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Appropriateness of red blood cell use in China in the last thirteen years: A systematic review

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Abstract

Objective: To determine both the rates of appropriate red blood cells (RBCs) use in China and where inappropriate use is particularly prevalent.

Background: In China, obtaining the comprehensive picture in unnecessary RBCs transfusion is helpful for understanding the strained blood supplies and targeting training of clinicians.

Study design: and methods: Eligible studies were mainly retrieved from four Chinese medical databases and four databases from abroad. In all studies, the appropriateness of RBCs transfusion in transfusion cases, blood request forms, or RBC units within the last thirteen years was determined by using national guidelines. Relationships between RBCs-transfusion appropriateness and type of RBCs-transfusion record, geographical region, level of hospital (LOH-2 and LOH-3), department type (operative vs. non-operative), and study quality (high vs. low) were analyzed by Chi-squared tests.

Results: On average, 72.30% (standard deviation, SD = 18.87%) of all cases/forms/units throughout China were appropriate. The appropriateness of RBCs-

transfusion differed significantly depending on RBCs-transfusion record type, they were 69.10%, 68.85%, and 75.64% for blood request forms, transfusion cases, and RBCs units, respectively ($p < 0.001$). The southwest and northeast were the most (80.62%) and the least (66.57%) appropriate transfusion areas, respectively. The coefficients of variances (CV) for the geographical regions differed significantly (0.029–0.39). LOH-3 were more appropriate than LOH-2 ($p < 0.001$). Non-operative departments were more appropriate than operative departments ($p < 0.001$). High-quality studies reported higher appropriate rate than low-quality studies (74.48% vs. 69.72%, $p < 0.001$).

Conclusion: In China, unnecessary RBCs transfusion was common and may exacerbate the current pressure on blood supplies. Clinicians in certain geographical regions, LOH-2, and operative departments should be targeted with training in transfusion medicine.

Keyword: Evidence-based medicine

1. Introduction

Red blood cells (RBCs) are the most clinically important of all blood components and cannot be substituted. The safety and adequacy of RBCs has always been a concern all around the world and especially in China whose blood collection and supply are unbalanced. In China, the inappropriate use of RBCs in the clinic has recently been reported, which may negatively impact the already limited blood supply of RBCs. Especially, due to developments in China's economy and society, the expansion of the medical security system covering both rural and urban areas has vastly increased the numbers and sizes of hospitals from all levels [1]. Specifically, between 2005 and 2013, the number of second-level hospitals (LOH-2) and third-level hospitals (LOH-3) increased by 30% and 89%, respectively. Moreover, the number of beds in LOH-2 and LOH-3 increased by 98% and 180%, respectively. This is significantly given that the number of beds in LOH-2 and LOH-3 accounted for 91.1% of all hospital beds in China [2]. These relatively rapid changes have in turn placed great pressure on blood component inventory, as shown by Xiao *et al*, they reported that the rapidly growing numbers of inpatients in China were the main cause of the sharp rise in the demand for blood components [3]. There is thus an urgent need to assess, with the aim of improving the appropriateness of blood transfusion occurring in LOH-2 and LOH-3.

Other possible problems hampering the appropriate administration of blood components in China include the fact that the rate of voluntary blood donation remains relatively low: in 2011, it was only 8.53 donors per 1000 [4] and it wasn't until 2016 that China's blood donation rate has achieved the rate recommended by World Health Organization (WHO). Moreover, the professional training system that teaches blood

transfusion physicians is not fully developed in China: transfusion medicine continues not to be listed in the national classification of disciplines and only five medical colleges currently teach transfusion medicine [5, 6]. As a result, there are very few well-trained professional transfusion medicine physicians in the blood transfusion departments in China, and even fewer personnel who can actively monitor and evaluate the clinical use of blood components at a local and national level [7]. These observations suggest that there may be substantial unreasonable use of RBCs throughout the hospital system and that this may strongly contribute to the increasing pressure on blood inventories in China [8].

Several studies have assessed the appropriateness of the clinical use of RBCs in specific areas and hospitals in China. However, many of the studies' results were discrepant and were unlikely to reflect the overall status in China accurately [9]. To obtain a more comprehensive picture of inappropriate RBCs transfusion in China, we performed a present systematic literature review on the clinical use of RBCs in China. We discovered that there was substantial unnecessary use of RBCs throughout China and that it was particularly prevalent in certain clinical departments, hospitals, and geographical regions. This information will help guide the targeted education of clinicians in transfusion medicine. It will also benefit subsequent research on the clinical use of RBCs.

2. Results

2.1. Study characteristics

In total, 979 papers were retrieved, among which 189 were related to RBCs transfusion. Of these, 115 (60.85%) were excluded during screening (Fig. 1). At last, we included 74 articles (39.15%) from four main Chinese databases. Among the number of these included articles, transfusion cases, blood request forms and RBC units were 40, 23 and 11, respectively. Of the 32 provinces/municipalities, 23 (71.88%) covered the appropriateness of RBCs transfusion in mainland China (except for Hong Kong & Macau). 226 LOH-3, 429 LOH-2, and 105,696 transfusion cases were totally assessed in these studies. Five studies examined RBCs use in a whole province, namely, Jiangxi [10], Hebei [11], Zhejiang [12], and Anhui [13, 14]. 26 studies assessed RBCs use in more than one hospital in a city or county. The remaining 43 studies focused on a single hospital. Among these papers, 11 were considered to be high-quality, while 63 were considered to be low-quality.

2.2. Appropriate RBCs use associated with different types of transfusion records

On average, 72.30% (SD = 18.87%) of all cases/forms/units throughout China were appropriate. The appropriateness and differences of clinical use between the types of RBCs-transfusion record were shown in Table 1.

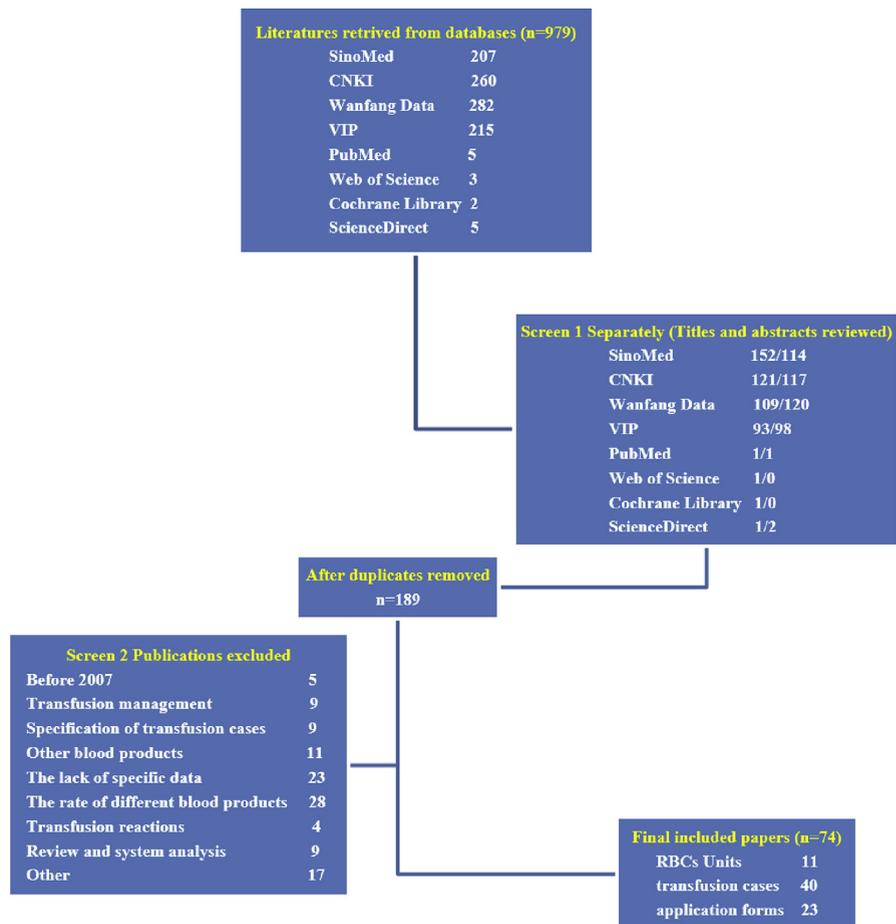


Fig. 1. Flowchart of study selection. Notes: The process in screen 1 was screened by two researchers, separately. The third researcher made the ultimate decision when the opinions of the first two researchers were different.

2.3. Appropriate RBCs use in different hospital levels

Of the studies that examined the appropriateness of transfusion cases/forms, 14 and 42 focused only on LOH-2 and LOH-3, respectively. Table 2 presented a detailed comparison between LOH-2 and LOH-3.

2.4. Appropriate RBCs use in clinical departments

The differences between different clinical departments were also observed in Tables 1 and 2. The operative departments had significantly lower appropriate transfusion rates than the non-operative departments regardless of the study objects ($p < 0.001$).

2.5. Appropriate RBCs use in different regions

The amount of research in the seven Chinese geographical regions varied markedly: 20 studies that included 143 hospitals and 47,780 transfusion cases were performed in

Table 1. The number and appropriate rate of different subjects.

Study subjects	Overall	Medicine	Surgery	Gynecology & obstetrics	Pediatrics
Request forms	24386 69.10%	8722 82.90%	15208 61.12%	318 78.61%	69 100%
Units of RBCs	39873 75.64%	13084 90.35%	20086 63.14%	4560 81.40%	2143 90.76%
Transfusion cases	24153 68.85%	7400 84.27%	13796 60.09%	2315 73.69%	642 87.07%
<i>P</i> value	<0.001	<0.001	<0.001	<0.001	<0.001

Notes: *P* values were acquired by performing comparisons between three groups in the same column. Then we also calculated *P* values between any two groups in the same column and the difference is significant unless noted otherwise. The overall appropriate rate between request forms and transfusion cases, $P = 0.556$ was obtained. $P = 0.075$ was obtained by comparing the statistics between request forms and transfusion cases in the surgery department. In the departments of gynecology and obstetrics, $P = 0.060$ was obtained by comparing the appropriateness of transfusion cases and blood request forms; $P = 0.219$ was obtained by comparing the appropriateness between application forms and RBCs units.

eastern China, whereas only 6 studies that included 7,271 cases were performed in northern China (Fig. 2). The cases/forms were most frequently appropriate in southwest China (80.62%), followed by northern China (79.34%), eastern China (78.25%), northwest China (78.22%), central China (71.07%), southern China (70.97%) and northeast China (66.57%). The appropriate rate of RBCs transfusion in various regions did not correlate significantly with the ratio of LOH-3 to LOH-2 ($r = 0.071$, $p = 0.879$) or the ratio of all cases from internal medicine and surgery ($r = 0.036$, $p = 0.939$). Although the average frequency of appropriate RBCs use in different areas was 74.95% (SD = 5.36%, acquired from group of cases/forms), the different areas differed markedly in terms of CV. For example, the CV of medicine in eastern China was 0.029, while the CV of surgery in northwest China was 0.387 (Fig. 3).

2.6. Frequencies of appropriate RBCs use reported in high- and low-quality studies

Eleven studies were classified as high-quality studies. The remaining 63 papers were recognized as being of low-quality. The high-quality studies reported appropriate RBCs use more frequently in the departments overall than the low-quality studies ($p < 0.05$). This was also observed within the operative departments, namely, surgery, gynecology and obstetrics ($p < 0.001$). However, this difference between the high-quality and low-quality studies was not observed in the non-operative departments ($p = 0.815$) (Table 3).

3. Discussion

In the 74 articles that met the screening criteria in this systematic review, the overall frequency of appropriate RBCs transfusion in China ranged from 53.60% to 93.60%

Table 2. The number and appropriateness of RBCs used in LOH-2 and LOH-3 according to clinical departments.

Level of hospital	Overall		Medicine		Surgery		Gynecology & obstetrics		Pediatrics	
	cases/forms	units	cases/forms	units	cases/forms	units	cases/forms	units	cases/forms	units
LOH-2	9918 66.51%	8879 77.45%	3789 84.58%	3280 91.46%	5560 54.93%	3683 61.85%	169 76.92%	1916 84.6%	400 71%	398 71.86%
LOH-3	28439 71.14%	14318 82.60%	8176 84.86%	5157 89.97%	17394 64.49%	7712 76.31%	2182 74.20%	1449 89.86%	687 89.08%	0 0
<i>P</i> value	<0.001	<0.001	0.701	0.023	<0.001	<0.001	0.434	<0.001	<0.001	-

Notes: The number of subjects and appropriateness were obtained from the integration of data from papers researching RBC units. *P* values were obtained by comparing the two groups in one column. No data concerning pediatrics were reported in LOH-3 in the group of RBC units.

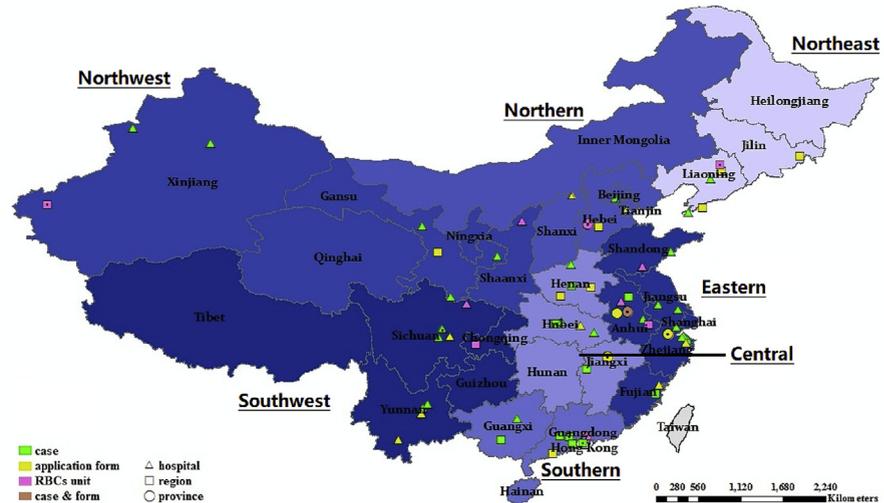


Fig. 2. The appropriate level of RBCs transfusion according to areas and characteristics of the studies.-
Notes: 1. Appropriate rate of RBC use ranging from high to low are southwest, northern, eastern, north-west, central, southern and northeast. The gray areas indicate areas (Hong Kong, Macao and Taiwan) from which data were not acquired. 2. The kinds of research reports used are indicated by different colors in the middle column of symbols. 3. The various shapes in the right column of symbols were used to express the scope of the literature covered. 4. The black dots in the middle of the shapes indicate high quality literature. Those without the black dot were of low quality.

for different research subjects. The research showed the most appropriate use of RBCs (93.60%) was reported in Shanghai by Tao et al at 2017 and the appropriate rate of RBCs transfusion in non-operative department was up to 98.89% (445/450) [15]. The second rate (91.07%) was reported in 2018 [16] and others suggested us that almost 25%–40% of all clinical use of RBCs in China had been unnecessary since 2006. This in turn suggested that the common inappropriate transfusion of RBCs might be one cause of the current excessive pressure on blood supplies in China.

The blood request form-based studies and studies focused on blood cases were significantly less likely to report appropriate RBCs use (69.10% and 68.85%) than the studies of RBC units-based studies (75.64%) ($p < 0.001$). In order to analyzed the reasons, we assessed whether the studies with different record types differed in terms of the nature of the main clinical departments, and found that there was good uniformity between the appropriate level of RBCs use in different types of transfusion records and between the ratio of cases from medicine and surgery (90.35%, 84.27%, 82.90% and 63.14%, 60.09%, 61.12% for RBC units, transfusion cases and request forms, respectively). In addition, we couldn't exclude completely that the characteristic of different record types confounded the analysis. For example, multiple RBC units sometimes were requested in a single request form, so it might be difficult for the researchers to determine the appropriateness of each unit. This problem also obvious when evaluating the appropriateness of transfusion cases including part inappropriate request forms. There were nine studies in which

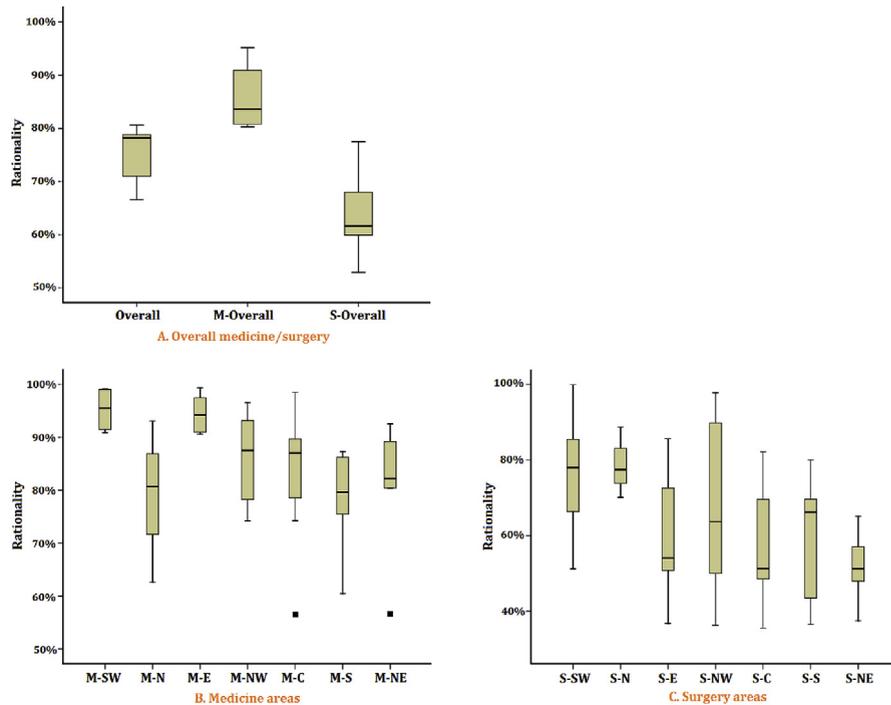


Fig. 3. The dispersion of appropriateness between areas. Notes: overall = the overall appropriate levels between areas; M-Overall = the overall appropriate levels between areas of medicine; S-Overall = the overall appropriate levels between areas of Surgery; M-SW = medicine of Southwest China; M-E = medicine of Eastern China; M-NW = medicine of Northwest China; M-N = medicine of Northern China; M-S = medicine of Southern China; M-C = medicine of Central China; M-NE = medicine of Northeast China; S-SW = surgery of Southwest China; S-E = surgery of Eastern China; S-NW = surgery of Northwest China; S-N = surgery of Northern China; S-S = surgery of Southern China; S-C = surgery of Central China; S-NE = surgery of Northeast China. We used medians, percentiles (25%, 75%), extreme values, and outliers to show the dispersion of appropriateness. The little black box, in the M-NE column indicates literature with the appropriateness of 56.66% in the Yanbian area of Jilin province. The black box in the column of M-C indicates the appropriateness of the literature in more than ten hospitals in the area of Zhoukou in Henan province and the appropriate rate is 56%.

Table 3. The number and appropriateness of cases/forms reported in high- and low-quality studies according to clinical departments.

Quality of papers	Overall	Medicine	Surgery	Gynecology & obstetrics	Pediatrics
Low	40620	13783	23736	2393	708
	69.34%	84.65%	60.30%	72.50%	85.59%
High	6571	1896	3969	240	466
	74.48%	84.44%	68.08%	92.08%	79.40%
<i>P</i> value	<0.001	0.815	<0.001	<0.001	<0.01

Notes: Subject number and appropriateness were obtained from the integration of data from papers researching cases/forms. *P* values were obtained by comparing two groups in the same column.

investigators classified transfusion cases as wholly or only partially appropriate cases [15, 17, 18, 19, 20, 21, 22, 23, 24]. These observations suggested that the most feasible study outcome variable for evaluating RBCs use appropriateness should be the blood request form.

Our study also showed that, regardless of record types, the operative departments were significantly less likely to use RBCs appropriate than other clinical departments. This might be explained by a study showed that while 78% of physicians in China were fully cognizant of the national guidelines regarding the clinical use of blood, only 60% of surgeons have grasped this knowledge [25]. Moreover, compared with non-operative departments, operative departments are exposed to variables that may elevate the risk of hemorrhage and death, thus making surgeons more prone to use RBC units. These variables include the experience of surgeons or anesthesiologists, the condition of patients, the duration of surgery, and the anesthetic and surgical techniques being used [26]. In addition, more than half of all medical disputes in China were related to surgeons, thus, surgeons may be prone to ordering transfusions in order to avoid any possible disputes [27, 28].

When different departments were examined, nearly all showed that the different outcome variables were associated with different degrees of appropriateness, except for gynecology and obstetrics departments and pediatrics departments. In gynecology and obstetrics departments, the appropriateness of RBCs transfusion between blood request forms and RBC units was similar ($p = 0.219$). This lack of difference might due to limited numbers of blood request forms ($n = 318$). This might also explained why the appropriateness of RBC transfusion was significantly different between the blood request forms ($n = 69$) and the transfusion cases ($n = 642$) in pediatric departments ($p < 0.001$). There was evidence that the three record types were quantitatively similar for the same specimen in pediatrics: Zheng *et al.* showed that 96.3% of the transfusion cases only included one application form, while 74.71% of the blood request forms only requested one unit of RBCs [29]. These quantitative similarities between three record types could help minimize confounders in pediatric studies.

To compare the appropriate use of RBCs in different regions of China, the arithmetic means of appropriate rate from internal medicine and surgery, other than from all the records surveyed, was calculated. We took into account not only the fact that the seven areas used quantitatively different transfusion records from mainly clinical departments but the fact that some departments had fewer transfusion cases (*i.e.* pediatrics, obstetrics and gynecology departments). Although the linear correlation between the appropriateness of RBCs transfusion in different areas and the ratio of LOH-3 to LOH-2 was not detected, the different rate between southwest and southern/northeast may be partly related to the number of LOH-3 involved in this analysis, LOH-3 accounted for 67% in southwest China, but only 33% and 51% in

northeast and southern China, respectively. To some degree, insufficient blood supervision and management may be partly responsible for the low rate of appropriate RBCs use in northeast China. For example, Jiang *et al.* reported that in Jilin province, which is one of the three provinces in northeast China, 65% of the clinical blood transfusion supervisors did not have a bachelor's degree and only 19.8% of staffs in the blood bank and clinical transfusion departments had specialized in clinical medicine. Moreover, transfusion medicine physicians only accounted for 20.8% and 9.7% of all staffs in transfusion departments in LOH-3 and LOH-2 respectively [30]. When comparing the appropriate transfusion of RBCs between medicine and surgery in different regions, it was found that the median appropriate rate of internal medicine was higher than that of surgery except in northern China (Fig. 3). Reviewing the raw data, it was found that only 3 studies in northern China had reported the appropriate rate of RBCs between medicine and surgery which suggested that the results in northern China might not be representative. In the regions of eastern, north Western and central China, the results all indicated that the rate of medicine was higher than that of surgery which further stated that some measures should be taken in surgery department to strengthen the appropriateness of RBCs transfusion.

Regardless of the type of records being used, LOH-3 were overall more appropriate in their RBCs use than LOH-2 ($p < 0.001$). This situation can be attributed to the following aspects, Firstly, compared to LOH-2, LOH-3 have more specialized clinical doctors who are experienced with complicated cases and have been trained to deliver blood transfusions accurately [31]. Secondly, LOH-3 all have an independent blood transfusion department, whereas in some LOH-2 (30.3%), the department of blood transfusion is still merged with the clinical laboratory [32]. This makes it difficult for the hospital transfusion committee to educate, train, monitor, and evaluate the clinical teams since the committee is not complete and is always a formality to some degree in LOH-2 [7, 33]. Thirdly, most Chinese regard blood transfusion as a very precious and effective medicine, while only 17% are cognizant of its disadvantages [34]. For this reason, doctors in LOH-2 are more likely to request blood or blood components in order to prevent medical disputes even though the request violate the Chinese national guidelines on clinical blood transfusion [25].

Our review also indicated that high-quality studies were significantly more likely to report appropriate use of RBCs than low-quality studies. Further analysis showed that 48.5% and only 31.1% of transfusion cases in high- and low-quality studies were from LOH-3, respectively. In addition, compared to low-quality studies, the assessment of RBCs transfusion is more objective and accurate for the clinical specialists participated in high-quality studies. Thus, the difference between high- and low-quality studies in terms of appropriate frequencies may partly reflect this study bias. Especially, these differences were more obvious in operative departments ($p < 0.001$) than in the non-operative departments (medicine, $p = 0.492$; pediatrics, $p = 0.258$). Thus, future studies should consider inviting clinical specialists to assess the

appropriateness of RBCs use in operative departments. WHO also emphasized that the hemoglobin level of a patient, while important, should not be the sole indicator for starting transfusion [26].

Our systematic review also had limitations. Firstly, we merged the data from transfusion cases and blood request forms, not only because both probably included the use of more than one unit of RBCs, but also because the number of studies using blood request forms was too limited to allow their division into enough categories for further analysis. Secondly, we excluded partially appropriate transfusion cases. This was partly because they accounted for a very small percentage of the transfusion cases analyzed in the present study (1741/58,669; 2.97%) but more importantly because of the lack of details regarding these cases. In any case, our systematic review supported the notion that there was widespread inappropriate clinical use of RBCs in China.

Therefore, measures should be taken immediately to improve appropriate blood use and avoid unnecessary blood transfusions in China. It was reported that about 60% of the cases of unreasonable clinical transfusion were attributed to the lack of conformity between prescribing and national guidelines [35]. To address the causes of this inappropriate use, several methods, such as: establishing a system of clinical blood management, evaluation [36], educating and training clinicians in transfusion medicine [37] can improve appropriate blood transfusions and minimize unnecessary transfusions. In addition, restrictive transfusion strategies aiming to avoid unnecessary blood usage and improve patient outcomes have become a worldwide movement. Several studies have reported that restrictive blood transfusion was beneficial for patients [38, 39]. Taking into account the differences between the transfusion guidelines of AABB [40] and the transfusion thresholds of RBCs determined by China (7 g/dl for surgery departments and 6 g/dl for internal medicine [41]), we could have provided more important and relevant data about clinical results (Tables 4 and 5). Unfortunately, all the researches included in this review did not

Table 4. RBCs transfusion guidelines in China.

Items	Contents
Surgery and trauma	<p>Purpose: RBCs are applied to improve the ability of blood to carry oxygen, provided that blood volume basic normal or low blood volume has been correct. Patients with low blood volume can be corrected with gel and crystal liquid applications.</p> <ol style="list-style-type: none"> 1. Hemoglobin >100 g/L, transfusion is not recommended. 2. Hemoglobin <70 g/L, transfusion should be considered. 3. Hemoglobin between 70-100 g/L, the decision of transfusion depending on the degree of anemia, Cardiopulmonary compensatory function, Presence of increased metabolic rate and age of patient <i>etc.</i>.
Internal medicine	<p>Adaptive objective: Chronic anemia patients accompanied by hypoxia symptoms, whose red blood cells were damaged, lost or dysfunctional. hemoglobin <60 g/L or hematocrit <0.2, transfusion should be considered.</p>

Table 5. Main recommendation of RBCs transfusion guidelines in AABB.

Main recommendation	Contents
Recommendation1	AABB recommends a restrictive RBC transfusion threshold of 7 g/dL in hospitalized hemodynamically stable adult patients, including critical care patients.
Recommendation2	For patients undergoing orthopedic surgery, cardiac surgery and those with pre-existing cardiovascular disease, AABB recommends a restrictive RBC transfusion threshold of 8 g/dL.

focus on the treatment effect of patients. There is no doubt that restrictive transfusion strategies will be a worthy recommendation not only for saving Chinese blood resources but also for determining a more restrictive transfusion threshold.

In conclusion, our review showed that unnecessary RBC transfusions are common in China and may be in a large part responsible for the increasing demands on the present limited blood supplies. We also showed that inappropriate blood transfusion is a particular acute problem in LOH-2, surgical departments, and certain regions of China. This information showed where measures to improve the appropriate use of blood will be particularly effective. Since people at many levels in Chinese society ranging from governments to hospitals to individual researchers and clinicians are currently paying more attention to the safety, availability, and appropriate use of blood than ever before, it is high likely that the unnecessary transfusion of blood can be rapidly reduced, thus not only minimizing the risks of transfusion but also alleviating the pressure on Chinese blood supplies.

4. Materials and methods

4.1. Data retrieval and screening

Four main medical databases in China, PubMed, Web of Science, the Cochrane library and Science Direct were searched by two researchers separately *via* basic queries or advanced searches with keywords with the search terms “blood”, “blood transfusion”, “blood use”, “blood component”, “clinical use”, “red blood cells”, “rationality”, “appropriateness” and “China” [8, 9]. Four Chinese medical databases were the China National Knowledge Infrastructure (cnki.net), Wanfang Data (wanfangdata.com.cn), SinoMed (sinomed.ac.cn), and CQVIP (cqvip.com). All databases were searched for articles published up to December 1, 2018. The retrieved articles were screened to ensure that they assessed the appropriateness of RBCs or blood component transfusion in China according to Technical Specification for Clinical Blood Transfusion standards, which were issued by the Former Chinese Ministry of Health on June 1, 2000 [41] (Table 4). Articles that didn't focus on the appropriateness of RBCs were excluded and the exclusion criteria as follows: repeated articles; studies that describe clinical blood

transfusion management; researches on the trend of clinical blood use; articles that report the appropriateness of other blood components; reviews and systematic analysis (Fig. 1).

4.2. Article classification and definitions

The articles that passed the screening were then classified according to the type of transfusion records, hospital level (LOH-2 and LOH-3), type of clinical department, geographical region, and study quality. Three kinds of research objects, namely: transfusion cases, blood request forms and RBC units were investigated in the literature. The data from the first two were integrated (cases/forms) for analysis. For the hospital level, LOH-2 are regional hospitals that provide medical and health services across several communities and are technical centers for regional medical prevention. LOH-3 are hospitals that provide medical and health services across regions, provinces, cities and the whole country. These hospitals are preventive technical centers with the ability of comprehensive medical treatment, teaching and scientific research. Operative departments included surgery, gynecology and obstetrics; however, non-operative departments consisted of medicine and pediatrics. Other clinical departments were not distinguished because detailed information on these departments was not described in the studies. Geographical region was defined as seven geographical districts, namely, northeast, northwest, northern, eastern, southwest, central, and southern China. These districts were obtained from an article called “Characteristics of Regional Social and Economic Development in Mainland China” [42]. Study quality was defined as high when RBC-transfusion records were both selected randomly and evaluated by clinical specialists. Studies that did not have these elements were regarded as low-quality studies.

4.3. Statistical analyses

All extracted data were coded, and then were placed in a Microsoft Excel 2007 table. The frequency of appropriate RBCs use was expressed as the appropriate rate. The appropriate level of RBCs use of all cases/forms/units throughout China was expressed as the mean \pm standard deviation (SD) of rates. Different groups were compared in terms of appropriate RBCs use frequency by using Chi-squared tests. Variability between the different geographical regions was expressed as coefficient of variation (CV). The arithmetic means of the appropriate rates of RBCs use in both medicine and surgery in every area were used to represent the appropriateness of this area. Correlations between appropriate rate of RBCs use in different regions and LOH-3/LOH-2 ratio or the ratio of all cases from internal medicine and surgery were assessed by Spearman correlation analysis. All statistical analysis was performed by using SPSS 20.0. Statistical significance was set at $p < 0.05$.

Declarations

Author contribution statement

Yujie Kong, Xiangming Wang: Analyzed and interpreted the data; Wrote the paper.

Yonghua Yin: Contributed reagents, materials, analysis tools or data.

Xue Tian, Ling Li, Jue Wang, Li Tian, Ning Song: Analyzed and interpreted the data.

Zhong Liu: Conceived and designed the experiments.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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