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# Antidepressant use and expenditure in the treatment of patients with depression: Evidence from China urban medical claims data



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ARTICLE INFO	A B S T R A C T
<i>Keywords:</i> Antidepressant Depression Expenditure China	Objectives: Few studies have analyzed the use of antidepressants among population suffering from depression in China. This study aimed to describe the prevalence and the cost of commonly prescribed antidepressants among patients with depression. <i>Methods:</i> This study used data that comprised 5% random sample of claims data from China's Urban Basic Medical Insurance between 2013 and 2016. We estimated the prevalence, calculated the proportions of those on antidepressant treatment as well as those on specific drugs. <i>Results:</i> Among 26 826 patients with depression, 62.31% were prescribed with antidepressants in urban China, and the estimated average annual total cost of antidepressants per patient was RMB887.7(USD140.9). The prevalence of antidepressant prescription was higher among patients aged 15–24 years, having URBMI insur- ance, with recurrent depression and having severe or moderate depression. Approximately 9.3% of patients used more than one type of antidepressants and 19% of patients have only one prescription of antidepressant in a year. <i>Conclusion:</i> Our analyses showed that antidepressant prescribing was prevalent among patients with depression, particularly in adolescents and youth groups, and are subject to variation with clinical features and different insurance scheme. Further investigation of antidepressant use patterns, such as duration, combination and switching, as well as treatment trajectories will facilitate our understanding of the pharmacotherapy practices of depressive disorders.

### 1. Introduction

Antidepressants are the most widely prescribed class of drugs and the evidence-based treatment that is recommended by international guidelines for severe, moderate, as well as the chronic courses of depression. The optimal use of antidepressant could reduce symptoms of low mood and motivation, along with the personal and social burden. The number of antidepressants available on the market has increased markedly during the past decades, providing with a great variety of treatment options for prescribers (Gomez-Lumbreras et al., 2019; Luo et al., 2020). Several factors, including clinical characteristics, reimbursement policies, drug profile were involved in the choice of an antidepressant. With the increasing prescription and widely spreading use of antidepressants, the investigation on the actual prescribing practices among patients with depression has become essential to ensure medication safety and to achieve the optimal therapeutic outcome.

Depression has become one of the major public health concerns in

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China. The prevalence of depression and the disability-adjusted life years attributable to depression rose rapidly during recent years (Ren et al., 2020; Phillips et al., 2009; Huang, 2010). However, few studies have analyzed the use of antidepressants among population suffering from depression in China. At the same time, the growing availability of electronic health insurance claims databases has provided the opportunity to obtain detailed assessments of drug consumption at a patient level and across various healthcare settings. Therefore, we aimed to describe the prevalence and the cost of commonly prescribed antidepressants, as well as the pattern of use in terms of socio-demographic characteristics and clinical conditions among patients with depression, based on the claims database of urban basic medical insurance, the predominant insurance program for the urban population of China.

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### 2. Methods

### 2.1. Data source

The data used in this study were 5% random sample of China Urban Employee's Basic Medical Insurance (UEBMI) and China Urban Residents' Basic Medical Insurance (URBMI) beneficiaries' insurance claims from January 2013 to December 2016. The sample was drawn using systematic random sampling strategy with a random start. In brief, every Kth record from a population of size N was selected, with the first sample record picked from a random number table. In such a way, a sample size of n was obtained, where N/n > = K. UEBMI and URBMI are the major health insurance schemes and covered more than 90% of urban residents in China mainland (Yu, 2015). The claims data, which were collected and sampled by China Health Insurance Research Association (CHIRA). included 84 cities (including both megacities like Beijing, Shanghai, Shenzhen etc. and small to mid-sized cities like Mianyang in Sichuan province and Datong in Shanxi province etc.) recorded beneficiaries' demographic information, diagnoses and cost of health services. Each beneficiary was assigned a sample weight that equals to the reciprocal of the selection probability to correct for systematic differences in probability sampling.

### 2.2. Diagnosis of depression

ICD-10 (the 10th revision of the International Statistical Classification of Diseases) was used to identify patients with depression. The principal diagnosis codes were F32.0-F32.3, F32.8, F32.9, F33.0-F33.3, F33.8 and F33.9. Diagnosis of depression was made by qualified clinical psychiatrists. Our study sample comprise 26 826 patients with depression identified between 2013 and 2016 in the claims data.

### 2.3. Medications

Antidepressant prescriptions were identified according to the World Health Organization Anatomical Therapeutic Chemical Index, and further classified into three categories: (1) N06AA, non-selective monoamine reuptake inhibitors (tricyclic antidepressants, TCAs) (2) N06AB, selective serotonin reuptake inhibitors (SSRIs) (3) N06AX, other antidepressants. We provide the prescription pattern of paroxetine, escitalopram, sertraline, mirtazapine, venlafaxine, citalopram, duloxetine and fluoxetine, which are the eight most commonly prescribed antidepressants in our dataset.

### 2.4. Sociodemographic and other health-related characteristics

Sociodemographic information was collected for each subject, including age (categorized into < 15, 15–24, 25–44, 45–64, > = 65), sex (male or female), insurance type (UEBMI or URBMI), diagnosis (single episode (ICD-10: F32.x) or recurrent depressive disorder (F33.x)) and degree (severe (F32.2/F32.3, F33.2/F33.3), moderate (F32.1, F33.1), mild (F32.0, F33.0) or other (F32.8/F32.9, F33.8/F33.9) of depression.

### 2.5. Ethical approval

Because the claims data we used were anonymized database and had no impact on patients' health and service utilization, the informed consent was exempted. This study was approved by the Ethics Committee of Beijing University of Chinese medicine (No.2019BZHYLL0201).

### 2.6. Statistical analysis

Antidepressant prescribing was defined as patients having a prescription of antidepressant. Annual period prevalence of antidepressant prescribing was calculated by dividing the number of patients having at least one prescription for an antidepressant in a calendar year by the total number of patients with depression in that calendar year in a database during the study period. We defined patients receiving multiple antidepressants as those who were prescribed with different antidepressants within the same round or in different rounds within the same year, while those who were only with one prescription of antidepressants in the same year were regarded as "patients receiving one prescription". Expenditure was defined as the annual average cost of antidepressants per patient. Subgroup analyses by age, sex, diagnosis, degree and insurance type, as well as drug classes. The software Stata version 15 for Mac (Stata Corp, College Station, TX, USA) was used for the statistical analysis.

### 3. Results

### 3.1. Prescription patterns of antidepressants among patients with depression

Table 1 provides the prevalence of antidepressant prescribing among patients with depression from 2013 to 2016 in urban China. Among 26 826 patients, 62.31% were prescribed with antidepressants, 46.95% were prescribed with SSRIs, 22.58% were prescribed with other antidepressants and only 2.27% were prescribed with TCAs. Paroxetine (13.52%), sertraline (11.68%), escitalopram (11.42%), mirtazapine (8.39%), venlafaxine(8.38%), citalopram(6.97%), fluoxetine (5.22%), and duloxetine(4.56%) were the eight most commonly prescribed antidepressants. The prevalence of antidepressant prescription was higher among patients aged 15–24 years, having URBMI insurance, with recurrent depression and having severe or moderate depression.

## 3.2. Expenditure patterns of antidepressants among patients with depression

Table 2 provides the annual average expenditure of antidepressants per patients. From 2013 to 2016, the annual average cost of antidepressants for patients with depression was RMB 887.73(USD 140.91). And cost for TCAs users, SSRIs users and other antidepressants users were RMB66.92(USD10.62), RMB789.12(USD125.26), and RMB817.60 (USD129.78), respectively. And escitalopram and duloxetine incurred higher cost than other type of antidepressants. The cost increased with increasing age, and higher among male patients, UEBMI beneficiaries, patients with recurrent depression and those having moderate depression.

## 3.3. Multiple antidepressants using and proportion of patients with only one prescription

The prevalence of patients using multiple antidepressants was reported in Fig. 1. Totally 9.27% of all patients with depression were prescribed with multiple antidepressants, and the prevalence ranges from 14.87% for all antidepressant users to 60.57% for mirtazapine users. The prevalence of patients only have one prescription in a year was reported in Fig. 2. 19.00% of all patients with depression having only one prescription in a year and the prevalence ranges from 21.70% for escitalopram users to 37.71% for fluoxetine users.

### 4. Discussion

This study provides a recent and a distinctive overview of antidepressant prescribing patterns among patients with depression in urban China. Overall, more than 60% of patients with depression used antidepressants. The most commonly prescribed antidepressants were selective serotonin reuptake inhibitors and we found that the prevalence and the cost of antidepressant prescribing varies with age and clinical features. Additionally, approximately 9.3% of patients used more than one type of antidepressant in a year, indicating switching to or combined

Prevalence of	antidepressant pr	escribing among 1	patients with depre	ssion in urban	China, 2013–201	[6 (N(%)).						
	All	XN06AX	XN06AB	XN06AA	Paroxetine	Escitalopram	Sertraline	Mirtazapine	Venlafaxine	Citalopram	duloxetine	fluoxetine
All	16,715(62.31)	6056(22.58)	12,595(46.95)	609(2.27)	3626(13.52)	3.64(11.42)	3133(11.68)	2252(8.39)	2248(8.38)	1871(6.97)	1222(4.56)	1400(5.22)
Age												
< 15	48(61.54)	4(5.13)	44(56.41)	0(0)	4(5.13)	4(5.13)	31(39.74)	1(1.28)	2(2.56)	1(1.28)	2(2.56)	3 (3.85)
15-24	432(69.34)	127(20.39)	337(54.09)	8(1.28)	53(8.51)	82(13.16)	140(22.47)	38(6.10)	62(9.95)	27(4.33)	22(3.53)	47(7.54)
25-44	4589(66.78)	1779(25.89)	3347(48.70)	121(1.76)	841(12.24)	944(13.74)	856(12.46)	597(8.69)	708(10.30)	429(6.24)	379(5.52)	384(5.59)
4564	7474(60.32)	2737(22.09)	5646(45.57)	305(2.46)	1788(14.43)	1319(10.65)	1335(10.77)	972(7.85)	1041(8.40)	845(6.82)	549(4.43)	609(4.92)
> = 65	3836(61.35)	1268(20.28)	2963(47.39)	141(2.25)	838(13.40)	660(10.55)	705(11.27)	580(9.28)	388(6.21)	553(8.84)	250(4.00)	323(5.17)
Sex												
Male	6217(62.22)	2249(22.51)	4647(46.51)	214(2.14)	1329(13.30)	1141(11.42)	1195(11.96)	846(8.47)	829(8.30)	651(6.52)	479(4.79)	520(5.20)
Female	10,162(62.64)	3666(22.60)	7690(47.40)	361(2.23)	2195(13.53)	1868(11.51)	1872(11.54)	1342(8.27)	1372(8.46)	1204(7.42)	723(4.46)	846(5.21)
Insurance ty	pe											
UEBMI	14,846(61.90)	5300(22.10)	11,210(46.74)	453(1.89)	3185(13.28)	2728(11.37)	2743(11.44)	1928(8.04)	1980(8.26)	1731(7.22)	1084(4.52)	1258(5.25)
URBMI	1533(68.68)	615(27.55)	1127(50.49)	122(5.47)	339(15.19)	281(12.59)	324(14.52)	260(11.65)	221(9.90)	124(5.56)	118(5.29)	108(4.84)
Diagnosis												
Single	15,625(61.79)	5627(22.25)	11,766(46.53)	525(2.08)	3278(12.96)	2875(11.37)	2925(11.57)	2087(8.25)	2095(8.28)	1783(7.05)	1129(4.46)	1342(5.31)
Recurrent	1090(70.92)	429(27.91)	829(53.94)	84(5.47)	348(22.64)	189(12.30)	208(13.53)	165(10.74)	153(9.95)	88(5.73)	93(6.05)	58(3.77)
Degree												
Severe	176(70.40)	103(41.20)	117(46.80)	5(2.00)	30(12.00)	43(17.20)	31(12.40)	39(15.60)	49(19.60)	15(6.00)	18(7.20)	15(6.00)
Moderate	567(86.30)	208(31.66)	464(70.62)	22(3.35)	145(22.07)	127(19.33)	103(15.68)	97(14.76)	71(10.81)	86(13.09)	38(5.78)	13(1.98)
Mild	160(59.26)	53(19.63)	128(47.41)	9(3.33)	28(10.37)	44(16.30)	36(13.33)	31(11.48)	23(8.52)	24(8.89)	5(1.85)	6(2.22)
Other	15,575(61.91)	5604(22.28)	11,701(46.51)	550(2.19)	3336(13.26)	2820(11.21)	2906(11.55)	2049(8.14)	2078(8.26)	1734(6.89)	1149(4.57)	1354(5.38)

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use with another antidepressant. And 19% of patients have only one prescription of antidepressant in a year, suggesting the un-sustained use.

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First of all, 62.31% patients with depression were prescribed with antidepressants in urban China, and the estimated average annual total cost of antidepressants per patient was RMB887.7(USD140.9). The prevalence was close to the result of one study based on the Medical Expenditure Panel Survey in United States, which showed that 69.4% of patients with major depressive disorder were prescribed with antidepressant in 2015 (Luo et al., 2020). However, comparison of results of our study with estimation from other countries is difficult owing to differences in the methods applied, data sources used, and population groups selected. The health insurance claims data with detailed records make our result more representative for this issue in urban China.

The most commonly prescribed four antidepressants among patients with depression in urban China were paroxetine, escitalopram, sertraline and mirtazapine, with most of the antidepressants were SSRIs and other antidepressants, which were far more prevalent than TCAs. This pattern is consistent with that of studies from United States (Luo et al., 2020) and European countries (González-López et al., 2015; Haller et al., 2019). SSRIs like escitalopram, paroxetine, and sertraline were recommended by the clinical guidelines as the preferred medication for depression treatment in most of countries, accounting for more than 60% of the market (Guidi et al., 2017; Stahl et al., 2017). And the average annual cost of escitalopram and duloxetine was higher than that of other antidepressants. The higher price of escitalopram was reported by one study based on hospital prescribing data of major cities in China (Yu et al., 2020). The safety and efficacy of escitalopram has been demonstrated by several studies (Pastoor and Gobburu, 2014), and it also have a cost-utility advantage over other antidepressants for the pharmacotherapy of major depression (Wade et al., 2008). Only 2.27% of patients with depression were prescribed TCAs despite its lowest annual average cost (RMB 66.92(USD10.62)). A similar pattern has also been observed in many other countries (Luo et al., 2020; Haller et al., 2019). The low prescribing rate may be explained by its disadvantages like cardiovascular side effects, significant drug interaction, as well as the higher overdose toxicity (Peretti et al., 2000; Spina and Scordo, 2002).

The age pattern of antidepressant prescribing in China revealed distinctive feature. The prevalence was highest among the age group of 15-24 years old. Most of these patients were prescribed sertraline, which has been considered to be a safe SSRI for children and adolescents with major depressive disorder for a long time. Sertraline was reported with lower risk to induce treatment-emergent extrapyramidal symptoms, compared to other SSRIs like paroxetine and fluoxetine. The age pattern of the antidepressant cost is also worth to mention. The annual average cost increased with increasing age. This pattern may be explained by the fact that the proportion of patients with recurrent depression and the proportion of patients prescribed with multiple antidepressants increased with increasing age in our sample (from 0.0% patients with recurrent depression in < 15 to 4.67% in 65+ age group, from 3.85% patients with multiple antidepressant prescription in < 15to 8.96% in 65+ age group), since commonly, the antidepressant costs were higher for patients in these two categories (Haller et al., 2019). The prescribing pattern in diagnosis and degree of depression is not surprising and consistent with studies in other countries (Luo et al., 2020). Depressive patients of more severe and longer duration symptoms and episodes tend to prefer pharmacotherapy treatment with antidepressants (Aikens et al., 2008; Van Schaik et al., 2004).

We also observed marked disparities of antidepressant use between UEBMI and URBMI participants, with higher proportion of prescribing prevalence but lower annual cost of antidepressants among patients with URBMI compared to that among patients with UEBMI. The disparities in insurance medical coverage, benefits and reimbursement rate between these two schemes may explain the observed associations. UEMBI, which targeted urban employees covered more services and medication and with a higher reimbursement rate (68%) than URBMI

	All	XN06AX	XN06AB	XN06AA	Paroxetine	Escitalopram	Sertraline	Mirtazapine	Venlafaxine	Citalopram	duloxetine	fluoxetine
All	887.73	817.60	789.12	66.92(6.27)	773.77(26.18)	1047.25(42.82)	572.60(21.23)	548.69	890.58(34.50)	668.92(28.92)	1082.13(56.61)	655.38(29.19)
	(14.99)	(22.75)	(14.69)					(30.33)				
Age												
< 15	288.74	206.16	300.53	0	218(-)	117(-)	339.12(67.86)	31.12(-)	187(-)	-	200.18(10.58)	268.49(-)
	(47.61)	(17.88)	(54.03)									
15-24	690.86	534.80	707.04	72.54(51.63)	402.18(133.12)	1050.69	488.60(78.01)	229.93	650.10(213.43)	706.50	678.474	811.03(274.51)
	(77.55)	(110.55)	(91.70)			(252.16)		(56.72)		(347.22)	(178.44)	
25-44	848.87	795.80	739.53	74.12(14.68)	681.94(49.90)	1101.37(81.09)	524.36(39.56)	472.61	855.19(61.26)	513.35(42.49)	1043.18(86.70)	543.90(38.60)
	(26.81)	(37.67)	(28.40)					(38.94)				
45-64	886.05	805.11	787.53	61.18(8.20)	764.55(37.10)	996.01(62.70)	570.96(31.34)	576.45	869.71(48.16)	696.16(43.76)	1113.50(89.69)	713.66(46.28)
	(22.43)	(34.63)	(21.30)					(58.14)				
> = 65	904.42	889.27	798.83	59.39(10.13)	772.89(54.39)	1033.54(92.56)	603.27(44.52)	603.10	1050.13(93.34)	743.66(57.91)	1093.82	630.20(57.58)
	(33.09)	(56.25)	(30.51)					(52.42)			(146.74)	
Sex												
Male	880.18	861.38	757.85	64.35(10.13)	776.03(50.35)	1038.95(76.49)	518.34(30.59)	576.96	898.50(57.10)	580.28(46.94)	1138.05(92.86)	565.69(39.71)
	(28.06)	(41.55)	(26.05)					(62.73)				
Female	868.79	784.53	782.11	63.62(7.39)	721.24(28.55)	1041.10(52.14)	586.34	528.83	884.76(44.20)	709.25(35.60)	1035.72(72.87)	692.77(38.74)
	(17.21)	(27.06)	(17.57)				(27.68))	(30.78)				
Insurance t	vpe											
UEBMI	885.75	823.24	785.63	63.91(6.53)	756.00(27.60)	1057.20(45.61)	565.78(22.16)	556.91	896.06(36.63)	670.57(29.33)	1083.18(59.75)	660.23(30.30)
	(15.91)	(24.48)	(15.50)					(33.87)				
URBMI	718.70	708.59	617.11	63.93(15.17)	568.32(58.21)	823.57(129.48)	494.91(47.63)	465.76	815.75(114.38)	569.96	956.09(199.09)	480.74(81.08)
	(39.72)	(63.02)	(38.87)					(60.11)		(116.97)		
Diagnosis												
Single	865.38	814.44	763.78	49.16(5.24)	733.91(26.67)	1025.25(43.13)	554.97(20.93)	552.85	884.89(35.73)	665.73(29.17)	1073.92(58.84)	628.51(28.00)
U	(15.27)	(23.69)	(14.77)					(32.24)				
Recurrent	1219.70	859.38	1173.76	161.40	1175.90	1459.64	816.53	501.76	981.10(131.41)	735.40	1202.55	1384.36
	(69.25)	(81.12)	(76.35)	(24.54)	(971.14)	(243.54)	(122.17)	(80.80)		(172.96)	(206.32)	(285.42)
Degree												
Severe	800.26	548.71	719.72	37.26(20.28)	474.84(78.28)	789.49(153.08)	730.66	321.36	580.64(112.66)	565.27	496.84(112.66)	352.18(72.25)
	(95.89)	(104.80)	(87.76)				(202.74)	(87.57)		(245.76)	. ,	. ,
Moderate	921.43	838.38	725.14	59.38(29.57)	680.79(80.12)	797.88(197.44)	505.36(78.57)	391.00	1131.19	427.97(54.15)	1366.14	1636.96
	(69.32)	(114.54)	(61.76)					(46.06)	(255.91)		(313.58)	(488.38)
Mild	717.63	674.88	586.67	58.70(31.58)	634.15(154.50)	550.39(220.22)	568.34	326.10	665.78(128.92)	394.86	2465.79	174.55(63.90)
	(105.61)	(146.69)	(90.14)				(176.80)	(62.62)		(114.78)	(1996.19)	. ,
Other	871.93	818.29	775.71	63.71(6.24)	747.60(27.27)	1056.40(45.41)	558.38(21.42)	560.71	892.08(36.43)	681.90(30.24)	1068.19(59.02)	634.55(28.25)
	(15.57)	(24.08)	(15.25)					(33.41)				

 Table 2

 Annual average expenditure of antidepressant among patients with depression in urban China, 2013–2016 (RMB(SE)).







Fig. 2. Proportion of patients with one prescription of antidepressant among patients with depression in urban China, 2013–2016(%).

(48%), which targeted elderly, children and unemployed population that not covered by other health insurance schemes in urban area (Yu, 2015). Additionally, the adverse selection has been reported for URBMI enrollment, with higher self-reported prevalence of non-communicable diseases among people with URBMI than those without insurance (Mao et al., 2019). Such possibility also echoes with clinical characteristics of our samples. The proportion of severe and moderate depression among patients with URBMI (9.59%) was higher compared to that among patients with UEBMI.

Patients who were prescribed with more than one antidepressants (multiple use of antidepressants) in a year referring to both patients with combination therapy and patients who switch previous monotherapy to a new drug in that year. Our study showed that 9.27% of patients with depression were prescribed with more than one antidepressants from 2013 to 2016, which were lower than the proportion reported by one study from United States (18.45% in 2015) (Luo et al., 2020). We also found that the proportion of multiple use was distinctively higher among users of mirtazapine, a noradrenaline and selective serotonin antagonist. Mirtazapine has been demonstrated to have a faster onset of action and higher efficacy than SSRIs for depression. For patients who fails to respond to the first antidepressant, switching to or combining SSRIs with mirtazapine is routinely recommended as an alternative therapeutic treatment (Blier et al., 2010).

The proportion of patients with only one prescription of antidepressant in a year is an indicator of a subgroup in which treatment is not sustained. Our result suggests that about 30% of patients that prescribed with antidepressant have only one prescription in a year, which were similar to the prevalence reported in other countries (Abbing-Karahagopian et al., 2014). For example, proportions of patients with one prescription reported in Denmark were 27% in 2008 (Abbing-Karahagopian et al., 2014). Besides, we found that such cases were more prevalent among users of TCAs and fluoxetine, which may be explained by its side effects and drug-drug interaction, as mentioned before.

### 4.1. Limitation

This study is subject to several limitations. First of all, extrapolation from our findings to the situation of patients with depression in China should be cautious because the claims database we used was restricted to urban population. Secondly, although the claims data provide detailed information on medication prescriptions, which can be considered complete, the information of reimbursement data does not reflect actual use. Thirdly, the cross-sectional data only allow us to investigate the antidepressant use in the selected year, we are unable to estimate the initiation of use among patients with depression. Additionally, we failed to investigate the dosage of prescribed antidepressant among patients with depression, since the information was unavailable in the dataset we acquired. Future research focusing on this important aspect to assess the appropriateness of antidepressants prescribing in China is warranted.

### 5. Conclusion

Our study represents the first detailed descriptions of antidepressant prescription patterns for patients diagnosed with depression in urban China. Overall, our analyses showed that antidepressant prescriptions are prevalent among patients with depression, particularly in adolescents and youth groups, and are subject to variation with clinical features and different insurance scheme. Further investigation of antidepressant use patterns, such as duration, combination and switching, as well as treatment trajectories will facilitate our understanding of the pharmacotherapy practices of depressive disorders. This study can be the first step to carry forward further investigation of routine data regarding antidepressant use in China.

#### CRediT authorship contribution statement

**Ruoxi Ding:** Visualization, Formal analysis, Writing – original draft, Writing – review & editing. **Yanshang Wang:** Visualization, Writing – original draft, Writing – review & editing. **Xin Ye:** Visualization, Writing – original draft, Writing – review & editing. **Dawei Zhu:** Writing – original draft, Writing – review & editing. **Xuefeng Shi:** Investigation, Supervision, Writing – original draft, Writing – review & editing. **Ping He:** Writing – original draft, Investigation, Supervision, Writing – review & editing.

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### **Declaration of Competing Interest**

The authors declare no potential conflicts of interest

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N/A

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