

*Original Research*

# Global research trends on the absence of vas deferens: a bibliometric and visualized study

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## Abstract

**Background and objectives:** To conduct a bibliometric analysis of publications on the absence of vas deferens (AVD) and explore hot topics regarding the subject. **Material and methods:** Publications about AVD research were retrieved from the Web of Science Core Collection (WoSCC). We conducted bibliometric analyses using CiteSpace and VOSviewer software. The results parameters were authors, number of publications, top institutions/countries, impact factor and citation analysis. In addition, network maps were presented to evaluate the collaborations between them. **Results:** A total of 918 articles were included in the analysis. Since 1998, the number of publications has gradually declined. Human reproduction (69) represented the most papers and was also the most co-cited journal. Silber Sj, Asch Rh and Patrizio P were leading researchers, and there were active collaborations among the top authors. The USA was the leading national contributor in this field, with 231 publications, and active cooperation between countries and institutions was observed. Hot topics included the themes of congenital bilateral absence, cystic fibrosis, infertility and mutations. **Conclusion:** Research papers on AVD gradually decreased after 1998. This historical overview of research on AVD will be useful for further research. Future research on specific areas regarding hot topics is recommended.

**Keywords:** Absence of the vas deferens (AVD); Bibliometric analysis; Cystic fibrosis transmembrane conductance regulator (CFTR); Cystic fibrosis

## 1. Introduction

Approximately one in every 10 couples experiences fertility difficulties, and male factors account for 20%–25% of the reasons for infertility. For male infertility patients, congenital bilateral absence of the vas deferens (CBAVD) accounts for 1%–2% [1]. If a patient has absence of the vas deferens (AVD), infertility is generally the reason that he comes to the male outpatient department for treatment. Diagnosis can usually be made by a clinician performing a physical examination, a semen examination and an auxiliary examination of imaging. AVD can be divided into CBAVD and congenital unilateral absence of the vas deferens (CUAVD). Some patients with CUAVD may be able to impregnate a partner naturally. However, due to the lack of bilateral vas deferens, CBAVD patients cannot impregnate a partner naturally, but the purpose of procreation could be achieved through assisted reproductive technology.

The database search revealed hundreds of research studies in the field of AVD with hidden data worthy of in-depth mining. However, systematic analysis, a summary of the literature regarding the development of publications, recognition in citations, locations for research, patterns of collaboration and analyses of keywords are all lacking. Bibliometrics has been widely developed to analyze the progress of a given event, as it includes quantitative measurements using statistical and geometric methods [2,3]. It is mainly aimed at the measurement characteristics

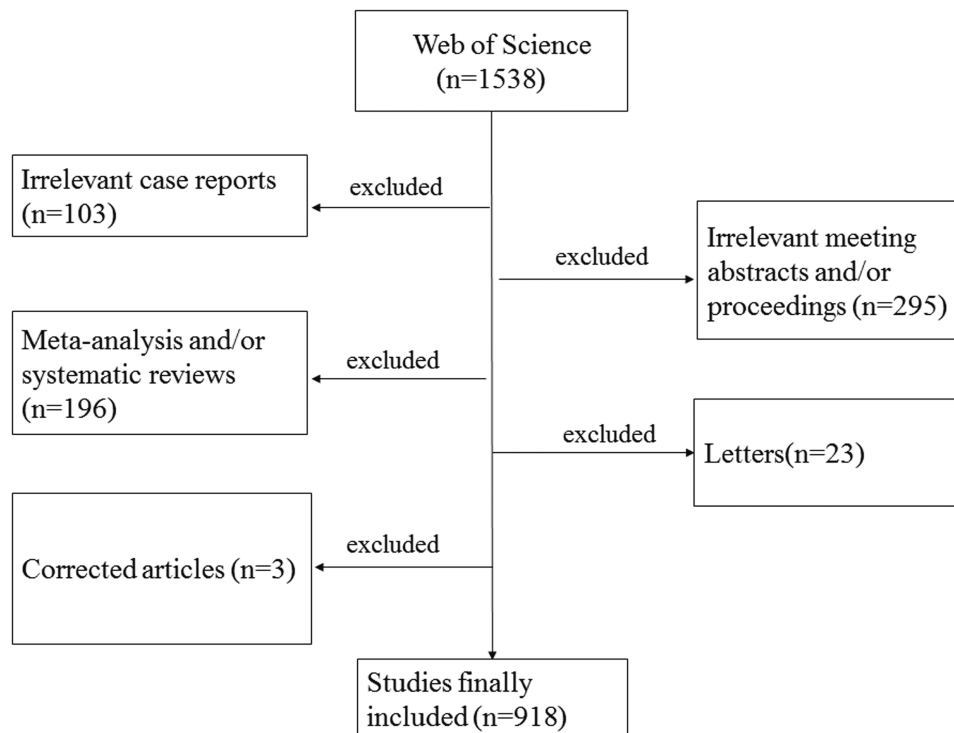
of data related to a specific topic, which are used to evaluate the development of this field and provide visual displays that have an important impact on scientific research [4]. Bibliometrics has been applied to explore the hot topics and frontiers of various disciplines. There are many bibliometric studies in medical journals [5,6], including urology [7].

As a rare disease, AVD has attracted research at a greatly increased rate, and many related articles have been published in academic journals. However, researchers have yet to systematically analyze the evolution of academic achievements in this field. Therefore, an innovative method is needed to make sense of AVD. In this study, VOSviewer and CiteSpace were mainly used to process the relevant literature on AVD included in the Web of Science Core Collection (WoSCC) database; development, hot topics and trends in this discipline were preliminarily explored through econometric analysis and mapping of scientific knowledge.

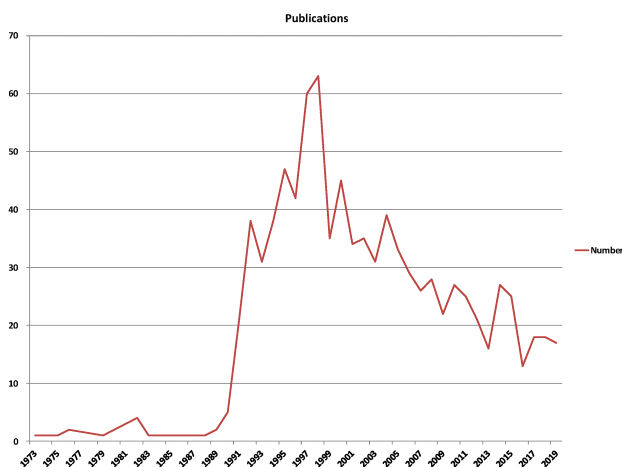
## 2. Methods

This research is a bibliometric analysis of publications retrieved from the WoSCC database on Dec 1, 2020. The search queries of the key words “absence of the vas deferens” were used to retrieve papers between 1970 and 2020. Two authors extracted the number of publications (including journals, authors, countries and institutions), citation frequency, and key word trends. Inclusion criteria were





**Fig. 1. Flow diagram of the included papers.**



**Fig. 2. The number of publications by year and the overall trend consistently kept gradually reducing from 1998 to 2019.**

publications about a study of AVD, including original research. Exclusion criteria were case reports, meeting abstracts, corrected articles, proceedings, systematic reviews and/or meta-analyses.

**Data analysis:** In this study, CiteSpace 5.7.R1 (Podia Labs, Inc., New York, NY, USA) (<Go to ISI>://WOS:000234932600008) and VOSviewer 1.6.15 (a software program developed by the Netherlands Leiden University, <http://www.vosviewer.com/>, Leiden, Netherlands) were used to visualize the collaboration network of keywords/countries/institutions/authors and perform co-

occurrence analysis. VOSviewer and CiteSpace are tools for information visualization and mapping of scientific knowledge and have been widely used by relevant institutions and personnel in the field of scientometrics. Burst keyword detection was also conducted to reveal the recurrent new keywords. Reference co-citation analysis and author co-citation analysis were conducted, and related knowledge maps were generated. For the process of analysis, the 50 most frequently found or cited papers were used to generate the network at 1-year intervals. For cluster analysis, log-likelihood ratio weighting was selected. Moreover, we used a timeline view to depict the changes in the trends of the field over time, and CiteSpace was used to visualize the timeline.

### 3. Results

A total of 918 publications met the inclusion criteria (Fig. 1). The volume of articles by year is shown in Fig. 2, where the overall growth trend gradually decreased from 63 articles in 1998 to 17 articles in 2019. A total of 918 publications were cited 27,042 times in total, and the average number of citations per article was 29.02. In these studies, the sources of financial support included the National Institutes of Health USA [8], United States Department of Health Human Services [9], National Institute of Diabetes Digestive and Kidney Diseases (NIDDK) [10], National Natural Science Foundation of China (NSFC) [11], and the NIH Eunice Kennedy Shriver National Institute of Child Health Human Development (NICHD) [12].

**Table 1. The top 15 productive and cited journals on the research of absence of vas deferens.**

Ranking	Journal	Frequency	IF (2019)	Cited (times)
1st	Human Reproduction	69	5.733	3717
2nd	Fertility and Sterility	50	6.312	1534
3rd	British Journal of Pharmacology	41	7.73	1311
4th	Journal of Urology	27	5.925	638
5th	Naunyn-Schmiedeberg's Archives of Pharmacology	18	2.05	317
6th	Journal of Andrology	16	1.951	154
7th	Andrologia	15	1.951	107
8th	Human Mutation	14	4.124	522
8th	Biology of Reproduction	14	3.322	499
10th	Molecular Human Reproduction	13	3.636	379
10th	European Journal of Pharmacology	13	3.263	122
12th	Clinical Genetics	12	3.578	237
12 th	Journal of Assisted Reproduction and Genets	12	2.829	69
14th	International Journal of Andrology	11	1.951	174
15th	Urology	10	1.924	156

IF, Impact Factor.

### 3.1 Analysis of leading journals and cited journals

A total of 331 academic journals have published documents about AVD. Table 1 shows the top 15 journals contributing to AVD study. Human Reproduction, as the top journal, published the most documents (69 papers), followed by Fertility and Sterility (50 papers), British Journal of Pharmacology (41 papers), and Journal of Urology (27 papers).

Table 1 presents the top 15 cited journals on AVD study. Human Reproduction was the most cited journal (3717 times), followed by Fertility and Sterility (1534 times), British Journal of Pharmacology (1311 times), and Journal of Urology (638 times).

### 3.2 Analysis of leading region/countries and institutions

The region/country collaborative network of AVD studies is shown in Fig. 3. Fig. 4 and Table 2 show the top 15 regions/countries contributing to AVD research. The United States was the top country with the most articles published (231), followed by France (112 papers), Italy (66 papers), England (63 papers), Germany (56 papers), China (42 papers), and Austria (38 papers). For betweenness centrality, the top seven countries were the United States (0.6), France (0.21), Italy (0.02), England (0.13), Germany (0.12), China (0.0), and Austria (0.0).

The institution collaboration network of AVD is shown in Fig. 5. The top 5 most productive institutions were Saint Luke's Hospital in Missouri (19 papers), University of Boston (17 papers), Institut National De La Santi Et De La Recherche Medicale (Inserm) (14 papers), Henri Mondor Hospital (13 papers), and The Johns Hopkins Hospital (13 papers).

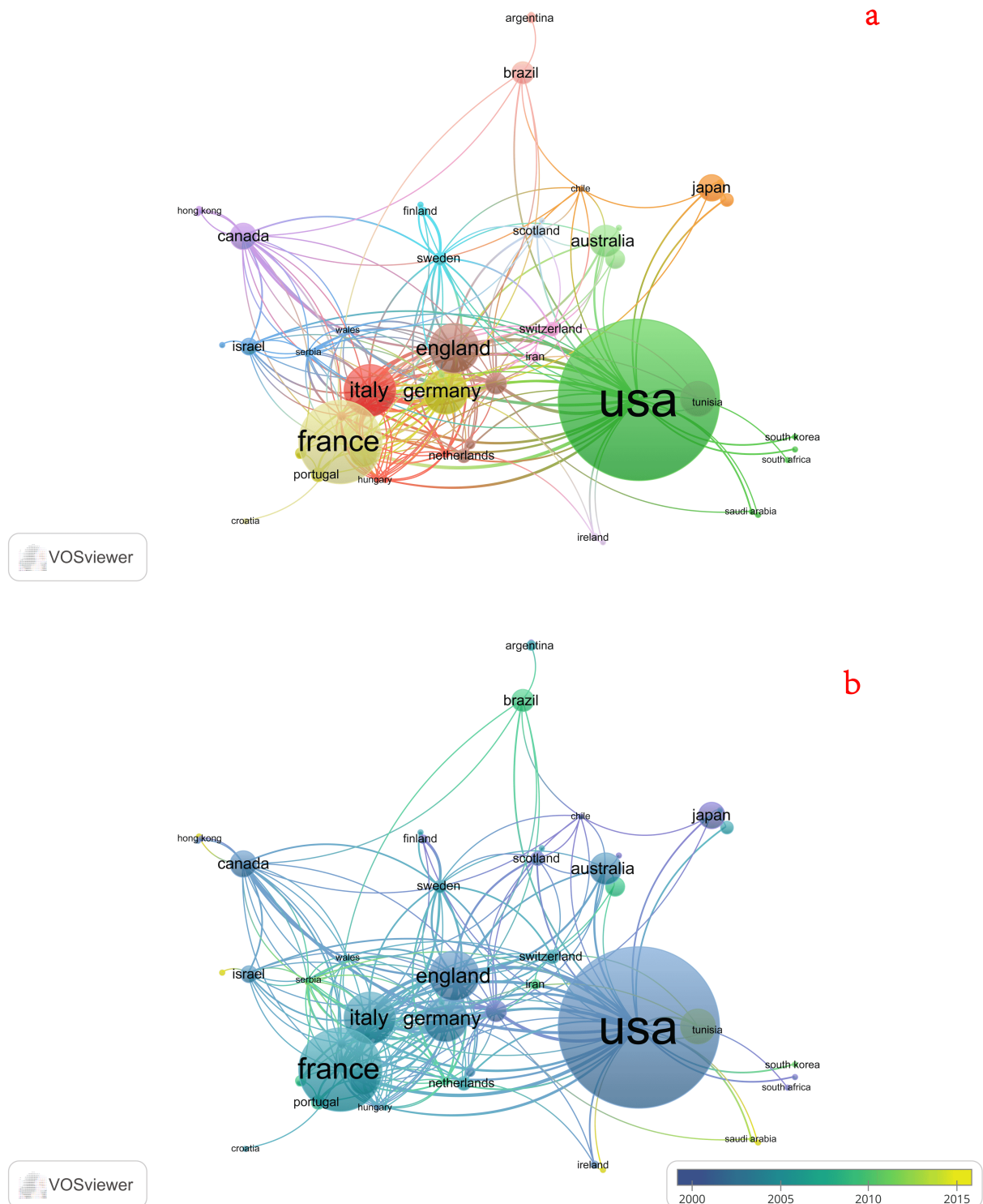
### 3.3 Analysis of authors and co-cited authors

The author collaboration network of AVD is shown in Fig. 6. In terms of frequency, Silber Sj (18 papers), Asch Rh (15 papers), Patrizio P (15 papers), Oates Rd (13 papers), Ord T (11 papers) and Girodon E (11 papers) were the six most productive authors. For co-cited authors, the top 5 authors with the largest numbers of citations were Silber Sj (1515 co-citations), Devroey P (1451 co-citations), Lissens W (1380 co-citations), Ferec C (1270 co-citations), and Casala T (1186 co-citations) (Table 3).

### 3.4 Analysis of co-occurring keywords and burst terms

A total of 3783 key words were identified, and the collaboration network of AVD is presented in Fig. 7. The main hot topics identified by key words included vas deferens (405), congenital bilateral absence (169), cystic fibrosis (164), congenital absence (145), mutations (131), men (127), cystic fibrosis genes (103), infertility (99), cystic fibrosis transmembrane conductance regulator (CFTR) genes (97), CFTR (93) and cystic fibrosis (93).

These words can be classified into 6 large clusters: "intracytoplasmic sperm injection", "congenital bilateral absence", "adrenoceptor mediating contraction", "glutathione s-transferases", "male rat" and "genetic risk". The timeline view from 1990 to 2019 is presented in Fig. 8 and encompasses the key word time evolution of clusters from the initial study focus on "cystic fibrosis, male infertility" to the current study dimension of "ADGRG2, DNA" research changes.



**Fig. 3.** The font size of each country/region's name represents the number of articles in the country/region. The thickness of the curved connecting line represents the collaborative intensity between countries/regions. (a) The country collaboration network of AVD research. (b) Different colors inside the circle represent different time intervals.

### 3.5 Co-cited references and burst references

We also presented the top 15 co-cited references about AVD study. Three articles (Rosenstein 1998, Chillon 1995

and Cohn 1998) were co-cited more than 600 times, 4 articles (Buratti 2001, Anguiano 1992, Siber 1995 and Cuppens 1998) were co-cited between 300 and 500 times, and



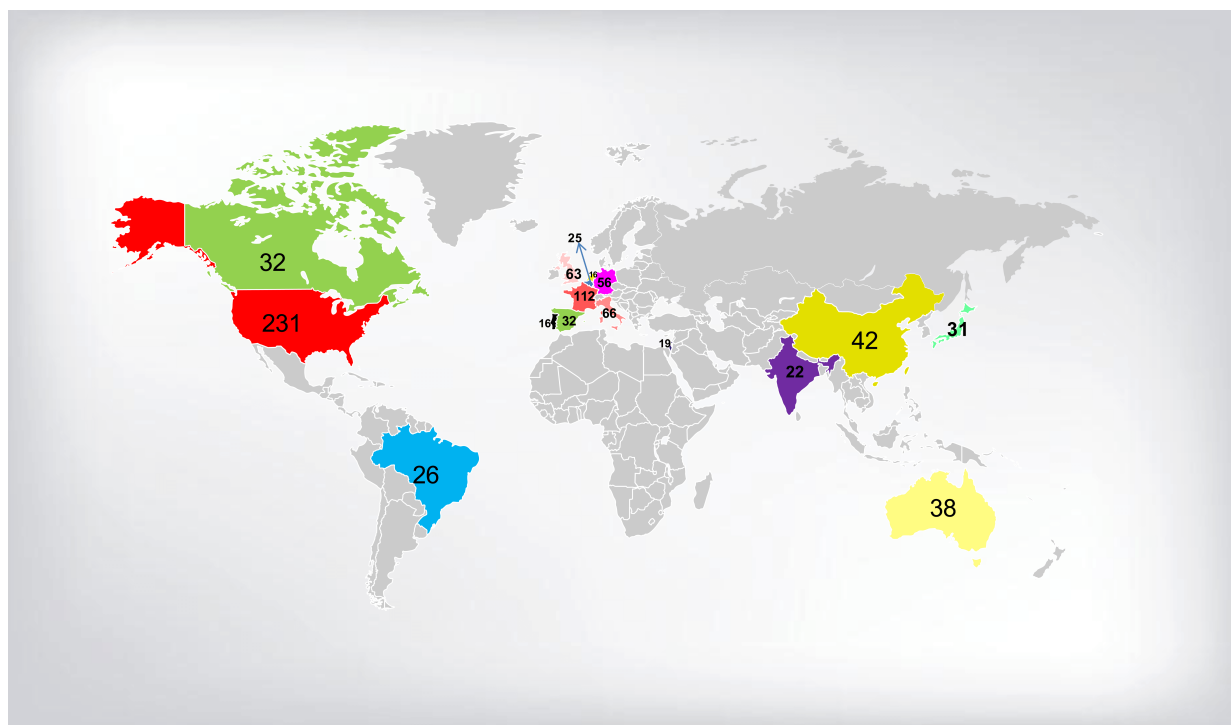


Fig. 4. The global distribution of the top 15 productive countries in AVD research.

Table 2. The top 15 productive and cited country on the research of absence of vas deferens.

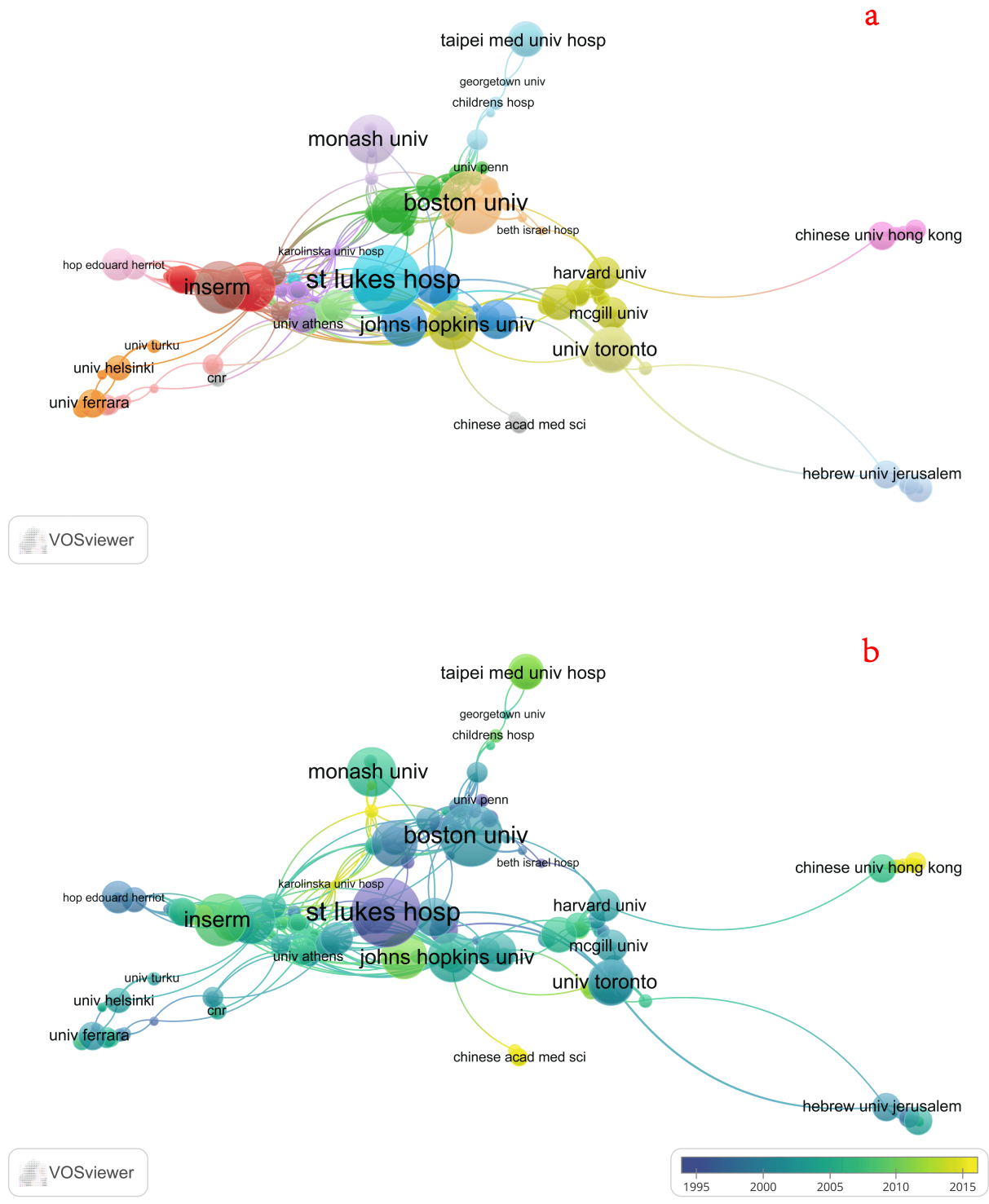
Ranking	Country	Frequency	Cited (times)
1st	USA	231	10560
2nd	France	112	4094
3rd	Italy	66	3061
4th	England	63	1951
5th	Germany	56	2161
6th	People's Republic of China	42	648
7th	Austria	38	857
8th	Spain	32	1628
8th	Canada	32	1071
10th	Jpan	31	534
11th	Brazil	26	323
12th	Belgium	25	2996
13th	India	22	132
14th	Israel	19	777
15th	Netherland	16	460
15th	Portugal	16	188

eight articles (Foster 2001, Silber 1994, Tournaye 1994, Saura 1992, Meredith 2004, Parr 1998, Noone 2001 and Bombieri 2011) were co-cited more than 200 times.

The strongest citation bursts in Fig. 9 present the top 20 references. The first reference [13] with citation bursts was presented in 1989; most of the papers were cited between 1990 and 1993.

## 4. Discussion

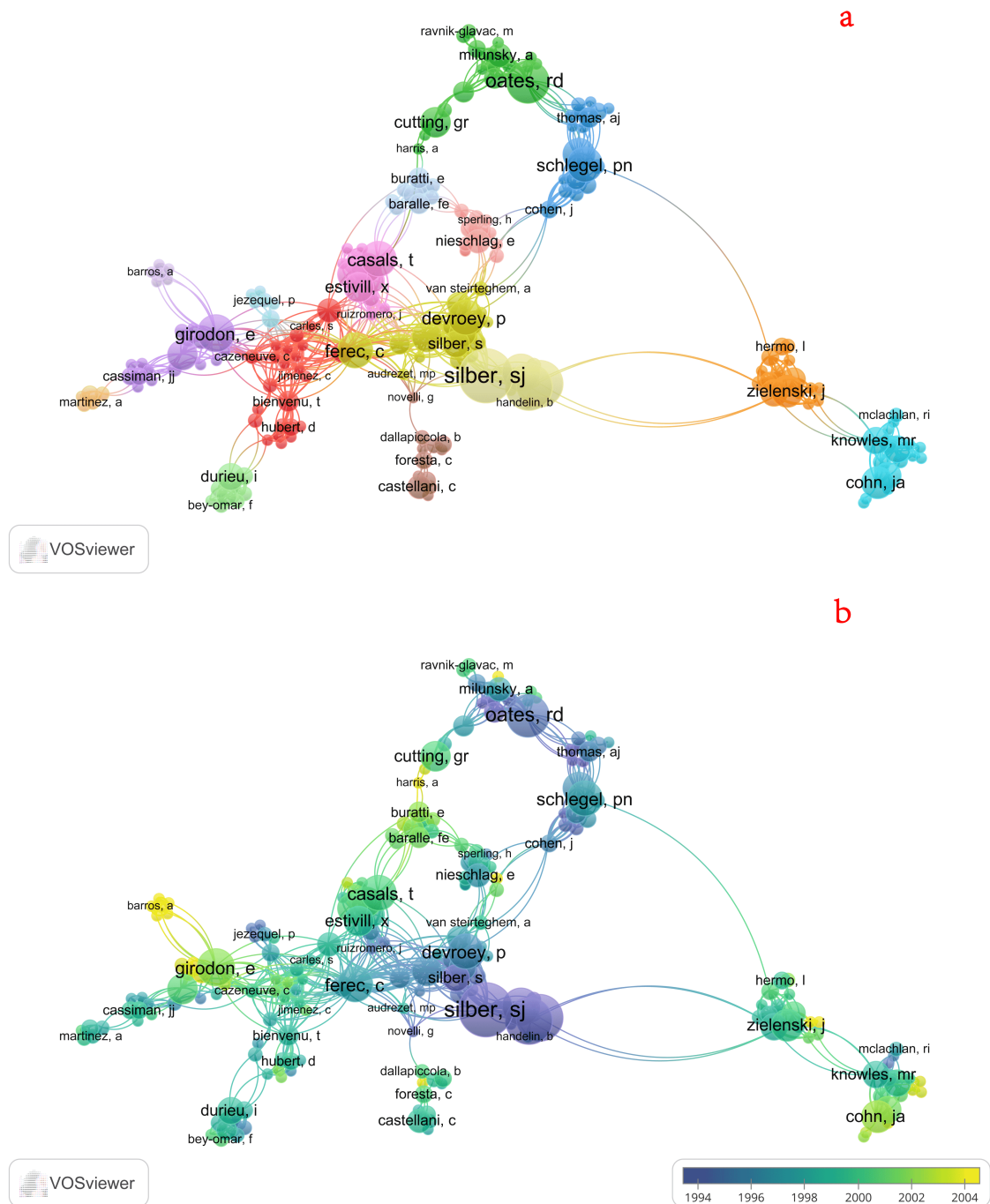
This is the first article to perform a bibliometric analysis regarding AVD including 918 research documents retrieved from WoSCC. This bibliometric analysis presents a comprehensive overview of the scientific literature in this field. In the present study, VOSviewer and CiteSpace were used to conduct bibliometric analysis of studies published on AVD, and the research status of global scholars was visually presented in the form of a scientific knowledge at-



**Fig. 5. The font size of each institution's name represents the number of articles in the institutions.** The thickness of the curved connecting line represents the collaborative intensity between institutions. (a) Institution collaboration network of AVD research. (b) Different colors inside the circle represent different time intervals.

las. Therefore, authors and teams engaged in or about to engage in this field can understand the current research status, which is conducive to the improvement of current and subsequent studies.

European and North American institutions are the most impactful regions for AVD study, with 231 publications by authors in the United States, followed by France, Italy, England, and Germany. Developed countries in Eu-



**Fig. 6.** The font size of each author's name represents the number of articles. The thickness of the curved connecting line represents the collaborative intensity between authors. (a) The authors collaboration network of AVD research. (b) Different colors inside the circle represent different time intervals.

rope and the United States occupy the top 5 countries where researchers are contributing to the literature. The reason why these countries have achieved so many publications in the past may be related to their large numbers of researchers, strong scientific interests, and large amounts of financial support. Although there are many countries in Asia, and the population of Asia represents more than half of the to-

tal population of Earth, only China and Japan are represented in the top 10 contributing countries, and there are few cited documents [14]. We also found that publications from China have increased rapidly, which may be related to the country's overall economic growth and social development [15,16].

**Table 3. The most productive authors on the research of absence of vas deferens (Top 20).**

Ranking	Author	Number of Publications	Cited (times)
1st	Silber Sj	18	1515
2nd	Asch Rh	15	539
2rd	Patrizio P	15	527
4th	Oates Rd	13	875
5th	Ord T	11	381
5th	Girodon E	11	649
7th	Deveroey P	10	1451
7th	Ferec C	10	1270
7th	Casals T	10	1186
7th	Schlegel Pn	10	600
11th	Cohn Ja	9	1035
11th	Zielenski J	9	385
11th	Goldstein M	9	356
11th	Starke K	9	305
11th	Des Georges Marie	9	138
11th	Claustres Mireille	9	138
17th	Lissens W	8	1380
17th	Cutting Gr	8	1173
17th	Estivill X	8	1029
17th	Gimenez J	8	367
17th	Ramos Md	8	367
17th	Girodon Emmanuelle	8	72
17th	Bieth Eric	8	87
17th	Goossens M	8	689

The number of papers on AVD in journals has been declining since 1998 but has been relatively stable in the past 3 years. Papers are funded mostly by the countries' national science foundations, which indicates that studies are giving more attention to the national scientific and technological aspects of the research. Publications are relatively concentrated in authoritative journals of reproduction, andrology and urology. Human Reproduction published the most documents, followed by Fertility and Sterility, Journal of Urology, Urology and Andrologia. Most of the papers published in the field of AVD are high quality. As the average number of citations for each article is as high as 29.02, this demonstrates that authors can obtain international recognition.

Silber Sj published the most articles and conducted relatively early studies on AVD. Following Asch Rh, Patrizio P, Oates Rd, Ord T and Girodon E rounded out the six most productive researchers; Silber Sj, Asch Rh, Patrizio P, Ord T and Deveroey are all from Saint Luke's Hospital in Missouri [17,18]. Global study teams tend to be scattered and lack cooperative research, which makes follow-up multicenter joint research increasingly important, especially in the era of big data. In addition, research efforts have obvious geographical features, and study teams are focused in the United States and Europe. Departments are concentrated in university teaching hospitals and reproductive cen-

ters, and andrology, urology and family planning institutes. Therefore, various countries and regions need to strengthen collaborations to obtain more research results.

The high-frequency keywords were mainly "congenital bilateral vas deferens, cystic fibrosis, gene mutation, male sterility, CFTR, and azoospermia", indicating that studies focused on the diagnosis, etiology and treatment of vas deferens deformities [19]. A key word cluster timeline map revealed the key word time evolution of each cluster, from the initial research focus on "cystic fibrosis, male infertility" to the current research dimension of "ADGRG2, CFTR" [20]. This indicates that research on AVD is performed at the level of gene and chromosome sequencing in genetic etiology.

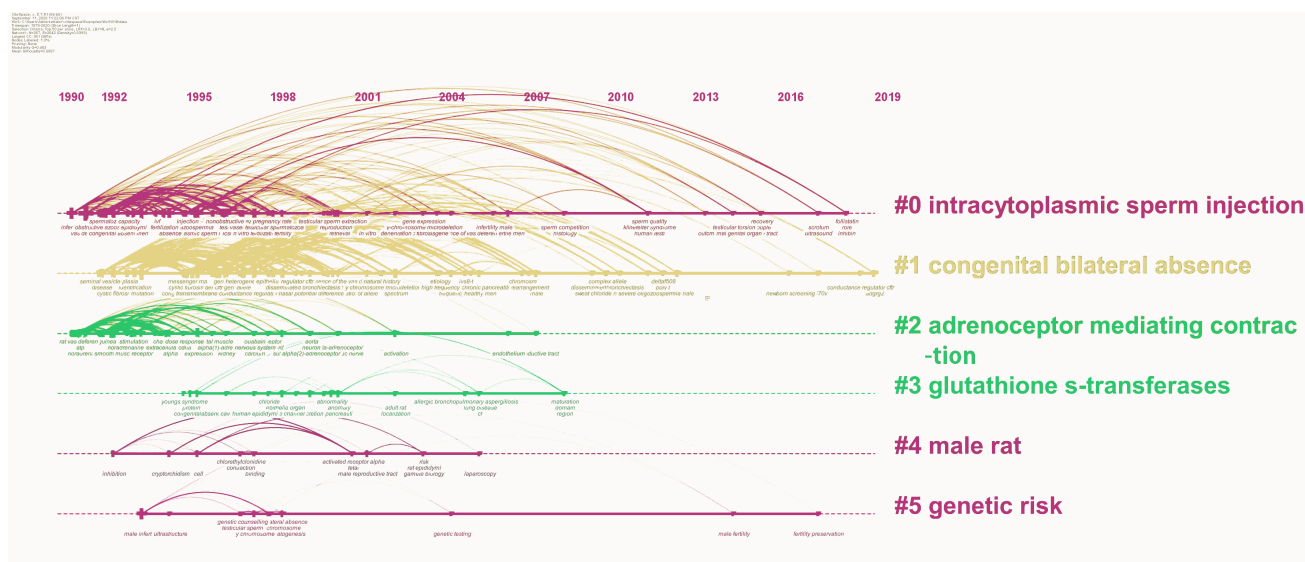
This study provides an analysis that employs bibliometric tools to assess the level of AVD research. This first bibliometric analysis of AVD research publications will help identify historical research priorities and establish future priorities in the development of this academic discipline. The authors discussed leading journals, countries, and contributors. For researchers in the field of AVD, hot topics and research centers can be tracked, which should enable individuals and institutions to strengthen exchanges and cooperation to promote the further development of the discipline. The present study analysis was based on

viewer

viewer







**Fig. 8. Timeline view of the knowledge map in the AVD field.** This view clearly presents the differences in the appearance time point and time span of six clusters.

### Top 20 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	1979 - 2020
SILBER S, 1987, LANCET, V2, P850	1987	4.1185	1989	1994	
BENHAM CD, 1987, NATURE, V328, P275, <a href="#">DOI</a>	1987	5.1943	1990	1995	
DEAN M, 1990, CELL, V61, P863, <a href="#">DOI</a>	1990	5.8411	1992	1997	
JEQUIER AM, 1990, FERTIL STERIL, V53, P1104	1990	4.2565	1992	1994	
SILBER SJ, 1988, FERTIL STERIL, V50, P525	1988	16.9133	1992	1996	
SILBER SJ, 1990, NEW ENGL J MED, V323, P1788, <a href="#">DOI</a>	1990	19.624	1992	1996	
ORD T, 1990, HUM REPROD, V5, P987, <a href="#">DOI</a>	1990	7.4926	1992	1995	
PATRIZIO P, 1989, FERTIL STERIL, V52, P1018	1989	4.2565	1992	1994	
ORD T, 1992, FERTIL STERIL, V57, P1103	1992	4.2565	1992	1994	
DUNN PM, 1988, BRIT J PHARMACOL, V93, P243, <a href="#">DOI</a>	1988	4.8101	1992	1995	
FRIEL DD, 1988, J PHYSIOL-LONDON, V401, P361, <a href="#">DOI</a>	1988	5.346	1992	1995	
RIGOT JM, 1991, NEW ENGL J MED, V325, P64	1991	5.8411	1992	1997	
KEREM BS, 1989, SCIENCE, V245, P1073, <a href="#">DOI</a>	1989	10.042	1993	1997	
ROMMENS JM, 1989, SCIENCE, V245, P1059, <a href="#">DOI</a>	1989	7.7123	1993	1997	
VONKUGELGEN I, 1989, N-S ARCH PHARMACOL, V340, P760, <a href="#">DOI</a>	1989	3.7679	1993	1994	
ANGUIANO A, 1992, JAMA-J AM MED ASSOC, V267, P1794, <a href="#">DOI</a>	1992	16.3742	1993	2000	
BURNSTOCK G, 1990, ARCH INT PHARMACOD T, V304, P7	1990	3.7679	1993	1994	
DAVIS RO, 1991, FERTIL STERIL, V56, P1128	1991	5.0266	1993	1994	
SILBER SJ, 1988, FERTIL STERIL, V49, P373	1988	4.991	1993	1995	
ASCH RH, 1992, FERTIL STERIL, V58, P190	1992	3.7679	1993	1994	

**Fig. 9. The top 20 references with the strongest citation bursts in the co-citation network.**

a retrieval strategy limited to WoS core databases (some databases, such as Medline, Embase-indexed journals, and Google Scholar, may provide broader coverage) and excluded non-English papers, which is a limitation. In addition, the outcomes of this study were generated by machine learning algorithms that may not have interpreted all data correctly and produced bias.

### Author contributions

HL and CM designed the study; HL, CM and JX conducted the literature search and analyzed the data. CM

wrote the paper. All authors read and approved the final manuscript.

### Ethics approval and consent to participate

Not applicable.

### Acknowledgment

Not applicable.

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## Conflict of interest

The authors declare no conflict of interest.

## Informed consent

No informed consent is needed for this type of study.

## Data availability statement

The raw data supporting the conclusions of this article are openly available in a public repository that does not issue DOIs. The data are openly available at <http://webofscience.com>. If needed during the review process, we could provide datasets to the editor or editorial staff upon request. Please contact [lihongjun@pumch.cn](mailto:lihongjun@pumch.cn).

## References

- [1] Hussein TM, Zakaria NH, Zahran AM. Clinical, laboratory and genetic assessment of patients with congenital bilateral absent vas deferens. *Andrologia*. 2011; 43: 16–22.
- [2] Zhang M, Gao M, Yue S, Zheng T, Gao Z, Ma X, *et al*. Global trends and future prospects of food waste research: a bibliometric analysis. *Environmental Science and Pollution Research*. 2018; 25: 24600–24610.
- [3] Chen C. CiteSpace II: Detecting and visualizing emerging trends and transient patterns in scientific literature. *Journal of the American Society for Information Science and Technology*. 2006; 57: 359–377.
- [4] Bornmann L, Leydesdorff L. Scientometrics in a changing research landscape: bibliometrics has become an integral part of research quality evaluation and has been changing the practice of research. *EMBO Reports*. 2014; 15: 1228–1232.
- [5] Miao Y, Zhang Y, Yin L. Trends in hepatocellular carcinoma research from 2008 to 2017: a bibliometric analysis. *PeerJ*. 2018; 6: e5477.
- [6] Baek S, Yoon DY, Lim KJ, Cho YK, Seo YL, Yun EJ. The most downloaded and most cited articles in radiology journals: a comparative bibliometric analysis. *European Radiology*. 2018; 28: 4832–4838.
- [7] Hui J, He S, Liu R, Zeng Q, Zhang H, Wei A. Trends in erectile dysfunction research from 2008 to 2018: a bibliometric analysis. *International Journal of Impotence Research*. 2020; 32: 409–419.
- [8] Plyler ZE, Birket SE, Schultz BD, Hong JS, Rowe SM, Petty CF, *et al*. Non-obstructive vas deferens and epididymis loss in cystic fibrosis rats. *Mechanisms of Development*. 2019; 155: 15–26.
- [9] Houzet L, Pérez-Losada M, Matusali G, Deleage C, Dereuddre-Bosquet N, Satie A, *et al*. Seminal Simian Immunodeficiency Virus in Chronically Infected Cynomolgus Macaques is Dominated by Virus Originating from Multiple Genital Organs. *Journal of Virology*. 2018; 92: e00133–18.
- [10] Pietrement C, Da Silva N, Silberstein C, James M, Marsolais M, Van Hoek A, *et al*. Role of NHERF1, cystic fibrosis transmembrane conductance regulator, and cAMP in the regulation of aquaporin 9. *The Journal of Biological Chemistry*. 2008; 283: 2986–2996.
- [11] Yang B, Wang X, Zhang W, Li H, Wang B. Compound heterozygous mutations in CFTR causing CBAVD in Chinese pedigrees. *Molecular Genetics & Genomic Medicine*. 2018; 6: 1097–1103.
- [12] Tomaszewski J, Joseph A, Archambeault D, Yao HH. Essential roles of inhibin beta a in mouse epididymal coiling. *Proceedings of the National Academy of Sciences of the United States of America*. 2007; 104: 11322–11327.
- [13] Silber S, Ord T, Borrero C, Balmaceda J, Asch R. New treatment for infertility due to congenital absence of vas deferens. *Lancet*. 1987; 2: 850–851.
- [14] Dou Y, Huang Q, He C, Meng S, Zhang Q. Rapid Population Growth throughout Asia's Earthquake-Prone Areas: a Multi-scale Analysis. *International Journal of Environmental Research and Public Health*. 2018; 15: 1893.
- [15] Xiong K, Wang L, Chen X, Cao Y, Xiang C, Xue L, *et al*. Analysis of projects received and funded in fields of emergency and intensive care medicine/trauma/burns/plastic surgery from National Natural Science Foundation of China during 2010–2013. *Zhonghua wei zhong bing ji jiu yi xue*. 2014; 26: 11–16. (In Chinese)
- [16] Wan Q, Xu Y, Dong E. Diabetic nephropathy research in China: Data analysis and review from the National Natural Science Foundation of China. *Journal of Diabetes*. 2015; 7: 307–314.
- [17] Patrizio P, Ord T, Silber SJ, Asch RH. Correlation between epididymal length and fertilization rate in men with congenital absence of the vas deferens. *Fertility and Sterility*. 1994; 61: 265–268.
- [18] Liu J, Lissens W, Silber SJ, Devroey P, Liebaers I, Van Steirteghem A. Birth after preimplantation diagnosis of the cystic fibrosis delta F508 mutation by polymerase chain reaction in human embryos resulting from intracytoplasmic sperm injection with epididymal sperm. *Journal of the American Medical Association*. 1994; 272: 1858–1860.
- [19] Bieth E, Hamdi SM, Mieusset R. Genetics of the congenital absence of the vas deferens. *Human Genetics*. 2021; 140: 59–76.
- [20] Ma C, Wang R, Li T, Li H, Wang B. Analysis of CNVs of CFTR gene in Chinese Han population with CBAVD. *Molecular Genetics & Genomic Medicine*. 2020; 8: e1506.