An Estimate of the Global Birth Prevalence of Achondroplasia

Alden Smith Pharm D [1], Alexandra Hill MPH [2], Sarah Anderson MSc [2], Dorthe Viuff PhD [3], Chelsea Catsburg PhD [2], Jonathan A Leff MD [1]
[1]Ascendis Pharma Inc, Palo Alto, CA; [2]BluePrint Orphan, New York, NY, [3] Ascendis Pharma A/S, Copenhagen, Denmark

BACKGROUND

- Achondroplasia (ACH) is the most common skeletal dysplasia[1]
- Little is known about its true birth prevalence, globally, as few recent studies have been published; studies vary by population, geography, and methodology
- With the advent of novel therapies, understanding the true prevalence is critical for clinical trial considerations

OBJECTIVE

- To estimate the global birth prevalence of ACH through meta-analysis of English-language literature available in PubMed

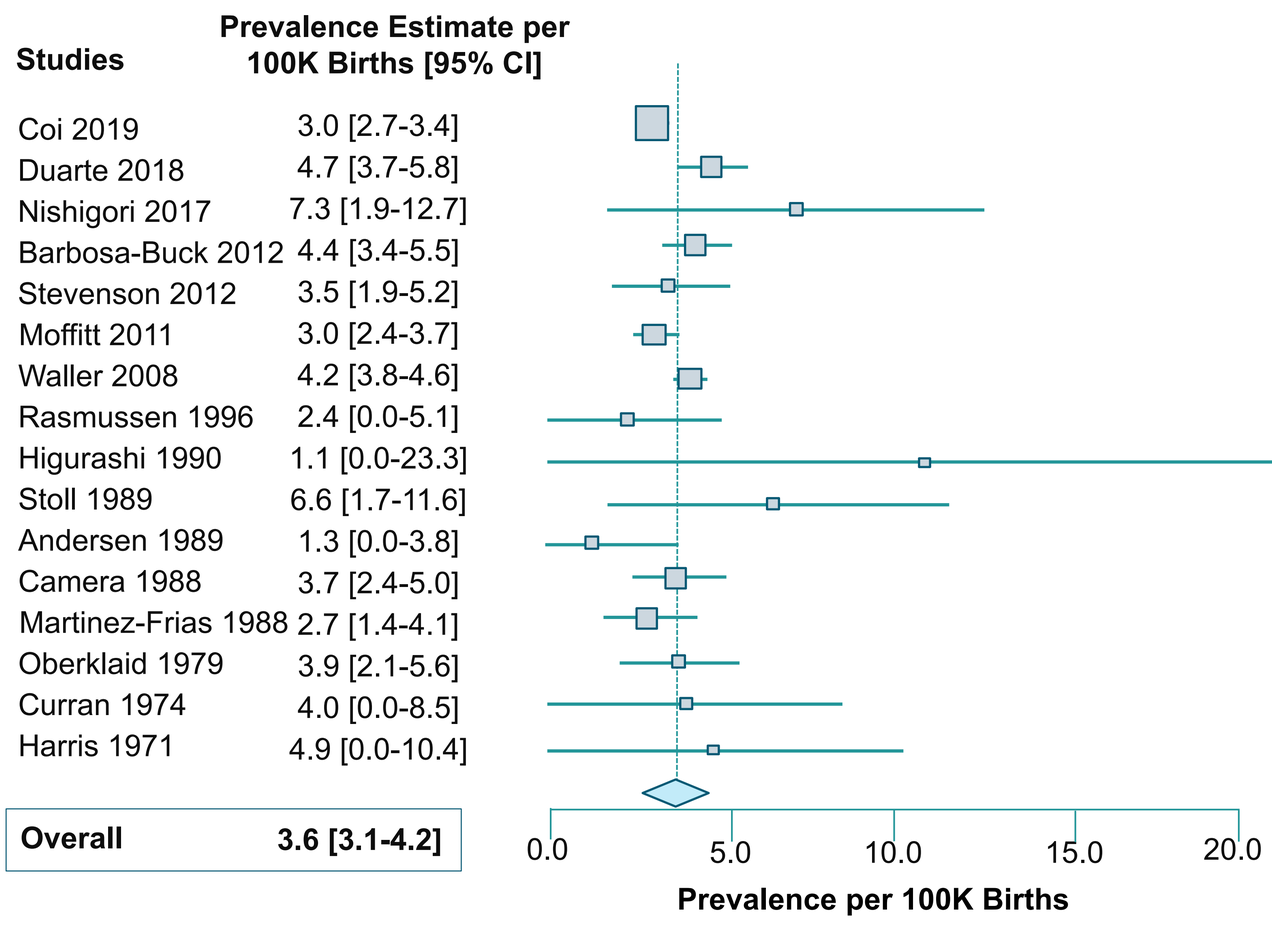
METHODS

- Comprehensive, targeted search of English language literature available in PubMed was conducted
  - Search terms used were MeSH “ACH” AND (“incidence” OR “prevalence” OR “epidemiology”)
  - Flow diagram based on PRISMA guidelines[2] was generated
- Abstracts were reviewed for relevance and full-text articles assessed for inclusion based on the following criteria:
  - Study rigor (using the STROBE checklist[3])
  - Case ascertainment methodology
- Studies were excluded if methodology was not clearly described, or if the results were based on outdated registries from developing countries
- Meta-analysis of birth prevalence estimates was conducted using a random effects model (‘meta’ package, R)
- Heterogeneity was assessed using forest plots and Cochran’s I^2

Table 1: Literature Estimates for Birth Prevalence of Achondroplasia

Source	Country	Observation/ Study Years	Achondroplasia Cases	Total Births	Birth Prev. per 100K
Coi 2019	Europe (multi-country)	1991-2015	350	11,475,410	3.1
Duarte 2018	Argentina	2009-2016	79	1,663,610	4.7
Nishigori 2017	Japan	2011-2014	7	95,994	7.3
Barbosa-Buck 2012	South America (multi-country)	2007-2007	68	1,544,496	4.4
Stevenson 2012	US	1999-2008	18	509,283	3.5
Moffitt 2011	US	1999-2006	91	2,993,421	3.0
Waller 2008	US	1968-2003	459	10,876,099	4.2
Rasmussen 1996	US	1972-1990	3	126,316	2.4
Higurashi 1990	Japan	1972-1985	3	27,472	10.9
Stoll 1989	France	1979-1986	7	105,374	6.6
Andersen 1989	Denmark	1970-1983	1	77,977	1.3
Camera 1988	Italy	1978-1985	31	838,717	3.7
Martinez-Frias 1988	Spain	1976-1985	15	553,270	2.7
Oberklaid 1979	Australia	1969-1975	19	492,889	3.9
Curran 1974	US	1964-1974	3	75,000	4.0
Harris 1971	UK	1951-1969	3	61,682	4.9

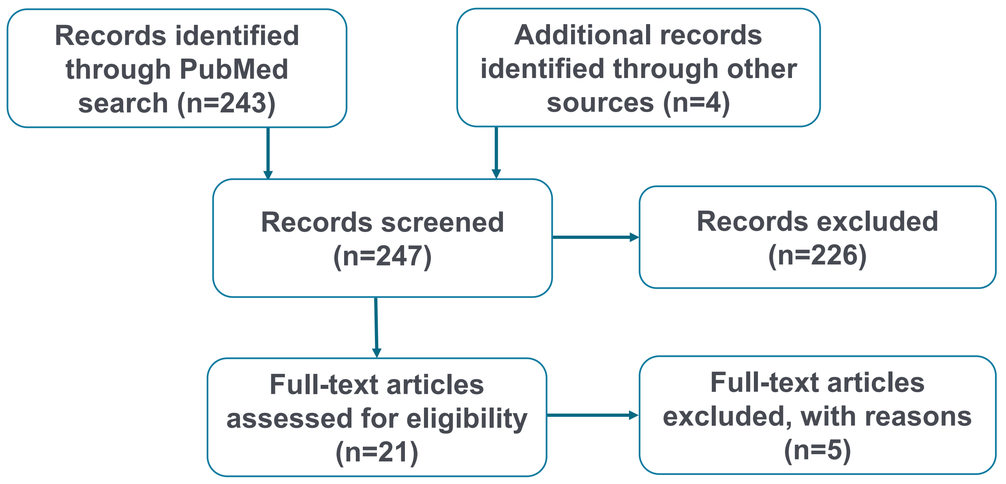
Figure 2: Forest Plot of Achondroplasia Birth Prevalence Estimates



RESULTS

- Search strategy yielded 21 papers referencing ACH birth prevalence **(Figure 1)**
  - 16 papers published between 1971-2019 met the inclusion criteria and were included in the meta-analysis **(Table 1)**
- Meta-analysis yielded point estimate for birth prevalence of ACH of 3.6 [95% CI 3.1-4.2] per 100K births **(Figure 2)**
- Studies exhibited moderate heterogeneity (I^2=63.9%; p-value=0.0003)

Figure 1: PRISMA Flow Diagram of PubMed Search Strategy



SUMMARY AND CONCLUSIONS

- The results of this analysis suggest the global birth prevalence of ACH was 3.6 per 100K or ~5,000 new cases worldwide, annually
- To our knowledge, this is the first estimate of the *global* birth prevalence of ACH
- Despite disparate study populations and periods, prevalence estimates were generally consistent across studies
- **Limitations:** Studies varied in their reporting of birth prevalence–some included still births and/or terminations, and others looked only at live births. These discrepancies were not adjusted for in this analysis. Because of this, it is feasible that the *live* birth prevalence of ACH is slightly lower than the overall birth prevalence
- **Conclusions:** These data can be used to inform planning strategies for therapeutic services and healthcare utilization, and to estimate potential study populations in the advent of novel therapies for ACH

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This study was sponsored by Ascendis Pharma A/S.