Medication Non-Adherence Identified at Home: A Systematic Review and Meta-analysis

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ABSTRACT

**Background:** Patients dwelling at home are at risk of medication non-adherence which is directly associated with poor treatment outcomes. This study aimed to estimate the prevalence rate of medication non-adherence occurring at patient’s home.

**Methods:** EMBASE, PUBMED/MEDLINE, SCOPUS and CINAHL were searched from their inceptions to January 2016. Original articles were included if they enrolled patients home domiciled and provided sufficient data for calculating the prevalence. The quality assessment of included studies was performed using Crombie’s items. Pooled estimates were obtained by using random-effect model. STATA was used for data analysis.

**Results:** Of 3398 articles identified, 13 met the inclusion criteria. The median prevalence of medication non-adherence detected in home settings was 38.6% [Interquartile range (IQR): 12.8-53%]. According to population, the median prevalence in elderly was 43.2% (IQR: 13.2-57.7%) whereas that in all-aged population was 8.4% (95% CI, 6.3-10.5%; $\chi^2$ 0.61; d.f.1; $F=0%$; $p=0.435$). Using pill count as a method of detection showed the highest medication non-adherence rate (70%, 95% CI; 61-79%). High income countries reported a higher levels of non-adherence to medications (median 46.8%, IQR: 26.4-57.7%) than lower middle-income countries (9.6%, 95% CI; 5.7-13.5%) or upper middle-income countries (8.4%, 95% CI; 6.3-10.5%; $\chi^2$ 0.61; d.f.1; $F=0%$; $p=0.435$). Medication involving cardiovascular, alimentary tract and metabolic and respiratory diseases were most implicated with non-adherence.

**Conclusion:** Non-adherence to medication detected at patients’ home was appreciable. Healthcare professional should be aware of adherence problems in community and further design an effective strategy for improving adherence to achieve desired therapeutic outcomes and safety.

**Keywords:** Home; Patient adherence; Patient compliance; Non-adherence; Non-compliance

How this fits in with quality in primary care?

**What do we know?**

Patients dwelling in their own homes or in community are vulnerable to have medication non-adherence because many are elderly and unsupervised. No systematic review and meta-analysis estimated the extent of this issue.

**What does this paper add?**

Medication non-adherence is evidently considerable in primary care settings with two in five patients dwelling in home encountered this problem, particularly in the elderly population. Cardiovascular treatments are most commonly subject to medication non-adherence and clinicians in primary care should monitor adherence closely in patients at home.

**Abbreviations:** AHRQ: Agency for Healthcare Research and Quality; ATC: Anatomical Therapeutic Chemical; CI: Confidence Interval; CINAHL: Cumulative Index to Nursing and Allied Health Literature; IQR: Interquartile Range

**Introduction**

The term ‘medication adherence’ is defined as the extent to which patient behavior in taking medication, a diet and/or executing lifestyle changes, accord with recommendations with health care providers [1]. Patients not adhering to their medications has been a crucial problem in pharmacotherapy and occurred at any stage of their treatment. Medication non-adherence also causes poor treatment outcomes, poor quality of life, and subsequent hospitalization and emergency room visits [2-4]. Apart from negative clinical outcomes, medication non-adherence further burdens healthcare systems and their resources. In the United States, spends $100 and $300 billion annually was attributable to non-adherence to medication, accounting for 3-10% of national health care budget [5], while the EU devotes €125 billion annually for this purpose [6].

Patients at home are vulnerable to medication non-adherence because (i) they live in an uncontrolled environment compared to that in hospitals, (ii) consume multiple medications both prescriptions and over the counter drugs, (iii) and little supervision at home [7]. The consequential non-adherence results in adverse outcomes and hospital admissions [8].
Many studies have assessed non-adherence of home domiciled patients, however, no systematic review has been conducted on this issue. Accordingly, this study aimed to quantify prevalence and nature of non-adherence to medications within domiciled settings.

**Methods**

**Search strategy**

A systematic search of PUBMED/MEDLINE, SCOPUS, EMBASE and CINAHL since their inception to January 2016 using keywords or of their synonyms; (“drug-related problem” OR “medication-related problem” OR “adherence” OR “compliance”) AND “home setting”. In addition, bibliographies of included articles were also screened for relevant studies.

**Eligibility criteria**

Original studies were included if they enrolled patients dwelling at home and reported the prevalence of medication non-adherence. Investigations in hospital settings or long-term care facilities or focusing on specific medications or medication groups were excluded.

**Study selection and data extraction**

The retrieved articles were screened independently by 2 investigators (P.M. and C.K.) against a pre-specified selection criteria. The studies meeting the eligibility criteria were then extracted using a standardized form. Information to be extracted were as follows: study characteristics (study design, setting, year, sample size), study population (age, sex), method used to measure non-adherence, prevalence rates of non-adherence to medications. Medications involved in non-adherence were classified according to the Anatomical Therapeutic Chemical (ATC) classification system [9]. We also contacted authors for raw data if necessary. Any disagreement was discussed until a consensus was reached.

**Quality assessment of studies**

The risk of bias of eligible studies was assessed using Crombie’s items which contain 7 criteria for quality of cross-sectional/prevalence studies as recommended by the Agency for Healthcare Research and Quality (AHRQ) [10]. In brief, 7-categories include (i) appropriate design, (ii) adequate description of data, (iii) report response rates, (iv) adequately represent the total sample, (v) clearly stated aims and likelihood of reliable and valid measurements, (vi) statistical significance, and (vii) adequate description of analyses. Articles were given quality scores ranging from 0-7. All disagreements were resolved by discussion.

**Data analyses**

Prevalence rates were expressed as the ratio of numbers of non-adhering patients to total patients, and these outcome measures were used for statistical pooling. The pooled prevalence and 95% confidence interval (95% CI) were derived using the random-effects model of the Dersimonian–Laird method assuming that the true effect size varies between studies [11]. To assess heterogeneity of prevalence rates among studies, we used standard χ² tests, and the F statistic. If F 75%, considerable heterogeneity is indicated and, median prevalence [interquartile range (IQR)] was reported instead of pooled estimates (95%CI). To explore potential heterogeneities, the average estimate was stratified by age group, i.e., “elderly” (>60 years) or “all age groups”, method for assessing medication non-adherence (“pill count”, “combination of pill count and interview”, “self-report”, “interview” and “case review”) and socio-economic status (“high income countries”, “upper middle-income countries” and lower middle-income countries”). All analyses were performed using STATA, v14.1 [12].

**Results**

**Search results**

Of 3398 articles identified from the databases searches, 738 duplicates were removed. After screening the title and abstract, some articles were removed: (a) irrelevant to non-adherence to medications (1133 articles); (b) reviews (401); (c) case reports (98) or case series (19); (d) were not human studies (87). The remaining 522 articles were fully assessed for eligibility and 511 were removed because the patients were not home domiciled (506 articles), or contained insufficient data to calculate prevalence rates of non-adherence to medications (5 articles). Two additional articles were identified by hand-searching. Thus, 13 articles [13-25] were included in the systematic review and meta-analysis (Figure 1).

All included studies (n=13) were cross-sectional studies, investigating medication non-adherence detected in patients living at home (Table 1), set in N. America (5 studies), Europe (3), Australia (2), Asia (2) and S. America (1). Five methods were employed to assess medication non-adherence: interview (7 studies), patient self-report via questionnaire (3), case note review (1), residual pill counting (1) and combined method of interview/pill count (1). According to population characteristics, eleven studies were conducted in elderly and three in the ‘all age groups’. Among the studies in the elderly, five studies [13,14,16,17,19] reported that more than 40% of subjects lived alone but not reported in the remainder.

The study qualities by Crombie item scores was 3-7 but 8/13 attracted scores >5 demonstrating good quality (Table 1).

**Definition used to assess medication non-adherence**

There was a variety of definitions used to determine medication non-adherence in the included studies. Four studies [13,14,21,25] employed a vague criteria described as “patients did not adhere to prescription direction”. Two studies [19,20] judged non-adherence based on Morisky scale. Five studies [17,22,24] defined patients with medication non-adherence if they missed a single dose or failed to take a drug [15-17,22,24] or an extra dose was taken [15,16]. One study [18] used the criteria developed by Strand et al. [26]. One study [23] classified patients as non-adoherent if the pill count was lower than 80% or greater than 110% of anticipated pill counts.

**Prevalence of non-adherence in home settings**

The 13 studies comprised a total of 4072 home residents of whom 995 were identified as non-adherent to medications.
Figure 1: Study selection flow diagram.

Table 1: Characteristics of 13 included studies.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year of publication</th>
<th>Survey year</th>
<th>Population</th>
<th>Crude rate prevalence (%)</th>
<th>Mean Age (year)</th>
<th>Men (%)</th>
<th>Adherence measure</th>
<th>Setting</th>
<th>Socioeconomic status</th>
<th>Crombie’s score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooper et al.</td>
<td>1982</td>
<td>NA</td>
<td>Elderly</td>
<td>48/111 (43.2)</td>
<td>70.5</td>
<td>41</td>
<td>Interview</td>
<td>United States</td>
<td>High income country</td>
<td>4.5</td>
</tr>
<tr>
<td>Darnell et al.</td>
<td>1986</td>
<td>NA</td>
<td>Elderly</td>
<td>78/155 (50.3)</td>
<td>71.6</td>
<td>28.4</td>
<td>Interview</td>
<td>United States</td>
<td>High income country</td>
<td>4.5</td>
</tr>
<tr>
<td>Zeppetella et al.</td>
<td>1999</td>
<td>1995-1997</td>
<td>Elderly</td>
<td>64/111 (57.6)</td>
<td>66.4</td>
<td>55.9</td>
<td>Interview and pill count</td>
<td>United Kingdom</td>
<td>High income country</td>
<td>3</td>
</tr>
<tr>
<td>Barat et al.</td>
<td>2001</td>
<td>1998</td>
<td>Elderly</td>
<td>92/348 (26.4)</td>
<td>75</td>
<td>43</td>
<td>Interview</td>
<td>Denmark</td>
<td>High income country</td>
<td>6.5</td>
</tr>
<tr>
<td>Thompson et al.</td>
<td>2001</td>
<td>1993-1995</td>
<td>Elderly</td>
<td>163/204 (80.0)</td>
<td>NA</td>
<td>30</td>
<td>Interview</td>
<td>Australia</td>
<td>High income country</td>
<td>5.5</td>
</tr>
<tr>
<td>Roughhead et al.</td>
<td>2004</td>
<td>NA</td>
<td>Elderly</td>
<td>132/1,000 (13.2)</td>
<td>Median, 74 (M), 75.5 (F)</td>
<td>38</td>
<td>Case note review</td>
<td>Australia</td>
<td>High income country</td>
<td>4</td>
</tr>
<tr>
<td>Roth et al.</td>
<td>2005</td>
<td>2002</td>
<td>Elderly</td>
<td>53/100 (53.0)</td>
<td>77.5</td>
<td>15</td>
<td>Self-reported</td>
<td>United States</td>
<td>High income country</td>
<td>6.5</td>
</tr>
<tr>
<td>Vik et al.</td>
<td>2006</td>
<td>2000</td>
<td>Elderly</td>
<td>123/319 (38.6)</td>
<td>82.8</td>
<td>21</td>
<td>Self-reported</td>
<td>Canada</td>
<td>High income country</td>
<td>7</td>
</tr>
<tr>
<td>Mastroianni et al.</td>
<td>2011</td>
<td>2008</td>
<td>All age group</td>
<td>21/280 (7.5)</td>
<td>NA</td>
<td>NA</td>
<td>Interview</td>
<td>Brazil</td>
<td>Upper income country</td>
<td>5</td>
</tr>
<tr>
<td>Fiss et al.</td>
<td>2011</td>
<td>2006-2008</td>
<td>Elderly</td>
<td>95/744 (12.8)</td>
<td>80.5</td>
<td>26.9</td>
<td>Self-reported</td>
<td>Germany</td>
<td>High income country</td>
<td>5.5</td>
</tr>
<tr>
<td>Turner et al.</td>
<td>2012</td>
<td>NA</td>
<td>Elderly</td>
<td>70/78 (70.0)</td>
<td>75</td>
<td>26</td>
<td>Pill count</td>
<td>United States</td>
<td>High income country</td>
<td>5</td>
</tr>
<tr>
<td>Kumar</td>
<td>2012</td>
<td>NA</td>
<td>Elderly</td>
<td>21/219 (9.6)</td>
<td>NA</td>
<td>NA</td>
<td>Interview</td>
<td>India</td>
<td>Lower income country</td>
<td>NA</td>
</tr>
<tr>
<td>Kongkaew et al.</td>
<td>2015</td>
<td>2015</td>
<td>All age group</td>
<td>35/381 (9.2)</td>
<td>56.7</td>
<td>30.18</td>
<td>Interview</td>
<td>Thailand</td>
<td>Upper income country</td>
<td>5.5</td>
</tr>
</tbody>
</table>

Abbreviations: NA: Not Applicable
Crude prevalence rate of medication non-adherence ranged from 7.5% [21] to 80% [17], with a number of population varied from 78 [23] to 1,000 [18]. Across the 13 studies, the median prevalence rate of medication non-adherence was 38.6% (IQR: 12.8-53%; $\chi^2$ 1033.2, d.f.12; $F$=98.8%, p<0.001).

When sub-grouped by age, the result showed that studies on elderly participants reported a higher prevalence rate (median=43.2%; IQR: 12.8-53%; $\chi^2$ 905.4, d.f.10; $F$=98.9%, p<0.001) than all-age groups (pooled prevalence=8.4%; 95% CI: 6.3-10.5%; $\chi^2$ 0.61, d.f.1; $F$=0%, p=0.435) (Figure 2). When sub-grouped by measurement methods, medication non-adherence rate was highest by pill-counting (70%; 95%CI, 61-79%), but lower when combining pill-count with interview (57.7%; 95% CI, 48.5-66.8%), by self-report (median=38.6%; IQR: 12.8-53%; $\chi^2$ 123.8, d.f.2; $F$=94.8%, p<0.001), by interview (median=26.4%; IQR: 9.2-50.3%; $\chi^2$ 688, d.f.6; $F$=99.1%, p<0.001) and case review (13.2%; 95% CI: 11.1-15.3%). When sub-grouped by socio-economic status, studies originating from high income regions [13-20,22,23] had a higher mean prevalence rate (median=46.8%; IQR: 26.4-57.7%; $\chi^2$ 858.4, d.f.9; $F$=99%, p<0.001) than studies conducted in upper middle-income [21,25] (8.4%; 95% CI: 6.3-10.5%; $\chi^2$ 0.61, d.f.1; $F$=0%, p=0.435) and lower middle-income countries [24] (9.6%; 95% CI: 5.7-13.5%) (Table 2).

**Medications involving non-adherence at patients’ home**

Only 3/13 studies [13,15,16] reported medication classes most associated with medication non-adherence were those treating cardiovascular, alimentary tract and metabolic and respiratory diseases (Table 3).

**Discussion**

This systematic review reveals that around two-fifth of patients dwelling at home did not adhere to their medication regimens. This was 5-fold higher than non-adherence rates on hospital admissions [27]. In addition, the prevalence rate of medication non-adherence identified in elderly was far greater than in adults (Table 2). Although some studies [28-30] found that younger participants were less adherent with their medication regimens than older people, but our meta-analysis demonstrated more medication non-adherence in the elderly.

**Figure 2:** Pooled prevalence of medication non-adherence in all age population.

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Prevalence estimate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mastroianni PC, et al. (2011)</td>
<td>7.5 (4.4, 10.6)</td>
</tr>
<tr>
<td>I-squared = 0.0%, p = 0.435</td>
<td>8.4 (6.3, 10.5)</td>
</tr>
</tbody>
</table>

**Table 2:** Subgroup analysis according to population, methods of measurement and socioeconomic status.

<table>
<thead>
<tr>
<th>Method to measure adherence problems</th>
<th>Prevalence estimate, % (95% CI)</th>
<th>Heterogeneity test</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elderly</td>
<td>Median 43.2 (IQR: 13.2-57.7)</td>
<td>905.4</td>
</tr>
<tr>
<td>All age group</td>
<td>8.4 (6.3-10.5)</td>
<td>0.61</td>
</tr>
<tr>
<td><strong>Method to measure adherence problems</strong></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Interview</td>
<td>Median 26.4 (IQR: 9.2-50.3)</td>
<td>688</td>
</tr>
<tr>
<td>Self-reported</td>
<td>57.7 (48.5-66.8)</td>
<td>123.8</td>
</tr>
<tr>
<td>Combined method of interview &amp; pill count</td>
<td>13.2 (11.1-15.3)</td>
<td>NA</td>
</tr>
<tr>
<td>Case note review</td>
<td>70 (61-79)</td>
<td>NA</td>
</tr>
<tr>
<td>Pill count</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td><strong>Socioeconomic status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High income countries</td>
<td>Median 46.8 (IQR: 26.4-57.7)</td>
<td>858.4</td>
</tr>
<tr>
<td>Upper middle income countries</td>
<td>8.4 (6.3-10.5)</td>
<td>0.61</td>
</tr>
<tr>
<td>Lower middle income countries</td>
<td>9.6 (5.7-13.5)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: CI: Confident Interval; IQR: Interquartile Range
Several reasons for medication non-adherence among elderly have been proposed. (i) Older people may have poor vision, hearing, and memory, (ii) difficulty in following instructions, opening drug containers, and handling small tablets [31], (iii) have inadequate education about the medication, recognizing adverse drug reactions, and competing prescription medications could be a barrier of adherence in older people [32]. Our study also identified that almost 40% of elderly patients in this study lived independently [13,14,16,17,19]. It is noteworthy that elderly who live alone without caretakers were at risk of medication non-adherence [16,33,34]. Thus, in order to increase the adherence rates among elderly, simplified treatment regimens, use reminder devices, and large easily read labels are needed.

Patients dwelling in the community or in their own home are particularly vulnerable for medication non-adherence because they consumed medications without supervision and are often overlooked by health care systems. In our study, the high prevalence of medication non-adherence in such patients provides much scope for improvement. To realize this, it requires continuous processes of identification of barriers to adherence, implementing effective strategies according to individual needs, and close monitoring of adherence. Furthermore, educating patients about their medications, disease, and how to self-monitor adverse events, thereby establishing more trusting relationships between patients and health-care providers as recommended [35,36]. Home-care, support by family members, and follow-up visits could further promote adherence [37,38]. While each factor above may incrementally foster adherence, multiple interventions appear to be more sustainable [39,40].

Our finding also revealed that pill-counts yielded the highest non-adherence rates and is objective, cheap and simple. However, if ideally, the number of pills prescribed and number consumed can be accurately accounted for, those lost to attrition or extra pills taken cannot be assessed thereby risking false adherence rates. Subjective methods (e.g. interview, self-report or case notes) seem to be popular in clinical practice due to their low cost, simplicity and immediate feedback, but risks under-reporting to please the clinical supervisor [41]. Thus, there is no ‘gold standard’ to quantify adherence. Multi-measure approach with clear defined treatment outcome is recommended provides estimations closest to reality [41,42] together with measuring ultimate treatment outcomes (e.g. hospital stay, morbidity and mortality rates).

Prevalence of medication non-adherence was greater in high-income countries compared to those studies conducted in upper and middle income countries. This finding may be contrary to some previous studies [43,44] which have suggested that people who had no insurance or low income were more likely to be non-adherent to medication. But even for people with health insurance, their health expenditures could still be a problem as more than 10% of elderly in the USA, for example, used less of their required medication because of cost [45]. Although majority of the included studies was conducted in high-income countries, the estimated prevalence rate might not reflect the situation of non-adherence to medications in all high income countries due to differences of healthcare system. In addition, we also need more studies in other hemisphere to draw a global conclusion. Apart from this, several factors may influence the prevalence rate of adherence including age of population, methods for measuring non-adherence, complexity of medication regimen, medical condition, living condition, gender, level of education and ability for self-care [31].

Drugs attracting non-adherence could be ranked as those treating cardiovascular, alimentary tract and metabolic, and respiratory disease which accords with a previous meta-analysis showing that ~50% of patients taking cardiovascular medications were non-adherent [46] and was associated with increased mortality [47]. Likewise, non-adherence to
medications for gastrointestinal tract, diabetes mellitus, and 
respiratory conditions had an increased risk of hospitalization 
and health-care expenditure [5,48,49]. Recent studies 
suggested that self-management, daily dose regimen and 
affordable therapies with minimal side-effects combined 
with effective patient-clinician communication improves 
medication adherence [50,51].

To our knowledge, this is the first systematic review and 
meta-analysis examining the extent and natures of medication 
non-adherence identified at home and have much strength. We 
applied a thorough search strategies including (i) wide range 
of well-recognized international bibliographic databases, (ii) 
hand searching for unpublished articles; and (iii) no languages 
restrictions. This was to ascertain that the included studies 
were representative. In addition, our study adheres to standard 
methodology of systematic review and meta-analysis as 
indicated by the PRISMA statement [52].

This study has some limitations that might affect the overall 
estimated prevalence rates. (i) Some missing data in the original 
included studies (e.g. number of non-adherent patients, their 
ages), despite our attempts to contact the studies’ authors, 
(ii) there was high heterogeneity between studies and where 
encountered, the results were summarized using the median rate 
and interquartile range, instead of a meta-analytic summary. We 
also need more studies in other hemisphere to draw a conclusion.

The findings from this meta-analysis have important 
implications. Based on considerable prevalence rate of 
medication non-adherence for home domiciled patients, 
healthcare professionals in primary care system should be aware 
of non-adherence problem occurring at patients’ home and 
closely monitored. Our estimated prevalence rate of medication 
non-adherence could serve as a point of reference for countries 
in which prevalence rates of non-adherence in home settings are 
poorly characterized.

Based on our review, studies examining the prevalence rate of 
medication non-adherence in children and/or pediatrics and 
factors that determine adherence to medications in general are 
lacking. Future study need to investigate these. In addition to 
the prevalence rate of medication non-adherence, further studies 
may include ultimate therapeutic outcomes stemmed from 
medication non-adherence (e.g. adverse outcomes, morbidity 
and mortality) to gain clear understanding the impact of 
medication non-adherence.

**Conclusion**

Non-adherence is clearly a major problem in home domiciled 
patients particularly in the elderly probably through the 
combination of polypharmacy, chronic disease, and cognitive 
decline. Identification of factors associated with medication 
non-adherence among patients dwelling at home is further 
needed.

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