



# Prevalence of Bovine Viral Diarrhea Virus in Ovine and Caprine Flocks: A Global Systematic Review and Meta-Analysis

Nai-Chao Diao<sup>1,2†</sup>, Zi-Yang Chen<sup>1,2†</sup>, Jun-Feng Shi<sup>1,2</sup>, Qi Wang<sup>1,2</sup>, Chen-Yan Sheng<sup>1,2</sup>, Bao-Yi Ma<sup>1,2</sup>, Yang Yang<sup>1</sup>, Yu-Han Sun<sup>1</sup>, Kun Shi<sup>1\*</sup> and Rui Du<sup>1,3,4\*</sup>

<sup>1</sup> College of Chinese Medicine Materials, Jilin Agricultural University, Changchun, China, <sup>2</sup> College of Animal Science and Technology, Jilin Agricultural University, Changchun, China, <sup>3</sup> Laboratory of Production and Product Application of Sika Deer of Jilin Province, Jilin Agricultural University, Changchun, China, <sup>4</sup> Key Laboratory of Animal Production, Product Quality and Security, Ministry of Education, Jilin Agricultural University, Changchun, China

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### \*Correspondence:

Kun Shi  
sk1981521@126.com  
Rui Du  
durui197101@sina.com

†These authors share first authorship

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**Background:** Bovine viral diarrhea virus (BVDV) is the causative agent of bovine viral diarrhea. It can infect cattle, sheep, pigs, and other animals, causing diarrhea, miscarriage, and stillbirth, among other symptoms, and it can result in huge economic losses to animal husbandry. There are reports on BVDV infection rates in sheep and goat herds from all over the world and this meta-analysis aimed to evaluate the prevalence of and risk factors for BVDV in sheep and goats.

**Results:** Using the data of 41,297 sheep and goats in 24 countries/regions to calculate a comprehensive prevalence rate for BVDV. The overall prevalence of BVDV infection in sheep and goats was estimated to be 8.6% (95% CI: 5.2–12.7) by immunological methods and 7.3% (95% CI: 2.7–13.7) by molecular methods. Analysis by national income level revealed that prevalence is higher in middle-income countries than in high-income countries ( $P < 0.05$ ). The study also compared prevalence rates by species of BVDV, sampling year, and test species, but did not find significant differences.

**Conclusion:** This systematic review and meta-analysis is the first to determine the global prevalence of BVDV in ovine and caprine flocks. The prevalence of BVDV in sheep and goat populations varies from region to region, and the situation is not optimistic in some countries.

**Keywords:** bovine viral diarrhea virus, ovine, caprine, prevalence, meta-analysis

## INTRODUCTION

Bovine viral diarrhea virus (BVDV) is currently classified as the genus *Pestivirus* and family *Flaviviridae*, it is a single-stranded, positive-sense RNA virus (1). The natural host of BVDV is cattle, but it can also infect goats, sheep, piglets, and other domestic and wild ruminants through transiently infected individuals and persistently infected (PI) animals (2). BVDV infection in goats typically result in reproductive-system diseases, but survival in PI goats that can survive are rare (3). The main clinical symptoms of BVDV include decreased productivity and fecundity, slow fetal growth, diarrhea, respiratory symptoms, reproductive dysfunction (such as abortion, teratogenicity, fetal mummification, and stillbirth), and immune dysfunction, all of which can be

complicated by infection (4–6). Two species of BVDV, i.e., BVDV-1 (Pestivirus A) and BVDV-2 (Pestivirus B), have been identified as bovine pestiviruses, together with the HoBi-like pestivirus (Pestivirus H) (7). Each species has multiple subgenomes: BVDV-1 can be divided into at least 21 subgenomes (1a-1u) and BVDV-2 can be divided into four subgenomes (2a-2d) (8). BVDV-1, BVDV-2, Border disease virus (BDV), and HoBi-like viruses have been identified from sheep and cattle (9). Cattle, sheep, and goats are the main domestic livestock across the world, and widespread infection with BVDV disease has caused huge economic losses to the livestock industry (10), with the cross-infection of a variety of animals making prevention and control of the disease difficult (11).

In economic terms, sheep and goats occupy an important position in the global livestock breeding industry. For example, in the Kyrgyz Republic (Kyrgyzstan), animal husbandry (especially sheep breeding) has always been the basis for supporting the livelihoods of local people. The contribution of agricultural production to the economy is vital (about 45% of total income) (12). Australia is the country with the largest number of sheep stock and is the largest exporter of wool in the world, widely known as the “country on the back of sheep.” Its developed sheep- and goat- farming industry is world-renowned and has been the lifeblood of the country’s agricultural development for many years (13). Similarly, sheep breeding is an important source of income for many agricultural countries in the world (14). Recent studies have shown that BVDV infection of sheep and goats can cause diarrhea, miscarriage of female animals, stillbirth and teratogenesis (3, 15, 16). Researchers have found BVDV in infected sheep fetal tissue, proving that the virus can be transmitted through the sheep placental barrier (17). Goats infected with BVDV have higher neonatal morbidity and mortality (18, 19). BVDV infection can cause immunosuppression and lead to mixed infection and secondary infection by other pathogens, seriously impact the sustainable development of the global livestock industry (20, 21).

To the best of the authors’ knowledge, no systematic assessment of the prevalence of BVDV infection in ovine and caprine flocks worldwide has been conducted. Understanding the epidemiology and epidemic dynamics of sheep and goat BVDV will help prevent and control disease caused by BVDV infection of sheep and goats and will help to evaluate the effectiveness of vaccination. Therefore, we conducted a systematic review and meta-analysis to estimate the prevalence of BVDV infection in sheep and goat populations worldwide. This article aims to comprehensively evaluate the prevalence of BVDV infection in sheep and goats by conducting a meta-analysis of articles that have been published around the world. Through this process, we evaluate the geographical distribution in terms of factors such as climate and altitude as well as the main factors affecting BVDV infection in sheep and goat herds to provide guidance on and suggestions for the prevention and control of BVDV.

**Abbreviations:** BDV, Border disease virus; ELISA, Enzyme-linked immunosorbent assay; SNT, Serum neutralization test; RT-PCR, Reverse transcription-polymerase chain reaction; OIE: World Organisation for Animal Health.

## MATERIALS AND METHODS

This systematic review and meta-analysis was performed strictly in accordance with the relevant requirements of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement (22) (**Supplementary Material 1**).

### Literature Retrieval Strategy

A literature search in Chinese and English was conducted, searching Chinese Web of Knowledge (CNKI), the Wanfang database, the Chongqing VIP database, PubMed, Science Direct, Web of Science, and Springer Link.

In Pubmed, we built Search Formula A: (Diarrhea Viruses, Bovine Viral [Mesh] OR BVDV OR Diarrhea Virus, Bovine Viral OR Bovine Viral Diarrhea Viruses OR Bovine Diarrhea Virus OR Bovine Diarrhea Viruses OR Diarrhea Virus, Bovine OR Diarrhea Viruses, Bovine OR Virus, Bovine Diarrhea OR Viruses, Bovine Diarrhea OR Bovine Pestivirus OR Bovine Pestiviruses OR Pestiviruses, Bovine). We then built Search Formula B: (sheep [MeSH Terms] OR Ovis OR Dall Sheep OR Ovis dalli OR Sheep, Dall OR Goats [MeSH Terms] OR Goat OR Capra OR Capras OR Sheep, Domestic OR Domestic Sheep OR Ovis ammon aries OR Ovis aries OR Mouflon OR Mouflons OR Ovis gmelini musimon OR Ovis aries musimon OR Small ruminants [MeSH Terms]). Finally, we used the logical “AND” with the two formulas to identify items satisfying both Search Formula A AND Search Formula B: (Diarrhea Viruses, Bovine Viral [Mesh] OR BVDV OR Diarrhea Virus, Bovine Viral OR Bovine Viral Diarrhea Viruses OR Bovine Diarrhea Virus OR Bovine Diarrhea Viruses OR Diarrhea Virus, Bovine OR Diarrhea Viruses, Bovine OR Virus, Bovine Diarrhea OR Viruses, Bovine Diarrhea OR Bovine Pestivirus OR Bovine Pestiviruses OR Pestiviruses, Bovine) AND (sheep [MeSH Terms] OR Ovis OR Dall Sheep OR Ovis dalli OR Sheep, Dall OR Goats [MeSH Terms] OR Goat OR Capra OR Capras OR Sheep, Domestic OR Domestic Sheep OR Ovis ammon aries OR Ovis aries OR Mouflon OR Mouflons OR Ovis gmelini musimon OR Ovis aries musimon OR Small ruminants [MeSH Terms]).

In Science Direct, we built the Search Formula: (“Diarrhea Viruses, Bovine Viral” OR BVDV OR Pestivirus) AND (sheep OR goat OR small ruminants) AND (prevalence). In Web of Science, we built the Search Formula: (“Diarrhea Viruses, Bovine Viral” OR BVDV OR Pestivirus) AND (sheep OR goat OR small ruminants) AND (prevalence). In SpringerLink, we built Search Formula: (“Diarrhea Viruses, Bovine Viral” OR BVDV OR Pestivirus) AND (sheep OR goat OR small ruminants) AND (prevalence). In the CNKI database, we used the term “BVDV” + “Viral diarrhea” AND “sheep and goats” + “small ruminants” (The words were spelled in Chinese; the “+” represents the Boolean operator “OR”). In the Wanfang database, we used the terms (BVDV OR Viral diarrhea) AND (sheep and goats OR small ruminants) (in Chinese). The types of articles found in the Wanfang database were limited to “papers in journals, degree theses and conferences.” In the VIP Chinese Journal Database, we used the search formulas: (BVDV OR Viral diarrhea) AND (sheep and goats OR small ruminants) (The words were spelled in Chinese and “OR”). The search strategies and search restrictions

are reported in **Supplementary Material 2**. Endnote (version X9.3.1) was used to catalog the articles retrieved.

## Inclusion and Exclusion Criteria

The following inclusion criteria were applied: (1) the research objects were sheep and goats; (2) sample size was  $>30$ ; (3) research content included the number of sheep and goats infected with viruses; and (4) research reports were published in Chinese or English.

The following exclusion criteria were applied: (1) reviews; (2) duplicate publications or studies with similar data; (3) incomplete, unclear, or obviously erroneous data that could not be resolved by contacting the authors; (4) research on BVDV vaccination; (5) other species besides sheep and goats; (6) the type of sample collected for the study is a fecal sample (Most of the material collected in the study was diarrhea, which may overestimate the positive rate and is not sufficiently representative of the true infection status of the herd).

## Quality Assessment

The quality of the selected literature depends on the level of proposal evaluation, formulation, and evaluation methods (23). Quality was scored using a method with a maximum of five points assigned to each study. The studies were graded according to whether they detailed random sampling, inspection methods, sampling time, had a sample size greater than or equal to 200, or contained four or more risk factors, with one point awarded for each of these criteria met. According to this standard, we defined a score of 4–5 as high quality, 2–3 as middle quality, and 0–1 as low quality.

## Literature Screening and Data Extraction

The screening of the literature was carried out by four trained reviewers. First, preliminary screening of the title and abstract of the literature was carried out, then the full text was evaluated and the statistics examined. The authors of the original studies were not contacted for more information, and no unpublished data were used. Any disagreements between reviewers were resolved by Zi-Yang Chen, the study author.

We referred to a standardized data collection table to extract the data contained in the article (24). The recorded information was as follows: first author; publication year; sampling time; country; national income level (according to World Bank data available at [https://data.worldbank.org/cn/indicator/NY.GNP.MKTP.CD?name\\_desc=false](https://data.worldbank.org/cn/indicator/NY.GNP.MKTP.CD?name_desc=false)), with national income level divided into low-income, middle-income, and high-income; immunological method (ELISA and SNT); feeding mode (free-range agriculture and concentrated agriculture); BVDV species (BVDV-1 and BVDV-2); test species (sheep and goat); subject age (under 1 year old, 1–2 years old, and over 2 years old); sample classification (aborted fetuses and serum). Article quality level (low quality, middle quality, high quality) was also recorded.

Geographic area and geographic factors (geographic factor data provided by the National Oceanic and Atmospheric Administration National Environmental Information Center at <https://gis.ncdc.noaa.gov/maps/ncei/cdo/monthly>) were also extracted, including the latitude and longitude, altitude, annual

average precipitation, and average annual temperature of the sampling area. We grouped latitude according to south or north, depending on position in relation to the equator. North and south were further divided into groups for every 30-degree section. The longitude subgroup was divided into west and east, with the 180-degree sections from the prime meridian to east and west each subdivided into 30-degree section groups. Altitude was divided into three groups according to international standards: 1,500–3,500 meters (medium altitude), 3,500–5,300 meters (high altitude), and  $>5,300$  meters (extreme altitude) (25). The average annual precipitation subcomponents were  $<200$  mm and 200–400 mm. The average annual temperature was divided into subgroups for every  $10^{\circ}\text{C}$ . Extracting the geographical factors presented some problems. If there was no weather station in the sampling area, we chose the station closest to the sampling location. The precipitation and average annual temperature data provided by the station was not always complete, so we chose the year closest to the sampling year to calculate averages. If no sampling year was given, we only extracted the latitude, longitude, and altitude of the sampling point.

## Statistical Analysis

A systematic review and meta-analysis of the included studies was conducted to calculate the combined prevalence of BVDV infection in sheep and goats. A meta-analysis of the ratio was performed using R software (version 4.0.0). According to previous research, double-arc-sine transformation (PFT) can be used to transform the observed rates to make them closer to (in line with) the normal distribution (26, 27). This part of the code is in **Supplementary Material 3**. The formula for PFT is as follows:

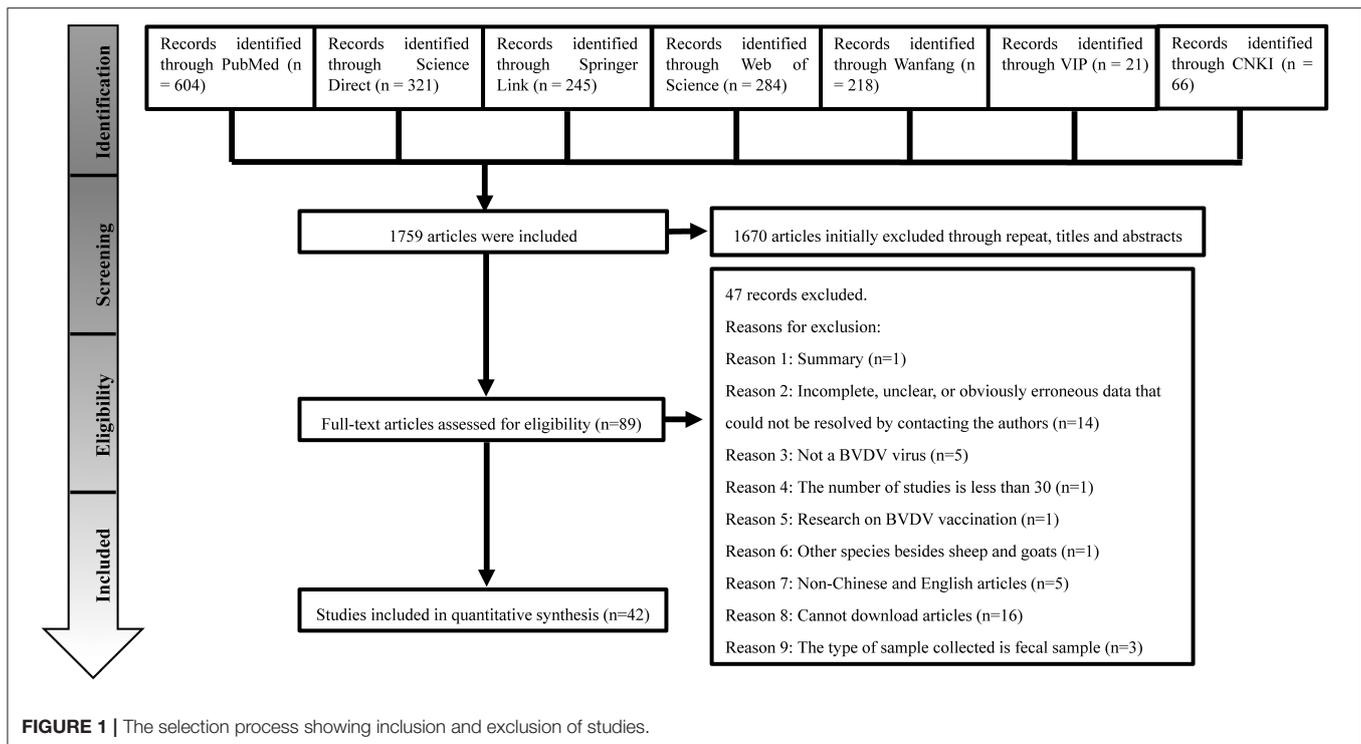
$$t = \arcsin(\sqrt{r/(n+1)}) + \arcsin(\sqrt{(r+1)/(n+1)})$$

$$se(t) = \sqrt{1/(n+0.5)}$$

$$p = (\sin(t/2))^2$$

Note:  $t$ : transformed prevalence;  $r$ : positive number;  $n$ : sample size;  $se$ : standard error.

To investigate whether the results have obvious heterogeneity, “meta” software package was used to calculate and prepare forest plots, using a random-effects model to predict heterogeneity (26, 28–30). The statistics  $I^2$  and Cochran's  $Q$  (represented as  $\chi^2$  and  $P$ -values) were used to assess variability.  $I^2 < 50\%$  represented low heterogeneity and  $I^2 > 50\%$  represented high heterogeneity, describing the percentage of difference between studies due to heterogeneity.  $P < 0.05$  was considered statistically significant. Funnel plots, Egger's test and “trim and fill analysis” were used to detect publication bias, with publication bias and heterogeneity subjectively judged through funnel plot symmetry. A symmetrical graph was taken as representing an absence of publication bias and heterogeneity; asymmetry suggested publication bias and heterogeneity. Egger's test, based on the  $P$ -value, was used to assess publication bias. When  $P \geq 0.05$ , the deviation was considered non-existent.  $P < 0.05$  was taken as indicative of publication bias. The trim and fill analysis uses an iterative algorithm that removes a very small sample of studies from the positive side of the funnel plot (the side of the funnel plot with the most studies in the literature), recalculates the total



effect size, and then gradually adds these originally removed studies to the formula and recalculates, repeating this until the funnel plot is left-right symmetric around the recalculated total effect size. A sensitivity analysis was conducted to further determine the stability of the results obtained. This was done by deleting one study at a time, merging the remaining studies, and judging the impact of the deleted study on the overall data by comparing the differences before and after.

The factors we investigated included sampling year (before 2000, 2001–2010, and after 2010), national income level (medium and high), feeding mode (free-range agriculture and concentrated agriculture), BVDV specie (BVDV-1 and BVDV-2), species tested (sheep and goats), age of test subjects (below 1 year old, 1–2 years old and over 2 years old), sample classification (aborted fetuses and serum), article quality level (low, middle, and high quality), latitude (0–30°N, 0–30°S, 30–60°N), longitude (0–30°E, 30–60°E, 60–90°E, 90–120°E, 120–150°E, 0–30°W, 30–60°W), altitude (<1,500 m, 1500–3500 m, 3500–5300 m), precipitation (<200 mm, 200–400 mm), and temperature (<0°C, 1–10°C, 10–20°C, 20–30°C).

## RESULTS

### Literature Screening Process and Results

Figure 1 shows the PRISMA flow diagram. A total of 1,759 records were identified through database searching. Of these, 42 studies were eligible for the meta-analysis. Of the retrieved articles, 11 datasets were based on molecular methods, and 31 datasets were based on immunological methods.

Studies were identified from 24 countries worldwide, including four countries in Africa, two countries in South America, two countries in North America, seven countries in Europe, two countries in Oceania, and seven countries in Asia. Twenty-two studies were conducted in middle-income countries, and 20 studies were conducted in high-income countries. According to our quality rating scale, nine study articles were of middle quality (2–3 points), the remaining 32 were of high quality (four or five points), and only one article was of low quality (0–1 point) (Table 1).

### Evaluation of Publication Bias

Four positive conversions were performed on the data (Tables 2, 3). The PFT conversion results were closer to the normal distribution, and we chose the combined results of the PFT conversion for meta-analysis. The extent of publication bias in the selected studies was evaluated and illustrated by funnel plots (Figures 2, 3). A random effects model ( $I^2 = 99\%$ ) was used and visualized with forest plots (Figures 4, 5). According to the results of Egger's test ( $P = 0.7739$  and  $P = 0.07888$ ), we considered that the included articles were not biased for publication (Supplementary Figures 1, 2, Supplementary Tables 1, 2). The trim and fill analysis showed that the included studies had minimal sample size bias (Supplementary Figures 3, 4).

### Sensitivity Analysis of the Included Literature

The sensitivity analysis (Supplementary Figures 5, 6) results showed that after removing one study, the reorganized results

**TABLE 1** | Included studies of BVDV infection in sheep and goats worldwide.

| Study ID                         | Sampling time  | Income level | Country                | Detection methods <sup>a</sup> | Positive samples/<br>total samples | Quality<br>score | Quality level |
|----------------------------------|----------------|--------------|------------------------|--------------------------------|------------------------------------|------------------|---------------|
| <b>Africa</b>                    |                |              |                        |                                |                                    |                  |               |
| Hyera et al. (31)                | 1987           | Middle       | Tanzania               | SNT                            | 424/1564                           | 5                | High          |
| Depner et al. (32)               | 1987–1989      | Middle       | Namibia                | SNT                            | 137/1736                           | 5                | High          |
| Feknous et al. (33)              | UN             | Middle       | Algeria                | SNT                            | 2/689                              | 3                | Middle        |
| Lysholm et al. (34)              | 2016.09        | Middle       | Botswana               | ELISA                          | 0/100                              | 4                | High          |
| <b>South America</b>             |                |              |                        |                                |                                    |                  |               |
| Rosadio et al. (35)              | UN             | Middle       | The Republic of Peru   | SNT                            | 1/34                               | 2                | Middle        |
| Julia' et al. (36)               | UN             | High         | Argentina              | SNT                            | 32/54                              | 2                | Middle        |
| <b>Asia</b>                      |                |              |                        |                                |                                    |                  |               |
| Okur-Gumusova et al. (37)        | UN             | Middle       | The Republic of Turkey | SNT                            | 463/2444                           | 4                | High          |
| Ataseven et al. (38)             | 2004.6–2005.2  | Middle       | The Republic of Turkey | SNT                            | 83/275                             | 5                | High          |
| Mishra et al. (39)               | 2004–2006      | Middle       | India                  | RT-PCR                         | 2/562                              | 5                | High          |
| Mishra et al. (40)               | 2004–2007      | Middle       | India                  | RT-PCR                         | 8/1561                             | 5                | High          |
| Yeşilbag and Gungor (41)         | 2004.4–2005.10 | Middle       | The Republic of Turkey | SNT                            | 124/388                            | 5                | High          |
| Yeşilbag et al. (42)             | UN             | Middle       | The Republic of Turkey | SNT                            | 0/137                              | 2                | Middle        |
| Safarpour Dehkordi (43)          | 2010           | Middle       | Iran                   | RT-PCR                         | 167/967                            | 4                | High          |
| Gianguasero et al. (44)          | 2007.9–2008.1  | High         | Japan                  | SNT                            | 1/165                              | 3                | Middle        |
| Li (45)                          | UN             | Middle       | China                  | SNT                            | 12/35                              | 3                | Middle        |
| Oem et al. (46)                  | 2009.11–2011.8 | High         | Korea                  | ELISA                          | 10/672                             | 5                | High          |
| Kalaiyarasu et al. (47)          | 2005–2010      | Middle       | India                  | ELISA                          | 187/569                            | 4                | High          |
| Mao et al. (48)                  | 2011–2013      | Middle       | China                  | RT-PCR                         | 31/238                             | 4                | High          |
| Mao et al. (49)                  | 2011–2013      | Middle       | China                  | RT-PCR                         | 29/236                             | 4                | High          |
| Chen et al. (50)                 | 2014.10–2016.6 | Middle       | China                  | RT-PCR                         | 58/195                             | 3                | Middle        |
| Bulut et al. (51)                | 2011–2015      | Middle       | The Republic of Turkey | RT-PCR                         | 40/396                             | 4                | High          |
| Deng et al. (52)                 | 2013.3–2016.4  | Middle       | China                  | ELISA                          | 38/217                             | 4                | High          |
| Tamer et al. (53)                | UN             | Middle       | The Republic of Turkey | SNT                            | 101/543                            | 4                | High          |
| Ma et al. (54)                   | 2013.4–2014.3  | Middle       | China                  | ELISA                          | 804/2187                           | 5                | High          |
| Hidayat et al. (55)              | 2020.7–10      | Middle       | Indonesia              | RT-PCR                         | 2/46                               | 4                | High          |
| <b>Europe</b>                    |                |              |                        |                                |                                    |                  |               |
| Løken et al. (56)                | 1980–1984      | High         | The Kingdom of Norway  | SNT                            | 166/3712                           | 4                | High          |
| Løken (57)                       | 1983–1984      | High         | The Kingdom of Norway  | SNT                            | 83/2335                            | 4                | High          |
| Graham et al. (58)               | 1999.6–9       | High         | UK                     | SNT                            | 14/918                             | 4                | High          |
| O'Neill et al. (59)              | 2001.5.17–6.26 | High         | Republic of Ireland    | SNT                            | 39/1448                            | 4                | High          |
| Krametter-Froetscher et al. (60) | UN             | High         | Austria                | SNT                            | 32/549                             | 3                | Middle        |
| Danuser et al. (61)              | 2005–2006      | High         | Switzerland            | ELISA                          | 827/5562                           | 5                | High          |
| Krametter-Froetschee et al. (62) | 2005–2006      | High         | Austria                | RT-PCR                         | 1/1196                             | 4                | High          |
| Czopowicz et al. (63)            | 2007.6–7       | High         | Poland                 | ELISA                          | 7/1060                             | 5                | High          |
| Casaubon et al. (64)             | 2009–2011      | High         | Switzerland            | ELISA                          | 9/500                              | 4                | High          |
| Decaro et al. (65)               | 2015–2016      | High         | Italy                  | RT-PCR                         | 27/1231                            | 4                | High          |
| Emma et al. (66)                 | 2018.6–11      | High         | Northern Ireland       | ELISA                          | 56/3372                            | 5                | High          |
| Potârniche et al. (67)           | 2014–2018      | High         | Poland                 | ELISA                          | 7/910                              | 5                | High          |
| <b>Oceania</b>                   |                |              |                        |                                |                                    |                  |               |
| Robinson (68)                    | UN             | High         | New Zealand            | SNT                            | 14/50                              | 1                | Low           |
| Evans et al. (69)                | UN             | High         | Australia              | ELISA                          | 0/875                              | 4                | High          |
| Evans et al. (70)                | 2018.8–10      | High         | New Zealand            | ELISA                          | 17/270                             | 4                | High          |
| <b>North America</b>             |                |              |                        |                                |                                    |                  |               |
| Silveira et al. (9)              | 2015–2016      | High         | US                     | SNT                            | 20/200                             | 4                | High          |
| Lamontagne et al. (71)           | UN             | High         | Canada                 | SNT                            | 89/700                             | 3                | Middle        |

Detection methods<sup>a</sup>: ELISA, enzyme-linked immunosorbent assay; RT-PCR, reverse transcription-polymerase chain reaction; SNT, serum neutralization test.

**TABLE 2** | Normal distribution test and conversion forms for the normal distribution of prevalence (Immunological methods).

| Conversion form | W       | P         |
|-----------------|---------|-----------|
| PRAW            | 0.79631 | 4.414e-05 |
| PLN             | NaN     | NA        |
| PLOGIT          | NaN     | NA        |
| PAS             | 0.91542 | 0.01788   |
| PFT             | 0.91019 | 0.01307   |

PRAW, original rate; PLN, logarithmic conversion; PLOGIT, logit transformation; PAS, arcsine transformation; PFT, double-arcsine transformation; NaN, meaningless number; NA, missing data.

**TABLE 3** | Normal distribution test and conversion forms for the normal distribution of prevalence (Molecular methods).

| Conversion form | W       | P       |
|-----------------|---------|---------|
| PRAW            | 0.89584 | 0.1643  |
| PLN             | 0.87417 | 0.08768 |
| PLOGIT          | 0.8911  | 0.1435  |
| PAS             | 0.93748 | 0.4914  |
| PFT             | 0.94008 | 0.5214  |

PRAW, original rate; PLN, logarithmic conversion; PLOGIT, logit transformation; PAS, arcsine transformation; PFT, double-arcsine transformation.

were consistent with the previous results, indicating that the systematic review and meta-analysis results were relatively stable and reliable.

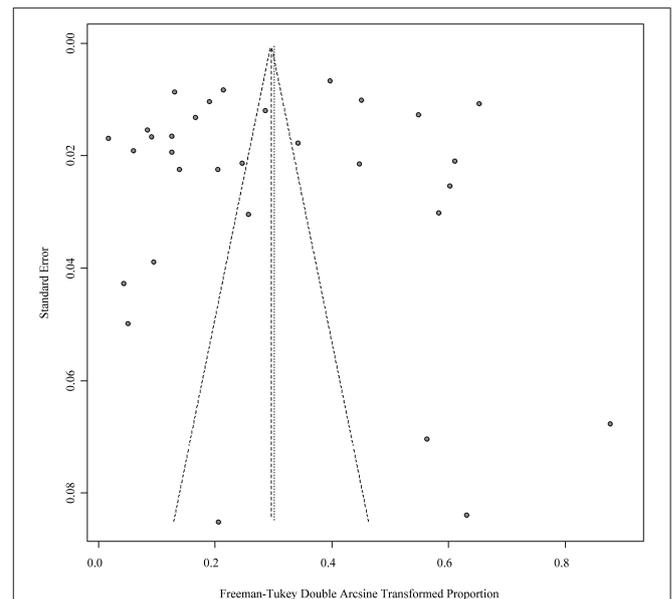
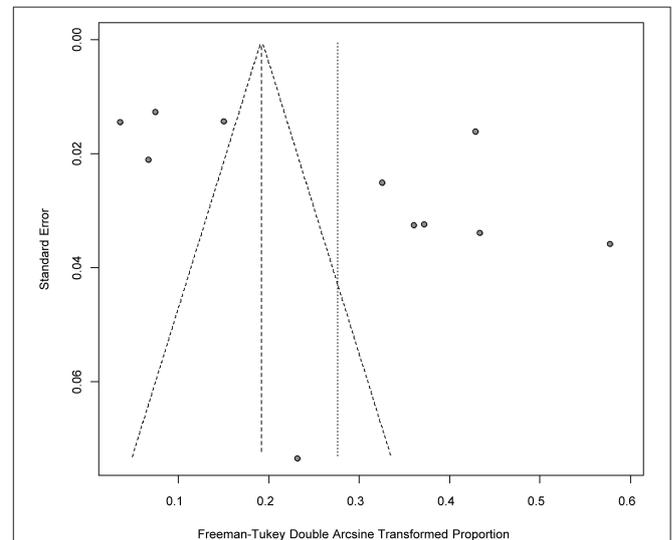
## Meta-Analysis

### Results Based on Immunological Methods

A total of 34,452 sheep and goats from 31 datasets were evaluated for detection of BVDV in their serum. The prevalence of BVDV infection in sheep and goats detected using immunological methods was 8.6% (95% CI: 5.2–12.7, 3,761/34,452; **Table 4**). In the regional subgroups, the prevalence for South America was 26.2% (95% CI: 0.0–87.8, 33/88; **Table 5**), which is higher than that of other regions. In terms of income-level subgroups, middle-income countries had the highest antibody prevalence of 14.9% (95% CI: 8.2–23.1, 2,338/10,701; **Table 4**).

As can be seen from **Table 4**, the prevalence is significantly different among age groups ( $P < 0.05$ ), with the prevalence of 31.8% (95% CI: 24.2–40.0, 919/2,812) for animals over 2 years old being higher than that of the other age groups. There is no significant difference between subgroups by sampling year.

Furthermore, in terms of BVDV species, the prevalence of BVDV-1 was highest (10.5%, 95% CI: 2.6–21.4, 911/7,725). When comparing prevalence between goats and sheep, the prevalence in sheep (11.4%, 95% CI: 6.4–16.8, 2,976/24,709) was higher than that in goats (8.7%, 95% CI: 4.5–14.1, 785/9,743). In terms of feeding mode, the prevalence was higher in concentrated agriculture (17.9%, 95% CI: 11.7–25.2, 2,591/13,778) than in free-range agriculture (5.3%, 95% CI: 1.6–10.8, 180/2,915). According to quality of study, the prevalence was highest in studies of low

**FIGURE 2** | Publication bias of studies by funnel plot (Immunological methods).**FIGURE 3** | Publication bias of studies by funnel plot (Molecular methods).

quality (28.0%, 95% CI: 16.3–41.4, 14/50; **Table 4**). There were no significant differences between the geographic factor subgroups.

### Results Based on Molecular Methods

A total of 6,845 sheep and goats from 11 datasets were evaluated for detection of BVDV in their aborted fetuses, and serum. Using the random-effects model, the prevalence of BVDV infection in sheep and goats detected using molecular methods was 7.3% (95% CI: 2.7–13.7, 403/6,845; **Table 6**). In the regional subgroups, the prevalence for Asia was 9.6% (95% CI: 3.3–18.6, 375/4,418; **Table 7**), which is higher than that for Europe (0.8%, 95% CI:

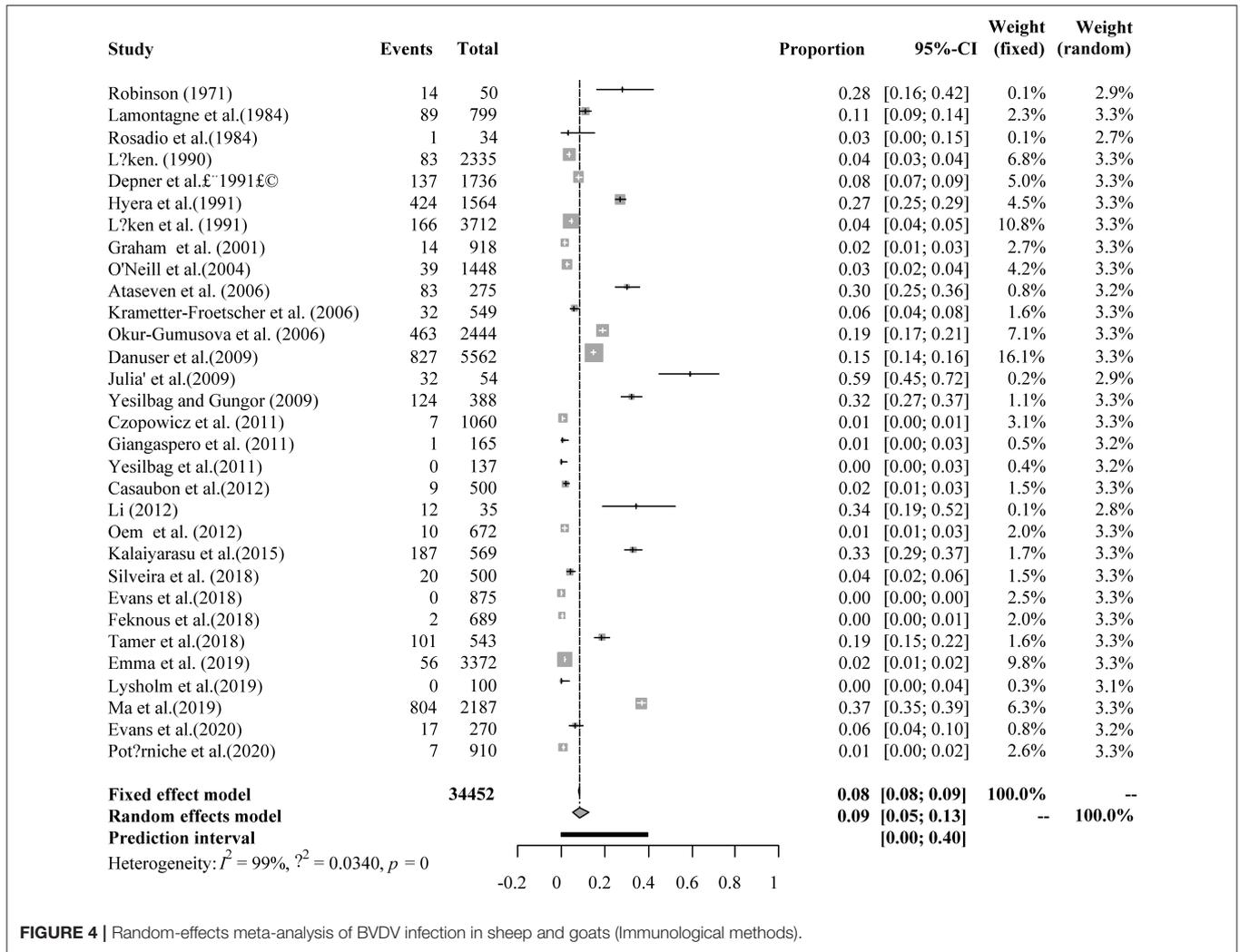


FIGURE 4 | Random-effects meta-analysis of BVDV infection in sheep and goats (Immunological methods).

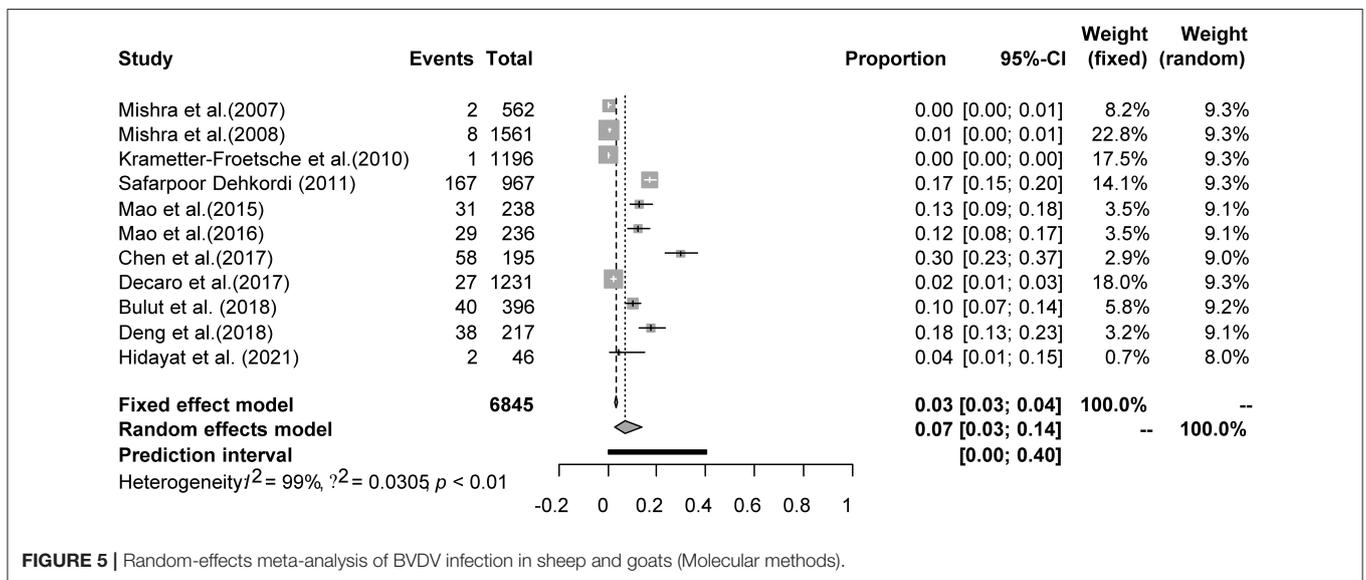


FIGURE 5 | Random-effects meta-analysis of BVDV infection in sheep and goats (Molecular methods).

**TABLE 4** | Association of different variables in the prevalence of BVDV infection in sheep and goats worldwide (Immunological methods).

|                          | No. studies | No. tested | No. positive | % (95% CI) <sup>a</sup> | Heterogeneity |         |                    | Univariate meta-regression |                      |
|--------------------------|-------------|------------|--------------|-------------------------|---------------|---------|--------------------|----------------------------|----------------------|
|                          |             |            |              |                         | $\chi^2$      | P-value | I <sup>2</sup> (%) | P-value                    | Coefficient (95% CI) |
| <b>Sampling years</b>    |             |            |              |                         |               |         |                    |                            |                      |
| before 2000              | 5           | 10,265     | 824          | 7.2% (2.0–15.2)         | 666.12        | <0.01   | 99.4%              | 0.664                      | 0.038(–0.132–0.207)  |
| 2001–2010                | 8           | 10,070     | 1,100        | 8.7% (3.0–16.7)         | 900.27        | <0.01   | 99.1%              |                            |                      |
| after 2011               | 8           | 8,597      | 1,093        | 6.4% (0.3–19.1)         | 2053.79       | 0.00    | 99.7%              |                            |                      |
| <b>Income level</b>      |             |            |              |                         |               |         |                    |                            |                      |
| Middle                   | 13          | 10,701     | 2,338        | 14.9% (8.2–23.1)        | 1299.75       | <0.01   | 99.1%              | 0.002                      | 0.173(0.064–0.281)   |
| High                     | 18          | 23,751     | 1,423        | 4.8% (2.6–7.8)          | 1356.71       | <0.01   | 98.7%              |                            |                      |
| <b>Method</b>            |             |            |              |                         |               |         |                    |                            |                      |
| ELISA                    | 11          | 16,077     | 1,924        | 5.2% (0.8–12.9)         | 2696.34       | 0.00    | 99.6%              | 0.146                      | 0.106(–0.040–0.249)  |
| SNT                      | 20          | 18,375     | 1,837        | 10.7% (6.6–15.6)        | 1674.50       | 0.00    | 98.9%              |                            |                      |
| <b>BVDV specie</b>       |             |            |              |                         |               |         |                    |                            |                      |
| BVDV-1                   | 5           | 7,725      | 911          | 10.5% (2.6–21.4)        | 438.91        | <0.01   | 99.1%              | 0.446                      | 0.051(–0.068–0.417)  |
| BVDV-2                   | 2           | 743        | 9            | 4.0% (0.0–24.8)         | 20.45         | <0.01   | 95.1%              |                            |                      |
| <b>Variety</b>           |             |            |              |                         |               |         |                    |                            |                      |
| Goat                     | 17          | 9,743      | 785          | 8.7% (4.5–14.1)         | 1038.64       | <0.01   | 98.5%              | 0.543                      | 0.038(–0.083–0.159)  |
| Sheep                    | 22          | 24,709     | 2,976        | 11.4% (6.4–16.8)        | 3305.43       | 0.00    | 99.4%              |                            |                      |
| <b>Age</b>               |             |            |              |                         |               |         |                    |                            |                      |
| <1 year                  | 3           | 1,772      | 180          | 13.0% (0.1–41.0)        | 318.52        | <0.01   | 99.4%              | 0.014                      | 0.275(0.056–0.494)   |
| 1–2 years                | 13          | 15,710     | 1,854        | 9.3% (4.3–16.0)         | 1667.66       | 0.00    | 99.3%              |                            |                      |
| >2 years                 | 3           | 2,812      | 919          | 31.8% (24.2–40.0)       | 36.87         | <0.01   | 94.6%              |                            |                      |
| <b>Feeding mode</b>      |             |            |              |                         |               |         |                    |                            |                      |
| Free-range agriculture   | 5           | 2,915      | 180          | 5.3% (1.6–10.8)         | 83.54         | <0.01   | 95.2%              | 0.019                      | 0.193(0.032–0.355)   |
| Concentrated agriculture | 13          | 13,778     | 2,591        | 17.9% (11.7–25.2)       | 1067.90       | <0.01   | 98.9%              |                            |                      |
| <b>Quality level</b>     |             |            |              |                         |               |         |                    |                            |                      |
| Low                      | 1           | 50         | 14           | 28.0% (16.3–41.4)       | 0.00          | -       | -                  | 0.601                      | –0.040(–0.188–0.109) |
| Middle                   | 8           | 2,462      | 169          | 8.4% (2.3–17.4)         | 264.72        | <0.01   | 97.4%              |                            |                      |
| High                     | 22          | 31,940     | 3,578        | 8.1% (4.3–12.8)         | 4037.40       | 0.00    | 99.5%              |                            |                      |
| Total                    | 31          | 34,452     | 3,761        | 8.6% (5.2–12.7)         | 4373.38       | 0.000   | 99.3%              |                            |                      |

CI<sup>a</sup>, Confidence interval.

Young sheep or goat: <1 year.

0.0–4.1, 28/2,427; **Table 7**). In terms of income level subgroups, middle-income countries had the highest viral prevalence at 9.6% (95% CI: 3.3–18.6, 375/4,418; **Table 6**).

As can be seen from **Table 6**, aborted fetuses samples had the highest prevalence at 13.6% (95% CI: 7.4–21.3, 207/1,363). The highest positivity rate in the sampling-year subgroup of was after 2011 at 11.6% (95% CI: 4.9–20.5, 225/2,559).

Furthermore, in terms of regarding BVDV species, the prevalence of BVDV-1 was highest (4.6%, 95% CI: 1.2–10.2, 129/4,837). When comparing viral prevalence between goats and sheep, the prevalence in sheep (7.1%, 95% CI: 1.3–16.4, 201/3,503) was higher than that in goats (7.0%, 95% CI: 1.4–15.8, 202/3,342). In terms of feeding mode, the prevalence was higher in free-range agriculture (27.0%, 95% CI: 17.5–37.8, 20/74) than in concentrated agriculture (9.0%, 95% CI: 2.7–18.5, 128/3,285). In terms of quality of study, the prevalence was highest in studies of middle quality (29.7%, 95% CI: 23.5–36.4, 58/195; **Table 6**). Among the geographic factor subgroups, the difference was significant in the longitude subgroup ( $P < 0.05$ ), with the highest

prevalence of 14.6% (95% CI: 8.5–21.8, 16/110; **Table 7**) in the 120–150°E group.

## DISCUSSION

Sheep and goats are some of the earliest-domesticated animals. Because of their excellent reproduction performance, their products are distributed all over the world (72). Their meat, milk, wool, and leather play important roles in daily life, especially in low-income and developing countries (73). Cattle of all ages are susceptible to infection by BVDV, and its distribution is worldwide although some countries have recently eradicated the virus (OIE). Sheep and goats are similar to cattle, and they can be infected with BVDV at all ages (74). Acute infection usually manifests as intestinal and respiratory symptoms, and latent infection usually does not occur after recovery. Infection in the early stages of pregnancy can cause miscarriage or infertility, and in middle and late pregnancy, it can lead to fetal malformation or

**TABLE 5** | Sub-group analysis of the prevalence of BVDV based on geographical factors (Immunological methods).

|                                     | No. studies | No. tested | No. positive | % (95% CI) <sup>b</sup> | Heterogeneity |         |                    | Univariate meta-regression |                       |
|-------------------------------------|-------------|------------|--------------|-------------------------|---------------|---------|--------------------|----------------------------|-----------------------|
|                                     |             |            |              |                         | $\chi^2$      | P-value | I <sup>2</sup> (%) | P-value                    | Coefficient (95% CI)  |
| <b>Region</b>                       |             |            |              |                         |               |         |                    |                            |                       |
| Africa                              | 4           | 4,089      | 563          | 5.4% (0.0–19.7)         | 541.22        | <0.01   | 99.4%              | 0.005                      | -0.182(-0.312--0.054) |
| Asia                                | 10          | 7,415      | 1,785        | 16.6% (8.5–26.8)        | 884.21        | <0.01   | 99.0%              |                            |                       |
| Europe                              | 10          | 20,366     | 1,240        | 3.1% (1.0–6.3)          | 1007.83       | <0.01   | 99.1%              |                            |                       |
| Oceania                             | 3           | 1,195      | 31           | 6.8% (0.0–24.3)         | 93.84         | <0.01   | 97.9%              |                            |                       |
| South America                       | 2           | 88         | 33           | 26.2% (0.0–87.8)        | 38.07         | <0.01   | 97.4%              |                            |                       |
| North America                       | 2           | 1,299      | 109          | 7.2% (1.8–15.7)         | 23.24         | <0.01   | 95.7%              |                            |                       |
| <b>Latitude</b>                     |             |            |              |                         |               |         |                    |                            |                       |
| 0–30°N                              | 1           | 569        | 187          | 32.9% (29.1–36.8)       | 0.00          | -       | -                  | 0.092                      | -0.172(-0.373-0.028)  |
| 0–30°S                              | 6           | 5,247      | 607          | 9.2% (1.2–23.1)         | 874.32        | <0.01   | 99.4%              |                            |                       |
| 30–60°N                             | 9           | 13,447     | 1,936        | 20.2% (11.6–30.3)       | 1270.76       | <0.01   | 99.4%              |                            |                       |
| <b>Longitude</b>                    |             |            |              |                         |               |         |                    |                            |                       |
| 0–30°E                              | 4           | 7,198      | 986          | 11.0% (4.8–19.4)        | 181.27        | <0.01   | 98.3%              | 0.205                      | 0.190(0.104–0.484)    |
| 30–60°E                             | 6           | 5,591      | 1,084        | 18.8% (8.9–31.1)        | 464.85        | <0.01   | 98.9%              |                            |                       |
| 60–90°E                             | 1           | 569        | 187          | 32.9% (29.1–36.8)       | 0.00          | -       | -                  |                            |                       |
| 90–120°E                            | 1           | 770        | 284          | 36.9% (33.5–40.3)       | 0.00          | -       | -                  |                            |                       |
| 120–150°E                           | 2           | 910        | 12           | 9.2% (0.0–63.4)         | 51.31         | <0.01   | 98.1%              |                            |                       |
| 0–30°W                              | 1           | 3,372      | 56           | 1.6% (1.3–2.1)          | 0.00          | -       | -                  |                            |                       |
| 30–60°W                             | 2           | 853        | 121          | 32.2% (0.0–82.1)        | 58.59         | <0.01   | 98.3%              |                            |                       |
| <b>Altitude</b>                     |             |            |              |                         |               |         |                    |                            |                       |
| <1500 m                             | 14          | 15,392     | 1,896        | 15.5% (8.8–23.7)        | 1960.24       | 0.00    | 99.3%              | 0.139                      | 0.153(-0.050–0.355)   |
| 1500–3500 m                         | 5           | 3,871      | 834          | 28.1% (13.5–45.6)       | 423.04        | <0.01   | 99.1%              |                            |                       |
| <b>Annual average precipitation</b> |             |            |              |                         |               |         |                    |                            |                       |
| <200 mm                             | 5           | 7,215      | 779          | 11.4% (3.2–23.5)        | 652.43        | <0.01   | 99.4%              | 0.280                      | 0.219(-0.178–0.615)   |
| 200–400 mm                          | 1           | 1,274      | 363          | 28.5% (26.1–31.0)       | 0.00          | -       | -                  |                            |                       |
| <b>Annual average temperature</b>   |             |            |              |                         |               |         |                    |                            |                       |
| <0°C                                | 1           | 1,274      | 363          | 28.5% (26.1–31.0)       | 0.00          | -       | -                  | 0.104                      | -0.293(-0.647–0.060)  |
| 1–10°C                              | 2           | 3,826      | 275          | 4.6% (0.1–14.5)         | 89.05         | <0.01   | 98.9%              |                            |                       |
| 10–20°C                             | 4           | 1,914      | 210          | 20.3% (2.9–47.8)        | 354.77        | <0.01   | 99.2%              |                            |                       |
| 20–30°C                             | 1           | 147        | 49           | 33.3% (25.9–41.2)       | 0.00          | -       | -                  |                            |                       |

CI<sup>b</sup>, Confidence interval.

stillbirth. For infection in the first trimester of pregnancy, only a very small number (around 1–2%, cattle; OIE) of fetuses survive and form PI animals, which remain PI for life and are usually seronegative, presenting serious problems for the prevention and control of the virus (75). Therefore, detailed knowledge of the epidemiological status of BVDV has become crucial for the development of effective prevention measures in sheep and goats.

We searched all the articles on the epidemiology of sheep and goat BVDV from 1971 to 2021. Our meta-analysis finally considered 42 documents covering six continents and 24 countries and a total of 41,297 sheep and goats. Sheep and goats are widely distributed around the world, and both often coexist in the same farm, regardless of the fact that intensive and free-range farming often intersects geographically (76). In order to pursue quality increase, other species are often introduced, increasing the transmission of the disease (34, 77). In addition, the use of public pastoral areas, as well as the cross-working of breeding or technical personnel methods can contribute to the

spread of BVDV, so we have analyzed and will discuss sheep and goats together. There are two main methods for detecting the prevalence of BVDV, namely immunological and molecular methods. In the studies, we considered 31 were based on immunological methods and 11 papers were based on molecular methods. In our statistical analysis, the total positive rate of immunological methods was 8.6% (95% CI: 5.2–12.7) and the total positive rate of molecular methods was 7.3% (95% CI: 2.7–13.7). Thus, the results of the two were essentially the same.

The immunological methods considered in this study are ELISA and SNT. The molecular method is RT-PCR. RT-PCR has high sensitivity and specificity. It is not affected by maternal antibodies, but may present false positives due to cross-contamination (78). Immunological and molecular methods have their advantages and disadvantages. In terms of detection sensitivity and accuracy, immunological methods cannot be compared with molecular methods (43, 79), but immunological methods have advantages over molecular methods in terms

**TABLE 6** | Association of different variables in the prevalence of BVDV infection in sheep and goats worldwide (Molecular methods).

| Variable/sub-groups      | No. studies | No. tested | No. positive | % (95% CI) <sup>a</sup> | Heterogeneity |         |                    | Univariate meta-regression |                      |
|--------------------------|-------------|------------|--------------|-------------------------|---------------|---------|--------------------|----------------------------|----------------------|
|                          |             |            |              |                         | $\chi^2$      | P-value | I <sup>2</sup> (%) | P-value                    | Coefficient (95% CI) |
| <b>Sampling years</b>    |             |            |              |                         |               |         |                    |                            |                      |
| 2001–2010                | 4           | 4,286      | 178          | 2.2% (0.0–10.5)         | 415.63        | <0.01   | 99.3%              | 0.070                      | 0.200(–0.016–0.416)  |
| after 2011               | 7           | 2,559      | 225          | 11.6% (4.9–20.5)        | 190.85        | <0.01   | 96.9%              |                            |                      |
| <b>Income level</b>      |             |            |              |                         |               |         |                    |                            |                      |
| Middle                   | 9           | 4,418      | 375          | 9.6% (3.3–18.6)         | 541.68        | <0.01   | 98.5%              | 0.096                      | 0.226(–0.040–0.493)  |
| High                     | 2           | 2,427      | 28           | 0.8% (0.0–4.1)          | 32.14         | <0.01   | 96.9%              |                            |                      |
| <b>BVDV specie</b>       |             |            |              |                         |               |         |                    |                            |                      |
| BVDV-1                   | 6           | 4,837      | 129          | 4.6% (1.2–10.2)         | 258.30        | <0.01   | 98.1%              | 0.110                      | 0.150(–0.002–0.301)  |
| BVDV-2                   | 3           | 3,354      | 16           | 0.4% (0.0–1.3)          | 15.22         | <0.01   | 86.9%              |                            |                      |
| <b>Variety</b>           |             |            |              |                         |               |         |                    |                            |                      |
| Goat                     | 8           | 3,342      | 202          | 7.0% (1.4–15.8)         | 415.84        | <0.01   | 98.3%              | 0.990                      | 0.001(–0.201–0.204)  |
| Sheep                    | 6           | 3,503      | 201          | 7.1% (1.3–16.4)         | 313.70        | <0.01   | 98.4%              |                            |                      |
| <b>Feeding mode</b>      |             |            |              |                         |               |         |                    |                            |                      |
| Free-range agriculture   | 1           | 74         | 20           | 27.0% (17.5–37.8)       | 0.00          | -       | -                  | 0.235                      | 0.240(–0.637–0.156)  |
| Concentrated agriculture | 7           | 3,285      | 128          | 9.0% (2.7–18.5)         | 311.61        | <0.01   | 98.1%              |                            |                      |
| <b>Sample</b>            |             |            |              |                         |               |         |                    |                            |                      |
| Aborted fetuses          | 2           | 1,363      | 207          | 13.6% (7.4–21.3)        | 12.15         | <0.01   | 91.8%              | 0.212                      | 0.140(–0.080–0.360)  |
| Serum                    | 8           | 5,244      | 165          | 5.3% (1.5–11.1)         | 363.47        | <0.01   | 98.1%              |                            |                      |
| <b>Quality level</b>     |             |            |              |                         |               |         |                    |                            |                      |
| Middle                   | 1           | 195        | 58           | 29.7% (23.5–36.4)       | 0.00          | -       | -                  | 0.057                      | –0.332(–0.673–0.010) |
| High                     | 10          | 6,650      | 345          | 5.8% (1.9–11.5)         | 600.40        | <0.01   | 98.5%              |                            |                      |
| Total                    | 11          | 6,845      | 403          | 7.3% (2.7–13.7)         | 720.35        | <0.0001 | 98.6%              |                            |                      |

CI<sup>a</sup>, Confidence interval.

Young sheep or goat: <1 year.

of batch detection and ease of operation. In terms of testing costs, immunological methods are more economical. In general, for clinical sample testing, immunological methods are recommended for large-scale screening in concert with, the use of molecular methods for retesting suspected or uncertain samples, ensuring accuracy.

The incidence of BVDV in sheep and goat populations may be related to management measures (80). Among the continental subpopulations, the prevalence of BVDV in Asian sheep and goats is relatively high. For Asia, the prevalence for immunological testing is 16.6% (95% CI: 8.5–26.8), and the prevalence for molecular testing is 9.6% (95% CI: 3.3–18.6), which are much higher than the corresponding values for Europe, where the prevalence for immunological testing was 3.1% (95% CI: 1.0–6.3) and the prevalence for molecular testing was 0.8% (95% CI: 0.0–4.1) (Tables 5, 7). According to income-level subgroup analysis, the prevalence of BVDV in sheep and goat herds in middle-income countries is higher than that in high-income countries, which is consistent with the results for the continental subgroups. However, there are several abnormal data revealed by the analysis. For example, the immunological prevalence rate in South America is 26.2% (95% CI: 0.0–87.8) and the immunological prevalence rate in Argentina is 59.3% (95% CI: 45.8–72.1). The actual epidemic situation in the region still needs more epidemiological analysis to support this data. It is noteworthy that Australia, a large agricultural country, has a

BVDV prevalence rate close to zero although Australia has not yet introduced an elimination plan (81). This shows that scientifically informed breeding and effective management systems are closely related to animal health.

We analyzed the data in terms of sampling-year subgroup, and the prevalence rate of BVDV in sheep and goat herds after 2011 was 11.6% (95% CI: 4.9–20.5) (Table 6). The decrease in prevalence from 2001 to 2010 may be related to programs initiated by certain European countries to prevent BVDV in livestock. For example, Austria launched a mandatory BVDV control plan in August 2004 (82), Switzerland has implemented a mandatory eradication plan since 2008 (61, 83). In the present study, we divided the breeding methods into free-range and intensive agriculture. The positive rate for immunological methods in intensive agriculture was 17.9% (95% CI: 11.7–25.2), which is higher than that of free-range agriculture at 5.3% (95% CI: 1.6–10.8). However, the results of molecular methods contradict those of immunological methods. The positive rate for intensive agriculture was 9.0% (95% CI: 2.7–18.5), which is lower than the positive rate for free-range agriculture, at 27.0% (95% CI: 17.5–37.8) (Table 6). The main reason for this result is that molecular methods use a relatively small sampling volume and have a certain pertinence.

Our meta-analysis also looked at geographical factors. We did not find significant differences in BVDV prevalence by latitude, altitude, average annual precipitation, or mean annual

**TABLE 7** | Sub-group analysis of the prevalence of BVDV based on geographical factors (Molecular methods).

|                                     | No. studies | No. tested | No. positive | % (95% CI) <sup>b</sup> | Heterogeneity |         |                    | Univariate meta-regression |                      |
|-------------------------------------|-------------|------------|--------------|-------------------------|---------------|---------|--------------------|----------------------------|----------------------|
|                                     |             |            |              |                         | $\chi^2$      | P-value | I <sup>2</sup> (%) | P-value                    | Coefficient (95% CI) |
| <b>Region</b>                       |             |            |              |                         |               |         |                    |                            |                      |
| Asia                                | 9           | 4,418      | 375          | 9.6% (3.3–18.6)         | 541.68        | <0.01   | 98.5%              | 0.096                      | 0.226(–0.040–0.493)  |
| Europe                              | 2           | 2,427      | 28           | 0.8% (0.0–4.1)          | 32.14         | <0.01   | 96.9%              |                            |                      |
| <b>Latitude</b>                     |             |            |              |                         |               |         |                    |                            |                      |
| 0–30°S                              | 1           | 46         | 2            | 4.4 (0.0–12.7)          | 0.00          | –       | –                  | 0.785                      | 0.057(–0.354–0.469)  |
| 30–60°N                             | 5           | 3,236      | 155          | 8.0% (1.6–18.7)         | 294.07        | <0.01   | 98.6%              |                            |                      |
| <b>Longitude</b>                    |             |            |              |                         |               |         |                    |                            |                      |
| 0–30°E                              | 3           | 2,679      | 54           | 2.7% (0.0–8.7)          | 83.22         | <0.01   | 97.6%              | 0.016                      | –0.215(–0.389–0.041) |
| 30–60°E                             | 1           | 126        | 14           | 11.1% (6.2–17.3)        | 0.00          | –       | –                  |                            |                      |
| 90–120°E                            | 3           | 367        | 73           | 13.8% (2.6–31.2)        | 28.72         | <0.01   | 93.0%              |                            |                      |
| 120–150°E                           | 1           | 110        | 16           | 14.6% (8.5–21.8)        | 0.00          | –       | –                  |                            |                      |
| <b>Altitude</b>                     |             |            |              |                         |               |         |                    |                            |                      |
| <1500 m                             | 4           | 1,730      | 62           | 5.5% (0.0–18.8)         | 146.42        | <0.01   | 98.0               | 0.574                      | –0.117(–0.525–0.291) |
| 1500–3500 m                         | 1           | 1,231      | 27           | 2.2% (1.4–3.1)          | 0.00          | –       | –                  |                            |                      |
| 3500–5300 m                         | 1           | 195        | 58           | 29.7% (23.5–36.4)       | 0.00          | –       | –                  |                            |                      |
| <b>Annual average precipitation</b> |             |            |              |                         |               |         |                    |                            |                      |
| <200 mm                             | 3           | 1,613      | 81           | 9.2% (0.0–36.0)         | 232.74        | <0.01   | 99.1%              | 0.635                      | 0.161(–0.503–0.825)  |
| 200–400 mm                          | 1           | 1,231      | 27           | 2.2% (1.4–3.1)          | 0.00          | –       | –                  |                            |                      |

CI<sup>b</sup>, Confidence interval.

temperature ( $P > 0.05$ ; **Tables 5, 7**). The BVDV virus prevalence was lower in sheep and goat flocks in the 0–30°E longitude region (**Table 7**). According to the regional subgroup analysis, BVDV prevalence was not high in European countries, which corresponds to the results for longitude. Although BVDV prevalence in Europe was low, the study data suggest that the European sheep and goat population is not insignificant and that many countries with low prevalence are at risk of importing the virus. Therefore, adequate disease prevention and good management and control are needed to ensure imported livestock do not introduce disease (84).

BVDV is further classified into two species, BVDV-1 and BVDV-2. In our subgroup study, the prevalence for BVDV-1 was higher than that for BVDV-2 (**Tables 4, 6**). BVDV-2 virus is understood to have been originally isolated from a serious outbreak of hemorrhagic fever syndrome in cattle. The virus then spread to the European continent through contaminated fetal bovine serum or other biological products. The propagation rate of BVDV-2 is lower than that of BVDV-1 (60, 85). In Krametter-Froetscher et al. (86), the main pestivirus in Austrian sheep and goat flocks was found to be BVDV-1. An analysis by the same author reported in another article showed that BVDV-1 comprised the main genetic population (87). Mishra et al. (39, 40, 88) conducted research on plague virus infections in Indian sheep and goat flocks and found that BVDV-1 was widespread. BVDV-1 is the most common BVDV species in Africa (8). In terms of virulence, BVDV-2 is more pathogenic than BVDV-1 (89). Under natural conditions, these two species can cause double infection (90), thereby enhancing the toxicity of the virus. Research reports indicate that the virulence of species or strains is a factor in economic losses (91). Therefore,

care should be taken to avoid the harm caused by mixed infection with BVDV-1 and BVDV-2 in the process of feeding and management.

In the age subgroup, we found that BVDV prevalence was highest in flocks of sheep and goats older than 2 years, and it was significantly higher than in flocks of sheep and goats under 1 year or 1–2 years old ( $P < 0.05$ , **Table 4**). The wide range of movement of adult sheep and the opportunities for contact with other species increase the risk of contracting the disease, which may also explain the high rate of positivity in adult sheep (61, 92, 93). Thus, decreasing movement between species and timely isolation of positive sheep and goats is essential for controlling BVDV disease and transmission.

There may be some limitations in our systematic review and meta-analysis, but these limitations are inevitable. First, although we retrieved a large number of papers using various retrieval methods, many of them were ineligible for inclusion. Second, there were very few reports from some countries and regions, or studies had small sample sizes. The actual epidemic situation in some surveyed countries and regions may not have been truly represented. Third, the quality of the included studies was uneven, meaning that the studies could not fully reflect the prevalence of sheep and goat BVDV in all areas, with more testing needed. Fourth, because of incomplete statistical information in the included articles, information was insufficient for complete analysis. For example, data such as season and gender were not analyzed in our systematic review and meta-analysis. Last, we only included research reports written in English and Chinese, which may have led to research in other languages being ignored, thereby affecting the results.

## CONCLUSION

In conclusion, despite their limitations, systematic reviews and meta-analysis studies provide a comprehensive overview of global antibody and virus prevalence in sheep and goats. We found a relatively high chance of infection in middle-income level countries and recommend better management of environmental health to reduce the risk of BVDV infection. The results of our study also indicate that ongoing surveillance of sheep and goats as well as ongoing implementation of integrated improvement strategy measures should be conducted. Furthermore, we recommend that additional surveys be conducted to further clarify the prevalence of BVDV worldwide.

## DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding authors.

## AUTHOR CONTRIBUTIONS

KS and RD conceptualized the study, with funding provided by RD. Data extraction was performed by Z-YC, Y-HS, YY, and B-YM. The database was established by Z-YC, and data

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## SUPPLEMENTARY MATERIAL

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