Identifying Unintentional Medication Discrepancies at Admission among Elderly Inpatients in Vietnam

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Abstract

Background Elderly patients are at high risk of unintentional medication discrepancies during transition care as they are more likely to have multiple comorbidities and chronic diseases that require multiple medications. The main objective of the study was to measure the occurrence and identify risk factors for unintentional medication discrepancies in elderly inpatients during hospital admission.

Methods A prospective observational study was conducted from July to December 2018 in a 800-bed geriatric hospital in Hanoi, North Vietnam. Patients over 60 years of age, admitted to one of selected internal medicine wards, taking at least one chronic medication before admission, and staying at least 48 hours were eligible for enrolment. Medication discrepancies of chronic medications before and after admission of each participant were identified by a pharmacist using a step-by-step protocol for the medication reconciliation process. The identified discrepancies were then classified as intentional or unintentional by an assessment group comprised of a pharmacist and a physician. A logistic regression model was used to identify risk factors of medication discrepancies.

Results Among 192 enrolled patients, 328 medication discrepancies were identified; of which 87 (26.5%) were unintentional. 32.3% of patients had at least one unintentional medication discrepancy. The most common unintentional medication discrepancy was omission of drugs (75.9% of 87 medication discrepancies). The logistic regression analysis revealed a positive association between the number of discrepancies at admission and the type of treatment wards.

Conclusions Medication discrepancies are common at admission among Vietnamese elderly inpatients. This study confirms the importance of obtaining a comprehensive medication history at hospital admission and supports implementing a medication reconciliation program to reduce the negative impact of medication discrepancy, especially for the elderly population.

Impact Of Findings On Practice

- This is the first study that assessed the occurrence of unintentional medication discrepancies and the associated risk factors in elderly patients at hospital admission in Vietnam.
- A step-by-step protocol for the medication reconciliation process was developed according to the World Health Organization's High 5s programm to identify medication discrepancy in the study population.
- The study supports the importance of implementing standard operating procedures to attain a complete preadmission medication history for patients as well as implementing a medication reconciliation program in Vietnam

Background

Medication discrepancies are defined as the variations in drug regimens (1) and can occur during the transition between healthcare facilities, including on admission, transfer, and discharge (2). The discrepancies (e.g. medication omission, addition of a new medication, change in medication dose, or change in the route of administration), especially those that are unintentional, can often lead to preventable medication errors and potentially be harmful to patients (3, 4). In practice, medication errors due to unintended discrepancies have been reported to occur in up to 50–70% of patients during transitions in care (5).

The majority of these medication discrepancies can be intercepted through medication reconciliation at all transitions in care (2). Many organizations have demonstrated that implementing medication reconciliation at all interface of care is an effective and necessary strategy for identifying medication discrepancies and thus ensuring patient safety (2) (6, 7). According to the World Health Organization (WHO), "medication reconciliation is the formal process in which health care professionals partner with patients to ensure accurate and complete medication information transfer at interfaces of care" (2). The Institute for Healthcare Improvement (IHI) defines medication reconciliation as the process of creating the most accurate list possible of all medications a patient is taking and comparing that list against the physician's order at all transition of care (6). The medication reconciliation service has proven to be successful in identifying most discrepancies, preventing harm to patients and associating with significant financial saving (4), (8), (9, 10). Currently, medication reconciliation has become a standard healthcare practice recommended by the WHO (11) and many countries (7, 12-14).

Among the population groups, elderly patients have a high risk of medication discrepancies, with a reported prevalence of 49.5% to 81.9% during transitions in care (15-19). Elderly patients are at high risk of medication discrepancies for several reasons. Firstly, they are more likely to have multiple comorbidities and chronic diseases. The prevalence of chronic disease in elderly patients was shown to range from 55% to 98% according to a systematic review (20). With multiple comorbidities, these patients are likely to be prescribed more medications, thereby increasing the risk of inappropriate prescribing (21), drug–drug interactions, drug–disease interactions,

adverse drug events (22), and medication errors (23). Elderly patients can also suffer from psychological (e.g. anxiety, depression, and dementia) and physiological factors (e.g. impaired hearing and vision function) that may impair their ability to communicate effectively with medical and healthcare staff, which may further contribute to medication discrepancies in this population. Elderly patients are, therefore, more vulnerable to medication discrepancies and should be a target population for medication reconciliation.

In Vietnam, obtaining the medication history from patients is the responsibility of doctors, nurses, and clinical pharmacists during ward rounds. However, the concept of medication reconciliation is still very new and has not been mentioned in any government documents or specialized professional practice standard guidelines. As such, there is no standard operating procedure for medication reconciliation in Vietnam. This is further attested by a literature search performed by our research team, showing no studies on this topic had been performed in Vietnam to date. Hence, the extent and clinical impact of unintentional medication discrepancies remain unknown as a potential clinical problem in Vietnam. Without this information, it is difficult to request the healthcare administrators to allocate appropriate resources to rectify this problem.

Methods

Aims of the study

The main objective of the present study was to assess the occurrence of unintentional medication discrepancies and identify the associated risk factors in elderly patients at hospital admission in Vietnam. The results are expected to support the importance of obtaining a comprehensive medication history at hospital admission and implementing a medication reconciliation program to reduce the negative impact of medication discrepancy, especially for the elderly population. This would also provide evidence to persuade the healthcare administrators in Vietnam to allocate additional resources to rectify this problem.

Ethics approval

This study was granted ethics approvals by The Hospital Science and Technology Committee at Friendship Hospital, Vietnam (approved on 28th March, 2018) and the Human Research Ethics Committee (HREC) at the University of Newcastle, Australia (Approval Number H-2018-0130).

Study setting and patient recruitment

This prospective observational study was conducted at Friendship Hospital, a 800-bed public geriatric hospital in Hanoi, which has 23 clinical units in total with 22,700 admissions in 2018. Patients over 60 years of age, admitted to 7 selected internal medicine units of the hospital, taking at least one chronic medication before admission, and staying at least 48 hours were eligible for enrolment. The selected internal medicine units were endocrine and metabolism, orthopedics, cardiovascular, respiratory, gastroenterology, psychiatry and neurology, and general internal medicine (coded from 01 to 07 respectively). Patients were excluded if they were unable to give consent due to their clinical conditions or refused to participate in the study. The patient recruitment process took place over 14 non-consecutive weeks from July 2018 to December 2018, with two weeks of recruitment for each unit. During this period, all patients who met the selection criteria and gave informed consent were included in the study.

Data collection

For each enrolled participant, the following information was collected: age, gender, comorbidity, current admission diagnosis, treatment unit, outpatient management status (i.e. whether the patient was managed as an outpatient by the study hospital), and the available sources for patients' medication information (e.g. electronic medical records, paper-based outpatient medical records, and paper-based inpatient medical records). The patients' medication history and the current treatment during the hospital admission were collected as part of the medication reconciliation process described below.

Process of identifying medication discrepancies

At the time of the study, there was no standard operating procedure (SOP) available for healthcare staff to obtain the medication history from patients and to reconcile the information with the admission medication prescriptions. The physician or nurse would normally collect the information regarding patients' preadmission medications during medical examination and record this in the patients' paper-based medical record without a SOP to perform any reconciliation for discrepancy. To identify any medication discrepancies at admission, the research group conducted a process of medication reconciliation independent of but did not interfere with the normal practice of other healthcare professional staffs in delivering care to the patients.

Using the information from the WHO High 5s programme, a step-by-step protocol for the medication reconciliation process was developed and training was provided for a group of study data collectors. Overall, the process of medication reconciliation for each participant consisted of the following key steps.

- *Step 1: Obtain the Best Possible Medication History (BPMH) list for patients*: The BPMH form suggested by the WHO High 5s programme was employed to obtain preadmission medication information of patients (2). The BPMH was obtained from multiple available sources, including patient interviews, computer−based medical record systems, and paper-based medical records. Patient interviews were conducted at the patients' bedside, using a structured form to guide the interview and record the data (**Supplementary file 1. Interview guide**).
- *Step 2: Identify medication discrepancies in chronic medications*: The list of admission medication prescriptions (i.e., the first 24 hours after admission of patients to the hospital) was collected from paper-based medical records for each patient. The list was then compared to the BPMH obtained by a study researcher as described above. Any differences between the chronic medications on the BPMH and admission medication prescription list was considered a medication discrepancy.

To examine the extent of the medication discrepancy resolution by physicians during the patients' hospital stay, the medication discrepancy was also assessed at 48 hours after admission and at the time of discharge using the same approach described above. After this time, each medication discrepancy was discussed with the physician to determine if it was intentional or unintentional. To ensure the accuracy of the process of medication discrepancy determination, several potential reasons such as diagnosis of a new clinical condition, occurrence of adverse drug events, or a specific medication was unavailable in the Department of Pharmacy at the hospital, were considered. Medication discrepancies that were accepted by the physician as being unreasonable were classified as unintentional medication discrepancies. Each unintentional medication discrepancy was then classified by drug class (according to the Anatomical Therapeutic Chemical Classification System – ATC) (24) and type of unintentional medication discrepancy (including omission of medication, change of medication, extra medication, or difference in dose or dosing frequency).

Data analysis

The collected data were analyzed by using the Statistical Package for Social Sciences (SPSS), version 20.0 (IBM statistics, Armonk, NY, United States). Percent and frequency were used to describe medication discrepancy. Chi squared (χ2) test was conducted to identify potential relationships between medication discrepancy and explanatory variables. In addition, the Backward Stepwise (Wald) method was employed to identify appropriate multivariate logistic regression models and risk factors associated with unintentional medication discrepancies. The regression analysis results were expressed as odds ratio with 95% confidence intervals. The influence of factors was considered to be statistically significant at $p < 0.05$.

Results

Demographics and baseline characteristics of the participants

During the study period, a total of 395 patients was admitted to the study units. Of these, 203 patients were excluded from the study – 14 were admitted for less than 48 hours, 127 were not taking any chronic medications or had no chronic disease, 30 refused to participate in the study, and 32 were unable to give consent. There was a total of 192 patients eligible to be included in the study (Figure 1).

The demographics and baseline characteristics of these 192 patients are shown in Table 1. The average age of the study participants was relatively high (75.6 ± 7.0 years) and 77.1% were males. Polypharmacy (at least 5 medications) before admission was seen in almost half of the patients (44.8%). The most common chronic diseases in the study participants were hypertension (86.5%), hyperlipidemia (61.5%), type 2 diabetes (45.3%), chronic coronary syndrome (37.0%), and osteoarthritis (25.5%). The average number of co-morbidities was 5.1 ± 1.8.

Table 1. *Demographics and baseline characteristics of the study participants*

Characteristics of Participants	Number of participants (%) (N=192)
Gender	
Male	148 (77.1)
Female	44 (22.9)
Age (years)	
Mean	75.6 ± 7.0*
Age group:	
60 - 65	13 (6.8)
66 - 85	165 (85.9)
>85	14 (7.3)
Activities of Daily Living (ADL)	
Independent	88 (45.8)
Dependent (≥1ADL)	104 (54.2)
Charlson Co-morbidity Index	
0	43 (22.4)
1 - 2	115 (59.9)
≥3	34 (17.7)
Number of comorbidities per patient	5.1 ± 1.8*
Top 5 common diseases	166 (86.5)
Hypertension	118 (61.5)
Hyperlipidemia	87 (45.3)
Type 2 diabetes	71 (37.0)
Chronic coronary syndrome	49 (25.5)
Osteoarthritis	

Number of preadmission medications per patient	
Mean	4.5 ± 2.2*
1-2	38 (19.8)
3-4	68 (35.4)
≥5	86 (44.8)
Number of preadmission chronic medications per patient	
Mean	
1-2	3.1 ± 1.5*
3-4	75 (39.1)
≥5	81 (42.2)
	36 (18.8)

Note: * Mean ± Standard Deviation

Medication discrepancies

Among the 192 patients recruited, there were 328 chronic medication discrepancies identified between the BPMH list and the 24-hour medication prescription (intentional and unintentional), with a mean ± SD of 1.7 ± 1.4 discrepancies per patient. All of the identified discrepancies had no documented reason in either the paper-based medical records or electronic medical records of patients. After discussion with the managing physicians, 87 discrepancies were classified as unintentional in 32.3% of patients (n=62). The frequency of medication discrepancies among the study population is presented in Table 2.

Table 2. Medication discrepancies at 24 hours after admission

Characteristics of MD	Number of participants (%)
Number of MD	328
Intentional MD	241 (73.5)
Unintentional MD	87 (26.5)
Number of MD per patient	1.7 ± 1.4*
0	40 (20.8)
1	55 (28.6)
2	48 (25.0)
3	29 (15.1)
≥ 4	20 (10.4)
Patients with no UMD	130 (67.7)
Patients with at least 1 UMD	62 (32.3)
1 UMD	42 (21.9)
2 UMDs	15 (7.8)
3 UMDs	5 (2.6)

Note: * Mean ± Standard Deviation; MD = medication discrepancy; UMD = unintentional medication discrepancy

Among the types of unintentional medication discrepancies, medication omission accounted for the highest proportion (75.9%), followed by medication change (21.8%) (Table 3). Dose change was the least likely reason for the unintentional medication discrepancies identified (2.3%). After the first 48 hours of admission, the number of unintentional medication discrepancies remained high (90.8%) and persisted until the time of discharge (77%) (Table 3).

Table 3. Type of unintentional medication discrepancies (UMD)

UMD	24 hours		48 hours		At Discharge	
	n	%	n	%	n	%
Medication omission	66	75.9	60	69.0	48	55.2
Medication change	19	21.8	17	19.5	17	19.5
Incorrect dose	2	2.3	2	2.3	2	2.3
Total	87	100	79	90.8	67	77.0

Cardiovascular agents were the most common drug classes involved in medication discrepancies among the study participants. This included lipid-modifying drugs (39 cases, 44.8%), antihypertension drugs (18 cases, 20.7%), and antithrombotic drugs (11 cases, 12.7%) (Table 4).

Table 4. *Unintentional medication discrepancies (UMD) according to drug class*

Drug class	ATC code	Number (n)	Percentage (%)
Lipid modifying agents	C10A	39	44.8
Antihypertensive agents	C02	18	20.7
Antithrombotic agents	B01A	11	12.7
Blood glucose lowering drugs	A10B	9	10.3
Beta-blocking agents	C07A	5	5.7
Dopaminergic agents	N04B	2	2.3
Calcium	A12A	1	1.1
Thyroid preparations	H03A	1	1.1
Antinematodal agents	PP02C	1	1.1

Risk factors associated with unintentional medication discrepancies

The occurrence of unintentional medication discrepancies was significantly higher among patients admitted to the orthopedics, respiratory, and gastroenterology units compared to those admitted to the endocrine and metabolism unit (odds ratios of 10.03, 5.44 and 6.98, respectively; p<0.05). In addition, the risk of medication discrepancy significantly increased among patients using a least 5 chronic medications (polypharmacy) before admission compared to patients taking only 1 or 2 chronic medications at preadmission (odds ratio 4.65, p < 0.05) (Table 5).

Table 5. Risk factors associated with unintentional medication discrepancies

Factors	No. of UMD* (%)	Odds ratio (95% CI)	P-value
Treatment Units			
Unit 01 (n=24)	4 (16.7)	1 (control)	-
Unit 02 (n=20)	11 (55.0)	10.03 (2.32 – 43.37)	0.002
Unit 03 (n=43)	13 (30.2)	3.00 (0.81 – 11.05)	0.100
Unit 04 (n=22)	9 (40.9)	5.44 (1.30 – 22.83)	0.021
Unit 05 (n=26)	13 (50.0)	6.98 (1.73 – 28.12)	0.006
Unit 06 (n=20)	7 (35.0)	3.79 (0.87 – 16.44)	0.075
Unit 07 (n=37)	5 (13.5)	1.04 (0.24 – 4.55)	0.956
Number of chronic medicines using before admission			
1-2 (n=75)	18 (24.0)	1 (control)	-
3-4 (n=81)	26 (32.1)	1.78 (0.83 – 3.81)	0.137
≥5 (n=36)	18 (50.0)	4.65 (1.82 – 11.87)	0.001

* 95% CI: 95% confidence intervals

Discussion

To the best of our knowledge, this is the first study to examine the occurrence of medication discrepancies among inpatients in Vietnam. Our study focused on elderly patients, as they are a particularly vulnerable population to medication discrepancies and other drug-related problems (e.g., inappropriate indication, dose, or adverse effects). The results showed an average of 1.7 (SD 1.4) medication discrepancies per patient at the time of admission and 32.3% of the study participants had at least one unintentional medication discrepancy regarding their chronic medications.

To interpret the results meaningfully, we compared our findings with similar studies conducted in other countries (from 2010 onwards). As shown in Table 6, the prevalence of unintentional medication discrepancies varied widely between the published studies from other countries. The studies that showed a much higher rate include those conducted by Belda-Rustarazo et al in 2015 (64.5%) (16), Vargas et al in 2016 (49.5%) (15), and Magalhães et al in 2014 (48.0%) (25). Similar and lower prevalence rates were reported in the study by Cornu et al in 2012 (40.9%) (17), Quélennec et al in 2013 (33.2%) (26), and Climente-Martí et al in 2010 (9.1%) (27). Reasons for the marked variation in results include differences in the study population, the definition of unintentional medication discrepancy used, and the protocol applied to conduct medication reconciliation. For example, the studies by Belda-Rustarazo et al (16), Vargas et al (15), and Magalhães et al (25) selected patients with at least 3 or 5 preadmission medications, whereas our study only required at least one preadmission medication. This may explain the lower rate of unintentional medication discrepancy in our current study when compared to those published studies. Furthermore, we only classified medication discrepancies as 'unintentional' after clarification and approval from the managing physicians, this could have reduced the proportion of unintentional medication discrepancies identified. Despite this, our study still found a relatively high prevalence of unintentional medication discrepancies, thus suggesting the need of improvement in the current practice of obtaining the medication history from patients and reconciliating this with the medications prescribed at hospital admission in Vietnam.

Table 6. *Summary of similar studies related to unintentional medication discrepancy (UMD) in elderly inpatients on hospital admission*

Authors and country	Year	Study population	Justification of UMD	Number of UMD	Prevalence of UMD	Common types of UMD (%)	Risk factors
Dong et al (present study), Vietnam	2018	192 patients aged over 60 using at least 1 chronic preadmission medication	Identified by researcher and confirmed by physician	87	32.2%	Medication omission (75.9%)	Treatment units; Using at least 5 chronic preadmission medications
Vargas et al, Spain (15)	2016	206 patients aged over 65 and using at least 5 preadmission medications	Identified by clinical pharmacist and confirmed by physician	359	49.5%	Medication omissions (65.1%)	Physician experience; Number of preadmission prescribed medications; Previous surgeries
Belda-Rustarazo et al, Spain (16)	2015	814 patients aged over 65 and using at least 5 preadmission medications	Identified by pharmacist and confirmed by physician	1175	64.5%	Medication omissions (73.6%)	Number of preadmission prescribed medications; Number of comorbidities
Magalhães et al, Brazil (25)	2014	58 patients (mean age 65) using at least 3 preadmission medications	Identified by researcher and confirmed by physician	32	48.0%	Different medication dose	Not reported
Quelennec et al, France (26)	2013	256 elderly patients	Identified by researcher and confirmed by physician	173	33.2%	Medication omissions (87.9%)	Not reported
Cornu et al, Belgium (17)	2012	199 patients aged over 65 and using at least 1 preadmission medication	Identified by pharmacist and confirmed by physician	681	40.9%	Medication omissions	Not reported
Climente-Martí et al, Spain (27)	2010	120 patients (mean age 76) using at least 1 chronic preadmission medication	Identified by pharmacist and confirmed by physician	14	9.1%	Medication omissions (92.7%)	Age

This study also found the number of unintentional medication discrepancies remained very high at 48 hours after admission (90.8%) and even persisted until the patient was discharged (77.0%). If these discrepancies were not identified and effectively communicated to the patient or the patient's general practitioner following hospital discharge, the unresolved medication discrepancies (e.g., omission of a vital medication) may continue indefinitely and can lead to adverse consequences for the patient.

The most frequent type of unintentional medication discrepancy identified was medication omissions (75.9%), followed by medication change (21.8%). Similarly, previous studies had also reported medication omission as the most common type of discrepancy (15, 16, 27, 28). Potential reasons for the unintentional omission of medications among patients at hospital admission or discharge include incomplete information regarding the patients' preadmission medication lists, issues surrounding the anamnesis of patients during interviews, and the complexity of patients' medication regimens. These findings suggest the need of strategies to identify and improve barriers in the transition of care pathways to ensure continuity and integration of care for the patient. Clinical pharmacists would be an invaluable resource to contribute in this area.

In term of medication class, unintentional medication discrepancy was identified mostly for cardiovascular drugs (e.g. lipid-modifying agents, antihypertensive agents, and antithrombotic agents), followed by blood glucose lowering drugs. Other medication reconciliation studies had also identified cardiovascular drugs as being one of the most frequent drug classes associated with medication discrepancies (15, 16, 25). Other frequently reported medication classes include drugs affecting the blood and hematopoietic system (16, 27), the nervous system (15), (16), and the gastrointestinal system (15), (27). This may suggest that some medication classes require special attention when implementing medication reconciliation procedures.

Associations between the number of unintentional medication discrepancies and the type of internal medicine unit as well as the number of medications at admission were found in the present study. The unintentional medication discrepancies were 10.03, 5.44 and 6.98 times more likely to occur among patients admitted to the orthopedics, respiratory, and gastroenterology units, respectively, compared to patients admitted to the endocrine and metabolism unit. Similar variations in the prevalence of unintentional medication discrepancy among hospital wards were also reported by other studies (27, 29). These variations may be due to the lack of a standard operating procedure for medication reconciliation in the different units of the study hospital. The different charactersitics of patients admitted to these units and the different specialties of the physicians in these units may also contribute. In resource-limited settings such as Vietnamese hospitals, this information could help the hospital administrators to strategically assign resources.

Furthermore, the likelihood of medication discrepancy was also significantly increased among patients taking at least 5 chronic medications prior to hospital admission compared to patients taking 1 or 2 preadmission chronic medications. This finding was again consistent with other studies regarding the risk factors of unintentional medication discrepancies (15, 29). These findings suggest that medication reconciliation by clinical pharmacists can be prioritized to elderly inpatients with polypharmacy at hospital admission if resources are limited.

There are a few limitations that should be considered when interpreting the findings of the present study. Firstly, the results may not represent the current practice of the whole country, as the study was only conducted at a single hospital in Vietnam. However, as mentioned above, the concept of 'medication reconciliation' is still very new in Vietnam and has not been mentioned in any official documents or specialized professional practice standards. Hence, there is a lack of standard operating procedures in Vietnamese hospitals for this practice. In addition, the study hospital is one of the biggest geriatric hospitals in Vietnam with large number of elderly patients admitted each year. Therefore, the current results are likely to be applicable to other Vietnamese hospitals. The second limitation is that the review of the medications prescribed was limited to only chronic medical conditions, which may have led to an underestimation of the prevalence of unintentional medication discrepancies. Lastly, the potential clinical impact of the unintentional medication discrepancies identified was not evaluated in the study due to a lack of appropriate assessment instrument. In fact, other studies have resorted to using a physician and a pharmacist to judge the clinical significance of the unintentional medication discrepancies (26, 27). Therefore, future studies about the clinical impact of unintentional medication discrepancies should be conducted in Vietnamese hospital settings to assess the severity of the problems. The cost-benefit analysis for the implementation of medication reconciliation services should also be explored to justify the resource allocation that is required.

Conclusion

This study found similar rate of medication discrepancies among elderly patients admitted to hospital in Vietnam compared to the results reported in other jurisdictions. The most frequent type of unintentional medication discrepancy was medication omission, which commonly occurred for drugs of the cardiovascular system. Another important observation from our study was that unintentional medication discrepancy persisted throughout the patients' hospital stay until discharge. Overall, our results support implementing a medication reconciliation program with officially endorsed standard operating procedures to attain a complete preadmission medication history for patients in Vietnam.

List Of Abbreviations

BPMH: Best Possible Medication History

CI: Confidence Intervals

MD: Medication Discrepancy

OR: Odd Ratio

SD: Standard Deviation

SOP: standard operating procedure

UMD: Unintentional Medication History

WHO: World Health Organization

Declarations

Authors' contributions

- Phuong Thi Xuan Dong: Conceptualization, Methodology, Data collection, Formal analysis, Writing – Original Draft, Writing – Review & Editing.
- Van Thi Thuy Pham: Conceptualization, Methodology, Writing – Review & Editing.
- Linh Thi Nguyen: Data collection, Formal analysis, Writing – Review & Editing.
- Thao Thi Nguyen: Data collection, Writing – Review & Editing.
- Huong Thi Lien Nguyen: Conceptualization, Methodology, Writing – Review & Editing.
- Susan Hua: Conceptualization, Methodology, Writing – Review & Editing, Supervision.
- Shu Chuen Li: Conceptualization, Methodology, Writing – Review & Editing, Supervision, Project administration.
- All authors read and approved the final manuscript

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Figures
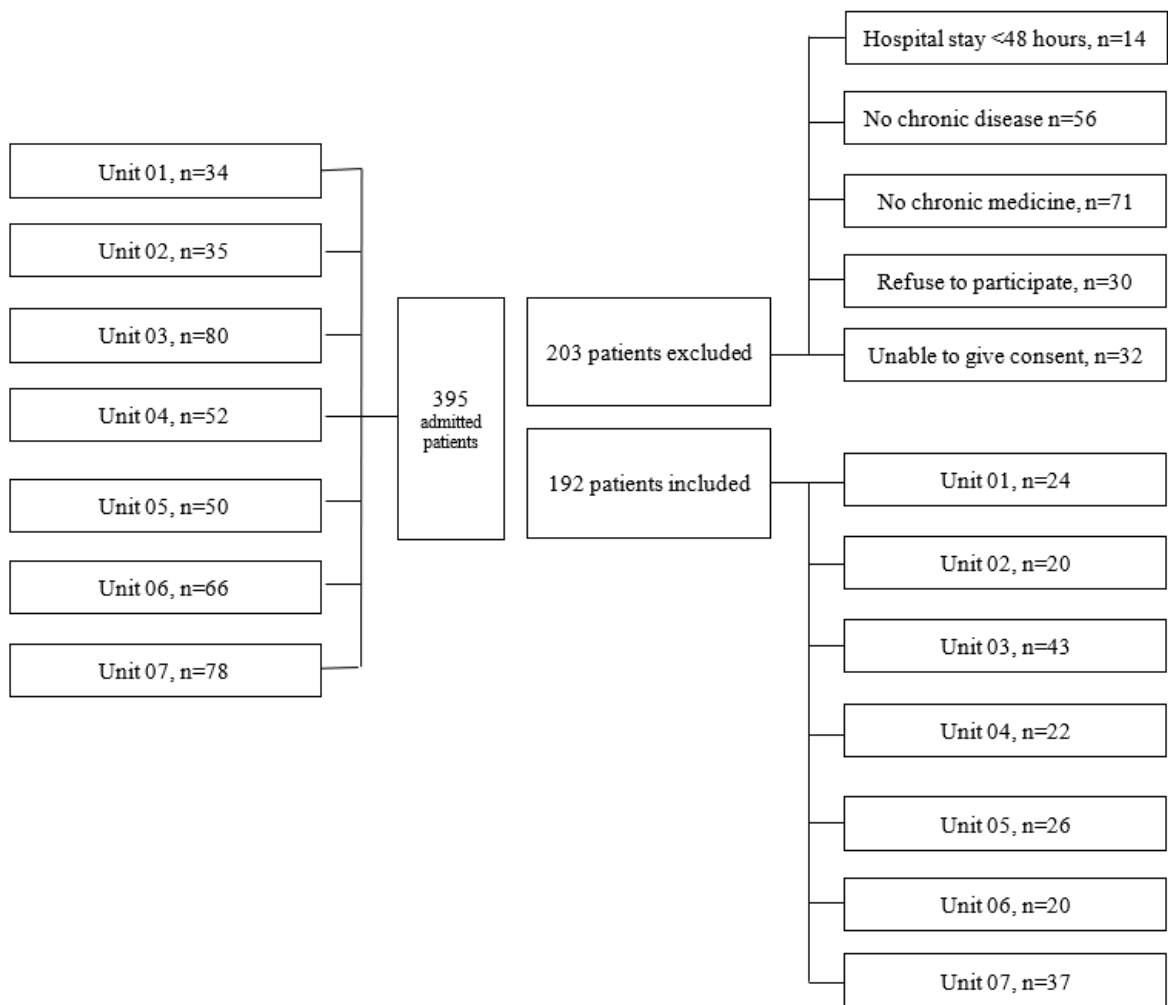
Figure 1

Flowchart of the patient recruitment process

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