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The drug will not work if the patient fails to take it

PERSPECTIVES

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Poor adherence leads to poorer patient treatment. Doctors in all specialties need to be aware of this phenomenon.

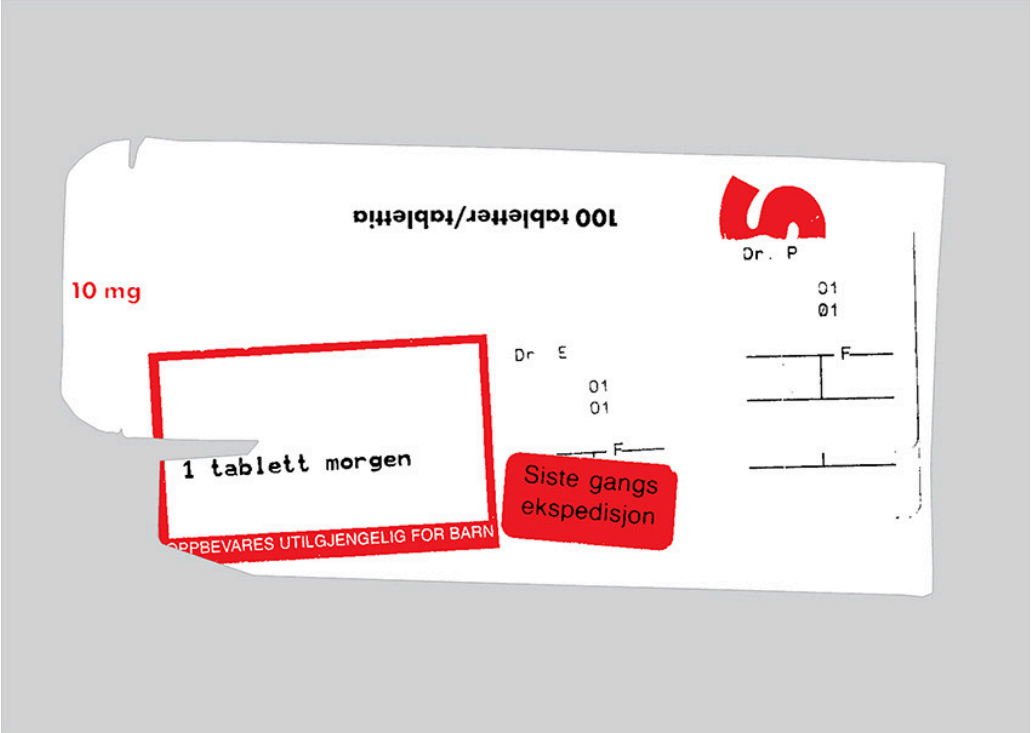

Illustration: Journal of the Norwegian Medical Association

Approximately one-half of all patients fail to take their medication as prescribed (1–3). This prevents the given treatment from exerting a beneficial effect and leads to increased morbidity and mortality (3–7). Improved adherence will help achieve savings for the healthcare system, as well as better results in clinical trials. The World Health Organization has stated: '*There is growing evidence to suggest that because of the alarmingly low rates of adherence, increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments*' (4).

The question of adherence is nevertheless often put aside during a busy clinical working day (4).

Poor effect of treatment

Poor adherence on the part of the patient may lead the doctor to conclude that the treatment has no effect. Unnecessary escalation and prolongation of the treatment are often the result (2, 7, 8). Costly and unnecessary examinations are often ordered (7). Hospitalisation may cause the patients to develop complications, for example hypoglycaemia or hypotension, because they actually consume the drugs as prescribed while hospitalised (2).

Poor adherence can also accelerate complications of chronic diseases that would otherwise have been prevented or delayed (2). Treatment of hypertension is a good example: poor adherence is the main reason for poor control of blood pressure in the population. Within one year of initiation of

antihypertensive treatment, adherence is below 50 % (9). Less than 25 % of those treated for hypertension achieve the desired blood pressure during treatment (4).

> ***«Poor adherence can also accelerate complications of chronic diseases that would otherwise have been prevented or delayed»***

Treatment of tuberculosis in developing countries is another example. Tuberculosis is becoming increasingly widespread, there is increasing treatment resistance and an increasing number of relapses and deaths. Much of this can be attributed to poor adherence (10). For HIV/AIDS, the rates of adherence vary from 37 % to 83 %, depending on the given treatment regimen (4). In sub-Saharan Africa, there is a high prevalence of concomitant tuberculosis and HIV infection. Providing effective treatment is difficult when adherence is poor for both diseases (10).

Health economic aspects

Improved adherence can lead to major health economic savings. In the United States, lack of adherence to medicinal treatment in the health services costs approximately USD 100–300 million each year, or 3–10 % of total health expenditure (2). Around 23 % of all nursing home admissions and 10 % of all hospital admissions can be related to poor adherence (11).

Improving adherence will thus help achieve direct savings for the health services due to fewer hospitalisations, shorter hospitalisation periods and less follow-up in outpatient clinics or by GPs. More indirect savings can be seen in the form of better quality of life for patients and maintenance of their work capacity (4, 12).

Adherence and clinical trials

In clinical trials, patients are followed more closely than in a normal course of treatment. Often, however, full adherence is not achieved. Four to five per cent of all participants in clinical trials never initiate the treatment (9). In clinical trials of chronic conditions, adherence rates of 43–78 % have been reported (6). This may lead to incorrect conclusions: adverse effects and therapeutic effects may be underestimated, while the recommended dosage can be overestimated (7, 8). This may in turn may render the economic analyses imprecise (8). In clinical trials, there should be greater emphasis on documenting the extent of adherence in relation to treatment effect (13).

What affects adherence?

The degree of adherence depends on several factors (7). A good relationship between the patient and the clinician is essential. Good, comprehensible information regarding the indications for treatment, its expected effect, possible adverse effects, how the medication should be taken and the duration of treatment are important (6). Patients often obtain information about the prescribed medication from multiple sources. In a study of 328 patients, it was found that more than 80 % had received contradictory information from different sources, including doctors, pharmacists and various mass media sources. Such contradictory information is unfortunate and can lead to reduced adherence (14).

> ***«A good relationship between the patient and the clinician is essential»***

The amount of time spent with the patient is crucial. Brief, hasty consultations have been shown to have a negative effect on adherence (4). Good continuity in the follow-up is also of great importance (2). Adherence tends to be best immediately prior to and after a consultation (6), and close follow-up will therefore often improve adherence.

Stress, forgetfulness, uncertainty regarding the diagnosis, concerns about possible adverse effects, low expectations for the therapeutic effect, fear of addiction and poor understanding of the health risks associated with non-adherence all have a negative effect. Low socioeconomic status, poverty, unemployment, lack of social network, cultural aspects and a number of other factors may also affect adherence negatively (4, 15).

Some patient groups are more susceptible to poor adherence than others. The proportion of the population over 60 years of age is increasing, leading to a greater number of patients with multimorbidity and often complex treatment regimens. Such patients consume approximately 50 % of all prescriptions issued and three times more prescriptions than the general population. This in itself increases the risk of poor adherence, and combined with declining levels of both physical and cognitive functioning, the risk of poor adherence increases even further (4).

Patients with psychiatric disorders have a generally lower level of adherence than those with somatic diseases. Patients who suffer from depression also have a lower rate of adherence to medications that are prescribed for somatic disorders (3, 16). Even sub-clinical depression is a risk factor for poor adherence (2). Some people occasionally forget to take their medication. The effect of this can be reduced if it is possible to prescribe drugs with a long half-life in relation to the dose interval, thus ensuring that the effect persists even when a dose has been forgotten or delayed (6, 17).

«Patients with psychiatric disorders have a generally lower level of adherence than those with somatic diseases»

Poor adherence is more common in conditions that are asymptomatic and where medication is used prophylactically. An example is the use of statins. Close to one in every six patients who are prescribed a statin never starts the treatment, and after two years, fewer than 60 per cent remain on the treatment. Adherence is poorer for primary prophylaxis than for secondary prophylaxis (17) and declines over time. After six months of treatment, there is often a clear reduction in adherence (6).

It has been shown that adherence increases with decreasing frequency of tablet administration per day. In a meta-analysis of 76 studies, it was found that adherence to medications taken once daily was 79 %, compared to 65 % for medications taken three times daily (18).

Interestingly, placebo-controlled trials have shown that patients who adhere well fare better, *irrespective* of whether they receive placebo or the study medicine. The fact that patients who adhere to their medication regimen also tend to follow other advice on health and disease ('the healthy adherer effect') shows that good adherence alone is a factor that has a bearing on morbidity and mortality (3, 13).

How can adherence be improved?

Technological or practical devices may be useful for increasing adherence. A pill dispenser is a good alternative. Involvement of family members or home-based care services will also help increase adherence (6). Mobile phone apps that provide reminders to take medication are also available (2). Practical challenges, such as problems with opening medication boxes, taking eye drops or using an inhaler, need to be identified.

More general measures include increased research on depot medications and implants, development of drugs with fewer adverse effects, and prevention and cure of diseases, which would render treatment unnecessary (1).

In any situation where the given treatment does not produce the expected effect, inadequate adherence should be considered before implementing other measures (6). Measures can be implemented to improve the adherence in individual patients. However, no single intervention has been shown to be effective in isolation, especially for chronic conditions (1, 4).

Writing and renewing prescriptions are often routine tasks. Studies have shown that doctors in general tend to overestimate the patients' degree of adherence to the prescribed treatment (8). Doctors are often busy, but increased awareness of adherence will go a long way. A simple question such as 'I know it can be difficult to remember to take your medications. Do you sometimes have problems with this?' can reveal poor adherence (16, 19). Spending time on this is likely to save time later on by diminishing the need for unnecessary consultations and an inflated use of resources.

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