Sample: practitioners and patients

A random sample of 10 of the 19 general practitioners in Ga-Rankuwa township at the time of the study was asked to participate. All patients over the age of 16 years presenting to their practitioner with either a new symptom (to be able to assess symptom and concern resolution) or with one of the three target conditions (hypertension, diabetes mellitus or asthma) were asked to take part. In order to demonstrate clinical differences of 20% with respect to each of the three target groups, 240 patients were required¹⁷. We aimed at having at least 10 practitioners with 25 patients per practitioner. When it became clear that we would not be able to gain anywhere near a sufficient number of patients in any of the three target groups required to test the fifth hypothesis, we stopped the data collection once we had sufficient patients to test the first four hypotheses.





Practitioner	n	Minimum	Maximum	Mean	SD	Median	Mode
1	26	0.50	2.00	1.29	0.45	1.00	1.00
2	21	0.67	3.00	1.56	0.53	1.50	2.00
3	26	1.00	2.00	1.49	0.47	1.50	1.00
4	28	1.00	3.00	1.34	0.54	1.00	1.00
5	24	0.67	2.00	1.50	0.46	1.50	2.00
6	26	1.00	2.00	1.25	0.34	1.00	1.00
7	3	1.00	2.00	1.33	0.58	1.00	1.00
Total	154						
Kruskall-Walli	is H =	10.658 df = 6	p = 0.099				

Table I: The patient-centred score and the practitioners

Patient-cen	tred	Percentage of patients who:		had symptom	had concern
score	n	understood	satisfied	resolution	resolution
0.00-1.00	73	40%	40%	58%	57%
1.01-2.00	40	35%	32%	37%	40%
2.00-3.00	41	32%	54%	40%	60%
Total	154				
Chi-square		0.77	3.96	5.64	3.88
Df		2	2	2	2
Р		0.679	0.138	0.059	0.143

Table II: The relationship between the patient-centred score and the patient outcomes

Analysis

The data were analyzed using the EPI 6 statistics programmes, primarily using the Chisquare test and the Kruskal-Wallis (K-W H) one-way analysis of variance. The results were controlled for a number of patient variables (age, gender, marital status, level of education and home language) and practice variables (the practitioner, use of interpreters, duration of the doctor-patient relationship, frequency of contact, whether the patient had seen his regular doctor and the duration of the consultation).

RESULTS

Patient, practitioner and practice characteristics

Of the 178 patients asked to take part in the study, 11 refused because they did not want to be late for work, so that 167 patients participated for a response rate of 94%. All of the interview forms and chart abstract forms were complete, but 16 of the audio-tapes were of inadequate sound quality for scoring for patient centredness, so that we had a complete data set for 154 (86%) of the participants. Very few patients had any of the three target conditions: five with hypertension, one with diabetes and none with asthma.

The ages of the patients ranged from 16 to 79 years with a mean of 36 years. Sixty percent were female and 57% were married (38% never married, 3% widowed, 1% divorced). A range of educational levels was present, with 11% not having completed primary school, 29% having completed primary school, 40% having completed high school and 20% having completed further education.

Patient-centred score and:	Kruskall-Wallis H	df	р
Age	5.15	3	0.161
Gender	0.11	2	0.946
Marital status	2.33	2	0.311
Level of education	1.254	3	0.7400
Language spoken at home	0.004	1	0.9485

Table III: The relationship between the patient-centred score and patient characteristicsn=154

Of the 10 general practitioners asked to participate, two could not be found, eight agreed to participate, but one eventually did not, leaving seven. Six of these doctors conducted between 21 and 32 consultations each. The seventh withdrew after five consultations, stating that his patients were not keen. Of the seven doctors who took part, six were solo practitioners, the other was a group practice consisting of four doctors of whom the three female partners took part. Only one of the solo practitioners was female. All were local Black South African doctors, except one Ugandan, who was the only one to have post-graduate training in family practice. The doctors had been in practice between two and 15 years.

None of the consultations involved an interpreter. About one third (34%) of the consultations were first visits. Another third (35%) were second, third or fourth visits. The remaining one third (31%) had seen their doctor at least five times and the maximum recorded was 18 times. Ninety-three percent said that they had a regular doctor and 72% stated that the doctor seen at the time of the study was their regular doctor. The consultations ranged from 1.0 to 10.8 minutes in length, with an average length of 3.6 minutes.

The patient-centred score

The patient-centred scores of the consultations ranged from 0.50 to 3.00. The distribution is shown in Figure 1. The mode, median and mean were 1.00, 1.25 and 1.40 respectively, with 25th and 75th percentiles of 1.00 and 2.00. The intra-rater reliability on 21 tapes scored independently six months apart was high (r=0.88). A total of 318 offers were recorded from the 154 audio-tapes scored, for an average of 2.06 offers per consultation. The patientcentred scores for the seven practitioners are shown in Table I.

Reasons for coming

393 reasons for attending were reported by patients during the 167 post-consultation interviews for an average of 2.35 reasons per consultation. The commonest reasons for attending were symptoms (76%), followed by specific expectations (19%), worries (4%) and problems of living (1%). A range of 40 different symptoms was presented. Worries were mainly a fear of having something seriously wrong such as cancer. Expectations included tablets, injections, sutures, xrays, pain relief, blood pressure checks, circumcisions, referrals, pap tests, preg-

Patient-centred score and:	Kruskall-Wallis H	df	р
Practitioner	10.658	6	0.099
Duration of relationship	1.410	3	0.703
Frequency of contact	0.377	2	0.828
Regular doctor	0.027	1	0.868
Duration of consultation	1.080	2	0.582

Table IV: The relationship between the patient-centred score and practice characteristicsn=154

Patient- characteristic	Percentage of 1 felt really understood	oatients who: were very satisfied	had symptom resolution	had concern resolution
n				
Age (years)				
16-25 34	37	44	63	59
26-35 43	31	54	46	63
36-45 43	36	32	42	39
46-79 34	50	25	52	58
Chi-square	3 27	8 26	2 /2	5 59
Df	2	2	2	2.30
DI	0 252) 0.0/1*	D 220) 0.124
г	0.552	0.041	0.550	0.154
Gender				
Male 61	30	39	38	52
Female 93	43	40	57	56
Chi-square (Yates)	2.06	0.06	4.43	0.14
P	0.151	0.962	0.035*	0.708
-		0.,01	00000	0.700
Marital Status				
Married 87	39	38	50	55
Never Married 60	33	47	50	57
Widowed/	<i>c</i> - 7	0	42	20
Divorced /	5/	0	45	29
Chi-square	1.73	0.66	0.14	2.51
Df	2	1	2	2
Р	0.42	0.42	0.93	0.36
Education				
Primary or less 58	32	25	47	50
Secondary 62	34	44	1/	54
Further 24	56	61	44	54
runner 94	50	01	00	54
Chi-square	6.08	12.21	4.27	1.33
Df	2	2	2	2
Р	0.047*	0.002*	0.118	0.514
Language				
Tswana 140	38	41	52	56
Other 14	39	25	31	44
	57		51	
Chi-square (Yates)	0.02	0.99	1.68	0.41
P	0.881	0.320	0.195	0.524

* Indicates p values that are signficant at the 0.05 level

Table V: The relationship between the patient characteristics and patient outcomes n=154

nancy tests and follow-up for conditions such as hypertension, diabetes mellitus, antenatal care and tuberculosis. Problems of living included unwanted pregnancy and sexual/marital problems. The main reason for coming was usually a symptom (79%), frequently an expectation (20%) and much less often a worry or a problem of living (1%).

Tests of the four hypotheses: the relationship between patient-centredness and patient outcomes *Patients feeling understood*

All patients either agreed (62%) or strongly agreed (38%) with the statement, "I really felt understood by this doctor." As shown in Table II, an association was not found between the patient-centred score

Patient- characteristic	Pe fe	ercentage of It really nderstood	f patients who: were very satisfied	had symptom resolution	had concern resolution
	n		outorieu	100010000	
Practitioner					
1	26	62	64	76	56
2	21	62	37	37	47
3	26	36	48	52	60
4	28	31	17	28	36
5	24	25	32	41	48
6	26	27	39	52	70
Chi-square		15.33	12.95	13.70	6.57
Df		5	5	5	5
Р		0.009*	0.023*	0.017*	0.259
Duration of rela	ationsk	bip			
Less than 1 yr	41	36	33	55	55
1 to 2 years	43	28	45	51	58
3 to 4 years	35	36	35	46	54
More than 4 yrs	35	54	46	46	48
Chi-square		6.31	1.91	0.94	0.75
Df		3	3	3	3
Р		0.097	0.590	0.814	0.861
Frequency of co	ntact ((during past	12 months)		
Once	52	42	35	52	48
2 to 4 times	54	41	46	57	59
5 or more times	48	29	37	39	57
Chi-square		2.18	1.46	3.21	1.32
Df		2	2	2	2
Р		0.335	0.481	0.201	0.515
Regular doctor					
Yes	112	39	43	48	54
No	42	35	30	55	55
Chi-square (Yate	s)	0.09	1.59	0.37	0.01
Р		0.760	0.206	0.545	0.927

* Indicates p values that are significant at the 0.05 level

Table VI: The relationship between the practice characteristics and patient outcomes n=154

and patients feeling understood. Asked about how well their doctor understood the importance of their main reason for coming, 50% said 'very well', 45% said 'well' and 5% said 'somewhat' or 'not at all well'. The mean patient-centred score was lower for the consultations of the patients who reported that their main reason was only 'somewhat' understood, rather than 'well' or 'very well' understood, but not statistically significantly so (mean patient-centred scores of 1.167, 1.354 and 1.459 respectively, K-W H =2.987 df=2 p=0.2245).

Patient satisfaction

Patient satisfaction was approached in three ways. Patients were asked how satisfied they were with the discussion of each of their reasons for coming, how satisfied they were with what was done about each one and were also asked, "Overall, how well did the doctor deal with (this reason for coming)?" Overall, patients were satisfied with their care. For example, with respect to satisfaction with discussion of "Half measures with respect to patient-centredness would seem not to be of value; rather, it would seem that patient-centredness is only effective once a reasonably high level of skill has been reached..."

their main symptom: 19% were 'very satisfied', 75% were 'satisfied', and 5% 'somewhat' or 'not at all satisfied'. With respect to satisfaction about what the doctor did or said about their main symptom: 52% were 'very satisfied', 30% were 'satisfied' and 18% were only 'somewhat' or 'not at all satisfied'. The third measure was "Overall, how well did the doctor deal with this problem?" Again, for their main symptom 40% stated 'very well', 53% said 'well' and 7% said 'somewhat' or 'not at all well'. No associations were found between the patient-centred score and the various measure of patient satisfaction. Table II shows the relationship between the patient-centred score and how well the patient thought the doctor had dealt with his or her main symptom.

Symptom resolution

Ninety percent of the patients presented with a symptom. Of these, almost all stated that they had either 'a great deal' (69%) or 'a fair amount' (26%) of discomfort prior to seeing the doctor and only a few had 'a little' (3%) or 'none' (1%). When asked, "At this time, after seeing the doctor, is the discomfort that you have: worse, about the same, better, much better?" 3% said worse, 48% said about the same, 49% said better. As shown in Table II, those who had had the least patient-centred consultations were somewhat more likely to report symptom resolution.

Concern resolution

At the post-consultation interview, patients were asked, "Before seeing the doctor, how worried were you that (your problem) might be something serious?" Most said 'very worried' (60%) or 'a fair amount worried' (30%); only a few said 'a little' (9%) and only one patient said 'not at all worried'. When asked, "At this time after seeing the doctor, how worried are you that (your problem) might be something serious?" 3% said 'more worried', 42% said 'about the same amount', 43% said 'less worried' and 11% said 'much less worried'. As shown in Table II, the relationship between the patient-centred score and concern resolution was not significant.

The relationship between the patient-centred score and patient and practice characteristics

Table III shows that there were no significant associations between the patient-centred score and the patient characteristics listed. The only small difference found was with respect to marital status, in that 43% of those widowed or divorced had experienced a more highly patient-centred consultation compared with only 29% of those who were married or had never been married. There were only seven in this group, so this difference was not statistically significant.

Table IV shows that practitioner/practice characteristic found to have an association approaching significance with the patient-centred score was the practitioner. Of note, consultations scoring higher for patient-centredness did not take longer than those scoring lower.

The relationship between patient outcomes and patient and practice characteristics

As shown in Table V, age, gender and level of education were associated with patient outcomes. Younger patients were more

likely to be satisfied, female patients were more likely to report symptom resolution and patients with further education were more likely to feel understood and to be satisfied.

As shown in Table VI, practitioners 1 and 2 were more likely than the other practitioners to have patients report feeling understood. Practitioner 1 was also more likely to have patients report satisfaction and symptom resolution. A greater percentage of patients who had seen their doctor for more than four years reported feeling understood than the other patients, but the difference failed to reach statistical significance.

Controlling the analysis for the individual practitioner did not reveal any new associations between the patient-centred score and patient outcomes.

DISCUSSION The sample

The sample

The random sample, comprising a sizeable proportion of all of the doctors in private general practice in Ga-Rankuwa at the time of the study, is likely to make these results representative of private general practice in the township. Three things particularly struck us about the resultant patient sample.

The first was its relatively high level of education. A much larger percentage of this sample had completed high school and had obtained further education than reported in a previous study involving much the same population, but a different sample, patients attending state practitioners⁹. This finding would be in keeping with the understanding that those with higher education are more likely to have jobs, higher paying jobs or jobs with medical aid and thus are more likely to attend private doctors than the state health services, which do not cater for private patients.

The second point was that patients with hypertension, diabetes mellitus and asthma are not obtaining their care from the private doctors in the township. The third thing was that most of these patients had a regular doctor and were seeing that doctor at the time of the study. This contradicts the common complaint by doctors in the township that their patients continually 'doctor-shop,' making continuity of care impossible.

Patient-centredness in Ga-Rankuwa township

The distribution of the patient-centred scores shows a lack of patient-centredness in general practice in Ga-Rankuwa.

Almost half of the consultations (47%) were given a patient-centred score of one or less, indicating that these consultations consisted of almost entirely closed responses by the doctor. Only four of the consultations received scores greater than two; that is, scores that would indicate that the doctor had specifically facilitated the patient's expression of thoughts, feelings or expectations. Only scores of 2.5 or above indicate truly



patient-centred consultations where this happens at least half of the time. Thus the patients in this study seldom had their worlds entered into⁶.

The finding of such a low frequency of patient-centred consultations was somewhat surprising given that the private doctors, compared with their state colleagues, sometimes pride themselves on their doctor-patient relationships. A study involving mainly state-employed practitioners in South Africa found a half of the scores were two or higher and 26% of the scores were 2.5 or greater⁹. However, this may point to the importance of post-graduate training in family medicine, as several of the doctors in the previous study had had family medicine training, whereas only one doctor in the present study had.

The relationship between patient-centredness and patient outcomes

We think that the failure to demonstrate significant relationships between patientcentredness and patient outcomes in this study is most likely due to the very few truly patient-centred consultations present.

Previous studies^{8,9} have shown a positive relationship between the same patientcentred score used in this study and the same patient outcomes, but mainly for those consultations scoring higher than 2, with the best results for those scoring 2.50 to 3.00. We lacked consultations with these scores in this study. In addition, those studies showed a dip in the results for consultations receiving intermediate patient-centred scores. For example, it was found that the percentage of patients who had their main symptom resolved was 54% if they had received a closed response to their main symptom (scored as a 1), 31% if they had received an open response (scored as a 2) and 75% if they had had their thoughts, feelings or expectations about their main symptom explored (scored as a 3)8. This study shows a similar result (consider Table II) in that 40 to 58% of patients who had consultations scored as a 1 have a positive outcome, followed by a dip for those consultations scored as 2 or thereabouts. There was no top quartile of consultations present with scores above 2.5 (see Figure 1) to be able to really test

the effectiveness of patient-centred consultations.

Conclusion

The degree to which a patient-centred approach is practised by the private general practitioners in Ga-Rankuwa township is low. Half measures with respect to patient-centredness would seem not to be of value; rather, it would seem that patient-centredness is only effective once a reasonably high level of skill has been reached. Further research into the long term effectiveness of a patient-centred approach is required.

References

- Balint M. The doctor, his patient and the illness. 2nd ed. London: Pitman Medical, 1964.
- Hodson M. Doctors and patients: a relationship examined. London: Hodder and Stoughton, 1967.
- Pendleton D, Hasler J. Editors. *Doctor-patient* communication. London: Academic Press, 1983.
- Barro AR. Survey and evaluation of approaches to physician performance measurement. J Med Educ 1973;489(suppl):1047-93.
- Bass MJ, Buck C, Turner L. Primary care physician actions influencing patient outcomes. Final report of OM 697 to the Ontario Ministry of Health. The University of Western Ontario, London, Ontario, 1984.
- Levenstein JH, McCracken EC, McWhinney IR, Stewart MA, Brown JB. The patient-centered clinical method. 1. A model for the doctorpatient interaction in family medicine. Fam Pract 1986;3:24-30.
- Weston WW, Brown JB, Stewart MA. Patientcentred interviewing. Part 1: Understanding patients' experiences. Can Fam Physician 1989;35:147-151.
- 8. Henbest RJ. *Patient-centred care: a review of the concept.* S Afr Fam Pract 1989; 10:454-463.
- Francis V, Korsch BM, Morris MJ. Gaps in doctor-patient communication. Patients' response to medical advice. N Engl J Med 1969;280:535-40.
- 10. Stewart MA. What is a successful doctorpatient interview? A study of interactions and outcomes. Soc Sci Med 1984;19:167-75.
- 11. Henbest RJ, Stewart MA. Patient-centredness in the consultation. 2. Does it really make a difference? Family Practice 1990;7:28-33.
- Greenfield S, Kaplan SH, Ware JE. Patient participation in medical care: effects on blood sugar and quality of life in diabetes. J Gen Int Med 1988;3:448-457.
- 13. Greenfield S, Kaplan S, Ware J. *Expanding involvement in care; effect on patient out comes.* Ann Int Med 1985;102:502-28.
- 14. The Headache Study Group. *Predictors of outcome in headache patients presenting to family physicians a one year prospective study.* Headache 1986;26:285-294.
- Henbest RJ, Fehrsen GS. Patient-centredness: Is it applicable outside the west? Its measurement and effect on outcomes. Family Practice 1992;9:311-317.
- Henbest RJ, Stewart MA. Patient-centredness in the consultation. 1. A method for measurement. Family Practice 1989;6:249-254.
- 17. Donner A. *Approaches to sample size estimation in the design of clinical trial. A review.* Stat Med 1984;3:199-214.