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Walid Makin Fahmy, Cibele Aparecida Crispim, Susan Cliffe



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**Association between maternal death and cesarean section in Latin America: a systematic literature review**

**Walid Makin Fahmy [Medical Doctor]**

Department of Obstetrics, Hospital e Maternidade Municipal Dr. Odelmo Leão Carneiro, Uberlândia, MG, Brazil.

**Cibele Aparecida Crispim [Professor]**

Faculty of Medicine, Universidade Federal de Uberlândia, Uberlândia, MG, Brazil.

**Susan Cliffe [Professor]**

Department of Public Health, London School of Hygiene & Tropical Medicine, London, United Kingdom.

**Corresponding author:** Walid Makin Fahmy, Phone/ Fax: +5534 3253-5600

Address: Rua Mata dos Pinhais, 410 - Bairro Jardim Botânico - CEP: 38410-655

Uberlândia – MG – Brazil

E-mail: fahmywm@hotmail.com.

**ABSTRACT**

**Background**

It is critically important to explore a possible relationship between cesarean section and maternal mortality in Latin America, where the highest cesarean section rates in the world are found. Our aim was to conduct a systematic literature review on the relationship between maternal death and caesarean section in Latin America.

**Methods**

We undertook a systematic review through six electronic databases. Studies that reported any association analysis between maternal mortality and the mode of delivery in Latin America were included. Papers that fulfilled the inclusion criteria were then read fully, and a quality assessment was conducted with the PROMPT tool.

**Results**

Seven articles were identified for final analysis, all of which were observational studies. Most of the studies were retrospective (6) and one was prospective. Of the retrospective studies, 3 were case control and 3 were cross-sectional. Most of the publications on this topic suggest that there may be an increased risk of maternal mortality with cesarean section compared with vaginal birth (odds ratio ranging from 1.6 to 7.08). However, it is evident that there is a lack of studies with this subject, especially those that take into account the differences in risk between women delivered by cesarean section or by vaginal birth.

**Conclusions**

Most of the articles showed that there may be an increased risk of maternal mortality with cesarean section compared with vaginal birth. However, it is clear that there is a limited number of studies published on this issue. Additional studies with a better methodological design should be conducted.

**Keywords:** Maternal death, Caesarean section, Vaginal birth.

## Introduction

The maternal mortality ratio (defined as the number of maternal deaths per 100,000 live births) has shown large variations in different regions of the world. This rate is higher in developing regions (230) compared with developed regions (16). Latin America has a maternal mortality ratio of 85<sup>1</sup>. It is currently known that the most important direct causes of maternal death are hypertensive disorders, hemorrhage, abortion, and sepsis<sup>2,3</sup>; however, the identification of other potentially novel risk factors might provide insights into other possible preventative approaches to maternal death.

Rates of caesarean section have increased in recent decades worldwide<sup>4-5-6</sup>. Recently, Betran et al.<sup>7</sup> analyzed 90% of the total number of live births worldwide between 1990 and 2014, and found that caesarean section rate increased 12.4% in this period. The largest absolute increase occurred in Latin America and the Caribbean (19,4%, from 22,8% to 42.2%)<sup>7</sup>. According to the last official data available in Brazil (2012), this country has the highest caesarean section prevalence in the world - 55.6%<sup>8</sup>. Although it is well established that a correct indication of caesarean section is extremely important and can save the lives of mother and newborn, studies have shown that this mode of delivery may expose women to an increased risk of morbidity<sup>9,10,11</sup> and mortality<sup>10,11</sup>.

The association between caesarean section and maternal death shows contradictory results in different countries<sup>12-17</sup>. While some studies have found no associations<sup>12-14</sup>, most of the evidence has shown a positive association in different degrees<sup>10,11,15,16,17</sup>.

Clark et al.<sup>16</sup>, in USA, found a maternal mortality ratio 10 times higher in caesarean section compared with vaginal birth; Deneux-Tharaux et al.<sup>15</sup> in France, maternal mortality ratio 3.6 times higher; and Gonzales et al.<sup>17</sup>, in Peru, maternal mortality ratio 5.5 times higher.

Interestingly, in studies conducted in countries that have cesarean section rates lower than 15% and high mortality rates (e.g., Sub-Saharan African countries), cesarean section is associated with lower maternal mortality ratios, which demonstrates a protective effect of this procedure<sup>13,14,18,19</sup>. On the other hand, countries with cesarean section rates of more than 30%, such as many in Latin America, cesarean section rates are associated with higher maternal mortality ratios<sup>17,20</sup>. This suggests that other variables may be involved in the relationship between the mode of delivery and maternal mortality.

It is critically important to explore if there is a relationship between cesarean section and maternal mortality in a region where the rate of caesarean section is the highest in the world and has presented the highest increase in recent decades. The aim of this study was to conduct a literature review on the relationship between maternal mortality and cesarean section in Latin America.

## **Methods**

### **Inclusion and exclusion criteria**

#### *Inclusion criteria:*

Searches were limited to publications relating to countries of Latin America (Argentina, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Guyana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname, Uruguay), written in English, Spanish or Portuguese, published between the year 2000 and 31 December 2015.

#### *Exclusion criteria:*

Articles that assess data from Latin America and other regions together, without differentiation; articles that do not allow for any type of comparison between the mode of delivery and maternal death; articles that used only descriptive analysis without an appropriate statistical analysis; articles whose data were collected before 1980.

**Literature search strategy:**

A systematic literature review on the relationship between maternal death and cesarean section in Latin America was carried out. The methodology of the systematic review involved an extensive search of all relevant published/unpublished data.

To ensure that the search terms already identified (maternal mortality, maternal death, cesarean section, vaginal birth and normal birth) were appropriate, as well as to discover others, an initial database search test was conducted in an exploratory manner. Terms added to the search strategy after this analysis were: caesarean, C-section, vaginal and normal delivery, mode, type and method of delivery. Moreover, an analysis was carried out to evaluate the feasibility of the study and to make adjustments, such as for the time period and geographic location.

Following the initial search, a wide range of electronic databases sources was used, accessed through PubMed, Global Health, Popline and the WHO library. Two important database of the Latin America region were also used: the Scientific Electronic Library Online (SCIELO) and Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS). SCIELO is an electronic virtual library that covers a selected collection of Latin American scientific journals. LILACS is the most important and comprehensive index of scientific and technical literature of Latin America and the Caribbean.

The database search was performed considering the literature published between the year 2000 and 31 December 2015. Three domains were identified in the search strategy (maternal mortality, mode of delivery and area of study). Within the domains, the Boolean Operator 'OR' was used to combine the search terms, whereas between the domains, the Boolean Operator 'AND' was used to combine the three domains (maternal mortality AND mode of delivery AND area of study).

Terms related to maternal mortality were 'maternal death' OR 'maternal mortality'. Terms related to mode of delivery were 'caesarean section' OR 'caesarean' OR 'cesarean' OR 'c-section' OR 'vaginal delivery' OR 'normal delivery' OR 'vaginal birth' OR 'mode of delivery' OR 'type of delivery' OR 'method of delivery'. Terms related to geographic location were 'Latin America' OR 'Central America' OR 'Argentina' OR 'Belize' OR 'Bolivia' OR 'Brazil' OR 'Chile' OR 'Colombia' OR 'Costa Rica' OR 'Ecuador' OR 'El Salvador' OR 'Guatemala' OR 'Guyana' OR 'Honduras' OR 'Mexico' OR 'Nicaragua' OR 'Panama' OR 'Paraguay' OR 'Peru' OR 'Suriname' OR 'Uruguay' OR 'Venezuela'. All of the words were translated into Spanish and Portuguese when searching the Latin America databases.

The specific details of the search results are demonstrated in Figure 1. A large number of literature articles were generated by the initial searches (1344), many of which were excluded as being unrelated to the search by a review of the title alone or a quick review of the abstract. Following the review of these abstracts, 316 articles were identified for full text consideration before this number was narrowed down to 7 final articles that met the inclusion criteria for the review. Excluded articles (n=309) did not procedure any statistical association between the mode of delivery and maternal death, or assess data from Latin America and other regions together, without differentiation. Articles that

evaluated data before 1980 were also excluded. In the final stage of the literature review, 7 final articles were selected.

Language restrictions were not applied in the search or in the selection process. Potentially eligible datasets included journal articles, registries, and published or unpublished information from government or other agencies, whether available in print or online. In addition, data from 'Grey literature' was also examined from contacted experts in the field.

Each title, abstract, full text, dissertation/thesis and grey literature was evaluated by the same author. Thus, 7 articles were considered in the final analysis.

### **Insert Figure 1**

### **Data extraction, synthesis and critical appraisal**

The papers that fulfilled the inclusion criteria were then read fully, and a quality assessment was conducted through critical appraisal by the author. The tool used for the evaluation was PROMPT, a structured approach to the critical evaluation of information (provenance, relevance, objectivity, method, presentation, timeliness<sup>21</sup>).

Key findings on the association between maternal mortality and the mode of delivery in Latin America were noted as necessary factors to take into consideration, including logistic regression (odds ratio) and the relative risk. Moreover, information regarding whether maternal death was secondary to complications of cesarean section or to underlying conditions and the difference between the risk of maternal death associated with planned or elective cesarean section, emergency cesarean section or intrapartum cesarean section were analyzed. Particular attention was given to the articles with analysis adjusted for confounders such as low or high risk pregnancy.



## Results

Seven articles were identified for final analysis. An overview of the data contained in the reviewed articles is presented in the Table 1.

Insert Table 1

Of the seven studies identified, all were observational studies. Most of the studies (6) were retrospective<sup>17, 22-26</sup>, and one was prospective<sup>20</sup>. Of the 6 retrospective studies<sup>17, 22-26</sup>, 3 were case-control<sup>22,24,26</sup> and 3 cross-sectional<sup>17,23,25</sup>.

Regarding the geographic area, most of studies were conducted in Brazil (4)<sup>22,23,25,26</sup>, one study in Mexico<sup>24</sup> and one in Peru<sup>17</sup>. One study was multicenter and analyzed data from 8 countries in Latin America (Argentina, Brazil, Cuba, Ecuador, Mexico, Nicaragua, Paraguay and Peru)<sup>20</sup> (Table 1).

The period of data collection began in the 1980s in 2 of the articles analysed<sup>22,23</sup>, the 1990s in 1<sup>24</sup>, and the 2000s in 4<sup>17,20,25,26</sup>. The period of data analysis of the studies was up to 5 years in 2<sup>20,25</sup>, between 5 and 10 years in 2<sup>22,26</sup>, and 10 or more years in 3<sup>17,23,24</sup>. (Table 1).

The number of live births, which corresponds to the sample size evaluated in the studies, ranged from 63,002 to 1,153,034. Most studies (4)<sup>24,25,26,17</sup> included populations larger than 100,000 live births, two studies<sup>20,23</sup> analyzed between 50,000 and 100,000 live births. One<sup>22</sup> study did not provide this information.

The data sources of the evaluated studies were a majority of clinical files or medical reports (4)<sup>20,22,23,24</sup> and epidemiological surveillance(4)<sup>17,22,25,26</sup>. Other methods were also used, including death certificates (1)<sup>22</sup>, maternal mortality committee databases (1)<sup>26</sup>, birth certificates (1)<sup>25</sup>, interviews (1)<sup>24</sup> and hospital surveillance (2)<sup>20,25</sup>.

The analysis of risk of maternal death and the mode of delivery adjusted for confounders are shown in Table 1. All studies that used logistic regression analysis (6)<sup>17,20,22,24,25,26</sup> showed that cesarean section was associated with a significantly higher risk of maternal death than vaginal birth. The adjusted ORs ranged from 1.6 to 7.08 (Table 1). In one study<sup>23</sup>, relative risk analysis indicated a positive association between cesarean section and maternal mortality (RR=10.7, 95% CI=3.07-37.77).

Data extracted from studies that separated elective, intrapartum and emergency cesarean section is presented in the Table 2. This type of sample stratification was performed in only two of the studies included in this review<sup>17, 20</sup>.

## Discussion

This systematic literature review aimed to explore the association between cesarean section and maternal mortality in Latin America. To the best of our knowledge, this is the first study to systematically review this association in the world region that has the highest cesarean section rates<sup>7</sup>. To date, most of the publications on this topic suggest an increased risk of maternal death following cesarean section compared with vaginal birth. However, it is evident that the lack of studies hinders our ability to draw more definitive conclusions. Thus, this association can only be confirmed by further studies, with appropriate methodological designs.

The positive association between cesarean section and maternal mortality in Latin America found in this review is consistent with previous studies from other geographical regions<sup>2,10,11,15,16,27-30</sup>. In general, evidences from other regions showed that women who underwent cesarean section had a higher risk of severe maternal

morbidity and mortality than women who underwent vaginal birth, independent of geographical area and clinical characteristics<sup>2,10,11,15,16,27-30</sup>. Kamilya et al.<sup>30</sup>, in India, showed that cesarean section was associated with a 3.01-fold increase in the risk of maternal mortality compared with vaginal birth. In the UK, Hall et al.<sup>28</sup> found an OR of 2.84 (95% CI 1.72-4.7) for elective cesarean section and 8.84 (95% CI 5.60–13.94) for emergency cesarean section compared with vaginal birth. Moreover, Souza et al.<sup>10</sup>, in Africa, Asia and Latin America, found an association between cesarean section and risk of death, as well as admission to the intensive care unit, blood transfusion and hysterectomy for both antepartum cesarean section without medical indications (adjusted OR= 5.93, 95% CI 3.88to 9.05) and intrapartum cesarean section without medical indications (adjusted OR=14.29, 95% CI 10.91 - 18.72). It is important to mention that the positive association between cesarean section and maternal death was not found by Althabe et al<sup>13</sup> in a multicenter study, O'Dwyer et al.<sup>12</sup> in Ireland, Liu et al.<sup>9</sup> in Canada, Cristina Rossi and Mullin<sup>31</sup> in developed countries and Volpe<sup>14</sup> in a global ecological study. This demonstrates the need for additional worldwide studies in this area.

It is important to highlight that all the 5 studies that presented analyses adjusted for clinical (4) or social (1) confounders<sup>17,22,24-26</sup> (Table 1), showed that cesarean section was associated with a significantly higher risk of maternal death than vaginal birth in Latin America. These adjustments can be considered a very important procedure in these studies, because some conditions - such as hypertensive disorders, heart disease and low socioeconomic conditions could be contributors to mortality and must be considered in statistical analyses.

Another approach that was used in the review of this topic was to analyze the performance of elective, emergency or intrapartum cesarean section, which can indicate

different degrees of risk. This information was considered only in two studies in the present review<sup>17,20</sup> (Table 2). Villar et al.<sup>20</sup> found that elective and intrapartum cesarean section were associated with a significantly higher risk for maternal death than for vaginal birth. Gonzales et al.<sup>17</sup> conducted a logistic model adjusted for some important confounders (Table 1), and found that, compared with vaginal birth, elective and emergency cesarean section were associated with a significantly higher risk of maternal death. Importantly, the maternal mortality ratio for cesarean section was approximately 5 times greater than that for vaginal birth in both studies<sup>17,20</sup>.

Two studies included in the present review did not adjust the analysis for any confounder. However, it is important to consider that Villar et al.<sup>20</sup> excluded emergency cesarean section without labor in their study, thus diminishing the chance of bias. Although Ramos et al.<sup>23</sup> did not adjust the analysis for any confounder, they considered, in the RR analysis, only the cases in which death could be attributed to the mode of delivery (surgical- and/or anaesthetic-related deaths in cesarean section, and hemorrhage and infection with vaginal birth). This can indicate that the lack of adjustment was not an important limitation.

This review has some limitations. Of the 20 countries in Latin America, only 8 were evaluated because there were no studies published in the other countries. Most of the studies were conducted in Brazil, which presents a better economic condition than other countries such as Bolivia, El Salvador, Guatemala and Honduras. It is also evident that there is a small number of studies. No peer review was performed and, despite our efforts to include all available studies, some could have been missed, and publication bias could exist. Heterogeneity of the populations (e.g., city residents, state residents, hospitals that do not represent the general population) can also be considered as a limitation.

An important aspect is that there were no publications in the literature of Latin America with an ideal study design and adequate power to establish the relationship between maternal mortality and the mode of delivery. In this sense, population-based analyses of maternal death should be conducted, and a prospective trial considering low risk and high risk planned vaginal birth and elective cesarean section (**with and without medical indication**) is warranted to resolve the current debate. Moreover, it is necessary to account for short- and long-term outcomes in successive deliveries throughout reproductive life<sup>32</sup>. Long-term complications such as uterine rupture, placenta previa or placenta accreta with subsequent pregnancy may impact maternal mortality<sup>33</sup>.

## Conclusions

All of the seven articles demonstrated that there might be a greater risk of maternal death with cesarean section than with vaginal birth. However, it is evident that the small number of studies and countries covered in the region limit the ability to establish these associations. Further studies are needed to address a better understanding of this issue.

Additional studies that control the maternal confounders, such as high-risk and low-risk pregnancies in planned vaginal and planned elective cesarean section should be conducted.

## Ethical Statement

- 1) Conflict of Interest  
None declared" / "Not applicable
- 2) Ethical Approval

This project is a literature review and, thus, involves data that have already been anonymised and for which confidentiality has been upheld. Thus, there are no ethical implications

### 3) Funding Sources

None declared" / "Not applicable

### 4) Clinical Trial

None declared" / "Not applicable

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Table 1: Outline of data extracted from the included studies

Author (year)	Population and geographical area	Study design	Period of data collection	Live births	Number of deaths	Maternal mortality ratio	Data analyses	Adjustment	Outcome
Cecatti et al. <sup>22</sup>	All maternal death of the Campinas, SP, Brazil	retrospective, case-control	1985 - 1991	no info	62	no info	Logistic regression	Maternal age, marital status, occupation, type of health insurance, parity, history of abortion, previous cesarean section, antenatal visits, complications during labor	OR of maternal mortality with cesarean section compared with vaginal birth=3.01 (1.37-6.55)
Ramos et al. <sup>23</sup>	Tertiary University Hospital in Porto Alegre, RS, Brazil	retrospective, cross-sectional	1980 - 1999	63,002	#81	109	Relative risk	Deaths attributed exclusively to complications of mode of delivery (cesarean section and vaginal delivery)	RR of maternal mortality with cesarean section, compared with vaginal birth= 10.7 (3.07-37.77)
Romero-Gutiérrez et al. <sup>24</sup>	Social Security Hospital in Leon, GUA, Mexico	retrospective, case-control	1992 - 2004	132,278	110	47.3	Logistic regression	Maternal age, marital status, antenatal visits, preexisting medical conditions, complications in previous	OR of maternal mortality with cesarean section compared with vaginal birth=1.6 (1.00-2.4)

								pregnancies	
Kilzaj et al. <sup>25</sup>	All maternal death of the Sao Paulo State, Brazil, from the public Sector	retrospective, cross-sectional	2001 - 2003	1,153,034	314	27.2	Logistic regression	Maternal age, hypertension, other disorders, problems and complications	OR of maternal mortality with cesarean section compared with vaginal birth=3.3 (2.6-4.3)
Villar et al. <sup>20</sup>	120 Latin America hospitals from 8 countries *	prospective	2004 - 2005	94,258	23	24.4	Logistic regression	None	OR of maternal mortality with emergency cesarean section, intrapartum cesarean section compared with vaginal birth=3.38 (1.07-10.65); 5.28 (2.05-13.62)
Leite & Araújo <sup>26</sup>	All maternal death of the Recife, PE state, Brazil	retrospective, case-control	2001 - 2005	120,071	#75	62.46	Logistic regression	Type of health insurance, maternal age, schooling, antenatal visits	OR of maternal mortality with cesarean section compared with vaginal birth=7.08 (3.54-14.17)
Gonzales et al. <sup>17</sup>	All maternal death of the city from Peruvian Public Health Facilities	retrospective, cross-sectional	2000 - 2010	563,668	241	43	Logistic regression.	Maternal age, BMI, anaemia, preeclampsia, prenatal care, twin pregnancy, urinary tract infection	OR of maternal mortality with elective and emergency cesarean section compared with vaginal birth=4.45 (3.21-6.18); 4.82 (3.44-

\*8 countries of Latin America: Argentina, Brazil, Cuba, Ecuador, Mexico, Nicaragua,

Paraguay and Peru. #late maternal death.

**Table 2. Outline of data extracted from studies that separated elective, intrapartum or emergency cesarean section**

Author (year)	Cesarean section (%)	General maternal mortality ratio	Crude maternal mortality ratio in vaginal birth	Crude maternal mortality ratio in cesarean section	Crude Elective cesarean section OR (95% CI) / (vaginal birth OR=1)	Crude Intrapartum or Emergency cesarean section OR (95% CI) / (vaginal birth OR=1)	Adjusted Elective cesarean section OR (95% CI) / (vaginal birth OR=1)	Adjusted Intrapartum or Emergency cesarean section OR (95% CI) / (vaginal birth OR=1)	Confounders/ Bias
Villar et al. <sup>20</sup>	33.7	24.4	11	50.3	3.38 (1.07 - 10.65)	5.28 (2.05 - 13.62)	Not calculated	Not calculated	Database includes only deaths associated with hospitalization and delivery, not adjusted for clinical confounders and/or high risk pregnancies
Gonzales et al. <sup>17</sup>	27	43	18	108	6.10	5.61	4.45 (3.21 - 6.18)	4.82 (3.44 - 6.75)	No adjustments for high risk pregnancies and database included only 43 public health facilities.

OR: odds ratio; CI – confidence interval.

**Highlights:**

A systematic review through six electronic databases was conducted.

Seven articles were identified for final analysis.

There might be a greater risk of maternal death with cesarean section than with vaginal birth.

Accepted manuscript

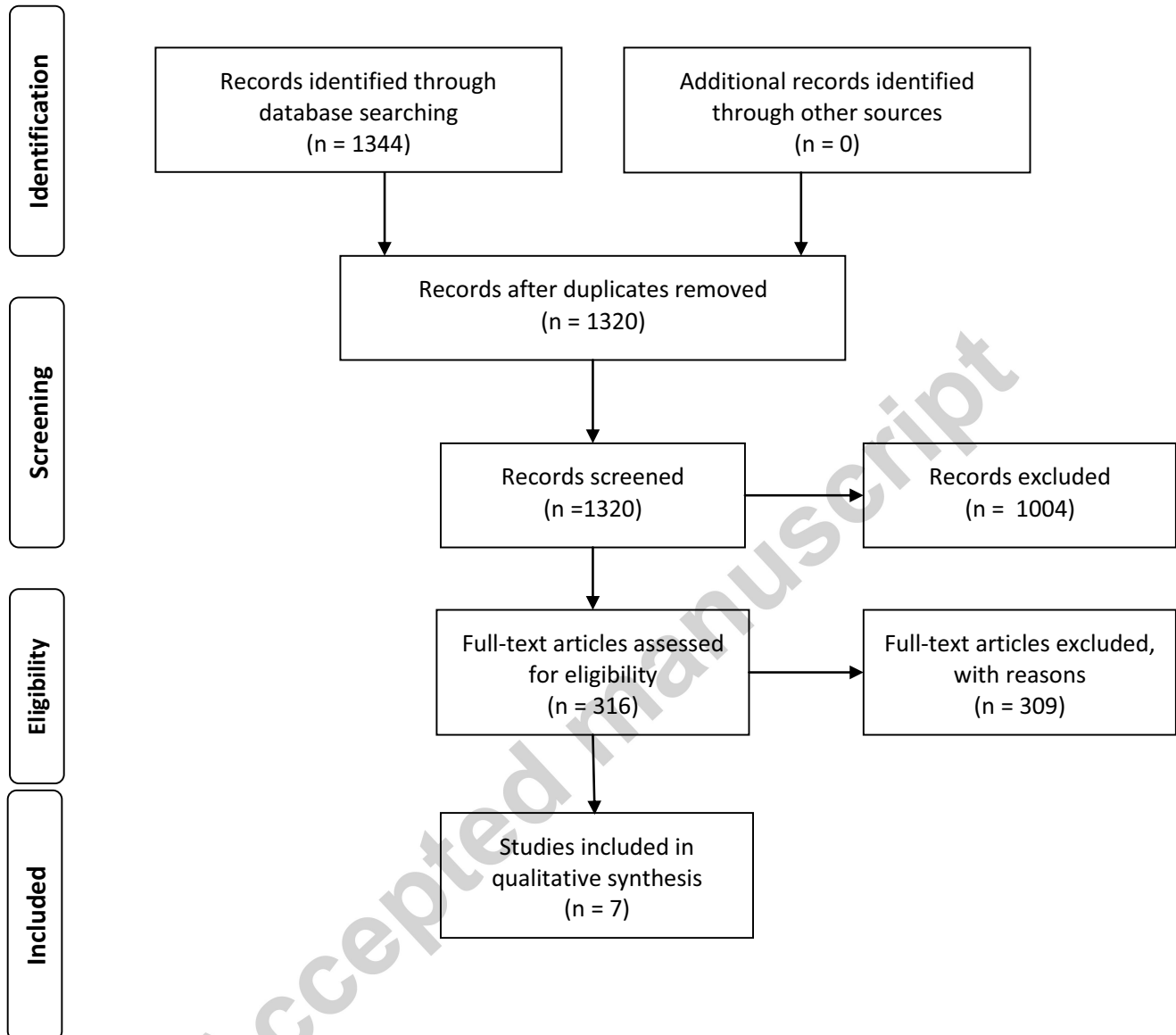


Figure 1. Flowchart of study identification and selection process.