Prevalence and factors associated with adherence to anti-hypertensives among adults with hypertension in a developed Asian community: A cross-sectional study

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Abstract
Introduction: Poor adherence to anti-hypertensive medications (AHM) results in hypertension treatment failure. Understanding and addressing the factors associated with adherence to AHM may potentially improve health outcomes. This study aimed to assess the prevalence and factors associated with patients’ adherence to AHM in a developed Asian community.

Methods: An assistant-administered questionnaire survey was conducted on multi-ethnic Asian adults aged 31–80 years with essential hypertension based on their electronic health records (EHR) at a public primary-care clinic. Data on their demographic characteristics, clinical measurements of blood pressure and body mass index, co-morbidities and prescriptions from the EHR, along with the Medication Adherence Report Scale-5 scores were collated, audited and analysed. A MARS-5 score of <25 indicated poor adherence. Logistic regression was used to identify factors associated with adherence to AHM.

Results: Data of 395 patients were analysed. Of these, 179 (45.3%) had poor adherence to at least one AHM. Bivariate analysis showed that poor adherence was significantly associated with lower mean age (59 years old vs. 63 years old), higher mean clinic diastolic blood pressure (76 mmHg vs. 73 mmHg) and higher mean weight (70.4 kg vs. 67.4 kg). Logistic regression showed that patients with no co-morbidities (such as diabetes mellitus, dyslipidaemia, stroke and ischaemic heart disease) had better medication adherence (MA; odds ratio=1.98; 95% confidence interval 1.14–3.45; p=0.02). There was no significant MA difference between the classes, dose frequency and number of AHM.

Conclusion: Almost half of the patients had poor adherence to at least one AHM. Co-morbidity significantly influenced their MA. Attention should be directed to patients with co-morbidities to assess their AHM adherence.

Keywords
Hypertension, medication adherence, primary care

Introduction
According to the World Health Organization (WHO) Global Burden of Disease Study, increased blood pressure (BP) due to essential hypertension is the leading risk factor for death and disability.1 It is the cause of 50% of heart disease, stroke and heart failure and 18% of overall deaths, and of at least 40% of deaths in people with diabetes. Nearly all (90%) of adults will develop hypertension by the time they reach 80 years old.1 Due to an aging population in developed communities such as Singapore,2 the associated increase in the prevalence of hypertension will threaten patients’ vascular health unless such risks are mitigated with evidence-based treatment, including the use of anti-hypertensive medications (AHM). With disease progression and more patients living with
hypertension over longer life-spans, the use of multiple AHM to optimise their BP control becomes inevitable.

Nevertheless, poor adherence to even a single AHM is one of the major causes of unsatisfactory blood-pressure control in more than two thirds of patients with hypertension. Adherence to hypertension pharmacotherapy is estimated to vary between 50% and 70%. A Malaysian study reported that 47% of patients had poor adherence to AHM. Adherence to multiple AHM is expected to pose even larger challenges in clinical practice.

Poor AHM adherence increases the risk of cardiovascular complications such as stroke and ischaemic heart disease and contributes to socio-economic burden. In their study of five large European economies, Mennini et al. found that by increasing the adherence to the current level of about 40% to an arbitrary 70%, €332 million would be saved from the number of preventable cardiovascular events.

Adherence to a medication regimen is generally defined as the extent to which patients take medications as prescribed by their health-care providers. Adherence behaviour is complex and influenced by multiple factors, including societal values and local cultural beliefs. The WHO Multidimensional Adherence Model characterised barriers into various domains, including patient, disease entity, therapeutics, equity, health system and service delivery hurdles. A systematic review by Alghurairi et al. found that among the 51 unique surveys, patient factors are the most prevalent among all barriers to AHM adherence.

Medication adherence (MA) varies depending on the types of AHM and drug regimens. A meta-analysis by Kronish et al. reported that mean adherence can range from 28% for beta blockers to 65% for angiotensin II receptor blockers. Hassan et al. reported that a complex medication regimen was associated with poor MA. Calderón-Larrañaga et al. showed that co-morbidities improved MA, whereas another study by Saadat et al. reported that when the number of co-morbid conditions increased, the proportion of patients with high adherence decreased. Hence, we postulated that demographic and medication-related factors and the presence of other co-morbidities similarly influenced AHM adherence in Asian patients.

In Singapore, hypertension has been in the top two medical conditions in multi-ethnic Asian patients who are being managed in public primary-care clinics (polyclinics) in the past five years. Recognising and understanding MA to AHM provide insights into the disease-management burden of essential hypertension. Measuring the magnitude of MA to AHM and identifying the respective modifiable factors will facilitate the development and prioritisation of interventions to address the barriers and improve health outcomes. Thus, this study aimed to determine the prevalence and factors associated with patients’ adherence to their AHM in an ambulatory primary-care setting.

**Methods**

**Study site**

This cross-sectional study was conducted in a typical public primary-care clinic (polyclinic) located in Sengkang, an estate in the north-eastern region of Singapore. The polyclinic provides comprehensive and subsidised primary-health-care services to a dense population of about 350,000 multi-ethnic Asian residents living within an area of 20 km². Its multidisciplinary teams of primary health-care professionals serve an active registry of about 19,000 patients with a diagnosis of essential hypertension.

**Study population**

**Inclusion criteria.** The target participants were patients with a diagnosis of essential hypertension and who had at least one AHM prescription in the past 12 months in their electronic health records (EHR) and prescription records. They included multi-ethnic Asian adults of both sexes and were aged 31–80 years old – the age range with a higher prevalence of hypertension.

**Exclusion criteria.** Participants were excluded if they had debilitating conditions which rendered them incapable of providing informed consent for the study, or if they were treated for hypertension by health-care providers other than those at Sengkang Polyclinic.

**Sample size**

Based on the poor adherence rate of 47% in the Malaysian study, the sample size needed to ensure that the 95% confidence interval estimate of the proportion to be within 5% of the true proportion was 383 participants. By allowing a 5% buffer for participants who may withdraw from the study or had incomplete data, the investigators planned to recruit 404 participants.

**Demographic and clinical information**

Demographic and clinical information such as age, sex, ethnic group, marital status, number of children, education level, housing type, occupational status, monthly income, further medical subsidy, smoking, physical activity, home blood-pressure measurement, awareness of the BP goal, clinic BP, duration of hypertension, regimens (types, classes and dose frequencies) of both the AHM and regular chronic medications, and co-morbidities were collected. To collect the data, trained research assistants helped the participants to complete a questionnaire, and further data were retrieved from the participants’ EHR by a single person only (the lead author).

**Instrument to assess AHM adherence**

Methods to measure MA can be direct, such as direct observed therapy and measurement of serum drug levels, and indirect, such as patient self-reporting via questionnaires, pill counts, prescription refill rates and electronic medication monitors. Direct methods are inherently difficult or expensive to execute, while most indirect methods are cheaper but susceptible to error and patient manipulation. Nonetheless, high reliability and validity have been reported in some of the self-report tools, which have been used in many adherence-related studies.
The Medication Adherence Report Scale-5 (MARS-5) was selected to measure AHM adherence in this study.\textsuperscript{19} It attained Cronbach alpha scores of 0.78 and 0.73 in two separate studies, indicating good internal reliability.\textsuperscript{20,21} The MARS-5 provides a quantitative measure of self-reported adherence and has been used for many other conditions such as hypertension, diabetes mellitus, chronic obstructive pulmonary disease, coronary artery disease and mental disorders.\textsuperscript{20,22–25} Other indirect methods such as pill counts and prescription refill rates were deemed less reflective of adherence, as patients may still refill the prescription or present with empty pill bottles when they had not completed the tablets given to them previously.

The MARS-5 contains five items regarding a participant’s non-adherent behaviour: forgets to take them, takes less than instructed, stops taking them, misses a dose or alters a dose. Participants rate their agreement on a five-point scale (ranging from ‘never’ to ‘always’). Scores of each of the five items are summed to give a total adherence score between 5 and 25. Good adherence is defined as a score of $\geqslant 25$, while a score of $\leqslant 24$ is considered poor adherence.\textsuperscript{26}

In this study, a participant could be treated with one or more AHM. The MARS-5 was used to assess MA to each AHM. If a participant was on more than one AHM, a score of $\leqslant 24$ to any AHM was classified as poor adherence.

\textbf{Charlson Comorbidity Index}

Co-morbidity has been shown to influence MA to AHM.\textsuperscript{14} The Charlson Comorbidity Index (CCI), first developed in 1986 for evaluating prognosis based on weightings for specific co-morbid conditions, was chosen for this study, as it has been validated in primary-care populations.\textsuperscript{27,28} After the co-morbidities of each participant were obtained from the EHR, the CCI was calculated by assigning weights of 1, 2, 3 and 6 for each of the existing co-morbid diseases to derive a total score. For example, a participant with uncomplicated diabetes (1 point) and localised solid tumour (2 points) would have a score of 3 according to the list of co-morbid diseases provided by Charlson et al.\textsuperscript{27} This standardised the reporting of co-morbidity for this study population.

\textbf{Definition of medication regimen complexity}

Medication regimen complexity can be defined by the number of medications and the number of times per day or ‘doses’ that the patient takes of a medication.\textsuperscript{29} For example, a patient with three AHM has a more complex regimen than with just two AHM, and taking one AHM t.i.d. is more complex than taking one AHM q.d.

\textbf{Recruitment and data-collection procedure}

Over three months in 2017, potential participants attending the study site were screened by trained research assistants and polyclinic nurses for eligibility for study enrolment. An information sheet describing the details of the study and contact methods for further clarification was given to each participant. Upon obtaining written consent after their doubts and queries were addressed, the research assistant interviewed the participants face to face using the approved questionnaire. The latter collected demographic and clinical information. The participant identified their respective medications from a catalogue showing photos of AHM which were available in the in-house polyclinic pharmacy. Next, they proceeded to evaluate their adherence to each of their respective AHM using the MARS-5.

BP height and weight were measured after the interview. The BP for each participant was measured after five minutes of rest with a validated and automated upper-arm digital sphygmomanometer (Model: GE Dinamap V100). Two measurements were taken three minutes apart. The set of lower BP readings was used for computation as an outcome in this study. Weight and height were measured with a digital standing scale with an attached ultrasonic sensor height-measuring module (Model: Avamech B1000-LAN).

\textbf{Statistical analysis}

SPSS Statistics for Windows v22.0 (IBM Corp., Armonk, NY) was used for all data analysis. Descriptive statistics were computed and expressed as the mean±standard deviation for continuous variables with normal distribution and as the median (interquartile range: Q1–Q3) for the non-parametric variables. Factors potentially associated with poor MA were analysed with bivariate analysis in which the chi-square test or Fisher’s exact test was used for categorical variables, and the Mann–Whitney U-test or independent t-test was used for continuous variables. Factors shown to be potentially significant in the bivariate analysis ($p<0.2$) were included in the multiple logistic regression analysis, with the relationships reflected by odds ratios (OR) and 95% confidence intervals (95% CIs). A $p$-value of $<0.05$ was considered statistically significant.

\textbf{Ethics approval}

The SingHealth Centralised Institutional Review Board approved this study (approval number: 2017/2221).

\textbf{Results}

\textbf{Demographic characteristics of study population}

Of the 404 participants recruited, nine were excluded because of incomplete data in the questionnaires. Hence, the data of 395 participants were analysed. Participants had a mean age of $61\pm7$ years, and $52.2\%$ were women. The majority were Singaporean citizens and permanent residents ($99.2\%$), of Chinese ethnicity ($79.5\%$), had at least secondary school education ($78.3\%$) and earned $<\text{SGD}\$4000 a month ($85.1\%$; Table 1).

The most prevalent co-morbidity was dyslipidaemia ($73.7\%$). A total of $38\%$ of participants had diabetes mellitus, $9.6\%$ had myocardial infarct and $4.7\%$ had stroke. The morbidity burden was low for this study population, with a CCI of 0 (IQR 0–2).

Participants had a median of 10 years (IQR 5–15 years) of hypertension. Almost two thirds of them measured their BP at home, but only $6.8\%$ of them were aware of the BP goal.
Table 1. Characteristics of the study population.

|                                | Frequency (%) | Poor adherence | Good adherence | p-Value |
|--------------------------------|---------------|----------------|----------------|---------|
| Total                          | 395 (100.0)   | 179 (45.3)     | 216 (54.7)     |         |
| Age                            |               |                |                | 0.01    |
| Sex                            |               |                |                | 0.28    |
| Male                           | 189 (47.8)    | 91 (48.1)      | 98 (51.9)      |         |
| Female                         | 206 (52.2)    | 88 (42.7)      | 118 (57.3)     |         |
| Ethnic group                   |               |                |                | 0.64    |
| Chinese                        | 314 (79.5)    | 141 (44.9)     | 173 (55.1)     |         |
| Malays                         | 26 (6.6)      | 10 (38.5)      | 16 (61.5)      |         |
| Indian                         | 47 (11.9)     | 23 (48.9)      | 24 (51.1)      |         |
| Eurasian                       | 8 (2)         | 5 (62.5)       | 3 (37.5)       |         |
| Marital status                 |               |                |                | 0.36    |
| Single                         | 21 (5.3)      | 12 (57.1)      | 9 (42.9)       |         |
| Married                        | 354 (89.6)    | 160 (45.2)     | 194 (54.8)     |         |
| Divorced/separated/widowed     | 20 (5.1)      | 7 (35)         | 13 (65)        |         |
| Number of children             |               |                |                | 0.07    |
| 0                              | 44 (11.1)     | 26 (59.1)      | 18 (40.9)      |         |
| 1 or 2                         | 210 (53.2)    | 86 (41)        | 124 (59)       |         |
| 3 or more                      | 141 (35.7)    | 67 (47.5)      | 74 (52.5)      |         |
| Education                      |               |                |                | 0.16    |
| No formal education/primary    | 125 (31.6)    | 49 (39.2)      | 76 (60.8)      |         |
| Secondary                      | 170 (43)      | 78 (45.9)      | 92 (54.1)      |         |
| Tertiary                       | 100 (25.3)    | 52 (52)        | 48 (48)        |         |
| Housing type                   |               |                |                | 0.70    |
| 1- to 2-room public housing    | 19 (4.8)      | 7 (36.8)       | 12 (63.2)      |         |
| 3- to 5-room public housing    | 350 (88.6)    | 161 (46)       | 189 (54)       |         |
| Condo/private apartment/landed | 26 (6.6)      | 11 (42.3)      | 15 (57.7)      |         |
| property/studio apartment       |               |                |                |         |
| Occupational status            |               |                |                | 0.43    |
| Working                        | 231 (58.5)    | 111 (48.1)     | 120 (51.9)     |         |
| Unemployed/looking for a job   | 67 (17)       | 28 (41.8)      | 39 (58.2)      |         |
| Retired                        | 97 (24.6)     | 40 (41.2)      | 57 (58.8)      |         |
| Monthly income (SGD)           |               |                |                | 0.12    |
| <2000                          | 267 (67.6)    | 114 (42.7)     | 153 (57.3)     |         |
| 2000–3999                      | 69 (17.5)     | 39 (56.5)      | 30 (43.5)      |         |
| ≥4000                          | 59 (14.9)     | 26 (44.1)      | 33 (55.9)      |         |
| Medical subsidy                |               |                |                | 0.97    |
| Yes                            | 210 (53.2)    | 95 (45.2)      | 115 (54.8)     |         |
| No                             | 185 (46.8)    | 84 (45.4)      | 101 (54.6)     |         |
| Duration of hypertension, median (IQR) | 10 (5–15) | 10 (5–15) | 10 (4.3–15) | 0.80    |
| Aware of BP goal               |               |                |                | 0.08    |
| Aware of BP goal               | 27 (6.8)      | 14 (51.9)      | 13 (48.1)      |         |
| Aware but reported wrong BP goal | 198 (50.1) | 99 (50) | 99 (50) |         |
| Not aware                      | 170 (43)      | 66 (38.8)      | 104 (61.2)     |         |
| Measure BP at home             |               |                |                | 0.89    |
| Yes                            | 242 (61.3)    | 109 (45)       | 133 (55)       |         |
| No                             | 153 (38.7)    | 70 (45.8)      | 83 (54.2)      |         |
| Smoking                        |               |                |                | 0.25    |
| Smoker                         | 43 (10.9)     | 23 (53.5)      | 20 (46.5)      |         |
| Non-smoker                     | 352 (89.1)    | 156 (44.3)     | 196 (55.7)     |         |
| Often takes part in regular physical activity (e.g. 30 minutes of walking four to five times per week) |     | | | 0.11    |
| Always/frequently              | 106 (26.8)    | 41 (38.7)      | 65 (61.3)      |         |
| Sometimes/rarely/never         | 289 (73.2)    | 138 (47.8)     | 151 (52.2)     |         |
| Clinic systolic BP, mean (SD)  | 138 (126.5–152) | 138 (127.5–152) | 137.75 (126.1–151.4) | 0.81    |
| Clinic diastolic BP, mean (SD) | 74 (67–81.5)  | 76 (66.5–84)   | 73 (67–80.3)   | 0.03    |
| Weight (kg), mean (SD)         | 68.4 (60.3–79.2) | 70.4 (61.5–81.3) | 67.4 (58.8–77.2) | 0.04    |
| Height (m), mean (SD)          | 1.61 (1.5–1.68) | 1.62 (1.5–1.69) | 1.61 (1.5–1.67) | 0.45    |
| BMI, mean (SD)                 | 26.4 (23.8–29.3) | 26.8 (23.8–29.6) | 26.2 (23.6–29.2) | 0.14    |
They had been prescribed a median of two (IQR 1–2) AHM, corresponding to a median of two (IQR 1–2) doses of AHM per day. They had a median of 4 (IQR 2–5) types of chronic medications (inclusive of AHM) daily.

### MA and associated factors

A total of 45.3% of the participants were found to have poor adherence. Using bivariate analysis, poor adherence was associated with younger participants (59 years old vs. 63 years old; \( p = 0.01 \)), higher clinic diastolic BP (76 mmHg vs. 73 mmHg; \( p = 0.03 \)) and higher mean weight (70.4 kg vs. 67.4 kg; \( p = 0.04 \); Table 1).

On multivariate logistic regression, participants without any co-morbidity such as diabetes mellitus, stroke, myocardial infarction or dyslipidaemia were more likely to have better adherence to AHM (OR=1.98; 95% CI 1.14–3.45; \( p = 0.02 \); Table 2). No multicollinearity existed among the variables in this analysis.

Variables related to medication regimen complexity — such as the number of regular chronic medications, the number of AHM, the number of doses of regular chronic medications and the number of doses of AHM — were not associated with a significant difference in MA. MA was also not associated with socio-economic status — such as monthly income, housing type, occupational status and medical subsidy. Morbidity burden as measured by the CCI was not associated with poor adherence.

Analysing the MARS-5 questions that were answered for all 656 individual AHM taken by the participants, the question that scored <5 (indicating poor adherence) most frequently (35.4%) was ‘I forget to take my anti-hypertensive medication’ (Table 2). The other four questions scored <5 for <15% of the responses.

On multivariate logistic regression analysis, participants without any co-morbidity such as diabetes mellitus, stroke, myocardial infarction or dyslipidaemia were more likely to have better adherence to AHM (OR=1.98; 95% CI 1.14–3.45; \( p = 0.02 \); Table 3). No multicollinearity existed among the variables in this analysis.

### Table 1. Frequency of MARS-5 question scoring <5.

| Question                                                                 | n (%) | Frequency (%) | Poor adherence | Good adherence | p-Value |
|--------------------------------------------------------------------------|-------|---------------|----------------|---------------|---------|
| I forgot to take my anti-hypertensive medication                         | 232 (35.4) | 309 (78.2) | 146 (47.2) | 163 (52.8) | 0.14    |
| I changed the dosage of my anti-hypertensive medication                 | 36 (5.5) | 86 (21.8) | 33 (38.4) | 53 (61.6) | 0.92    |
| I stopped taking my anti-hypertensive medication for a while           | 67 (10.2) | 0 (0–2) | 0 (0–2) | 0 (0–2) |         |
| I decided to skip one of my anti-hypertensive medication dosages        | 97 (14.8) | 4 (2–5) | 4 (2–5) | 4 (2–5) | 0.79    |
| I use my anti-hypertensive medication less than is prescribed          | 31 (4.7) | 2 (1–2) | 2 (1–2) | 2 (1–2) | 0.22    |

*Good adherence is defined as a MARS-5 score of >=25, and poor adherence is defined as a MARS-5 score of <25.

AHM: anti-hypertensive medication; BP: blood pressure; IQR: interquartile range; SD: standard deviation.

### Table 2. Factors associated with good medication adherence using multivariate logistic regression.

| OR (95% CI) | p-Value |
|-------------|---------|
| Age         | 1.02 (0.99–1.05) | 0.13 |
| Number of children | 1 | – |
| Education | 1.26 (0.61–2.60) | 0.54 |
| Monthly income (SGD) | 1.18 (0.64–2.16) | 0.59 |
| Often takes part in physical activity | 1.38 (0.85–2.25) | 0.19 |
| Aware of BP goal | 1.13 (0.49–2.62) | 0.77 |
| Not aware | 1.72 (0.73–4.07) | 0.22 |
| Clinic diastolic BP | 0.98 (0.96–1.003) | 0.09 |
| BMI | 0.99 (0.94–1.03) | 0.59 |
| Any cardiovascular co-morbidities | 1.31 (0.79–2.17) | 0.30 |
| Number of doses of AHM | 1.03 (0.74–1.44) | 0.86 |

Model chi-square value=3.456, \( p = 0.063 \), Nagelkerke \( R^2 = 0.099 \). BMI: body mass index.

### Table 3. (Continued)
MA to specific anti-hypertensive agents

There was no significant difference in MA between the drug classes ($p=0.78$; Figure 1). The drug class with the highest proportion of good adherence was diuretics (65.1%), followed by angiotensin-converting enzyme inhibitors (ACEI; 62.4%), beta blockers (58.6%), calcium channel blockers (CCB; 57.6%) and angiotensin II receptor blocker (ARB; 56.4%). Two participants were on hydralazine, one was on methyldopa and no patients were on alpha blockers. The most frequently used AHM class was CCB ($n=238$), followed by ARB ($n=133$), beta blockers ($n=128$), ACEI ($n=101$) and diuretics ($n=43$).

Discussion

At 45.3%, the prevalence of poor MA to AHM is significant in this study. This indicates that almost one in two patients are not fully adherent to their AHM. This may directly or indirectly contribute to the top causes of death in Singapore, which are related to stroke and ischaemic heart disease.30 Likewise, the prevalence of poor MA is also known to range between 41% and 56.5% in similar studies undertaken in Asia.5,31–33 It is indeed a prevalent but preventable barrier towards optimal vascular health in Asians.

Co-morbidities have a variable effect on AHM adherence. In our study, the participants without other cardiovascular co-morbidities such as stroke, myocardial infarct, diabetes or dyslipidaemia were twice more likely to have good adherence than those with these co-morbidities. This result contradicts the findings by Calderón-Larrañaga et al., who reported that participants with vascular co-morbidity (i.e. diabetes, dyslipidaemia and obesity) were less likely to have poor adherence.14 Pittman et al. and Lee et al. found that higher co-morbidity scores were associated with better adherence.9,35 In contrast, studies by Holmes et al., Raebel et al., Yoon et al. and Ghembaza et al. also showed that having more co-morbidities was associated with worse adherence.36–39 Doctors in public primary-care clinics may spend less time educating patients on the importance of good hypertension control when they need to focus on other vascular co-morbidities as well. With more co-morbidities, the burden of having more medications to adhere to may affect patients psychologically, leading to less adherence. Adherence to multiple medications may also be affected by poorer health literacy, which was not explored in our study. This finding is a grave concern, since patients with more vascular co-morbidities have a greater cardiovascular risk.

The subset of the study population with poor MA tended to be younger (Table 1). We postulated that they might not have recognised the potential complications of hypertension and failed to appreciate the importance and relevance of MA to their AHM. After all, essential hypertension is largely asymptomatic. There is a need to review the modalities and delivery of patient education in treatment adherence by the multidisciplinary primary health-care team at the polyclinics. The use of patient decision support aids has been shown to be a more holistic tool to garner patients’ commitment to their treatment, including their AHM.40 It provides patients with evidence-based information on the effectiveness and potential adverse effects of the various AHM and serves to gather their feedback on any concerns about their medications. Such a tool will be evaluated for their effectiveness in enhancing MA in future research.

Our study did not find medication regimen complexity to be associated with MA. Medication regimen complexity often impacts on MA negatively. A systematic review by Pantuzza et al. found that in most studies, increased regimen complexity reduced pharmacotherapy adherence.11 Studies specific to adherence to AHM that were done by Bader et al., Ramli et al. and Ghembaza et al. showed that greater treatment
complexity led to poorer adherence. On the other hand, Tajeu et al. found that polypharmacy was associated with a decreased risk of poor adherence. Most AHM that are being used nowadays are only administered once a day, simplifying the regimen. The pill burden did not seem to influence MA. Patients with good MA had a median of two AHM compared to one among those with poor MA – although the result was not statistically significant (Table 1).

Several meta-analyses have been performed to determine the effect of AHM drug classes on adherence. Lemstra et al. reported that ARB had better adherence than ACEI, CCB or diuretics. Diuretics had worse adherence than ACEI or CCB. Kronish et al. showed similar results, with ARB having the best adherence rate followed by ACEI, CCB, diuretics and beta blockers. Our findings, although not significantly different statistically, seemed to be the reverse, with diuretics having the best adherence and ARB the worst. This may be a little surprising and also concerning, since ARB is known for its renoprotective and cardioprotective properties and has a more favourable adverse-effect profile compared to diuretics. In the subset of our study population treated with diuretics, 88.4% of them were prescribed hydrochlorothiazide as the second- or third-line therapy in low doses of 12.5–25 mg q.d. Potential adverse effects are fewer and less severe, since they are dose dependent. In contrast, ARB and ACEI are mostly used as first-line medications at the study site, often escalating to the maximal tolerable doses to achieve BP control when adverse effects are more likely to occur.

Forgetting to take medications is a form of unintentional medication non-adherence and features prominently in many studies done on MA. Studies by Bhandari et al., Mohammad et al. and Hsu et al. revealed that forgetting to take AHM was the most commonly reported cause of non-adherence, ranging from 21.4% to 55.1%. In our study, forgetting to take medication was the most frequently reported reason using the MARS-5. Cognitive impairment can possibly lead to forgetting, but our study did not measure this outcome. The younger patients could be distracted by their work commitments, resulting in ‘forgetting’ to take their AHM. With high penetrance of mobile technology in Singapore, the use of smartphone applications to remind patients to take their AHM has vast potential to improve MA. A prototype of such an app is currently being evaluated in a separate study. The institution is also currently undertaking service transformation, with plans to collect patient-reported outcomes and other data systematically at the pre-consultation stage of the patient’s visit to the polyclinic. The MA assessment can be integrated seamlessly into the phase, which can be executed remotely or via tablets. It can also be individualised to the patients’ specific medications, which will be retrieved from the e-prescription system. Such data, once channelled to the EMR, should alert the attending physicians to discuss and address the MA with their patients.

**Strengths and limitations**

The study has identified a significant barrier towards optimal control of essential hypertension. MA is potentially modifiable and amenable to enhancement, leveraging on mobile health technology, infrastructure and system change to identify, measure the magnitude and present opportunities for interventions to address this barrier.

However, the results of the study should be interpreted in the light of its limitations. We were unable to determine if cognitive impairment influences adherence. The cross-sectional and observational nature of the study did not allow for causal inferences to be made, and we do not have observations of adherence over time. The questionnaire for data collection, including the MARS-5, contained variables that were self-reported, and this may led to recall bias. Furthermore, adherence studies based on informed consent may have targeted a self-selected group of participants who might give socially desirable responses. Both recall and selection biases may lead to an over-estimation of adherence. Yet, this method had revealed a significant dimension of this barrier, despite such limitations.

**Conclusion**

Prevalence of poor adherence to AHM is almost 50% in an Asian population with hypertension. Concurrent vascular diseases is twice more likely to be associated with poor adherence. The co-morbidity burden, medication regimen complexity and AHM drug class did not seem to influence MA. Physicians should pay attention to patients with co-morbidity to assess their adherence to AHM. Interventions leveraging on innovations to automate the assessment of MA and alerting the physicians of patients at risk of poor adherence are being developed for future research.

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**Authors’ contributions**

C.Y.G.K. and N.C.T. were involved in the conception/design of the study. Y.L.E.K. conducted the statistical analysis. C.Y.G.K. and N.C.T. drafted the manuscript. All authors approved the final version of the manuscript.

**Availability of data and materials**

The data sets generated and/or analysed during the current study are available from C.Y.G.K.

**Informed consent**

Written informed consent was obtained from all subjects before the study.

**Ethical approval**

Ethical approval for this study was obtained from the SingHealth Centralised Institutional Review Board (approval number: 2017/2221).
Conflict of interest
The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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