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ORIGINAL RESEARCH

Continued Use of Medications Withdrawn Internationally for Safety Concerns: Insights from an Urban Employed Population in China

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Purpose: Some drugs approved for marketing are later withdrawn in other countries due to safety concerns. This study aimed to examine the use of such drugs in China and explore factors associated with continued prescribing.

Methods: A 5% random sample of the Urban Employee Basic Medical Insurance (UEBMI) database (2019–2021) from a province in China was used. Withdrawn drugs were identified from two global databases, the Onakpoya dataset and the WITHDRAWN 2.0 database that included withdrawals from 1950 to 2020. Generalized linear mixed models incorporating hospital random effects were applied, adjusting for individual-level covariates (age, sex, ethnicity, occupation, and supplementary public servant medical benefits) and institution-level covariates (medical institution level, hospital ownership and type, and region of treatment).

Results: We included 293,859 insured individuals, of whom 16,510 (5.62%) received at least one withdrawn drug. Thirty-eight such drugs were prescribed, 26 of which remained available without restriction in China. Overall use declined from 6.21% in 2019 to 5.46% in 2021. Mean per-person spending on withdrawn drugs declined from 402.88 yuan in 2019 to 258.36 yuan in 2021. The reductions in usage and spending were mainly observed in inpatient prescribing. Nervous system medications were most frequently used (27.3% of outpatient and 52.2% of inpatient uses) and accounted for the largest share of expenditures (40.3%). Greater use was observed among men, retirees, and those with supplementary public servant medical benefits, as well as in tertiary, private, and general hospitals.

Conclusion: Drugs withdrawn internationally for safety concerns continued to be prescribed in China, despite overall declines in use. Efforts to strengthen post-marketing surveillance, improve alignment between domestic regulatory actions and global safety evidence, and enhance prescribing oversight—particularly in higher-level hospitals—may help reduce avoidable patient exposure to unsafe medications.

Keywords: drug withdrawal, real-world data, medication utilization, pharmacovigilance

Introduction

Ensuring the safety of approved medicines is essential for patient care. Yet despite increasingly sophisticated regulatory systems, new evidence continues to emerge after marketing approval showing that some approved drugs have serious or even fatal risks. When serious adverse reactions are suspected or when risks outweigh benefits, regulatory authorities may withdraw a drug from the market.[1] For example, the anti-obesity drug sibutramine, approved in 1999, was withdrawn globally in 2010 after being linked to increased risks of myocardial infarction and stroke.[2] Timely withdrawal of unsafe drugs is essential to reduce medication-related harm. Between 1993 and 2011, 17 approved drugs were

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withdrawn in the US after more than 112 million prescriptions had been issued.[3] The withdrawal of rofecoxib (Vioxx) alone was estimated to have caused 88,000–139,000 cases of myocardial infarction or stroke among US users.[4]

Despite growing international attention to drug safety, withdrawal decisions vary markedly across regulatory jurisdictions. Among 121 drugs withdrawn for safety concerns between 1960 and 1999, 42.1%, 5.0%, and 3.3% were withdrawn only in Europe, North America, and the Asia–Pacific region, respectively, while 49.6% were removed globally.[5,6] Even between countries with advanced regulatory capacity, decisions often differ: from 1971 to 1992, the UK withdrew nearly three times as many drugs as the US.[7,8] More recent comparisons show substantial timing discrepancies; for example, most drugs withdrawn in both China and the US between 1999 and 2021 were not withdrawn in the same year.[9]

Consequently, drugs withdrawn for safety concerns in one country may remain available elsewhere. A global assessment of 137 national essential medicines lists found that 136 countries listed at least one withdrawn drug, and more than one-quarter listed ten or more.[10] A study in Argentina identified 17 such drugs still available locally.[11] Our previous multi-city study in China identified at least 21 withdrawn drugs that continued to be used. This evidence suggests a global pattern of persistent use of withdrawn medications.

Despite the importance of this issue, empirical evidence remains limited. Existing studies typically document lists of withdrawn drugs or compare regulatory decisions across countries but rarely quantify real-world use within healthcare systems. Few studies have examined patient- or institution-level determinants of continued prescribing, and none to our knowledge have done so using large-scale population-based data. Addressing this gap is critical for understanding the reasons withdrawn drugs persist in practice, identifying vulnerable populations, and informing regulatory and policy actions to strengthen drug safety.

In this study, we used patient-level data from a provincial Urban Employee Basic Medical Insurance (UEBMI) database in China from 2019 to 2021. Within the Chinese healthcare system, we quantified the utilization of withdrawn drugs in other markets for safety concerns and examined patient and institutional characteristics associated with the use of these drugs.

Methods

Data Source and Study Population

We used a 5% random sample of the UEBMI database from a province with a medium-low economic development level in China from January 2019 to December 2021. UEBMI covers urban employees and retirees, including staff in government agencies, public institutions, state-owned enterprises, private companies, and social organizations. In this province, the UEBMI program insured approximately 6.77 million, 7.14 million, and 7.56 million individuals in 2019, 2020, and 2021, respectively.

UEBMI claims data include patient demographics, prescription drug information, and reimbursement records. Because the provincial platform expanded over time, the 2021 data contained a larger and more complete beneficiary population. Only individuals with at least one prescription record were included in the analysis. We excluded prescription records that had missing information such as missing drug name, place, or date of prescription.

Drugs Withdrawn for Safety Concerns

Drugs withdrawn for safety concerns were defined as medications removed from the market in at least one country or region due to safety concerns. We identified such drugs using two global databases: Onakpoya's dataset, which includes 462 withdrawals from 1953 to 2014, and the WITHDRAWN 2.0 database, which records 647 withdrawals between 1950 and 2020.[12,13] Any medication listed in either database was considered a withdrawn drug and included in our analysis, ensuring comprehensive coverage across sources. Both sources provide information on the timing and region of first withdrawal, reasons for withdrawal, and classification based on the Anatomical Therapeutic Chemical (ATC) system. The Onakpoya dataset additionally rates the strength of supporting evidence according to the Oxford Centre for Evidence-Based Medicine levels (1= highest quality; 2=randomized clinical trials; 3=non-randomized, cohort, or follow-up studies;

4=case series, and 5 = mechanistic reasoning). To ensure that medications were not re-introduced to market, we excluded medications that had later been reintroduced for alternative indications or formulations.

We also examined the regulatory status of these drugs in China during the study period, including whether they remained in regular use, were restricted by formulation, or were listed in the National Key Monitoring Drug Catalogue for Rational Use, a national policy tool used to regulate the inappropriate use of adjuvant medications.[14]

Prescription Information

Prescription records provided information on generic drug names, ATC classifications, reimbursement categories, and expenditures. The primary outcomes were whether a patient used any withdrawn drug with safety concern, the total expenditure associated with withdrawn drug, and the proportion of withdrawn drug spending relative to total drug expenditure. Reimbursement categories were defined using the National Reimbursement Drug List (NRDL, 2019–2020). Category A drugs are reimbursed at the highest rate, category B drugs at a rate approximately 10% lower, and category C drugs are excluded from the NRDL and must be paid entirely out of pocket.

Covariates

To identify factors associated with the use of withdrawn drugs, several individual and institutional characteristics were examined. Individual-level covariates included age, sex, and ethnicity, categorized as Han, Miao/Dong/Buyi, or other minority groups. Occupation was coded using the 2017 Industrial Classification for National Economic Activities and grouped by income level based on national urban wage statistics from 2019–2021.[15,16] Categories included agricultural and fishery workers, industrial and service workers, public sector employees such as teachers and healthcare workers, and professionals in high-technology or specialized industries. All individuals were enrolled in UEBMI; some also received supplementary public servant medical benefits, which provide additional reimbursement for high-cost care, chronic disease management, and catastrophic illness.[17]

Institutional covariates included the level of the healthcare facility (tertiary, secondary, primary or others), hospital ownership (public or private), and hospital type (general or specialized), based on National Health Commission criteria.[18] Prescription encounters were classified as within-province or out-of-province, as the latter often involve different reimbursement procedures.

Statistical Analysis

Baseline characteristics were summarized using means and standard deviations for continuous variables and frequencies with percentages for categorical variables. Factors associated with the use of withdrawn drugs were examined using generalized linear mixed models (GLMMs) with hospital random effects. The models adjusted for individual-level covariates (age, sex, ethnicity, occupation, and supplementary public servant medical benefits), institution-level covariates (medical institution level, hospital ownership and type, and region of treatment), and city because these factors are potential factors associated with the use of withdrawn drugs. Multicollinearity was assessed using variance inflation factors (VIFs), all of which were below 5. Statistical analyses were conducted using Stata version 17.0 (StataCorp, College Station, TX, USA), and a two-sided p-value < 0.05 was considered statistically significant.

Subgroup Analyses

Subgroup analyses were conducted by care setting (outpatient vs. inpatient) to examine whether the factors associated with withdrawn drug use differed between settings.

Results

Characteristics of the Study Population

A total of 293,859 participants were included, contributing 855,835 prescription records. The mean age was 48.03 years (SD 16.61), and 49.46% were male. The majority were of Han ethnicity (82.06%), while Miao/Dong/Buyi ethnic groups accounted for 6.42% (Table 1). Overall, 69.26% of participants were actively employed, with public sector employees

Table 1 Characteristics of Study Population

	2019	2020	2021
Number of participants	73657	77431	142771
Number of prescriptions	221304	220221	414310
Age, years	48.76 (16.46)	48.46 (16.57)	47.41 (16.68)
Sex, male	37206 (50.51)	38809 (50.12)	69352 (48.58)
Race/ethnicity			
Han	59378 (80.61)	62556 (80.79)	119206 (83.49)
Miao/Buyi/Dong	5264 (7.15)	5349 (6.91)	8255 (5.78)
Others	9015 (12.24)	9526 (12.30)	15310 (10.72)
Working (vs. retired)	49500 (67.20)	53053 (68.52)	100960 (70.71)
Occupation			
Agriculture and fishery workers	7808 (10.60)	8766 (11.32)	29650 (20.77)
Industrial and service workers	11058 (15.01)	11674 (15.08)	25532 (17.88)
Public sector employees	40993 (55.65)	42325 (54.66)	65946 (46.19)
Professionals	13798 (18.73)	14666 (18.94)	21643 (15.16)
With additional insurance subsidy	8222 (11.16)	8180 (10.56)	13884 (9.72)

Notes: Continuous variables were presented as mean (standard deviation) and categorical variables were presented as number (percentage).

constituting the largest occupational group (55.65%). In addition, 10.86% of participants received supplementary public servant medical benefits. Demographic characteristics did not vary substantially from 2019 to 2021.

Withdrawn Drugs for Safety Concerns

Using the two-step screening process, we identified 38 drugs withdrawn for safety concerns that were prescribed at least once during the study period (STable 1). Of these, 25 were identified in both databases, while 13 were found only in Onakpoya's database. Most drugs (32 drugs, 84.21%) had been withdrawn in two or more countries. According to ATC classification, the most common therapeutic classes were nervous system medications (7 drugs, 18.42%), gastrointestinal drugs (7, 18.42%), and cardiovascular drugs (4, 10.53%). The first year of market withdrawal for these drugs ranged from 1965 to 2011.

Regarding the strength of supporting evidence, rosiglitazone was withdrawn based on level 1 evidence (systematic review) and parecoxib on level 2 evidence (randomized trial). The majority of withdrawals (26 drugs, 68.42%) were supported by level 4 evidence (case series or observational data), and two drugs (5.26%) were withdrawn solely on the basis of animal studies.

A total of 26 drugs (68.42%) remained available without restrictions during the study period in China, including 22 prescription drugs and four over-the-counter drugs (STable 1). Others were subject to various regulatory actions. For example, aprotinin (injection form), aminopyrine, and phenolphthalein were banned in 2007, 2020, and 2021, respectively. Ganglioside, bovine tissue extract, and cinepazide maleate were included in the National Key Monitoring Drug Catalogue for Rational Use in 2019 and subsequently removed from the National Reimbursement Drug List (NRDL) in 2020.

Usage and Expenditure of Withdrawn Drugs for Safety Concerns

Between 2019 and 2021, 16,510 patients (5.62%) received at least one withdrawn drug, with a prevalence of 3.60% in outpatient and 8.65% in inpatient settings (Table 2). Overall use declined significantly—from 6.21% in 2019 to 5.46% in 2021 ($p<0.05$)—driven mainly by reduced inpatient prescribing (9.83% to 8.24%, $p<0.05$).

In 2019, mean per-person spending on withdrawn drugs was 402.88 yuan, representing 4.93% of total drug costs (243.10 yuan in outpatient vs. 554.40 yuan in inpatient settings, Table 2). Per-person expenditures decreased steadily from 2019 to 2021, driven primarily by reductions in inpatient spending. By 2021, mean expenditures had decreased to 258.36 yuan overall, including 211.31 yuan for outpatient, and 312.81 yuan for inpatient care.

Table 2 Usage and Expenditures of Withdrawn Drugs Due to Safety Concerns

	2019	2020	2021
Use of withdrawn drugs, number (percentage)			
Overall	4574 (6.21)	4146 (5.35)	7790 (5.46)
Outpatient	2465 (3.61)	2437 (3.36)	5094 (3.72)
Inpatient	2243 (9.83)	1853 (8.13)	2993 (8.24)
Expenditures of withdrawn drugs, yuan[a]			
Overall	402.88 (4.93)	317.64 (3.65)	258.36 (3.55)
Outpatient	243.10 (8.31)	267.26 (9.23)	211.31 (8.60)
Inpatient	554.40 (4.99)	359.21 (3.16)	312.81 (2.99)

Notes: [a]Mean expenditures (proportion of drug expenditures attributed to withdrawn drugs).

Nervous system drugs were the most frequently used withdrawn medications. Among patients who received at least one withdrawn drug, 27.27% of outpatient users and 52.17% of inpatient users were prescribed a nervous system drug, accounting for 40.33% of total withdrawn drug expenditures (STable 2). Codeine was consistently the most commonly used individual drug, used by 21.21% of patients in 2019, with utilization increasing to 30.44% in 2021 (STable 3). Ganglioside ranked as the second most frequently used withdrawn drug in 2019 (12.18%) but its use declined sharply to 3.07% by 2021. In terms of expenditures, ganglioside accounted for more than half of total withdrawn drug spending in 2019 (51.78%), decreasing to 33.70% in 2020 and 13.41% in 2021.

In 2019, six withdrawn drugs were classified as Category A under the NRDL. However, only two retained Category A status in both 2020 and 2021 (STable 4). The numbers of Category B and Category C drugs increased accordingly. Category B drugs accounted for the largest share of withdrawn drug spending in 2021 (81.80% of outpatient and 54.63% of inpatient expenditures). In contrast, the share of Category A drugs declined steadily over time, from 19.59% to 9.56% in outpatient care and from 12.36% to 2.70% in inpatient care.

Associations Between Patient and Healthcare Institution Characteristics and Use of Withdrawn Drugs

After adjusting for demographic, occupational, and institutional factors, the likelihood of being prescribed a withdrawn drug declined significantly over time (compared to 2019, OR = 0.87, 95% CI: 0.84–0.91 for 2020; OR = 0.84, 95% CI: 0.80–0.87 for 2021, Table 3). Male patients (OR = 1.07, 95% CI: 1.04–1.10), retirees (OR = 1.20, 95% CI: 1.16–1.25), and those with supplementary public servant medical benefits (OR = 1.16, 95% CI: 1.12–1.20) were more likely to receive withdrawn drugs than their counterparts, while older adults (≥65 years) were less likely (OR = 0.90, 95% CI: 0.87–0.94). Prescriptions from tertiary, private, and general hospitals were more likely to include withdrawn drugs, whereas primary or lower-level facilities had lower odds (OR = 0.34, 95% CI: 0.29–0.40).

Subgroup analyses by care setting showed broadly similar patterns. Withdrawn drug prescribing declined in both outpatient and inpatient services, although the decline was more substantial in inpatient care (OR = 0.70, 95% CI 0.65–0.75 for 2021 vs. 2019; STable 5) compared with outpatient care (OR = 0.99, 95% CI 0.94–1.04; STable 6). Male, retired, and patients with supplementary medical benefits were consistently more likely to use withdrawn drug. Age patterns differed by setting: adults ≥65 years were less likely to receive withdrawn medications in outpatient care (OR = 0.76, 95% CI 0.72–0.79) but more likely in inpatient care (OR = 1.14, 95% CI 1.04–1.19). Primary or lower-level facilities consistently showed reduced prescribing risk in both settings.

Discussion

In this population-based study using real-world insurance data from a province in China, we identified the continued use of 38 drugs that had been withdrawn in other countries for safety concerns. Between 2019 and 2021, approximately 5.6% of insured patients received at least one withdrawn drug. Although the overall prevalence and expenditures associated with withdrawn drugs declined over time, a substantial proportion of patients continued to be exposed to medications

Table 3 Associations Between Patient and Institution Characteristics and Use of Withdrawn Drugs for Safety Concerns

	Number of Prescriptions	Use of Withdrawn Drugs, n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]
Year				
2019	221304	7186 (3.25)	1.0 (Ref)	1.0 (Ref)
2020	220221	6642 (3.02)	0.92 (0.89, 0.95)***	0.87 (0.84, 0.91)***
2021	414310	12017 (2.90)	0.90 (0.87, 0.93)***	0.84 (0.80, 0.87)***
Age, years				
< 65	581597	16568 (2.85)	1.0 (Ref)	1.0 (Ref)
≥ 65	274238	9277 (3.38)	1.04 (1.02, 1.07)**	0.90 (0.87, 0.94)***
Sex				
Female	404964	12139 (3.00)	1.0 (Ref)	1.0 (Ref)
Male	450871	13706 (3.04)	1.06 (1.03, 1.09)***	1.07 (1.04, 1.10)***
Race/ethnicity				
Han	727676	22352 (3.07)	1.0 (Ref)	1.0 (Ref)
Miao/Dong/Buyi	45394	1121 (2.47)	1.03 (0.96, 1.10)	1.02 (0.95, 1.09)
Others	82765	2372 (2.87)	0.99 (0.94, 1.04)	0.95 (0.90, 1.00)
Working status				
Working	459303	12103 (2.64)	1.0 (Ref)	1.0 (Ref)
Retired	396532	13742 (3.47)	1.14 (1.11, 1.17)***	1.20 (1.16, 1.25)***
Occupation				
Agriculture and fishery workers	134421	4332 (3.22)	1.0 (Ref)	1.0 (Ref)
Industrial and service workers	136488	4076 (2.99)	0.94 (0.90, 0.99)*	0.94 (0.90, 0.99)*
Public sector employees	413739	12333 (2.98)	1.02 (0.98, 1.06)	0.99 (0.95, 1.03)
Professionals	171187	5104 (2.98)	0.95 (0.90, 0.99)*	0.96 (0.92, 1.01)
Insurance				
No additional subsidy	687912	19624 (2.85)	1.0 (Ref)	1.0 (Ref)
With subsidy	167923	6221 (3.70)	1.11 (1.08, 1.15)***	1.16 (1.12, 1.20)***
In-province visit				
Yes	853142	25781 (3.02)	1.0 (Ref)	1.0 (Ref)
No	2693	64 (2.38)	1.76 (1.25, 2.46)**	1.22 (0.87, 1.72)
Healthcare institution				
Tertiary	373829	15635 (4.18)	1.0 (Ref)	1.0 (Ref)
Secondary	274037	6881 (2.51)	0.99 (0.87, 1.14)	0.96 (0.84, 1.10)
Primary or others	207969	3329 (1.60)	0.36 (0.31, 0.42)***	0.34 (0.29, 0.40)***
Public or private institution				
Public	728957	22869 (3.14)	1.0 (Ref)	1.0 (Ref)
Private	126878	2976 (2.35)	1.02 (0.92, 1.12)	1.16 (1.05, 1.28)**
General/specialized				
Specialized	59858	1733 (2.90)	1.0 (Ref)	1.0 (Ref)
General	795977	24112 (3.03)	1.05 (0.90, 1.21)	1.20 (1.04, 1.39)**

Notes: [a]Adjusted model included calendar year, age, sex, race/ethnicity, working status, occupation, insurance, whether or not in-province visit, types of healthcare institution, and city. *p<0.05, **p<0.01, ***p<0.001.
Abbreviations: CI, confidence interval; OR, odds ratio.

with known safety concerns. The findings highlight persistent gaps between global pharmacovigilance decisions and local clinical practice.

Our findings are consistent with earlier evidence suggesting that some drugs withdrawn in one jurisdiction remain available elsewhere. A global assessment of 137 national essential medicines lists found that 136 countries listed at least one withdrawn drug while a study in Argentina identified 17 drugs withdrawn in international markets were still in local use.[10,11] Our study demonstrates that, even within a well-regulated healthcare system such as China's, global safety withdrawals are not always mirrored by timely domestic action. We found that more than two-thirds of the withdrawn

drugs prescribed in China had been removed in more than one country. Yet 26 of these drugs remained available without restriction in China during the study period, underscoring how international regulatory decisions do not always translate into domestic action or clinical practice changes.

The therapeutic distribution of withdrawn drugs in our study—dominated by nervous system, gastrointestinal, and cardiovascular agents—aligns with patterns observed globally, reflecting classes with historically higher rates of post-marketing safety concerns.[19] Codeine and ganglioside were among the most frequently used and incurred highest expenditures in our sample, echoing their widespread historical use in China and other markets prior to tighter regulation.[20,21] The use and expenditures of ganglioside declined after its inclusion in the National Key Monitoring Drug Catalogue for Rational Use in 2019 and removal from the National Reimbursement Drug List in 2020,[22] suggesting that targeted policy interventions can be effective in curbing inappropriate use.

Despite overall progress, our results reveal persistent disparities in withdrawn drug use across demographic and institutional subgroups. However, the magnitude of most patient-level associations was modest. For example, male sex, retirement status, and insurance subsidy were associated with slightly higher odds of receiving withdrawn drugs, while older age was associated with a modestly lower likelihood after adjustment. These effect sizes suggest that, although statistically significant, individual demographic factors may have limited clinical impact on prescribing patterns. The elevated risk among retirees and those with better insurance coverage may reflect greater healthcare utilization or access to higher-tier facilities,[23] whereas the lower odds among older adults may indicate more cautious prescribing or closer medication review.

In contrast, institutional characteristics showed substantially larger and more policy-relevant differences. Prescriptions from tertiary hospitals and private or general hospitals were associated with significantly higher odds of withdrawn drug use, whereas primary or lower-level facilities showed much lower use. This pattern may reflect differences in clinical roles and formulary scope across hospital tiers. Tertiary hospitals manage more complex cases and maintain broader formularies, which may increase exposure to legacy or adjunctive drug use.[24] In contrast, primary care institutions typically have more limited formularies and focus on the management of common conditions and chronic diseases, which may inherently constrain the use of withdrawn drugs. Subgroup analyses revealed that the overall decline in withdrawn drug use was more pronounced in inpatient settings, which was largely driven by decline in the use of ganglioside after being included in the National Key Monitoring Drug Catalogue for Rational Use. By contrast, outpatient prescribing showed a slower decline, highlighting the need for oversight.

The continued use of drugs withdrawn from international markets in China underscores a broader challenge faced by countries-including high-income settings- in harmonizing pharmacovigilance practices across countries or regions. Medications withdrawn in one country may remain in clinical use elsewhere due to difference stem from differences in adverse event reporting systems, domestic epidemiology, therapeutic alternatives, and perceptions of benefit–risk balance.[9,25] However, delayed withdrawal or incomplete restriction can expose large populations to avoidable risks, especially when safer therapeutic alternatives exist.[26]

China has made significant progress in post-marketing surveillance, including the establishment of the National Adverse Drug Reaction Monitoring System and the Key Monitoring Drug Catalogue for Rational Use.[27] Nevertheless, our findings indicate that gaps remain in the translation of safety signals into prescribing practice. Several policy mechanisms may help reduce the continued use of withdrawn drugs. These include strengthening real-time pharmacovigilance and signal detection, expanding the key monitoring lists, and linking safety-based regulatory actions to reimbursement and hospital formulary management. In addition, integrating alerts on internationally withdrawn drugs into electronic prescribing and clinical decision support systems may help clinicians avoid prescribing high-risk medications. More timely data sharing and closer coordination across regulatory agencies could also reduce regulatory lag and promote greater international alignment in post-marketing drug safety governance.

This study has several strengths. It leverages a large, population-based administrative database capturing both inpatient and outpatient services, enabling comprehensive assessment of real-world prescribing patterns. By integrating internationally curated withdrawal databases, we identified drugs withdrawn for safety concerns with robust evidence. The inclusion of both individual- and institution-level factors further provides insights into drivers of continued use. However, some limitations must be acknowledged. First, the UEBMI database represents the urban employed population

and may not generalize to rural residents or uninsured groups. Second, prescription data lack clinical context and we were not able to determine indication appropriateness or dosage. Third, underreporting of over-the-counter drug use could underestimate total exposure. Fourth, not all drugs withdrawn abroad should necessarily be deemed inappropriate in China, given potential differences in patient populations, indications, and regulatory frameworks. Fifth, we relied on international databases and public records, some drugs with less-documented withdrawals may have been missed.

Conclusion

In summary, this study identified ongoing clinical use of 38 drugs that had been withdrawn internationally for safety concerns. These findings highlight the need to strengthen post-marketing drug surveillance, align national regulatory actions with global safety evidence, and enhance rational prescribing oversight.

Data Sharing Statement

The data supporting the findings of this study are not publicly available. Requests for access may be directed to the corresponding author (blyu@pku.edu.cn).

Ethics and Consent

This study was approved by the Institutional Review Board at Guizhou Medical University (2024-160). Individual participant consent was waived because of anonymous data.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declared no conflicts of interest in this work.

References

1. Aronson JK. Post-marketing drug withdrawals: pharmacovigilance success, regulatory problems. *Therapie*. 2017;72(5):555–561. doi:10.1016/j.therap.2017.02.005
2. Alomar M, Palaian S, Al-tabakha MM. Pharmacovigilance in perspective: drug withdrawals, data mining and policy implications. *F1000Research*. 2019;8:2109. doi:10.12688/f1000research.21402.1
3. Saluja S, Woolhandler S, Himmelstein DU, Bor D, McCormick D. Unsafe drugs were prescribed more than one hundred million times in the united states before being recalled. *Int J Health Serv*. 2016;46(3):523–530. doi:10.1177/0020731416654662
4. Lenzer J. FDA is incapable of protecting US "against another Vioxx". *BMJ*. 2004;329(7477):1253. doi:10.1136/bmj.329.7477.1253
5. Fung M, Thornton A, Mybeck K, Wu JHH, Hornbuckle K, Muniz E. Evaluation of the characteristics of safety withdrawal of prescription drugs from worldwide pharmaceutical markets-1960 to 1999. *Ther Innov Regul Sci*. 2001;35(1):293–317. doi:10.1177/009286150103500134
6. Lee KH, Kim GJ, Kim JH. Correlation between drug market withdrawals and socioeconomic, health, and welfare indicators worldwide. *J Korean Med Sci*. 2015;30(11):1567–1576. doi:10.3346/jkms.2015.30.11.1567

7. Davis C, Abraham J. Mapping the social and political dynamics of drug safety withdrawals in the UK and the US. University of Sussex; 2002. Available from: https://sussex.figshare.com/articles/report/Mapping_the_social_and_political_dynamics_of_drug_safety_withdrawals_in_the_UK_and_the_US_/23374409/1. Accessed November 13, 2025.
8. Lexchin J. Drug withdrawals from the Canadian market for safety reasons, 1963–2004. *CMAJ*. 2005;172(6):765–767. doi:10.1503/cmaj.045021
9. Li Y, Jiang Y, Wang H, Zhang L, Yang Y. Safety-related drug withdrawals in china between 1999 and 2021: a systematic investigation and analysis. *Drug Saf*. 2022;45(7):737–745. doi:10.1007/s40264-022-01185-0
10. Charles O, Onakpoya I, Benipal S, et al. Withdrawn medicines included in the essential medicines lists of 136 countries. *PLoS One*. 2019;14(12):e0225429. doi:10.1371/journal.pone.0225429
11. Buschiazzo H, Dorati C, Iusef Venturini N, et al. Medicines withdrawn in other countries due to safety concerns: should they continue to be available in the Argentine pharmaceutical market? *Rev Fac Cien Med Univ Nac Cordoba*. 2022;79(3):241–247. doi:10.31053/1853.0605.v79.n3.35443
12. Onakpoya IJ, Heneghan CJ, Aronson JK. Post-marketing withdrawal of 462 medicinal products because of adverse drug reactions: a systematic review of the world literature. *BMC Med*. 2016;14:10. doi:10.1186/s12916-016-0553-2
13. Gallo K, Goede A, Eckert OA, Gohlke BO, Preissner R. Withdrawn 2.0-update on withdrawn drugs with pharmacovigilance data. *Nucleic Acids Res*. 2024;52(D1):D1503–D1507. doi:10.1093/nar/gkad1017
14. Guo X. Circular on issuing the first batch of national key monitored rational drug use drug list (Chemical Drugs and Biological Products) _ documents of state council departments _ Chinese government network. Available from: https://www.gov.cn/zhengce/zhengceku/2019-11/19/content_5453479.htm. Accessed November 14, 2025.
15. Classification of National Economic Industries. National bureau of statistics of China. Available from: https://www.stats.gov.cn/sj/tjbz/gmjjhyfl/. Accessed November 14, 2025.
16. National Data. Available from: https://data.stats.gov.cn/easyquery.htm?cn=C01. Accessed November 14, 2025.
17. Lin Z. Notice of the general office of the state council forwarding the opinions of the ministry of labor and social security and the ministry of finance on implementing medical subsidies for national civil servants opinions on implementing medical subsidies for national civil servants __state council gazette No. 21, 2000 _ Chinese government website. Available from: https://www.gov.cn/gongbao/content/2000/content_60249.htm. Accessed November 14, 2025.
18. 2022 China health statistics yearbook. Available from: https://www.nhc.gov.cn/mohwsbwstjxxzx/tjtjnj/202305/49beded3bd984669bfe9089c6f231cf5.shtml. Accessed November 14, 2025.
19. Kocadal K, Saygi S, Alkas FB, Sardas S. Drug-associated cardiovascular risks: a retrospective evaluation of withdrawn drugs. *North Clin Istanb*. 2018;6(2):196. doi:10.14744/nci.2018.44977
20. Xiang C, Pan M, Shen Q, et al. Clinical consumption of compound opioid analgesics in china: a retrospective analysis of national data 2015-2018. *Biol Pharm Bull*. 2021;44(9):1316–1322. doi:10.1248/bpb.b21-00347
21. Wu X, Wu W, Wang Z, et al. More severe manifestations and poorer short-term prognosis of ganglioside-associated Guillain-Barré syndrome in Northeast China. *PLoS One*. 2014;9(8):e104074. doi:10.1371/journal.pone.0104074
22. Wen X, Wang Y, Chen X, Liu Y, Mao Z. The impact of key monitoring policy on the usage of policy-related drugs in Hubei Province, China. *Front Pharmacol*. 2023;14. doi:10.3389/fphar.2023.1088723
23. Beijing Municipal Healthcare Security Bureau. Headlines & updates _ work dynamics _ urban employee medical insurance | what are the reimbursement rates for outpatient and inpatient medical expenses? Check here. Available from: https://ybj.beijing.gov.cn/swdt/2020_gzdt/202501/t20250120_3994118.html. Accessed November 21, 2025.
24. Qian D, Lucas H, Chen J, Xu L, Zhang Y. Determinants of the use of different types of health care provider in urban China: a tracer illness study of URTI. *Health Policy*. 2010;98(2):227–235. doi:10.1016/j.healthpol.2010.06.014
25. Frank C, Himmelstein DU, Woolhandler S, et al. Era of faster FDA drug approval has also seen increased black-box warnings and market withdrawals. *Health Affairs*. 2014;33(8):1453–1459. doi:10.1377/hlthaff.2014.0122
26. Onakpoya IJ, Heneghan CJ, Aronson JK. Delays in the post-marketing withdrawal of drugs to which deaths have been attributed: a systematic investigation and analysis. *BMC Med*. 2015;13:26. doi:10.1186/s12916-014-0262-7
27. Hou Y, Li X, Wu G, Ye X. National ADR monitoring system in China. *Drug Saf*. 2016;39(11):1043–1051. doi:10.1007/s40264-016-0446-5