

Higher rates of complications and health-care resource use in achondroplasia compared to the general population: a matched cohort study using the CPRD-HES database

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Background

- Achondroplasia (ACH) is a rare, genetic skeletal dysplasia, resulting in disproportionate short stature and multiple complications.
- We estimated disease burden and health-care resource use (HCRU) in ACH patients compared to general population controls.

Methods

- Matched retrospective cohort study using Clinical Practice Research Datalink (CPRD-GOLD,) linked to Hospital Episode Statistics (HES) in England.
- Study index date was first ACH record within study period of 01/01/1987 to 31/12/2018.
- Control patients defined as those without evidence of skeletal/growth disorders.
- ACH cases index date matched (1:4) to controls by age, sex, general practitioner (practice-level) and linkage ability to HES.
- Event rates per 100 person-year calculated for a pre-defined set of complications, medical imaging (x-rays, DEXA, MRI scans etc), inpatient surgeries and HRCU overall and by age-group.
- Rate ratios (RR) and 95% confidence intervals (95%CI), accounting for matching, used to compare between cohorts.

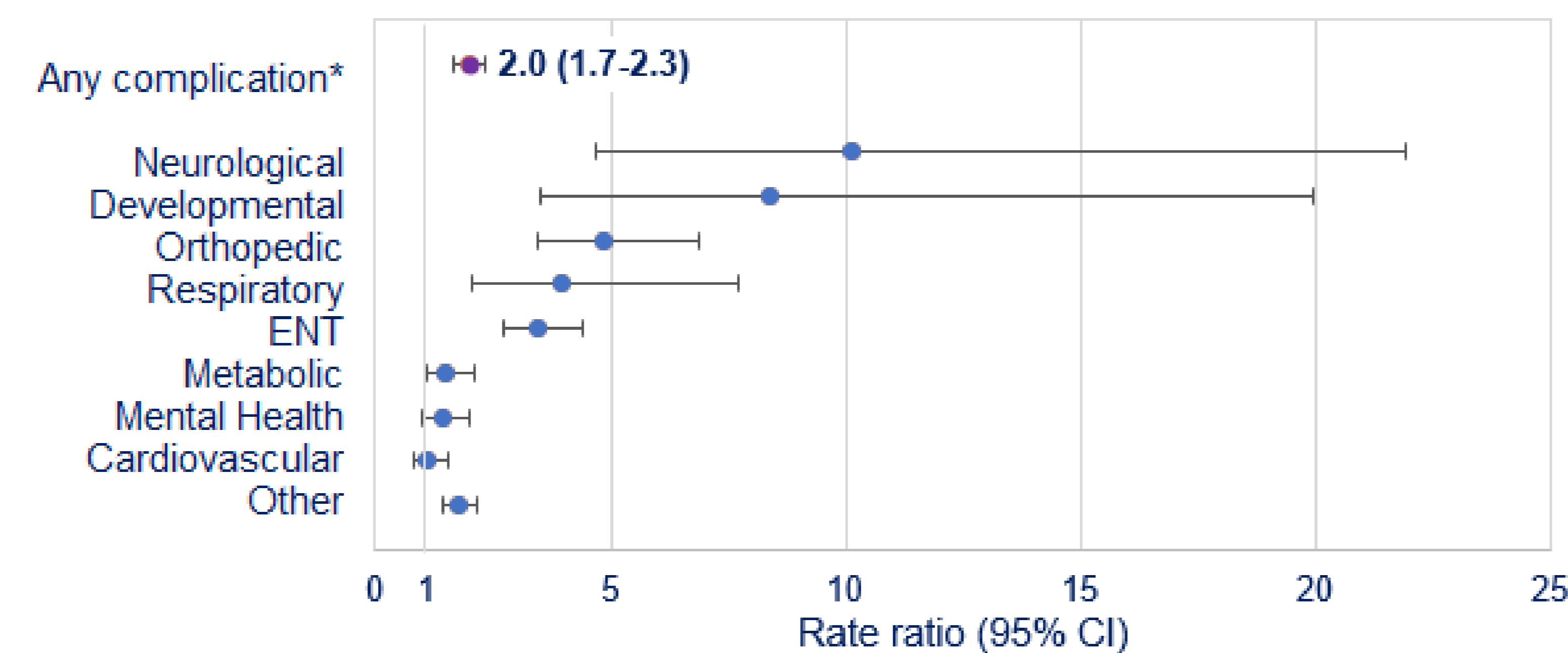
Results

- We identified 275 ACH cases and 1,064 matched controls; 51% females, median age 28 years (y) (IQR 7-40y). Median follow-up time in primary care was 8.9y (ACH) and 11.4y (controls); HES inpatient was 21.7y, 15.7y in outpatient and 6.7y in imaging datasets for both cases and controls.

Results

- Considering all pre-defined complications, complications were twice as likely to be reported among ACH cases vs. controls, **RR=2.0, 95%CI 1.7-2.3** (Fig. 1).

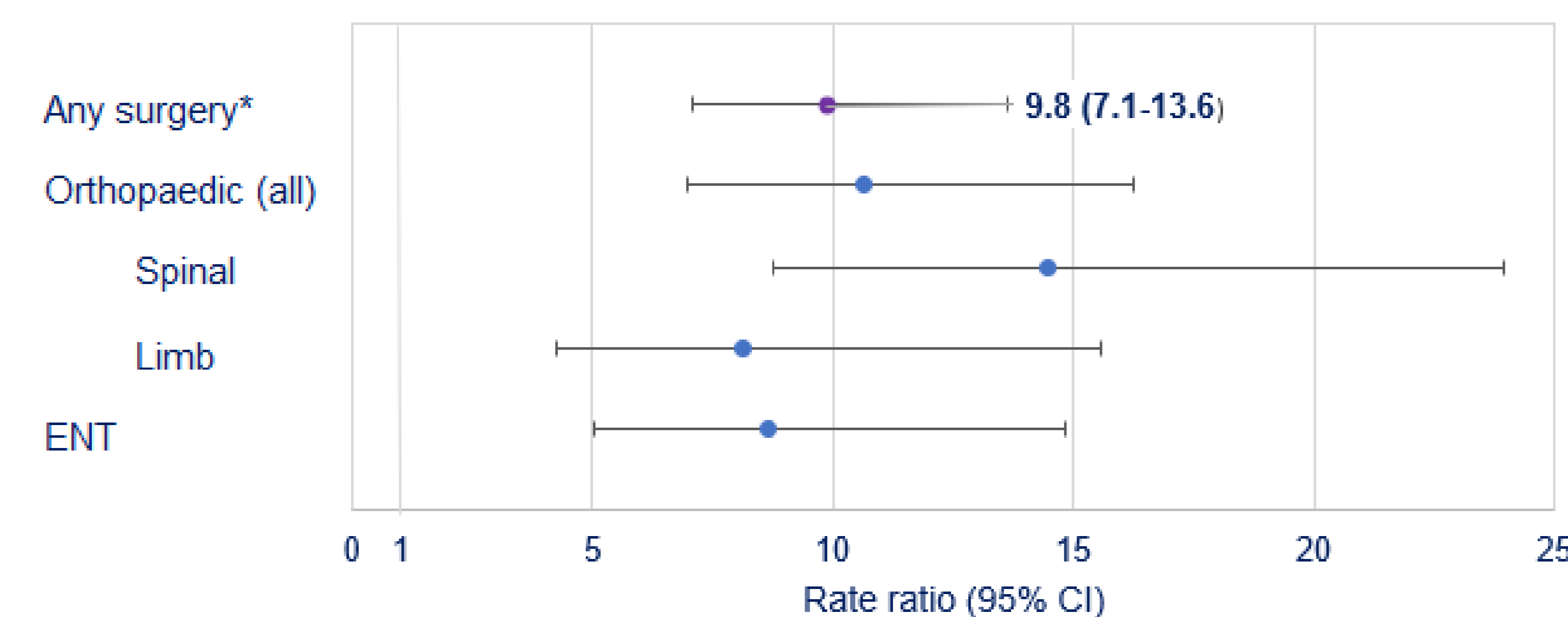
Fig. 1: Rate ratio (95%) for complications in ACH cases vs. matched controls



*Any complication as defined as any of those in body systems stated. Other includes gastrointestinal, headache, pain and gynaecological.

- For surgeries often associated with these complications, a 10-fold higher surgical burden was seen in ACH cases vs. controls (**RR=9.8, 7.1-13.6**) (Fig.2). Surgeries were mainly orthopaedic procedures (e.g. spinal decompression [RR=13.1, 7.9-21.9] or bone fixation [RR=16.0, 7.2-35.8]) and ear/nose/throat (ENT) procedures (e.g. grommet insertion [RR=13.1, 5.5-31.2] or tonsillectomy/adenoidectomy [RR=4.0, 2.2-7.1]).

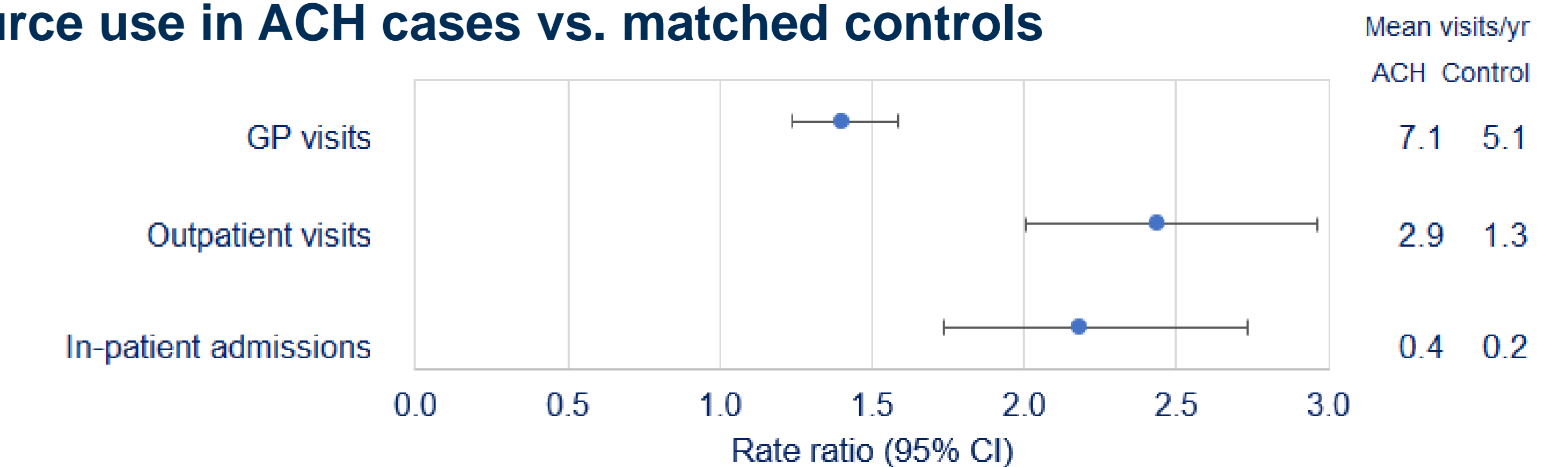
Fig. 2: Rate ratio (95%) for surgical procedures in ACH cases vs. matched controls



*Any surgery includes additional categories of Cardiovascular (stents), Neurological (shunt/ventriculostomy) and Respiratory (ventilation, tracheostomy) which are not individually reported on the figure due to CPRD rules around reporting of small cell sizes (either cases or controls had <5 instances of the specific surgical type).

- ACH cases reported more than double the rate of medical imaging vs. controls (**RR=2.5, 2.0-3.1**). The majority were skeletal images, of which spinal imaging, was substantially more common among cases (RR=7.5, 4.9-11.4).
- Furthermore, ACH patients reported significantly more primary care (GP visits) and secondary care use (hospital outpatient and in-patient admissions) than controls (Fig. 3).

Fig. 3: Rate ratio (95%) and mean number of annual visits for health care resource use in ACH cases vs. matched controls



- Mean length of inpatient hospital stay was 4.1 days (SD 13.2) in ACH cases and 2.3 days (SD 6.5) among controls.
- Differences in rates of outcomes were seen by age-groups:
 - Complications: In ACH cases, rates of developmental, ENT, neurological and respiratory events were higher among children (<18y). CV, mental health, metabolic and orthopaedic events were higher among adults (≥18y).
 - Surgeries: In ACH cases, ENT surgeries were higher in children and spinal decompression surgeries in adults.
 - Health care use: Among cases and controls, GP visits followed a U-shape distribution, where highest rates were seen among the youngest (≤10y) and oldest (≥60y). In contrast to controls, higher rates of hospital outpatient and in-patient visits were reported in ACH children (<18y) compared to adults.

Conclusions

- In a real-world clinical setting, ACH patients experience significantly higher rates of complications, surgeries, medical imaging and healthcare resource use compared to an appropriate matched general population cohort, consistently throughout life.
- These findings may have impact for proactive clinical management and patient education in this patient population.