Medication non-adherence in a cohort of chronically ill Australians

A case of missed opportunities

Tracey-Lea Laba, Tom Lung, Stephen Jan, Anish Scaria, Tim Usherwood, Jo-anne Brien, Natalie A Plant, Stephen Leeder

Background and objectives
This study investigated the effect of management – including home medicines reviews and chronic disease management plans funded through the Medicare Benefits Schedule – on self-reported medication non-adherence.

Methods
An observational cohort study including 244 individuals with an exacerbation of chronic illness enrolled into the Care Navigation randomised controlled trial of integrated care. Non-adherence was measured using the Morisky-Greene-Levine self-reported adherence tool.

Results
The cohort comprised an equal number of older men and women with, on average, three chronic diseases, receiving between five and 10 unique medications each month and visiting a general practitioner (GP) more than 50 times in the year prior to completing the questionnaire. Forty per cent reported non-adherence, which was greater in males (relative risk [RR]: 1.73; 95% confidence interval [CI]: 1.25, 2.54) and in patients reporting a recent fall (RR 1.40; 95% CI: 1.02, 1.89). GP-initiated chronic disease management programs did not influence adherence.

Discussion
Despite almost weekly contact with GPs, two in five patients were non-adherent. Better methods of encouraging adherence are needed.
little research has focused specifically on adherence by people with multiple chronic illnesses, especially in Australia. Even fewer studies have examined the impact of coordinated care. While patient, disease, socioeconomic and therapy-related factors have typically been implicated as barriers to adherence, the impact of health system–related factors such as access to resources to manage chronic diseases has received very little attention. To address these gaps in evidence, and given the interest in delivering coordinated care to people with complex chronic diseases in Australian general practice, we investigated the impact of health system–related factors on medication adherence reported by participants in the CN trial. In particular, we investigated the influence of home medicine reviews and chronic disease management plans funded by the Medicare Benefits Schedule (MBS) alongside patient characteristics on levels of non-adherence.

**Methods**

**Population**

Our study included all participants with chronic illness admitted to Nepean Hospital and enrolled in the CN trial who completed a self-report medication adherence questionnaire 12 months after randomisation and for whom we had access to administrative claims data. The inclusion criteria of the CN trial are described elsewhere. In brief, individuals comprised:

- patients aged ≥70 years (or ≥45 years for Aboriginal and Torres Strait Islander Australians) with three or more hospital admissions during the preceding 12 months
- patients aged ≥16 years with at least one previous respiratory-related or cardiac-related hospital admission
- patients determined by a CN nurse as likely to benefit from receiving CN.

Excluded from the CN trial were:

- previous CN recipients
- those medically unable to participate
- those admitted to hospital more than one business day prior to randomisation
- those not providing written informed consent.

For our study, the CN trial population was treated as a single cohort comprising participants from the two arms of the trial. This was because no effect of the intervention was found in the analysis of the trial. Of 500 participants in the CN trial, 308 provided detailed demographic and clinical variables (eg age, gender, employment status, comorbidities) by telephone interview 12 months after randomisation. Of these, 299 completed a self-reported adherence questionnaire, becoming eligible for inclusion in this analysis.

We excluded Department of Veterans’ Affairs entitlement holders (n = 9) and anyone not consenting to administrative data linkage (n = 46), because we lacked access to their administrative claims data needed to measure health system factors of interest.

**Primary outcome**

Using the validated and extensively used Morisky-Greene-Levine questionnaire, self-reported non-adherence was assessed 12 months following randomisation. This questionnaire includes four Yes/No questions:

1. Do you ever forget to take your medications?
2. Are you careless at times about taking your medications?
3. When you feel better, do you sometimes stop taking your medications?
4. If you feel worse when you take your medications, do you sometimes stop taking them?

As in other research, respondents answering ‘Yes’ to one or more of the questions were classified as non-adherent.

**Covariates**

In addition to the self-reported clinical and demographic characteristics, the health system–related variables measured were:

- the number of emergency department presentations and hospital admissions in the previous 12 months, recorded in a CN database of electronic medical records
- the number of GP visits and the presence of chronic disease-specific management plans and team care arrangements or DMMRs/RMMRs in the previous 12 months, as coded in the MBS at the time of the study and recorded in individually linked MBS records (refer to Table 1 for specific item codes used).

Finally, the average number of unique medications dispensed monthly for each participant over the previous 12 months was calculated using individually linked Pharmaceutical Benefits Schedule (PBS) administrative records of government-funded medications dispensed outside of public hospitals.

**Statistical analysis**

Correlations between all covariates were checked using the Pearson correlation coefficient, with >0.4 taken to indicate significant correlation. Continuous explanatory variables were plotted against the primary outcome (ie non-adherence), and those not linearly distributed were collapsed into categorical variables appropriate for the distribution (eg number of medications, number of GP consultations).

The association of covariates with non-adherence (relative to adherence) was analysed using the Poisson regression with robust error variance.

The Hosmer-Lemeshow purposeful selection of variables strategy was chosen to help guide the selection of a parsimonious model with numerically stable estimates and small standard errors.

Covariates with a univariate P value of 0.25 were selected as candidates for the multivariate analysis and iteratively removed from the model if they were non-significant (α = 0.2) and were not confounders (ie change in parameter estimate <15% compared with full model).

Covariates originally excluded from the multivariate model were individually re-added and retained at the P = 0.15 level. The model was then iteratively reduced as before but only for the variables that were additionally added. Given the aims of the study, the health system–related variables (emergency department and hospital admissions, GP visits, chronic disease-specific management plans and team care arrangements, DMMRs/RMMRs in the previous 12 months, as coded in the MBS at the time of the study and recorded in individually linked MBS records (refer to Table 1 for specific item codes used)).
RMMRs) and CN treatment assignment were retained throughout the model-building process and in the final model.

We conducted 1000 bootstrap replications to estimate 95% confidence intervals (CIs) for the coefficients of the iteratively reduced complete case multivariate model. Analyses were performed using SAS, version 9.3.

Written informed consent had been obtained from all participants in the study. Ethics approval was granted by Sydney West Area Health Service Human Research Ethics Committee – Nepean Campus (HREC/09/NEPEAN/55) and ratified by the University of Sydney Research Integrity office (ACTRN12609000554268).

Results
The mean age of participants was 70 years; 51.2% were male, 83.7% were dependent on social welfare and 2.5% resided in nursing homes. Fifty-two per cent received the intervention. Participants reported having, on average, three chronic diseases, and more than one-third reported having fallen in the month prior to interview.

In the 12 months prior to interview, 54.5% had received between five and 10 prescribed medications monthly; 54.1% had, on average, visited a GP more than once weekly; 16.0% had had a government-rebated, GP-initiated DMMR or RMMR; and more than two-thirds had experienced a GP-initiated chronic disease management plan. On average, participants had visited the emergency department three times and had been admitted to hospital twice (Tables 1, 2).

Of the 244 participants, 40.2% (n = 98) self-reported as non-adherent. Table 3 provides the univariate and multivariate rate ratios for non-adherence compared with adherence. After controlling for intervention arm assignment in CN trial and for other health system variables, males were at higher risk of reporting non-adherence (relative risk [RR]: 1.73; 95% CI: 1.25, 2.54). Participants who had reported a fall in the month prior to completing the questionnaire were at higher risk of reporting non-adherence compared with those who had not fallen (RR: 1.40, 95% CI: 1.02, 1.89). We found no other statistically significant associations between non-adherence and other demographic, clinical or therapy-related factors, nor with any of the health system–related variables assessed.

Discussion
In this Australian cohort of older people with multiple chronic illnesses, who were in frequent contact with their general practice and receive a hospital-based coordinated care program, the extent of...
self-reported medication non-adherence was 40%. The non-adherence estimate is similar to the range of 20–50% for chronic disease reported in the broader literature,2 but is substantially lower than the 82% non-adherence rate estimated in a Spanish study of a multimorbid cohort recently discharged from hospital, a study that used the same validated self-reported measure of non-adherence.13

Given that our study was conducted among a cohort derived from a clinical trial and that self-reporting measures are potentially subject to social desirability bias (ie providing responses that are viewed favourably),23 it is possible that our figure underestimates the extent of non-adherence within the broader multimorbid population. Nevertheless, only gender and falls history were significantly correlated with non-adherence.

Considering the extensive contact these patients had with a general practice in the preceding 12 months, including chronic disease management programs and services, this high rate of non-adherence is alarming and disappointing. Importantly, the relatively low uptake of specific collaborative medication management services (ie DMMRs/RMMRs), for which the majority of patients could have qualified,24 raises questions about the practical accessibility of such services. This might reflect administrative and time-related barriers, as recently reported by some Australian GPs.25 Alternatively, this finding, alongside the observed lack of GP awareness of medication-specific services,25 could signal an inadequate focus of current chronic disease management services with respect to medication adherence in general practice.

Our findings highlight the fact that surveillance of non-adherence and the use of adherence support services are needed for patients with multimorbidity, particularly men and those who have recently fallen. With the majority of patients in this study visiting a GP almost weekly, general practice seems the optimal, albeit not the only, place for intervention. Whether further funding for new services is needed or whether such services should be part of currently reimbursed general practice is debatable. On the one hand, emphasis on appropriate use of medications would ideally accompany any prescribing decision during a consultation. However, the reported difficulties of accurately detecting non-adherence in general practice23,24 and the time and cost pressures of the fee-for-service model might be barriers to such routine implementation.

### Table 2. Characteristics of the study cohort by gender (frequency and % unless otherwise reported)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Male (n = 125)</th>
<th>Female (n = 119)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Care Navigation treatment group</td>
<td>56 (44.8%)</td>
<td>71 (59.7%)</td>
</tr>
<tr>
<td>Age (mean, SD)</td>
<td>69 (10.8)</td>
<td>72 (12.5)</td>
</tr>
<tr>
<td>Financial constraints</td>
<td>33 (26.4%)</td>
<td>35 (29.4%)</td>
</tr>
<tr>
<td>Income source: pension/social welfare</td>
<td>98 (79.7%)†</td>
<td>102 (70.6%)§</td>
</tr>
<tr>
<td>Nursing home resident</td>
<td>2 (1.6%)†</td>
<td>2 (1.7%)§</td>
</tr>
<tr>
<td>Social isolation</td>
<td>30 (24.0%)</td>
<td>32 (26.9%)</td>
</tr>
<tr>
<td>Physical disability</td>
<td>58 (46.4%)</td>
<td>40 (33.6%)</td>
</tr>
<tr>
<td>History of falls in the last month</td>
<td>42 (36.2%)†</td>
<td>44 (38.3%)§</td>
</tr>
<tr>
<td>Visual and/or hearing impairment</td>
<td>101 (80.8%)</td>
<td>96 (80.7%)</td>
</tr>
<tr>
<td>Deterioration in health-related quality of life, 12 months*</td>
<td>48 (38.4%)</td>
<td>37 (31.1%)</td>
</tr>
<tr>
<td>Number of reported chronic conditions (mean, SD)</td>
<td>3 (1.5)</td>
<td>3.2 (1.6)</td>
</tr>
<tr>
<td>Average number of medications per month</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>46 (36.8%)</td>
<td>40 (33.6%)</td>
</tr>
<tr>
<td>5–10</td>
<td>61 (48.8%)</td>
<td>72 (60.5%)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>18 (14.4%)</td>
<td>7 (5.9%)</td>
</tr>
<tr>
<td>Domiciliary or residential medication review in previous 12 months†</td>
<td>19 (15.2%)</td>
<td>20 (16.8%)</td>
</tr>
<tr>
<td>Number of GP visits, previous 12 months†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>55 (44.0%)</td>
<td>57 (47.9%)</td>
</tr>
<tr>
<td>&gt;50</td>
<td>70 (56.0%)</td>
<td>62 (52.1%)</td>
</tr>
<tr>
<td>Chronic disease management, previous 12 months†</td>
<td>84 (67.2%)</td>
<td>88 (73.9%)</td>
</tr>
<tr>
<td>GP mental health treatment plan, previous 12 months†</td>
<td>14 (11.2%)</td>
<td>18 (15.1%)</td>
</tr>
<tr>
<td>Number of ED† visits, previous 12 months (mean, SD)</td>
<td>2.3 (2.8)</td>
<td>2.9 (3.5)</td>
</tr>
<tr>
<td>Hospital admissions, previous 12 months (mean, SD)</td>
<td>1.8 (2.2)</td>
<td>2.2 (2.7)</td>
</tr>
</tbody>
</table>

*Deterioration in EQ-5D utility score between baseline and 12 month visit
†Medicare Benefit Schedule item codes: GP visits: 3, 4, 20, 23, 24, 34–37, 43, 44, 47, 51–54, 57–60, 65, 92, 93, 95, 96, 597, 599, 5000, 5003, 5010, 5020, 5023, 5028, 5040, 5043, 5049, 5060, 5063, 5067; chronic disease management plans and practice nurse chronic disease services, mental health treatment plans, and Team Care Arrangements: 712–14, 716–19, 721, 723, 729, 732, 735, 739, 743, 747, 750, 758, 2700, 2701, 2702, 2710, 2712, 2713, 2715, 2717, 10997; medication reviews: 900, 903
‡Missing: n = 2 income source; n = 1 nursing home resident; n = 9 history of falls
§Missing: n = 3 income source; n = 1 nursing home resident; n = 1 history of falls
GP, general practitioner; ED, emergency department
Community pharmacists are trained in medication management. As a part of their professional practice, they are tasked with ensuring the optimal use of dispensed medications. Under the fifth and sixth community pharmacy agreements, they have financial incentives to encourage adherence, including offering in-store medicines use reviews and dose administration aids. However, unlike DMMRs/RMMRs, these pharmacist services, not being medical services, do not qualify for reimbursement through MBS (and so could not be captured nor accounted for in our study), do not require the pharmacist to undertake additional accreditation to participate and do not require collaboration with the patient’s GP.

With the remuneration of community pharmacies’ non-dispensing services a contested and divisive area of health policy, one solution might be to invest

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Comparison against reference</th>
<th>n</th>
<th>Univariate rate ratio</th>
<th>P</th>
<th>Bootstrapped rate ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CN treatment group</td>
<td>CN versus standard care</td>
<td>244</td>
<td>0.82 (0.60, 1.11)</td>
<td>0.193</td>
<td>0.89 (0.62, 1.25)</td>
<td>0.488</td>
</tr>
<tr>
<td>Age, increasing</td>
<td></td>
<td>244</td>
<td>0.98 (0.97, 0.99)</td>
<td>0.007</td>
<td>0.99 (0.98, 1.01)</td>
<td>0.188</td>
</tr>
<tr>
<td>Male</td>
<td>Male versus female</td>
<td>244</td>
<td>1.80 (1.29, 2.50)</td>
<td>0.001</td>
<td>1.73 (1.25, 2.54)</td>
<td>0.003</td>
</tr>
<tr>
<td>Financial constraints</td>
<td>Yes versus no</td>
<td>244</td>
<td>1.20 (0.87, 1.65)</td>
<td>0.271</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Income source</td>
<td>Received income vs social welfare</td>
<td>239</td>
<td>1.33 (0.94, 1.90)</td>
<td>0.111</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Resident of nursing home</td>
<td>Yes versus no</td>
<td>239</td>
<td>0.63 (0.12, 3.47)</td>
<td>0.597</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Social isolation</td>
<td>Yes versus no</td>
<td>244</td>
<td>1.17 (0.84, 1.63)</td>
<td>0.341</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mental disability</td>
<td>Yes versus no</td>
<td>244</td>
<td>1.63 (1.01, 2.62)</td>
<td>0.044</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Physical disability</td>
<td>Yes versus no</td>
<td>244</td>
<td>1.43 (1.06, 1.94)</td>
<td>0.020</td>
<td>1.25 (0.93, 1.75)</td>
<td>0.154</td>
</tr>
<tr>
<td>History of falls in the last month</td>
<td>Yes versus no</td>
<td>231</td>
<td>1.24 (0.91, 1.70)</td>
<td>0.181</td>
<td>1.40 (1.02, 1.89)</td>
<td>0.030</td>
</tr>
<tr>
<td>Visual and/or hearing impairment</td>
<td>Yes versus no</td>
<td>244</td>
<td>1.06 (0.71, 1.58)</td>
<td>0.774</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Health-related quality of life deterioration, 12 months*</td>
<td>No change versus relative decline</td>
<td>244</td>
<td>0.99 (0.72, 1.37)</td>
<td>0.970</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Number of reported chronic conditions</td>
<td></td>
<td>244</td>
<td>0.99 (0.90, 1.10)</td>
<td>0.903</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Average number of medications per month</td>
<td>5–10 versus 0–4</td>
<td>244</td>
<td>0.66 (0.48, 0.91)</td>
<td>0.012</td>
<td>0.75 (0.52, 1.06)</td>
<td>0.090</td>
</tr>
<tr>
<td></td>
<td>&gt;10 versus 0–4</td>
<td>244</td>
<td>0.88 (0.54, 1.44)</td>
<td>0.609</td>
<td>0.95 (0.58, 1.48)</td>
<td>0.860</td>
</tr>
<tr>
<td>Domiciliary or residential medication review in previous 12 months†</td>
<td>Yes versus no</td>
<td>244</td>
<td>0.60 (0.34, 1.04)</td>
<td>0.070</td>
<td>0.68 (0.33, 1.12)</td>
<td>0.171</td>
</tr>
<tr>
<td>Number of GP visits in previous 12 months</td>
<td>&gt;50 versus ≤50</td>
<td>244</td>
<td>0.75 (0.55, 1.02)</td>
<td>0.067</td>
<td>0.79 (0.57, 1.07)</td>
<td>0.139</td>
</tr>
<tr>
<td>Chronic disease management, previous 12 months (GP or practice nurse)</td>
<td>Yes versus no</td>
<td>244</td>
<td>1.16 (0.81, 1.65)</td>
<td>0.414</td>
<td>1.21 (0.85, 1.86)</td>
<td>0.358</td>
</tr>
<tr>
<td>GP mental health management in previous 12 months</td>
<td>Yes versus no</td>
<td>244</td>
<td>1.39 (0.96, 2.01)</td>
<td>0.079</td>
<td>1.35 (0.86, 2.02)</td>
<td>0.146</td>
</tr>
<tr>
<td>Number of emergency department visits in the past 12 months</td>
<td></td>
<td>244</td>
<td>1.00 (0.95, 1.05)</td>
<td>0.936</td>
<td>1.00 (0.94, 1.05)</td>
<td>0.895</td>
</tr>
<tr>
<td>Number of hospital admissions in the last 12 months</td>
<td></td>
<td>244</td>
<td>0.98 (0.92, 1.05)</td>
<td>0.595</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Deterioration in EQ-5D utility score between baseline and 12 month visit
†Variables that have not been reported are excluded from the adjusted model
CI, confidence interval; CN, Care Navigation; GP, general practitioner
in technology to better connect GP services with the services provided by community pharmacists rather than create and fund ‘new’ adherence services.\textsuperscript{29,30} This is particularly relevant with respect to pharmacists’ dispensing of generic medications, whose different colours, shapes and sizes could confuse patients. Alternatively, the inclusion of pharmacists in the ‘Health Care Home’, as done in other contexts, could be explored.\textsuperscript{5,31} In any case, rigorous evaluation of the effectiveness of such services on both adherence and clinical outcomes is needed, with investment decisions guided by suitable cost-effectiveness and financial impact analyses that take into account implementation and scale.

While the association between non-adherence and gender corroborates other findings,\textsuperscript{32} the apparent correlation of non-adherence with a recent history of falls requires further investigation. Many medications can increase the risk of falls in the elderly.\textsuperscript{33} Non-adherence might reflect the patient’s appropriate response in the face of a falls-inducing adverse drug reaction.

On the other hand, the pharmacodynamic changes that occur with ageing and the characteristics of medication use – such as duration of use, drug–drug interactions and changes in medication use, including as a result of non-adherence – might be associated with an increased risk of falls.\textsuperscript{34} Further work considering the appropriateness of therapy, the number and pattern of an individual’s chronic diseases,\textsuperscript{35} as well as the longer-term impact of a fall on adherence, is needed to unpack this relationship.

The lack of any statistically significant association between the number of prescribed medications and non-adherence was surprising. Although we have allowed for an adequate number of observations per covariate in the multivariate analysis, the small overall sample size may be masking the true difference in outcomes between the different groups. Given the multiple comparisons (covariates) in the final model, we also cannot exclude the possibility of false positive results.

Furthermore, as our sample was a sub-group of participants enrolled in a randomised controlled trial that was conducted in one region of Australia, the generalisability of these findings to the broader population might be limited. In particular, the extent of federally funded non-MBS adherence services provided by community pharmacies might differ between our cohort and the general Australian population. Further, we could only explore the variables that were collected in the CN trial. It is also possible that we have underreported the number of chronic disease management services provided; for example, general practice management plans that were ongoing but not claimed during our study timeframe would not have been captured.

Finally, as there is no ‘gold standard’ measure of adherence, self-reporting can be subject to bias (eg recall bias given no recall period is specified with this instrument). Although the use of a more objective measure of adherence would be ideal, the ease of administration and relatively lower burden on the participants dictated our use of a self-reporting tool.

Implications for general practice

In this study, two in five patients with multiple chronic conditions enrolled in the CN trial reported medication non-adherence. Current GP programs to support chronic disease management, including collaborative home medicines reviews, did not influence adherence.

We recommend greater emphasis being placed, through existing MBS GP items, on addressing non-adherence in such patients. It is important for prescribers to regularly ask patients about their medication adherence and, if necessary, to discuss strategies for promoting this.\textsuperscript{36} Connecting GPs with the medication management skills of pharmacists might address this striking unmet clinical need.

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References


