

Hospital information system-based pharmacovigilance for elderly patients: practices and results

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Abstract

Objectives: To evaluate the effect of a pharmacovigilance system on potentially inappropriate medication prescriptions for elderly patients.

Method: The retrospective study was conducted at Shaanxi Provincial People's Hospital, China, after approval from the ethics review committee, and comprised data from May 2020 to April 2021, and comprised prescriptions related to elderly patients aged at least 65 years. Number of medication risk assessment entries, number of intervened medical orders on outpatients and inpatients number of medical order prompts, and number of physician communication with prescription-checking pharmacists were noted. Potential drug interaction rate was compared between pre- implementation from May to October 2020 and post-implementation from November 2020 to April 2021. Besides, the usage of sedatives and hypnotics and potentially inappropriate medication was noted for the period from January to June 2021 to evaluate the sustained effect of pharmacovigilance system. Data was analysed using SPSS 19.

Results: A total of 118 drugs were involved in the 3911 entries of outpatient prescription warnings, of which 19 drugs accounted for 3156 (80%). Besides, a total of 113 drugs were involved in the 3999 entries of inpatient prescription warnings, of which 19 drugs accounted for 3199 (80%) The overall prevalence of potentially inappropriate medication related to sedatives and hypnotics decreased post-intervention as warning percentage was 16.1% in January and 6.7% in June among outpatients. On inpatients, the warning percentage was 30.6% in January and 6.1% in June.

Conclusions: The pharmacovigilance system could reduce potentially inappropriate medication and provide deeper technical support for the safety of medical behaviour and individualised treatment of patients.

Key Words: Pharmacovigilance, Drug safety, Potentially inappropriate medication, Elderly patients, Risk management. (JPMA 73: 525; 2023) DOI: 10.47391/JPMA.6428

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Introduction

With rapid development and improvement of living standards, the average life expectancy of humans has increased. The ageing of the population has become a serious problem faced by all countries. Multiple diseases are often found in an elderly person concurrently, and most are chronic. A wide variety of drugs are available for treatment, but have prominent drugs interaction problems. Additionally, the pharmacokinetics in the elderly population is quite different from that of other age groups. Therefore, drugs easily accumulate in the body and cause adverse reactions¹.

In 1991, the criteria for determining inappropriate medication use in sanatorium residents were published for the first time by American geriatric experts², known as the Beers criteria. Subsequently, the Beers criteria have

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been updated several times by the American Geriatrics Society (AGS) following a comprehensive and systematic evaluation and analysis of relevant studies³⁻⁵. A list of drugs that should be avoided in elderly patients as such, and under specific disease conditions, drugs to be used with caution in elderly patients, marking of evidence level and strength of recommendation for each item was established. To date, the criteria for potentially inappropriate medication (PIM) use in older adults applicable to each local area have been formulated by many countries based on the Beers criteria to monitor and guide rational medication usage among the elderly⁶⁻¹¹. However, it is unrealistic to assume that the list of PIMs in older adults and specific risk contents are remembered by every physician, nurse practitioner or pharmacist. This highlights the need for processes to support prescribers in making rational choices, such as a software that may issue warnings when PIMs are prescribed. A pharmacovigilance system (PVS) was established in Shaanxi Provincial People's Hospital to issue PIM alerts. The current study was planned to evaluate the effect of

the PVS on PIM prescriptions for the elderly in a tertiary care setting.

Materials and Methods

The retrospective study was conducted at Shaanxi Provincial People's Hospital, China, after approval from the ethics review committee and comprised data from May 2020 to April 2021.

International and domestic guidelines and consensus documents³⁻⁵ on medication use for elderly patients were identified to establish PVS rules. The content was embedded in the medical order running software. The real-time audit of different dimensions was conducted on the issued medical orders, and the medical orders were intercepted or prompted on the hospital information system (HIS) to ensure medication safety.

The contents were updated in real time in line with evidence-based medicine (EVM) International and domestic guidelines and consensus documents published by the National Centre for Adverse Drug Reaction Monitoring¹². The PVS was intended for use in adults 65 years and older in all ambulatory, acute, and institutionalised settings of care. Hospice and palliative care settings were excluded. Five types of risk assessment are conducted: PIM related to diseases or symptoms in older adults; medications used cautiously in older adults; drugs interactions that should be avoided in older adults; drugs that should be avoided; an drugs that should be reduced in dose in patients with renal insufficiency.

Each risk assessment rule was collated with EVM, and source of recommendation was marked. The risk assessment rule entries were classified and summarised. By comparing the list of risky drugs with the list of drugs used in the hospital, the list of drugs that posed risks to

elderly patients and risk assessment rules for the hospital were screened to establish and complete the document information.

The risk assessment rules were imported into the HIS in batches (Figure). The real time audit of different dimensions was conducted on the medical orders issued according to the different contents of the entries in the PVS. In case of risks, early warning was conducted, with warning levels divided into three situations: interception, prompting, or online communication with prescription-checking pharmacist. For drugs that are prohibited for older adults or the combination of drugs with serious interactions or where the drugs have a significant impact on the original disease, such a medical order was directly intercepted by the system and a dialogue box explained the reasons for interception and evidence. In view of the situation that older adults use drugs with caution or require drug dose reduction or in case of drug interactions with low potential risks, only the prompt dialogue box was shown by the system, explaining the reason and EVM. The level of risk was determined by physicians according to the specific situation, and whether or not to modify the medical order was determined by them. In cases where the physician had objections or doubts on the warning content, communication was conducted online with prescription-checking pharmacists to change the disposition of the medical orders.

In the current study, prescriptions related to elderly patients aged at least 65 years were evaluated. Number of medication risk assessment entries, number of intervened medical orders on outpatients and inpatients, number of medical order prompts, and number of physician communication with prescription-checking pharmacists were noted. Potential drug interaction rate was compared

between pre-implementation phase from May to October 2020 and post-implementation phase from November 2020 to April 2021. Besides, the usage of sedatives and hypnotics, like estazolam, clonazepam, diazepam, zolpidem and alprazolam, and PIM was noted for the period from January to June 2021 to evaluate the sustained effect of pharmacovigilance system.

Data was analysed using SPSS 19. Data was presented as mean $\pm$ standard error of the mean (SEM). Differences between groups were analysed using paired samples t-test. The level of statistical significance was set at $p < 0.05$.

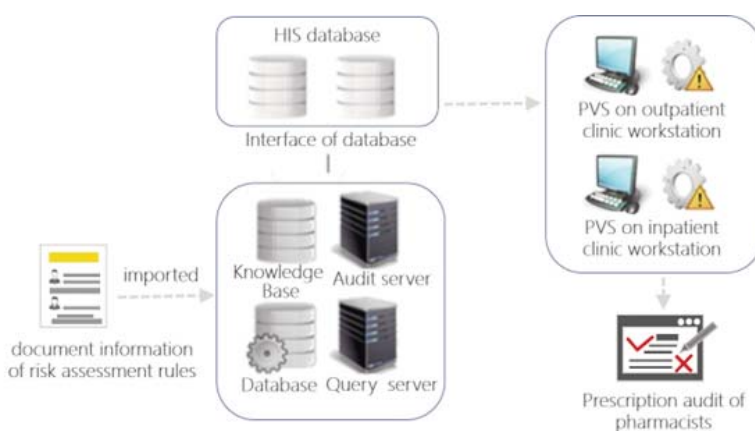


Figure: Structure of pharmacovigilance system (PVS).

HIS: Hospital information system

Results

A total of 343 drugs posing risk to the elderly were classified, involving 1164 warnings. Through cross-comparison between the list of risky drugs and list of drugs used in the hospital, a total of 418 drugs, including generics of an original drug, were screened, and 10,663 audit rules were summarised.

The PVS was implemented on a trial basis in the Neurology, Respiratory, Cardiology, Nephrology and Gastroenterology departments. The PVS provided 3911 warnings related to 1767 outpatients (10.5% of the total number of outpatients). Among these, prescriptions were

intercepted 349 times. Communications between physicians and pharmacists were 138 times. Finally, 263 medical orders were changed by physicians.

Among the inpatients, the PVS provided warnings 3999 times and 844 patients (23.7% of the total number of inpatients) were involved. Among these, the prescriptions were intercepted 230 times. Communications between physicians and pharmacists were 120 times. Finally, 146 medical orders were changed by physicians.

A total of 118 drugs were involved in the 3911 entries of outpatient prescription warning, of which 19 drugs accounted for 3156 (80%) (Table 1), and most of them

Table-1: Details of 80% early warning quantity among outpatients.

Drug name	Warning level	Warning contents	Quantity/piece (Percentage,%)
Zolpidem tablets	Prompt	Adverse reactions are similar to those of benzodiazepines (delirium, falls and fractures). Increased rate of emergency visits and hospitalisations, traffic accident, hypnosis and prolonging sleep time have poor effects; therefore, the drug should be avoided in older adults.	472 (12.1)
Alprazolam tablets	Prompt	The sensitivity of older adults to benzodiazepines increased, and the metabolism of long-acting preparations slowed down. Older adults are at increased risk for impaired cognitive function, delirium, falls, fractures and traffic accidents; therefore, the drug should be avoided in older adults.	429 (11.0)
Aspirin enteric-coated tablets	Prompt	The risk of haemorrhage caused by aspirin is significantly increased in the elderly population, which may promote fluid retention and aggravate heart failure. The drug should be used with caution in older adults in case of asymptomatic heart failure and should be avoided in case of symptomatic heart failure.	367 (9.4)
Ibuprofen suspension	Prompt	There are poor analgesic effects of commonly used oral doses and higher risk of neurological adverse reactions, such as delirium, compared with other opioids. There are safer alternatives. Avoid long-term use unless alternative drugs are ineffective and patients can take gastric mucosa-protective agents (proton pump inhibitors or misoprostol).	207 (5.3)
Clopidogrel bisulfate tablets	Prompt	Risks are caused by elderly patients when using the drug: (1) adverse reactions against the blood system (thrombocytopenia, neutropenia, gastrointestinal bleeding, purpura, epistaxis, eye haemorrhage, haematuria and intracranial haemorrhage) and (2) neurological adverse reactions (headache, dizziness, confusion and hallucination).	189 (4.8)
Eszolam tablets	Interception	The drug should be avoided in elderly patients because of adverse reactions in the central nervous system.	186 (4.8)
Ibuprofen sustained-release capsules	Prompt	There are poor analgesic effects of commonly used oral doses and higher risk of neurological adverse reactions, such as delirium, compared with other opioids. There are safer alternatives. Avoid long-term use unless alternative drugs are ineffective and patients can take gastric mucosa-protective agents (proton pump inhibitors or misoprostol).	174 (4.4)
Paroxetine tablets	Prompt	Antidepressants used alone or in combination have a strong anticholinergic effect, which leads to sedation and postural hypotension and severe central adverse reactions; therefore, the drug should be avoided in elderly patients.	160 (4.1)
Niergoline tablets	Prompt	It may cause water and sodium retention and lead to high blood pressure. Switch to acetaminophen or aspirin and closely monitor blood pressure.	136 (3.5)
Clonazepam tablets	Interception	The drug should be avoided in elderly patients because of adverse reactions in the central nervous system.	127 (3.2)
Sertraline tablets	Prompt	It may aggravate or lead to syndrome of abnormal secretion of antidiuretic hormone or hyponatraemia. Blood sodium level should be closely monitored when starting medication or adjusting dose, and the drug should be used with caution in elderly patients.	110 (2.8)

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Drug name	Warning level	Warning contents	Quantity/piece (Percentage,%)
Duloxetine enteric-coated tablets	Prompt	It may aggravate or lead to syndrome of abnormal secretion of antidiuretic hormone or hyponatraemia. Blood sodium level should be closely monitored when starting medication or adjusting dose, and the drug should be used with caution in elderly patients.	103 (2.6)
Pantoprazole sodium enteric-coated capsules	Prompt	There is a risk of bone loss and fracture caused by <i>Clostridium difficile</i> infection. The drug should be avoided in elderly patients for >8 weeks, unless used in a high risk population.	99 (2.5)
Rivasaban tablets	Prompt	Increased risk of gastrointestinal bleeding compared with warfarin. Gastrointestinal bleeding increased in older adults aged ≥ 75 years who were treated with venous thromboembolism or atrial fibrillation compared with other direct oral anticoagulants. The drug should be used with caution in the long-term treatment of venous thromboembolism or atrial fibrillation in older adults aged ≥ 75 years.	95 (2.4)
Diazepam tablets	Interception	The drug should be avoided in elderly patients because of adverse reactions in the central nervous system.	86 (2.2)
Oxaprozin enteric-coated capsules	Interception	It may cause water and sodium retention and lead to high blood pressure. Elderly patients should avoid using it and switch to acetaminophen or aspirin instead.	72 (1.8)
Omeprazole enteric-coated capsule	Prompt	There is a risk of bone loss and fracture caused by <i>Clostridium difficile</i> infection. The drug should be avoided in elderly patients for >8 weeks, unless used in a high risk population.	59 (1.5)
Quetiapine fumarate tablets	Interception	It may aggravate or lead to syndrome of abnormal secretion of antidiuretic hormone or hyponatraemia. Blood sodium level should be closely monitored when starting medication or adjusting dose, and the drug should be used with caution in elderly patients	43 (1.1)
Insulin glargine injection	Prompt	If no improvement is made to the management of hyperglycaemia, it will cause a higher risk of hypoglycaemia regardless of the nursing environment. In case of using short-acting or fast-acting insulin and not using basal or long-acting insulin concurrently, the dose is adjusted according to the current blood glucose level.	42 (1.1)
Subtotal			3156 (80.1)

Table-2: Details of 80% early warning quantity among inpatients

Drug name	Warning level	Warning content	Quantity/piece (Percentage,%)
Omeprazole sodium injection	Prompt	There is a risk of bone loss and fracture caused by <i>Clostridium difficile</i> infection. The drug should be avoided in elderly patients for >8 weeks, unless used in a high risk population.	529 (13.2)
Clopidogrel bisulfate tablets	Prompt	Risks are caused by elderly patients when using the drug: (1) adverse reactions against the blood system (thrombocytopenia, neutropenia, gastrointestinal bleeding, purpura, epistaxis, eye haemorrhage, haematuria and intracranial haemorrhage) and (2) neurological adverse reactions (headache, dizziness, confusion and hallucination).	517 (13.0)
Aspirin enteric-coated tablets	Prompt	The risk of haemorrhage caused by aspirin is significantly increased in the elderly population, which may promote fluid retention and aggravate heart failure. The drug should be used with caution in older adults in case of asymptomatic heart failure and should be avoided in case of symptomatic heart failure.	396 (10.0)
Furosemide injection	Prompt	It may aggravate or lead to syndrome of abnormal secretion of antidiuretic hormone or hyponatraemia. Blood sodium level should be closely monitored when starting medication or adjusting dose, and the drug should be used with caution in elderly patients.	317 (7.9)
Pantoprazole sodium enteric-coated capsules	Prompt	There is a risk of bone loss and fracture caused by <i>Clostridium difficile</i> infection. The drug should be avoided in elderly patients for >8 weeks, unless used in a high risk population.	290 (7.3)
Rivasaban tablets	Prompt	Increased risk of gastrointestinal bleeding compared with warfarin. Gastrointestinal bleeding increased in older adults aged ≥ 75 years who were treated with venous thromboembolism or atrial fibrillation compared with other direct oral anticoagulants. The drug should be used with caution in the long-term treatment of venous thromboembolism or atrial fibrillation in older adults aged ≥ 75 years.	157 (3.9)
Niergoline tablets	Prompt	It may cause water and sodium retention and lead to high blood pressure. Elderly patients should avoid using it and switch to acetaminophen or aspirin instead.	151 (3.8)

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Drug name	Warning level	Warning content	Quantity/piece (Percentage,%)
Mannitol injection	Prompt	It may aggravate or lead to syndrome of abnormal secretion of antidiuretic hormone or hyponatraemia. Blood sodium level should be closely monitored when starting medication or adjusting dose, and the drug should be used with caution in elderly patients.	122 (3.1)
Insulin aspart injection	Prompt	If no improvement is made to the management of hyperglycaemia, it will cause a higher risk of hypoglycaemia regardless of the nursing environment. In case of using short-acting or fast-acting insulin and not using basal or long-acting insulin concurrently, the dose is adjusted according to the current blood glucose level.	120 (3.0)
Doxophylline injection	Prompt	Risks are caused by elderly patients when taking the drug: (1) adverse cardiac reactions (atrial fibrosis, atrial flutter and tachycardia); (2) neurological adverse reactions (epilepsy, insomnia and irritability) and (3) nausea and diarrhoea (dose dependence).	86 (2.2)
Alprazolam tablets	Prompt	The sensitivity of older adults to benzodiazepines increased, and the metabolism of long-acting preparations slowed down. Older adults are at increased risk for impaired cognitive function, delirium, falls, fractures and traffic accidents; therefore, the drug should be avoided in older adults.	83 (2.1)
Pantoprazole sodium injection	Prompt	There is a risk of bone loss and fracture caused by <i>Clostridium difficile</i> infection. The drug should be avoided in elderly patients for >8 weeks, unless used in a high risk population.	82 (2.1)
Insulin glargine injection	Prompt	If no improvement is made to the management of hyperglycaemia, it will cause a higher risk of hypoglycaemia regardless of the nursing environment. In case of using short-acting or fast-acting insulin and not using basal or long-acting insulin concurrently, the dose is adjusted according to the current blood glucose level.	78 (2.0)
Spironolactone tablets	Prompt	It may aggravate or lead to syndrome of abnormal secretion of antidiuretic hormone or hyponatraemia. Blood sodium level should be closely monitored when starting medication or adjusting dose, and the drug should be used with caution in elderly patients.	73 (1.8)
Furosemide tablets	Prompt	It may aggravate or lead to syndrome of abnormal secretion of antidiuretic hormone or hyponatraemia. Blood sodium level should be closely monitored when starting medication or adjusting dose, and the drug should be used with caution in elderly patients.	50 (1.3)
Omeprazole enteric-coated capsule	Prompt	There is a risk of bone loss and fracture caused by <i>Clostridium difficile</i> infection. The drug should be avoided in elderly patients for >8 weeks, unless used in a high risk population.	42 (1.1)
Promethazine hydrochloride injection	Interception	Symptoms of Parkinson's disease may be aggravated; therefore, the drug should not be used.	38 (1.0)
Cisplatin injection	Prompt	It may aggravate or lead to syndrome of abnormal secretion of antidiuretic hormone or hyponatraemia. Blood sodium level should be closely monitored when starting medication or adjusting dose, and the drug should be used with caution in elderly patients.	35 (0.9)
Insulin detemir injection	Prompt	If no improvement is made to the management of hyperglycaemia, it will cause a higher risk of hypoglycaemia regardless of the nursing environment. In case of using short-acting or fast-acting insulin and not using basal or long-acting insulin concurrently, the dose is adjusted according to the current blood glucose level.	33 (0.8)
Subtotal			3199 (80.0)

were psychotropic, cardiovascular as well as cardio and cerebrovascular drugs. A total of 3510 (89.7%) warning levels were mainly prompts. Drugs that were intercepted included three sedatives and hypnotics (estazolam, clonazepam, diazepam), one nonsteroidal anti-inflammatory drug (NSAID) (oxaprazine) and one psychotropic drug (quetiapine). PVS had great influence on the usage of sedatives and hypnotics (estazolam, clonazepam, diazepam, zolpidem, alprazolam). The usage of the five drugs decreased significantly over the January-June period. Number of prescriptions of the five drugs were 38 (0.5% of total number of prescriptions), 35 (0.5%), 40 (0.6%), 41(0.6%) and 152 (2.2%) respectively in January 2021. The proportion decreased to 21 (0.4%), 15 (0.3%), 17

(0.3%), 20 (0.4%) and 103 (2%) respectively in June 2021 ($t=6.325$, $p=0.003$).

A total of 113 drugs were involved in the 3999 entries of inpatient prescription warning, of which 19 drugs accounted for 3199 (80%) (Table 2), and most of them were psychotropic and cardiovascular drugs. 3733 (93.3%) warning levels were mainly prompts.

The overall prevalence of PIM decreased during the 6 months. On outpatients, warning percentage was 16.1% in January 2021 and 6.7% in June 2021. On inpatients, warning percentage was 30.6% in January 2021 and 6.1% in June 2021. Besides, the potential drug interaction rate was also reduced. Interaction was 83 (2.7% of the total

number of inpatients) on inpatients and 186 (0.8% of the total number of outpatients) on outpatients during pre-intervention. Interaction decreased to 72 (2% of the total number of inpatients) on inpatients and 166 (0.6% of the total number of outpatients) on outpatients during post-intervention.

Discussion

According to the World Health Organisation (WHO), the ageing population will exceed 1.5 billion in 2050, accounting for 16% of the global population. As shown in the National Annual Report on Adverse Drug Reaction (ADR) Monitoring (2018), of the 1.499 million reports received, elderly patients aged >65 years accounted for 27.7%¹³. Such patients have a high risk of adverse drug events¹⁴⁻¹⁵. Therefore, the implementation of PVS contributes to prompting clinicians and pharmacists of the medication risk in real time. More attention should be given when issuing or reviewing medical orders so as to reduce the occurrence of drug injury events, and to play a role in popularising health sciences for the public¹⁶⁻¹⁷.

In the present study, the drugs with the highest incidence of early warning were anti-insomnia drugs, including zolpidem, alprazolam, diazepam and estazolam. It is found that >50% of the elderly have insomnia, and 23% of them have severe insomnia¹⁸, which may be the reason for the high frequency of use of such drugs in elderly patients. During the rule formulation, the warning level of anti-insomnia drugs with high risk and long half-life was set as interception, whereas drugs with short and medium half-life were still maintained as prompts, considering that the extremely high warning frequency would easily lead to 'vigilance fatigue'. Taking diazepam as an example, the long half-life can easily lead to a 'hangover phenomenon' in the early morning after using the drug in elderly patients, that is, drowsiness, dizziness, sleepiness and disorientation, which is similar to the symptoms of drunkenness. The present study revealed that accidental injuries in the elderly population, such as falls and fractures, are associated with long-term use of long-acting sleeping pills, such as diazepam¹⁹⁻²⁰. It is recommended that physicians must analyse the cause of insomnia before using the drug. First, psychological or behavioural therapy should be considered, or short-acting hypnotics should be used for treatment²¹, PVS indeed had great influence on the usage of sedatives and hypnotics.

Antiplatelet and anticoagulant drugs are second only to anti-insomnia drugs. The high incidence of cardiovascular and cerebrovascular diseases contributes to the frequent use of these drugs²². For secondary prophylaxis with

definite evidence, the warning level is prompt. Proton pump inhibitors (PPIs) are commonly used by older adults. ADR caused by long-term treatment have been recorded in numerous studies²³, such as induced infection, bone loss and fracture risk. However, this situation is usually overlooked in treatment. Prompts are provided by the PVS for such problems.

The vast majority of elderly patients have chronic pain, such as arthritis, gout and other diseases. NSAIDs are still the first choice for pain relief²⁴, indirectly resulting in an increase in the number of individuals with peptic ulcers. The older the patient, the worse the physiological functions of the body and the weaker are liver and kidney functions¹. The ability of prostaglandin synthesis is weakened, which leads to a decrease in gastrointestinal mucosal defence function, and NSAIDs-related peptic ulcer is more likely to develop²⁵. Prompts are provided by the PVS for the course of NSAIDs, thereby reducing the risk factors.

The use of two or more centrally acting drugs counts for most of the early warning of drug interaction. Two sedative and hypnotic drugs were used alternately. Antidepressants were used in combination with sedative and hypnotic drugs. It might increase the central adverse reactions in elderly patients. Fortunately, after PVS warning, the potential drug interaction rate hugely decreased. It reduced the potential risk of ADRs.

Furthermore, the early warning frequency of insulin was also high in the present study. Elderly patients have relatively large blood glucose fluctuations and high probability of hypoglycaemia because of their special fitness²⁶. Insulin is commonly used in elderly patients with diabetes. Great progress has been made in insulin-related research and development, including continuous optimisation of pharmacokinetics or administrative methods, but ADRs, such as allergic reactions, hypoglycaemia and weight gain, are still inevitable. In case of severe hypoglycaemia, consciousness will be lost and even life will be endangered²⁷. Therefore, insulin should be used with caution in older adults. If insulin is inevitably used, medication education and blood glucose monitoring for patients should be strengthened²⁸. Therefore, early warning of insulin is indispensable.

Elderly patients were still at risk although PIM prescriptions reduced. Most (60%-70%) pharmacist interventions were accepted. Although these interventions were performed in some cases after ignoring the initial alert, pharmacist interventions are frequently ignored. The benefits of PVS were ease of access and the provision of specific warnings to

physicians when prescribing PIMs. However, polypharmacy has been continuously prescribed in elderly patients that is associated with a higher prevalence of PIM. These issues should be addressed by de-prescribing to minimise prescription of multiple medicines and to withdraw PIM in elderly patients²⁹⁻³⁰.

In terms of limitations, the current study was conducted at a single hospital, and the results may not be applicable to other hospitals due to their unique PVS alert requirements. Moreover, because of limited data access, observations were conducted only in the Neurology, Respiratory, Cardiology, Nephrology and Gastroenterology departments. Therefore, findings may not be generalisable.

Conclusions

The PVS could reduce PIM and provide deeper technical support for the safety of medical behaviour and individualised treatment of patients. With the establishment of PVS, inappropriate prescription can be effectively reduced.

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Conflict of Interest: None.

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