

# The impact of age and frailty on surgery-induced inflammatory response: a systematic review protocol

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## Introduction

- Surgery is proinflammatory
  - Complex inflammatory response<sup>1</sup>
  - Tightly regulated balance between pro- and anti-inflammatory response
  - Dysregulation of the inflammatory response can have significant negative consequences
- Ageing and immunosenescence<sup>2</sup>
  - Elderly patients undergo surgery at a high rate
  - Dysregulated balance between pro- and anti-inflammatory response occurs with aging<sup>1,2</sup>
  - Post-operative complications are more common and more serious in elderly patients, especially if *frail*<sup>1</sup>
- Frailty
  - Aggregate expression of risk of adverse health outcomes based on age- and disease-related deficits
  - Prevalence increases with increasing age
  - 2-3 fold increase in risk of postoperative adverse events, independent of age
- The mechanism of age/frailty-related dysregulation of inflammatory response is poorly understood
- Deeper exploration of mechanisms underlying frailty- and age-attributable surgical risks is required

## Research Question

1. Does age or frailty status impact the surgery-induced immune response as measured by levels of biomarkers (primary outcome)?
2. Do age or frailty-related changes in biomarkers predict adverse clinical outcomes (secondary outcomes)?

## Methods

- Systematic literature review guided by an *a priori* registered study protocol
- Search: Electronic search strategy developed with information specialist; Cochrane, PubMed/Medline, Embase, CINAHL databases searched; manual search of reference lists of included articles
- Inclusion criteria:
  - Study Design: observational or experimental studies
  - Population: adults (>18 yrs.) undergoing surgeries under general or neuraxial anesthesia
  - Exposure:  
Age: patients grouped into relatively older age groups  
Frailty: frail patients based on multi-dimensional frailty instruments
  - Comparator:  
Age: patients grouped into relatively younger age group  
Frailty: non-frail patients based on multi-dimensional frailty instruments
  - Outcomes:  
Primary: level/activity of inflammatory biomarkers in any time frame  
Secondary: medical/surgical complications, all-cause mortality in any time frame
- Exclusion criteria: surgeries under local anesthesia, case report studies, pediatric populations, animal studies
- Data Screening/Extraction: Two independent reviewers (AP, WK)
- Planned Analysis: Pooled outcomes to assess individual and absolute differences. Depending on data available, sub-group analyses may be performed on confounding factors
- Risk of Bias: assessed using Cochrane Risk of Bias Tool for RCTs and ACROBAT-NRSI for non-randomized trials
- Reporting: All results will be reported in accordance with PRISMA guidelines

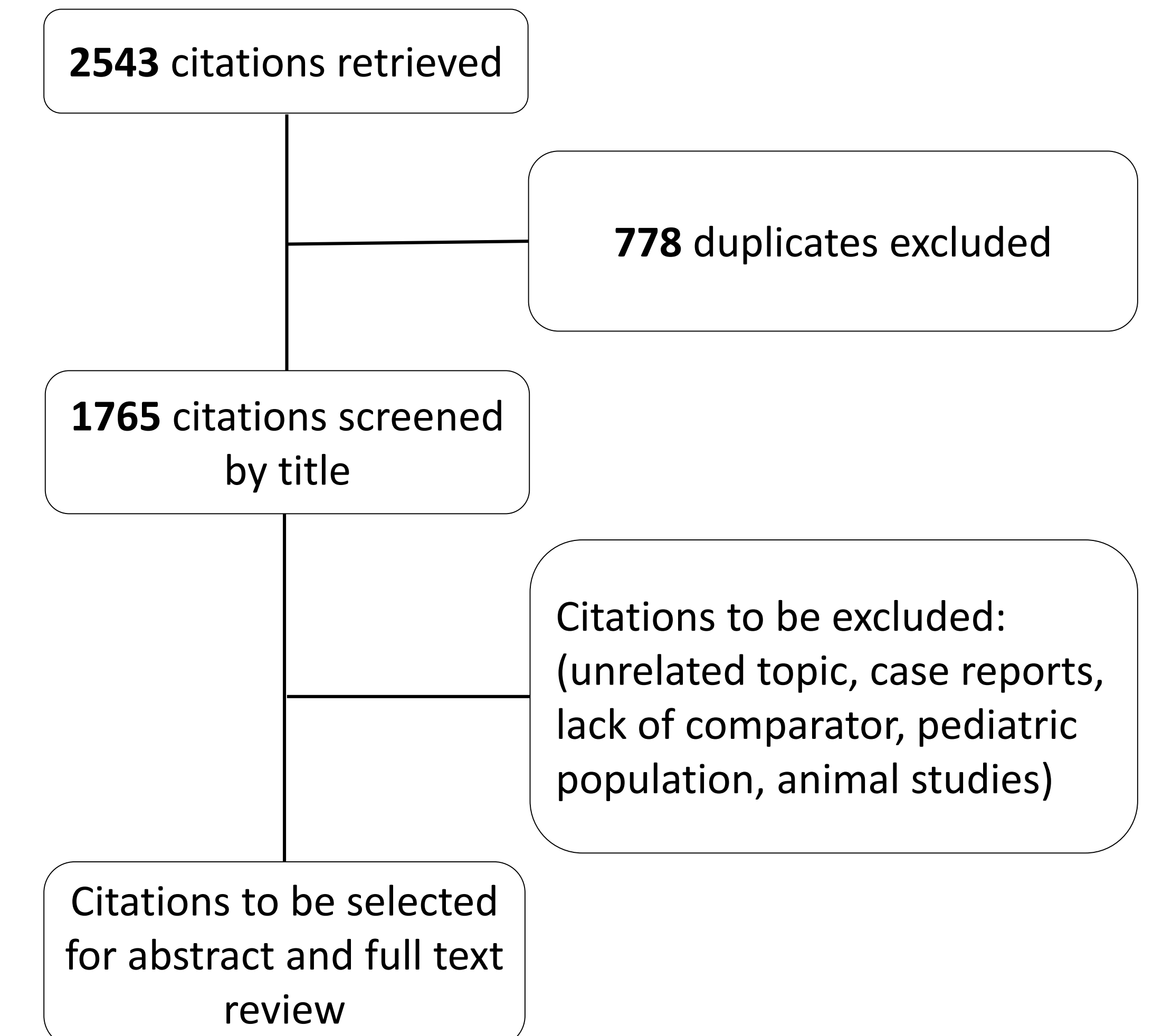


Figure 1. PRISMA flow diagram summarizing on-going study selection

## Discussion

- Study screening underway
- Results will assist in understanding mechanism of frailty- and age-related changes in inflammatory biomarkers
- May have implications to guide future research, especially in inflammatory-modulating therapies, to improve perioperative outcomes in the elderly/frail

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## References

1. Best Pract Res Clin Anaesthesiol.2011;25(3):413-25.
2. Aging Clin Exp Res. 2015;27(6):927-33.
3. J Gerontol. 2001;56(3):146-57.