

## Appendix 1 Full search strategy

This appendix provides the complete search strategies used in the databases included in this review. Searches were performed between January 2007 and May 2025 across PubMed, Scopus, and IEEE Xplore.

PubMed

("adult height" OR "final height" OR "predicted adult height" OR "height prediction")

AND ("central precocious puberty" OR "early puberty" OR "GnRH agonist" OR "GnRHa" OR "growth hormone" OR "GH therapy")

AND ("machine learning" OR "artificial intelligence" OR "predictive model" OR "statistical model")

Filters: Publication date from 2007/01/01 to 2025/05/31; English language.

Scopus

TITLE-ABS-KEY ("adult height" OR "final height" OR "predicted adult height")

AND TITLE-ABS-KEY ("precocious puberty" OR "GnRH agonist" OR "GnRHa" OR "growth hormone")

AND TITLE-ABS-KEY ("machine learning" OR "artificial intelligence" OR "predictive model" OR "regression analysis")

AND (LIMIT-TO (LANGUAGE, "English"))

AND (PUBYEAR > 2006 AND PUBYEAR < 2026)

IEEE Xplore

("machine learning" OR "artificial intelligence" OR "data mining")

AND ("height prediction" OR "growth prediction")

AND ("children" OR "girls" OR "puberty")

Publication Years: 2007–2025

**Table S1** Summary of clinical and methodological characteristics for all included studies, detailing study type, regimen, initiation and duration, adherence measurement, baseline assessment methods (bone age, predicted adult height, target height, mid-parental height), genetic or familial context, and notable findings

Ref	Short citation	Study type / population	Regimen (drug/dose)	Initiation timing	Duration	Adherence measure	Baseline methods (BA / PAH / TH-MPH)	Genetic / familial	Notes
(1)	Carel <i>et al.</i> , 2009 ( <i>Pediatrics</i> )	Consensus statement on GnRHa use	–	–	–	–	Defines diagnostic and follow-up BA methods (Greulich-Pyle); PAH criteria standardized	MPH guidelines referenced	Establishes CPP treatment criteria
(2)	Berberoğlu, 2009 ( <i>JCRPE</i> )	Review: precocious vs. normal variant puberty	–	–	–	–	Defines BA-CA gap >1 year as criterion; PAH by BP tables	Parental height context	Differentiates pathologic vs. variant puberty
(3)	Labarta <i>et al.</i> , 2021 ( <i>JCRPE</i> )	Review/guidance on short stature assessment	N/A	N/A	N/A	N/A	Charts, BA methods (GP), SDS thresholds	MPH/TH stressed	Framework for auxology tools
(4)	Palmert & Dunkel, 2012 ( <i>NEJM</i> )	Clinical review—delayed puberty	–	–	–	–	BP caveats in delayed puberty; Tanner staging	Familial pubertal timing	Diagnostic context for pubertal variability
(5)	Lemaire <i>et al.</i> , 2018 ( <i>PLoS ONE</i> )	AH model validation (iCPP)	Not a regimen study	Retrospective validation	–	–	Model vs. BP; height SDS; TH SDS; LH/FSH ratio	TH from parental heights	Outperforms BP in CPP prediction
(6)	Collett-Solberg <i>et al.</i> , 2019 ( <i>GRS Perspective</i> )	Expert guidance (short stature)	N/A	N/A	N/A	N/A	Auxology methods; BA interpretation caveats	Family history/genetics pointers	Frames etiology and response criteria
(7)	Dotremont <i>et al.</i> , 2023 ( <i>Front Endocrinol</i> )	Early puberty/poor PAH; combo vs. controls	GH 0.05 mg/kg/day + triptorelin 3.75 mg q4w	B2–B3; BA 10–12 years; PAH <–2.5 SDS	48 mo combo	Clinic + labs	BA by GP; PAH by BP; TH by Tanner	TH/MPH used	Protocolized GH + GnRHa trial
(8)	Alaaraj <i>et al.</i> , 2022 ( <i>Acta Biomed</i> )	EFP cohort (Qatar)	Triptorelin 3.75 mg monthly	Mean 7.7±0.7 years (EFP)	≈ 3 years	Monthly injection log	BA advance ≈ +1.9 years; PAH & MPH-SDS	MPH used	Regional Middle Eastern data
(9)	Park & Lee, 2023 ( <i>IEEE Access</i> )	AH prediction ML model (CPP)	N/A	–	–	–	Parental + child height; RMSE <3.5 cm	Parental height central	Segmented ML improves fit
(10)	Shmoish <i>et al.</i> , 2021 ( <i>JCEM</i> )	Healthy cohorts (AH ML)	N/A	–	–	–	Auxology to age 6; validated ML model	TH constructs	High performance, calibrated
(11)	Swaiss <i>et al.</i> , 2017 ( <i>Saudi Med J</i> )	CPP; treated vs. untreated (Jordan)	GnRHa depot (brand NR)	Start ≈ 7.1 y	3.0±1.4 years	3-monthly visits; non-compliant excluded	Baseline PAH; BA/CA ratio	TH/MPH framework	FAH 158.5 vs. 151.2 cm
(12)	Cho <i>et al.</i> , 2023 ( <i>Sci Rep</i> )	CPP; mono vs. combo therapy	Leuprolide 1.87–3.75 mg q28d + GH 0.6 IU/kg/week	GH added ≈ 6.9 mo post-GnRHa	≈3 years	Clinic follow-up	BA (GP); PAH (BP accel.); TH/MPH	MPH used	Combo ↑ FAH gain vs. mono
(13)	Spataru <i>et al.</i> , 2022 ( <i>BMC MIDM</i> )	Adherence risk ML (r-hGH)	r-hGH via easypod™	<18 years start	Predict 3/6/9 months	Device-logged < 85 % cutoff	Adherence metrics (time-series)	–	RF best predictor
(14)	Tuvemo, 1999 ( <i>Acta Paediatr</i> )	RCT: GnRHa ± GH (adopted girls)	Buserelin 300 µg × 6/day + GH 0.1 U/kg/day	< 9.5 years; B2–B3 (mean 8.3 y)	2 years active	Alarm watch; 3-months visits	PAH +2.7 cm gain at 2 years	–	Classic trial evidence
(15)	Ilyas <i>et al.</i> , 2020 ( <i>LNCS</i> )	DL for height planning	N/A	–	–	–	BA/PAH details NR	–	DL methods paper
(16)	Spataru <i>et al.</i> , 2021 ( <i>JES Abs.</i> )	Adherence risk ML (r-hGH)	r-hGH via easypod™	First 3 months → predict 4–12 months	–	Device-transmitted	Adherence features	–	RF optimal model
(17)	Chen <i>et al.</i> , 2024 ( <i>Front Endocrinol</i> )	Meta-analysis (ML for CPP diagnosis)	N/A	–	–	–	AUC ≈0.90; Sens ≈0.82; Spec ≈0.85	–	Diagnostic performance pooled
(18)	Chen <i>et al.</i> , 2023 ( <i>Diagnostics</i> )	ML for GnRH test outcome	N/A	–	–	–	BA (GP); PAH (local); Tanner; labs; MPH	MPH used	Diagnostic ML + LIME interpretability
(19)	Loftus <i>et al.</i> , 2022 ( <i>Digital Health</i> )	Federated learning methods	N/A	–	–	–	–	Privacy/multi-center	Core privacy-preserving framework
(20)	Araujo-Moura <i>et al.</i> , 2025 ( <i>Int J Public Health</i> )	Pediatric risk ML (transfer learning)	N/A	–	–	–	–	–	TL improves cross-cohort AUC ≈0.82