Nonadherence to medicines: the scale of the problem

Rachel Elliott PhD, MRPharmS

This is the first in a series of articles on how adherence with prescribed medications can be improved and the cost of wasted medicines reduced. Here, Professor Rachel Elliott provides an overview of the scale of the problem and the clinical and economic consequences.

England’s ageing population now receives 50 per cent more prescriptions items per capita for conditions such as heart disease, stroke, diabetes, COPD and asthma than in 1990.1 Prescription items increased by 374.5m to 961.5m from 2001 to 2011, cardiovascular medicines having the highest number – 292.4m.2

Favourable outcomes in long-term conditions depend significantly on self-management by patients, including appropriate medicines use, and expansion of evidence-based medicine and financial incentives for evidence-based prescribing rely upon patients’ adherence to those medicines.

Adherence to medication is defined as the extent to which individuals take their medication as prescribed.3 Persistence is the length of time from initiation to discontinuation of treatment.

Extent of nonadherence
Reported adherence ranges from 4 to 100 per cent4 due to a wide variety of patient populations, diseases and medicines considered, compounded by varying study designs, definitions and measurement of adherence. About 25 per cent of medicines prescribed for long-term conditions is probably not taken as directed.4 Low adherence is commonly reported in key prevalent diseases such as COPD: 33 per cent,5 schizophrenia: 52 per cent,6 asthma: 67 per cent7 and diabetes: 78 per cent.8

Adherence reduces over time: one study reported adherence to antidepressants falling, for example, from 95 per cent at one month to 52 per cent at two months, 37 per cent at three months and 18 per cent at six months.9 Adherence tends to increase with disease severity, illustrated in a study of COPD where adherence in the mildest condition was 6 per cent, rising to 73 per cent in the most severe disease.10

Figure 1. Estimated avoidable costs from suboptimal use of medicines worldwide, 2011: nonadherence accounts for 57 per cent (US$269 billion) of the total (US$475 billion); after reference 14

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Does nonadherence matter?

If a medicine has been prescribed appropriately, nonadherence represents a lost opportunity to improve or maintain a patient’s health status.

The potential consequences of nonadherence divide into health benefits forgone (poor health-related quality of life, increased hospitalisations and premature mortality) and wider economic burden (personal, health and social cost).

Clinical consequences of nonadherence

Research across different diseases demonstrates direct correlation between adherence rates and improved health outcomes, as illustrated by examples in Table 1.

The effect of nonadherence on patient outcome is specific to the pathology of the disease and the pharmacology of the medicine. For example, the consequences of nonadherence in epilepsy and asthma will become apparent very quickly. However, in diseases such as type 2 diabetes and hypertension, nonadherence may take many years to lead to morbidity and associated costs, so assessment needs to allow an appropriate time interval after nonadherence begins. This variation in time to effect of nonadherence can also influence patients’ decisions to take their medicines.

Economic impact of nonadherence

In 1993, the US Task Force on Compliance roughly estimated total US costs due to medicines nonadherence to be over US$100 billion, a combination of health care (direct) costs of over US$30 billion and societal (indirect) costs of more than $50 billion.13

A more recent global estimate from 186 countries sets the impact of nonadherence at US$269 billion in 2011, 57 per cent of the impact of all suboptimal medicines use (see Figure 1).14

However, these estimates have limited usefulness because they use unclear or poor methodology in estimation of costs and are based on major assumptions.

Furthermore, costing nonadherence as a ubiquitous phenomenon across population groups and disease states does not encourage anyone to do anything about it, or policy-makers to direct resources to it. These estimates do not tell us what proportion of that cost is preventable.

‘Bottom-up’ or patient-based estimates of economic impact of nonadherence use information on disease

Table 1. Three examples of the effect of medication nonadherence on treatment outcomes

<table>
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<tr>
<th>Disease, country of origin, patient sample</th>
<th>Effect of adherence on outcomes</th>
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<td>Diabetes USA 11532 adults in a managed-care organisation</td>
<td>nonadherent (&lt;80% adherence) patients had:</td>
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<td>- higher all-cause hospitalisation (23.2 vs 19.2%, p&lt;0.001)</td>
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<td>- higher all-cause mortality (5.9 vs 4.0%, p&lt;0.001)</td>
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<td>in multivariable analyses, medication nonadherence remained significantly associated with increased risks for:</td>
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<td>- all-cause hospitalisation (odds ratio 1.58; 95% CI 1.38–1.81; p&lt;0.001)</td>
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<td>- all-cause mortality (odds ratio 1.81; 95% CI 1.46–2.23; p&lt;0.001)</td>
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<td>Post-MI USA 1521 adults discharged with aspirin, beta-blockers and statins after MI hospitalisation</td>
<td>patients who discontinued use of all medications at 1 month had:</td>
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<td>- lower 1-year survival (88.5 vs 97.7%; log-rank p&lt;0.001) vs patients who continued to take 1 or more medication(s)</td>
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<td>in multivariable analysis, medication discontinuation remained significantly associated with:</td>
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<td>- higher mortality (hazard ratio 3.81; 95% CI 1.88–7.72)</td>
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<td>results were consistent when evaluating discontinuation of aspirin, beta-blockers and statins separately12</td>
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<tr>
<td>COPD multicountry 6112 adults with moderate to severe COPD in an RCT (inhaled salmeterol 50µg + fluticasone propionate 500µg with placebo and each drug individually)12</td>
<td>nonadherent (&lt;80% adherence) patients had:</td>
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<td>- higher exacerbation-related hospitalisation (27 vs 15%, p&lt;0.001)</td>
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<td>- higher all-cause mortality (26.4 vs 11.3%)</td>
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<td>in multivariable analyses, medication adherence remained significantly associated with decreased risks for:</td>
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<td>- exacerbation-related hospitalisation (rate ratio 0.58, 95% CI 0.44–0.73, p&lt;0.001)</td>
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<td>- all-cause death (hazard ratio 0.40; 95% CI 0.35–0.46, p&lt;0.001)12</td>
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treatment and follow-up, usually from models informed by epidemiological data. This method is more complex than the ‘top-down’ approach but is able to give more specific estimates of costs by disease and patient type, and can provide estimates of variation between and within groups.

In England, the estimated opportunity cost of the health gains foregone because of nonadherence is in excess of £930 million per annum in just five diseases: \(^{15}\)

- asthma (£130 million)
- type 2 diabetes (£100 million)
- high-cholesterol/coronary heart disease (statins for primary and secondary prevention £120 million)
- hypertension (£390 million)
- schizophrenia (£190 million)

The authors estimated that improving adherence from current levels to 80% per cent across these five areas would save the NHS £500 million per annum.

There are very few studies that use prospective patient-linked data in a real cohort of patients to estimate economic impact of nonadherence, particularly in the UK, although this situation is likely to change as use of health care administrative data becomes more widespread.

### Wastage versus nonadherence

There is a perception in the UK that patients ‘waste’ medicines. The gross annual cost of NHS primary and community care prescription medicines wastage in England is currently about £300 million per year. \(^{15}\)

The economic impact of nonadherence is not just about medicines wastage. There is evidence of considerable public and professional concern about wastage, and reductions in its scale and costs would not only be financially desirable but might also be politically popular. However, this needs to be looked at alongside adherence more generally.

The value of the forgone therapeutic gains associated with medicines nonadherence may well be significantly in excess of the acquisition cost of all wasted medicines that have to be physically disposed of. \(^{15}\)

### What can we do about nonadherence?

Most research points to nonadherence incurring an increased cost to patient, healthcare provider and society. Interventions to improve adherence are variably effective and usually costly. \(^{18}\)

Interventions to improve adherence are often not based on the reasons for nonadherence, assume patient education is the (only) action required, or are too complex and will never be embedded into practice. Many studies of interventions are designed poorly as trials \(^{16}\) and economic evaluations \(^{17}\) so they are unlikely to be taken up by commissioners.

Many patients have problems with their medicines and have information needs, but rarely discuss these concerns with their prescriber. Furthermore, prescribers rarely ask, so are generally unaware of patients’ behaviour regarding following instructions, experimentation and self-medicating with other therapies. \(^{18,19}\)

The body of evidence for reasons for nonadherence is extensive, \(^{3} \) but this evidence is often not used to train prescribers or to design interventions. Prescribers who think they know about adherence and how to communicate with patients may overestimate adherence \(^{20}\) and be reluctant to voice suspicions about nonadherence. \(^{21}\)

This comes at a time when efficient medicines use could not be more important in the face of economic pressures on the public sector budget and policy drivers such as medicines optimisation and patient empowerment. Priority areas are diseases that have a known high preventable morbidity associated with nonadherence, such as diabetes, hypertension, hypercholesterolaemia, asthma, COPD, depression and schizophrenia.

For decision-makers and managers placing emphasis on improving health outcomes, it is highly likely that improving adherence to existing, effective medicines could have a bigger impact on patient health than diverting resources to developing more new medicines.

### References


### Declaration of interests

None to declare.

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