

Profiling patient attitudes to phosphate binding medication: a route to personalising treatment and adherence support

¹Angel Marie Chater, ¹Rhian Parham, ²Steve Riley, ³Alastair J. Hutchison & ¹Rob Horne*

¹Centre for Behavioural Medicine, UCL School of Pharmacy, University College London

e-mail: a.chater@ucl.ac.uk, tel: 0207 8741273

e-mail: rhi_parham@hotmail.com, tel: 0207 8741273

e-mail: r.horne@ucl.ac.uk, tel: 0207 874 1293

²School of Medicine, Cardiff University, University Hospital of Wales, Cardiff

e-mail: rileysg@cf.ac.uk, tel: 02920742702

³Renal Unit, Manchester Royal Infirmary, Manchester Academic Health Sciences Centre, Central Manchester University Hospitals NHS Trust, Manchester M13 9WL

e-mail: Alastair.Hutchison@cmft.nhs.uk, tel: 0161 276 4488

*Corresponding Author: Professor Rob Horne, Director, Centre for Behavioural Medicine, Department of Policy & Practice, UCL School of Pharmacy, University College London, Mezzanine Floor, BMA House, Tavistock Square, London WC1H 9JP.

Email: r.horne@ucl.ac.uk

Tel: + 44 (0) 207 874 1293

Conflicts of interest: No conflict of interest has been declared by the authors.

Word count: 5864 (4117 excluding abstract and references)

ATTITUDES TO PBM

ABSTRACT

Objective: Nonadherence to phosphate binding medication (PBM) compromises the efficacy of treatment for chronic kidney disease (CKD), but its causes are poorly understood. This study sought to explore patient attitudes towards PBM and to evaluate the utility of the Necessity-Concerns Framework for understanding adherence to PBM. **Design:** A sample of two hundred and twenty-one dialysis patients currently prescribed PBM were surveyed from eight UK renal units. **Main Outcome Measures:** Demographic data and clinical information, alongside the Beliefs about Medication Questionnaire (BMQ) and the Medication Adherence Report Scale (MARS) were reported. **Results:** Low adherence to PBM was predicted by reduced beliefs in personal need for PBM (OR = .34; 95% CI: .14-.83; $p < .05$), and increased concerns about PBM (OR = 3.17; 95% CI: 1.87-5.37; $p < .001$). Patients were categorised into attitudinal groups based on their beliefs about PBM and being 'skeptical' of PBM (low necessity beliefs, high concerns) was most associated with low adherence. **Conclusion:** Strategies to improve adherence to PBM should aim to elicit and address patients' beliefs about their personal need for PBM and their concerns about this medication.

KEYWORDS

Beliefs, chronic kidney disease, nonadherence, phosphate binding medication, attitudes

INTRODUCTION

As renal function worsens in patients with chronic kidney disease (CKD), excess dietary phosphate contributes to increased serum phosphate levels (Almirall and Valenzuela, 2006; Delmez and Slatopolsky, 1992; Isakova, et al., 2009). Hyperphosphataemia in individuals with end stage renal disease (ESRD) has been associated with secondary hyperparathyroidism, renal osteodystrophy and increased risk of cardiovascular mortality (Almirall and Valenzuela, 2006; Savica et al., 2006; Thompson et al., 1994). Despite being an important goal of treatment in CKD, control of serum phosphate is often inadequate, partly due to poor adherence to phosphate binding medication (PBM) (Bame et al., 1993; Curtin et al., 1999; Delmez and Slatopolsky, 1992). PBM are used to reduce the absorption of phosphate in the blood by binding to it in the gastrointestinal tract. They are, therefore, usually required to be taken when eating to bind to any phosphate that may be present in ingested food. The treatment regime is often complex, with a high pill burden and unpleasant side effects and there may be no noticeable effect on symptoms (Karamanidou et al., 2008). This can be linked to the treatment regimes of other chronic illnesses such as HIV, where complex treatment regime, pill burden and treatment beliefs are often barriers to adherence (Mills et al., 2006). A systematic review of studies investigating the prevalence and causes of nonadherence to PBM (Karamanidou et al., 2008) revealed that reports of nonadherence to PBM range from 22-74%, and that associations between demographic and clinical factors and nonadherence to PBM are limited, with younger age being the only consistent predictor of poor adherence to PBM (Bame et al., 1993; Boyer et al., 1990; Horne et al., 2001). A further finding of this review was that whilst psychosocial predictors of adherence (e.g. patients' beliefs about medicines) have been less frequently assessed in the context of renal disease, significant associations with adherence often result when their effects are considered

ATTITUDES TO PBM

(Karamanidou et al., 2008). These findings are consistent with reviews of adherence in other chronic illnesses (Horne et al., 2006; World Health Organization, 2003) which suggest that nonadherence is best understood as a variable behaviour rather than a fixed characteristic with multifactorial components that can change over time (Kane & Robinson, 2010). The key to developing more effective methods for improving adherence may, therefore, lie in understanding the factors which influence medication-taking behaviour from the patients' perspective.

Over the last decade, new theories attempting to explain medication nonadherence and inform interventions to help patients get the best from their medicines have emerged, including the Perceptions and Practicalities Approach (Horne, 2001). There is hence a continuing need for innovative approaches, informed by theories of adherence behaviour (Campbell et al., 2007; Haynes et al., 2005; Horne et al., 2006).

While there are many causes of treatment nonadherence, these can be theoretically categorized as intentional or unintentional. Unintentional nonadherence occurs when an individual wants to follow treatment recommendations but is prevented from doing so by barriers such as poor comprehension, difficulties administering doses, restricted access to medication or because they simply forget to take it; these *practical* barriers to adherence, therefore, represent limitations in capacity and resources that affect an individual's ability to take a medication. Intentional nonadherence occurs, however, when an individual decides not to start treatment, to stop taking medication, or chooses to take it in a way which differs from the prescriber's recommendations. To understand intentional nonadherence, *perceptual* factors such as the beliefs, attitudes and preferences which influence a patient's motivation to start and continue with treatment need to be examined. However, there is most certainly an

ATTITUDES TO PBM

overlap between these two concepts of perceptual and practical barriers (for example, one may perceive a barrier when they are less motivated to take their medication, which could perhaps be overcome if they felt the treatment was necessary). Therefore, understanding these concepts together is important to support the development of interventions to facilitate adherence that can be tailored to address the practical and perceptual barriers unique to an individual, with a view that ‘one size does not fit all’ and a need for more personalized treatment approaches.

The application of this approach in adherence interventions, which can be easily applied in practice, requires a simple framework for conceptualising and capturing patients’ attitudes to medication and identifying the salient beliefs that influence adherence to medication. The Necessities-Concerns Framework (NCF; Horne and Weinman, 1999) posits that adherence decisions are influenced by beliefs about the *necessity* of a medication for maintaining or improving one’s health, and *concerns* about the potential adverse effects of adhering to a prescribed treatment. The utility of the NCF in explaining adherence to treatment has been shown in a variety of chronic illness groups including HIV (Horne et al., 2004, Horne et al., 2007), cardiovascular disease (Horne and Weinman, 1999), asthma (Horne and Weinman, 2002), depression (Aikens et al., 2005; Hunot et al., 2007), and inflammatory bowel disease (Horne et al., 2009). While associations between treatment beliefs and nonadherence have previously been explored in the context of renal disease (Butler et al., 2004; Horne et al., 2001), there is an overall paucity of research exploring the beliefs that patients with CKD hold specifically about phosphate binding agents, and the role of these beliefs in adherence behaviour. A recent study by Wileman et al (2011), however, reported from a sample of 76 patients, an association between beliefs held specifically about PBM and nonadherence, whereby doubts about personal need for PBM were associated with self-reported intentional

ATTITUDES TO PBM

nonadherence to PBM and increased concerns about PBM were associated with higher serum phosphate levels. The present study adds to this evidence by investigating a larger sample, providing sufficient power to reveal potential associations regarding dialysis patients' beliefs about PBM (perceived need for PBM, concerns about PBM), and the role of such beliefs in adherence to PBM, using a measure of both intentional and unintentional nonadherence to PBM in an attempt to profile their attitudes towards their medication. This type of attitudinal profiling will identify the characteristics of those who are *most* at risk of overall nonadherence.

DESIGN

Procedure

This cross-sectional survey was part of a routine service evaluation conducted across eight UK renal units (Parham et al., 2009). A convenience sample was used; during a one week period, audit questionnaires were distributed by nursing staff to evaluate the experiences of patients who were prescribed PBM. Patients were approached by a nurse while waiting to go onto dialysis (in the waiting room) and those who consented were asked to complete the survey.

Measures

Demographic and Clinical Details

Data was extracted on patients' age, gender, ethnicity, and level of education. The product(s) that they were currently taking as a PBM and approximately how many tablets they took per

ATTITUDES TO PBM

day was also noted. Length of time on dialysis, and the dialysis modality that they were currently receiving (peritoneal dialysis or haemodialysis) was also reported.

Beliefs about Medication

Patients' beliefs about PBM were assessed using the Beliefs about Medicines Questionnaire (BMQ; Horne et al., 1999), which has been previously validated in renal patients (Horne & Weinman, 1999). The BMQ comprises two sub-scales assessing patients' beliefs about the *necessity* of prescribed medication for controlling their illness (11 items; Cronbach's $\alpha = .80$), and *concerns* about the potential adverse consequences of taking it (9 items; Cronbach's $\alpha = .87$). An example item from the necessity scale is "My health at present depends on this medicine" while an example item from the concerns scale includes "I sometimes worry about becoming too dependent on this medicine". Respondents indicate their degree of agreement with each individual statement on a 1-5 point Likert scale, ranging from strongly disagree to strongly agree. A mean score for each of the two sub-scales is computed, giving a score ranging from 1-5 for both the necessity and the concerns scales. The BMQ used in the present study included additional PBM-specific items (e.g. "This medicine will effectively control my phosphate levels").

Adherence to Phosphate Binding Medication

Adherence to PBM was measured using the Medication Adherence Report Scale (MARS; Horne, 1997). The MARS is a 5-item self-report measure which has been validated against electronic adherence monitors (Cohen et al., 2008) and has demonstrated good psychometric qualities in a range of illnesses (George et al., 2005; Horne and Weinman, 2002; Mardby et al., 2007). Respondents indicate how often they engage in each of five nonadherent behaviours (e.g. "I take less than instructed") on a 1–5 point Likert scale ranging from always

ATTITUDES TO PBM

to never. The MARS used in the present study included two phosphate-binder specific items, making this a 7-item MARS (Cronbach's $\alpha = .83$). Scores for each MARS item were summed to give a total score ranging from 7 to 35, with higher scores indicative of higher levels of adherence. The MARS data was analysed in two ways. To examine the potential distinction between intentional and unintentional nonadherence, two sub-categories were created. An example question from the intentional category includes; "I decide to miss a dose" and from the unintentional category includes; "I forget to take them". Based on the distribution of scores, cut-off points were generated for intentional, unintentional and overall adherence. Due to the positively skewed nature of adherence scores, the mean score was taken as cut off points for unintentional (12), intentional (18) and overall (28) adherence, which were then used to classify patients into high and low adherence groups.

RESULTS

Patients

Data was extracted from two hundred and twenty-one questionnaires. The demographic and clinical details of the sample are shown in Table 1. Just over half of the sample were male (52%) with a mean age of 58 years ($SD = 14.24$; $n = 12$ age not stated); the vast majority of patients in this sample were Caucasian (82%). Nearly a half of the sample had been educated past high school level, with 24% educated through further education and 18% through higher education. The mean time on dialysis was 52 months (4 years, 4 months); 23% of patients had been on dialysis for up to one year, while 15% had been on dialysis for more than 10 years. The majority of patients were receiving haemodialysis (80%). Sevelamer hydrochloride

ATTITUDES TO PBM

and calcium carbonate were the most commonly prescribed PBM types (54% and 45% respectively).

TABLE 1 HERE

Beliefs held about phosphate binding medication (necessity, concerns)

In terms of necessity for medicine, a third of respondents (28%) scored below the scale midpoint for the necessity scale (i.e. <3 out of a range of 1-5), indicative of lower beliefs in the need for PBM. Over half (54%) of the patients did not agree that without PBM they would be very ill, 41% did not endorse the role of PBM in their future health, and a third of the sample (32%) harboured doubts about the efficacy of PBM in the control of phosphate. A similar number (31%) expressed doubt or uncertainty about their understanding of why they needed to manage their phosphate levels (see Figure 1).

FIGURE 1 HERE

A third of respondents (29%) scored above the scale midpoint for the concerns, indicative of increased concerns about PBM. Figure 2 provides a profile of the concerns held about PBM amongst the sample. Most prevalent were concerns about the long-term effects of PBM (39%); with a fifth of patients (22%) experiencing unpleasant side effects of PBM.

FIGURE 2 HERE

Adherence to PBM

ATTITUDES TO PBM

Based on a dichotomisation of total MARS scores (with patients scoring ≤ 28 classified as low adherers, and those scoring >28 classified as high adherers), a third of patients ($n = 68$; 32%) were classified as low adherers with the rest of the sample ($n = 153$) classified as high adherers. In total, 41% of the sample reported that they forgot to take their PBM, with 38% indicating that they forgot to take PBM at mealtimes. Almost one in three (29%) reported taking PBM without food. Nearly a quarter (23%) of the sample reported that they altered the dose of PBM, 21% reported that they took less than instructed, and a similar proportion (19%) reported that they omitted doses. Furthermore, 14% reported that they stopped taking their PBM at least sometimes, often or always (see Figure 3).

FIGURE 3 HERE

Demographic and clinical factors, beliefs about PBM (necessity, concerns) and reported adherence

Demographic and clinical variables were compared between those classified as high and low adherers. While low adherence was associated with younger age ($t(208) = -2.78$; $p < .01$), no significant associations were found between adherence behaviour and gender or level of educational attainment. When the specific types of adherence were taken into account, it was shown that younger age was significantly related to low intentional adherence ($t(205) = -3.64$; $p < .001$), but not unintentional $p > .05$. Due to a low sample in some of the ethnicity groups, patients were categorized into Caucasian ethnicity and non-Caucasian ethnicity and Chi square analysis was conducted to reveal that low adherence was associated with non-Caucasian ethnicity ($\chi^2(1) = 9.42$, $p < .01$). Looking at the different types of adherence, it

ATTITUDES TO PBM

was confirmed that there were significant differences for ethnicity and intentional adherence ($\chi^2 (1) = 6.56, p < .01$) but not unintentional ($p > .05$), with the non-Caucasian participants more likely to be intentionally low adherers.

A significant negative correlation was found between age and concerns about PBM ($r = -.178; p < .01$), and an independent t-test confirmed that concerns about PBM were significantly ($t (204) = -2.50; p < .01$) higher ($M=2.57, [SD=.73]$) in patients of non-Caucasian ethnicity than those of Caucasian origin ($M=2.96, [SD=.92]$). Furthermore, women were more likely to show concerns than men ($\chi^2 (1) = 5.44, p < .05$). There was no significant association with educational level.

In relation to necessity beliefs, there were no significant associations found between age, gender, ethnicity or education level.

Beliefs about PBM (necessity, concerns) were compared between the low and high adherence groups. Low adherence was associated with reduced beliefs in personal need for PBM ($t (205) = 4.99; p < .001$), and greater concerns about PBM ($t (204) = -6.98; p < .001$); see Figure 4, and this was regardless of the type of adherence being tested. No significant associations were found between the clinical variables (number of tablets taken, dialysis duration, dialysis type) and adherence behavior, and this was also the case when the different types of adherence were taken into account.

FIGURE 4 HERE

Predictors of adherence to PBM

Key demographic characteristics, in addition to those variables shown to have a statistically significant association with adherence (set a priori at $p < .05$) were entered into a logistic regression analysis; gender, age, ethnicity (Caucasian vs. non-Caucasian, and treatment beliefs (necessity, concerns). Low adherence to PBM was associated with reduced beliefs in personal need for PBM (OR = .34; 95% CI: .14-.83; $p < .05$), and increased concerns about PBM (OR = 3.17; 95% CI: 1.87-5.37; $p < .001$); see Table 2.

TABLE 2 HERE

Attitudinal analysis

Patients were categorised into ‘attitudinal groups’ based on their beliefs about PBM (Aikens et al., 2005); these groups were created by splitting BMQ necessity and concerns scores at the median value. A third of the sample (33%) was classified as ‘Skeptical’ of PBM, holding doubts about personal need and increased concerns about PBM. A similar proportion (32%) was ‘Accepting’ of PBM, endorsing the necessity of PBM whilst holding low concerns about its potential adverse effects. Over a fifth of patients (21%) were classified as ‘Ambivalent’, endorsing the necessity of PBM but concerned about its potential adverse effects. The lowest proportion of patients (14%) were found to be ‘Indifferent’ to PBM, neither convinced of its need nor concerned about taking it (see Figure 5).

ATTITUDES TO PBM

A chi-square analysis demonstrated statistically significant differences in the proportion of low adherers in the attitudinal sub-groups ($\chi^2 (3) = 27.04, p < .001$). While only 10% of individuals in the Accepting group were classified as low adherers, 30% of the Indifferent, 36% of the Ambivalent and 52% of patients in the Skeptical sub-groups were classified as low adherers.

FIGURE 5 HERE

DISCUSSION

The aims of this study were to investigate the beliefs that are held about phosphate binding agents, to assess reports of intentional and unintentional nonadherence to PBM, and to explore the role of treatment beliefs in the prediction of nonadherence to PBM. The study findings indicate that a sizeable proportion of patients harboured doubts about their personal need for PBM, with doubts expressed by the sample in areas such as the role of PBM in maintaining current and future health. Concerns about taking PBM were also widely reported, with apprehension about the potential long term adverse effects of PBM most prevalent. Previous research (Parham et al., 2009) has suggested that patients are highly dissatisfied with the information that they had received about PBM, particularly relating to the potential problems of taking PBM (e.g. risk of side effects) which supports this notion.

A third of the sample were classified as nonadherent to PBM, which is consistent with previously reported rates of nonadherence as measured by self-report in this patient population (Karamanidou, et al 2006). Both unintentional and intentional nonadherence to PBM was evident; while incidences of forgetting to take PBM were most notable (including

ATTITUDES TO PBM

forgetting to take PBM at mealtimes), intentional nonadherence was also reported, with approximately one in five patients reporting that they altered or missed doses of PBM. These findings lend support to previous research by Riley et al., (2007) in which a third of dialysis patients reported missing doses of PBM at least once a week.

Bivariate analyses of factors associated with low adherence to PBM revealed that younger age was related to low adherence, specifically intentional low adherence. This finding adds to previous research in renal failure patients (Bame et al., 1993, Boyer et al., 1990, Horne et al., 2001), specifying the intentional nature of low adherence in younger people, and may reflect differences in lifestyle factors that may affect an individuals' adherence to treatment (Boyer et al., 1990), or may be due to the manifestation of differing age-related attitudes towards medicines (indeed, concerns towards PBM were also found to be higher in younger people).

Non-Caucasian ethnicity was found to be associated with low adherence, specifically intentional low adherence and increased concerns. This research adds to the literature that confirms significant relationships between low adherence to PBM and ethnicity (Curtin et al, 1999; Leggat et al, 1998; Morduchowicz et al, 1993) while also specifying that such nonadherence in this sample was intentional.

Relationships between poor adherence and clinical factors, including pill burden, were not found in the present study. It is interesting to note from a review of the literature exploring adherence to PBM (Karamanidou et al., 2008) that although 'tablet burden' may be deemed a barrier to adherence for many patients, a causal relationship between this barrier and low adherence cannot be inferred from a review of studies.

ATTITUDES TO PBM

Lower adherence to PBM was found to be associated with treatment beliefs whereby reduced beliefs in personal need for PBM, and greater concerns about PBM were indicative of low adherence. This relationship was found to be significant in a logistic regression analysis (i.e. even when controlling for the effects of demographic variables which were found to be significantly associated with nonadherence in preliminary analyses). This finding, which supports an association between beliefs about PBM and poor adherence, is consistent with studies which have explored this relationship in other chronic illness groups (e.g. Aikens et al., 2005; Horne and Weinman, 1999; Horne et al., 2001; Horne and Weinman, 2002; Horne et al., 2004; Horne et al., 2007; Horne et al., 2009; Hunot et al., 2007). Furthermore, the creation of attitudinal groups based on patient's beliefs about PBM offered further insight into the relationship between treatment beliefs and adherence behaviour. The highest proportion of low adherers was found amongst those who were classified as 'Skeptical' of PBM (low necessity, high concerns), while the smallest proportion of low adherers were found amongst those who were 'Accepting' of PBM (high necessity, low concerns), a finding which is consistent with the premise of the Necessities-Concerns Framework (Horne and Weinman, 1999). It is possible in the context of renal disease that the doubts held amongst patients about personal need for PBM may be compounded by the fact that patients may not experience any noticeable impact of adherence on symptoms (Karimanidou et al., 2006); the findings of this study indicate that any such doubts need to be elicited and addressed in efforts to improve adherence. Moreover, it is suggested that the value of being able to identify those who fall into differing attitudinal groups in clinical practice may allow for the identification of those who may be most at risk of nonadherence to PBM, and hence inform the content of patient consultations, particularly where a need for improved outcomes is paramount.

ATTITUDES TO PBM

The findings of the current study extend those reported by Wileman et al. (2011) who found an association between reduced beliefs in the necessity of PBM and intentional nonadherence (as measured by self-report). In this study, no relationship was found between reported concerns about PBM and intentional nonadherence, yet an association between concerns about PBM and higher serum phosphate was reported. In the context of the high pill burden of PBM and reports of unpleasant side effects common to this patient population (Chiu et al 2009), Wileman et al (2011) noted their surprise at the finding of a lack of an association between treatment concerns and intentional nonadherence and acknowledged that this non-significant finding may have been due to a small sample size and hence a lack of statistical power. The current study, conducted in a larger sample, finds support for the role of both doubts about personal need, and concerns about PBM in the prediction of self-reported nonadherence to PBM.

There are a number of limitations to this study which should be acknowledged. Adherence was measured using a self-report scale. While this method has been criticized due to the risk of obtaining socially desirable responses, a sizeable proportion of the patients in this study reported incidences of nonadherence to PBM. The self-report scale used in the present study (i.e. the MARS) is worded in a non-judgmental manner in a bid to minimize instances of biased responses and has been validated against electronic adherence monitors (Cohen et al., 2008). While an alternative, objective, measure of adherence to PBM is the measurement of serum phosphate, this can be problematic as it is not possible to specify between adherence to PBM, dietary restrictions and attendance for dialysis. The MARS, therefore, has the advantage of high specificity for nonadherence to PBM. It must also be noted that this study is limited by its cross-sectional design, whereby it is not possible to conclude causality (i.e. that patients' beliefs *cause* nonadherence); as such a future prospective longitudinal design

ATTITUDES TO PBM

would allow for an enhanced exploration of whether treatment beliefs cause nonadherence. Furthermore, there were significantly fewer participants from ethnic backgrounds in this study, therefore, these were pooled together to compare against Caucasian. This dichotomy does not allow the data to be generalisable to the population as a whole. Finally, as the data represents a clinical audit, we could only analyse a distinct set of variables that were collected from the measures being used in the service. Therefore, we should note that we are not concluding that beliefs about medication are more important than clinical or socio-demographic variables (that may be underrepresented in this study), but more that they should be taken into consideration in combination with these factors.

CONCLUSION

There is a paucity of research concerning dialysis patients' beliefs (perceived necessity, concerns about adverse effects) about and nonadherence to PBM using validated methods. The results outlined in this study provide evidence that poor adherence to PBM continues to be an unremitting problem amongst individuals with CKD, and that nonadherent behaviour cannot be explained by demographic or clinical factors alone. The current findings indicate that a considerable proportion of patients prescribed PBM harbour doubts about the necessity of PBM and concerns about its potential adverse effects. The study findings are in line with the findings of a systematic review (Karaminidou et al, 2006), which suggest that psychosocial factors appear to be the most promising predictors of nonadherence in this context. Overall, the finding that beliefs about PBM were predictive of reported adherence indicates that further research is warranted in this context in efforts to inform the content of adherence interventions. Indeed, strategies to improve adherence to PBM will need to elicit and address perceptual barriers (e.g. beliefs about personal need for PBM, concerns about its

ATTITUDES TO PBM

potential adverse effects) to adherence to PBM, while also focusing on younger people and ethnic groups who may be more at risk of intentional nonadherence.

ACKNOWLEDGEMENTS

This work was supported by an unrestricted educational grant from Shire Pharmaceuticals. In addition, we would like to thank Natalie Bidad who assisted with preparing the manuscript for publication, and all of the staff and patients who were involved in this research.

REFERENCES

Aikens, J.E., Nease Jr., D.E., Nau, D.P., Klinkman, M.S., Schwenk, T.L. (2005). Adherence to maintenance-phase antidepressant medication as a function of patient beliefs about medication. *Annals of Family Medicine* 3, 23-30.

Almirall, J., Valenzuela, M.P. (2006). The safety of phosphate binders. *Expert Opinion on Drug Safety* 5, 675-86.

Bame, S.I., Petersen, N., Wray, N.P. (1993). Variation in hemodialysis patient compliance according to demographic characteristics. *Social Science and Medicine* 37, 1035-43.

Betts, D.K., Crotty, G.D. (1988). Response to illness and compliance of long-term hemodialysis patients. *ANNA Journal* 15, 96-100.

ATTITUDES TO PBM

Boyer, C. B., Friend, R., Chlouverakis, G., Kaloyanides, G. (1990). Social support and demographic factors influencing compliance of hemodialysis patients. *Journal of Applied Social Psychology* 20, 1902-1918.

Butler, J.A., Peveler, R.C., Roderick, P., Smith, P.W.F., Horne, R., Mason, J.C. (2004). Modifiable risk factors for non-adherence to immunosuppressants in renal transplant recipients: A cross sectional study. *Nephrology Dialysis Transplantation* 19, 3144-3149.

Campbell, N.C., Murray, E., Darbyshire, J., Emery, J., Farmer, A., Griffiths, F., et al. (2007). Designing and evaluating complex interventions to improve health care. *British Medical Journal* 334, 455-459.

Cohen, J.L., Mann, D.M., Wisnivesky, J.P., Leventhal, H., Musumeci, T., Halm, E.A. (2008). Assessing the validity of the Medication Adherence Reporting Scale (MARS). Inner City Asthmatic Adults. 10th International Congress for Behavioural Medicine, Tokyo, Japan.

Cummings, K.M., Marshall, H.B., Kirscht, J.P., Levin, N.W. (1982). Psychological factors affecting adherence to medical regimens in a group of haemodialysis patients. *Medical Care* 20, 567-580.

Curtin, R.B., Svarstad, B.L., Keller, T.H. (1999). Hemodialysis patients' noncompliance with oral medications. *ANNA Journal* 26, 307-16.

Delmez, J.A., Slatopolsky, E. (1992). Hyperphosphatemia: its consequences and treatment in patients with chronic renal disease. *American Journal of Kidney Disease* 19, 303-17.

ATTITUDES TO PBM

Denhaerynck, K., Manhaeve, D., Dobbels, F., Garzoni, D., Nolte, C., De Geest, S. (2007). Prevalence and consequences of nonadherence to haemodialysis regimens. *The American Journal of Critical Care* 16, 222-235.

George, J., Kong, D.C., Thoman, R., Stewart, K. (2005). Factors associated with medication nonadherence in patients with COPD. *Chest* 128, 3198–3204.

Haynes, R.B., Yao, X., Degani, A., Kripalani, S., Garg, A.X., McDonald, H.P. (2005). Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews*.

Horne, R. (1997). The nature, determinants and effects of medication beliefs in chronic illness. PhD Thesis. University of London.

Horne, R. (2001). Compliance, adherence and concordance. In *Pharmacy Practice* (eds Taylor, K. & Harding, G.). London: Taylor and Francis.

Horne, R. (2006). Beliefs and adherence to treatment: the challenge for research and clinical practice. In *The Power of Belief: Psychosocial Influence on Illness, Disability and Medicine*. (eds Halligan, P.W. & Aylward, M.), Oxford: Oxford University Press.

Horne, R., & Weinman, J. (1999). Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *Journal of Psychosomatic Research* 47, 555–567.

ATTITUDES TO PBM

Horne, R., Weinman, J., Hankins, M. (1999). The Beliefs about Medicines Questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology & Health* 14, 1–24.

Horne, R., & Weinman, J. (2002). Self-regulation and self-management in asthma: exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. *Psychology & Health* 17, 17–32.

Horne, R., Sumner, S., Jubraj, B., Weinman, J. & Frost, S. (2001). Haemodialysis patients' beliefs about treatment: Implications for adherence to medication and fluid-diet restrictions. *International Journal of Pharmacy Practice*, 9, 169-175.

Horne, R., Buick, D., Fisher, M., Leake, H., Cooper, V., Weinman, J. (2004). Doubts about necessity and concerns about adverse effects: identifying the types of beliefs that are associated with non-adherence to HAART. *International Journal of STD & AIDS* 15, 38–44.

Horne, R., Cooper, V., Gellaitry, G., Leake, H. & Fisher, M. (2007). Patients' perceptions of Highly Active Antiretroviral Therapy in relation to treatment uptake and adherence: The utility of the Necessity-Concerns Framework. *JAIDS*, 45, 334-341.

Horne, R., Parham, R., Driscoll, R., Robinson, A. (2009). Patients' attitudes to medicines and adherence to maintenance treatment in inflammatory bowel disease. *Inflammatory Bowel Diseases* 15, 837–844.

ATTITUDES TO PBM

Hunot, V., Horne, R., Leese, M. N. & Churchill, R. C. (2007). A cohort study of adherence to antidepressants in primary care: the influence of antidepressant concerns and treatment preferences. *The Primary Care Companion to The Journal of Clinical Psychiatry*, 9, 91-99.

Isakova, T., Gutiérrez, O. M., Chang, Y., Shah, A., Tamez, H., Smith, K., ... & Wolf, M. (2009). Phosphorus binders and survival on hemodialysis. *Journal of the American Society of Nephrology*, 20(2), 388-396.

Kane, S. V., & Robinson, A. (2010). Review article: understanding adherence to medication in ulcerative colitis—innovative thinking and evolving concepts. *Alimentary Pharmacology & Therapeutics*, 32(9), 1051-1058.

Karamanidou, C., Clatworthy, J., Weinman, J. & Horne, R. (2008). A systematic review of the prevalence and determinants of nonadherence to phosphate binding medication in patients with end-stage renal disease. *BMC Nephrology*, 9, 2.

Leggat, J.E., Jr., Orzol, S.M., Hulbert-Shearon, T.E., Golper, T.A., Jones, C.A., Held, P.J., Port, F.K. (1998) Noncompliance in hemodialysis: predictors and survival analysis. *American Journal of Kidney Disease*, 32, 139–145.

Mardby, A.C., Akerlind, I., Jorgensen, T., (2007). Beliefs about medicines and self-reported adherence among pharmacy clients. *Patient Education and Counselling* 69, 158–164.

ATTITUDES TO PBM

Mills, E. J., Nachegea, J. B., Bangsberg, D. R., Singh, S., Rachlis, B., Wu, P., ... & Cooper, C. (2006). Adherence to HAART: a systematic review of developed and developing nation patient-reported barriers and facilitators. *PLoS medicine*, 3(11), e438.

Morduchowicz, G., Sulkes, J., Aizic, S., Gabbay, U., Winkler, J., Boner, G. (1993). Compliance in hemodialysis patients: a multivariate regression analysis. *Nephron* 64, 365–368.

Parham, R., Riley, S., Hutchinson, Horne, R. (2009). Patients' satisfaction with information about phosphate binding medication. *Journal of Renal Care*, 35, 86–93.

Riley, S. Bradley, R., Carig, K., & Wells, L. (2007). Examining patient perceptions of phosphate binders. *British Journal of Renal Medicine* 12, 19-21.

Savica, V., Calo, L. A., Monardo, P., Santoro, D. & Bellinghieri, G. (2006). Phosphate binders and management of hyperphosphataemia in end-stage renal disease. *Nephrology Dialysis Transplantation* 21, 2065-8.

Thompson, G. R., Naoumova, R., Sidhu, P. & Underwood, R. (1994). Predicting coronary heart disease. *Lancet* 343, 670-1.

Wileman, V., Chilcot, J., Norton, S., Hughes, L., Wellsted, D., & Farrington, K. (2011). Choosing not to take phosphate binders: the role of dialysis patients' medication beliefs. *Nephron Clinical Practice* 119:c205-c213

ATTITUDES TO PBM

World Health Organisation (2003). *Adherence to Long-term Therapies: Evidence for Action*,
World Health Organization.