REVIEW

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The impact of catastrophic events on the sex ratio at birth: A systematic review

Lilybeth Fontanesi | **Maria Cristina Verrocchio** ⬤ | **Melissa D'Ettorre** | **Giulia Prete** | **Francesco Ceravolo** | **Daniela Marchetti**

Department of Psychological, Health and Territorial Sciences, G. d'Annunzio University of Chieti-Pescara, Chieti, Italy

Correspondence
Maria Cristina Verrocchio, Department of Psychological, Health and Territorial Sciences, G. d'Annunzio University of Chieti-Pescara, Via dei Vestini 31, 66100 Chieti, Italy.
Email: mc.verrocchio@unich.it

Abstract

Objective: The impact of maternal stress on birth outcomes is well established in the scientific research. The sex ratio at birth (SRB), namely the ratio of male to female live births, shows significant alteration when mothers experience acute stress conditions, as proposed by the Trivers-Willard Hypothesis. We aimed to synthetize the literature on the relationship between two exogenous and catastrophic stressful events (natural disasters and epidemics) and SRB.

Methods: A systematic search was run in Scopus, PubMed, Web of Science, and Cochrane Library, until March 9, 2023. The search produced 1336 articles and 25 articles met the inclusion criteria. We found seven case–control studies and 18 observational studies. Most of studies investigated the impact of earthquakes and other natural disasters. Only seven studies examined the effect of epidemics or pandemics.

Results: The results of the studies seem inconsistent, as 16 studies found a decline in SRB, three found a rise, four did not record any change and two studies gave contradictory results. The period and population analyzed, the source of information, the method of variance analysis in the SRB, and the failure to assess confounding variables may have influenced the incongruence of the results.

Conclusion: Our findings contribute to improve the knowledge about the relationship between socio-ecological factors and SRB. Future studies should investigate the mechanisms by which this relationship impacts public health, in particular the health of pregnant women and their newborn, through an accurate and consistent methodology that also includes confounding factors.

1 | INTRODUCTION

Sex ratio at birth (SRB), or the secondary sex ratio, is defined as the ratio of male to female live births and is characterized by a remarkable homogeneity across the population, ranging from 102–109 male to 100 female births (James & Grech, 2017; Mathews & Hamilton, 2005; United Nations DESA Population Division, 2011). This ratio can be influenced by maternal conditions and/or environmental stressors (Schacht

et al., 2019). Maternal stress during pregnancy can be related to personal factors—such as a significant loss, anxiety, or depression (Grech, 2018; Hansen et al., 1999; Schnettler & Klüsener, 2014)—or environmental determinants such as wars (Grech, 2014; James, 2009) and terrorist attacks (Masukume et al., 2017) or natural disasters (Saadat, 2008). According to the literature, the effects of maternal stress include reduced birthweight (Ding et al., 2021; Kim et al., 2017; Parayiwa & Behie, 2018; Suzuki et al., 2016; Witt et al., 2014), birth defects (Carmichael et al., 2014; Goenjian et al., 2011; J. Li et al., 2021; F. Li et al., 2021; Tan et al., 2009), shorter gestational length (Mahrer et al., 2021; Menclova & Stillman, 2020), small for gestational age (Ding et al., 2021), increased proportion of preterm births (Ding et al., 2021; Freedman et al., 2021; Parayiwa & Behie, 2018), and infant mortality (Heron, 2018). In fact, maternal stress can influence maternal inflammation, pregnancy, and birth complications; the second and third trimesters appear to be associated with the highest risks of developing these conditions (Di Renzo et al., 2007; Obel et al., 2007; Walsh et al., 2019). It should be noted that male fetuses are biologically weaker and may be more readily affected by these conditions and diseases than female ones are (Kirchengast & Hartmann, 2009). Thus, miscarriage and premature deaths are more common for boys than for girls (McCarthy, 2019), which may potentially affect the SRB in favor of females.

For these reasons, SRB and its fluctuations are considered in the literature to be a valuable indicator of general population health and that of gestating women in particular (Bernard et al., 2022; Davis et al., 1998). Trivers and Willard (1973) suggest that "natural selection should favour the ability of parents to adjust the sex ratio of the offspring according to their capacity to invest in parenting" to explain variations in SRB; mammalian females, including humans, are therefore subject to adaptive mechanisms to adjust the sex ratio of offspring in response to maternal conditions in order to achieve optimal reproductive rewards. Trivers and Willard (1973) stated that (1) the reproductive success of male offspring is more variable and resource-dependent than that of female offspring, (2) maternal conditions are associated with the offspring condition, and (3) maternal conditions are positively related with reproductive success. The Trivers–Willard hypothesis (TWH) suggests that mothers in good and stable physical and socio-economic conditions during pregnancy are more likely to give birth to boys, while those experiencing poor conditions are more likely to give birth to girls. Therefore, it follows that female individuals are more likely to have at least some reproductive success when carried under suboptimal conditions, compared to male individuals who experienced

the same conditions (Trivers & Willard, 1973). Consequently, this hypothesis predicts a decrease in the percentage of male births in places where women are subjected to stressful events (James & Grech, 2017; Wu, 2021).

In line with these considerations, natural disasters and adverse local and global events such as epidemics or pandemics provide a unique opportunity for studying the effects of stressful catastrophic events on SRB and for testing the TWH. Natural disasters are sudden and acute events generated by a geophysical system that disrupt a population to the point of exceeding its management capacities (Lafortune et al., 2021). The World Health Organization refers to a natural disaster as "an act of nature of such magnitude as to create a catastrophic situation in which the day-to-day patterns of life are suddenly disrupted and people are plunged into helplessness and suffering and, as a result, need food, clothing, shelter, medical and nursing care and other necessities of life, and protection against unfavorable environmental factors and conditions" (Assar, 1971, p. 24). For example, after an earthquake, an entire population can be evacuated and the government can declare a state of emergency, leading to a considerable number of people requiring assistance in the following months (D'Alfonso et al., 2012). Therefore, natural catastrophes typically represent a source of intense psychological stress (Han et al., 2021; Itoh et al., 2022; Kotozaki & Kawashima, 2012; Lugović-Mihić et al., 2021; Mondal et al., 2013; North & Pfefferbaum, 2013; Wakashima et al., 2019).

Moreover, global adverse circumstances such as epidemics and pandemics are extremely stressful events that may create heavy psychological and emotional burdens for the general population (J. Li et al., 2021; F. Li et al., 2021; Shigemura et al., 2009; Van Bortel et al., 2016). Epidemics are high-impact health emergencies that may cause elevated rates of morbidity and a significant death toll (Peters, 2016). Furthermore, epidemics and pandemics (epidemics that not only affect a specific population but also are spread over multiple countries and continents) may bring many changes into people's everyday lives, drastically altering daily routines, and causing financial pressures and social isolation, as well as uncertainty for the future. They threaten the lives of many people, and the fear of contagion aggravates the situation, as was the case during the recent COVID-19 pandemic (Abdoli, 2022; Bali et al., 2016; Cori et al., 2021). Research has highlighted a significant prevalence of psychological distress among different population groups resulting from the emergency conditions and other aspects of epidemics, such as fear of contagion, job loss, and uncertainty about the future (Krishnamoorthy et al., 2020; Traylor et al., 2020; Wong et al., 2010; Xiong et al., 2020).

A recent narrative review focused on the length of the interval between the occurrence of a few natural catastrophes and their impact on SRB (Fukuda et al., 2020). The review described 13 natural disasters (nine earthquakes, one flood, one hurricane, one volcanic eruption, and London smog), examining whether or not the events triggered a change in SRB (Fukuda et al., 2020). According to the results, there was a decline in SRB, with more females being born than males, after 11 of the 13 analyzed events. Nevertheless, the authors highlighted the necessity of understanding the causes of inconsistencies between the results (Fukuda et al., 2020). Moreover, the review by Fukuda et al. (2020) did not apply a systematic methodology, account for epidemics and pandemics, or discriminate between the effects of stress on pregnant women and toxic environmental factors on SRB.

To our knowledge, research articles on natural disasters, epidemics/pandemics, and their impact on SRB have not been systematically reviewed so far. Therefore, this study aims to systematically review the current evidence on the effects of these two exogenous factors on fluctuations of SRB within populations. In particular, it makes an attempt to determine whether stress-related mechanisms may induce a general decline in SRB, as proposed by the TWH.

2 | MATERIALS AND METHODS

2.1 | Search strategy

To perform a robust systematic review of the available publications, an exploratory and preliminary search of the literature was performed to identify all keywords referring to the effects of natural disasters and epidemics/pandemics on SRB. The search terms were identified after this process; when possible, general terms were preferred (e.g., catastrophic event, environmental disaster, and epidemic or pandemic). When necessary, specific keywords for single events were included to guarantee finding all the relevant literature (e.g., coronavirus disease 19, poliomyelitis, Ebola, and Spanish flu).

The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). The PRISMA checklist is available as supplementary material. Major medical, health, and psychological literature databases, including PubMed, Cochrane Library, Web of Science, and Scopus, were consulted. The literature search included all publication years until the date of the systematic search (March 9, 2023). Based on the type of catastrophic event, two sets of keywords were used for the systematic search. For natural disasters, the keywords

were "sex ratio" AND birth* AND "natural catastroph*" OR calamit* OR "natural disaster*" OR "catastrophic event*" OR "natural hazard*" OR "environmental disaster*" OR earthquake* OR tsunami* OR flood* OR alluvion* OR storm* OR hurricane* OR cyclone* OR avalanche* OR "london smog" OR fire* OR "volcanic eruption*." For epidemics and pandemics, the keywords were "sex ratio" AND birth* AND epidemic OR epidemia OR pandemic OR pandemia OR "coronavirus disease 19" OR "COVID-19" OR "severe acute respiratory syndrome" OR "sars-cov" OR "middle east respiratory syndrome" OR "mers-cov" OR poliomyelitis OR ebola OR zika OR variola OR diphtheria OR pertussis OR "Spanish flu" OR measles OR mumps OR rubella. The keywords were searched in the title, abstract, and keywords fields on Scopus and in all fields for Web of Science, PubMed, and Cochrane Library.

2.2 | Inclusion and exclusion criteria

Studies were considered eligible and included in the systematic review if they: (1) were original research articles; (2) were published in English or Italian; (3) included a sample of births; (4) considered exposure to a natural disaster or an epidemic/pandemic; and (5) investigated the impact of a natural disaster or an epidemic/pandemic on SRB. Consequently, studies were excluded if they: (1) included animal subjects; (2) consisted of reviews, opinions, or commentaries or were theoretical articles; (3) were published in languages other than English and Italian; (4) did not consider a natural disaster or an epidemic/pandemic; or (5) did not investigate the impact of an event on SRB.

2.3 | Study selection and data extraction

Upon completion of the search in the electronic databases, all results were exported to Mendeley, and duplicates were removed. Two reviewers screened the titles and abstracts of studies identified with the search strategy for inclusion/exclusion. The reviewers resolved disagreements through discussion and consensus. The same two authors independently reviewed the full text of all qualifying articles to determine their final inclusion in the review. A list of possible articles was generated, and inconsistencies were resolved through a consensus involving a third reviewer. A narrative summary of the evidence taken from the final compilation of the included papers was conducted. We extracted data from all the included articles, including the authors (year of publication), type of study design (case–control or

observational), sample characteristics (i.e., total sample size, gender), information about the stressful catastrophic event (natural disasters or epidemics/pandemics, intensity, distance), outcome measurements (i.e., SRB computation), and main findings on the effect of the catastrophic event on SRB. Due to incomplete data or substantial differences in the studies included in this review (e.g., in the research design, measurement, indices, and statistical analysis used), a quantitative synthesis of the evidence (meta-analysis) was not performed.

2.4 | Data quality assessment

A quality assessment of the eligible studies included in the review was performed, depending on the study design, by referring to the National Institutes of Health Study Quality Assessment Tool for Case–Control Studies (NIH, 2019a) and the National Institutes of Health Study Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (NIH, 2019b), which consisted of 12 and 14 items, respectively. These tools evaluated several domains of potential bias, such as sample (e.g., specific study population, consistent criteria for the selection of cases or controls), exposure measures (e.g., valid and reliable tools, levels of exposure), and outcome measures (e.g., clear and valid tool, confounding variables). The NIH Quality Assessment Tools include "yes" or "no" or "cannot determine" (CD) and "not applicable" (NA) as possible responses. The data quality was assessed by two independent reviewers, and all disagreements were resolved through discussions with the involvement of a third reviewer. According to the guidelines for determining the overall quality rating (NIH, 2019a; NIH, 2019b), the studies were awarded a rating of good, fair, or poor. A "good" study had the least risk of bias, and we considered its results to be valid. A "fair" study was still considered to be valid, albeit susceptible to some bias. Finally, a "poor" study was associated with a significant risk of bias.

3 | RESULTS

3.1 | Search results and study characteristics

A total of 1336 articles were identified from searching the aforementioned databases. Of these papers, 123 items consisted of duplicates and were thus excluded. After screening at the level of title and abstract, another 1162 studies were excluded because they did not meet the

inclusion criteria, two records were not retrieved, and 49 full texts were independently assessed for inclusion by two authors. Finally, 25 research articles were identified as eligible for the systematic review presented here. The reasons for the exclusion of full texts and other details of the study selection are provided in the PRISMA 2020 Flow Diagram (Figure 1).

Overall, 18 studies investigated natural disasters, while seven studies examined epidemics/pandemics. All studies measured SRB using records from national or local birth registers. Most of the studies considered ($N = 12$) were conducted in Asia. The remaining studies were conducted in Europe ($N = 5$), the United States ($N = 3$), South America ($N = 2$), Africa ($N = 1$), and Australia ($N = 1$). Finally, one study (Shifotoka & Fogarty, 2013) used global data from 184 countries. The main findings of each study were organized and described according to research design (case–control vs. observational). Overall, we identified seven case–control studies and 18 observational studies. Figure 2 provides a graphical summary of the main results.

3.2 | Study quality

We used the NIH Study Quality Assessment Tool for Case–Control Studies (NIH, 2019a) and the NIH Study Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (NIH, 2019b) to assess the quality of eligible studies in this review. Some of the questions used to assess their quality were not applicable (Table 1 and Table 2), so the studies had a maximum potential score of 8, 9, or 10. Of the 25 studies included, only one study was rated "poor" in quality (Fukuda et al., 2018), nine studies were rated "fair" in quality, and 15 studies were rated "good," with Torche and Kleinhaus (2012) receiving the highest score of the case–control studies and Catalano et al. (2013) receiving the highest score of the observational studies. The overall quality assessments for all included studies are displayed in Table 1 and Table 2.

3.3 | Case–control studies

No case–control studies were identified regarding epidemics or pandemics. Only studies related to catastrophic events such as earthquakes were found, among which a decrease in SRB was reported in six studies, relative to only one study finding no differences in SRB after the given catastrophic event. Table 3 summarizes the sample characteristics, SRB measures, and detailed results.

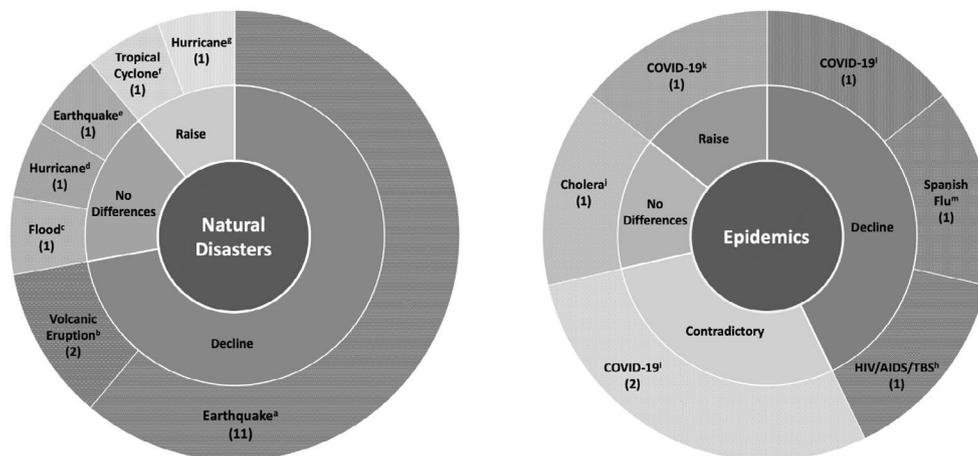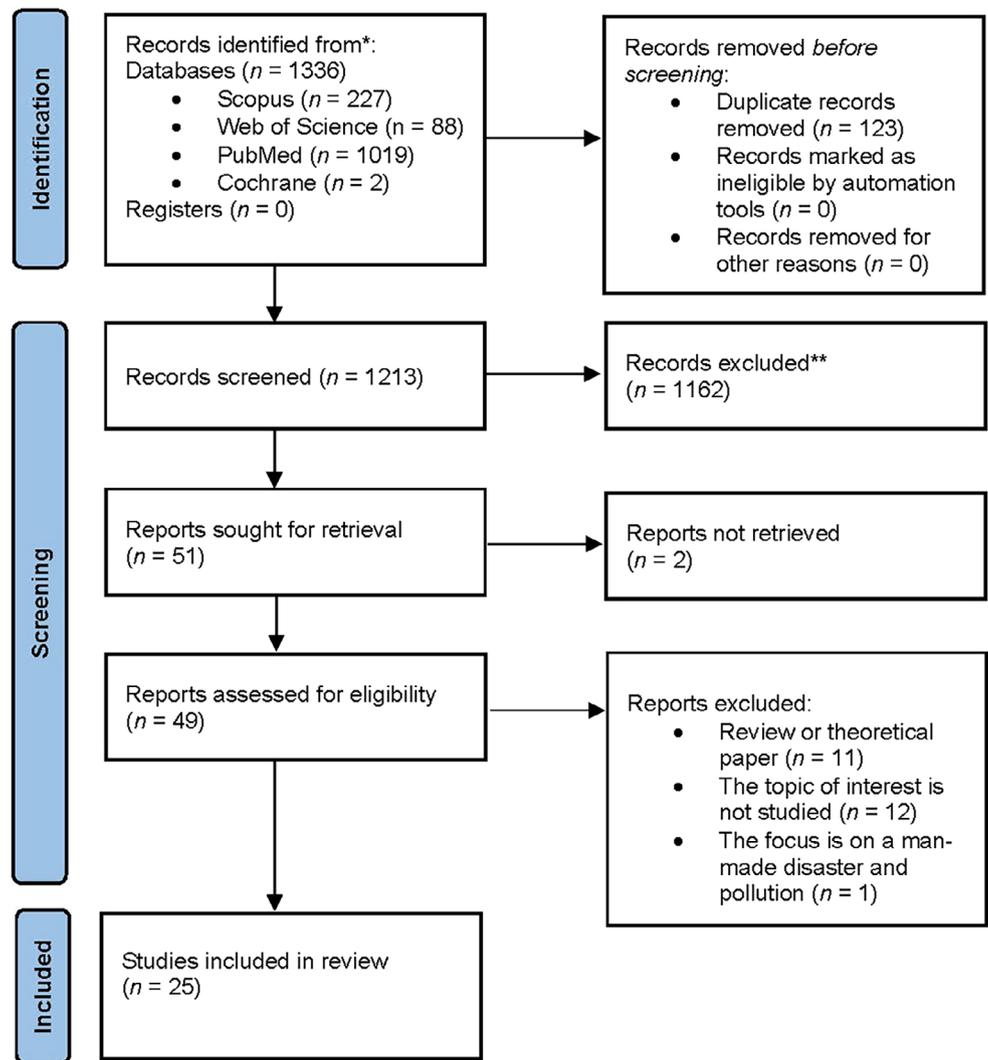**FIGURE 1** PRISMA flow diagram of included studies.

FIGURE 2 Summary of the main results. (A) Catalano et al., 2013; D'Alfonso et al., 2012; Doğer et al., 2013; Fukuda et al., 1998; Fukuda et al., 2018; Hamamatsu et al., 2014; Nandi et al., 2018; Saadat, 2008; Suzuki et al., 2016; Torche & Kleinhaus, 2012; Tourikis & Beratis, 2013. (B) Catalano et al., 2020; Grech & Borg, 2016. (C) Nasir, 2019. (D) Long et al., 2021. (E) Tan et al., 2009. (F) Parayiwa et al., 2023. (G) Grech & Scherb, 2015. (H) Shifotoka & Fogarty, 2013. (I) Inoue & Mizoue, 2022; Masukume et al., 2023. (J) Madrigal, 1996. (K) Saadat, 2021. (L) Masukume et al., 2022. (M) Schacht et al., 2019.

TABLE 1 Summary of the quality assessment for each study using the NIH study quality assessment tool for case–control studies.

Author, date	Clearly stated research question	Specific study population	Sample size justification	Uniform eligibility criteria	Consistent criteria to select cases or controls	Cases clearly differentiated from controls	Random selection of cases and controls	Use of concurrent controls	Exposure or risk prior to outcome	Clear, valid, reliable, consistent exposure measure	Blinding of outcome measures	Statistical analysis (confounding variables)	Total	Applied checklist points	Overall rating
Saadat, 2008	Yes	No	NA	Yes	Yes	No	NA	NA	Yes	Yes	NA	CD	5	8	Fair
Tan et al., 2009	Yes	Yes	No	Yes	Yes	No	NA	NA	Yes	Yes	NA	CD	6	9	Fair
D'Alfonso et al., 2012	Yes	Yes	No	Yes	Yes	No	NA	NA	Yes	Yes	NA	CD	6	9	Fair
Torche and Kleinhaus, 2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	NA	No	9	10	Good
Doğer et al., 2013	Yes	Yes	NA	Yes	Yes	Yes	NA	NA	Yes	Yes	NA	Yes	8	8	Good
Suzuki et al., 2016	Yes	Yes	NA	Yes	Yes	Yes	NA	NA	Yes	Yes	NA	Yes	8	8	Good
Nandi et al., 2018	Yes	Yes	NA	Yes	Yes	Yes	NA	NA	Yes	Yes	NA	Yes	8	8	Good

Abbreviations: CD, cannot determine; NA, not applicable.

3.3.1 | Decline in SRB

There is a significant decline in SRB according to studies conducted in Bam (Saadat, 2008), Wenchuan (Tan et al., 2009), L'Aquila (D'Alfonso et al., 2012), Tarapaca (Torche & Kleinhaus, 2012), Gölcük (Doğer et al., 2013), East Japan (Suzuki et al., 2016), and Gujarat (Nandi et al., 2018). Two studies (D'Alfonso et al., 2012; Saadat, 2008) found a reduction in male births at 9 and 11 months after an earthquake, respectively. One study reported a significant decline in SRB 4 months after an earthquake (Doğer et al., 2013). Torche and Kleinhaus (2012) also identified a significant decline in SRB among pregnant women exposed in the third month of gestation. Five studies used data from national and local databases (Doğer et al., 2013; Nandi et al., 2018; Saadat, 2008; Suzuki et al., 2016; Torche & Kleinhaus, 2012), while D'Alfonso et al. (2012) used data from a local clinic situated close to the earthquake epicenter. The studies using the national and local databases compared data from affected and non-affected areas to assess the impact of the considered earthquakes (Doğer et al., 2013; Nandi et al., 2018; Saadat, 2008; Suzuki et al., 2016; Torche & Kleinhaus, 2012). Meanwhile, D'Alfonso et al. (2012) selected different time periods to analyze the birth cohort within the same area.

3.3.2 | No differences in SRB

Tan et al. (2009) assessed the changes in SRB following the Wenchuan earthquake and compared the ratio of male infants before and after the event. The authors revealed that the catastrophic event had an important impact on maternal well-being, as well as on the levels of birth defects, which increased following the earthquake; however, these did not have an impact on the SRB.

3.4 | Observational studies

Regarding the observational studies, 10 papers confirmed a significant decline, three studies showed a rise, and three studies found no differences in SRB after a stressful catastrophic event. Additionally, two studies yielded contradictory results. These latter studies focused on different types of natural disasters and epidemics/pandemics. All the data for the observational studies were obtained from national databases on birth, public health, or mortality, except for Shifotoka and Fogarty (2013), who retrieved their information from the World Health Organization database. Most of these studies observed changes in SRB by comparing the number of births before and

TABLE 2 Summary of the quality assessment for each study using the NIH study quality assessment tool for observational cohort and cross-sectional studies.

Author, date	Clearly stated research question	Specific study population	Rate of eligible persons	Uniform eligibility criteria	Sample size justification	Exposure measured prior to outcome	Suitable timeframe between exposure and outcome	Levels of exposure	Exposure measures clearly defined	Exposure assessed more than once over time	Clear, valid, reliable, consistent outcome measure	Blinding of outcome measures	Loss to follow-up	Statistical analysis (confounding variables)	Total	Applied Checklist point	Overall Rating
Madrigal, 1996	Yes	Yes	Yes	Yes	NA	No	Yes	No	No	NA	Yes	NA	NA	CD	6	10	Fair
Fukuda et al., 1998	Yes	Yes	Yes	Yes	NA	No	Yes	No	Yes	NA	Yes	NA	NA	CD	7	10	Fair
Tourikis & Beratis, 2013	Yes	No	Ye	Yes	NA	No	Yes	Yes	Yes	NA	Yes	NA	NA	Yes	8	10	Good
Catalano et al., 2013	Yes	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	NA	Yes	NA	NA	Yes	9	10	Good
Shifotoka & Fogarty, 2013	Yes	No	Yes	No	NA	No	Yes	Yes	Yes	NA	Yes	NA	NA	Yes	7	10	Fair
Hamamatsu et al., 2014	Yes	Yes	Yes	Yes	NA	No	Yes	No	Yes	NA	Yes	NA	NA	Yes	8	10	Good
Grech & Scherb, 2015	Yes	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	NA	Yes	NA	NA	CD	8	10	Good
Grech & Borg, 2016	Yes	Yes	Yes	Yes	NA	No	Yes	No	Yes	NA	Yes	NA	NA	CD	7	10	Fair
Fukuda et al., 2018	Yes	Yes	CD	Yes	NA	No	Yes	No	CD	NA	Yes	NA	NA	CD	5	10	Poor
Schacht et al., 2019	Yes	Yes	Yes	Yes	NA	No	Yes	No	Yes	NA	Yes	NA	NA	Yes	8	10	Good
Nasir, 2019	Yes	Yes	Yes	Yes	NA	No	Yes	No	Yes	NA	Yes	NA	NA	Yes	8	10	Good
Catalano et al., 2020	Yes	No	Yes	Yes	NA	No	Yes	No	Yes	NA	Yes	NA	NA	CD	6	10	Fair
Long et al., 2021	Yes	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	NA	Yes	NA	NA	CD	8	10	Good
Saadat, 2021	Yes	Yes	Yes	Yes	NA	No	Yes	No	Yes	NA	Yes	NA	NA	No	7	10	Fair
Inoue & Mizoue, 2022	Yes	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	NA	Yes	NA	NA	No	8	10	Good
Masukume et al., 2022	Yes	Yes	Yes	Yes	NA	No	Yes	No	Yes	NA	Yes	Na	NA	Yes	8	10	Good
Parayiwa et al., 2023	Yes	Yes	Yes	Yes	NA	No	Yes	No	Yes	NA	Yes	NA	NA	Yes	8	10	Good
Masukume et al., 2023	Yes	Yes	Yes	Yes	NA	No	Yes	No	Yes	NA	Yes	NA	NA	Yes	8	10	Good

Abbreviations: CD, cannot determine; NA, not applicable.

TABLE 3 Case–control studies.

Authors	Country/region	Event	Sample characteristics	SRB	Results
Saadat, 2008	Southern Iran	Bam earthquake (December 2003)	- Total births: N = NR M = NR F = NR - AR and NAR births 11 months after the earthquake: N = 2920 (469 AR and 2451 NAR) M = 219; 1304 (AR; NAR) F = 250; 1147 (AR; NAR)	- Data from National Organization for Civil Registration	- Decline in the SRB (0.467) 11 months after the earthquake. - The reduction in the SRB in Bam was statistically significant ($\chi2 = 6.68$; $df = 1$; $p = 0.009$).
Tan et al., 2009	Southwestern China	Wenchuan earthquake (May 2008)	- Pre- and post-earthquake births: N = 13 003 (6638 pre-earthquake and 6365 post-earthquake) M = NR F = NR	- Data from local hospitals of Du Jiang Yan and Peng Zhou - Ratio of male infants (%)	- No significant differences were found in SRB after the Wenchuan earthquake ($p > 0.05$).
D'Alfonso et al., 2012	Italy	L'Aquila earthquake (April 2009)	- Pre- and post-earthquake births: N = 1826 (1026 pre-earthquake and 800 post-earthquake) - M = NR - F = NR	- Records from the Clinical Obstetrics and Gynecology Department of the San Salvatore Hospital, L'Aquila	- Decline in the SSR 9 months after the earthquake, but the overall reduction was not statistically significant. - SSR was 0.62 for January 2010, while it was 0.96 for January 2008 ($p = 0.23$). - Decline in SSR in the first trimester of 2010 compared to the same period of 2008 ($p = 0.13$). - Statistically differences in SSR were found comparing the first trimester of 2010 to the second: 0.82 versus 1.27 ($p = 0.031$).
Torche & Kleinhaus, 2012	Northern Chile	Tarapaca earthquake (June 2005)	- AR and NAR births: N = 13 989 (6874 AR and 7115 NAR) - M = 3510; 3649 (AR; NAR) - F = 3364; 3466 (AR; NAR)	- Data from Chilean Ministry of Health	- Decline in the SSR for those exposed to the earthquake in the third month of gestation, but it was not statistically significant − 5.1% ([CI: −10.5, 0.3] $p = 0.07$). - Counterfactual simulation estimated a decline in the SSR among those exposed in the third month of gestation by 5.8% ([CI: −11.3, −0.3%] $p = 0.039$). - Significant decline in SSR for those exposed to the earthquake in the 8th month of gestation [−5.1% (CI: −0.10%, 0.00) $p = 0.05$].

TABLE 3 (Continued)

Authors	Country/region	Event	Sample characteristics	SRB	Results
Doğer et al., 2013	Turkey	Gölcük earthquake (August 1999)	- AR and NAR births: $N = 1\ 563\ 098$ (627 743 AR and 935 355 NAR) M = 800 742 F = 762 356	- Data from Turkey Statistics Institute - Male proportion: M/F	- Significant decline in SSR in the 4th month and 8th month after the earthquake, comparing AR to NAR ($p = 0.001$ and $p = 0.024$). - SSR in April 2000 was significantly lower than the same months in 2001–2002 ($p = 0.032$ and $p = 0.049$, respectively).
Suzuki et al., 2016	Eastern Japan	Great East Japan earthquake (March 2011)	- EAR, MAR and NAR births: $N = 1\ 367\ 610$ (56 501 EAR; 537 031 MAR; 774 078 NAR) M = 28 896; 275 853; 397 844 (EAR; MAR; NAR) F = 27 605; 261 178; 376 234 (EAR; MAR; NAR)	- Data from Ministry of Health, Labour and Welfare of Japan	- Significant decline in the SSR in EAR at 4–11 weeks of gestation in the 2011 group than 2010 group (49.8% and 52.1%, respectively; $p = 0.009$). - Significant decrease in the SSR between 2010 and 2011 groups (51.7% vs. 50.9%) in NAR at 4–11 weeks of gestation ($p = 0.001$).
Nandi et al., 2018	India	Gujarat earthquake (January 2001)	- AR and NAR births: $N = 153\ 117$ (18 865 AR and 134 252 NAR) M = 10 125; 71 002 (AR; NAR) F = 8740; 63 250 (AR; NAR)	- Data from District-Level Household Survey of India	- The effect of the earthquake was a 2.2 percentage point reduction in the boy-birth rate (equivalent to a 4.1% decrease from a baseline of 53.5% share of boy-births) in the affected districts. The effect was only weakly significant at the 10% level.

Abbreviations: AR, affected region; EAR, extremely affected region; F, females; M, males; MAR, moderately affected region; NAR, not affected region; NR, not reported; SRB, sex ratio at birth; SSR, secondary sex ratio; TC, severe tropical cyclones.

after a catastrophic event, without specifying, however, the radius of the area or the distance from the area affected by the analyzed event. Table 4 summarizes the sample characteristics, the assessment of SRB, and the detailed results of the observational studies.

3.4.1 | Decline in SRB

Five studies investigated the impacts of earthquakes in Kobe (Fukuda et al., 1998; Fukuda et al., 2018), Tohoku, Kumamoto (Fukuda et al., 2018), Zakynthos Island (Tourikis & Beratis, 2013), and East Japan (Catalano et al., 2013; Hamamatsu et al., 2014). These studies showed a significant decline in SRB from 7 to 12 months after the earthquake. Two studies focused on volcanic eruptions at Eyjafjallajökull (Grech & Borg, 2016) and

Laki (Catalano et al., 2020). Three studies examined the impact of different epidemics—namely, HIV/AIDS and tuberculosis (Shifotoka & Fogarty, 2013), the Spanish Flu (Schacht et al., 2019), and the COVID-19 pandemic (Masukume et al., 2022).

3.4.2 | Rise in SRB

Parayiwa et al. (2023) analyzed the areas most affected by the Marcia and Yasi tropical cyclones, finding an increase in SRB after Cyclone Yasi and no variations in SRB after Cyclone Marcia. Grech and Scherb (2015) had previously shown a significant rise in SRB after a natural disaster. These authors investigated the impact of Hurricane Katrina as a stressful event on related disparate rainfall events on SRB in Alabama, Florida, Mississippi, and in

Louisiana, using the Centers for Disease Control and Prevention database (Grech & Scherb, 2015). In this study, the only relevant result is an association between heavy rainfall and a significant rise in SRB in the southern United States (Grech & Scherb, 2015). Finally, Saadat (2021) noticed a rise in SRB after the COVID-19 pandemic in Iran, around 10–13 months after the beginning of the pandemic.

3.4.3 | No differences in SRB

Three observational studies failed to identify variations in SRB following catastrophic events. Madrigal (1996) did not find any significant differences in SRB shortly after the cholera and whooping cough epidemics in Escazú. Nasir (2019) examined the impact of floods and conflict shocks on several birth outcomes in Pakistan, not finding any differences in the areas affected by floods. Finally, Long et al. (2021) studied the effect of Hurricane Katrina using IBM MarketScan and found no variations in SRB within the general population after the hurricane.

3.4.4 | Contradictory results

Two studies (Inoue & Mizoue, 2022; Masukume et al., 2023) investigated the effects of the COVID-19 pandemic on the variation in SRB and identified conflicting results. Masukume et al. (2023) found a decline in SRB after 3 months following the beginning of the pandemic in England and Wales, but they also registered a rise in the ratio after 6 months. Inoue and Mizoue (2022) also observed contradictory results, finding the reverse of the study by Masukume et al. (2022). Inoue and Mizoue (2022) registered a decline in SRB after 9 months within the areas most affected by COVID-19 in Japan and a rise in the less affected areas 6 months after the peak of pandemic.

4 | DISCUSSION

The present systematic review aimed to analyze the effect of natural disasters and epidemics/pandemics on SRB according to the results of 25 papers on the subject, which were narrowly selected according to PRISMA guidelines (Page et al., 2021). This section discusses the hypothesized mechanisms derived from the reviewed studies that may have led to a decline, an increase, or no change in SRB, emphasizing any contradictory results and providing methodological suggestions for future studies.

4.1 | Decline in SRB

Of the 16 studies reporting a decline in SRB, 11 analyzed the SRB ratios after earthquakes, two following volcanic eruptions, and three after a pandemic. Regarding the first catastrophic event, through the information reported by the authors, it was possible to infer that the earthquakes occurred around the first trimester of gestation in nine out of 11 cases. However, the maternal stress–problem pregnancy mechanism may have been related to post-traumatic situations; a negative mental health status related to the traumatic experience of a natural disaster may negatively affect pregnancy in subsequent trimesters (Di Renzo et al., 2007; Fothergill & Peek, 2004; Obel et al., 2007; Walsh et al., 2019; Zahran et al., 2012). These findings may support the TWH regarding the maternal conditions associated with the fetus and with reproductive success (Trivers & Willard, 1973). The same can be concluded for Grech and Borg (2016) on SRB after the Eyjafjallajökull eruption and Masukume et al. (2022) on the COVID-19 pandemic. In fact, two studies reported a decrease in SRB following the Spanish flu (Schacht et al., 2019) and tuberculosis/HIV (Shifotoka & Fogarty, 2013). These studies only partially support the TWH: regions with a high prevalence of the disease had a lower quality of life, and women who were more affected by prenatal and perinatal conditions had access to fewer economic and social resources, which may in turn have impacted the SRB according to the first statement of the TWH. This interpretation may also explain the oscillation in the SRB of 80 annual birth cohorts in Sweden studied by Catalano et al. (2020), suggesting that social factors may be responsible for the decrease in SRB following the Laki eruption.

4.2 | Rise in SRB

Grech and Scherb (2015) previously analyzed the effects of Hurricane Katrina on variations in SRB and found an increase of male newborns over female ones. The authors explained that the amount of radiation in the heavy rainfalls that followed the hurricane may have affected the X chromosome, which appeared to be more vulnerable to ionic radiation exposure. That may have led to the skew toward a higher female fetus mortality and a lower number of females conceived (Grech & Scherb, 2015; Scherb & Grech, 2021). The same explanation could be applied to the evaluation of the results obtained by Parayiwa et al. (2023), which identified a rise in SRB after Cyclone Yasi followed by heavy rainfalls. Saadat (2021) observed a rise in SRB 10 and 13 months after the beginning of the pandemic; the author suggested that due to

TABLE 4   Observational studies.

Authors	Country/region	Event	Sample characteristics	SRB	Results
Madrigal, 1996	Costa Rica	Cholera and Whooping cough (1856; 1892; 1896; 1898)	- Total births: $N = 10\ 957$ $M = 5471$ $F = 5453$	- Data from Parish of San Miguel de Escazú - Number of male births per 100 female births	No association was found between SSR and epidemics.
Fukuda et al., 1998	Japan	Kobe earthquake (January 1995)	- Total births (1993–1996) $N = 159\ 285$ $M = 82\ 130$ $F = 77\ 155$ - October 1995's births: $N = 3932$ $M = 1971$ $F = 1961$	- Data from Hyogo Prefecture and from the published welfare statistics in Japan - Male proportion: $M/(M + F)$	- Decline in the SRB (0.501) 9 months after the Kobe earthquake. - The reduction in SRB in October 1995 was statistically significant ($p = 0.04$; one-tailed).
Torche & Kleinhaus, 2012	Greece	Seismic sequence in the Island of Zakynthos (April–May 2006)	- Total births (2004–2010): $N = NR$ $M = NR$ $F = NR$ - March–April 2007's births: $N = 79$ $M = 30$ $F = 49$	- Data from Statistical Bureau of Greece - Male proportion: M/F	- Decline in the SSR (0.612) 13 months after the earthquakes (March–April 2007). - SSR in March–April 2007 was significantly lower than during the 6 years period from 2004 to 2006 and from 2008 to 2010 ($OR = 0.57$, 95% CI = 0.36–0.91, $p = 0.023$). - SSR in March–April 2007 was significantly lower than SSR during the same months 3 years before and after the earthquakes ($OR = 0.50$, 95% CI = 0.31–0.82, $p = 0.007$).
Catalano et al., 2013	Japan	Great East Japan earthquake (March 2011)	- AR and NAR births: $N = NR$ $M = 18\ 028; 433\ 901$ (most affected areas; all areas left) $F = NR$	- Data from Ministry of Health, Labour and Welfare of Japan	- Significantly fewer observed male births than expected for AR e NAR after the earthquake ($p < 0.003$; one-tailed test).
Shifotoka & Fogarty, 2013	184 Countries	HIV/AIDS TB (2009)	- Total births: $N = NR$ $M = NR$ $F = NR$	- Data from WHO Global Observatory database, the United Nation database and the Central Intelligence Agency World Factbook - Number of male births per 100 female births	- Significant negative correlation ($r = -0.58$, $p < 0.001$) between SRB and national HIV/AIDS prevalence was found. - Significant negative correlation ($r = -0.48$, $p < 0.001$) between SRB and national TB prevalence was found. - Populations with the highest quartile of HIV/AIDS and TB

TABLE 4 (Continued)

Authors	Country/region	Event	Sample characteristics	SRB	Results
					prevalence had a reduced SRB compared with those with the lowest quartiles: −0.022 (95% CI −0.031 to −0.013) and − 0.016 (95% CI −0.028 to −0.004), respectively.
Hamamatsu et al., 2014	Japan	East Japan earthquake (March 2011)	- Total births: $N = 582\,136$ (225 791 AR; 356 232 NAR; 113 foreign born) M = NR F = NR	- Data from website of the Demographic Survey of Japan - Number of male births per 100 female births	- Male births for all Japan in October 2011 (SSR = 102.9, $n = 89\,180$) were lower than the empirically estimated 95% CI. - NAR male births (SSR = 102.6, $n = 53\,761$) in October 2011 were lower than the empirically estimated 95% CI. - AR male births decreased from expected SSR 104.8 to 103.4 ($n = 35\,410$) during the disaster-impact period, remaining within the empirically estimated 95% CI.
Grech & Scherb, 2015	Southern USA	Hurricane Katrina (August 2005)	- Total births: $N = 3\,903\,660$ M = 1 996 966 F = 1 906 694	- Data from website of the Centers for Disease Control and Prevention - Male proportion: M/(M + F)	- Significant rise of male proportion 8–10 months (April to June 2006) after the hurricane from 1.052 to 1.071 with SOR of 1.018 (95% CI 1.005, 1.032, $p = 0.007$).
Grech & Borg, 2016	Iceland	Eyjafjallajökull eruption (April 2010)	- Total births: $N = 110\,594$ M = NR F = NR	- Data from Statistics Iceland - Male proportion: M/(M + F)	- Significant decline in M/T for September and November 2010 was noted after the Eyjafjallajokull eruption. - M/T dipped to <20th percentile, at 0.488 and 0.489, respectively, 3 to 5 months after the eruption.
Fukuda et al., 2018	Japan	Kobe earthquake (January 1995); Tohoku earthquake (March 2011); Kumamoto earthquake (April 2016)	- Total births: N = NR M = NR F = NR	- NR	- SRB was significantly lower in January 2012 (0.953) after the Tohoku earthquake than the same month from 2006 to 2011 ($p = 0.020$). - SRB was significantly lower in February 2017 (0.963) than the same month from 2011 to 2016 ($p = 0.039$).

TABLE 4 (Continued)

Authors	Country/region	Event	Sample characteristics	SRB	Results
Schacht et al., 2019	Utah	Spanish flu (1918–1920)	- Total Births: $N = 106\ 645$ (15 205 SF period and 91 440 other periods) M = NR F = NR	- Data from Utah Population Database - Male proportion: M/F	- Significant decrease in male births ($B = -0.077$, $SE = 0.022$, $p < 0.001$) during SF period was observed.
Nasir, 2019	Pakistan	Floods (2010 and 2011)	- Total births: $N = 14\ 075$ M = NR F = NR	- Data from the Pakistan Demographic and Health Survey	- No significant differences in the probability of female birth after the exposure to floods were found.
Catalano et al., 2020	Sweden	Laki Eruption (June 1783)	- 80 annual birth cohorts: N = NR M = NR F = NR	- Data from Human Mortality Database - Male proportion: M/F	- Decline in SSR was noted after the Laki volcano eruption in Sweden. - The odds of male birth dropped 2.6% in 1784.
Long et al., 2021	USA Sweden	Hurricane Katrina (August 2005)	- Total births $N = 3\ 134\ 062$ (USA) and 3 260 304 (Sweden) M = NR F = NR	- Data from IBM Health MarketScan dataset - Swedish National Patient Register	- No significant association between Hurricane Katrina and variations of SRB was found.
Saadat, 2021	Iran	COVID-19 (February 2020)	- Total births $N = 5\ 274\ 898$ (4 075 425 I1, 849 959 I2, and 349 514 I3) M = 2 718 658 (2 099 500 I1, 438 396 I2, and 180 762) F = 2 556 240 (1 975 925 I1, 411 563 I2, and 168 752 I3)	- Data from National Organization for Civil Registration database - Male proportion: M/F	- Statistically significant rise of SRB in I3 (10–13 months post-epidemic) compared I1 (36 months pre-epidemic) ($\chi^2 = 5.25$, $df = 1$, $p = 0.022$). - No significant differences of SRB between I2 and I1.
Inoue & Mizoue, 2022	Japan	COVID-19 (February 2020)	- Total births: $N = 7\ 835\ 985$ M = 4 017 899 F = 3 818 086	- Data from Ministry of Health, Labour and Welfare of Japan - Number of male births per 100 female births	- Significant reduction in SRB (102.9) in December 2020 for all Japan than the lower bound of 95% PI (103.12). - Considering different levels of exposure, only severely affected prefectures showed a significant decline of SRB in December 2020 than the lower bound of 95% PI. - A significant increase of SRB for less affected prefectures in September 2020 than the upper bound 95% PI was found.

TABLE 4 (Continued)

Authors	Country/region	Event	Sample characteristics	SRB	Results
Masukume et al., 2022	South Africa	COVID-19 (March 2020)	- Total births: $N = 8\ 151\ 364$ $M = 4\ 113\ 288$ $F = 4\ 038\ 076$	- Data from Statistics South Africa - Male proportion: $M/(M + F)$	- Decline in SRB (0.499) for June 2020 was noted after the COVID-19 pandemic began in South Africa. - Significant reduction of observed SRB for June 2020 than predicted ratio (0.504) ($p = .045$).
Parayiwa et al., 2023	Australia	Tropical cyclones Yasi (February 2011) and Marcia (February 2015)	- Total births (severely affect areas) $N = 54\ 635$ (34 360 Yasi TC and 20 275 Marcia TC) $M = 28\ 261$ (17767 Yasi TC and 10 494 Marcia TC) $F = 26\ 374$ (16593 Yasi TC and 9781 Marcia TC)	- Data from Queensland Perinatal Data Collection (Q-PDC) - Male proportion: $M/(M + F)$	- A significant association between early pregnancy exposure to TC Yasi and higher proportion of male birth (IRR = 1.08, 95% CI = 1.00−1.17, $p = 0.041$) was found. - No significant changes in SRB after TC Marcia were found.
Masukume et al., 2023	UK (England and Wales)	COVID-19 (March 2020)	- Total births $N = 6\ 108\ 030$ $M = 3\ 133\ 915$ $F = 2\ 974\ 115$	- Data from Office National Statistics - Male proportion: $M/(M + F)$	- Significant decline in the SRB (0.5100) in June 2020, which was below the 95% *PI* (0.5102–05179). - Significant rise in the SRB (0.5171) in December 2020, which was above the 95% *PI* (0.5085–0.5162).

Abbreviations: AR, affected region; F, females; I1, first interval; I2, second interval; I3, third interval; M, males; NAR, not affected region; NR, not reported; SF, Spanish flu; SOR, sex odds ratio; SRB, sex ratio at birth; SSR, secondary sex ratio; TB, tuberculosis.

the restraint measures (i.e., lockdown), couples had more sex and more children were born, as SRB rates were positively correlated with parental coital rates (James, 2008).

4.3 | No differences in SRB

After the Wenchuan earthquake, Tan et al. (2009) observed a higher number of birth defects, but they did not find any significant alterations in the SRB, in contrast with the findings obtained through a similar study by Fukuda et al. (2018). However, according to the hypothesis made by the authors based on the existing literature, the number of males born with a birth defect should have significantly increased relative to the values obtained through the studies conducted prior to the earthquake period (Tan et al., 2009). According to Tan et al. (2009), this could be related to the sampling methodology, which would have only included a small part of the areas

affected by the earthquake. It can also be hypothesized that the absence of variations in SRB after the earthquakes in those specific areas could be related to political and social issues—the administrative under-reporting and delayed registration of females, as well as sex-selective abortive procedures, may have significantly skewed the sex ratios in the general population (Wang, 2017). In 2008, when the earthquakes hit the Wenchuan region, the male-to-female ratio in China was one of the highest registered (1.069:1.00). Similarly, higher rates of sex-selective abortion and "the son preference" (Chao et al., 2021) may have affected the results of Nasir (2019), who found no differences in SRB following heavy floods that occurred in Pakistan. Madrigal (1996) suggested that insignificant fluctuation in SRB in Costa Rica after two epidemics was due to maternal protective factors (better life conditions). These theories were confirmed by Long et al. (2021), who stated that variations in SRB could be attributed primarily to non-

adaptive factors, such as socio-cultural influences, rather than genetic or adaptive factors.

4.4 | Contradictory results

While Masukume et al. (2023) identified a decline in SRB, the same authors first registered a rise in the number of recorded male births relative to the number of recorded female births (December 2020). The authors hypothesized that this variation may have been due to a general reduction in overall live births compared to prior Decembers in the examined areas, suggesting little sexual activity (Masukume et al., 2023). Similarly, Inoue and Mizoue (2022) found a decline in SRB in December 2020 in Japan but observed a rise in the sex ratio in September 2020. They suggest that these differences may have been due to a colossal sport event (the Rugby World Cup) hosted by Japan from September to November 2019, which had a huge positive economic impact on the country. This would support the hypothesis that variations in SRB are subject to at least some adaptive mechanisms but also to social and economic pressures, which would make it difficult to make specific predictions about sex ratio modifications.

5 | IMPLICATIONS FOR RESEARCH

Although most of the reviewed studies scored "good" or "fair" in the quality assessment, the soundness of the results was not totally supported by the methodological choices of the reviewed papers. All the reviewed studies were conducted with a case–control or observational design, so any associations found here are not causal inferences. Most of the studies explored an association between natural disasters and SRB, whereas a smaller amount of data were available regarding the impacts of epidemics on SRB. Specific factors should be considered in the analysis of SRB variations that may have an impact on the relationship between catastrophic events and SRB, as well as time frames, distances, and confounding or moderator variables.

5.1 | Time frame and distance

The reviewed studies considered different time frames, ranging from several months after the catastrophic event (e.g., Masukume et al., 2023; Saadat, 2008) or years before and after (e.g., Doğer et al., 2013; Torche & Kleinhaus, 2012) to the month (Torche &

Kleinhaus, 2012) or the week of exposure during the gestational period (Parayiwa et al., 2023; Suzuki et al., 2016). Furthermore, some studies investigated the population of a specific area near or in the middle of the epicenter of the catastrophic event (D'Alfonso et al., 2012; Doğer et al., 2013; Nandi et al., 2018; Saadat, 2008; Suzuki et al., 2016; Torche & Kleinhaus, 2012), while other studies included a larger portion of the population.

5.2 | Variables associated with variations in SRB

Few studies have controlled for the effect of possible confounding or moderator variables in the variation of SRB; for example, seasonality refers to the fluctuation in births during a specific period. Seasonality is a source of non-trend variation in births, which varies among populations. For example, high temperatures in summer may reduce conception through a reduced copulatory rate or decreased fecundability (e.g., decreased sperm quality; Darrow et al., 2009) or, in western societies, a peak in conception appears to manifest during the holidays (Wood et al., 2017). Other factors that should be considered in the analysis of SRB variations include environmental factors such as the effect of radiation after heavy rainfall (Grech & Scherb, 2015). In addition, socio-economic factors may influence people's quality of life through social, political, and legal factors, as in the impact of a state's abortion policy on the induced abortion of female fetuses in China and Pakistan.

More accurate and consistent research methods should be employed and compared to obtain more reliable evidence. In order to investigate variations in SRB and test how the TWH applies to our species, future studies should employ a shared paradigm that includes (a) a mixed method design to compare groups—for example, within and between, before and after the event, affected and not affected areas; (b) comprehensive data from national registers; (c) a shared measure to assess the variation in SRB (e.g., prediction or counterfactual); and (d) a deeper analysis of possible confounding or moderator variables. Finally, researchers should also consider that the period of gestation that may be more vulnerable to stressful events and thus identify the influence of the environment on maternal and fetal well-being.

6 | LIMITATIONS OF THE SYSTEMATIC REVIEW

Although this paper contributes to knowledge on the variation of SRB after catastrophic events, our findings

should be interpreted with consideration of the limitations of the systematic review performed here. First, we only retrieved studies published in the English language; we may have thus missed some other relevant contributions. Second, we did not search the gray literature and conference abstracts, and we only included published research articles. The exclusion of unpublished studies in the review may indicate a degree of publication bias, although tests could not be performed. Third, we did not register our systematic review with PROSPERO, an international database of prospectively registered systematic reviews used to avoid duplication, reduce the opportunity for reporting bias, and compare the completed review with the registered protocol. However, this may be a methodological limitation that does not affect our results.

7 | CONCLUSION

The systematic review provided here explored the effects of natural catastrophes and epidemics on SRB; most of the studies reported a decline in SRB following catastrophic events, appearing to generally support the TWH. Even if testing the TWH in our species is not a simple task, studies on large populations generally start from the assumption that when the socio-ecological factors are disadvantageous, such as when natural catastrophes occur, this may result in a decrease in SRB, with important implications for maternal and newborn health. Nevertheless, although most of the analyzed studies identified a decrease in SRB, some research reported an increase in or no change to the SRB. Therefore, further work involving more accurate and consistent methodologies should be undertaken to acquire a better understanding of the mechanisms that lead to SRB variations.

Our considerations point to a question on the relationship between SRB and public health and to the importance of explaining changes in human SRB over time. In fact, unusual variances in the sex ratio may represent an important warning sign of prenatal, perinatal, and postnatal health complications, since many studies have reported an increase of birth defects and fetal deaths in response to environmental perturbations. Moreover, it is important because catastrophic events due to climate change and the possibility of future pandemics will only increase. Additionally, more empirical studies should be conducted to examine the association between natural disasters, maternal stress, post-traumatic symptoms, environmental and socio-economic conditions, and their impact on declines in SRB.

AUTHOR CONTRIBUTIONS
Lilybeth Fontanesi: Conception and design, analysis, and interpretation of data for the work, drafting the work and revising it critically for important intellectual content, final approval to be published. **Maria Cristina Verrocchio:** Drafting the work and revising it critically for important intellectual content, final approval to be published. **Melissa D'Ettorre:** Data collection, drafting the work, final approval to be published. **Giulia Prete:** Drafting the work, final approval to be published. **Francesco Ceravolo:** Data collection, drafting the work, final approval to be published. **Daniela Marchetti:** Conception and design, analysis, and interpretation of data for the work, drafting the work and revising it critically for important intellectual content, final approval to be published. All authors have approved the final version of the paper.

ORCID
Maria Cristina Verrocchio https://orcid.org/0000-0003-2549-1152

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.