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# Determining the effect of seminal plasma supplementation on sperm motility in males with asthenozoospermia: a systematic review protocol

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| Keywords: | Subfertility < GYNAECOLOGY, Reproductive medicine < GYNAECOLOGY, Systematic Review |
| | |

# Determining the effect of seminal plasma supplementation on sperm motility in males with asthenozoospermia: a systematic review protocol

*Nathalie Willathgamuwa[1], Manodya Nammunige[1], Hiranthika Thennakoon[1], Tanuri Ayanga[2], Manushi Dinasha[2], Nishadi Rodrigo[3], Prassana Logenthiran[4]*

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## Abstract

**Introduction:** Male infertility, defined as the inability to impregnate a fertile female, arises from various factors, among which sperm motility plays a pivotal role in determining reproductive potential. Seminal plasma, a complex fluid comprising diverse proteins, serves to nourish and support sperm, thereby facilitating their function within the female reproductive tract for successful conception. Normozoospermia denotes normal sperm motility in males, whereas asthenozoospermia indicates reduced sperm motility. This review seeks to assess the feasibility of augmenting sperm motility in men with asthenozoospermia through supplementation with seminal plasma or specific seminal plasma proteins.

**Methods and analysis:** A systematic literature review following Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) guidelines will be conducted. PubMed and Google Scholar databases will be systematically searched using predefined keywords and Boolean operators. The search strategy will encompass terms related to asthenozoospermia, normozoospermia, seminal plasma proteins, sperm motility, and sperm movement. Additionally, reference lists of relevant articles will be scrutinized for additional studies. Inclusion criteria will encompass human studies published as original research articles between 2019 and 2023. Data extraction will be performed using a standardized form, encompassing author details, country of origin, publication year, study design, participant characteristics, outcomes, and conclusions. The risk of bias within the selected studies will be evaluated using the Robvis visualization tool.

**Ethics and dissemination:** Ethical approval is not required for this systematic review. The findings will be disseminated through publication in a peer-reviewed scientific journal and presentation at relevant conferences.

**PROSPERO registration number:** CRD42024526439

## Strengths and limitations of this study

Strengths of this study will include its comprehensive search strategy following PRISMA guidelines, encompassing both PubMed and Google Scholar databases. Additionally, by including human studies published between 2019 and 2023, it will ensure the relevance and currency of findings. The standardized data extraction form will enhance consistency and rigorousness in data collection and analysis.

However, limitations may arise from the availability of studies comparing the effects of seminal plasma supplementation and different seminal plasma proteins from normozoospermic individuals on sperm motility in individuals with asthenozoospermia. Moreover, the effectiveness of seminal plasma supplementation may be influenced by various factors such as the specific proteins used, dosage, and individual differences among participants, which could introduce heterogeneity across studies.

## Introduction

Infertility is defined as the incapacity to achieve pregnancy after engaging in frequent, unprotected sexual activity for a year or longer (1). It is a complicated concern involving biological, behavioral, and environmental factors. Male infertility is characterized by abnormal sperm parameters, such as low count, abnormal morphology, and reduced motility (2). Sperm morphology refers to the specific structure and form of the spermatozoa, while count measures the total number of sperms in a sample. Sperm motility, which involves forward progression and lateral head displacements, is essential for male fertility as it directly affects the sperm's ability to move through the female reproductive system and fertilize the oocyte (3).

Asthenozoospermia, defined as reduced sperm motility, can significantly impact male fertility. It hinders the sperm's ability to fertilize the oocyte, leading to infertility (4). Normozoospermia, on the other hand, is when sperm parameters are within the normal range, as specified by semen analysis protocols of World Health Organization (WHO). These parameters, including morphology, count, and motility, are considered essential for optimal fertility (5). To evaluate male infertility, (a) progressive sperm motility which refers to the forward movement of sperm in a straight line, which is essential for successful fertilization; and (b) non-progressive sperm motility which includes any other type of movement, such as twitching or vibrating, that doesn't contribute to forward progression are assessed during a semen analysis (3).

Seminal plasma, the acellular fluid fraction of seminal fluid, carries sperms and proteins, enzymes, and bioactive compounds during ejaculation. It plays a crucial role in the functioning capacity of the spermatozoa (6). Research shows that seminal plasma elements can regulate sperm motility, controlling its direction and speed (7). Seminal plasma supplementation involves adding seminal fluid, which contains various proteins, hormones, and nutrients, to assist in reproductive processes such as artificial insemination or *in vitro* fertilization. So, by understanding the effects of seminal plasma supplementation (mixing of seminal plasma in homogenous and heterogenous manner) and proteins on sperm motility could help develop new treatments for asthenozoospermia, enhancing fertility outcomes.

## Methods and analysis

This systematic review protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO) in April 2024 under the registration number CRD42024526439 (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42024526439). The PRISMA (Preferred Reporting Items for Systematic review and Meta-Analysis) 2020 checklist (8) was used to elaborate the protocol.

## Review question

The research question was tailored to be specific and pertinent within the context of existing literature and available resources (9). The systematic literature review will address the following research question formulated according to the PICO (patient/population, intervention, comparison and outcomes) (10) criteria:

"Does seminal plasma supplementation and different seminal plasma proteins (I) compared to no seminal plasma supplementation or different seminal plasma proteins (C), affect the sperm motility (O) in individuals diagnosed with asthenozoospermia (P)?"

## Study selection

The PRISMA (Preferred Reporting Items for Systematic review and Meta-Analysis) flow chart will be used in the study screening and selection process (Figure 1). Five reviewers (NW, MN, HT, TA, MD) will conduct the study selection process according to the PRISMA flow chart.

## Inclusion Criteria

The study inclusion criteria will consist of studies only published in English language between 2019-2023. Furthermore, original studies based on human population will be included.

## Exclusion Criteria

Studies will be excluded if they do not meet the predefined inclusion criteria or if they fail to provide relevant data on seminal plasma supplementation and its effects on sperm motility in males with asthenozoospermia. Additionally, studies published before 2019 or after 2023 will not be considered. Non-human studies, review articles, editorials, conference abstracts, and case reports will also be excluded. Studies with insufficient data or unclear methodologies will be excluded to ensure the reliability and validity of the findings. Furthermore, non-English language studies will be excluded due to limitations in translation resources. Finally, studies involving participants with conditions other than asthenozoospermia or those receiving concurrent treatments that may confound the effects of seminal plasma supplementation will be excluded to maintain homogeneity and focus within the review.

## Search strategy

The systematic literature review will encompass studies examining the impact of seminal plasma supplementation and various seminal plasma proteins on sperm motility in males diagnosed with asthenozoospermia. The search strategy will be conducted using Google Scholar and PubMed databases, utilizing keywords and Boolean operators 'AND' and 'OR'. Additional sources will be explored through related articles identified in PubMed and Google Scholar. Filters will be applied to limit results to human studies, original research articles published between 2019 and 2023.

The following search strategy will be used, (((((Asthenozoospermia) AND (normozoospermia)) AND (seminal plasma proteins)) OR (sp proteins)) AND (sperm motility)) OR (sperm movement).

## Data collection

A data extraction form will be used to collect data from the selected studies. The data extraction form will include the authors, country, year, study design, study sample, age range, results obtained, and conclusion of the selected studies. Five reviewers (NW, MN, HT, TA, MD) will extract data using separate Microsoft Excel spreadsheets and the information will be combined into a single spreadsheet. NR and PL will review the final spreadsheet.

## Critical appraisal

The assessment of the selected studies will involve using the Robvis visualization tool (https://www.riskofbias.info/welcome/robvis-visualization-tool). This will be carried out to evaluate both the quality and potential bias risk associated with the chosen studies.

## Data synthesis

The data synthesis for this systematic literature review will involve aggregating and analyzing findings from studies investigating the effects of seminal plasma supplementation and various seminal plasma proteins on sperm motility in males with asthenozoospermia. Through a comprehensive review of the selected articles, data on key outcomes such as changes in sperm motility parameters, including velocity, progressive motility, and total motile sperm count, will be extracted, and synthesized. The synthesis will involve comparing and contrasting results across studies, identifying trends, and assessing the overall impact of seminal plasma supplementation and specific proteins on sperm motility in both asthenozoospermic and normozoospermic individuals. Additionally, any variations in outcomes related to different types of seminal plasma proteins or supplementation will be examined to provide insights into potential factors influencing sperm motility improvement. The evidence synthesis will be ensured and the risk of bias due to selective publication will be controlled by following the steps previously described for critical appraisal of the studies and quality of evidence evaluation.

## Discussion

The findings of this systematic review will contribute to understanding the potential of seminal plasma supplementation in improving sperm motility among males with asthenozoospermia. If the included studies demonstrate a positive effect, it could pave the way for novel therapeutic interventions in male infertility. However, discrepancies in study methodologies, including variations in seminal plasma composition, dosage, and administration methods, may limit the generalizability of the findings. Additionally, the lack of standardized protocols across studies may hinder the ability to draw definitive conclusions. Further research addressing these limitations is

warranted to establish the efficacy and safety of seminal plasma supplementation in clinical practice.

## Ethics and Dissemination

This study will be based on previous published literature and no human or animal population will be involved. Therefore, ethical approval is not required. The dissemination of findings through publication in a peer-reviewed journal and presentation at conferences will facilitate knowledge translation and guide future research in this field.

## Authors' contributions

NW, MN, HT, TA, MD, NR and PL conceptualized and designed the protocol, drafted the initial manuscript. NR and PL reviewed the manuscript. NW, MN, HT, TA, MD and NR defined the concepts and search items, data extraction process and methodological appraisal of the studies. NR and PL planned the data extraction and statistical analysis along with NW, MN, HT, TA, MD. NR and PL provided critical insights. All authors have approved and contributed to the final written manuscript.

## References


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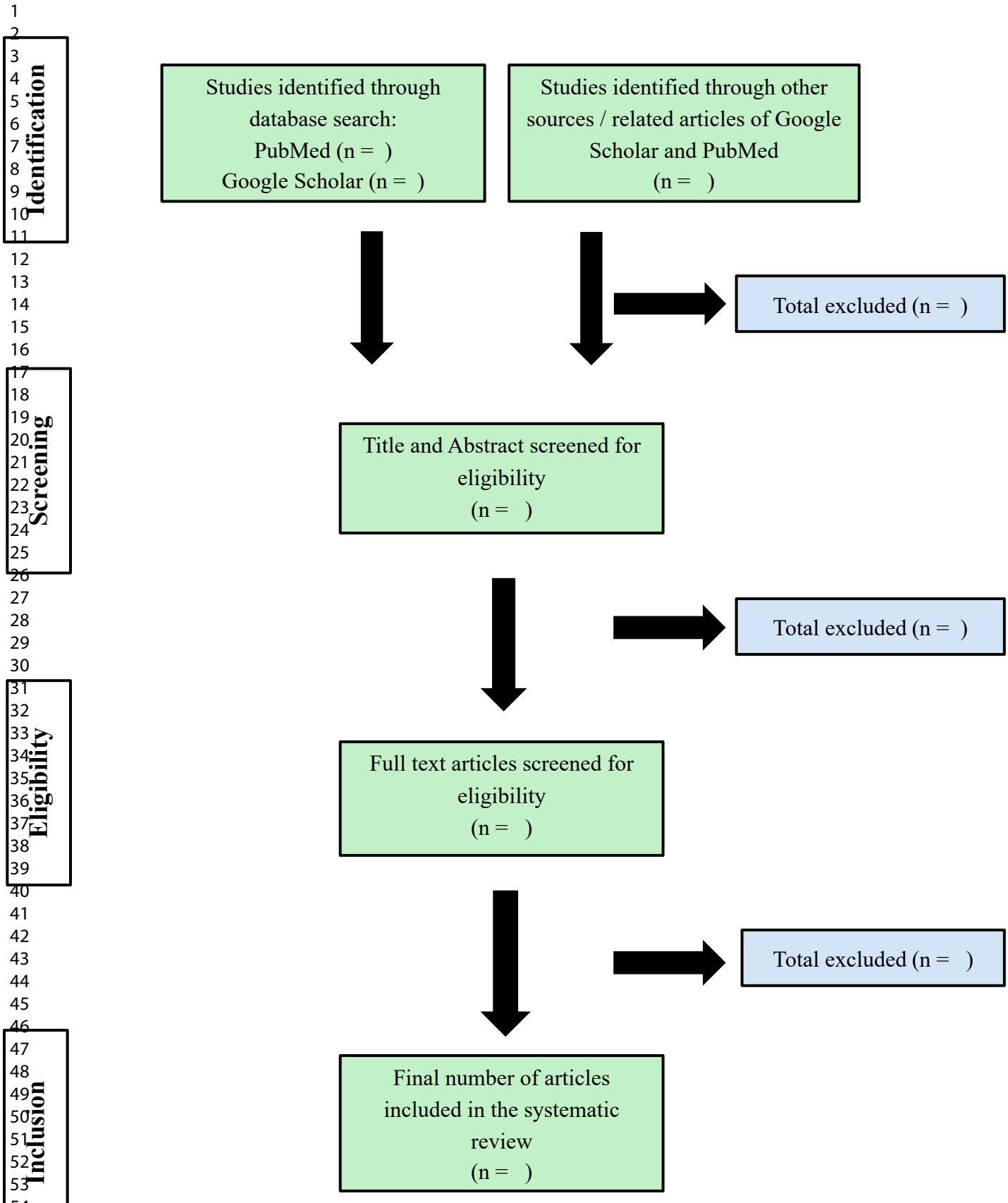
10. Higgins JP, Green S (Eds. ). Cochrane Handbook for Systematic Reviews of Interventions. Vol S38.; 2008.


## Legend

**Figure 1: PRISMA flow chart**


Identification
Studies identified through database search:
PubMed (n = )
Google Scholar (n = )
Studies identified through other sources / related articles of Google Scholar and PubMed
(n = )
Total excluded (n = )
Screening
Title and Abstract screened for eligibility
(n = )
Total excluded (n = )
Eligibility
Full text articles screened for eligibility
(n = )
Total excluded (n = )
Inclusion
Final number of articles included in the systematic review
(n = )

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| Date Submitted by the Author: | 23-Oct-2024 |
| Complete List of Authors: | Willathgamuwa, Nathalie; Coventry University<br>Nammunige, Manodya; Coventry University<br>Hiranthika Piyumali, Thennakoon Mudiyanselage; Coventry University<br>Nissanka, Tanuri; Metropolia University of Applied Sciences<br>Dinasha, Withanage Dona; Metropolia University of Applied Sciences<br>Rodrigo, Nishadi; Uva Wellassa University, Department of Anatomy<br>Logenthiran, Prassana; University of Sri Jayewardenepura, Department of Physiology |
| Primary Subject Heading: | Reproductive medicine |
| Secondary Subject Heading: | Reproductive medicine, Sexual health |
| Keywords: | Subfertility < GYNAECOLOGY, Reproductive medicine < GYNAECOLOGY, Systematic Review |
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Manuscript word count: 2107

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Financial disclosure: None

Conflict of interest: None

Number of figures: 1

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## Abstract

**Introduction:** Male infertility, defined as the inability to impregnate a fertile female, arises from various factors, among which sperm motility plays a pivotal role in determining reproductive potential. Seminal plasma, a complex fluid comprising diverse proteins, serves to nourish and support sperm, thereby facilitating their function within the female reproductive tract for successful conception. Normozoospermia denotes normal sperm motility in males, whereas asthenozoospermia indicates reduced sperm motility. This review seeks to assess the feasibility of augmenting sperm motility in men with asthenozoospermia through supplementation with seminal plasma or specific seminal plasma proteins.

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**Ethics and dissemination:** Ethical approval is not required for this systematic review. The findings will be disseminated through publication in a peer-reviewed scientific journal and presentation at relevant conferences.

**PROSPERO registration number:** CRD42024526439

## Strengths and limitations of this study

- Comprehensive search strategy will follow PRISMA guidelines, ensuring methodological rigor.
- Both PubMed and Google Scholar databases will be searched to ensure a broad inclusion of relevant studies.
- Inclusion of human studies published between 2019 and 2023 will ensure up-to-date findings.
- A standardized data extraction form will be used to promote consistency and reliability in data collection.
- Potential limitations include the variability of seminal plasma proteins, dosage, and individual participant differences, which may introduce heterogeneity in study comparisons.

## Introduction

Infertility is defined as the incapacity to achieve pregnancy after engaging in frequent, unprotected sexual activity for a year or longer [1]. It is a complicated concern involving biological, behavioral, and environmental factors. Male infertility is characterized by abnormal sperm parameters, such as low count, abnormal morphology, and reduced motility [2]. Sperm morphology refers to the specific structure and form of the spermatozoa, while count measures the total number of sperms in a sample. Sperm motility, which involves forward progression and lateral head displacements, is essential for male fertility as it directly affects the sperm's ability to move through the female reproductive system and fertilize the oocyte [3].

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## Methods and analysis

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## Review question

The research question was tailored to be specific and pertinent within the context of existing literature and available resources [10]. The systematic literature review will address the following research question formulated according to the PICO (patient/population, intervention, comparison and outcomes) criteria [11]:

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Studies will be excluded if they do not meet the predefined inclusion criteria or if they fail to provide relevant data on seminal plasma supplementation and its effects on sperm motility in males with asthenozoospermia. Additionally, studies published before 2019 or after 2023 will not be considered. Non-human studies, review articles, editorials, conference abstracts, and case reports will also be excluded. Studies with insufficient data or unclear methodologies will be excluded to ensure the reliability and validity of the findings. Furthermore, non-English language studies will be excluded due to limitations in translation resources. Finally, studies involving participants with conditions other than asthenozoospermia or those receiving concurrent treatments that may confound the effects of seminal plasma supplementation will be excluded to maintain homogeneity and focus within the review.

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warranted to establish the efficacy and safety of seminal plasma supplementation in clinical practice.

## Ethics and Dissemination

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## Authors' contributions

NW, MN, HT, TA, MD, NR and PL conceptualized and designed the protocol, drafted the initial manuscript. NR and PL reviewed the manuscript. NW, MN, HT, TA, MD and NR defined the concepts and search items, data extraction process and methodological appraisal of the studies. NR and PL planned the data extraction and statistical analysis along with NW, MN, HT, TA, MD. NR and PL provided critical insights. PL acted as guarantor. All authors have approved and contributed to the final written manuscript.

## Patient and Public Involvement

This study is based entirely on previously published literature, with no involvement of human or animal participants. As such, ethical approval is not required. Patients and the public were not involved in the design, conduct, reporting, or dissemination plans of this research. However, the dissemination of findings through publication in a peer-reviewed journal and presentations at relevant conferences will promote knowledge translation and help guide future research in this field, potentially informing studies that involve patient or public engagement in the future.

## References


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2. Boitrelle F, Shah R, Saleh R, Henkel R, Kandil H, Chung E, et al. The Sixth Edition of the WHO Manual for Human Semen Analysis: A Critical Review and SWOT Analysis. Life. 2021 Dec;11(12):1368.
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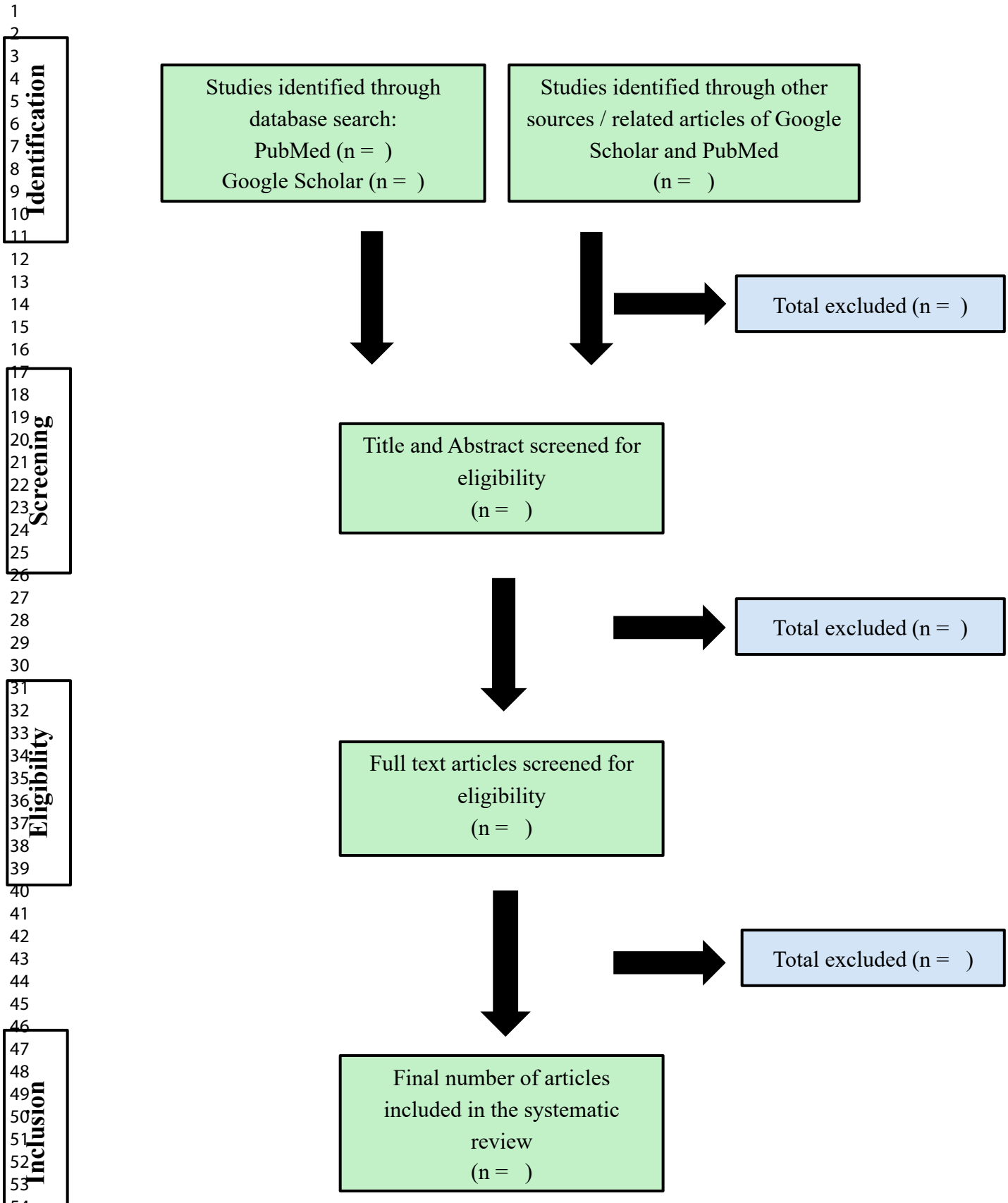
**Legend**

Figure 1: PRISMA flow chart

Appendix 1: PRISMA-P 2015 checklist

Appendix 2: Search strategy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Google Scholar (n = )
Studies identified through other sources / related articles of Google Scholar and PubMed
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Total excluded (n = )
Screening
Title and Abstract screened for eligibility
(n = )
Total excluded (n = )
Eligibility
Full text articles screened for eligibility
(n = )
Total excluded (n = )
Inclusion
Final number of articles included in the systematic review
(n = )

## Search strategy

| Database | Search strategy | Filters |
|---|---|---|
| Google Scholar | (((((Asthenozoospermia) AND (normozoospermia)) AND (seminal plasma proteins)) OR (sp proteins)) AND (sperm motility)) OR (sperm movement) | 2019 – 2023<br>Human studies<br>Original research |
| MEDLINE (PubMed) | | |