## INPLASY PROTOCOL

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# Aggression in group housed male mice – a systematic review

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**Review question / Objective:** By systematically reviewing articles investigating male mouse aggression we wanted to map how the literature in the field support, or not, the available recommendations on how to prevent aggression in group housed male mice, and to detect knowledge gaps that ought to be filled. We also wanted to address and describe how aggression have been measured in the literature, since this may influence the possibility to translate outcomes to normal husbandry conditions and contribute to useful recommendations.

**Condition being studied:** Aggression between male cage mates is one of the main problems in laboratory mouse husbandry, affecting both animal welfare and scientific quality.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 December 2022 and was last updated on 19 December 2022 (registration number INPLASY2022120078).

#### INTRODUCTION

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#### **METHODS**

Participant or population: Male mice housed in a laboratory environment.

Intervention: Not applicable.

**Comparator: Not applicable.** 

Study designs to be included: Experimental studies.

Eligibility criteria: Abstracts will be screened to identify empirical studies on group or single housed male mice, investigating aggression, social dominance, wounds, stereotypies, stress, physiological parameters or details of the husbandry, such as group size, cage cleaning procedures or enrichment. All records that match these criteria will be included and screened in fulltext. To be included the article have to: i) be available as full text and written in English: ii) investigate the effects of group housing of male mice (or male mice and castrated male/female mice); iii) investigate aggression or social dominance. Studies that do not have a specific aim to measure aggression but still drew conclusions about aggression will also be included. Studies of wild mice or other rodents than mice are excluded.

Information sources: We conducted a systematic literature search on the 12th of December 2018 using the online databases Medline, Embase and Web of Science via the University Library at Karolinska Institutet, Sweden. Additional articles from reference lists of three relevant and recent literature reviews were also included.

Main outcome(s): Studies designed to understand the causes of male mice aggression use different methodological approaches and are heterogeneous, using different strains, environmental enrichments, housing conditions, group formations and durations. This systematic review elucidates that the problem with aggression is complex and that one solution will not be appropriate for all animal facilities and all research projects. Be aware that the method used to study aggression might influence whether or not results are relevant for home cage aggression. It is therefore important to evaluate the method used to study aggression before drawing conclusions on whether or not the reported results can be implemented in daily practice.

Quality assessment / Risk of bias analysis: The methodology, treatment, outcome of experiments as well as additional relevant information were extracted from the included articles. Two authors extracted information independently. The data was then verified by an author who had not performed the data extraction.

Strategy of data synthesis: The original conclusions from the reviewed articles were extracted and summarized and has in no way been re-analysed.

Subgroup analysis: Not applicable.

Sensitivity analysis: We have not performed any statistical analyses and therefore we have not performed a sensitivity analysis.

Language restriction: English only.

**Country(ies) involved:** The study was performed in Sweden and all authors are Swedish.

Keywords: aggression; animal welfare; environmental enrichment; group formation; housing conditions; in-juries; resident-intruder; social defeat; social dominance; wound scoring.

### **Contributions of each author:**

Author 1 - Elin Weber - The author contributed to the development of the inclusion and exclusion criteria and drafted the manuscript.

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