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medicines **partnership**

A question of choice — compliance in medicine taking

a preliminary review

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Foreword

Non-compliance with prescribed medication is an age-old problem. The most recent systematic review of compliance by McGavock and colleagues (1996), conducted under the auspices of the Concordance Co-ordinating Group, showed that, despite the ability of medicines to prevent, relieve and even cure many forms of ill health, people often do not take them as prescribed. Since then, new and potentially more effective medicines have been launched that may be easier to take and have fewer side effects than their predecessors. Given these developments, it is not unreasonable to suppose that overall compliance rates should have improved. This update was commissioned by the Task Force on Medicines Partnership to test this hypothesis by reviewing more recent evidence across eleven therapy areas and amongst two broad patient groups.

The literature review presented here is enriched by the inclusion of views of individual patients and patient support groups about the issues that are important to them in medicine taking. This perspective serves as a useful counterpoint to the more academically focused research papers, and reminds us that non-compliance is often a considered decision by people making their own choices about the benefits and disadvantages of medicines. At the same time, it is clear that many people want more information about their conditions and treatments, and better dialogue with health professionals.

The results of the review demonstrate that non-compliance continues to be a significant problem across all therapy areas investigated. It is particularly interesting to see the impact and opportunity cost of non-compliance in new areas such as statin therapy. In the context of a rising drugs bill and the key role of medicines in promoting health, the review underlines the vital importance of maintaining a clear focus on improving compliance and making better use of medicines.

The review's findings illustrate some of the barriers to obtaining robust data in this field such as the difficulties inherent in measuring non-compliance. It enables us to draw some general conclusions about the major factors affecting compliance with prescribed medicine, such as:

- prevention versus treatment
- complexity of regimen
- extent of unwanted effects
- patients' own views about their illnesses and how they are best treated

The review also points towards strategies that work in practice to improve compliance. It supports the view that involving patients as partners in managing their own condition is key to more effective use of medicines; and that, although an understanding of the condition and treatment is critical, provision of information alone is not the solution. The evidence shows that the cost of effective interventions can be significant, while applicability across different therapy areas and patients is uncertain. The results complement those of the recently published World Health Organisation report (2003), which highlights the need to develop strategies to improve adherence as an essential element in reducing the global burden of disease.

The Task Force on Medicines Partnership enjoyed working with Sarah Carter and David Taylor at the University of London School of Pharmacy and Ros Levenson, an independent researcher, to create this useful resource for those involved in the fields of medicine taking and use. We hope that this publication will contribute to a better understanding of the issues involved in taking medicine, by linking the research evidence with the views of patients and patient representatives. We are particularly grateful for the contributions of individual patients and patient groups, that have added so much to the review.

The potential to improve health outcomes through better compliance represents an enormous opportunity and one that should be pursued with energy and determination. It is clear to us from this work and from other aspects of the Task Force programme, that the way forward is through focused, action-based research exploring practical solutions that involve patients in treatment decisions and support them in medicine taking. This work needs to concentrate on high priority conditions and patient groups, experimenting with and fine tuning interventions that have been shown to be promising, with rigorous evaluation to establish what works and how it can be delivered cost-effectively for the benefit of patients. We look forward to taking forward this exciting agenda.

Joanne Shaw
Director
Medicines Partnership

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1 Introduction

Methodology

This report was commissioned as a preliminary rapid review of literature relating to compliance. It provides an overview of the research published from 1996 onwards, and is intended to update and complement McGavock's study.

The terms used to describe medicines use which does not fully conform to professionals' recommendations include **non-compliance**, **non-adherence** and **lack of concordance**. Each has different meanings and implications. Because this paper concentrates mainly on evidence relating to the extent to which patients take or do not take their medicine as prescribed, we use **compliance** as the most straightforward word available. It remains the most widely cited term in the national and international literature on this topic.

This report looks at medication compliance in the following conditions:

- arthritis
- cancer
- coronary heart disease (CHD)
- depression
- diabetes
- epilepsy
- hormone replacement therapy (HRT)
- osteoporosis
- Parkinson's Disease
- renal disease
- post-transplantation care

Each topic report includes, where possible:

- information on compliance rates
- adverse health outcomes as a consequence of non-compliance
- factors found to be related to non-compliance
- interventions addressing non-compliance
- information on specific patient groups such as older people and adolescents

Other issues relating to compliance rates are discussed as appropriate.

The information presented here is not the result of a structured systematic review, so there were no strict inclusion or exclusion criteria. In some cases, several studies revealed similar findings, but only one study is referenced to illustrate the relevant observations. Similarly, individual studies are not necessarily described in detail.

The review is intended to be a representative sample of the literature which has become available since the mid-1990s. It is the result of a thorough search of databases, peer reviewed journals, condition-specific journals and websites. Individual specialists in some conditions were also contacted, particularly in cases when little published literature was found.

The databases and journals searched were:

Databases	Journals
MEDLINE	*British Medical Journal*
EMBASE	*The Lancet*
Ingenta	*Journal of the American Medical Association*
PubMed	*Pharmaceutical Journal*
Web of Science	*International Journal of Pharmacy Practice*
Cochrane Review Database	Condition-specific journals
BIDS International Bibliography of the Social Sciences	
Medicines Partnership database	

The key words used in the searches were 'adherence', 'compliance' and the name of the disease or condition. An example of a Boolean search was

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((adherence) OR (compliance)) AND (arthritis)
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The term 'concordance' was not found to be a useful search word in the context of this review.

Only articles published in English between 1996 and 2002 were scanned for inclusion in the review. Hand searches of reference lists of relevant articles were also conducted. Most of the research cited was carried out in the UK or the US; the rest took place in Europe.

The methodological quality of the studies was not evaluated for the purposes of this report, although all were published in peer-reviewed journals. Reported limitations of individual studies were noted in the review. The studies referred to in the reports varied in terms of:

- the number of participants involved
- definitions of compliance (for example, some researchers classified non-compliance as taking less than 90% of medication, some as taking less than 75%, and some used the dropout rate from clinical trials as a measure)
- measures of compliance used (for example, pill counts or self-reported consumption)
- measures of factors associated with non-compliance (note that the omission of some unquantified variables does not necessarily mean they were not significant)
- the types of intervention used to improve compliance rates

Patient perspectives

The views of patients and their organisations, highlighted at the beginning of each chapter, were sought by telephone interview. For each condition, views were sought from:

- At least one key voluntary organisation. Where there were several relevant organisations, organisations which were user-focused and/or user-led were

selected, rather than professionally focused ones. Most of the organisations were national, one was regional and one was Europe-wide. The organisations that contributed were:

- Arthritis Care
- CancerBACUP
- British Heart Foundation
- Rethink
- Diabetes UK
- National Society for Epilepsy
- National Osteoporosis Society
- European Federation of Neurological Associations
- Parkinson's Disease Society
- North East Kidney Patients Association

- Between two and six people with each condition, identified via their patient organisation, to explore personal opinions on what had influenced decisions about compliance with the prescribed medication for their condition.

It should be noted that these interviews are not intended to give a comprehensive picture of the views of patients and their organisations. Rather, they are intended to add patients' perspectives to the range of points identified from the literature.

Summary — key points

- Non-compliance in medicine taking is a long-standing problem in all therapeutic areas, including the treatment of cancer, arthritis and depression, the prevention of transplant rejection, and the lowering of heart attack and stroke risks.
- There is strong evidence that, despite the introduction of new medicines which have fewer side effects and are more convenient to use, many people still do not take them as prescribed — even when not doing so can have life-threatening consequences.
- Medicines prescribed for preventive purposes are especially likely not to be taken as prescribed. This may be because people do not feel immediately threatened and, in the case of symptomless conditions such raised cholesterol levels and hypertension, feel no obvious benefit at the time when medicines are taken.
- Factors associated with poor compliance include:
  - complex regimens involving multiple doses and several medicines
  - unwanted side effects
  - concerns about the value or appropriateness of taking medicines in particular contexts
  - denial of illness, especially among younger people
  - confusion or physical difficulties associated with medicine taking, which most frequently affect older people

- Effective ways of improving compliance rates involve the complementary use of educative, practical, and emotionally and behaviourally supportive interventions, rather than the provision of information alone. There is evidence that, regardless of the specific knowledge imparted, self-management programmes which help to raise people's sense of self-efficacy and confidence promote better medicine taking.
- Health professionals should respect patients' autonomy, and accept that increasing compliance with prescribing instructions is not as important as meeting patients' individual needs and priorities. Patients need help to make informed choices about treatment. For example, there is a need to differentiate clearly between situations where varying the timing or quantity of medicine doses may do little harm or even be beneficial, and situations in which there is a high probability of adverse clinical outcomes.
- Compliance rates are difficult to measure, especially when patients fear the consequences of telling professionals the truth. Future research into compliance in medicine taking should seek to assess the effectiveness of interventions, and also the health gain generated relative to their cost. Failure to address objectively the economics of improving compliance could hamper future developments in this field.
- Improvements in self-management skills and compliance in medicine taking can generate significant benefits for individuals and the population as a whole. Providing better access to modern pharmaceutical care — combining medication reviews with other forms of timely and appropriate support for patients and carers — represents an important route towards better and more cost-effective medicines use.

2 Compliance across medical conditions

Factors influencing compliance

Up to 80% of patients may be 'non-compliant' in their medicine taking (Dunbar-Jacob 2001), although the actual figure varies significantly between patient groups and types of illness. The figure is normally very much lower in contexts where there is an immediate risk of harm.

Factors that are predictive of, or associated with, non-compliance include:

- demographic indicators (e.g. age, gender and socio-economic status)
- medication characteristics (e.g. side effects, complexity of regimen)
- psychosocial issues (e.g. social support, family functioning, self-esteem).

Relatively few studies mention individuals' and groups' attitudes, beliefs and perceptions. However, a paper by Horne and Weinman (1999) reported a study which linked patients' beliefs about medication, classed as general or specific, to compliance. General beliefs were grouped into:

- those about the *intrinsic nature* of medicines (e.g. the extent to which they are perceived as harmful)
- those relating to the *way in which medicines are used by doctors*

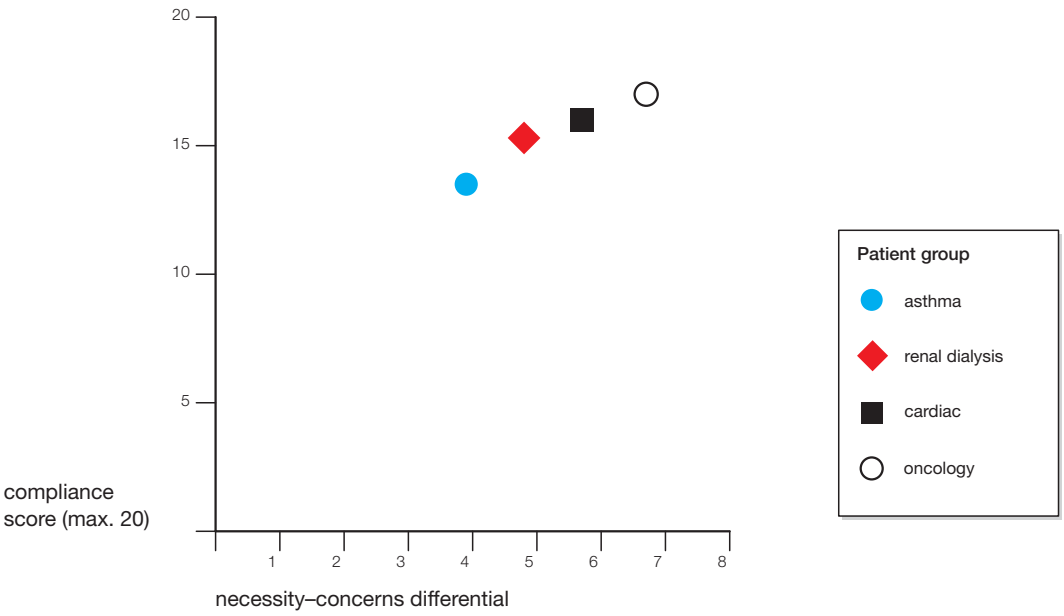
Specific beliefs about medications include whether a medication is perceived as necessary for maintaining the user's health, and whether there might be adverse consequences such as side effects or dependency.

The authors looked at whether beliefs affected compliance in four different chronic illness groups (asthma, cardiac conditions, renal failure needing haemodialysis, and cancer) and the extent to which medication-related beliefs differ in and between groups. They found that specific beliefs about medicines were the strongest predictor of compliance, accounting for 19% of the observed variance. Demographic variables were less significant.

Patients who believed that their medication was necessary for good health reported a higher rate of compliance, whereas those who had more concerns about medicine use reported poorer compliance. Figure 1 shows the strong relationship between patients' beliefs and their reported adherence. The x axis represents the extent to which patients believe that the need to taking the medicines outweighs their concerns about potential adverse effects (mean value 5.2); the y axis represents their reported adherence (scores range from 4 to 20). Of the four groups, the asthma patients were the least likely to believe that their medicines were necessary and the most likely to say that their costs outweighed their benefits. They were also the least compliant.

This study highlights the importance of taking beliefs about medication into account when addressing compliance issues, and shows that reasons for non-compliance differ between illness groups. Consequently, efforts to improve compliance may need to be tailored to meet the specific requirements of defined sets of medicine takers.

Figure 1. Effects of patients' beliefs about their medicines on their reported compliance



From Horne and Weinman (1999)

Interventions to improve compliance

Roter et al (1998) conducted a meta-analysis of 153 studies published between 1977 and 1994, which evaluated a range of interventions intended to improve compliance. It was found that they generally had a weak to moderate effect on (measures of) compliance. However, even modest improvements in appropriate areas could save lives and costs.

Combined-focus interventions were more successful than single-focus ones. The most effective were a combination of educational, behavioural and affective communications, which educated patients about their illness and treatment, taught behavioural strategies to enable people to cope better with symptoms and medication taking, and addressed emotions and moods.

The authors suggested that ideally interventions should address patient satisfaction, empowerment, understanding of illness, quality of life, functional status and psychological well-being. These aspects are fundamental to the notion of **concordance**.

More recently an updated Cochrane Review of interventions to improve compliance has been published (Haynes et al 2002). It states that the literature 'remains surprisingly weak' and that there are "only a few relatively rigorous trials … [which]… provide little evidence that medication adherence can be improved consistently, within the resources usually available in clinical settings, and that this will lead predictably to improvements in treatment outcomes.' Many studies included in the review lacked the statistical power needed to detect clinically important effects, due mainly to small sample sizes.

There is a strong case for concluding that compliance-related interventions should be designed to help the patient make an informed choice about their medicine

taking, rather than to 'improve compliance' *per se* (Horne 2001). Professionally led initiatives appear likely to be most useful when:

- they are targeted at well defined illness group(s)
- there is adequate demographic and psychosocial profiling of the patients involved
- the beliefs, expectations and preferences of patients are taken sympathetically into account
- patients' lifestyles are given similar attention
- outcome analyses have sufficient statistical power
- definitions of non-compliance are clinically appropriate
- the measure(s) of compliance and health outcome used are robust and relevant
- the resources necessary to execute interventions are properly evaluated and available as required in practice

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3 Compliance in arthritis care

Patients' views about taking medication for arthritis

The main issues raised by people with arthritis and their organisations were about the importance of the person with arthritis being in control, for which good information is seen as essential. There were also major concerns about unwanted effects of medication and how these weigh up against perceived benefits.

❝ *We do not like the word 'compliance'. It sticks in the craw. We are committed to the principles of concordance and to empowering people with arthritis. Empowered people make their own choices. It is about information, being heard, having your health beliefs heard and valued even if they mean that you do not take medications."* Arthritis Care

❝ *Older people especially feel unhappy about taking something that is not time-limited. The idea of medication for life is often uncomfortable…People also want to be in control. They want to know what they can do for themselves and prescribed medicines may be outside those parameters."* Arthritis Care

❝ *People need answers to questions like can I get pregnant while taking these pills? Can I have a drink? Can I take them with my other pills? These questions come up every day on the helpline and people ought to be getting this information from their doctors."* Arthritis Care

❝ *A lot of the disease-modifying drugs are toxic, so you have to decide what is worse — the disease or the drugs. I give it a lot of thought. I have two young grandchildren and my daughter is pregnant so I take the medication as I really need the mobility. I might have to trade that off against the itchiness and liver problems."* Woman in her 50s

❝ *I do read the leaflets but I often think I should not be taking stuff because of the other things I take, but I take what the doctor advises. The doctor makes time for me when I want to see him. I don't have any problems with side effects, but I wouldn't know if they were side effects."* Woman in her 80s

❝ *The doctors wish to make you better, which is not possible with rheumatoid arthritis. But you know how you feel and you may be able to accept possible long-term joint damage against feeling better today…It can be difficult to give up a medication that is making you feel better because of the side effects it is causing, if those side effects are not apparent to you and just show up in a blood test."* Woman in her 50s

❝ *It can be difficult getting at the pills. You have to remember to ask for a non-childproof bottle. Then they give you blister strips and they can be awkward. The edges of the foil are tough and sharp… I can sometimes forget whether I have taken my painkillers. Some pills come in strips of ten. For things like paracetamol or coproxamol that you can only take eight a day it would be best if the strips came in eights. Then you'd know if your strip was empty you could not take any more that day."* Woman in her 50s

❝ *Paying for medication can put people off. It's OK for me as I am also diabetic, but some people with arthritis have to ask the pharmacist which is the most important pill as they can't afford them all."* Woman in her 50s

Research evidence

Background

Arthritic conditions involve damage to and inflammation of joints and their linings, typically leading to persistent pain, stiffness and swelling. Rheumatic disorders resulting from trauma, auto-immune responses and other causes can affect children and young adults, but are most prevalent in later life.

Symptom-relieving drugs such as aspirin and anti-inflammatories are often prescribed to relieve pain and reduce swelling. *Disease-modifying* drugs are prescribed to slow or arrest the underlying pathological process. The significance of compliance issues differs between the two types of drug.

Patients taking symptom-relieving medication may sometimes decide to miss doses on days when their pain is less severe, or choose to give their body a 'break' from drugs. This 'noncompliant' behaviour might on occasions lead to increased pain or more limited mobility. But it also has the potential to generate physical as well as psychological benefits — in addition to the issues of control and personal autonomy involved, people taking symptom-relieving medication may find it easier to do activities which further harm the musculo-skeletal system.

Non-compliance with disease-modifying treatment may compromise the future health of the individual and incur costs for the NHS. Where medicines prevent disease progression, failure to use them to best effect could lead to avoidable disability and additional longer-term care needs. But the scale of the latter burden cannot be estimated here, partly because many of the studies in this field do not report which drugs have been prescribed, but refer simply to 'treatment' or ' the medication'.

Non-compliance rates

In a US study conducted by Chewning et al (2001) one-third of arthritis patients attending hospital rheumatology clinics had 'adjusted' their medication during the previous week. Of these, 61% intentionally added or missed a dose; the rest just forgot. About half of the patients were on eight or more different medications at one time. As the number of drugs increased, patients became more likely to change their regimen without seeking professional advice. It was also found that many physicians typically altered patients' prescriptions every six months, which further reduced recorded compliance.

Despite the relatively high rate of non-compliance observed in the treatment of arthritis, a review by Brus et al (1997) could not determine whether improved compliance led to better health status. This underlines the point that, where the main aim of therapy is to reduce symptomatic distress, non-compliance is not necessarily harmful.

Factors affecting compliance

Park et al (1999) examined compliance in rheumatoid arthritis (RA) patients aged 35–84 for a period of four weeks, using the Medication Event Monitoring System (MEMS), with which each opening of patients' medication containers is recorded and analysed. Older adults (aged 55–84) and those who coped well with arthritis-

related moods were more likely to be better compliers. Poorer compliance was found amongst middle-aged adults (aged 34-54), those with busy lifestyles and those with cognitive deficits. No relation was found between compliance and the severity of the condition, medication load or physical function.

Viller et al (1999) observed that women with arthritis are more likely to take their medicines as prescribed than men are. Higher compliance rates were also associated with high satisfaction with contacts with health care professionals, and above-average knowledge about the nature of the condition and its treatment. However, it should not be assumed from this that such factors *directly* promote better compliance — they may be linked to other more fundamental variables, such as **self-efficacy** levels.

Self-efficacy — which in this context may be defined as confidence in one's abilities to take medicines to good effect and cope with illness successfully — has been found to be important in arthritis care (Volkoff et al 1999, Brus et al 1997). The extensive research base underpinning initiatives such as the DoH's Expert Patient Programme indicates that raising an individual's sense of self-efficacy in medicine taking and other health maintenance contexts can change behaviour, and improve the experience of illness in the long term (DoH 2001). This may in part explain why higher levels of compliance sometimes appear to be associated with lower levels of experienced disability than might otherwise be expected for given levels of physical impairment.

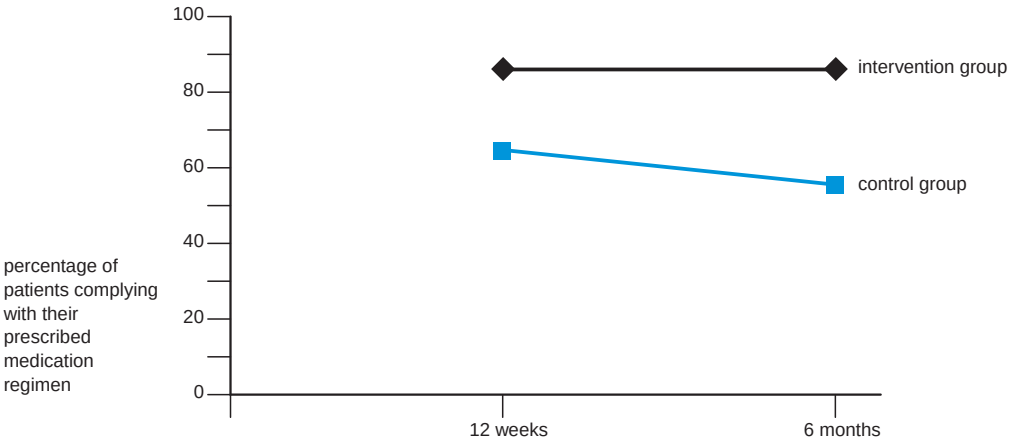
Interventions to improve compliance

Patient education programmes are often offered to patients with arthritis in conjunction with their medical treatment. The level of observed compliance is often used as a measure of the success of such programmes, which usually involve providing information about the condition, its causes and treatments, although there is limited evidence from any field that information provision *per se* markedly changes patient behaviour, other than at times when new problems become apparent. Strategies to cope with the disease may also be taught.

Studies evaluating such interventions with arthritis patients have shown varying results. Brus et al (1998) examined the effects of a patient education programme on compliance in patients with recent-onset RA who had been prescribed sulphasalazine. Outcomes were measured by pill counts. Defined compliance rates exceeded 80%, with no difference between the intervention and control group. This high rate of compliance may have been due to an 'experimenter' effect — that is, the patients may have taken their medication because they knew they were being studied.

A more recent study conducted by Hill et al (2001) evaluated a programme where patients receiving D-penicillamine received seven 30-minute sessions of the specified intervention. Figure 2 (overleaf) shows that at 12 weeks 86% of patients in the intervention group were compliant compared with 64% in the control group (who received their usual care). The same proportion of patients in the intervention group remained compliant at the end of the study, whereas the figure for the control group had dropped to 55%. Health status had improved significantly in both groups.

Figure 2. Effects on compliance of an information programme for arthritis patients



From Hill et al (2001)

In young people with RA, behavioural interventions, where medicine-taking behaviour is targeted by, for example, a reward system, have been found to be the most effective in improving compliance (Lemanek et al 2001).

The Arthritis Self-Management Programme (ASMP) was developed at the Stanford University Arthritis Centre (Lorig and Holman 1993). It has been systematically evaluated at Stanford over the past 14 years. Due to its success, the approach in the ASMP has since been adapted for other conditions such as diabetes and chronic pain, and for long-term illnesses generally. It is designed to help patients cope better, understand more and take an active role in managing their condition. It typically involves a series of group sessions led by trained volunteers who themselves have arthritis. Participants have access to information about how to deal with pain, fatigue and depression, the appropriate use of medicines, and how to communicate more effectively with family members and health professionals. They also agree targets for changed behaviour with their peers, and report back on their achievements to the wider group. These experiences of 'mastery' raise self-confidence levels, and are considered by Professor Lorig and her colleagues to be the most important element of programmes like the ASMP.

The programme has been evaluated in arthritis patients in the UK (Barlow et al 2000). At 4 months, compared with a waiting list control group, self-efficacy was enhanced. There was more evidence of positive health behaviours such as exercise, relaxation and communication with doctors, and participants were less depressed, tired and anxious. A similar pattern was found at 12 months, suggesting long-term benefits. Over the evaluation period, observed physical functioning remained stable.

Specific patient groups

Research has been done on arthritis in children and adolescents. A study in Finland revealed that nearly one-fifth of 13- to 17-year-olds felt that they complied poorly with their arthritis treatment, and only 11% were confident that they complied fully. The lowest level of compliance in the regimen was with their medication (Rn 2000).

Kyngas and Rissanen (2001) analysed questionnaires completed by Finnish adolescents. Their work identified several factors which were predictive of better (self-reported) compliance:

- willpower (7 times more likely to comply than those with 'insufficient willpower')
- support from parents, doctors and nurses (7 times more likely to comply)
- good motivation (5 times more likely to comply)
- positive attitude towards disease and treatment
- no threat to social, physical and emotional well-being
- no fears of complication
- no uncontrolled pain

These results indicate that predictors of compliance are varied and differ in degrees of controllability. Studies like that reported above depend for their validity and meaning on the quality of the questionnaires or other research instruments used, and how their findings are interpreted. For example, 'willpower' may equate to self-efficacy — confidence in one's ability to carry out the required behaviour. Interventions involving the provision of information, therapy management, behaviour modification and parental monitoring have been found to be effective in both clinical and non-clinical settings in improving compliance in the context of juvenile RA (Kroll et al 1999).

Summary

People with arthritis may choose not to comply with prescribed medication or other therapeutic regimens for reasons which are in many cases rational in professional as well as lay terms. However, a range of interventions — most notably lay-led self-management programmes — have the potential to reduce non-compliance.

Support which increases people's sense of self-efficacy, and helps them to be active managers of their own illness, has been shown to improve the outcomes they experience with arthritis. There is as yet little substantive evidence that improved rates of compliance with medication are associated with improved biomedical outcomes for arthritis. But as more effective disease-modifying agents are introduced, achieving better compliance will become more important in arthritis care.

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4 Compliance with treatment for asthma

Patients' views about taking medication for asthma

The major issue facing patients in relation to asthma medicine appears to be a lack of understanding of how to use it most effectively, rather than concerns about adverse effects. Many patients, even having had the condition for many years, have never understood the different kinds of medication available and how they should be used. Some remain on repeat prescriptions for year after year with sub-optimal symptom control, developing their own approaches to managing their condition, and unaware that they could be feeling much better.

❝ *Most people with asthma have a little or no involvement in the decision over what medication they are prescribed. They simply take the advice of their doctor or asthma nurse. What is even more worrying is that, they are rarely called back for a review of their medication — our National Asthma Panel research showed that less than 50% of people with asthma were having medication reviews."* National Asthma Campaign

❝ *People with asthma are the best people to take an active role in the control of their condition — especially in terms of medication. We encourage patients to sit down with their GP or asthma nurse and fill in a personal asthma plan — a guide, based on the changes in their asthma, of how much medication to take and when to take it. It really helps people get asthma under control."* National Asthma Campaign

❝ *Cost is a real deciding factor in whether or not people with asthma take their medication. A female caller to the Asthma Helpline was failing to pick up her own prescriptions and was sharing her daughter's inhaler because she could not afford asthma medication. 94% of people with asthma believe that free prescriptions are vital to effective asthma control*"* National Asthma Campaign

❝ *Free prescriptions for people with asthma would go a long way to helping them take their medication regularly. But many still do not know how to take their medication properly because they haven't been shown — let alone developing a personal asthma plan to manage their medication. A better partnership with their doctor or nurse is what's really needed if people with asthma are going to take their medication."* National Asthma Campaign

❝ *I've got quite bad asthma but I always used to try to keep my inhaler use to a minimum. You don't want to be dependent on it. But then a nurse explained to me that I shouldn't feel bad about keeping my symptoms under control. It's made me feel much better about taking it and my health has really improved."* Woman in her 30s

❝ *I take my reliever inhaler (salbutamol) twice a day as well as when I have symptoms. It's what I've always done. The doctor never said not to use it with this new (combination) inhaler that I have had for about six months now."* Woman in her 50s

❝ *I have just changed to a new doctor but my previous doctor never reviewed my treatment — just kept on giving me repeat prescriptions for over four years. When I get my asthma symptoms I just use my blue inhaler for about two to three days and it seems to help me OK. Sometimes I'll use the brown one, but only when it's really bad."* Man in his 30s

* *National Asthma Panel*

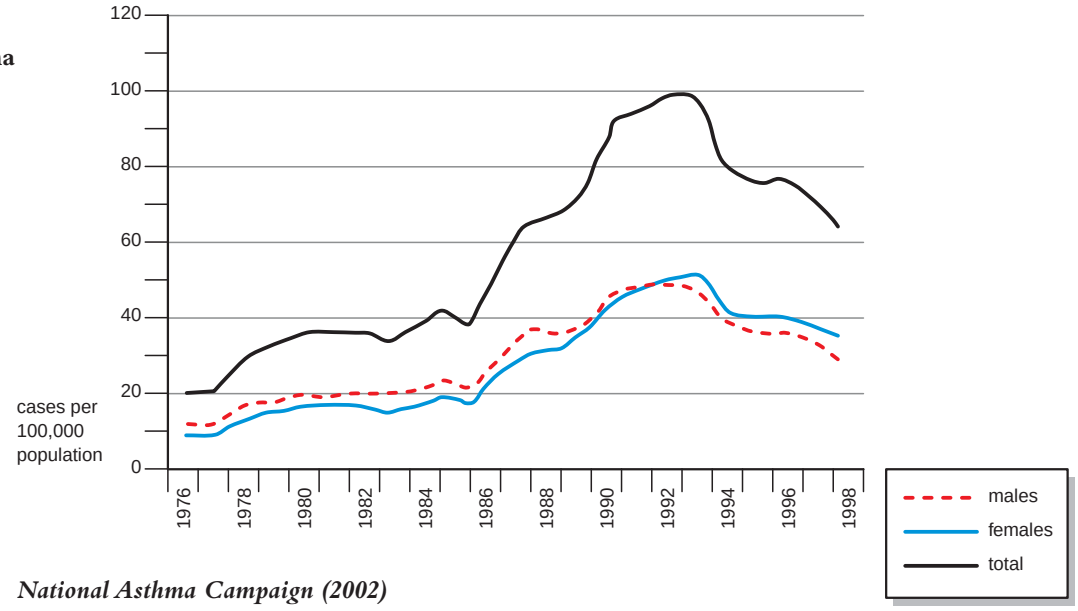
> *I smoke 20 cigarettes a day and think that the asthma nurse would be cross with me if I told her the truth about my smoking. I am afraid to give up. That's why I never attend reviews. A friend of mine who did stop smoking then died a year later from lung cancer and I don't want that to happen to me."* Woman in her 60s

Research evidence

Asthma is a chronic inflammatory disease of the airways which can be exacerbated by factors such as dust, pollutants, pollen, tobacco smoke, exercise and viral infections. Symptoms include coughing, wheezing and shortness of breath. Statistics show that asthma was the cause of death for nearly 1300 people in England and Wales in 2002. Nearly three-quarters of these were people over the age of 55, 17% were aged between 25 and 55, and 5% were under 25 years old (Office of National Statistics 2002).

Research shows that although the incidence of asthma has dramatically decreased since the early 1990s, it is still higher than in the mid-1970s (Figure 3). An estimated 1.4 million children and 3.7 million adults are currently being treated in the UK (National Asthma Campaign 2001).

Figure 3. New episodes of asthma in England and Wales



National Asthma Campaign (2002)

Drug treatments for asthma can be divided into those which prevent attacks (**preventers**) and those which are intended for symptomatic relief (**relievers**). **Inhaled corticosteroids (ICS)** have an anti-inflammatory effect and can be used to prevent asthma attacks. **Leukotriene antagonists** also have anti-inflammatory as well as bronchodilatory properties, and can be taken orally as asthma preventers. Acute symptomatic asthma is treated with a **β2 agonist**; these drugs work on the airway smooth muscle to relieve bronchoconstriction.

Asthma treatment has five steps according to severity:

Step 1 Occasional relief bronchodilators

Step 2 Regular inhaled preventer therapy

Step 3 High-dose inhaled corticosteroids, or standard-dose inhaled corticosteroids plus long-acting inhaled $\beta 2$ agonist

Step 4 High-dose inhaled corticosteroids plus regular bronchodilators

Step 5 As Step 4 plus regular corticosteroid tablets

Cost of managing asthma

Asthma has been estimated to cost the NHS an amount approaching £1 billion per year (National Asthma Campaign 2001). Das Gupta and Guest (2003) recently analysed data from over 4500 UK asthma patients between 1993 and 1998 to determine the primary care costs of managing asthma. Their results revealed that costs increase with the severity of the condition — the estimated annual primary care cost per patient are:

- Patients with mild asthma (step 1) **£35**
- Patients with moderate asthma (steps 2–3) **£150**
- Patients with severe asthma (steps 4–5) **£535**

Drugs account for between 72% and 80% of these costs, and GP consultations account for the remainder. There is a probable association with more severe illness and greater health care usage.

Non-compliance rates

Asthma patients are typically advised to take preventer medication such as an ICS or a leukotriene antagonist on a daily basis, supplemented with a relief inhaler if symptoms arise. Noncompliance problems typically involve the under-use of preventer medicines. This increases the risk of acute episodes, and so leads to a relative over-use of relief medication and in some cases hospital emergency care.

Voluntary guidelines written in 2003 by the British Thoracic Society and the Scottish Intercollegiate Guidelines Network recommend that all patients admitted to hospital with severe asthma should be followed up for at least a year by a specialist and should be checked regularly on drug and inhaler use (Higgins and Douglas 2003).

A recent analysis of data from UK asthma patients over five years revealed that 25% of patients have compliance rates estimated at 30% or less (Das Gupta and Guest 2003). They also found that compliance rates, measured by the time elapsed between prescriptions issued for medication, tended to increase with age and severity of asthma. Table 1 (overleaf) shows the estimated compliance rate of two groups of patients at year 5 of the study: patients with mild to moderate asthma (on treatment Steps 2/3) at year 5; and patients with moderate to severe asthma (on treatment Steps 4/5) at year 5, all of whom had been diagnosed as having mild to moderate asthma two years previously.

Table 1. Estimated compliance rates with patients prescribed twice-daily inhaled corticosteroids

Age	Mild to moderate asthma at year 5	Moderate to severe asthma at year 5
Under 16 years	48%	42%
16–69 years	60%	66%
Over 69 years	69%	73%

From Das Gupta and Guest (2003)

The situation is similar in the USA. One review stated that rates are typically around 50% (Fish and Lung 2001). However, reported rates do differ due to variations in methods of measuring compliance (or non-compliance,) populations, medications and levels of asthma severity.

Results of the European Community Respiratory Health Survey showed large variations in compliance rates across the world (Cerveri et al 1999); for example:

- The percentage of patients who responded 'yes' to the question 'If you are prescribed medicine for your breathing, do you normally take all of the medicines?' was 67% on average; but it ranged from 40% in the USA to 78% in Iceland and around 65% in the UK.
- When asked 'When your breathing gets worse, and you are prescribed medicines for your breathing, do you normally take all of the medicines?', 77% of UK patients answered 'yes', slightly higher than the average of 72%.

Adverse effects of non-compliance

Non-compliance is thought to contribute to between 18% and 48% of asthma deaths (National Asthma Campaign 2001). Non-compliance can also lead to increased hospitalisation rates (Cerveri et al 1999).

There are also non-medical costs which contribute to a decreased quality of life. According to the 1996 Health Survey for England, nearly 20% of adults with respiratory problems reported that their symptoms disturbed their sleep at least once a week and affected their speech. Symptoms also interfered with daily activities for 50% of sufferers, and 20% reported lost work days (Joint Health Surveys Unit 1998).

Factors affecting compliance

The reasons for non-compliance are often complex. However, several factors are consistently related to poor medicine taking in people with asthma; in summary, these are:

- ***Patient-related factors***
  - misunderstanding treatment
  - forgetting
  - patients' beliefs

  - misunderstanding the condition
  - denial
  - embarrassment
  - lack of social support
- ***Treatment-related factors***
  - fear of, or experience of, side effects
  - complex regimen
  - frequent dosing
  - method of administration
- ***Condition-related factors***
  - no, or mild, symptoms
  - severe symptoms

If patients misunderstand their treatment, the regimen prescribed, medication devices or the condition itself, this is likely to lead to poor compliance (Fish and Lung 2001). Professional observers report a lack of knowledge about the chronic nature of asthma which can affect, for example, the patient's ability to judge whether and when to use preventer or reliever medication.

Frequent dosing and complex regimens are also linked to poor compliance. Some studies have shown that less frequent dosing promotes better compliance (Fish and Lung 2001) although others found equivocal results (Moller 1999). However, less frequent dosing may not suit all patients. One caveat here is that if a patient forgets to take his or her medication, the impact will be greater with a once-daily dose than a with more frequent dose (Hyland 1999).

Several studies have found that patients often simply forget to take their medication (e.g. Buston and Wood 2000). This may again be linked with complex regimens.

Fear of the adverse effects of prolonged medicine taking is common in asthma patients, as in other chronic conditions (Bender 2002), although it is not certain whether the fear is justified by the reality. Side effects of the medication used include palpitations, nausea, vomiting and immunosuppression.

The method of administering medicine is also regularly cited as a reason for poor compliance (Cochrane et al 1999). Some studies have found that oral therapy seems to be preferred and better adhered to than inhaled medication (Kelloway et al 1994), possibly due to it being easier and less embarrassing to administer in public.

Patients' beliefs about their condition and treatment can also have an impact on compliance. Adams and colleagues conducted in-depth interviews with asthma patients and found that they seemed to fall into two broad categories — **deniers** and **accepters** (Adams et al 1997):

- The deniers refused to acknowledge that asthma was the condition causing their symptoms. They hid their diagnosis, and their treatment, from friends, family and work colleagues. They tended to see asthma sufferers as a stigmatised group and did not like to perceive themselves as having a chronic illness. None of these patients were taking prophylactic medication, despite it being prescribed for them, yet all were taking more than optimal amounts of reliever treatment. Preventative medication brought fears of dependency and lack of control. The

daily use of preventer treatment was also seen as synonymous with accepting that one was 'asthmatic'.

- Accepters, on the other hand, freely admitted to being asthma sufferers. They believed they kept their condition under control, partly by taking the appropriate medication and partly due to their personality. They prided themselves on their ability to cope well. Unlike the deniers, who perceived asthma as an acute condition, the accepters understood its chronic nature and the importance of control. The accepters took preventer treatment regularly and were aware that it is only effective when used this way. They all agreed that reliever medication was simply used to treat an 'attack'.

Interventions to improve compliance

As well the many factors related to non-compliance, several factors have been found to improve medicine taking by people with asthma. The literature suggests two main components: **a simple regimen** and **better patient understanding** of their illness and treatment.

The relative complexity of the regimen is usually investigated by comparing compliance with once-daily dosing and with more frequent dosing. An analysis by Das Gupta and Guest (2003) found that significantly more patients taking once-daily ICS were 'high' compliers than those taking twice-daily doses. A review by US researchers concluded that twice-daily dosing was more effective in terms of compliance than medication taken three or four times a day, but no more effective than once-daily medication (Fish and Lung 2001).

Patients' understanding and knowledge about asthma and its treatment has been explored in a variety of ways. Fish and Lung (2001) conducted a review of studies. Two reports, one published in a peer-reviewed journal and the other a US Expert Panel Report, highlighted the importance of:

- information on the pathophysiology of asthma (explaining what happens to the body during an attack)
- the ability to recognise symptoms
- awareness of environmental triggers
- understanding of how medications work, especially the difference between preventers and relievers
- demonstrations of how to use medication devices
- information about side effects

The authors suggest that information should be reinforced at each visit to the clinician, and by the patient's pharmacist. They also suggest that verbal information should be supported with brief written information, all of which should be individualised to the patient's lifestyle and routine, health beliefs, concerns, age, education and culture.

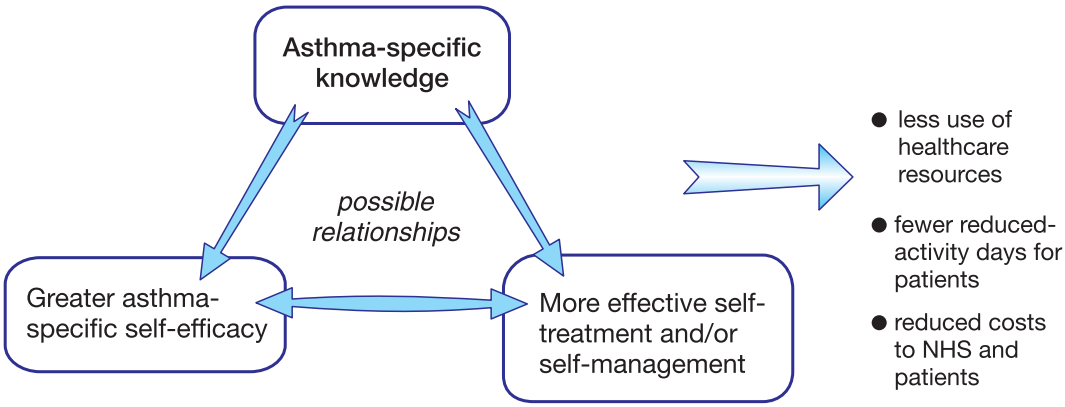
However, earlier studies have shown that, while information is essential, it is not sufficient by itself to improve compliance in other chronic conditions (DoH 2001). Self management programmes are often used both to informing patients about their condition and to encourage them to manage it effectively. Such programs have

been shown to be effective in decreasing asthma symptoms and negative emotions, and in increasing quality of life and compliance (Put et al 2003).

One important effect of self-management programmes may be to increase patients' context-specific sense of self-efficacy (confidence in managing their condition). One recent study revealed that both self-efficacy and compliance increased in asthma patients randomly assigned to an individualised asthma management programme (Put et al 2003).

However, another study found that neither general nor asthma-specific self-efficacy directly predicted adequate self-treatment or self-management behaviour, as measured by responses to a hypothetical situation; however, asthma-specific knowledge did. This knowledge was also found to predict asthma-specific self-efficacy (van der Palen et al 1997). So it is possible that asthma patients who know and understand about their condition are more likely to achieve both self-efficacy and effective self-management (Figure 4).

Figure 4. Knowledge, self-efficacy, effective self-treatment and self-management in asthma patients



A review of self-management and educational programmes showed that they can reduce the use of healthcare resources such as hospital and GP visits, for both adults and children; for patients, the number of limited activity days is also significantly reduced (Liljas and Lahdensuo 1997). Programmes directed at patients with moderate to severe asthma produced the largest savings.

Specific patient groups

Children and adolescents

The parents of children with asthma are often in charge of their medicine management, so most studies investigating compliance in children have focussed on parents.

As with adult patients, parents' misunderstanding of treatment is associated with non-compliance in children with asthma. In a study published in the USA, Farber and colleagues (2003) found that 23% of parents did not understand that inhaled anti-inflammatory medicine should be used daily as a preventer rather than when symptoms begin; this misunderstanding was associated with a slight decrease in compliance.

Parents' beliefs about treatment also influence compliance, although it is not yet possible to distinguish cause and effect. Irvine et al (2002) found that parents whose children's prescriptions for preventer medication were collected irregularly were less likely to perceive the treatment as effective and were more reluctant to administer it.

Interventions to increase compliance in children seem to be effective. A recent Cochrane review examined 32 clinical trials of self-management education programmes in 2- to 18-year-olds (Wolf et al 2003). The programmes in the trials taught self-management strategies for attack prevention, attack management and/or social skills, in either individual or group settings.

The review found that education programmes were associated with moderate improvement in measures of airflow and in levels of self-efficacy; and with modest reduction in absence from school, days of restricted activity and emergency visits. Greater effects for most outcomes were generally found in patients with moderate to severe asthma, rather than in patients with mild to moderate symptoms.

Adolescents with asthma have additional issues which can affect medicine taking. Several studies have reported that denial, family conflict and embarrassment predict non-compliance (WHO 2003; Buston and Wood 2000). Fish and Lung (2001) suggest that internet chat-rooms may provide peer support, and that healthcare professionals should recognise adolesecents' desire for autonomy and direct the consultation to the patient as much as possible, rather than to parents.

Older people

Little research has been conducted on elderly asthma patients as a specific group. However, a recent World Health Organisation report (WHO 2003) concluded that forgetfulness and polypharmacy were related to non-compliance in this population.

Ethnic minorities

Research shows that black and south Asian asthma patients are more likely than white patients to be admitted to hospital due to their condition, despite little evidence to show that the prevalence or severity is higher than in other populations (Gilthorpe et al 1998; Partridge 2000).

Some evidence suggests that this may reflect poorer management of asthma. In one UK study, Asian males were significantly less likely to self-report full compliance than white European males; and Asian females were significantly less likely to carry out self-management (Moudgil and Honeybourne 1998).

Poor compliance and self-management may, in turn, reflect poorer understanding of the condition and its treatment. Research conducted in Britain has shown that south Asians born in the UK are more likely to be on regular treatment than those born abroad (Ormerod et al 1999). Asian females were also less likely to understand the role of their medication than their white European counterparts (Moudgil and Honeybourne 1998). This suggests possible ineffective patient education and communication difficulties in ethnic minority populations.

Summary

Asthma medication is effective when taken as prescribed. However, both adults and children commonly under-use preventer medication and over-use reliever medication. This is frequently due to misunderstanding of asthma and its treatment. Patients often find it difficult to come to terms with the diagnosis; this can also affect medicine taking. Interventions which teach strategies for prevention and relief of acute attacks are effective in improving illness management.

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5 Compliance with treatment for cancer

Patients' views about taking medication for cancer

Issues raised by and on behalf of people with cancer included

- the quality of information available to them
- how to raise concerns while on medication
- concerns about unwanted effects
- occasional issues about remembering to take medication.

Some patients expressed a desire to comply with medication that was linked to their gratitude for the care received, and some were reluctant to cease medications even if they were no longer strictly necessary.

> *When I first took Tamoxifen, I had to ask when to take it — mornings or when. I had to read and ask and no-one tells you."* (Woman, 72, had breast cancer and bone cancer secondaries)

> *..the Tamoxifen makes the menopause start at once. This is not made widely known enough. You have both to contend with — the cancer and the Tamoxifen and the menopause. Not enough is said about it."* (Woman, 62, had breast cancer)

> *I had good explanations, but it does sometimes need a bit more time. If you are throwing up, you need to be able to talk about not just the medication, but your diet and lifestyle. When you eat may be important so you can take the medication."* (Woman, 43, had Hodgkin's disease)

> *The information leaflets — if you can read them and many of them are very small print — many people are terrified to take the medicines. I found them over-informative. So I read them all once and then didn't bother to read them again."* (Woman, 43, had Hodgkin's disease)

> *Patients should be aware of side effects and should have a chance to discuss if the medication is really necessary. The medical profession do tend to work in generalisations but there are factors like age and gender which can affect things and you need to be able to follow things up for your own situation."* (Woman, 72, had breast cancer and bone cancer secondaries)

> *Some people can't be bothered to take it [Tamoxifen]. But as far as I am concerned, I have done the basics and everyone has rallied round. Now it is up to me to continue the good work…It is our job to carry on. It's like it is no good having a heart bypass and going back to 60 cigarettes a day."* (Woman, 62, had breast cancer)

> *I was most meticulous about taking medication. I just accepted the fact I should take it. You are concerned for the quality of life, so you do take it. The patient needs to be aware that the medication is prescribed for a particular reason."* (Woman, 72, had breast cancer bone cancer secondaries)

> *Some people do tend to forget to take their medication. I kept all the boxes by my kettle where I have my first cup of tea. I always went through the ritual of counting them out and checking them."* (Woman, 43, had Hodgkin's disease)

> *I did some research and there was no scientific reason to stay on [Tamoxifen] after 5 years but they were doing some tests on people taking it for 5, 10 and 15 years, and that's why I stayed on it. I asked the surgeon if he was surprised I was staying on it and he said no, it's like taking a dummy from a baby."* (Woman, 62, had breast cancer)

Research evidence

One in every three UK citizens will contract cancer at some point in their lives. Each week 5000 people in this country are diagnosed with cancer. The great majority are over 60. But a number of relatively rare forms of cancer affect children and young adults; and breast cancer is still a major cause of mortality and morbidity in women of working age (despite recent rapid declines in British death rates, associated to a significant degree with the use of the medicine tamoxifen).

Treatment strategies vary enormously depending on the type of cancer, the progression of the tumour, and the age of the patient (Cancer Research UK 2002). Survival rates for all the neoplastic diseases are improving. However, most forms of treatment for advanced cancer are still essentially palliative.

The most cost effective forms of anticancer medication are preventive interventions such as nicotine replacement therapy, either prescribed or bought over the counter, to help people stop smoking tobacco. Preventive interventions are not considered here, but it should be emphasised that the distinctions between preventative, curative and palliative treatments for cancer raise a range of different compliance issues.

The literature on medication compliance in cancer patients is limited, because most treatment is administered in hospital and other settings, under the direct supervision of health professionals. However, the use of oral therapies such as tamoxifen is increasing, in part because it is usually better tolerated than, so preferred to, intravenous chemotherapy (Liu et al 1997). The issue of compliance in cancer patients is therefore likely to become more important in the future, although so far most research has been conducted in the context of clinical trials, and uses dropout rates as the measure of compliance.

This is not an ideal measure as there are many reasons why patients withdraw from trials; inability or unwillingness to take medication is only one of them. For example, regular hospital attendance for tests may become too demanding, and participants may not have the time or motivation to complete questionnaires or self-reports. Conversely, patients involved in clinical trials are likely to be more motivated to follow treatment, and are more closely monitored and supported than members of the general oncology population.

Non-compliance rates

Partridge and his colleagues reviewed compliance with oral antineoplastic agents in 2002. They found relatively few published studies, with measures and definitions of compliance varying significantly between the studies they identified. So any meaningful comparison is limited. But the evidence shown in Table 2, summarising Partridge et al's findings, indicates that compliance rates in cancer treatment are variable, and sometimes very poor.

Table 2. Non-compliance with prescribed oral antineoplastic agents among adults

Type of cancer	Measure of non-compliance	Definition of non-compliance	Rate of non-compliance
Haematological malignancies	Serum levels of drug metabolites	Serum levels below expected threshold	83%
Breast cancer	Self-report	Taking less than 90% of prescribed medicine	47%
Breast cancer	Self-report Pill count MEMS*	Taking less than 80% of prescribed medicine	2% 8% 15%
Hodgkin's disease or non-Hodgkin's lymphoma	MEMS	Not described	—
Small cell lung cancer	MEMS	Not described	7%
Ovarian cancer	MEMS	Not described	3%

* *Medication Event Monitoring System — a medication dispenser containing a microchip that records when the container is opened*

From Partridge et al (2002)

In addition to the studies summarised in Table 2, Veronesi et al (1998) compared dropout rates among two groups of women involved in clinical trials. One group were receiving tamoxifen as an adjuvant (that is, additional) therapy after cancer surgery; the other group were healthy, hysterectomised women prescribed tamoxifen as a preventative treatment for breast cancer. More than a quarter of the prevention group dropped out of the study; of these 17% did so because of adverse events, and 72% for other reasons such as 'side effects', fear, no longer being interested in the study, being advised by their doctor to quit, and reluctance to continue taking drugs.

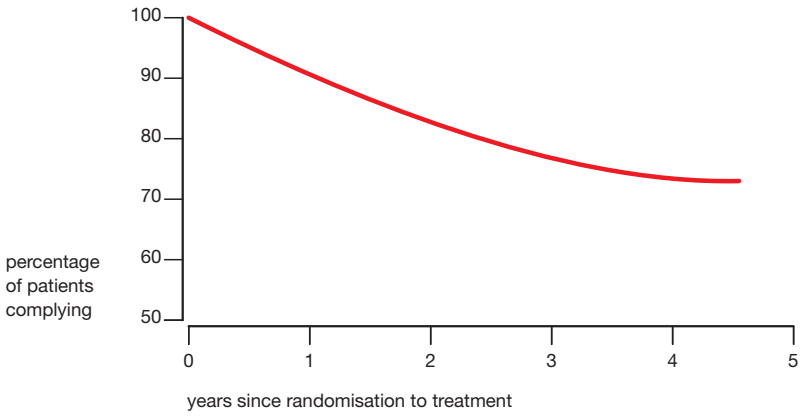
Significantly fewer patients (15%) in the adjuvant therapy group dropped out of the study. This highlights the differences between compliance with medication offered as a preventative, and medication perceived as curative. Higher numbers of dropouts in the prevention group may reflect lower motivation, fewer cues for compliance (such as symptoms), and lower perceived vulnerability.

Other trials evaluating tamoxifen as a preventative agent have shown dropout rates of around one-third — 36% in the Royal Marsden Tamoxifen Chemoprevention

Study (Powels et al 1998) and 29% in the National Surgical Adjuvant Breast and Bowel Project (Fisher et al 1998).

According to correspondence in the *Lancet* in March 1999 (Cuzick and Edwards) compliance in the International Breast Cancer Intervention Study, which evaluated the effect of a daily dose of tamoxifen for five years in 'at-risk' women aged 35–70, was 90% after one year, 83% after two years, and 74% after four years (Figure 5).

Figure 5. Compliance in tamoxifen use



From Cuzick and Edwards (1999)

There is also evidence of non-compliance in the form of taking too much self-administered anti-cancer medication. Patients may believe that taking more medication will lead to better health and/or a stronger preventive or curative effect, although in reality it may reduce therapeutic impact and lead to increased toxicity and side effects (Partridge et al 2002).

Adverse effects of non-compliance

In the few available studies evaluating non-compliance and therapeutic outcome, noncompliant patients tended to have shorter relapse-free and total survival times (Partridge et al 2002). This finding needs to be interpreted with care, because the reasons for withdrawing from clinical trials can include treatment failure.

Factors affecting compliance

The Partridge et al (2002) review found no research on factors predictive of compliance (or non-compliance) in cancer patients. Variables linked to (non)compliance in other illnesses are likely to be relevant to cancer care; but, in contrast to other conditions, some studies revealed no relationship between the prevalence of side effects and compliance. This suggests that patients being treated for cancer are significantly more willing to tolerate adverse consequences of medicine taking, compared with people whose conditions are seen as less life-threatening.

Interventions to improve compliance

Partridge et al's (2002) review included a few studies which attempted to improve compliance; these showed that educational programmes, behavioural modification techniques (such as practising taking medicines), and using cues and reminders can be effective.

There is also evidence compliance with cancer treatment regimens can be improved by providing care in patients' homes. Borras and colleagues (2001) analysed compliance in adult patients receiving chemotherapy for colorectal cancer in an outpatient clinic, compared with compliance in a home setting. Forty-two patients were randomly assigned to the outpatient treatment group, and 45 to home treatment. Voluntary withdrawal, not related to disease progression or unacceptable toxicity of the therapy, was classed as non-compliance.

Voluntary withdrawal was significantly higher in the outpatient treatment group (14%) than the home group (2%). The authors speculated that this difference may be due to the impact of adverse side effects on daily life, which can be more manageable at home. They concluded that, in the therapeutic and social context studied, home treatment is a safe, acceptable and economically realistic alternative to hospital treatment. They noted that chemotherapy for other cancers may not produce the same results.

Specific patient groups

Partridge et al's (2002) review also revealed poor compliance in the paediatric oncology population (Table 3, page 33). Again, measures and definitions of compliance varied between studies.

Adolescents were the least compliant cancer patients. Those most at risk tended to have a poorer understanding of their illness than their peers, and to have less perceived vulnerability and higher levels of denial, compared with those who were compliant. The relationship between parental involvement and compliance also appeared to be important.

These observations are consistent with other research. According to Spinetta et al (2002) the reasons for refusal, non-compliance and abandonment of anticancer treatment in children and adolescents include:

- physical discomfort
- misunderstanding and uncertainty about benefits of medication
- poor communication regarding diagnosis and regimen
- frustration with length of treatment
- fear of side effects
- poor understanding of the seriousness of the illness

Social support, religious beliefs and psychological distress in parents can also have an effect on compliance rates in paediatric cancer care.

Table 3. Non-compliance with prescribed oral antineoplastic agents among children and adolescents

Type of cancer	Measure of non-compliance	Definition of non-compliance	Rate of non-compliance
Leukaemia or non-Hodgkin's lymphoma	Level of drug metabolite in urine	Level lower than expected	33%
Leukaemia, Hodgkin's disease, non-Hodgkin's lymphoma, other malignancies	Self-report and parent report	More than one missed dose per month	35%
	Serum bioassay	Not described	—
Hodgkin's disease, acute lymphocytic leukaemia (ALL)	Biological markers	Level lower than expected	50%
ALL	Level of drug metabolite in urine	Level lower than expected	42%
ALL	Level of drug metabolites in blood	Level lower than expected	10%
ALL	Level of drug metabolites in blood	Level lower than expected	2%

From Partridge et al (2002)

Summary

Much evidence on compliance in taking anticancer medicines relies on clinical trial dropout rates. It indicates that 'non-compliance' is higher in patients taking cancer medication regimens perceived to be for preventive rather than curative purposes. This is likely to have important future implications as better oral anticancer therapies become available, and management of the disease becomes more oriented to its long-term control and the prevention of relapses, as opposed to relatively heroic attempts to 'cure' acute late stage illness.

Young adults with cancer are in particular need of targeted care and support. There is evidence that people who are realistically aware of the risk that cancer presents to them, and the possible benefits of treatment are often willing to persist with therapy, despite sometimes unpleasant side effects, and in some cases the prospect of only small increases in life expectancy. But this should not be taken to imply that patients should or could be frightened into taking cancer treatments. Approaches which allow people to avoid denial, feel confident and make informed decisions, in what may be testing personal circumstances, are more likely to succeed.

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6 Compliance in coronary heart disease

Patients' views about taking medication for coronary heart disease

People taking medicines for coronary heart disease talked about the need to fit their regime in with their lifestyle — otherwise it could be difficult to remember to take the medication. Several people indicated that compliance was aided by good partnerships with health professionals. There were some concerns about unwanted effects and a lot of issues about the need for information which ideally would be linked to sources of reassurance and support.

❝ *I had a heart attack in 1998 and after that I did a cardiac rehab course. We had talks from the pharmacist and that was really helpful, telling us things we wouldn't have known ..also, he explained about when to take the medication, what time of day, when in relationship to meals etc. if you understand all this you are more likely to take it right."* (Woman, 49, diabetic, had heart attack in 1998)

❝ *I recently got in trouble with my GP. I take the aspirin and the BP tablets in the morning and I am supposed to take the cholesterol ones at night. But if we have been out I find it hard to remember it at night — it doesn't fit in with my routine so I had been taking it in the mornings."* (Man, 61, had coronary artery bypass graft 8 years ago)

❝ *Taking the medications is not a problem, except I have to take one dose of the beta blockers in the middle of the day. Fifty percent of the time I may forget to take that particular dose on time and have to take it later."* (Man, 56, had heart attack two years ago)

❝ *I have to take tablets for irregular heartbeat and I hate taking them. I really enjoy the outdoor life and you have to keep out of the sun. It doesn't fit in with my lifestyle and how I like to live. But I do take it as I'd be a fool not to."* (Woman, 49)

❝ *The doctor has given me permission to vary the beta blockers according to my own needs."* (Man, 56, had heart attack two years ago)

❝ *I take the tablets even though I don't like taking tablets. I sort of think they make it worse. Sometimes I get vertigo and you blame it on the pills. But then I think, perhaps it's the weather and perhaps it's me. I try not to blame the tablets. If the tablet is going to do you good, you have to take them."* (Woman, 78, has heart failure)

❝ *More information on the medications [after a bypass] would be really useful, and there is a need for more education but the question is when. If you do too much beforehand it can frighten people. At the time of giving out the tablets the nurses are so busy. Also, at the time, I was in such a poor state that I wouldn't have taken it in."* (Man, 71, recovering from triple bypass)

❝ *There can be a conflict between specialists. One says take this and one says take that. There is a lack of cross-information between specialists."* (Man, 78, had aortic aneurysm repaired in 1995)

❝ *With taking medication I try to achieve a reasonable balance compared to the alternatives [of not taking medications]. I recognise the seriousness of the alternatives."* (Man, 56, had heart attack two years ago)

> *I'm a devil for not taking tablets if I'm not careful, I have an in-built resistance to taking them. It stems from my mother as she would always say pills don't do you any good. I have changed my attitude now, but as soon as I can knock the drugs off I do. ..I don't like drugs but if someone convinces me I'll take them."* (Man, 71, recovering from recent triple bypass)

> *Some people don't take their tablets because they feel so lousy and can't be bothered. You need someone behind you with a big shooter up your backside."* (Man, 71, recovering from recent triple bypass)

Research evidence

Despite falling age-specific mortality rates, coronary heart disease (CHD) is still the most common single cause of death in the UK (British Heart Foundation 2002). Major risk factors for CHD include raised (LDL) cholesterol levels and high blood pressure, as well as smoking and obesity. The links between these factors and other major causes of avoidable ill health in populations such as that of modern Britain (including stroke, type 2 diabetes and lung cancer) mean that the prevention and long term treatment of CHD and its sequelae may represent the most important challenge facing the NHS today.

Relevant forms of pharmaceutical care include the use of low-dose aspirin and other anti-platelet aggregation treatments, antihypertensives and lipid-lowering drugs (LLDs, the most important of which are the statins). In addition, medicines such as nitrates can help relieve CHD-related symptoms such as angina (heart pain), but cannot modify the underlying progression of the disease.

Statins are currently the fastest growing component of medicines spending in the UK. The recent Wanless report estimated that the cost of prescribing statins in the UK will rise from £700 million now to £2100 million by 2010. Given anticipated price adjustments, this implies a four- to five-fold increase in volume.

People with or at risk from CHD are likely to require treatment for many years, if not for life. Clinical trials show that appropriate CHD medication regimens can deliver major health gains cost effectively. But poor compliance reduces their benefits. One key problem is that conditions such as hypertension and hyper-lipidaemia are asymptomatic. Patients are not as motivated to take medicines for these as for health problems which cause tangible symptoms before causing major harm.

Non-compliance rates

At the five-year follow-up of the West of Scotland Coronary Prevention Study (WOSCOPS) a quarter of participants were classed as non-compliant, defined as taking less than 75% of the medication they were prescribed (Shepherd et al 1995). However, compliance and discontinuation rates are often worse than this in practice. For instance, Sung et al (1998) reported that only about one-third of patients took at least 90% of their lipid-lowering treatment. Other investigators have estimated discontinuation rates in this context to be 50% after one year and 85% after two years (Insull 1997).

Adverse health outcomes

A review conducted by McDermott et al (1997) found that non-compliance with CHD treatment was associated with a lower survival rate. Patients with or at risk for CAD (coronary artery disease) or congestive heart failure and who were classified as noncompliant with prescribed treatment, were twice as likely to die as those who were compliant. Non-compliance may also increase morbidity. One study included in the McDermott et al review found that up to 43% of hospitalised cardiovascular disease patients were noncompliant, while another found that non-compliance was one of the two most common reasons for hospital admission.

Patients termed compliant in the WOSCOPS study (those who took at least 75% of the lipid-lowering drugs prescribed for them) appeared to reduce their risk of death from specific causes and need for surgical procedures more than non-compliant patients (Figure 6, based on Shepherd et al 1995). However, this does not necessarily imply a direct causal link — other factors in people's lives may also have a protective effect as well as increasing their ability to comply.

Factors affecting compliance

As in other areas of medication, many factors have been associated with compliance with CHD treatment regimens. Those cited in the recent literature include:

Poor compliance

Demographic factors

- female
- under 45 years
- over 75 years
- lower socio-economic status
- non-white

Medication related factors

- twice-daily dosing (compared with once-daily)
- multiple drug regimens
- taking preventative as opposed to curative treatment, especially if the condition is asymptomatic
- fear of adverse side effects
- not being convinced of the need for treatment

Physical and psychological factors

- co-morbidities, including depression and dementia
- feeling in good health
- lack of knowledge about disease

Good compliance

Medication related factors

- use of statins compared with other lipid-lowering drugs
- prior good compliance

Provider related factors

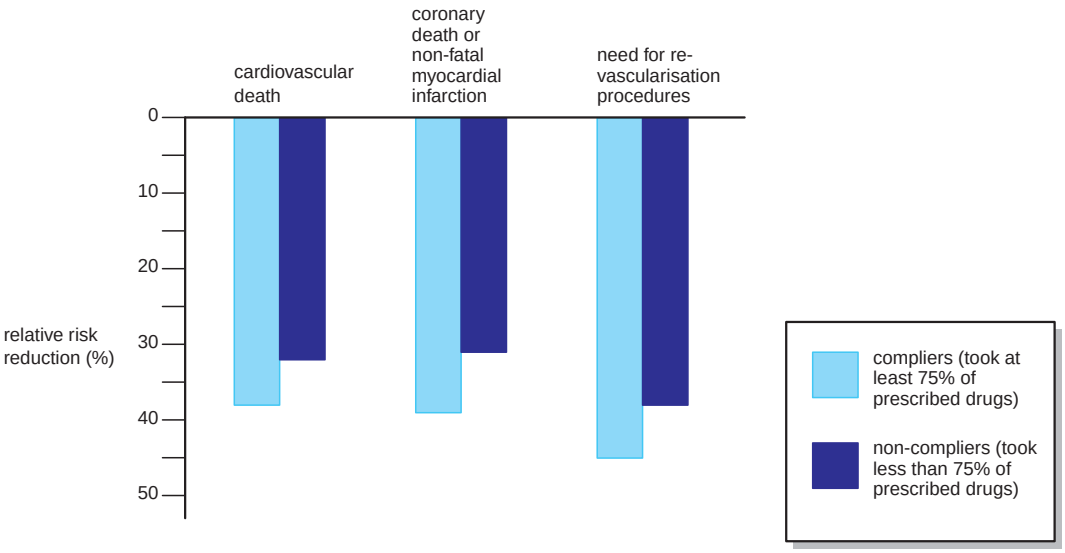
- good relationship with physician

Physical and psychological factors

- feeling in bad health

From LaRosa and LaRosa (2000); Benner et al (2002); Larsen et al (2002)

Figure 6. Medication compliance rates and reduction in the risk of cardiovascular disease (CVD)



Based on Shepherd et al (1995)

Interventions to improve compliance

The causes of non-compliance with CHD treatment are multi-factorial and multi-dimensional, as are the most successful approaches to reducing it. The available literature highlights three main areas of intervention:

- ***Patient-focused***
  - simple regimens tailored to patients' lifestyle
  - explicit patient education and instruction
  - involving the family
- ***Provider-focused***
  - regular contact
  - reminding patients of appointments
  - supplying compliance aids
  - allowing patient to feel comfortable asking questions
- ***System-focused***
  - using pharmacists
  - providing lipid management via lipid clinics

From LaRosa and LaRosa (2000); National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III; 2001)

Pharmacists are potentially well placed to provide counselling about the importance of compliance with cardiovascular medication regimens (Rybacki 2002). Previous studies have shown that pharmacists' interventions enhance knowledge about medicines, but have little effect on compliance rates. However, Blenkinsopp et al (2000) designed an intervention to improve compliance with treatments for hypertension, grounded in patients' own beliefs and experiences and delivered in community pharmacies.

Information from patient interviews was used to construct a brief questioning protocol to enable community pharmacists to ask patients about their views on their treatment. According to self-reports, compliance in both the intervention and control groups was similar at baseline (around 50%). After the study, it increased in the intervention group to nearly 63%. Patients in the intervention group also collected more prescriptions than controls. The authors attributed the success of the intervention to its being tailored in response to patients' needs, and to the time and attention spent on patients by pharmacists.

Specific patient groups

There is more research evidence about cardiovascular medication compliance for older people than for other age groups. There has been little research on CHD medication compliance among ethnic minorities, despite the relatively high prevalence of cardiovascular conditions in groups such as Pakistanis and Bangladeshis, and immigrants from Ireland (Joint Health Surveys Unit 2001).

In the US, research has been conducted among patients over 65 taking lipid-lowering medication such as statins, niacin, clofibrate, cholestyramine, gemfibrozil, probucol and colestipol. Average 'persistance' with their medication during one year (measured by analysing dispensed prescriptions) was around 60% (Avorn et al 1998). The highest compliance rate was with statins (64% day-to-day) and the lowest with cholestyramine (37%).

Rates tend to decrease over time. A Canadian study compared two-year compliance rates in three cohorts of patients, all aged 66 or over:

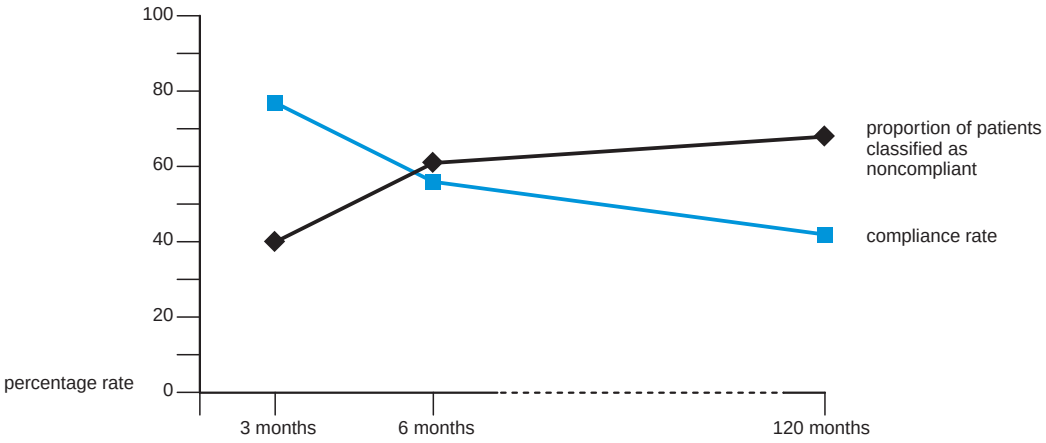
- those with recent acute coronary syndrome (ACS)
- those with chronic coronary artery disease (CAD)
- those who had been prescribed statins but had no evidence of coronary disease

Compliance was defined as a repeat statin prescription being dispensed at least once every 120 days after the initial prescription. It was initially recorded as being more than 70% at 3 months for all cohorts, but continuously decreased over the two-year period. At two years the compliance rate was found to be 40% in the ACS cohort, 36% in the CAD cohort and 25% in the 'no disease' cohort. This suggests that patients taking statins for what they perceive to be preventive reasons are unusually poor compliers (Jackevicius et al 2002).

A US study by Benner et al (2002) followed more than 34,000 statin users aged 65 and over. It showed that people took their medicine as prescribed 79% of the time in the first 3 months of treatment. This rate fell to 56% at 6 months and 42% at 120 months. The proportion of patients classified as noncompliant at 3, 6 and 120 months was 40%, 61% and 68% respectively (Figure 7).

These are important findings, because clinical trials suggest that statins (unlike treatments such as aspirin) may be effective in reducing mortality and morbidity in patients with coronary artery disease only after at least one to two years of continuous treatment. It is possible that in the US, more than in the UK, economic and allied factors may discourage long-term medicine by those sections of the population most at risk of developing heart disease and related conditions. However, the available evidence suggests that non-compliance with CHD related medication programmes is also a significant problem in the UK.

Figure 7. Compliance with statin use



From Benner et al (2002)

Summary

Providing effective treatment for the prevention and control of coronary heart disease is one of the most important tasks facing the NHS. The appropriate use of medicines can significantly reduce cardiovascular disease-related morbidity and mortality. However, research evidence indicates that non-compliance is an important problem in this area, especially among patients taking preventative medicines such as statins.

As well as causing harm to individuals, non-compliance represents a waste of NHS resources and may endanger the achievement of public health improvement goals. Improving performance in this area and related fields such as diabetes prevention and care is a high priority objective, to which professionals such as pharmacists should in future be able contribute more effectively.

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7 Compliance with treatment for depression

Patients' views about taking medication for depression

People with depression said that their attitudes to taking medication varied according to how they felt at different stages. There were numerous concerns about unwanted effects, and about the quality of information about the risks and benefits of medication. Sometimes people varied how they took their medications with or without professional advice. There was some concern from the national voluntary organisation, Rethink, that the cost of medication undermined compliance for some people.

> *At first I just wanted something. I needed something as I was in such a state and I needed to try something. I was aware I needed help ..When I first started feeling better I heard birds sing and that lifted my spirits and I knew something was better. But as I felt better I have sometimes tried to stop [medication] as I feel so good now ...I felt so well I thought I could cope without medication. It led me into a false sense of security."* (Man, 38, with depression and schizophrenia)

> *At that time [when the depression started] I was quite happy to take medication ... In my third spell, following a suicide attempt, they gave me lithium and I read up about it. I came off it because of what I read about the effect on the liver and kidneys ... At one stage I was referred to a reflexologist, she was someone to talk to and was influential at that stage. She believed medication was a poison to the system so I came off the medication."* (Man, 61)

> *If people are given more information they'd be more likely to take the medication, if there is a positive approach e.g. "these are the things to look out for, and if you have a problem, come back to me"... The doctor and nurse did not tell me about side effects, but when I went back and said that I have problems like I need to scratch myself all over, then they told me."* (Man, 38, with depression and schizophrenia)

> *I don't bother reading the leaflets — well I do now. But at first the leaflets are not simple. They are too much as you are depressed and not feeling on top of the world. It would be better if there was just a card with the most vital bits of information. When I was depressed I just did not want to read ... It would be good if the person who prescribes the medicines could talk more about them. It wouldn't have stopped me taking the pills as I needed to get well in the head. But I would have liked to have an honest explanation of possible side effects, such as weight gain."* (Man, 38, with depression and schizophrenia)

> *I got to the point of thinking: what is me and what is the medication? So I took myself off the medication. I told my psychiatrist and he said if I had problems to let him know. When I went back, he said "You're doing OK. We could probably have taken you off the medication years ago"."* (Man, 61)

> *I have sometimes started on a high dose and when I steadied I felt I could do with less, so I reduced the dose. When I am under stress I take a half or quarter tablet more. I don't make an appointment with the psychiatrist first. I wait for my appointment to come round then I tell him. That approach works. In fact, he compliments me on it."* (Woman, 54, with depression)

> *I get a season ticket and that is equivalent to a week's incapacity benefit."* (Woman, reported by Rethink)

Research evidence

The World Health Organisation has estimated that, by the year 2020, unipolar depressive illness will rank second (after ischaemic heart disease) among the causes of disability worldwide. Yet despite the scale of this problem and the importance of controlling it effectively, information on compliance in depression therapy is relatively limited (Pampallona et al 2002). (The treatment of manic/bipolar depression and other depressive psychoses are not discussed in this report.

Depression is often a chronic condition. At least half the people who are diagnosed as depressed will experience a recurrence. Many clinicians argue that patients should take medication for long periods of time, perhaps for life, to protect against relapses. But others point out that the evidence available on the effectiveness of drug treatments (compared with placebo medicines) is — particularly for mild to moderate depression — relatively weak.

Medication compliance is a well established issue in the care of depression. There is evidence that more than 50% of depressed patients discontinue treatment prematurely (Katon et al 1996). The reasons for poor compliance include unpleasant side effects and not feeling better. In addition, beliefs and attitudes to treatment can be a major influence (Demyttenaere 2001). Despite the fact that severe depression may be disabling enough to demand hospital admission and is potentially life threatening, the nature of the illness means that sufferers may underestimate their capacity to respond to treatment.

Non-compliance rates

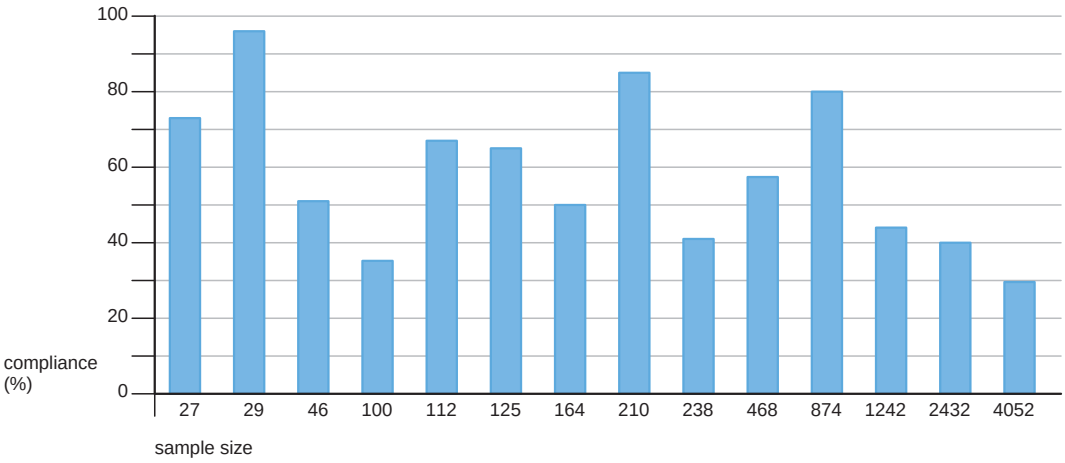
Reported rates of non-compliance with medical treatments prescribed for unipolar depression vary considerably. A recent review examined 32 relevant studies (Pampallona et al 2002). Most used direct measures of compliance, such as pill counts; some used the number of therapeutic appointments kept. Only four studies used composite measures of medication intake. The review cited medication compliance rates from 14 epidemiological studies, varying from 30% to (a questionable) 97% (Figure 8). Some other non-randomised clinical trials have reported compliance rates below 10% in groups that received no intervention beyond their drug treatment.

A review of studies conducted between 1975 and 1996 in the US showed that patients on antidepressants took an average of 65% of the prescribed amount. These rates contrasted with an observed 76% compliance in physical disorders (Cramer and Rosenheck 1998). Other research has claimed that depressed patients are three times more likely to be non-compliant with medical treatment recommendations in general, as compared to non-depressed patients (DiMatteo et al 2000).

Differences between antidepressants

Compliance rates may also vary between classes of drug and dosing regimens. For example, in the US Claxton et al (2000) found that compliance with a once-weekly dose of fluoxetine was higher (86%) than with a once-daily dose (79%). Similarly in the Netherlands, when patients changed from a once-daily dose of fluoxetine to a once-weekly dose, compliance did not decrease, while those who remained on the daily dosage became less compliant over time (de Klerk 2001).

Figure 8. Compliance in epidemiological studies of unipolar depression



From Pampallona et al (2002)

Many studies have compared compliance in relation to the newer selective serotonin re-uptake inhibitors (SSRIs) with the older tricyclic antidepressants (TCAs). SSRIs tend to have fewer, and more tolerable, side effects than TCAs. Unsurprisingly, this appears to have an effect on compliance.

Thompson et al (2000) assessed compliance using pill counts, patient questionnaires and a device called the Medication Event Monitoring System (MEMS), a medication dispenser containing a microchip that records when the container is opened. The MEMs provides a useful indicator of compliance, although the medication is not necessarily consumed each time the container is opened. They found that the level of compliance with fluoxetine was higher than with the TCA dothiepin on all outcome measures, although the differences were not statistically significant. An increased level of compliance seemed to translate into improved health outcomes — patients taking fluoxetine scored better on the health transition scale of 36-item Short-Form Health Survey Questionnaire and showed an improvement on the Hamilton Depression Rating Scale, although there may not be a direct causal relationship with compliance.

Better tolerance of SSRIs has been generally reflected in lower dropout rates from clinical trials, compared with those of TCAs (Barbui et al 2000).

Adverse health outcomes

Depending in part on how bad the depression is, symptoms can recur if medication is stopped before the patient has made a full recovery (Melfi et al 1998; Sood et al 2000). But taking antidepressants as prescribed can be difficult for patients, especially when side effects appear before symptoms are relieved. There is strong evidence that even with drugs like dothiepin, which many prescribers have believed to be the safest of the TCAs, there are significant associations with conditions like ischaemic heart disease (Hippisley-Cox et al 2001). But the literature on adverse health outcomes from non-compliance with antidepressant medication is limited.

Factors affecting compliance

Several variables have been found to influence whether people take antidepressants as prescribed. The recent review by Pampallona et al (2002) found the following factors correlated with better compliance:

- ***Demographic factors***
  - female
  - married
  - relatively high educational status
  - high IQ
- ***Medication-related factors***
  - lack of severe side effects
  - lack of relapse
  - previous use of antidepressants or psychiatric treatment
- ***Provider-related factors***
  - prescription by psychiatrist
  - referral to private psychiatrist
  - non-emergency referral
- ***Social factors***
  - good social adjustment
  - diagnosis other than personality disorder and substance abuse

A review by Delgado (2000) emphasised the importance of a patient's 'personal model of illness' in relation to compliance. This model encompasses their attitudes, beliefs and expectations about their illness and treatment. Kadam et al (2001) found that many depressed patients do not perceive medication to be an effective response to their needs.

Interventions to improve compliance

In their review of the literature, Pampallona et al (2002) found few quantitative studies on interventions to increase compliance in depressed patients. Most studies investigated a variety of interventions, and it was not possible to determine which components of the intervention (or combinations of components) had been effective. Studies also tended to present aggregated data relating to both major and minor depressive episodes and mixed diagnoses, so the authors could not assess whether an intervention worked better for some diagnostic sub-groups than others. There was a tendency, however, for interventions with more components (for example, patient education plus management changes plus a medication clinic) to produce better results. This is consistent with findings in a variety of other conditions.

One UK randomised controlled trial compared the effects of antidepressant drug counselling and providing information leaflets, on compliance with prescribed medication programmes for depression (Peveler et al 1999). The drug counselling consisted of:

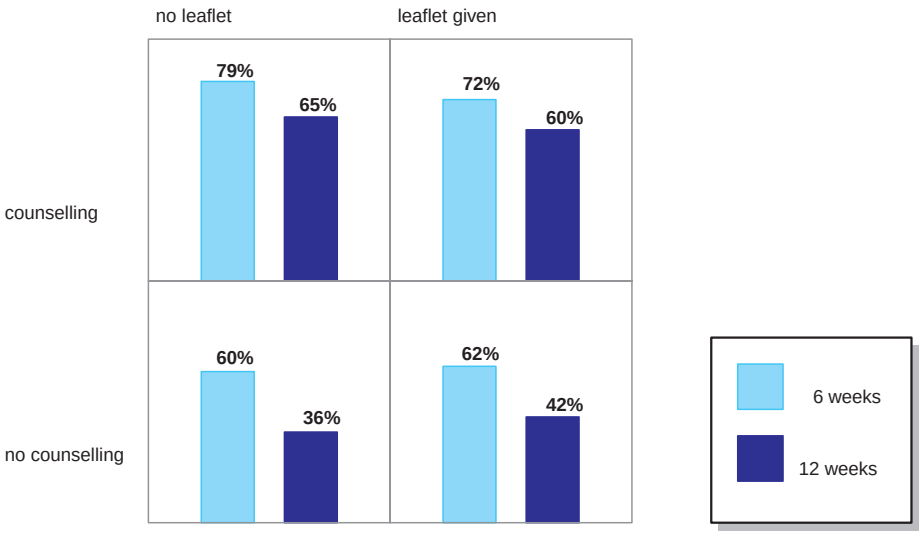
- assessments of daily routine and lifestyle, and attitudes to treatment
- education about depression

- self-help support and resource provision
- discussion of side effects and medication management
- advice on compliance

The leaflet contained information about the medicine prescribed, its side effects and what to do if a dose was missed. As shown in Figure 9, significantly higher percentage of patients (65%) who received drug counselling at the beginning of their treatment continued medication to 12 weeks, compared with those who received no intervention (36%), or just the leaflet (42%). But this did not affect their depressive symptoms

An 'attention control' group confirmed that these results were not simply due to the extra attention given to patients. The investigators concluded that the information leaflet had no significant effect on compliance with antidepressant medication regimens.

Figure 9. Proportion of patients who continued to take antidepressant treatment



From Peveler et al (1999)

Specific patient groups

Few studies have focused exclusively on treatment compliance in depressed elderly, adolescent, or ethnic minority populations. These patient sub-groups are likely to have specific issues related to compliance.

Carers of elderly depressed people took part in focus groups for a UK study conducted by Boyle and Chambers (2000). They were found to have little knowledge of depression, or its medication. They nevertheless took an active role in trying to ensure compliance. Such observations highlight the need for health care professionals to support the carers of older people with depression in their efforts to help deliver effective treatment programmes, and to provide them with relevant information.

Summary

Non-compliance with drug treatments for depression is high. Factors that may affect it include side effects, lack of efficacy, relatively complicated dosing patterns and lack of belief in the appropriateness of drug treatment for this form of mental distress.

Depressed patients appear less likely than others to be compliant with any form of medication. This has important implications in other fields, such as the prevention and treatment of CHD. Information leaflets appear to have little or no impact on compliance rates. However, therapeutic counselling has been shown to help people with depression to take antidepressant medicines for extended periods. There is evidence that patients who are given relevant support continue with their treatment for longer than non-supported patients. The extent to which increased compliance is likely to lead to improved long term health outcomes amongst patients with mild to moderate depression is debatable. But for people with severe depression, the benefits of increased compliance may be much more significant.

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8 Compliance with treatment for diabetes

Patients' views about taking medication for diabetes

Diabetes UK and people with diabetes agreed that providing sound information about diabetes and its management as well as information about medications is necessary to enable people to take their medications correctly and control their disease. As with other conditions, there were misgivings about the leaflets that accompanied medication packs. Some people indicated that compliance might vary with age, and young people might find it particularly difficult to adhere to strict medication regimes. The means by which medication was administered was an important factor, as was the complexity of the medication regime.

❝ *I am geared to doing it all properly, as if not I would put my heart and kidneys and nerves at risk."* (Man, 69, with type 1 diabetes)

❝ *When I was diagnosed the GP went through everything. He said what diabetes was, how it was to be treated, and the importance of taking the tablets. I listened to what he said and try to carry out what I am told."* (Man, 76, with type 2 diabetes)

❝ *The pressure on staff at diabetic clinics and in hospitals is such that they don't get a lot of time to talk to people — maybe just 15 minutes. And you can't take it all in in that time."* (Man, 69, with type 1 diabetes)

❝ *In the doctor's surgery, the end of the interview is when he tends to write the prescription. It could be more helpful if the doctor explained more about the medication and what it should do."* (Man, 71, takes tablets for diabetes)

❝ *The product information sheets — I am not sure if they are good or bad. Some people are scared off by them."* (Man, 71, takes tablets for diabetes)

❝ *As a teenager I did go through a rebellious stage — a lot of young diabetics do. It's about not wanting to be different. And in those days you had to do urine tests not blood tests and I hated urine tests so I didn't bother. When I look back, my blood sugars must have been sky high."* (Woman, 49, with type 1 diabetes since age 10)

❝ *The advent of "pens" has made giving the insulin very easy. Now, if I am going to a lunch at the Rotary, I can wait till I sit down at table and depending on the number of units I think I need, I can pull up my shirt and do it without anyone even noticing it!"* (Man, 69, with type 1 diabetes)

❝ *You can feel bad and forget to take your tablets. I am taking 15 or 16 tablets and you can forget. But now I know if I forget to take something I feel sweaty and I think what have I done wrong? When I am on holiday I use a box to remind me what to take. When I am at home I write it down on a bit of paper. I keep a chart for my own sake. If I go out I take the tablets with me."* (Man, 76 with type 2 diabetes)

Research evidence

Diabetes is a chronic condition, associated with loss of the ability to produce or respond appropriately to insulin. As well as being life-threatening in itself, via the risk of hypo- or hyperglycaemic crises, its long term complications include cardiovascular diseases such as coronary heart disease (CHD) (Hu et al 2002), renal failure and blindness.

Type 1 diabetes is sometimes referred to as **early onset** diabetes. It always requires treatment with insulin. **Type 2** diabetes, sometimes referred to as **late onset** diabetes, is associated with obesity and lifestyle. Its treatment may involve the use of insulin, but often relies on dietary and lifestyle changes coupled with oral medication. Its prevalence is rising in the UK and worldwide.

Currently, about 1.4 million people have been diagnosed with diabetes in the UK. It is thought that this figure could double by 2010 (Diabetes UK 2002). Control generally requires frequent monitoring of blood glucose levels, and attendance at hospitals and clinics. Research in the UK and elsewhere has confirmed that good blood glucose control in patients with type 2 diabetes reduces complications and risk of death (Stratton et al 2000). Most of the literature available is either on compliance with aspects of diabetes control other than medication taking (such as dietary modification and keeping NHS appointments); or control of the condition as assessed by markers such as serum glycosylated haemoglobin.

Non-compliance rates

Recent research from Scotland revealed that, among 2920 type 2 diabetes patients, adequate compliance (defined as taking more than 90% of prescribed medication) was found in less than one-third of those prescribed sulphonylureas and/or metformin. Patients taking both drugs achieved only 13% compliance (Donnan et al 2002).

Factors affecting compliance

Research among patients with diabetes indicates that simple regimens where patients take only one type of drug, once a day, yield better compliance. Decreases in compliance of 22% for each increase in frequency of daily dosing have been found (Dailey et al 2001; Donnan et al 2002).

Psychological and social variables such as family support, good relationships with health professionals, absence of chronic stress and the ability to take on the challenges posed by the disease have been shown to have an influence on compliance (Lo 1999).

A long-acting insulin, Glargine, has recently been launched; it works at a consistent level for 24 hours. It is hoped that this type of insulin will lower the risk of night-time hypoglycaemia and improve blood glucose control. A preliminary investigation by the National Institute for Clinical Excellence (NICE) recommends that Glargine be prescribed to people with type 1 diabetes (Diabetes UK 2002; NICE 2002). However, it might also benefit some people with type 2 diabetes.

Interventions to improve compliance

Self-management programmes can be effective in improving blood glucose control and quality of life in patients with diabetes (Naquib 2002). Multidimensional programmes which enable participants to manage and cope with their illness in everyday life, are likely to produce better, longer lasting, results than didactic approaches which aim to impart specific information rather than raise people's overall confidence levels. According to Naquib and other sources, the most effective self-management programmes:

- include behaviour change strategies
- recognise and understand the importance of the patient's personal and unique experience of living with diabetes
- are patient-centred
- take social, emotional, cultural and psychological aspects into account
- include personalised goal-setting
- include social learning variables such as problem-solving skills and self-efficacy
- involve health professional and patient working as partners

Medication compliance has not always been measured in evaluatiing such interventions.; but it is almost certain to be improved.

(See also information on the Arthritis Self-Management Programme on page 15 in Section 2.)

Specific patient groups

Compliance with diabetes treatment regimens among children is usually good, as parents typically take responsibility for enforcement. However, as young people reach adolescence and their parents become less involved, compliance tends to decline. The drive towards independence from parents, the wish to have a similar lifestyle to their peers, and the other physical, emotional and social changes during adolescence, can all affect a young person's willingness and ability to manage her or his lifestyle and take regular treatment.

Research in this area has associated various psychological factors with observed compliance levels. According to a hypothetical model constructed by Kyngas (1999) these factors include encouragement and support from parents, fear of complications, will power, motivation, experience of results, and a sense of normality. Some of these influence compliance directly, others indirectly.

Ott and colleagues (2000) found that prior experience of successfully managing treatment tended to enhance patients' self-efficacy, which then led to increased compliance. This finding is consistent with research in areas such as arthritis care.

Support from others may also be important for young adults with diabetes. Kyngas et al (1998) found that actions of doctors, nurses and parents that were described as 'motivating' were associated with better compliance. Perceived parental acceptance of the young person's autonomy was also related to good compliance. Poor compliance was linked to routine or negligent medical actions, parental discipline and control, and domination by friends. However, these findings should be

interpreted with care — for example, parents should not be unfairly blamed for causing the problems they struggle to help resolve.

In a recent Cochrane review assessing various components of treatment regimens for adolescents with diabetes, Hampson et al (2001) concluded that educational and psychosocial interventions have small to medium benefits. They are more likely to be effective if they enable patients to understand the relationships between the different aspects of diabetes management. For example, demonstrating how regular self-monitoring of blood glucose can be used to guide other behaviours, such as lifestyle adjustment, makes it more meaningful and more likely to be done.

Multi-component interventions were more successful with adolescents than those focusing on just one aspect of management. Positive parental involvement also had beneficial effects upon compliance. However, there was little evidence that family-based interventions were any more effective than individual- or group-based ones. There were indications that the optimal time for intervening is in the early months after diagnosis. The reviewers pointed out that different approaches might be required for younger as opposed to older adolescents. Interventions may need to be tailored to the individual.

For people who develop type 2 diabetes in later life, the challenges faced are similar to those experienced by people with or at high risk of coronary heart disease (CHD; see Section 4, pages 35–40). Whether medication is seen as preventive rather than bringing immediate health benefits is, for example, one of the key variables likely to affect compliance.

Summary

Non-compliance with type 2 diabetes treatment is high, due in part to its major impact on daily life. Given that it is essentially a 'lifestyle condition', medication regimens that fit into people's existing routines are more likely to be accepted. The available research indicates that interventions that raise self-efficacy and enable service users to be confidently and actively involved in controlling the management of their illness are most likely to be effective in improving compliance rates.

Young adults with type 1 diabetes need facilitative, well informed, parental and professional support in taking control over the treatment-related aspects of their lives. Their need for independence and normality demands appropriate recognition for them to be protected as effectively and efficiently as possible.

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9 Compliance with treatment for epilepsy

Patients' views about taking medication for epilepsy

The National Society for Epilepsy (NSE) and the people who were interviewed drew attention to several factors that may affect how people with epilepsy take their medication. As well as the stigma associated with epilepsy, unwanted effects, both actual and potential, are important. The intervewees point out that a feeling of control is valued, and that people need good support and information to make choices. Other issues are particularly relevant to children and young people; and to people with learning disabilities. Some people with epilepsy may find it difficult to get supplies of their medication. Finally, decisions about compliance may be taken with other people in mind, as relationships and work can suffer if seizures are uncontrolled.

❝ *For some, side effects are so severe that regardless of the effectiveness of the medication, they may not find it acceptable. Some specialists feel that seizure control should not be at the expense of quality of life. But it varies.* " (NSE)

❝ *I have had side effects and have gone back to the doctor. I needed to feel in control of my medication. I have had double vision, dizziness, loss of appetite, things like that. Some people with epilepsy have those side effects and don't realise that a change of dose or change of medication can be helpful.*" (Woman, 40)

❝ *Also, there are the effects the drugs have, like not being able to have much alcohol. And there are side effects. I feel doped out a lot of the time, though I don't notice it so much now as I am used to it and I no longer know what I would otherwise feel like.*" (Man, 36)

❝ *When I started the phenobarbitone I was not really informed how difficult it is to come off. Time creeps up and after a bit the doctor will say it's difficult to take you off. I wasn't made aware of the long-term difficulties. So I have been boxed into a corner a bit.*" (Man, 36)

❝ *Children always have an issue about being different. At school I used to have to take medication at lunchtime and that made me feel different.*" (Woman, 40)

❝ *There was a period when I was prescribed Epilim, but I took no medication for months. I was at university and as it happened I had a completely seizure-free period. It wasn't a decision, I was just an irresponsible youth! Now I can see clearly the relationship between taking the drugs and the consequences. When I was younger I couldn't see the consequences [of not taking them]. It was a threat rather than a reality.*" (Man, 36)

❝ *You may think the seizures have gone away so you don't need the medication. That may be right or it may be that the seizures have abated because you are taking medication.*" (Woman, 40)

❝ *If you are epileptic, getting hold of the drugs can be difficult. Phenobarbitone is a restricted drug and sometimes it is difficult to get hold of. And Lamotrigine in different tablet forms, they don't hold a huge stock. You may have to go back to the chemist. You can phone through or post your prescription but when they don't have it all in and you have to go*

back you feel like punching him. If you are epileptic and can't drive, getting medications can be difficult. You have to be highly motivated." (Man, 36)

> *"Personally, if I take my drugs or not, it's up to me. But if I have seizures and my fiancee is concerned about me, then I have a responsibility to others as well. And to my colleagues. There is a pressure on me and overall I think you have to take the drugs as prescribed. I do what I'm told on the drug front, Epilepsy is difficult because of letting people down. But there are times when I feel: forget it, I'm going to stop taking these pills now. But to be honest, I don't have a choice."* (Man, 36)

Research evidence

Epileptic seizures are the result of abnormal brain activity. Recurrent seizures — related to brain lesions acquired before or after birth — can cause physical, cognitive and psychosocial disability, and premature death. Lifelong medication may be needed in order to control seizures. Epilepsy is still not well understood by many people, and may be associated with forms of social stigma. Using medicines to control seizures is not always straightforward. Trade-offs may need to be made between the total elimination of seizures and the maintenance of high levels of cognitive function.

Seizures can occur at any age. Their reported incidence is highest among children, adolescents and older people. Epilepsy is more prevalent amongst people with learning disabilities than it is in the general population. It sometimes occurs in conjunction with cerebral palsy. People with learning difficulties and their carers may require special help in medicines management.

Non-compliance rates

Buck et al (1997) found that 72% of patients taking anti-epileptic drugs (AEDs) said they never miss taking their medication. 15% reported missing doses less than once a month, 9% missed more than once a month and 4% said that, at least once a week, they did not take their treatment as prescribed. Half those contacted reported side effects, ranging from tiredness and memory problems to depression and headaches.

Adverse health outcomes

Non-compliance with AEDs can increase the chance of seizure recurrence, which may be harmful or even fatal. Hanna et al (2002) conducted an audit of epilepsy-related deaths. Of the deceased patients who had not received secondary care, 11% had a record of very poor medication compliance; 7% had decided not to take the recommended dose; and 7% took their medication irregularly. The frequency, type or severity of seizures do not in themselves appear to influence compliance rates (Buck et al 1997).

Factors affecting compliance

Studies have identified many variables associated with medication compliance in epilepsy. They include:

Factors related to good compliance	Factors related to poor compliance
Age over 60	Age under 60
Age over 19	Teenager (age under 19)
Once-daily dose	Four-times daily dose
Feeling that it is important to take medication as prescribed	Feeling stigmatised
Finding GP easy to talk to	Experience of side effects
Concerned about health or health risks	
Absence of barriers, such as costs, inability to obtain medication	

From Buck et al (1997); Buelow and Johnson (2000); Garnett (2000)

Seizures and anti-epilepsy medicines may make patients forgetful, which can raise levels of involuntary non-compliance.

Interventions to improve compliance

People with epilepsy often say that they want more information about their condition and how to cope with it. Ridsdale et al (1997) evaluated a nurse-run clinic that provided an information and disease monitoring service. The medical records obtained showed that, before attending the clinic, just 25% of patients had been identified as needing advice on medicine compliance. After intervention by the clinic, this figure rose to 80%. Ridsdale et al expressed concerns that many noncompliant patients are going undetected, and hence that opportunities to improve health outcomes amongst people with epilepsy are being overlooked.

A report by Garnett (2000) advised clinicians to emphasise the importance of compliance when therapy is initiated, and to enquire about it at each visit. They stressed that medication regimens should be kept as simple as possible and, as far as practicable, incorporated into the patient's lifestyle. Information should be given on side effects and possible drug interactions. Similarly, patients themselves should make sure they understand their condition and the need for long-term therapy. However, the authors did not give any evidence that these factors improve compliance.

Patient education and empowerment programmes have improved compliance in a range of contexts. However, a review of patients with epilepsy reported that such interventions generally increase knowledge but not compliance (Buelow and Johnson 2000). This effect could have resulted from an inappropriate concentration on providing instruction and direction about medicine taking, rather than on opportunities to raise patients' sense of self-efficacy.

New measures of compliance

Williams et al (2001) reported that hair analysis can be a useful technique to monitor medication compliance in patients with epilepsy. However, as with other assay-based compliance monitoring techniques (for example, in asthma care), important ethical issues must be taken into account. Medicines use should never be monitored covertly, and patients' fully informed consent should be obtained before samples are collected. Similarly, information which might affect individuals' entitlements to disability and allied benefits should not be passed on to third parties without informed patient consent.

Specific patient groups

Epilepsy is more prevalent in older people than in adults of working age. Older people may be particularly susceptible to the adverse consequences of seizures, which can include physical injury, loss of confidence and reduced independence. Treatment may be problematic, because interactions with other forms of medication and age-related changes in metabolism can increase vulnerability to side effects.

It has been suggested that medication compliance among older people could be improved by providing of written instructions, careful explanations to patients and their carers, and the use of monitored dosing systems (MDS). Patients with poor vision, deafness, cognitive impairment or difficulty with dexterity should receive additional support (Stephen and Brodie 2000). However, the value of providing written aids, such as leaflets on medication options, has not been conclusively demonstrated. Structured interpersonal support is likely to be of more value.

Teenagers with epilepsy may feel isolated and stigmatised, that their independence and ability to join in with their peers is threatened, and that their condition is not adequately understood. These feelings, along with other normal adolescent concerns, are likely to affect compliance. Young adults may stop taking their medication in order to fit in with their friends, or because they are denying their illness. Research in Finland by Kyngas (2000, 2001) with 300 teenagers aged 13–17 revealed that 22% said they fully complied with their treatment regimen; 44% reported satisfactory compliance; and 34% poor compliance. The highest level of compliance was for medication, compared to other regimen components such as lifestyle changes.

Psychological and social factors often contribute to non-compliance with treatment regimens in adolescence. Young people who felt supported by their parents and doctor, and had good motivation, were ten times more likely to comply than those who did not. Those who did not feel their condition to be a threat to their social well-being were eight times more likely to comply than those who perceived it as such a threat. Family environment has also been shown to be important in determining compliance with medication, and other aspects of treatment (Mitchell et al 2000; Otero and Hodes 2000).

No literature was found on compliance with AED regimens among ethnic minorities, although the reported prevalence of epilepsy may vary between social and groups. For example, reported incidence is lower in South Asians than in the rest of the population (Wright et al 2000). However, factors such as limited access to expert diagnosis and fear of the social stigma associated with epilepsy and learning disability may mask underlying prevalence rates in some communities.

Summary

The immediate impact of epilepsy on an person's life is such that those living with it are normally aware of their condition and its risks, and well motivated to control it. So medication is accepted despite its side effects. But non-compliance in relation to specific aspects of epilepsy medication and other treatment regimens is relatively common — as in other areas of long-term illness care.

The limited available research evidence is consistent with the view that multi-faceted communication, and support programmes designed to promote empowerment rather than just compliance, are most likely to be effective. The needs of adolescents and young adults with epilepsy, and of people with learning disabilities, require special attention; so may the needs of people from minority groups which may lack full access to adequate health care.

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10 Compliance with hormone replacement therapy (HRT)

Patients' views about taking hormone replacement therapy

The main issues raised by women on HRT related to the unwanted effects of the medication and the way in which it was administered. There were also significant concerns about information leaflets. Access to timely advice seemed to enhance compliance for women on HRT.

❝ *When I started HRT it started as a normal dose, 1.25, I think it was. I could not tolerate it. I was sick and all that jazz — giddiness, nausea, weakness, tremors… I changed the brand and had the same problems, so I went back to the GP and said: Listen, I can tell you from my body that if there is such a thing as a half-dose, that would be perfect. They hadn't told me about the half dose, but my body said to me: that's too much, half is just what I need."* (Woman, 54)

❝ *One thing is that I am not western … and my body framework is smaller than a western woman. Yet they give me the dose indicated in the BNF and they don't take my size into account…They treat the condition, not the person. So that affects what I decide to do."* (Woman, 54)

❝ *I found implants great — no side effects and they worked straight away. It was right from day one and much less fuss than tablets or a patch — all done and dusted."* (Woman, 45)

❝ *I sit in the car before I see my consultant and make a note of what I am going to say — and I have known her four or five years. I get so frightened that I won't be able to articulate what I want, especially as my condition is hormonal and I can't always control my emotions with the doctor. I have fought to be treated with respect. It's OK now. But I have had to fight to take my husband in with me. There seems no formal way for him to get reassurance. Also, it's an emotional thing and sometimes it's the person affected by my emotions that needs to explain."* (Woman, 40)

❝ *I read the leaflets but they are so generic. I could come down with plague and my symptoms would be covered… I like the latest leaflets that say how many in a thousand get the side effects. This took me a while to understand. But the fact that a symptom is common is reassuring. Yes, that would reassure me, not put me off as I would see it as something quite usual."* (Woman, 40)

❝ *Sometimes I have supplemented HRT with homeopathic preparations. Maybe that has been when I could not see the doctor immediately. When I had IVF there was a helpline and a doctor was always on call. That was fantastic. An HRT helpline would be tremendous."* (Woman, 40)

Research evidence

Hormone replacement therapy (HRT) contains synthetic oestrogen and progesterone to replace diminishing hormone levels at the time of menopause. HRT can be used to relieve unpleasant symptoms such as hot flushes, vaginal dryness and sleep disturbances, and offset other difficulties associated with ageing. It has also been found to be effective in preventing osteoporosis (see Section 9, pages 64–66) and certain other conditions.

However, HRT increases the risk of developing breast cancer. Rather than protecting against cardiovascular disease (as had been assumed until recently) it can increase the risk, at least among a proportion of users, such as those with undiagnosed or diagnosed type 2 diabetes (Roussouw et al 2002).

HRT is primarily a symptom-relieving treatment, typically used in the context of normal ageing. 'Non-compliance' is therefore not equivalent to not taking proven therapies to prevent or treat conditions like breast cancer or heart disease. Taking HRT may significantly affect the well-being of patients or those around them; but the rights and responsibilities of individuals carefully to assess the potential costs and benefits, and to make informed decisions geared to meeting their personal needs, must clearly be respected.

Non-compliance rates

Poor compliance/continuation rates with HRT are well documented. Faulkner et al (1998) conducted a retrospective longitudinal analysis of over 28,000 new HRT users in the US. Patients were classified as noncompliant if they took less than 75% of their prescribed medicine. After one year, more than half were noncompliant.

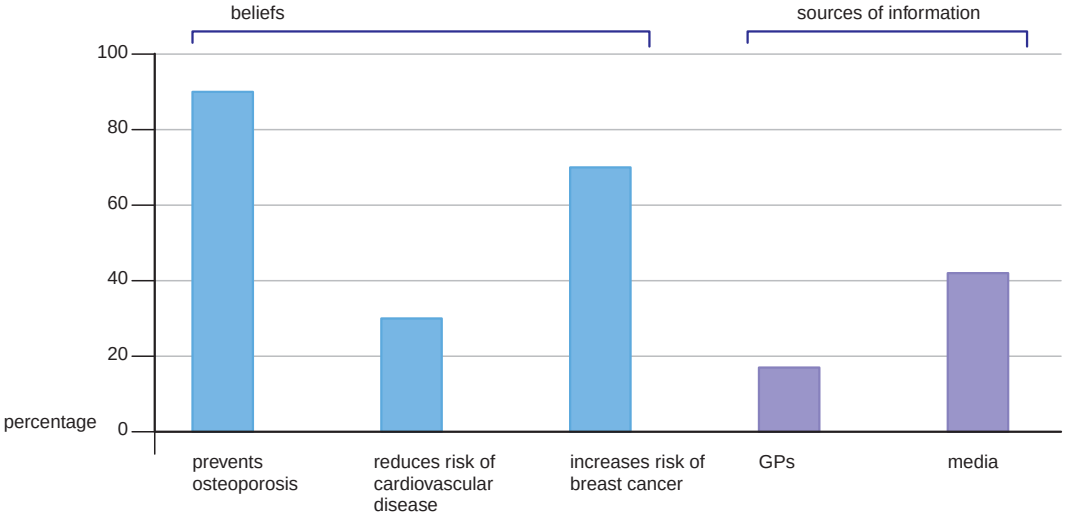
Another recent analysis found that around a quarter of women stop taking HRT within six months, and very few continue on the therapy for more than one or two years (Sturdee 2000). One possible explanation is that some women use HRT to allow themselves gradually to come to terms with the menopause. Some may adjust to it more rapidly than others, and decide to stop taking HRT relatively quickly.

Researchers in Denmark found higher rates of compliance among women needing HRT to counter the effects of surgically induced menopause. Hee (1999) looked at oestrogen replacement therapy (ERT) in perimenopausal women after they had had a hysterectomy and removal of their fallopian tubes and ovaries. 89% were still compliant three years after discharge. This high rate was attributed to initiation while in hospital, the quality of information given at discharge, and low incidence of side effects. This group also had good knowledge about HRT (Figure 10, page 61).

Differences between therapies

Clinical trials and results from 'real life' research have shown that different forms of HRT can yield different rates of compliance. Women taking continuous (every day) combined HRT were more likely to persist with the treatment than those taking sequential therapy, which includes a monthly break for a withdrawal bleed (Hill et al 2000). Evidence indicates that this is because women dislike monthly bleeding (Sturdee 2000).

Figure 10. Women's knowledge about HRT

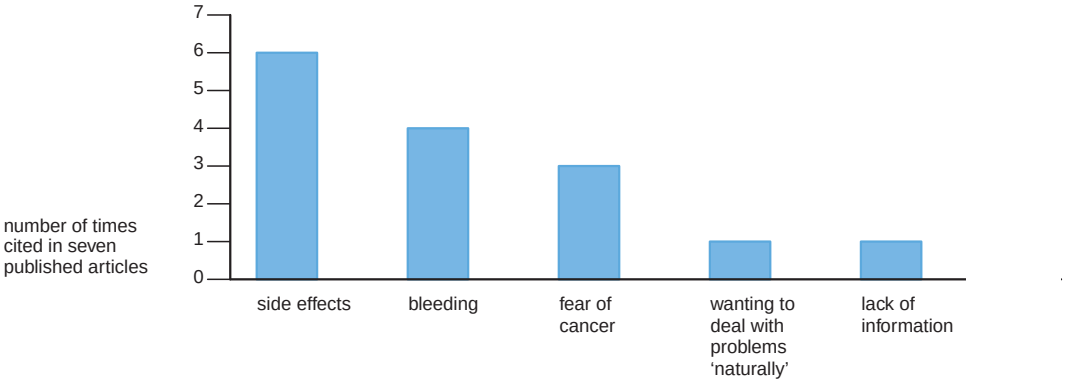


From Hee (1999)

Factors affecting compliance

Figure 11, which combines data from seven studies, shows the reasons given by women for not taking HRT as prescribed or for discontinuing it. Most commonly, women say they stop because of side effects or because they dislike bleeding.

Figure 11. Reasons for HRT non-compliance or discontinuation



From Berman et al 1997; Bjorn and Backsrom 1999; Brockie 2000; Faulkner et al 1998; Panay and Studd 1997; Sarrel 1999; Sturdie 2000

Recently, there has been considerable publicity about the **long-term health risks** of taking HRT. A review of four trials involving both healthy women and those with a previous history of cardiovascular disease (Beral et al 2002) concluded that, overall, HRT produced a significant increase in the risk of breast cancer, stroke and pulmonary embolism. The risk of colorectal cancer and fractured neck of femur was decreased, and there was no change in the risk for endometrial cancer or coronary heart disease. The increased risks were greater than any reduction in risk for other conditions. The effects of HRT did not differ between types or combinations of ingredients, nor were they influenced by patients' characteristics such as ethnicity, age, smoking behaviour or previous illnesses.

Interventions to improve compliance

From the research available, there seem to be three main ways of increasing compliance with, or prolonging the use of, prescribed HRT:

- follow-up and better communication with health professionals (Bjorn and Backsrom 1999; Sarrel 1999; Sturdee 2000)
- being offered a choice of administration routes, dosages or combinations (Sturdee 2000; Kenemans et al 2001)
- adequate information provision about benefits, risks and side effects (Bjorn and Backsrom 1999)

Summary

When HRT is prescribed for controlling menopausal symptoms, non-compliance and discontinuation rates are predominantly linked to unwanted monthly bleeds with sequential therapy, and fears of an increased cancer risk. Non-compliance is often the result of an intentional, rational, decision made by the woman, after weighing up the costs and benefits of the treatment.

Such decisions should be respected. However, higher compliance rates in some parts of Europe may indicate a need to investigate differences in quality of care and patient support. There is evidence that the supportive provision of clear information about and a range of choices in using HRT can significantly influence patterns of HRT use.

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11 Compliance with treatment for osteoporosis

Patients' views about taking medication for osteoporosis

The National Osteoporosis Society and individuals with osteoporosis agreed that treatments for osteoporosis can be a problem. Patients stressed that the severity of symptoms had made them highly motivated to take medication as prescribed. However, the complicated ways in which some medicines had to be taken, and the lack of immediate visible effects of treatment, both affected compliance.

> *My impression is that the number of patients who keep taking [medication] can be quite poor, especially after six months. I would think that this is because it is quite difficult to take the medication. You have to take it with a full glass of water, on an empty stomach and not eat immediately afterwards. Patients who are elderly may be quite concerned about all that. Also, sometimes people may read about the side effects and it can scare the life out of them …*
>
> *There can be side effects — gastric upsets and muscular aches and perhaps some people who have other aches and pains too may not want to take that on.*
>
> *Also, it is a medication that does not make you feel better and if people can't actually see it is making them better, they may not continue."* (Nurse — National Osteoporosis Society)

> *I understand that patient information leaflets do give the number of the National Osteoporosis Society helpline. That is good as patients who are considering whether to take the medication may welcome the advice from an independent source."* (Nurse — National Osteoporosis Society)

> *Initially the medication used to be by injection. Then I went on to a nasal spray supplied by an American drug company. When they stopped providing it to the specialist unit I had to come off it because of funding. So I went on to another medication. That was more of a nuisance as I had to take it as soon I got up on an empty stomach and I had to stay upright and not have anything else for a bit as it can cause a problems with the oesophagus. I used to miss my cup of tea when I woke up."* (Woman, 75)

> *I always do take the medication. Osteoporosis is so awful that if you have a medication and it helps, you take it and it is wonderful. It's so nasty that you wouldn't want to suffer. It should also prevent further fractures. I impress on my daughter to have a bone density scan as the medication can be preventive."* (Woman, 75)

> *There are no side effects for me. But if there were I know there are other things to try. They have told us that. They are very good at this clinic."* (Woman, 75)

> *Doctors not working together can affect how I take my medication. I always try to rely on the expert. But if there is a problem I have to make my own decision. When it goes wrong I work out what is the problem. If a sewing machine breaks down while you are sewing, you look at what could be the problem."* (Woman, 54)

Research evidence

Osteoporosis is a progressive systemic skeletal disease characterised by low bone mass and deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. Its reported prevalence is nearly 15% in western women aged between 50 and 59. It increases to 70% in women over 80 (National Osteoporosis Society 2002). In severe cases it can cause extreme pain (in the spine, for instance) and serious disability, and may be life-threatening.

Preventive measures include weight-bearing exercises, stopping smoking and ensuring adequate intake of calcium and vitamin D. Various treatments can increase bone formation or reduce bone reabsorption, including hormone replacement therapy (HRT), bisphosphonates (such as risedronate), and calcium and vitamin D supplementation. Such treatments have been shown to reduce the risk of fractures by 30%–50% (Delmas 2002). However, there is good evidence that adverse side effects or concerns about treatment can affect compliance and consequently efficacy (Fordham 2000).

There have been studies on compliance with earlier forms of oral bisphosphonate therapy. But within the criteria of this review no literature on compliance with osteoporosis treatment and prevention, other than hormone replacement therapy, was found. This brief analysis therefore focuses on compliance with HRT for treatment of osteoporosis (see also Section 8, pages 59–63).

Non-compliance rates

In a systematic review of HRT trials, Torgerson and Bell-Syer (2001) found non-compliance rates ranging from 12% to 52%, with an average of 30%. Patients who were noncompliant in HRT trials faced a risk of fracture up to three times higher than that of controls. Continuation with such treatment is also poor. One study reported that only about half of patients continue to take HRT for osteoporosis prevention for more than a year (Fordham 2000).

Some research has shown that compliance may be improved by offering a range of HRT preparations. Compliance was higher in both hysterectomised women and those with intact uterus when offered a choice of HRT alternatives as a primary osteoporosis prevention (78% and 67% respectively) compared to a randomised preparation (65% and 48% respectively;Vestergaard et al 1997).

Factors affecting compliance

Non-compliance with HRT relates to uncertainties about its risks and benefits, and the return of vaginal bleeding (Ahmed et al 1996; Figure 11, page 61). Age has been shown to be correlated with compliance levels, although not in a consistent direction — Vestergaard et al (1997) reported decreasing compliance with HRT with increasing age in women taking it as a preventive medicine; Torgerson and Bell-Syer (2001) reported better compliance in older women.

Interventions to improve compliance

Research in Europe has shown that continuous and intermittent doses of HRT produce equivalent increases in bone mineral density (BMD). Intermittent therapy may be favoured for fewer side effects and ease of use, therefore improving compliance.

Summary

Non-compliance with HRT regimens prescribed for the prevention of osteoporosis has similar root causes to non-compliance with HRT for menopausal symptom relief. Little compliance-related research has been conducted on other treatments for osteoporosis.

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12 Compliance with treatment for Parkinson's Disease

Patients' views about taking medication for Parkinson's Disease

The main issue for people with Parkinson's Disease (PD) is the balancing act required to achieve the optimum benefits and the fewest unwanted effects. Linked to this is the desire of people with PD to maximise their control over the disease and the medication. Remembering to take pills can also be an issue where people follow complex regimes that may involve taking medication every two and a half hours.

❝ *Side effects, yes, I live with an incredibly dry skin, but that I can live with. The Pergolide can cause hyperactivity and send me climbing the walls and I can't live with that and have to drop it down a bit. You do tend to learn to live with things and you tend to see how it is tomorrow."* (Woman, 52)

❝ *In the morning I have the PD symptoms but as the day goes on, I pick up the drug reactions .Taking the pills puts you back in control of your symptoms … As the drugs are assimilated, you switch on, it is very marked. First there is a tenuous control and then you go 'wow' — now I can write, do things, walk, and you are back in control."* (Man, 60)

❝ *I don't take [my medications] by the book. Tweaking and fiddling for yourself is much better. For instance, half tablets of Pergolide taken more often suit me better. The doctor knows about this and says sort out your best regime."* (Woman, 52)

❝ *Patients who are involved in groups and the PD society — they are in the driving seat. Loners might believe that what the doctor says is gospel and they don't cope so well with their condition. Older people tend to think doctor knows best, but us younger ones have to live with it longer and we talk among ourselves and we are less compliant! It is my body and I know how it feels."* (Woman, 52)

❝ *…You have to plan and have your wits about you to make it work for you. For example if I am singing in the choir and the concert starts at 7.30 I have to take the medication an hour and a quarter before, but the pick up of the drug depends on when you have eaten, so I might eat early at 4 or 4.30 so when I take the medication there is no hindrance to it being absorbed."* (Man, 60)

❝ *Patient information sheets are better than they were but they are so safety conscious and everything than can go wrong is put down automatically."* (Woman, 52)

❝ *I use a pill timer. It contains the pills too. This is imperative as I lead a busy and active life. It is used widely by younger PD patients. It is important as if you are late taking a pill, you do suffer."* (Woman, 52)

❝ *There is an issue for people with PD about taking their drugs when they are in hospital. When they go in to hospital they are forced into ward rounds and drug rounds and the times the drugs are given may not suit you — very likely not. There is a big campaign to keep hold of your own medication in hospital if you are compos mentis."* (Man, 60)

Research evidence

One in 500 (100,000) people in the UK have Parkinson's Disease. The risk of developing PD increases with age. Symptoms usually appear after the age of 50, and are the result of a prolonged process of dopaminergic neural cell loss. Nearly 4000 people were reported to have died from the disease in England and Wales in 2001 (Office for National Statistics 2002).

Dopamine and acetlycholine in the nervous system are involved in the co-ordination of movement. In Parkinson's Disease, there is an imbalance between these neuro-transmitters, caused by a relative and absolute loss of dopamine-producing cells. Parkinson's Disease is a debilitating, progressive illness characterised by muscle stiffness, slowness of movement and tremor.

Treatment involves drugs that restore the balance between dopamine and acetylcholine. Some increase the level of dopamine, slow its breakdown, or otherwise stimulate dopaminergic receptors (dopamine agonists). Others block the action of acetylecholine (anticholinergics). Medicines provide symptomatic relief, although they can have adverse side effects such as nausea, hallucinations, drowsiness, dry mouth and constipation. Use of L-dopa to treat Parkinson's Disease eventually causes significant permanent side effects characterised by dyskinesias — abnormal facial and other movements.

It has, however, recently been suggested that partial dopamine receptor agonists might have a *disease-modifying* effect, slowing the rate of PD progression as well as relieving symptoms. If this were to be demonstrated, compliance-related issues would become more important. At present there is very little literature on compliance in Parkinson's Disease.

Non-compliance rates

Within the criteria used in this review, no research was found on compliance rates with PD medication. However, some research has been conducted on patients' knowledge about their medication. Evans et al (2000) interviewed patients and found that understanding is often poor. They reported that 35% of those surveyed had to consult a list of possible medicines when asked for the name, dose and frequency of their medication. Even with the list, only 40% could answer correctly. Of those who attempted this question by memory, only 20% answered correctly.

Differences between drugs

As with treatments for many other conditions, compliance with PD medication is thought to be higher with simpler, lower frequency, regimens. There may be opportunities to modify therapy to increase acceptability and ease of use. For instance, a once-daily dose of the dopamine agonist cabergoline has been reported to be as effective and well tolerated as a thrice-daily dose of bromocriptine (Marsden 1998).

Factors affecting compliance

Treatments for Parkinson's Disease can cause side effects such as nausea, dizziness and headaches. For each individual the unwanted effects of some drugs are likely to be less distressing than those of others. Appropriate therapeutic strategies should help to maintain compliance levels.

Compliance levels may also be affected by a person's mobility and dexterity, along with other factors affecting their physical and psychological ability to take medicines as recommended. The symptoms of Parkinson's Disease may make it difficult for those with the condition to open containers, or to attend clinics. Professionals, family members and other carers can help patients to avoid or cope with such problems, if they are alert to them and motivated to provide relevant support.

Summary

There is little evidence available about compliance in Parkinson's Disease. However, people with PD have been shown to have relatively poor levels of knowledge about the medicines they have been prescribed, which although offering symptomatic relief have a range of unwanted side effects. They may also be affected by practical difficulties caused by impaired physical co-ordination. Compliance levels are related to such variables. Professional and lay carers can help people with Parkinson's Disease to use medicines as prescribed, and increase their well-being, by offering relevant support sensitive to each individual's needs.

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13 Compliance with treatment for psychotic conditions

Patients' views about taking medicines for severe mental illness

Key points emerging from interviews with patients include:

- Service users feel that the medical model tends to prevail over other models of understanding and treating severe mental health problems; and that this often results in a professional preference for medications rather than other therapies and support systems.
- There are significant concerns about adverse effects and about taking medications for a long period.
- Some service users feel that they are listened to and supported when they have concerns about their medications; others do not.
- There are continuing concerns about information about medication, although there are also some recent examples of very good practice.
- Service users often wish to retain a degree of control and to exercise choices about how they take medications.

> *It depends who you talk to. The psychiatrist is all about medications, all the medical model. My care co-ordinator is kind of not anti-medication, but thinks it is peripheral to other lifestyle approaches… My CBT therapist is pragmatic and thinks it's OK to be on medications as a way of staying out of hospital and having the therapy. It is difficult to work out my own views among the views of all the others.* (Woman, 47, with schizophrenia and depression)

> *I realise there is something weird about my brain chemistry and I do need medication.* (Man, 57, with schizophrenia)

> *The medication helps a lot. I don't mind taking it…It's like a buffer to help with the voices. Even if it's sedative, it stops you doing anything stupid. You've just got to stick at it. It's not an instant-win. You have to do it long-term.* (Man, 24, with schizophrenia)

> *The drugs suppress you or slow your brain down, but they don't address mental illness which is caused by underlying issues and problems. These issues are never addressed by people who think drugs are a cure…Those who prescribe drugs need to change their outlook to holistic care and treatment, and not just drugs. Care plans are generally: take these drugs and you'll be all right. Talking therapies etc disappear off the agenda and drugs rule. Psychiatrists need to identify real problems and issues, like benefits and housing, and put them in the care plan.* (Woman, 41, with bipolar affective disorder)

> *You are not always taken seriously about side effects…Many think that if the side effects are not on the leaflet, they don't exist. Finding a doctor to yellow-card it is really hard. You feel the onus is on you to prove the side effects.* (Woman, 37, with bipolar affective disorder)

> *For nine years I tried 18 different drugs and had toxic reactions to all of them. I could never get the professionals to understand and each time they just prescribed new drugs. I felt like I was going to die. Even with the three drugs that I could barely tolerate I felt so suppressed — I couldn't eat and I was sleeping far too much. I was like a zombie.* (Woman, 41, with bipolar affective disorder)

> *Taking medications is a love/hate relationship. The more recognition of the setbacks, the more you can accept the benefits. You feel you have made the decision and have not been coerced.* (Woman, 37, with bipolar affective disorder)

> *I have not been given good information about side effects. I have 35 years of the mental health system and not once was I given adequate information. You have to find everything out for yourself. There's an information blackout.* (Man, 57, with schizophrenia)

> *If you say something to any kind of doctor, they are not about to rock the boat if you are still taking the medication. My GP is excellent but my psychiatrist and I fight a lot. He thinks side effects are better than symptoms. I don't always agree … Having no symptoms is not the be-all and end-all of life. It is also important to be comfortable with one's life.* (Woman, 47, with schizophrenia and depression)

> *It's frustrating. Sometimes I go to a psychiatrist or GP and come away cross because there isn't an answer long term. I am stuck with medication for the rest of my life. I have been through 27 different medications, and what I am on now is the best compromise. But I still feel I am thinking through fog.* (Woman, 47, with schizophrenia and depression)

> *I have never been listened to by psychiatrists, nurses, pharmacists etc. They pretend you haven't spoken. Psychiatrists sometimes feel threatened as they know I know more than they do. Their whole work is diagnosis, then prescribe the drug.* (Woman, 41, with bipolar affective disorder)

> *Don't get cross with people who stop taking their medications. The grass is always greener … If I have not got symptoms, the side effects seem worse so I might want to stop. But then when I have symptoms I might prefer the side effects. It's permanently a question of trying to find the middle ground.* (Woman, 47, with schizophrenia and depression)

Research evidence

At any given time about one person in 250 will have a psychotic illness such as schizophrenia or bipolar affective disorder (Department of Health 1999). These potentially severe and enduring conditions are a major cause of disability, and are associated with a significantly raised risk of suicide. This review mainly describes medication compliance issues among people living with a diagnosis of schizophrenia, about which there is a significant body of relevant research. However, findings relating to compliance with prescribed medication among people with bipolar affective disorder are also discussed.

In the past 50 years there has been a major decline in the number of NHS beds occupied by patients with mental health problems — from around 150,000 (in England and Wales) in the mid 1950s to 30,000 today. This has been accompanied by a shift away from custodial to therapeutic and recovery-based models of care,

and a considerable growth in community-based services (Bell 2005). But despite such progress many individuals and families affected by mental illness still feel stigmatised and excluded from normal patterns of social interaction and personal opportunity.

For example, unemployment rates among people with severe mental illness are high. The disabilities and handicaps they experience largely relate to environmentally determined forms of disadvantage. Despite the biomedical realities underlying such conditions, the experience of 'having schizophrenia' (or any other psychotic disorder) is still very much a function of the way people labelled with these diagnoses are treated by the society around them.

The purpose of pharmaceutical and all other forms of psychiatric care — in addition to providing symptomatic relief as and when possible and necessary — is to enable people with mental health problems to gain greater control over and satisfaction with their lives. Hence, the issue of compliance with prescribed psychiatric medication regimens is important, and unusually sensitive. This is because of concerns about compulsion, and past patterns of care and treatment primarily intended to protect the public rather than individual patients' interests.

Effective psychotropic drug use can be of great value in helping people diagnosed as having psychoses to regain and/or maintain fulfilled lives. Yet coercive and demeaning approaches to giving drugs such as antipsychotics — which can force medication on individuals in the mistaken belief that its benefits will automatically outweigh its costs — may cause harm not only to those immediately involved, but indirectly to the wider community.

Schizophrenia

About one in every hundred people experience one or more episodes of schizophrenia or schizophreniform illness at some point in their lifetime. Symptoms are most likely to present first in late adolescence. According to the voluntary sector organisation Rethink, about a quarter of all those diagnosed as having schizophrenia recover within five years. Around two-thirds experience fluctuating symptoms over many years, and approximately 10%–15% experience severe long-term incapacity (Rethink 2005).

There is, however, evidence that outcomes in less industrialised nations may be significantly better that those recorded in countries such as the UK. In this country there seem to be significant variations in incidence rate and outcome between ethnic and other social groupings.

The drugs currently used to treat schizophrenia in part serve to block dopamine receptors in the cerebral cortex. Awareness of this led some observers to believe that schizophrenia results from overproduction of, or an undue sensitivity to, the neurotransmitter dopamine. But this view now appears too simplistic. The fundamental causes and mechanisms of schizophrenic illness remain unknown. Theories range from the possibility that genetically determined brain development abnormalities are involved, through to the idea that prenatal and/or postnatal infections have a significant role. It has also been suggested — but not proven — that using cannabis during adolescence may increase a person's risk of developing schizophrenia.

It is more widely accepted that psychological pressures related to emotionally charged criticism, prejudice and social rejection can play an important part in precipitating or maintaining schizophrenic illness. Some authorities believe these factors might ultimately be found to be of central significance in triggering the brain changes characteristic of the condition.

The symptoms of schizophrenia can be described as either *positive* or *negative*. Positive symptoms include hallucinations, illusions (in all sensory forms), delusions, disordered thinking and feelings of paranoia. Negative symptoms are less dramatic. But they tend to be more persistent, and can be highly disabling. Examples include becoming withdrawn, uninterested in social contact, and slow to think, move and talk.

Bipolar affective disorder

Bipolar affective disorder, or manic depression, is characterised by states of mind that fluctuate from manic episodes (*highs*) to depressive episodes (*lows*), with periods of normal mood in between. Individuals vary greatly in the rate at which their manic depression *cycles* between highs and lows.

As with schizophrenia the lifetime incidence of the disorder is about one in a hundred, and symptoms usually first appear in late adolescence or early adulthood. The fundamental causes of bipolar affective disorder are also unknown. But it is reasonable to assume that its occurrence is likely to be related to a combination of genetic factors and exposure to stressful life events and other environmental triggers.

Episodes of mania are typified by loss of inhibition, feelings of self-importance and being easily distracted. Episodes of depression are normally characterised by feelings of worthlessness, negativity, and loss of energy and interest in everyday activities. Some individuals with a bipolar affective disorder experience hallucinations and paranoia during psychotic episodes.

Antipsychotic medication

Antipsychotic medicines are appropriately prescribed to control the symptoms of schizophrenia and acute mania. The *typical antipsychotics* (such as chlorpromazine) were first introduced in the early 1950s. Although often effective in controlling florid psychotic symptoms such as hallucinations, they can also produce extra-pyramidal side effects. These include tremors, shaking, uncontrolled movements and restlessness. A more severe condition caused by these drugs, *tardive dyskinesia*, is characterised by involuntary movements of the tongue, mouth, face and jaw, which may not be reversible when treatment is stopped.

As well as blocking dopamine, many typical antipsychotics also block the action of the neurotransmitter acetylcholine. This can result in *anticholinergic* or *antimuscarinic* side effects such as a dry mouth, constipation, blurred vision and low blood pressure. Patients may be prescribed additional medicines to counteract these side effects, resulting in complex treatment regimens. Other side effects of typical antipsychotics include weight gain, altered libido, nausea and urinary retention, as well as a rare but potentially fatal complication known as *neuroleptic malignant*

syndrome, with symptoms including stiffening of the body and a high temperature. Anyone developing it needs urgent medical help.

Since the start of the 1990s a range of alternative *atypical* antipsychotic drugs has been increasingly widely prescribed. The first medicine in this class — still considered the most effective for a proportion of patients with difficult to treat symptoms — was clozapine. It was initially produced at the end of the 1950s, but its development was problematic. In about one in 100 users it can cause potentially fatal episodes of agranulocytosis, in which the formation of white blood cells is damaged. This leaves patients very vulnerable to infection. So clozapine use needs to be carefully monitored, and — as with all other forms of antipsychotic medication — it should not be initiated without the informed consent of those taking the drug, or that of their properly appointed representatives.

Other, more recently marketed, atypical antipsychotics include risperidone, quetiapine, zotapine and olanzapine. The mechanisms underlying their clinical actions appear to differ from those of the typical antipsychotics — they can be more effective in controlling negative symptoms, and there is evidence that they are less likely to cause some of the severe reactions associated with older treatments. However, they may still cause distressing side effects such as weight gain and sexual dysfunction, and may also be associated with additional problems.

Both typical and atypical antipsychotics can be delivered by depot injection. The advantage of this is that patients requiring long-term treatment need only a single injection every few weeks. But there are possible disadvantages — dosing flexibility may be lost, and service users may feel that control of their treatment has been removed from them. People with long-term mental health problems may sometimes fear that depot injections are used to enforce compliance.

Antipsychotic (as well as antidepressant) medications are today also prescribed for people with a bipolar disorder, depending on whether an individual is experiencing an acute high/manic or a low/depressed episode. However, the appropriate use of medicines containing lithium salts can often prevent such crises. These drugs were introduced in the late 1940s, but were not widely prescribed until the late 1960s.

The main concern with lithium therapy is that it is relatively easy to build up a potentially fatal toxic level in the blood. To avoid this there must be regular monitoring. Symptoms of lithium toxicity include fatigue, muscular weakness, poor co-ordination, drowsiness, tremor, diarrhoea and vomiting. Other adverse reactions associated with the therapeutic use of lithium can include weight gain, nausea, diarrhoea, tremor and blurred vision.

Rates of non-compliance

As in all other areas of pharmaceutical care, reported rates of non-compliance in severe mental illness vary greatly. One recent review of the literature calculated an average rate of compliance from ten studies to be 41% — so 59% of patients were found not to be compliant (Dolder, Lacro, Leckband and Jeste 2003). In another review one-third of patients with schizophrenia were classified as non-compliant and one-third as partially compliant (Oehl, Hummer and Fleischhacker 2000).

Previous work by the authors of the first study reviewed 39 articles published since 1980, and estimated the mean non-compliance rate in patients with schizophrenia

to be just over 40% (Lacro, Dunn, Dolder, Leckband and Jeste 2002). Similarly, a large-scale survey of views on mental health medicines reported that 44% of patients said that they had at some point stopped taking their medication without the support of their doctor (Hogman and Sandamas 2000). A study of people with bipolar affective disorder being treated on an outpatient basis found 27% to be partially compliant, with 12.5% having poor compliance (Colom, Vieta, Martinez-Aran, Reinares, Benabarre and Gasto 2000).

A recent more comprehensive review calculated non-compliance rates among patients with psychoses using data from 86 studies published worldwide from 1980 onwards. The mean rate of reported non-compliance was just over 25% (Nosé, Barbui and Tansella 2003). This study also found that the figure tended to decrease with increasing sample size. This may partly explain the higher proportion in other studies, although variances in any form of medicine taking can also be expected to vary between different social contexts and care settings.

Very few studies have specifically looked at compliance with recommended lithium therapy among bipolar affective disorder patients. A review published in the 1980s reported rates of between 9% and 57% (Cochran 1986). More recently, high rates of compliance have been reported (Macleod and Sharp 2001), although the authors acknowledged that this may have been because their study's participants were recruited from a lithium maintenance clinic, which compliant patients would be more likely to attend.

Despite evidence of differences between the side effect profiles of typical and atypical antipsychotic drugs, there are mixed results from studies comparing compliance in these two medication groups. Some studies have found that patients taking typical antipsychotics tend to experience more severe side effects, and also to receive less information about their illness, medicines and side effects (Hogman and Sandamas 2000); unsurprisingly, they were also more likely to be non-compliant than those receiving atypicals. However, this is not necessarily attributable entirely to the properties of the medicines involved; other aspects of therapeutic quality may also have been involved.

Similarly, a study of 288 (war) veteran patients in the US showed that those receiving atypical antipsychotics were slightly more compliant than those taking typical antipsychotics (Dolder, Lacro, Dunn and Jeste 2002). However, a further review reported that only three out of five studies analysed showed a trend towards greater compliance in patients perscribed atypical antipsychotics. Of these, two found only a partial association or nonsignificant trend (Lacro et al 2002). No association was found between drug type and compliance in a study of patients with bipolar affective disorder (Colom et al 2000).

Adverse health outcomes

The extent to which early and sustained use of antipsychotic medicines protects against (or might cause) long-term neurological and allied brain changes in people with schizophrenia is unknown. There is as yet no substantive evidence to this effect. However, there are clear associations between compliance with medication regimens, and factors such as relapse rates, (re) hospitalisation rates, and the incidence of serious unwanted events including suicides, assaults and (very rarely) murders. One study estimated that non-compliant patients have a six-month to

two-year risk of relapse — on average, 3.7 times higher than the risk for compliant patients (Fenton, Blyler and Heinssen 1997).

It should not be uncritically assumed that the benefits identified above always result directly from compliance with antipsychotic drug treatment. In some cases, compliance may be an indicator, rather than a cause, of psychological competency and/or better underlying mental health. But there is no doubt that, in many cases, a combination of medicine taking and other forms of care and support does protect individuals with schizophrenia or bipolar affective disorder against relapses, which may personally endanger and disadvantage them and their families.

Increasing rates of compliance with antipsychotic treatment may also have benefits at a wider societal level. People with schizophrenia and other forms of psychotic illness are still often stigmatised and perceived as 'violent' and 'dangerous'; improved compliance could help reduce community concerns and hence the social exclusion experienced by these people. Such progress might also go hand-in-hand with more productive patterns of working between the NHS and agencies such as the police. This could in turn reduce the amount of stigmatising, negative media coverage of severe mental ill health.

Factors affecting compliance

Several factors are known to affecting compliance with antipsychotic medication; these include:

- ***Patient-related factors***
  - lack of insight into the illness
  - co-morbid alcohol or substance abuse
  - poor social functioning
  - youth
  - male sex
  - presence or severity of symptoms
- ***Environment-related factors***
  - lack of social support
  - stigma of illness
  - living alone
- ***Healthcare professional-related factors***
  - poor therapeutic relationship
- ***Treatment-related factors***
  - presence or severity of side effects
  - delayed onset of therapeutic effects
  - complex treatment regimen

Patient-related factors

Several analyses have revealed patient-related factors consistently linked with non-compliance. These include lack of insight into the illness, co-morbid alcohol or substance abuse, and poor social functioning (Gray, Wykes and Gournay 2002; Lacro et al 2002; Oehl et al 2000; Nosé et al 2003). Attitudes towards medication

may also affect compliance. Some reviews have found that — as might be expected — people with mental health problems who perceive that they derive positive direct or indirect benefits from their medication (such as allowing them to make new friends, or keeping them out of hospital) are likely to achieve better compliance (Gray et al 2002).

Mixed results have been found in the contexts of patients' age and sex; typically, young males are relatively poor at compliance (Lacro et al 2002; Nosé et al 2003).

The presence and severity of ongoing symptoms such as delusions or feelings of persecution are also often associated with poor compliance (Lacro et al 2002).

Similar results have been found specifically in bipolar patients. A recent review reported lack of insight, substance abuse and relative youth to be predictive of non-compliance (Vieta 2005).

Environment-related factors

Recent literature indicates that lack of social support is consistently associated with non-compliance (Oehl et al 2000; Nosé et al 2003). Related risk factors include experience of stigma, and living alone (Oehl et al 2000).

Factors relating to healthcare professionals and quality of care

The available literature suggests that the quality and amount of contact with healthcare professionals influences medication taking, with inpatients tending to be more compliant than outpatients (Oehl et al 2000). This may well be due to increased supervision. Additionally, a good therapeutic relationship between the patient and the clinician, in which the clinician is seen to be interested in the patient as a person, has been found to be a strong predictor of compliance (Lacro et al 2002; Nosé et al 2003; Oehl et al 2000).

This is fully consistent with the concept of **concordance** — the view that decisions about medicine taking should be based on an informed and voluntary agreement between the prescriber and the user, and that such decisions are likely to result in improved compliance rates.

Treatment-related factors

Compliance is affected by the presence and severity of side effects, especially weight gain, sexual problems, delusions, paranoia, and the disturbances which may occur during the first few hours of therapy (Oehl et al 2000; Gray et al 2002). Other factors include delayed onset of therapeutic effect, and treatment efficacy not meeting patients' expectations

Patients receiving depot injections have been found (virtually by definition) to be better compliers, and simple regimens are reportedly easier to comply with than complex ones (Oehl et al 2000). This too is logical, and consistent with the evidence available in all other areas of medicine taking.

In a review of literature specifically looking at compliance in patients with bipolar affective disorder, poor compliance was linked to high rates of hospitalisation and to the side effects of lithium (Vieta 2005).

Interventions to improve compliance

There has been much research on interventions designed to improve compliance rates in patients taking antipsychotic medications. A major systematic review and meta-analysis of worldwide studies using controlled trials has recently been published (Nosé, Barbui, Gray and Tansella 2003). It reported that improved clinical practices can significantly improve compliance rates. Its authors found the strongest evidence of efficacy in studies recruiting homogenous populations of patients with schizophrenia. Other research, including patients with less precise diagnoses and those with disorders said to show 'psychotic features', was less conclusive.

Interventions aimed at coherently assessing medication compliance, rather than simply increasing the frequency of outpatient or post-discharge appointments, were found to be more effective. Interventions with a shorter follow-up period (less than six months) also tended to be more successful, indicating that the benefits of compliance support tend to decrease over time.

Nosé et al found robust data on the impact of educational interventions and the value of specific service policies such as pre-discharge contacts between patients and community teams. They therefore suggested that education about medication problems and benefits should be frequently and routinely repeated; and patients should be offered pre-discharge contacts with community based team members, even if they received such support during previous admissions.

Dolder and colleagues (2003) undertook a similar investigation, reviewing 23 research studies published since 1980. Four were classified as being based on educational strategies; two on behavioural reinforcement; and five on affective strategies, seeking to promote enhanced compliance through emotional support and social relationships. The other twelve involved combinations of these approaches.

In 15 of the 23 studies, antipsychotic medication compliance improved in the intervention group. These included one of the education-based interventions, four of the affective strategy-based studies, both the behavioural ones, and most of the combination strategies. In general, the education-only strategies mainly showed secondary gains in knowledge about and insight into treatment; interventions using combinations of educational, behavioural and affective components resulted in decreased hospitalisation rates, reduced psychopathology scores and increased social functioning.

Interventions involving more additional sessions tended to be more successful. This may have been due to patients taking a relatively long time to form good relationships with therapists, and so to gain from the intervention. However, it is unclear from this work which is more important over time — repetition of key messages, or a better relationship with the therapist.

The authors concluded that the active components of combination interventions are difficult to isolate, and commented that the use of multiple strategies may sometimes reduce the impact of the most effective elements of single-strategy interventions. The overall body of literature on compliance in medicine, and effective communication in healthcare more widely, generally supports combination approaches, involving multiple routes and frequent repetition of messages.

Psycho-education interventions aim to encourage compliance by informing patients about the nature of their (mental) illness and how it might impair rational judgements, and about the value of accepting ongoing treatments. They also try to increase insight and provide coping skills. In the context of bipolar affective disorder, research indicates that such programmes can enable patients to identify early signs of relapse, lengthen time to first manic relapse, improve occupational and social functioning, decrease the severity of depressive symptoms, and increase compliance (Vieta 2005).

Compliance therapy

One approach to improving compliance with recommended treatments for psychotic illnesses is known as *compliance therapy*. It was developed by Kemp et al (1996), with financial support from a major pharmaceutical company and other sources, and is mainly based on motivational interviewing and cognitive–behavioural techniques.

Compliance therapy involves three phases:

- During the first phase, patients review their illness history and their previous experience of medicines. This allows them to acknowledge their problems and concerns, and to explore and clarify their perception of these problems. It also uncovers potential barriers to treatment compliance. Talking about psychotic symptoms helps to 'normalise' them, reducing feelings of stigmatisation. Patients are also encouraged to think of times when treatment was useful, and to emphasise the benefits of being in control of treatment decisions.
- In the second phase the patient and therapist discuss patients' reluctance to take medication, covering topics such as side effects and illness denial. The therapist should also clarify and correct misconceptions about treatment, and encourage consideration of the pros and cons.
- In the final phase, the therapist aims to reduce feelings of stigmatisation and alienation by highlighting the prevalence of mental illness and making comparisons with chronic physical illnesses. The concept of maintenance treatment is introduced, with emphasis on the importance of being stable and staying well in order to achieve certain life goals. By discussing the patient's symptoms, the therapist aims to help them recognise signs of relapse.

The available research indicates that illness insight and medication compliance rates can be considerably improved by compliance therapy, and that its effects last for at least six months (Kemp, Hayward, Applewhaite, Everitt and David 1996). But it is unclear to what extent benefits endure for longer periods.One randomised controlled trial of the long-term effect of compliance therapy found that, at 12 months, it was no more effective than non-specific counselling in promoting compliance and stimulating positive attitudes towards treatment, insight, better levels of functioning or quality of life (O'Donnell, Donohoe, Sharkey et al 2003).

This relatively recent study involved only a small number of participants (26 in the intervention group and 24 in control group at the 12-month follow up) and recruited only those with a clear diagnosis of schizophrenia. Previous research showing the positive effects of compliance therapy, including that of Kemp et al, involved people with a more heterogeneous set of diagnoses. This might partly

explain variations in the reported findings, although such a conclusion appears to conflict with the findings of wider reviews. It is more likely that the effects of all forms of compliance support decrease over time (Nosé et al 2003), so careful attention needs to be paid to providing refresher and/or maintenance courses in community settings.

Compliance therapy may also be useful in encouraging compliance with lithium-based medication programmes by people with bipolar affective disorder. An exploratory study was conducted with eight participants by Scott and Tacchi (2002), who reported significantly improved attitudes towards lithium and compliance, as measured by both self-report and serum plasma levels. Such findings are encouraging, and deserve further validation among a larger sample.

The value of training health professionals in the delivery of compliance therapy has also been researched. Junior psychiatrists reported finding it useful and relevant to their work. It helped inform their awareness of the causes of non-compliance, such as the fear of stigma and desire for personal autonomy; and its personal costs in terms of phenomena such as decreased social functioning (Surguladze, Timms and David 2002). Training community mental health nurses in the use of compliance therapy has also been found to be valuable, and linked to significant improvements in their patients' psychopathology, attitudes towards medication and compliance rates (Gray, Wykes, Edmonds, Leese and Gournay, 2004).

Overall, compliance therapy appears promising. However, the exclusion of some patients in the available studies restricts the generalisability of study results. Those classified as 'non-English speaking' were often excluded from the intervention studies, so it's unclear how these patients would respond to the therapy. It may be especially important that these patients are counselled about their medication if language is a barrier to the understanding of their treatment regimen. Similarly, some studies excluded patients with co-morbid substance or alcohol abuse. As they are more likely to be non-compliant, it would be useful to know whether compliance therapy would be successful in these patients.

Discussion

Until relatively recently, it was commonly assumed that people with psychotic disorders could not gain insight into the nature of their illnesses, or take responsibility for controlling their own treatment. But just as the residential location of people with severe mental health difficulties has increasingly moved out of large confining hospitals into community-based settings, there is now a growing awareness that it is often possible for people who have experienced psychoses to be positively involved in their treatment, and to recover satisfactory lives.

Yet many challenges remain to be overcome, not least in relation to the variable efficacy and often unpleasant side effects of the medicines currently available. Present areas of concern include:

- The special needs of black and other ethnic community members, who are often relatively unwilling to seek professional help for mental health problems and so may remain untreated until severe symptoms become manifest. They may also be exposed to perceived and actual prejudice, and are more likely than other

population groups to suffer enforced rather than voluntarily agreed patterns of mental health treatment (Department of Health 2005).

- The recorded growth in illicit drug and alcohol misuse in modern Britain, and the special difficulties this is linked with in people with mental illnesses.
- The ongoing political debate about reforming mental health legislation, with ignorance and complex sectional conflicts making it difficult to achieve a fair and workable balance between the protection of public safety and public service efficiency, and the provision of high quality personal care, choice and human rights protection for people who develop severe mental health problems (Richardson 2005).

However, such issues should not detract from awareness of advances that have already been achieved in supporting appropriate medicine taking, or in providing further opportunities to help ensure that people suffering mental health crises are provided with appropriate pharmaceutical care, alongside other effective support. For example, advanced treatment directives are increasingly seen as an effective resource for enabling people with psychotic disorders to decide while they are well how they should be treated should they suffer a relapse. Linked with other advances in compliance support and concordance-based professional practice, such strategies have a substantial potential further to improve the effective, beneficial use of antipsychotic medicines in the 21st century.

Summary

Reported compliance rates with antipsychotic medicine regimens vary considerably. The available evidence indicates that around 40% of patients with severe mental illness do not take their medicines as prescribed.

The causes of non-compliance in antipsychotic medicine taking are — as in all other areas of pharmaceutical care — multifactorial, and complex. Interventions such as compliance therapy have been shown to be successful in improving medicine taking by people with diagnoses such as schizophrenia and bipolar affective disorder. They typically involve a combination of educational, cognitive and behavioural modification strategies.

But different sub-groups of antipsychotic medicine users may benefit from different components of such interventions to differing degrees, and the effects may in many cases be relatively short lived. These observations can partly be taken to highlight the need for sustained and well co-ordinated personal support in medicine taking and related issues for people with long-term mental health problems while they are well and living in the community.

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14 Compliance with treatment for renal disease

Patients' views about taking medication for renal disease

The issues raised by patients with renal disease are similar to those that are important to other patients. In particular, there are concerns about inadequate information about medication and about the medication's side effects. Nevertheless, patients gave no specific indications of difficulties in complying with medication. People who are active in kidney patients' organisations and who therefore may be more knowledgeable than average, report that they often acquire more knowledge than the staff who advise them.

❝ *I never didn't take medication or vary the dosage but I would sometimes query it with the doctor."* (Man, 58)

❝ *Most people comply with the medication in the main, but maybe with some deviation that they think they can get away with."* (Man, 58)

❝ *I was given all the information about the medication that I was going to be on, but you get the information at the wrong time, when you are very stressed. For example when you have been diagnosed with renal failure or when you are going on dialysis. You get bombarded and it is difficult to retain the information. People may not remember that they have been told things."* (Man, 58)

❝ *There is not enough information, especially about side effects. You are more likely to take the medication if you know the pros and cons."* (Man, 36)

❝ *Some are afraid of side effects. They think: OK maybe if I don't take the medication for a couple of days the side effects will go away."* (Man, 58)

❝ *I take it all — having half a kidney makes me take it all. I must not take anything that is not prescribed and I must take everything that is prescribed. I became aware of the importance of taking as prescribed, including taking things at the right time of day. It is such a little penalty for the quality of life I enjoy. People say: don't you get fed up with taking these pills and I say, no, not compared to the alternative."* (Man, 78, has had renal problems since aortic aneurysm in 1995)

Research evidence

Kidney failure which, without medical intervention, will lead to death is termed **end-stage renal disease** (**ESRD**). It can be treated by dialysis or kidney transplantation. Dialysis typically requires a complex medication regimen (frequently involving therapy for high blood pressure, diabetes and/or anaemia — states that can in part cause, or be caused by, ESRD), dialysis sessions, and fluid–diet restrictions. Non-attendance at dialysis sessions is rare, since missing just a few is likely to prove fatal. Non-compliance with prescribed medication regimens is more common, although still potentially very harmful. For patients who have had a renal transplant, immunosuppressive therapy must be taken continuously to ensure that the donated organ is not rejected (see also Section 12, pages 88–92).

Non-compliance rates

Greenstein and Siegal (1998) found that one-fifth of patients who underwent a renal transplant were noncompliant (as measured by self-reporting, and defined as one or more medication doses missed within the previous four weeks). A similar proportion of haemodialysis patients interviewed by Horne et al (2001) reported 'sometimes' missing a dose of medicine. Four per cent confessed that they missed doses 'often' or 'very often'.

When evaluating home dialysis, Bernardini and Piraino (1998) reported that 35% of patients were noncompliant in their medicine taking.

According to a review by Wolff et al (1998), non-compliance rates in children and adolescents with ESRD are around 40%, with some studies finding rates as high as 70%. Within these overall figures non-compliance with prescribed medicine taking was the most commonly form reported.

Adverse health outcomes

Non-compliance with medication regimens for ESRD can have serious, possibly fatal, consequences. Treatments for conditions such as high blood pressure and anaemia are important for the prevention of complications. Inadequate compliance with immunosuppressive medication after a kidney transplant can result in rejection, and possibly loss, of the organ. Douglas, Blixen and Bartucci (1996) found that 61% of patients who were identified as noncompliant before their transplant lost their organ, or died after transplant.

Non-compliance with dialysis treatment can also have consequences such as peritonitis and more days spent in hospital (Bernardini and Piraino 1998).

Factors affecting compliance

Horne and colleagues (2001) assessed the beliefs of 47 haemodialysis patients, aged 20–84, about their treatment, and about compliance with their prescribed medication regimens. Using the 'Beliefs about Medicines Questionnaire' (BMQ) they looked at patients' specific beliefs and concerns about their medication, and their general views about doctors, the intrinsic properties of medicines and the degree to which they saw medicines as harmful. The research showed that concerns about long-term effects and dependence on medication correlated with intentional non-compliance. However, non-compliance with medication was not related to the belief that their medicines were ineffective or unnecessary. Younger patients reported poorer compliance.

Among patients performing home peritoneal dialysis, there were no differences in age, race, gender or health between compliers and non-compliers (Bernardini and Piraino 1998).

Specific patient groups

Factors linked with non-compliance in children and adolescents with ESRD include:

- Systemic factors (organisation of health care)
  - feeling dependent
  - feeling powerless
- Illness- and treatment-related factors
  - treatment being intrusive into family and social life
  - suicide attempts
- Interrelational factors (between health care providers and patients)
  - insufficient information
  - no communication about non-compliance
  - unjustified or inappropriate criticism of reported non-compliance
- Patient and family factors
  - parents and families do not accept the seriousness of the disease

From Wolff et al (1998)

The available evidence indicates that non-compliance in children and adolescents usually has multiple reasons. But Wolff et al (1998) found that the majority of patients with kidney disease attributed non-compliance to emotional conflicts, or to crises such as those related to the experience of dependence in hospital and/or within the family. Compliance improved in nearly a quarter of patients after these crises were resolved.

Predictors of compliance appear to differ between ethnic groups. In renal transplant patients aged between 6 and 20, Tucker et al (2001) found that, among African–American children, motivation and self-efficacy levels predicted compliance. However, in Caucasian children, cues and reminders to take medication improved compliance most significantly. This highlights the importance of taking social and cultural context into account when researching and addressing medication compliance.

Interventions to improve compliance

Pharmaceutical interventions such as medication reviews have been shown to be effective in reducing the number and doses of drugs patients take, and in improving compliance. The *Pharmaceutical Journal* (July 2000) reported on a UK pharmacist-run medicine review scheme for patients with renal disease. Pharmacists explained the best times for taking the prescribed medication, and asked patients about compliance. The clinics helped more than a quarter of patients to reduce the dose of the drugs they were taking. Sixteen per cent were prescribed fewer drugs, and 14% had their medication changed to a more appropriate preparation.

Chisholm et al (2001) evaluated the impact of a clinical pharmacy service on compliance in renal transplant patients prescribed immunosuppressive medication. The clinical pharmacist reviewed medication regimens, with a view to eliminating unnecessary drugs and/or doses and providing treatment designed to maximise therapeutic outcome and minimise side effects. S/he counselled patients on their

therapy and how to take it properly. The rate of compliance for the intervention group was significantly higher than that of the control group.

For children and adolescents, the provision of understandable information, and support with coping and training programmes to improve management of the disease has been recommended (Wolff et al 1998). The overall evidence again emphases the value of approaches which raise patients' self-confidence levels and self-management skills, as opposed to merely didactic forms of information provision.

Summary

Despite severe potential consequences, reported medication non-compliance rates in patients with end-stage renal disease are high. Recent work by Horne et al (2001) identified concerns about long-term effects and dependence on medication as significant correlates with non-compliance. However, the reasons for failing to take medicines as prescribed are often non-intentional, and linked to practical difficulties experienced in daily living. Such observations highlight the importance of holistic support for patients when it is especially important to reduce non-compliance rates.

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15 Compliance in post-transplantation care

Patients' views about taking medication for post-transplantation care

When we interviewed people with a transplanted kidney or heart, they stressed the importance of taking medications according to directions, in the knowledge that those who fail to do so do not survive long-term. But our interviewees may not be entirely typical of transplant patients as a whole, because post-transplantation non-compliance is, in practice, relatively common.

Unwanted effects of medication were a significant issue; and, as with many other groups of patients, control was important. Recipients of successful transplants also expressed a moral obligation to look after the organ that they had been given.

❝ *I don't vary what I take at all. You get into a routine. I find it's the best way."* (Woman, 63, has kidney transplant)

❝ *8 days after my transplant I met a guy who had his transplant for 22 years. I asked how he did it and he said: I still cycle every day… I go to the pub and have a drink every other day and I take my pills dead on time. He said the secret is to take the pills and enjoy yourself. I listen to patients far more than the doctors, but only the long-term guys."* (Man, 40, has heart transplant)

❝ *The medication is actually damaging my kidney. The drugs that are meant to keep me alive are also damaging the kidney."* (Man, 36, has kidney transplant)

❝ *I don't have severe side effects. Some people have terrible side effects like skin cancer. I do wonder what motivates them to keep going. It can be bad in the summer when you have to cover up all the time but it's just the price we pay."* (Woman, 63, has kidney transplant)

❝ *There is not enough information given on side effects. When I did ask, they wanted to send me to a psychologist. If you are referred and you don't accept, the next doctor just reads "refused" and if you've ignored advice you are not taken seriously."* (Man, 40, has heart transplant)

❝ *You know you have the take the medication but you don't want to. I take mine begrudgingly. I have had no control over this disease and the medication is the only control I have."* (Man, 36, has kidney transplant)

❝ *We have a duty to keep the transplant — someone has actually given the organ. There is a duty to yourself, the donor and society. It is a big responsibility."* (Woman, 63, has kidney transplant)

Research evidence

Almost 3000 solid organ transplants were carried out in the UK and Ireland in 2001. But about two and a half times as many people were known to be waiting for a transplant that year (UK Transplant 2002). Post-transplant patients must take immunosuppressive medication to ensure good organ function, and avoid rejection. Despite the importance of this treatment, many post-transplant patients are reported to be noncompliant.

Non-compliance takes various forms (Laederach-Hofmann and Bunzel 2000). For example, patients may decide to take 'drug holidays' — they repeatedly and abruptly discontinue, and later resume, their medication. 'White coat compliance' is said to occur when patients who have been noncompliant for a period begin taking their medication shortly before a check-up. As a result both the clinician and the patient may wrongly believe that the patient is safe from the consequences of failing to take the prescribed medication.

Non-compliance rates

A review of research on non-compliance rates with immunosuppressive therapy reported figures ranging from 2% to 68% (Chisholm 2002). Laederach-Hofmann and Bunzel (2000) conducted a comprehensive review of issues in compliance with post-transplant treatment. The rate of persistent non-compliance was greatest for exercise, followed by medicine taking. Other components of the regimen were diet, not smoking, avoiding alcohol, and attending clinics.

Post transplant service users tend to become less compliant over time. There are reports that they experience more difficulties with their treatment regimens as time goes on (Dew et al 1996). In one study of renal transplant patients, 95% were compliant five months after the operation, but only half continued to be so after 12 months (Chisholm et al 2000).

However, the available evidence suggests that patients are much more likely to be compliant in their medicine taking after a re-transplantation. Troppman et al (1995) followed 14 patients who had lost their first kidney transplant due to non-compliance, and had subsequently received repeat transplants. Health professionals had ensured that these patients were fully aware of the importance of taking their medication as prescribed. More than four years later, all 14 patients had retained a functioning kidney, with 12 patients showing full compliance throughout the observation period.

Adverse health outcomes

The consequences of non-compliance with immunosuppressive medication are increased morbidity and mortality. There is compelling evidence that non-compliance is linked to organ rejection and loss, and increased risk of death (Laederach-Hofmann and Bunzel 2000).

Research conducted in 1989 (Rovelli et al) revealed that nine out of ten patients who were noncompliant rejected their organ or died, compared with less than one-fifth of those who took their medication as recommended.

More recently it has been found that as many as one-third of renal graft losses can be attributed to non-compliance (Gaston et al 1999), and that nearly two-thirds of noncompliant renal transplant patients who lose their transplanted organ die between one and three years afterwards (Douglas et al 1996). De Geest et al (2001) reported that nine out of ten late acute heart transplant rejections appeared to be caused by non-compliance.

Factors affecting compliance

The most commonly cited factors associated with medication compliance or noncompliance in post-transplantation care are, according to two recent reviews (Laederach-Hofmann and Bunzel 2000; Chisholm 2002):

- experience of side effects
- the number of drugs prescribed (some patients may be expected to take eight different drugs at different times of day, and with varying doses at different times)
- frequency of doses
- lack of social support

Other less frequently cited factors included depression, stress, low self-esteem and self-efficacy, lack of confidence in the drugs, and having a living related donor (LRD) rather than a cadaveric one (Laederach-Hofmann and Bunzel 2000; Chisholm 2002).

Interventions to improve compliance

Compliance has been found to vary considerably between transplant patient groups. Individual behaviour cannot be easily predicted, but there is evidence of a positive correlation between compliance rates before and after an organ transplant. Hence likely compliance might to some extent be assessed before the transplant, and patients given appropriate education, counselling and support. The evidence also indicates that, as far as practicable, treatment regimens should be designed around patients' preferences, with patient involvement wherever possible. For example, patients should be able to choose their medication as tablets or liquid. This is particularly important in children.

Oral and written information, videotapes, computer-based decision aids, the Internet, and interactive videoconferencing can all be used to enhance compliance (Chisholm 2002). Peer group-based communication and empowerment programmes, recognising the value of patient-to-patient information exchanges and support, are also beneficial.

Other recommendations have included simplifying medication regimens when possible, improved medicine management via monitoring and appropriately timed follow-up consultations, and inclusion of the patient's partner in the therapeutic process (Laederach-Hofmann and Bunzel 2000). Pharmaceutical care has been shown to be effective in addressing compliance issues in post transplant patients. As noted on page 86, Chisholm and colleagues (2001) evaluated the impact of a clinical pharmacy service on renal transplant patients' compliance with immuno-suppressive medication. This involved history taking, medication review, and providing relevant advice to patients.

HeartNet, an Internet-based psychosocial service for heart transplant recipients and their families, was evaluated by Dew et al (2002). The website included information, workshops to improve coping and compliance, access to communication with healthcare team members, and a discussion forum with other patients. Among those who accessed the website, medication compliance rates improved, and symptoms of depression and anxiety significantly declined.

Specific patient groups

Non-compliance is often encountered among children and young adults, and is one of the major causes of mortality in paediatric liver transplant recipients. D'Antiga et al (2002) found that of 20 children with acute rejection after a liver transplant, three were not adequately immunosuppressed due to non-compliance.

Children and young adults who experience psychological distress and side effects from medication, and are from dysfunctional families, are less likely to be compliant with their medication than others (Griffin and Elkin 2001). Some medication can produce appearance-altering side effects such as excessive body hair, trembling hands and weight gain. This makes it particularly difficult for adolescents, who are often especially concerned with their body image. Non-compliance rates have been found to be between 40% and 60% in 14- to 21-year-old transplantees (Bunzel and Laederach-Hofmann 2000).

Griffin and Elkin (2001) found that the following interventions might be effective in improving compliance in young transplant patients:

- educational programmes
- psychological interventions designed to reduce psychological and/or family stress
- emphasising the importance of support from family and friends, and from support groups
- behavioural programmes which reward good compliance
- providing the amounts and types of information desired by the patient
- good communication, which ensure that medical recommendations are understood and discussed

There is some evidence that in the US, African–Americans may be less compliant with immunosuppressive therapy after an organ transplant than members of other ethnic groups (Prieto et al 1997). The authors emphasised the importance of taking cultural differences into account when studying compliance, although such behaviour may in part be explained by general factors related to class and deprivation, independent of specific social group characteristics.

Other problems

Around half of all heart transplant patients show impaired cognitive function as a result of cardiovascular insufficiency, and around a quarter have residual cognitive deficits following their transplant operations. These can affect compliance (Gross 1998).

A recent article in the *Lancet* described a young girl experiencing complications after a second renal transplant. Her mother eventually found a hoard of between

one and two months' worth of immunosuppressive therapy in her room. It was concluded that she had a longstanding 'tablet phobia', which was subsequently improved with hypnotherapy (Watson 2002).

Summary

Despite potentially fatal consequences, medication non-compliance is high in post-transplant patients. The complexity of their overall treatment regimens is in part responsible for this, along with a wide range of other factors commonly associated with non-compliance.

Work by Troppman et al (1995) found that people do not always retain previous noncompliant behaviour after a second transplant. Whether this was due to more rigorous patient selection and 'contracting' arrangements, more information provision, more acceptable medication regimens, counselling, an increased emotional realisation of the importance of compliance, or a combination of factors is not known. But it suggests that compliance rates can change, provided that people are appropriately motivated and supported.

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16 Medicine taking by older people

Research evidence

Around half of all NHS medicines are prescribed for people over retirement age, although they represent only about 20% of the UK population (Department of Health 2001; Office of Health Economics 2000). The recent National Service Framework (NSF) on the care of older people highlighted the importance of medicines taking and effective medicines management in this section of the community.

There is conflicting evidence as to whether older people are more or less likely to be noncompliant than members of other age groups. Some research suggests that older people are more vigilant than younger people about health issues, and more likely to stick to a regimen prescribed for them (Park et al 1999).

However, a recent study (Cline et al 1999) found that, despite receiving written and verbal information, 27% of older people discharged from hospital after heart failure were classed as noncompliant 30 days later. The majority remembered receiving oral information, but less than one in four recalled any written information they were given. Nine per cent did not remember receiving any information at all. Half the patients surveyed could not recall the dose of their medication and nearly two-thirds did not know what time of day to take them (Figure 12).

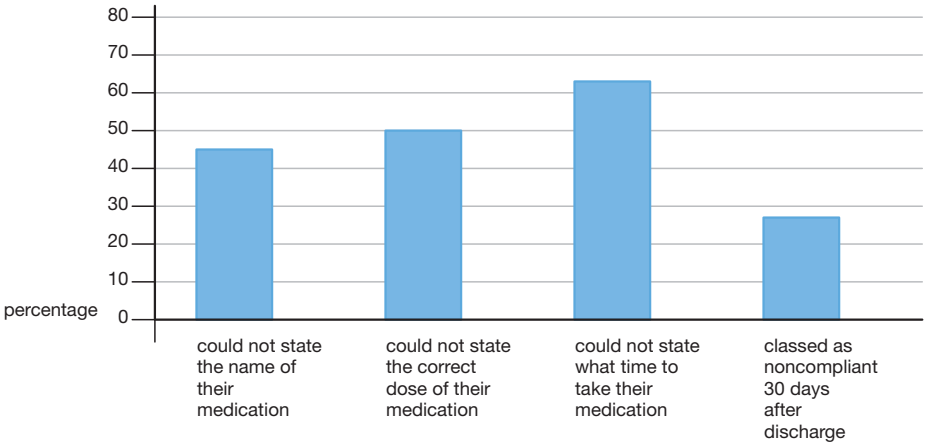

Figure 12. Knowledge about medication in elderly patients discharged from hospital

From Cline et al (1999)

In a subsequent Danish study, 40% of elderly patients did not know the purpose of their medication, only 20% knew of the consequences of non-compliance, and less than 6% knew about possible side effects of the drugs prescribed for them (Barat et al 2001).

Elderly patients are more likely than average members of the overall population to:

- be living alone
- be taking multiple medicines with high dose frequencies
- have decreased dexterity and/or cognitive functioning

Combined with lack of knowledge, these factors can lead to unintentional non-compliance. But there is also evidence that older people are as likely as people in

any other age group to make a rational and intentional decision to change or stop their medication without seeking professional advice. One study published in the *Pharmaceutical Journal* found that one-third of the older patients surveyed had altered their medication regimens, primarily because of experienced side effects, adjustments made in response to symptom changes, and the perceived inefficacy of treatments prescribed (Lowe and Raynor 2000).

Older service users identified as being at risk from the possible ill effects of non-compliance should be offered management services designed to resolve medication-related problems that influence compliance. Medication reviews by community pharmacists, carried out in patients' homes, have been successful in improving compliance and reducing the incidence of medication-related problems. Specific actions included modifying medication containers, supplying large-print labels, synchronising repeat medicine supply, tailoring the regimen to suit the patient, and stopping unnecessary prescribing (Raynor et al 2000).

Summary

Older people — defined as those aged 60 and over — now take more than 50% of all NHS prescribed medicines. Some, although by no means all, face special challenges in medicine taking, and are at particular risk of the unwanted effects of poly-pharmacy. Community and other pharmacists can play a valuable role in helping to reduce medication-related problems in this group provided they recognise its plurality and the need to treat all service users with appropriate respect for their autonomy as adults.

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17 Medicine taking by black and ethnic minority patients

Research evidence

According to the 2001 Census results, the population of Great Britain at the start of the twenty first century was structured as follows:

- White 92%
- Black 2%
- Indian 2%
- Pakistani, Bangladeshi and other Asian . 3%
- Other 1%

Source: Office for National Statistics

Among children and adolescents, and in many inner-city areas the proportion of ethnic minority members in the British community is higher than this. In London as a whole, for example, whites now form less than 80% of the total population. In a few areas of the UK, whites are in a minority. There are few published studies on compliance in medicine taking in ethnic minority communities. Most studies included in this preliminary review did not mention the ethnicity of trial or survey participants, and it is unlikely that related cultural differences were taken into account in the analysis of their results.

However, the incidence of given diseases vary considerably between ethnic groups. For example, South Asians living in the UK (Indians, Bangladeshis, Pakistanis and Sri Lankans) experience, along with people of Irish origin, higher premature death rates from coronary heart disease than other groups (BHF 2002), while black people are at relatively high risk from conditions such as stroke and prostate cancer. People who have come to the UK from new Commonwealth countries are at significantly higher than average risk of contracting renal disease and thus needing dialysis and/or a transplant.

Against this epidemiological background, ethnicity and culture influence some health-determining behaviour — for example, participation in screening programmes and attendance at follow-up appointments (Courtenay et al 2002; Meyerowitz et al 1998). It is likely that compliance with prescribed medication also differs between ethnic groups in the UK. Courtenay et al (2002) found differences in compliance between ethnic groups in the US European–Americans reported better compliance than Asian–Americans and people of Hispanic origin. Such variations may in part have been due to educational and socio-economic and linked variables and varying access to care, as well as to differences in beliefs about illnesses and their treatment and in learnt coping strategies.

Prieto et al (1997) also emphasised the influence that ethnic and cultural factors can have on compliance. They pointed out that groups differ in their attitudes, values and beliefs about health and illness. For example, Mexican–Americans tend to believe that health is equated with the absence of pain. This view could affect compliance, particularly with preventive treatments and medication for

asymptomatic conditions. Additionally, some cultures fatalistically attribute their good or poor health to God, and attach less importance to self-care than others. In some cultures it is not unusual for a patient's whole family to be involved in treatment decisions, while in others individual autonomy is more highly valued.

It would be wrong to assume that any ethnic sub-group is culturally homogenous; but overall differences between groups may be relevant to compliance. When assessing compliance, then, health professionals and researchers may find it useful to consider collective differences, as well as factors such as language and income. Measures of compliance may also need to be modified and validated for different ethnic or cultural groups. In some cases, it may be advisable to assess patients from a cultural perspective before making decisions about their individual treatment.

Tangrea (1997) argued that clinical trials should be as inclusive as possible in terms of minority populations. Similarly, in relation to studies of compliance and intervention to enhance it, it may be argued that:

- the design and management of trials should recognise the needs of diverse ethnic groups
- healthcare facilities which primarily serve minority populations should be included rather than excluded
- health professionals from minority backgrounds should be encouraged to participate
- investigators should be sensitive to ethnic and cultural beliefs

Figure 13 illustrates how factors related to ethnicity and culture may influence medicine taking.

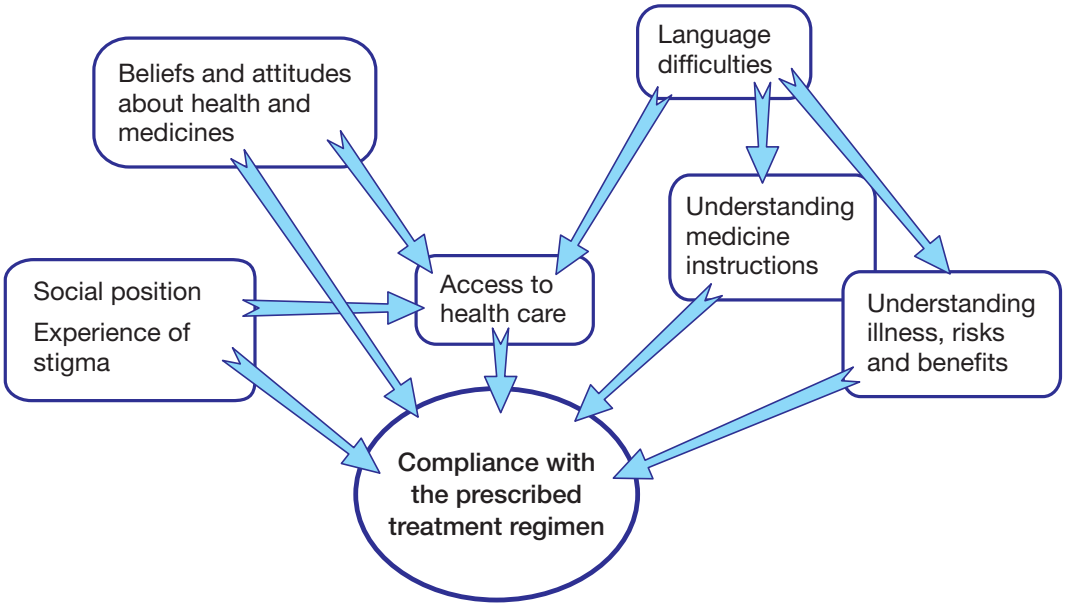

Figure 13. Possible cultural influences on compliance with medicine taking

Summary

Ethnic and cultural variations influence medicine taking in a variety of ways. Research on compliance should take into account the different needs of individuals and groups with minority backgrounds. This is relevant to the achievement of national and local public health targets for the reduction of health inequalities.

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18 Conclusions

The behaviour referred to in this review as non-compliance in medicine taking is widespread across all therapeutic fields. It affects groups ranging from post-transplant patients taking life-saving immunosuppressive treatment, to people with diabetes, arthritis or depression, and people who have been prescribed medicines to reduce their risk of attacks or strokes. It is a serious problem in all these contexts.

Compliance is difficult to study

The study of noncompliant medicine taking is challenging for many reasons. Outside professionally controlled environments, it is difficult to measure, although effective use of medicines is often most problematic in everyday community settings. Health service users often find it difficult to be honest with health professionals about how they really take medicines. This may be particularly true where they are uncertain about or reject the reasons for prescribing, but feel inhibited about openly questioning them.

... but basic conclusions can be drawn

Nevertheless, a number of basic conclusions about non-compliance in medicine taking can be drawn from the evidence in this review:

- More complex medication regimens are associated with low compliance rates. Multiple daily doses and/or multiple medicines make it harder for patients to comply; simpler regimens make compliance easier.
- Above-average rates of unwanted side effects are linked to lower compliance rates.
- People whose beliefs about their illness, and how best to live with it, are in conflict with those of their doctor or pharmacist, are less likely to take their treatment as recommended than those who have reached agreement with their professional advisers. Achieving agreement requires communication skills on both sides.
- Non-intentional non-compliance is higher among populations affected by cognitive and/or physical impairments.

The medicine's perceived role is important

Medicines are least likely to be taken as intended by the prescriber if they are seen as having a preventive — as distinct from a curative or short term distress-relieving — role. This may be because patients feel no immediate sense of threat, nor any obvious incentive to take treatments for conditions which do not currently make them feel unwell.

... as are patients' views and beliefs about medicines

In some cases, adhering to recommended treatment regimens unequivocally results in better outcomes for patients. But in others the situation is less clear-cut, either because the effect on health outcomes is likely to be slight (or even negative) or because of counter-balancing social and psychological considerations. Factors relating to professional power and authority and the financial incentives of medicine manufacturers and health care providers, may weigh against the rights, needs, and personal priorities of patients.

Young people have particular needs

In all age groups, patterns of support which build self-confidence and self-efficacy are more likely to promote effective medicine taking. In some patient groups, most notably young adults with long-term conditions, denial of illness may lead to problems with taking medicine. Such problems are often found in young people at the threshold of independence from their parents, who are seeking to identify as normal members of their chosen peer groups. Interventions which these young people see as critical, judgmental and/or blaming are particularly likely to be unhelpful.

Multi-component interventions are most effective

There is evidence that modern pharmaceutical care, involving procedures such as medication reviews and the provision of timely help with problems such as side effects, can improve the quality of medicine taking. Yet, as Cochrane reviews published since the mid 1990s have emphasised, interventions made by any professional can reduce medication non-compliance rates only to a limited extent, especially in the context of everyday practice and resource constraints.

Strategies which combine educational inputs with practical advice and emotional and peer group support are moderately effective. But single interventions, such as simply supplying information leaflets or giving routine instruction when a medicine is dispensed, appear to have little value.

Much of the available literature, including recorded comments from patients, appears to assume that providing more and better information will in itself promote better, more effective, medicine taking. This may well be true at certain times, such as when a person is coming to terms with a new diagnosis. But the available evidence indicates that successful strategies to change medicine taking and other health-related behaviours must also focus on enabling people to act on information which is already available to them. For this, people need more confidence in their ability to manage their own care, and to cope with the challenges they face in life.

A cultural change is required

To date it appears that this can best be achieved via lay-led group programmes, rather than conventional professional direction and support. But the value of the latter should not be discounted altogether. The available evidence, though incomplete, supports the view that holistic, patient-centred, approaches — like **concordance** (patient–professional partnership in prescribing and medicines management) — are required to address poor compliance. Such strategies must be based on an informed respect for patient autonomy (Coulter 2002).

Recognition of this throughout the culture of the NHS, and health care systems elsewhere in the world, is one of the most important challenges facing health professionals and managers. Publications such as the Wanless report (2002; prepared on behalf of the Treasury) have highlighted the importance of developing self-management and more constructive professional/patient relationships at all levels of health care, in order to improve value for the increasing amount of money devoted to the health service.

Future research on improving compliance in medicine taking needs to demonstrate convincingly the cost effectiveness of proposed interventions, and to identify high-priority innovations which have significant benefits relative to the resources needed to deliver them.

The potential impact is very significant

But the most important conclusion of this review is that in many areas of medicine taking, —from mental health care to the treatment of kidney and other transplant patients — reducing levels of non-compliance can still deliver significant new benefits to both individuals and populations. For example, addressing non-compliance in relation to the primary and secondary prevention of coronary heart disease (CHD) and its sequelae is still a vital priority, despite progress such as that already made in implementing the CHD National Service Framework (NSF) in England and Wales. The distress, disability and avoidable mortality associated with cardiac disease, type 2 diabetes, smoking and obesity illustrate how better use of medicines and health-protecting knowledge could greatly increase human well-being.

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