The systematic review and meta-analysis of X-ray detective rate of Kashin-Beck disease from 1992 to 2016

Xi Wang1,2,†, Yujie Ning1,†, Amin Liu1, Xin Qi1, Meidan Liu1, Pan Zhang1 and Xiong Guo1*

Abstract

Background: Kashin-Beck disease (KBD) is a serious human endemic chronic osteochondral disease. However, quantitative syntheses of X-ray detective rate studies for KBD are rare. We performed an initial systematic review and meta-analysis to assess the X-ray detective rate of KBD in China.

Methods: For this systematic review and meta-analysis, we searched five databases (PubMed, Web of Science, Chinese National Knowledge Infrastructure (CNKI), WanFang Data and the China Science and Technology Journal Database (VIP)) using a comprehensive search strategy to identify studies of KBD X-ray detective rate in China that were published from database inception to January 13, 2018. The X-ray detective rate of KBD was determined via an analysis of published studies using a random effect meta-analysis with the proportions approach. Subgroup analysis and meta-regression were used to explore heterogeneity, and study quality was assessed using the risk of bias tool.

Results: A total of 53 studies involving 14,039 samples with X-ray detective rate in 163,340 observations in total were included in this meta-analysis. These studies were geographically diverse (3 endemic areas). The pooled overall X-ray detective rate for KBD was 11% (95%CI,8 – 15%; Z = 13.14; p < 0.001). The pooled X-ray detective rate estimates were 11% (95%CI, 6 – 17%; Z = 7.06; p < 0.001) for northeast endemic areas, 13% (95%CI, 7 – 20%; Z = 7.45; p < 0.001) for northwest endemic areas, and 8% (95%CI, 5 – 12%; Z = 7.90; p < 0.001) for southwest endemic areas. There was a significant relationship between the survey year and the X-ray detective rate of KBD.

Conclusions: Our systematic review found that the summary estimate of the X-ray detective rate of KBD was 11% and, that KBD X-ray positive rate ranged from 8.00 to 15.00% depending on the study. Further research is required to identify effective strategies for preventing and treating KBD.

Keywords: Kashin-Beck disease, Meta-analysis, X-ray detective rate, Correlation analysis

Background

Kashin-Beck disease (KBD) is a serious, endemic chronic osteochondral disease in humans that is distributed from northeast to southwest China, affecting 378 counties in 13 provinces [1]. According to reports from the National Health Commission of China in 2017 [2], the prevalence of KBD in the 13 provinces of China are 1.04% in Hebei, 0.27% in Shanxi, 3.90% in Inner Mongolia, 0.08% in Liaoning, 0.55% in Jilin, 0.49% in Heilongjiang, 0.21% in Shandong, 1.78% in Henan, 5.54% in Sichuan, 2.00% in Tibet, 2.25% in Shaanxi, 1.85% in Gansu and 5.12% in Qinghai Province. KBD is also a major public health problem that results in serious health consequences for patients, including symmetrical enlargement of the phalanges, brachydactyly, joint deformity, and even dwarfism [3], which leads most patients with KBD to partially or completely lose their working capacity and self-care abilities. This outcome not only seriously impacts patient quality of life but also increases the medical burden on society [4].

The diagnosis and degrees of KBD is a crucial first step in the public health approach to confirm this type
of osteochondrosis in China. X-ray image, considered as an important diagnostic criterion for KBD, could reflect the damage of articular cartilage before any clinical manifestations. For example, X-ray image can detect the lesions at epiphysis and metaphysis. However, the lack of consensus in diagnosing KBD has resulted in wide variations in reported X-ray detective rate. For example, according to reports of a national survey of KBD prevalence in 2005 [5], National KBD surveillance group found that the X-ray detective rate of KBD was less than 3.00% in the east part of endemic region and was more than 10% in the west part of endemic region, some endemic region in west were 25%. In another analysis of national surveillance on KBD condition from 2000 to 2007, Liu et al. showed that the average X-ray detective rate of KBD in west endemic region has decreased from 21.75% in 2000 to 7.30% in 2007 [6]. Therefore, a number of controversies remain related to estimating the X-ray detective rate of KBD.

To data, few studies have synthesized the results of KBD X-ray detective rate studies. Given the large number of X-ray detective rate studies that have been published in recent decades and the absence of nationwide quantitative estimates of the X-ray detective rate of KBD, it is an opportune time to perform a full systematic review and quantitative analysis of KBD X-ray detective rate.

Here, we report the results of such a study in China to emphasize the need for more accurate nationwide and regional estimates of KBD X-ray detective rate. To analyze the wide variations in X-ray detective rate estimates, we investigated the influence of studies’ demographic and methodological characteristics.

**Methods**

**Search strategy and selection criteria**

A comprehensive four steps search strategy was used to identify the relevant studies in this systematic review and meta-analysis. The study followed the Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) guidelines [7]. We searched the following academic databases from January 1st 1990 up to January 13th 2018: PubMed, Web of Science, Chinese National Knowledge Infrastructure (CNKI) (articles in Chinese), WanFang Data (articles in Chinese) and the China Science and Technology Journal Database (VIP) (articles in Chinese). We used the following combinations of keywords as the search terms: “X-ray detective rate” or “X-ray” or “detection rate” and “Kashin-Beck disease” or “KBD” or “endemic osteochondrosis.” The language was limited to English or Chinese. We also reviewed the references cited in the studies and review articles to avoid missing studies. All publications were screened independently based on titles and abstracts, followed by retrieval; the full text publications were screened by two reviewers using the eligibility criteria described below. We searched the scientific literature systematically for observational cross-sectional studies that reported the X-ray detective rate of KBD. We excluded studies that were reviews, conference abstracts, or used qualitative methods only.

![Fig. 1 PRISMA flowchart showing the study selection process](image-url)
| Study                  | Year    | Areas           | Case(n) | Total(n) | X-ray detective rate (%) [95%CI] | Age (year) | Study | QS | Comprehensive Preventive Measures                                                                 |
|-----------------------|---------|-----------------|---------|----------|----------------------------------|------------|-------|----|------------------------------------------------------------------------------------------------|
| Zhang et al. 2005     | Heilongjiang (NE) | 270       | 1699    | 15.89 (14.15,17.63) | 7–12 Rep 10 | 1. Changing grain; 2. Supplemental Se |
| Su et al. 2012        | Jilin (NE)  | 8         | 742     | 1.08 (0.34,1.82)   | 7–12 Rep 10 | 1. Changing grain; 2. Water improvement |
| Tao et al. 2012       | Inner Mongolia (NE) | 54       | 929     | 5.81 (4.31,7.32)    | 7–12 Rep 9 | 1. Changing grain |
| Xun et al. 2009       | Inner Mongolia (NE) | 397      | 2281    | 17.40 (15.85,18.96) | 7–12 Rep 10 | 1. Changing grain; 2. Changing dietary patterns; 3. Improved economic conditions; 4. Water improvement |
| Xun et al. 2007       | Inner Mongolia (NE) | 67       | 871     | 7.69 (5.92,9.46)    | 7–12 Rep 10 | 1. Changing grain |
| Yuan et al. 1998      | Inner Mongolia (NE) | 297      | 863     | 34.41 (31.24,37.58) | 7–13 Rep 9 | 1. Changing grain; 2. Supplemental Se |
| Yuan et al. 1998      | Inner Mongolia (NE) | 386      | 1693    | 22.80 (20.8,24.8)   | 7–13 Rep 9 | 1. Changing grain; 2. Supplemental Se |
| Liu et al. 2001       | Inner Mongolia (NE) | 172      | 2498    | 6.89 (5.89,7.88)    | 7–13 Rep 10 | 1. Changing grain |
| Liu et al. 2001       | Inner Mongolia (NE) | 172      | 2498    | 6.89 (5.89,7.88)    | 7–13 Rep 10 | 1. Changing grain |
| Yung et al. 1994      | Henan (NE)  | 4         | 155     | 2.58 (0.08, 5.08)   | 7–12 Rep 8  | 1. Supplemental Se |
| Zhang et al. 1995     | Inner Mongolia (NE) | 308      | 687     | 4.43 (4.11,4.85)    | 7–12 Rep 10 | 1. Changing grain |
| Wang et al. 2011      | Beijing (NE) | 25        | 2055    | 1.22 (0.74,1.69)    | 7–12 Rep 10 | 1. Changing grain; 2. Changing dietary patterns; 3. Improved economic conditions; 4. Collective relocation |
| Wang et al. 2011      | Shandong (NE) | 576       | 5935    | 9.70 (8.95,10.46)   | Rep 8       | 1. Changing dietary patterns; 2. Improved economic conditions; 3. Collective relocation |
| Chen et al. 2011      | Shaanxi (NW) | 41        | 3091    | 1.33 (0.92,1.73)    | 7–12 Rep 10 | 1. Water improvement |
| Yu et al. 2011        | Henan (NE)  | 17        | 1928    | 0.88 (0.46,1.30)    | 7–12 Rep 10 | 1. Supplemental Se; 2. Changing grain |
| Yu et al. 2000        | Henan (NE)  | 200       | 567     | 3.52 (3.14,3.92)    | 3–7 Pro 8   | 1. Supplemental Se |
| Yang et al. 1994      | Henan (NE)  | 4         | 155     | 2.58 (0.08, 5.08)   | 7–12 Rep 8  | 1. Supplemental Se |
| Wang et al. 2011      | Shaanxi (NW) | 49        | 259     | 18.92 (14.15,23.69) | 7–16 Rep 9  | 1. Changing dietary patterns; 2. Supplemental Se; 3. Improved economic conditions |
| He et al. 2010        | Shaanxi (NW) | 32        | 355     | 9.01 (6.03,12.00)   | 6–13 Rep 9  | 1. Changing dietary patterns; 2. Water improvement; 3. Improved economic conditions |
| Xie et al. 2010       | Shaanxi (NW) | 1        | 505     | 0.20 (–0.19,0.59)   | 7–12 Pro 10 | 1. Changing grain; 2. Water improvement; 3. Collective relocation |
| Xie et al. 2008       | Shaanxi (NW) | 2        | 610     | 0.33 (–0.13, 0.78)  | 7–13 Pro 10 | 1. Changing dietary patterns; 2. Supplemental Se; 3. Water improvement; 4. Improved economic conditions |
| Lv et al. 2009        | Shaanxi (NW) | 37        | 8747    | 0.42 (0.29,0.56)    | 7–13 Rep 10 | 1. Changing dietary patterns; 2. Supplemental Se; 3. Water improvement; 4. Improved economic conditions; 5. Returning farmland to forest |
| Xu et al. 2004        | Shaanxi (NW) | 69        | 3059    | 2.26 (1.73, 2.78)   | 7–12 Rep 10 | 1. Supplemental Se; 2. Water improvement; 3. Collective relocation |
| Cao et al. 2004       | Shaanxi (NW) | 151       | 944     | 16.00 (13.66, 18.33) | 7–12 Rep 10 | 1. Supplemental Se |
| Yang et al. 2005      | Shaanxi (NW) | 4         | 110     | 3.64 (0.14, 7.13)   | 7–12 Rep 9  | 1. Changing grain |
| Wang et al. 2001      | Shaanxi (NW) | 60        | 524     | 11.45 (8.72, 14.18) | 7–12 Rep 9  | 1. Supplemental Se |
| Chen et al. 2004      | Shaanxi (NW) | 26        | 840     | 3.09 (1.92, 4.27)   | 7–12 Rep 10 | 1. Changing grain; 2. Supplemental Se; 3. Water improvement |
| Sun et al. 1992       | Shaanxi (NW) | 299       | 970     | 30.82 (27.92,33.73) | 3–13 Rep 9  | 1. Supplemental Se |
| Xu et al. 2009        | Shaanxi (NW) | 487       | 2844    | 17.12 (15.74, 18.51)| 7–12 Rep 10 | 1. Supplemental Se |
| Xie et al. 2011       | Shaanxi (NW) | 38        | 2248    | 1.69 (1.16, 2.22)   | 7–12 Pro 10 | 1. Supplemental Se |
| Lv et al. 2002        | Shaanxi (NW) | 441       | 3324    | 13.27 (12.11, 14.42) | 6–13 Rep 10 | 1. Supplemental Se; 2. Water improvement |
| Zhang et al. 2002     | Shaanxi (NW) | 500       | 2107    | 23.73 (21.91, 25.55)| 7–12 Rep 10 | 1. Supplemental Se |
| Yi et al. 2016        | Shaanxi (NW) | 6         | 1744    | 0.34 (0.07, 0.62)   | 7–12 Rep 9  | 1. Changing grain; 2. Water improvement |
| Cui et al. 2013       | Gansu (NW)  | 82        | 2254    | 3.68 (2.90, 4.46)   | 7–12 Rep 10 | 1. Supplemental Se |
| Ge et al. 2008        | Gansu (NW)  | 345       | 4367    | 7.90 (7.10, 8.70)   | 7–12 Rep 10 | 1. Supplemental Se |
| Liu et al. 2007       | Gansu (NW)  | 56        | 567     | 9.88 (7.42, 12.33)  | 7–12 Rep 10 | 1. Supplemental Se; 2. Changing grain |
Data extraction and quality assessment

Data were extracted by three reviewers. The following data were extracted: 1) study first author, 2) year and areas of publication, 3) number of KBD patients in the sample, 4) X-ray detective rate of KBD in the sample, and 5) age range of the sample. One reviewer crosschecked for accuracy. After removing duplicate studies, two reviewers screened the titles and abstracts using the eligibility criteria, with independent verification by other two reviewers. For suitable studies, we obtained the full text, and scrutinized the text against eligibility criteria, with independent verification by other two reviewers. The study quality was assessed by two reviewers using the standardized Risk of Bias Tool (Additional file 1), which was designed to assess population-based prevalence studies, as part of the data extraction strategy. To assess the risk of bias, the reviewers rated each of the ten items using a dichotomous ratings system with the following categories: low risk and high risk. An overall score was calculated by adding all the items rated as low risk. Thus, higher scores indicated a lower risk of bias and a stronger method quality.

Data analysis

A random-effect meta-analysis using the proportions approach [8] was used to quantify the X-ray detective rate of KBD. Traditional meta-analysis approaches face the problem that X-ray detective rate proportions approach the limits of 0% or 100%. Thus, a few revised procedures, such as the recently developed metaprop Stata command [8], have been explored to solve this problem. The command metaprop pools proportions and uses the score statistic and the exact binomial method, with the option to incorporate the Freeman-Tukey double arcsine transformation, to compute 95% confidence intervals. A random-effects model within metaprop was chosen due to the considerable heterogeneity across studies in terms of both the measurement of frailty and the samples studied. In random-effects models, the effect sizes of the observed studies are considered to represent a distribution of possible effects; random-effects meta-analysis incorporates both within-study variance and between-study heterogeneity [9]. Studies reporting area estimates were trisected into three groups according to the measurement type, as follows: “northeast,” “northwest” and “southwest.” The X-ray detective rate of KBD was

Table 1 Selected characteristics of the studies included in this systematic review and meta-analysis (Continued)

| Study       | Year | Areas     | Case(n) | Total(n) | X-ray detective rate (%) [95%CI] | Age (year) | Study | QS | Comprehensive Preventive Measures |
|-------------|------|-----------|---------|----------|----------------------------------|------------|-------|----|-----------------------------------|
| Zhang et al.| 2014 | Gansu (NW)| 31      | 1019     | 3.04 (1.99, 4.10)                | 7–12       | Rep   | 10 | 1. Supplemental Se                 |
| Bai et al.  | 2002 | Gansu (NW)| 484     | 802      | 60.22 (56.83, 63.61)             | 3–13       | Pro   | 10 | 1. Supplemental Se                 |
| Luo et al.  | 2012 | Gansu (NW)| 21      | 610      | 3.44 (2.00, 4.89)                | 7–14       | Rep   | 10 | 1. Supplemental Se                 |
| Li et al.   | 2004 | Qinghai (NW) | 383     | 1194     | 32.08 (29.43, 34.72)             | 7–12       | Rep   | 10 | 1. Supplemental Se; 2. Water improvement |
| Ding et al. | 2001 | Qinghai (NW) | 566     | 1290     | 43.88 (41.68, 46.58)             | 7–12       | Rep   | 9  |                                  |
| Ding et al. | 2003 | Qinghai (NW) | 291     | 1446     | 20.12 (18.06, 22.19)             | 7–12       | Rep   | 10 | 1. Water improvement; 2. Supplemental Se; 3. Changing dietary patterns |
| Li et al.   | 2006 | Qinghai (NW) | 2228    | 5122     | 43.50 (42.14, 44.86)             | 7–12       | Rep   | 9  | 1. Water improvement; 2. Supplemental Se |
| Bao et al.  | 1998 | Qinghai (NW) | 195     | 436      | 44.72 (40.06, 49.39)             | 7–12       | Rep   | 10 |                                  |
| Li et al.   | 2002 | Qinghai (NW) | 168     | 407      | 41.28 (36.49, 46.06)             | 7–12       | Rep   | 10 |                                  |
| Zhao et al. | 2016 | Tibet (SW) | 1388    | 43,034   | 3.23 (3.06, 3.39)                | 7–12       | Pro   | 9  | 1. Supplemental Se; 2. Changing grain; 3. Collective relocation; 4. Improved economic conditions |
| Zhao et al. | 2011 | Tibet (SW) | 15      | 431      | 3.48 (1.75, 5.21)                | 7–12       | Pro   | 10 |                                  |
| Gong et al. | 2004 | Tibet (SW) | 73      | 611      | 11.95 (9.38, 14.52)              | 4–12       | Pro   | 10 | 1. Supplemental Se                 |
| A et al.    | 2015 | Sichuan (SW) | 182     | 14,189   | 1.28 (1.10, 1.47)                | 7–12       | Rep   | 10 | 1. Supplemental Se                 |
| Wang et al. | 2005 | Sichuan (SW) | 551     | 3149     | 17.50 (16.17, 18.82)             | 7–12       | Rep   | 10 | 1. Supplemental Se                 |
| Zhang et al.| 2009 | Sichuan (SW) | 24      | 1243     | 1.93 (1.17, 2.70)                | 7–12       | Rep   | 10 | 1. Supplemental Se; 2. Changing dietary patterns |
| Li et al.   | 2003 | Sichuan (SW) | 314     | 1600     | 19.63 (17.68, 21.57)             | 7–12       | Rep   | 10 | 1. Supplemental Se; 2. Changing dietary patterns |
| Deng et al. | 2008 | Sichuan (SW) | 675     | 8689     | 7.77 (7.21, 8.33)                | 7–13       | Rep   | 10 | 1. Improved economic conditions; 2. Changing dietary patterns |
| Hunag et al.| 2010 | Sichuan (SW) | 373     | 13,472   | 2.77 (2.49, 3.05)                | 7–12       | Rep   | 10 | 1. Improved economic conditions; 2. Collective relocation; 3. Changing grain |
| Deng et al. | 1999 | Sichuan (SW) | 569     | 2224     | 25.58 (23.77, 27.40)             | 7–12       | Rep   | 10 | 1. Improved economic conditions |

QS: quality score; Rep: retrospective cohort study; Pro: prospective cohort study. NE: northeast; NW: northwest; SW: southwest
quantified overall and by measurement type. In addition to weighted estimates, the 95% confidence interval (CI) was reported along with z tests (weighted estimate divided by the standard error of the weighted estimate) and associated p values as metrics of precision.

Heterogeneity was assessed by using the chi-square test of the Q statistic, which was quantified by the $I^2$ values. We also calculated $I^2$ as a “signal-to-noise” ratio of excess dispersion to total dispersion, with values of 25% (indicating that all of the heterogeneity is low), 50% (indicating that all of the heterogeneity is moderate) and 100% (indicating that all of the heterogeneity is high and requires further examination and explanation) [10]. Publication bias and bias associated with small study effects were assessed visually with funnel plots, Egger’s linear regression and Begg’s rank correlation test [11]. To explain the significant observed heterogeneity, stratified analyses and a random-effects meta-regression were performed. Our main factors of interest were the study design (retrospective vs. prospective), geographic region, mean age, study year and study quality score. A sensitivity analysis was also performed by excluding one study at a time to assess whether one or more studies influenced the overall results. $P \leq 0.05$ indicated statistical significance.

Results

Included studies

The results of study identification, screening, eligibility, and inclusion are shown in the PRISMA flow diagram (Fig. 1). We identified 947 reports, 790 of which were without data, 79 with unqualified data, 10 with incomplete data, and 15 duplicates. Finally, 53 published studies, involving 14,039 samples with X-ray detective rate in 163,340 observations in total, were considered to be eligible and included in the meta-analysis [12–62] (Table 1). The 53 studies selected for the meta-analysis were

![Fig. 2 Forest plot of pooled estimated X-ray detective rate of KBD with 95% CI](image)
geographically diverse and included three parts of the KBD endemic area, with 15 studies from the northeast endemic area, 28 studies from the northwest endemic area and 10 studies from the southwest endemic area.

Meta-analysis
The overall estimated X-ray detective rate of KBD was 11% (95%CI, 8–15%; Z = 13.14; \( p < 0.001 \)). Heterogeneity statistics (Q = 19,151.88; \( I^2 = 99.73\% \)) indicated that there was significant and substantive heterogeneity in the X-ray detective rate of KBD across studies (Fig. 2). To confirm the stability and liability of the meta-analysis, a sensitivity analysis was performed by recalculating the pooled KBD X-ray detective rate when any single study was deleted. The results show that the pooled X-ray detective rate (14%; 95%CI, 11–18%) did not change significantly. A visual inspection of the funnel plot revealed slight asymmetry (Fig. 3), but both Begg’s test (Z = −1.14, \( P = 0.259 \)) and Egger’s test (t = 0.32, \( P = 0.747 \)) showed no potential risk of publication bias.

Subgroup results
To provide a range of KBD X-ray detective rate estimates in the KBD endemic areas, estimates were stratified by the northeast, northwest, and southwest endemic areas. The estimated X-ray detective rate of KBD in the northeast was 11% (95%CI, 6–17%; Z = 7.06; \( p < 0.001 \)). The estimated X-ray detective rate of KBD in the northwest was 13% (95%CI, 7–20%; Z = 7.45; \( p < 0.001 \)). The estimated X-ray detective rate of KBD in the southwest was 8% (95%CI, 5–12%; Z = 7.90; \( p < 0.001 \)) (Fig. 2).

Meta-regression
Meta-regression was performed to explore potential sources of heterogeneity. Survey year, age, study quality score and KBD endemic areas were tested as potential sources of heterogeneity. Only survey year (t = −5.82; \( P = 0.000 \)) was significantly associated with the detected heterogeneity (Table 2). We therefore further tested the correlation between KBD X-ray detective rate and potential sources of heterogeneity. There was a negative correlation between KBD X-ray detective rate and survey year(r = −0.6326, \( P = 0.0001 \)) (Fig. 4 and Additional file 2: TableS1).

Discussion
Despite substantial heterogeneity among the studies included in our study, we generated a precise estimate of the X-ray detective rate of KBD based on data from 53 published articles that involved 14,039 samples with

| Covariate | coefficient | 95%CI   | t-value | P-value |
|-----------|-------------|---------|---------|---------|
| Survey year | −0.0164 | −0.0220, −0.10937 | −5.82 | 0.000 |
| age | −0.0315 | −0.07480, 0.01173 | −1.43 | 0.153 |
| QS | −0.0091 | −0.06712, 0.04890 | −0.31 | 0.758 |
| EA | 0.0064 | −0.04004, 0.05286 | 0.27 | 0.787 |
X-ray detective rate in 163,340 observations in total in China via a systematic review and meta-analysis of studies published from 1992 to 2016.

In the report of a national survey of Kashin-Beck disease prevalence in 2005 [5], the X-ray detective rates of 11 spots were not more than 3% in the east part of endemic areas. The X-ray detective rates more than 10% in 5 of the 10 spots in the western parts, with the highest one being 25% (Qinghai Province). The X-ray detective rates were 0.96 and 5.04% in Sichuan, 5.56 and 6.02% in Shaanxi, 10.53% and 0 in Inner Mongolia, 14.71 and 16.98% in Gansu, 12.10 and 25% in Qinghai. The average detective rate was 5.21% in all spots. In our meta-analysis, the average detective rate was 11%, and the X-ray detective rate of KBD in the northeast was 11, 13% in the northwest and 8% in the southwest by subgroup analysis. In our meta-analysis, the X-ray detective rates data were selected from the studies published from 1992 to 2016, which were more comprehensive and persuasive than the survey in one year. But the trend of the two results above is consistent, the highest X-ray detective rate was northwest.

Moreover, the X-ray detective rate of KBD may be reflective of other mechanisms that are beneficial for preventing KBD. Although the average the X-ray detective rates of KBD was 5.21% in the report of a national survey of Kashin-Beck disease prevalence in 2005, the X-ray detective rates of KBD in some endemic areas in the northwest remained as high as 25%, and the high X-ray detective rates of KBD demonstrated that this disorder remains an important problem for some underdeveloped endemic areas. In addition, KBD is more common in some endemic areas than previously thought, which has important implications for researchers focusing on children with KBD.

To our knowledge, this review was the first to perform a systematic review and meta-analysis reporting KBD X-ray detective rates estimates in China. The aim of this study was to explore the overall X-ray detective rate of KBD in China from 1992 to 2016.

In this study, differences among X-ray detective rates estimates in different KBD endemic areas in China may be caused by intertwined factors, such as demographic and socioeconomic characteristics, life styles, and health and nutrition status. Interestingly, there was a negative correlation between KBD 1992 to 2016 and survey year, indicating that the mean X-ray detective rate decreased progressively. The comprehensive preventive measures such as improving drinking water and grain, relocating residents in endemic areas and improving balanced nutrition in KBD endemic areas may be the main reasons for the decreased X-ray detective rates of KBD, specifically the comprehensive preventive measures used in most of endemic areas. In Yi’s study, local residents ate grain purchased outside of the endemic areas instead of grain grown in endemic areas, and the condition of the drinking water was also improved [41]. In another study, the comprehensive preventive measures against KBD included supplemental Se, water supply improvements and altered dietary patterns [50]. For decades, it has been recommended that patients with KBD and residents living in endemic areas should prevent and cure KBD with supplemental Se, improved drinking water conditions, and altered the grains and improving dietary patterns. The measures above did decrease the risk of KBD in endemic areas. Recently, researchers have been developing and improving new diagnostic techniques for KBD and exploring the etiology and pathogenesis of KBD, which are the key to controlling and even eliminating KBD.
This systematic review and meta-analysis included 53 published articles that involved 14,039 samples with X-ray detective rate in 163,340 observations in total in China, and there is no potential risk of publication bias. Meta-regression analyses were conducted to find potential sources of heterogeneity. In addition, a sensitivity analysis was performed to confirm the robustness of our results. Nevertheless, several limitations should be acknowledged when interpreting the findings of our study. First, because KBD occurs primarily in China, the 53 articles included in this meta-analysis were all from Asia, which could lead to a bias in statistical analyses and the estimation of X-ray detective rate on a global scale due to the variability of the sample size and the unbalanced distribution of the studies. Second, most of the studies (45/53) included in this study were retrospective observational studies, which are considered to provide moderate evidence. Thus, the conclusion drawn in this analysis is restricted by this study type. Finally, heterogeneity was observed in the study, which was not surprising as heterogeneity often exists in such meta-analyses of overall X-ray detective rate. Although subgroup and meta-regression analyses suggested that geographic region and survey year could explain a portion of the observed heterogeneity, the remaining heterogeneity among the studies was not explained by the examined variables.

Conclusions
In conclusion, our meta-analysis found that the estimated the overall X-ray detective rate of KBD was 11% and ranged from 8 to 15% depending on the study. Further research is required to identify effective strategies for preventing and treating KBD.

Additional files

Additional file 1: Risk of Bias Tool: criteria for assessment of quality. (DOCX 13 kb)

Additional file 2: Table S1. The correlation between the mean prevalence and potential sources. QS: quality score. (DOCX 14 kb)

Abbreviations
CI: Confidence Interval; CNKI: Chinese National Knowledge Infrastructure; KBD: Kashin-Beck Disease; PRISMA: Systematic reviews and Meta-analysis

Acknowledgements
Not applicable.

Funding
This work is supported by the General Financial Grant from the China Postdoctoral Science Foundation (2017M613153), the General Financial Grant from the China Postdoctoral Science Foundation (2017 M623197), the National Natural Science Foundation of China (81472924), the National Natural Science Foundation of China (81803179), the National Natural Science Foundation of China (81803178), the National Key R&D Program of China (China-Korea, grant no. 2016YFE0119100). The Fundamental Research Funds for the Central Universities and Shaanxi Natural Science Basic Research Project – General Project (Youth) (grant no. 2018JQ8025 and 2018JQ8012).

The Fundamental Research Funds for the Central Universities. Innovative Training Program Fund for College Students (201610698090).

Availability of data and materials
Not applicable.

Authors’ contributions
XW, YJN, and XG designed the study. AML, XQ, MDL performed the analysis and interpretation of the data. XW, YJN, PZ and XG analyzed the results and drafted the manuscript. All authors critically reviewed and amended the manuscript, and all authors read and approved the final manuscript.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details
1School of Public Health, Xi’an Jiaotong University Health Science Center, Key Laboratory of Trace Elements and Endemic Diseases, National Health and Family Planning Commission, No.76 Yanta West Road, 710061 Xi’an, People’s Republic of China. 2Xi’an Jiaotong University Global Health Institutes, No.76 Yanta West Road, Xi’an 710061, People’s Republic of China.

Received: 23 April 2018 Accepted: 7 February 2019
Published online: 14 February 2019

References
1. Guo X, Ma WJ, Zhang F, Ren FL, Qu CJ, Lammi MJ. Recent advances in the research of an endemic osteochondropathy in China: Kashin-Beck disease. Osteoarthr Cartil. 2014;22:1774–83.
2. The National Health Commission of China. The prevention and control status of Kashin-Beck disease in 2017.
3. Xiong G. Diagnostic, clinical and radiological characteristics of Kashin-Beck disease in Shaanxi Province, PR China. Int Orthop. 2001;25:147–50.
4. Wang X, Zhang P, Ning Y, Yang L, Yu F, Guo X. Serum and hair zinc levels in patients with endemic Osteochondropathy in China: A meta-analysis. Biol Trace Elem Res. 2017.
5. group NKBdm. Report of a National Survey of Kashin-Beck disease prevalence in 2005. Chinese Journal of Endemiology. 2006;25:670–2.
6. Liu H, Zhou LW, YQ L. Analysis of National Surveillance on Kashin-Beck disease condition from 2000 to 2007. Chinese Journal of Endemiology. 2009;28:554–6.
7. Panic N, Leoncini E, de Belvis G, Ricciardi W, Boccia S. Evaluation of the endorsement of the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement on the quality of published systematic review and meta-analyses. PLoS One. 2013;8:e83138.
8. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. Arch Public Health. 2014;72:39.
9. Borenstein M, Hedges LV, Higgins JP, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. Res Synth Methods. 2010;1:97–111.
10. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327:557–60.
11. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315:629–34.
12. Zhang CN, Zhang W, ZS N. Summary of 14 years’ monitoring of kaschin - beck disease in Helongjiang province. Chinese journal of control of endemic. Diseases. 2005;2006:1–3.
13. Su HM, Qiao H, Y L. Analysis of monitoring results of kaschin - beck disease in Songyuan from 2009 to 2011. Chinese journal of control of endemic. Diseases. 2012;27:142–3.
14. H T. Analysis of monitoring results of Kaschin - Beck disease in Erdos City in 2011. Inner Mongolia Medical Journal. 2012;24:24–5.
15. Xun H, Wang Q, Yu YF. JY C. Analysis of 17 - year monitoring results of Kashin - Beck disease in Wushenqi of inner. Inner Mongolia medical. Journal. 2009;41:211–3.
16. Xun H, Wang Q, Yu YF. JY C. Surveillance of Kashin - Beck disease in Nalin River township, Wushenqi, Inner Mongolia from 2000 to 2006. Inner Mongolia medical. Journal. 2007;39:621–2.
17. Yuan F, JX Z. Current status and dynamics of Kashin - Beck disease in Huanqi. Chinese journal of control of endemic. Diseases. 1998, 13:162–3.
18. Yuan F, Jx Z. Present situation and dynamic analysis of Kashin Beck disease in Hulan Buru league. Chinese journal of control of endemic. Diseases. 1998, 13:162–3.
19. Liu QB, Liu XH, Zhang JX, Wang G, Fan J, Liu XB, et al. Evaluation of the effect of changing food for the prevention of Kashin - Beck disease in Hulunbeier league, inner. Chinese Journal of Epidemiology. 2002;21:117–9.
20. Zhang JX, JG Z. 1990-1994 report of Huakao Kashin-Beck disease. Study on Prevention and Control of Endemic Diseases in inner. 1995,20:125–6.
21. Zhou JC, Zhang MQ, C L. study on the evaluation model for eliminating Kashin - Beck disease in Huairou district Beijing. Chinese journal of control of endemic. Diseases. 2013;28:283–4.
22. Wang JR, Zhang J, HR C. Dynamic observation and analysis of Kashin - Beck disease in Chunhua County of Shaanxi Province. Studies of Trace Elements and Health. 2011;28:37–8.
23. Yu YH, Cui CL, YT Y. Prevalence of Kashin - Beck disease in Henan Province. Henan. J Prev Med. 2011;22:237–8.
24. Yu HY, Xing RX, Yang GM, Cui C, Standard PXH. Range of selenium concentration in selenium iodide in Kaschin disease and Keshan disease area in Henan province. Henan Journal of Preventive Medicine. 2001;12: 260–51.
25. Yang WZ, Wang DS, Wang YC, Wu XJ, Bai JC, Surveillance JW. Analysis of Kaschin - Beck disease in Shanxi County of Henan Province. Henan Journal of Preventive Medicine. 1994,5:56–6.
26. HJ W. Report on 32 - year monitoring of Kaschin - Beck disease in Beijing. Medical Journal of Chinese People's Health. 2011;23:1481–2.
27. He XQ, M Z. Surveillance and analysis of prevention and treatment of Kashin - Beck disease in Nanxheng County of Shaanxi Province in the past 20 years. Journal of Preventive Medicine of Anhui province. 2010;16:180–1.
28. Xie L, Chen W, Jin L, Yang G, PJ Y. Monitoring report of Kashin - Beck disease and selenium in 2007 and 2008. Modern Preventive Medicine. 2010; 37:924–5.
29. Xie L, Chen W, Jin L, G Y. Analysis of monitoring results of Kaschin - Beck disease in Xi'an from 2006 to 2007. Chinese journal of control of endemic. Diseases. 2008;23:307–8.
30. Lv XY, Xu GY, P C. Report on monitoring of Kaschin - Beck disease in Shaanxi Province in 2007. Chinese journal of control of endemic. Diseases. 2009;24:309–10.
31. Xu GY, Cao XG, XY L. Report of Kaschin-Beck disease prevalence and selenium salt monitoring in Shaanxi province from 2001 to 2003. Chin J End. 2004;23:556–7.
32. Cao XG, Zhang BD, Qin ZR, Lv XY, Xu GY, Liu HL, et al. The monitoring report of Kaschin-Beck disease prevalence rate in Yuyang county of Shaanxi. Chin J End. 2004;23:369–70.
33. Yang G, Chen W, Xie L, L J. Surveillance Report of Kashin - Beck Disease in Jinjing Village, Zhouzhi County, Xi'an, from 2001 to 2003. Chin J End. 2005; 24:704.
34. Wang FQ, ZW W. Surveillance report of Kashin-Beck disease from 1996 to 2000 in Linyou County, Shaanxi Province. Endemic Diseases Bulletin. 2001; 1665.
35. Chen W, Yang G, Jing L, Yao PI, L X. Analysis on monitoring results of Kaschin-Beck disease flow monitoring points in Xi'an from 2001 to 2002. Occupation and Health. 2004;20:79–80.
36. Sun J, Che WF, Han W, Wu YX, Xu JF, BK W. An investigation on the relation between improvement of Kashin-Beck disease and Environmental selenium level. Endemic Diseases Bulletin. 1992;716–8.
37. Xu GY, Cao XG, XY L. Analysis on monitoring data of Kashin-Beck disease in Shaanxi province during 19 years. Chin J End. 2009;24:442–6.
38. Xie L, Chen W, Jing L, Yang G, PJ Y. Analysis on monitoring results of Kashin-Beck disease in Lantian county of Xi'an city from 2001 to 2008. Modern Preventive Medicine. 2011;38:2382–4.