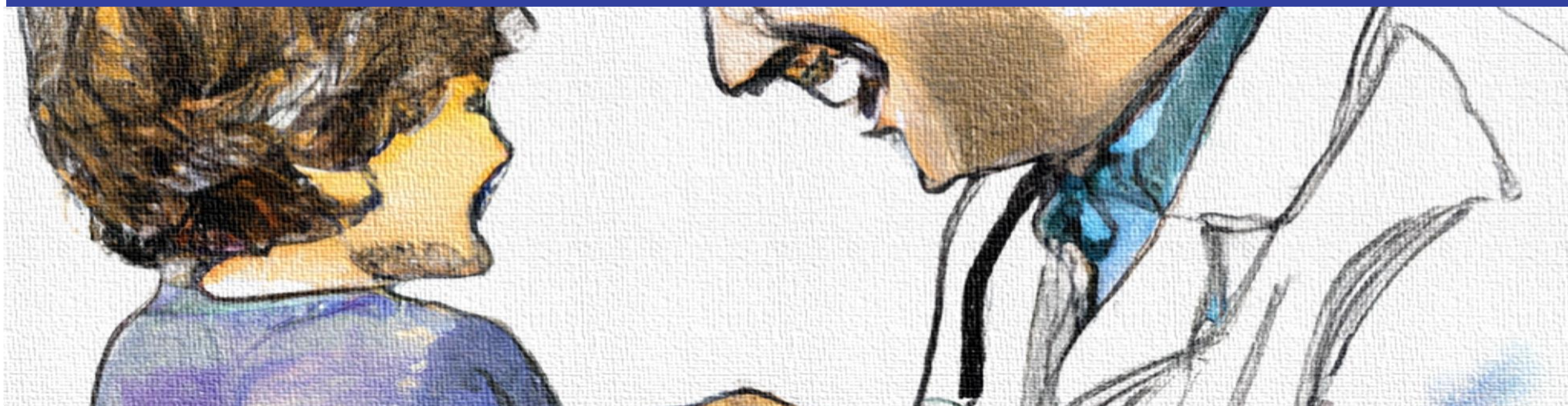


# Tailored pain management strategies are needed during childhood incorporating critical developmental stages such as puberty

Rachele Simonte<sup>1</sup>, Ruth Zaslansky<sup>2</sup>, Francesca Oppitz<sup>3</sup>, Alinde Hindriks<sup>3</sup>, Wolfgang Buhre<sup>3</sup>, Edoardo De Robertis<sup>1</sup>, Lisette Vernooij<sup>3</sup>, Winfried Meissner<sup>2</sup>, Ulrike Stamer<sup>4</sup>, Mienke Rijdsdijk<sup>3</sup>

<sup>1</sup> Dept of Medicine and Surgery, University of Perugia, Italy | <sup>2</sup> Dept Anesthesiology & Intensive Care, Jena Uni Hospital, Friedrich Schiller University, Germany | <sup>3</sup> Pain Clinic, Dep of Anesthesiology, University Medical Centre Utrecht, Netherlands | <sup>4</sup> Dept Anesthesiology & Pain Medicine, Bern Uni Hospital Switzerland



## BACKGROUND AND AIMS

Many children experience moderate to severe pain after routine surgical procedures. Factors contributing to postsurgical pain in children are underestimation of pain due to difficulties in pain assessment in different age groups, and inadequate training of healthcare providers. However, patients factors also play a role, as pain perception is influenced by various biological and psychological factors, with age being a significant modulator [1,2]. Adequate treatment of postsurgical pain will remain a challenge if we do not understand these relations.

This study investigates the association between age and postoperative pain intensity, aims to identify ages with the highest pain prevalence, and analyzes differences between the sexes.

## METHODS

Data were obtained from the PAIN OUT INFANT registry, including patients aged 4-18 years, undergoing appendectomy, tonsillectomy, spinal surgery, orthopedic surgery or hernia repair.

The primary endpoint was the association between age (years) and worst pain (NRS) on the first postoperative day stratified for sex. For missing data, multiple imputation was performed, and results were pooled using Rubin's rules. Linear regression was performed to assess the association between age and pain. An interaction term was added between age and sex to investigate potential differences in pain between sexes. Models were adjusted for a priori selected confounders including surgery type, duration of surgery, total morphine oral equivalent (from start of surgery up to 24 hours after surgery mg/kg) and use of regional anesthesia techniques.

The association between total opioid consumption and age was analyzed by calculating the Oral Morphine Equivalent per kilogram for each patient. A Mann-Whitney U test was conducted comparing opioid administration above and below the age of twelve and for girls and boys

## RESULTS

Of the 2004 included patients, mean age was 10.6±3.8 years and 51% were female.

LOESS lines indicate an age-related increase in worst pain scores, peaking around twelve years of age, particularly in girls (Figure 1). This was confirmed in our linear regression model showing that girls exhibited higher levels of pain compared to boys, with pain intensity increasing with age (interaction coefficient; 0,09 95% CI: 0,01-0,16 p=0.031) (Table 1). Other covariates significantly influencing pain scores were surgery type (lower pain scores in hernia surgery and higher in appendectomy compared to orthopedic surgery, Figure 2), total morphine oral equivalent and regional anesthesia use.

Patients under 12 years received lower perioperative opioid doses compared to older patients across all procedures (0.8±1.2 mg/kg vs 1.1±1.6 mg/kg), girls received higher doses of opioids compared to boys (1.01±1.46 mg/kg vs 0.82±1.26 mg/kg, p<0.001).

## CONCLUSION

In this large cohort of pediatric patients undergoing 5 different surgical procedures, we found that older girls experienced increased levels of pain compared to boys, notably peaking around the age of 12. Furthermore, there is a progressive increase in administration of opioids associated with age as well as among girls. We will investigate this further.

Our findings align with a recent meta-analysis focused on experimental pain, which demonstrated significantly higher pain intensity in girls compared to boys, particularly after the age of 12 [3]. This underscores the imperative for tailored pain management strategies during childhood incorporating critical developmental stages, such as puberty, in personalized pain management plans.

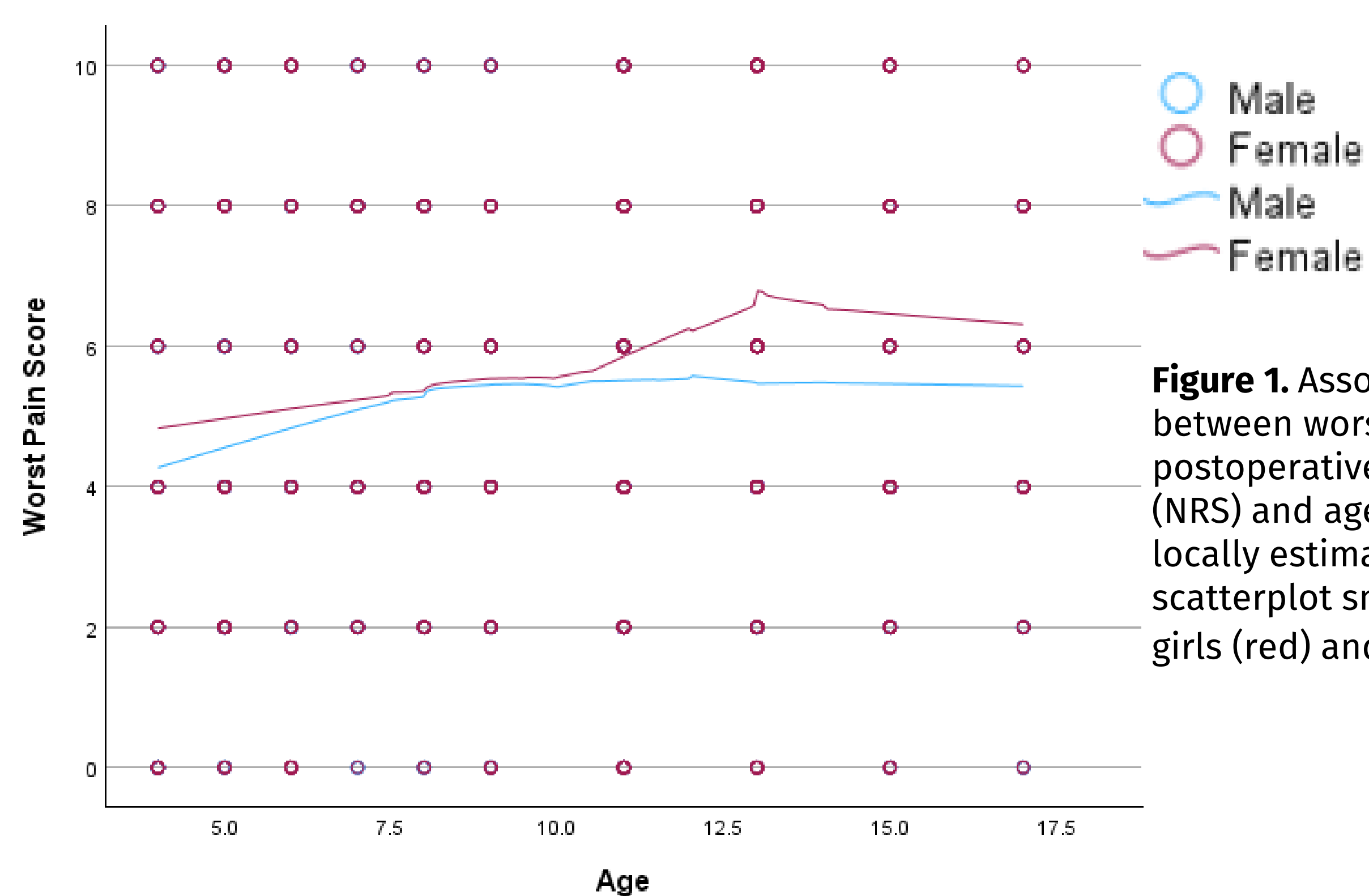


Figure 1. Association between worst postoperative pain score (NRS) and age (years) with locally estimated scatterplot smoothing for girls (red) and boys (blue).

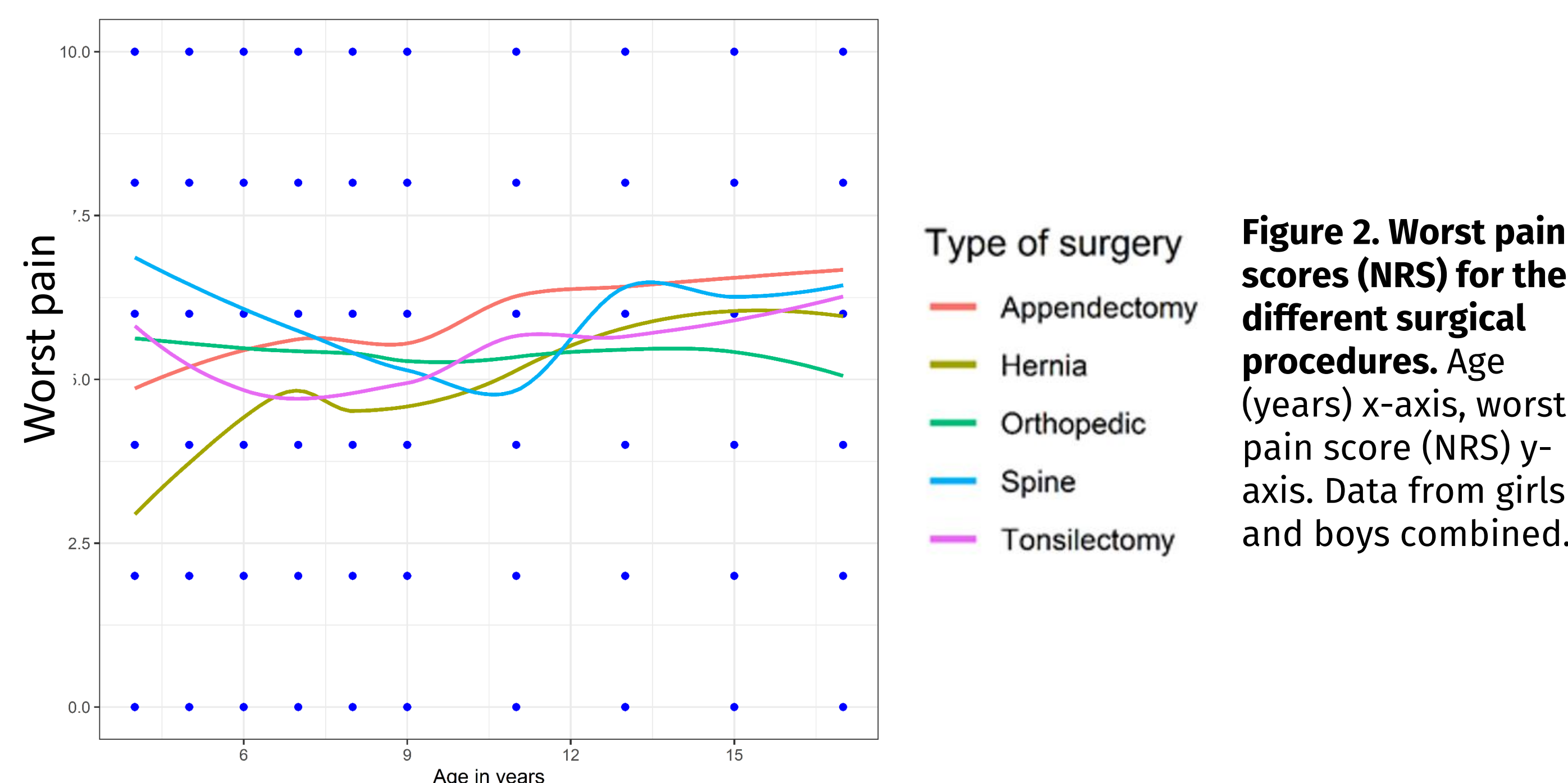


Figure 2. Worst pain scores (NRS) for the different surgical procedures. Age (years) x-axis, worst pain score (NRS) y-axis. Data from girls and boys combined.

Variable	Estimate (β)	2.5%	97.5%	p-value
(intercept)	5.18	4.40	5.96	<0.001
Age	0.01	-0.05	0.06	0.773
Sex (ref female)	-0.53	-1.41	0.34	0.229
Surgery type (ref orthopedic surgery)	Ref	ref	ref	Ref
Hernia repair	-1.12	-1.70	-0.54	<0.001
Tonsillectomy	-0.06	-0.65	0.52	0.832
Appendectomy	0.57	0.14	1.00	0.009
Surgery time	0.00	0.00	0.00	0.895
Total morphine oral equivalent (mg/kg)	0.15	0.00	0.31	0.045
Received regional anesthesia	-0.56	-0.93	-0.18	0.003
Age:sex interaction	0.09	0.01	0.16	0.031

Table 1. Linear regression model for the association between age (years) and postsurgical pain (NRS). We did not include spine surgery in our final model as most children received this procedure at older age (mean age 12,01 ± 3,30)

## REFERENCES

[1] Chow et al. Health Psychol. 2023 Oct;42(10):723-734, [2] Sim et al. Paediatr Anaesth 2024 Aug;34(8):701-719, [3] El Tumi et al. Eur J Pain. 2017 Jul;21(6):955-964.