

Encouraging adherence to long-term medication

SUMMARY

Non-adherence to medicines is common in patients with chronic disease and in those prescribed preventive medication. It can be intentional, unintentional, or both.

Non-adherence reduces the effectiveness of prescribed medicines and may lead the prescriber to escalate treatment unnecessarily and potentially dangerously.

Patient education, shared decision making, pharmacist support and motivational interviewing reduce intentional non-adherence.

Interventions to reduce unintentional non-adherence address patient factors including misunderstanding, confusion or forgetfulness, and factors beyond the patient's control such as cost.

Patients should be asked about adherence at every consultation. A collaborative communication style is effective, using the patient's own expressions and responding to their cues. Normalising non-adherence, and starting with open questions then following up with more specific probes, can also help.

Electronic reminders, such as text messaging, have been shown to increase medication adherence.

Tim Usherwood

Professor of General Practice
University of Sydney
Honorary Professorial Fellow
The George Institute for Global Health
Sydney

Keywords

dose administration aids, medication reviews, patient adherence, polypharmacy

Aust Prescr 2017;40:147–50

<https://doi.org/10.18773/austprescr.2017.050>

Introduction

In developed countries approximately 50% of patients living with chronic disease do not adhere to treatment recommendations.¹ A similar proportion do not take preventive medicines as prescribed.² Some patients do not start their prescribed drugs. Of those who do, many subsequently discontinue. Non-adherence is a major reason why treatments shown to be efficacious in trials are often less effective in clinical practice.

Non-adherence can be classified as intentional or unintentional.³ Both reasons may contribute to non-adherence in an individual.

Intentional non-adherence

Intentional non-adherence is when a patient actively decides not to take a drug or follow treatment recommendations. It is likely to reflect the patient's attitudes to medicines in general, and their specific beliefs and concerns about the treatment recommended and the disease being treated.⁴ A study of 99 adults and young people living with asthma identified several themes that predicted adherence to preventer medication. These included the perceived necessity of treatment, safety concerns, acceptance of disease chronicity, beliefs about treatment effectiveness, ease of use and satisfaction with asthma management.⁵ The opinions of friends and family, concerns about adverse effects, and

experience of adverse effects were particularly salient. Studies of intentional non-adherence to other types of medication for a wide range of diseases have shown similar results.⁶ These findings illustrate the importance of patients' own experiences and the views of significant others in informing the decision to take medicines.

Unintentional non-adherence

Unintentional non-adherence is unplanned by the patient. Causes include misunderstanding or forgetfulness, and factors beyond the patient's control such as an inability to access prescribed treatment. Multiple studies have shown that treatment complexity, cognitive impairment, cost and other practical difficulties (e.g. opening medicine bottles or difficulty swallowing pills) may reduce adherence.¹

Detecting non-adherence

Non-adherence reduces the patient's potential to benefit from treatment. It may also lead to unnecessary and potentially dangerous escalation of medicines.

Clinicians are poor at detecting non-adherence. In a study of 1169 patients being treated for hypertension, their doctors recognised non-adherence in fewer than half of those whose pharmacy records indicated significant gaps in dispensing. Prescribers often

Full text free online at nps.org.au/australianprescriber

147

Novo Nordisk Exhibit 2390
Mylan Pharms Inc v Novo Nordisk A/S

intensified treatment even when they suspected significant non-adherence.⁷ Patients should be asked about adherence at every consultation, and a poor response to treatment should always prompt detailed enquiry. A number of standardised questionnaires have been developed to measure adherence but they are not readily incorporated into routine clinical use and their psychometric properties are limited in that setting.⁸

A small number of studies have examined different styles of questioning by prescribers for detecting non-adherence.⁹⁻¹¹ Effective strategies include a collaborative style, using the patient's own expressions in responding to their utterances and cues, normalising non-adherence, and starting with open questions then following up with more specific probes (see Box).

In one study, questions that asked directly about missed doses were almost four times more likely to elicit disclosure of non-adherence than other question types.¹¹ Disclosure can be followed up with a more detailed enquiry and discussion of ways to promote adherence and overcome barriers.

Addressing intentional non-adherence

A systematic review explored patient-centred interventions to improve adherence, including patient education, shared decision making and pharmacist support.¹² Many educational interventions resulted in better adherence and greater patient knowledge. However, their impact on adherence typically decreased over time. Shared decision making (including the use of decision aids) increased patient

knowledge, but adherence improved in only two out of four studies.¹² Adherence also improved with interventions by pharmacy staff, when they were tailored to patient needs, often involving both face-to-face and telephone encounters.

Motivational interviewing is a patient-centred counselling technique that aims to encourage behaviour change by reinforcing positive intentions and challenging negative ideas. It has been shown to improve adherence in a variety of settings.^{13,14} However, not all studies show benefit and the time pressures of routine clinical practice can limit applicability.¹⁵

Reducing unintentional non-adherence

Interventions that address unintentional non-adherence seek to reduce barriers and improve the patient's ability to take medicines as prescribed. A wide range of strategies has been studied.

Cost

Out-of-pocket cost is a well-recognised barrier to accessing medicines.¹⁶ In a recent survey, the Australian Bureau of Statistics reported that 7.6% of patients who had received a prescription delayed getting the medicine, or did not get it at all, due to cost. The proportion was even higher in areas of disadvantage.¹⁷ Prescribers may be able to reduce the impact of cost by, for example, prescribing generic or lower cost medicines when appropriate. Pharmacists may also assist patients by recommending lower cost brands.

Drug regimen

Patients can be confused by the number and variety of medicines they need to take. Adherence has long been known to be inversely associated with the complexity of the regimen.¹⁸ Prescribers should aim to simplify this as much as possible. Discussion with a pharmacist may assist, particularly with tailoring appropriate preparations, formulations and packaging for the individual (e.g. people with an inability to swallow).¹⁹ These consultations may be rebatable in Australia using the Medicare medication management review items. It may be possible to reduce the frequency of administration, introduce combination medicines, or even deprescribe in some instances.²⁰ It is good practice to provide patients with a printed list of their medicines and the times of day when they should be administered. Alternatively, the patient may be encouraged to use a smartphone app such as the NPS MedicineWise MedicineList+. The patient's understanding of their regimen should be checked. For patients with cognitive impairment, the support of a carer to encourage or assist with administration is essential.

Patients should be asked about adherence at every consultation

Box Asking about adherence to medicines during a consultation

Doctor: *How are you going with taking your pills?*

[Open question using the patient's usual name for their tablets]

Patient: *Yes, good*

Doctor: *Remembering to take them regularly?*

[Gentle probe question]

Patient: *Yes, usually*

Doctor: *Many people forget to take their pills occasionally*

[Normalising statement responding to patient's answer to the probe question]

Patient: *Hmm*

Doctor: *Just thinking about the last couple of weeks – have you missed taking your pills on any occasion?*

[Specific probe asking directly about missed doses]

Brand swapping when medicines are dispensed may cause confusion and impair adherence. Pharmacists have a responsibility to educate patients if they swap brands, and prescribers should explain to patients and carers when they may be offered a choice.

Fixed-dose combinations can be helpful for patients on multiple medicines, and have been shown to improve adherence in some circumstances.²¹ Starting treatment with combination medicines has a strong evidence base in the management of HIV and other infections. For conditions such as hypertension, the evidence for starting with more than one medicine is mixed, but the strategy should be considered.²²

Patient reminders

Reminder packaging, which incorporates a date or time for a medicine to be taken, is an effective way of promoting adherence and has been shown to improve biological outcomes in type 2 diabetes and hypertension.²³ Drug administration aids are a form of reminder packaging and may be particularly helpful for patients prescribed multiple medicines. However, they are not suitable in all circumstances.²⁴ The stability of some drugs may be compromised by repackaging.²⁵ Patients with impaired cognition, eyesight or dexterity often have difficulty using them. Repackaging by the pharmacist may increase the cost to the patient and filling a compartmentalised box at home can lead to errors. Also, such boxes are rarely childproof.²⁶

There is strong evidence that regular reminders are an effective strategy for increasing adherence.²⁷

Electronic devices can assist with this. In a randomised controlled trial, 143 adults with asthma

used combination fluticasone propionate/salmeterol inhalers with attached electronic monitoring devices. The device recorded inhaler activation and provided twice-daily reminders for missed doses to those in the intervention group. Over six months, adherence was over 50% higher in the intervention group than in the control group.²⁸

A meta-analysis evaluating the use of text messaging in adults with chronic disease found it doubled the odds of adherence across 16 randomised controlled trials. The effect was not dependent on message characteristics such as personalisation, two-way communication or daily frequency.²⁹

As new information and communication technologies develop, new strategies for promoting and monitoring adherence are emerging. An example is 'smart pills' which send a signal to an external monitor when a tablet has been ingested. The signal can be linked to automated adherence reminders and to a medication reconciliation system.³⁰

Conclusion

Medicines do not work if they are not administered. Non-adherence, whether by intent or due to cost, complexity, or forgetfulness, is a major cause of reduced effectiveness and hence of preventable morbidity and mortality. Evidence-based strategies are available to address both intentional and unintentional non-adherence. ◀

Tim Usherwood is a member of the Editorial Executive Committee of Australian Prescriber.

REFERENCES

1. Sabaté E, editor. Adherence to long-term therapies: evidence for action. Geneva, Switzerland: World Health Organization; 2003.
2. Naderi SH, Bestwick JP, Wald DS. Adherence to drugs that prevent cardiovascular disease: meta-analysis on 376,162 patients. *Am J Med* 2012;125:882-7.e1. <https://doi.org/10.1016/j.amjmed.2011.12.013>
3. Hugtenburg JG, Timmers L, Elders PJM, Vervloet M, van Dijk L. Definitions, variants, and causes of nonadherence with medication: a challenge for tailored interventions. *Patient Prefer Adherence* 2013;7:675-82. <https://doi.org/10.2147/PPA.S29549>
4. Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychol Health* 1999;14:1-24. <https://doi.org/10.1080/08870449908407311>
5. Foster JM, Smith L, Bosnic-Anticevich SZ, Usherwood T, Sawyer SM, Rand CS, et al. Identifying patient-specific beliefs and behaviours for conversations about adherence in asthma. *Intern Med J* 2012;42:e136-44. <https://doi.org/10.1111/j.1445-5994.2011.02541.x>
6. Laba TL, Essue B, Kimman M, Jan S. Understanding patient preferences in medication nonadherence: a review of stated preference data. *Patient* 2015;8:385-95. <https://doi.org/10.1007/s40271-014-0099-3>
7. Meddings J, Kerr EA, Heisler M, Hofer TP. Physician assessments of medication adherence and decisions to intensify medications for patients with uncontrolled blood pressure: still no better than a coin toss. *BMC Health Serv Res* 2012;12:270. <https://doi.org/10.1186/1472-6963-12-270>
8. Lam WY, Fresco P. Medication adherence measures: an overview. *Biomed Res Int* 2015;2015:217047. <https://doi.org/10.1155/2015/217047>
9. Steele DJ, Jackson TC, Gutmann MC. Have you been taking your pills? The adherence-monitoring sequence in the medical interview. *J Fam Pract* 1990;30:294-9.
10. Bokhour BG, Berlowitz DR, Long JA, Kressin NR. How do providers assess antihypertensive medication adherence in medical encounters? *J Gen Intern Med* 2006;21:577-83. <https://doi.org/10.1111/j.1525-1497.2006.00397.x>
11. Callon W, Saha S, Korhuis PT, Wilson IB, Moore RD, Cohn J, et al. Which clinician questions elicit accurate disclosure of antiretroviral non-adherence when talking to patients? *AIDS Behavior* 2016;20:1108-15. <https://doi.org/10.1007/s10461-015-1231-7>
12. Kuntz JL, Safford MM, Singh JA, Phansalkar S, Slight SP, Her QL, et al. Patient-centered interventions to improve medication management and adherence: a qualitative review of research findings. *Patient Educ Couns* 2014;97:310-26. <https://doi.org/10.1016/j.pec.2014.08.021>

13. VanBuskirk KA, Wetherell JL. Motivational interviewing used in primary care. A systematic review and meta-analysis. *J Behav Med* 2014;37:768-80. <https://doi.org/10.1007/s10865-013-9527-4>
14. Hill S, Kavookjian J. Motivational interviewing as a behavioral intervention to increase HAART adherence in patients who are HIV-positive: a systematic review of the literature. *AIDS Care* 2012;24:583-92. <https://doi.org/10.1080/09540121.2011.630354>
15. Foster JM, Smith L, Usherwood T, Sawyer SM, Reddel HK. General practitioner-delivered adherence counseling in asthma: feasibility and usefulness of skills, training and support tools. *J Asthma* 2016;53:311-20. <https://doi.org/10.3109/02770903.2015.1091473>
16. Sinnott SJ, Buckley C, O'Riordan D, Bradley C, Whelton H. The effect of copayments for prescriptions on adherence to prescription medicines in publicly insured populations; a systematic review and meta-analysis. *PLoS One* 2013;8:e64914. <https://doi.org/10.1371/journal.pone.0064914>
17. Australian Bureau of Statistics. 4839.0 - Patient experiences in Australia: summary of findings, 2015-16. 15 November 2016. www.abs.gov.au/ausstats/abs@.nsf/mf/4839.0 [cited 2017 Jul 1]
18. Vermeire E, Hearnshaw H, Van Royen P, Denekens J. Patient adherence to treatment: three decades of research. A comprehensive review. *J Clin Pharm Ther* 2001;26:331-42. <https://doi.org/10.1046/j.1365-2710.2001.00363.x>
19. Cooper JA, Cadogan CA, Patterson SM, Kerse N, Bradley MC, Ryan C, et al. Interventions to improve the appropriate use of polypharmacy in older people: a Cochrane systematic review. *BMJ Open* 2015;5:e009235. <https://doi.org/10.1136/bmjopen-2015-009235>
20. Le Couteur D, Gnjidic D, McLachlan A. Deprescribing. *Aust Prescr* 2011;34:182-5. <https://doi.org/10.18773/austprescr.2011.095>
21. Webster R, Patel A, Selak V, Billot L, Bots M, Brown A, et al. Effectiveness of fixed dose combination medication ('polypills') compared with usual care in patients with cardiovascular disease or at high risk: a prospective, individual patient data meta-analysis of 3140 patients in six countries. *Intern J Cardiol* 2016;205:147-56. <https://doi.org/10.1016/j.ijcard.2015.12.015>
22. National Heart Foundation of Australia. Guideline for the diagnosis and management of hypertension in adults - 2016. Melbourne: National Heart Foundation of Australia; 2016. www.heartfoundation.org.au/images/uploads/publications/PRO-167_Hypertension-guideline-2016_WEB.pdf [cited 2017 Jul 1]
23. Mahtani KR, Heneghan CJ, Glasziou PP, Perera R. Reminder packaging for improving adherence to self-administered long-term medications. *Cochrane Database Syst Rev* 2011;CD005025. <https://doi.org/10.1002/14651858.CD005025.pub3>
24. Elliott RA. Appropriate use of dose administration aids. *Aust Prescr* 2014;37:46-50. <https://doi.org/10.18773/austprescr.2014.020>
25. Haaywood A, Llewelyn V, Robertson S, Mylrea M, Glass B. Dose administration aids: pharmacists' role in improving patient care. *Australas Med J* 2011;4:183-9. <https://doi.org/10.4066/AMJ.2011.693>
26. Barker R. When is child-resistant packaging not child resistant? *Aust Prescr* 2013;36:194. <https://doi.org/10.18773/austprescr.2013.084>
27. Schedlbauer A, Davies P, Fahey T. Interventions to improve adherence to lipid lowering medication. *Cochrane Database Syst Rev* 2010;CD004371. <https://doi.org/10.1002/14651858.CD004371.pub3>
28. Foster JM, Usherwood T, Smith L, Sawyer SM, Xuan W, Rand CS, et al. Inhaler reminders improve adherence with controller treatment in primary care patients with asthma. *J Allergy Clin Immunol* 2014;134:1260-8.e3. <https://doi.org/10.1016/j.jaci.2014.05.041>
29. Thakkar J, Kurup R, Laba TL, Santo K, Thiagalingam A, Rodgers A, et al. Mobile telephone text messaging for medication adherence in chronic disease: a meta-analysis. *JAMA Intern Med* 2016;176:340-349. <https://doi.org/10.1001/jamainternmed.2015.7667>
30. Granger BB, Bosworth H. Medication adherence: emerging use of technology. *Curr Opin Cardiol* 2011;26:279-87. <https://doi.org/10.1097/HCO.0b013e328347c150>