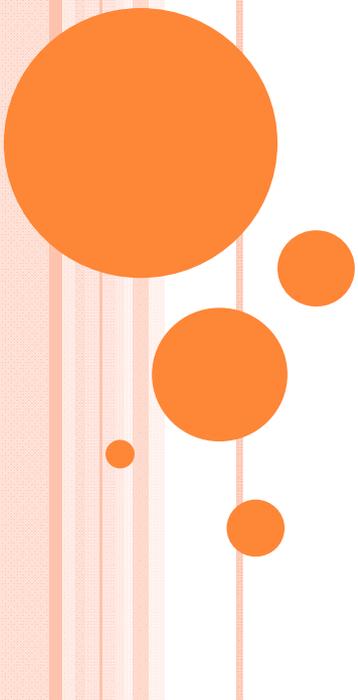


# THE USE OF GONADOTROPIN-RELEASING HORMONE ANALOGUES (GNRHA) IN CHILDREN WITH CENTRAL PRECOCIOUS PUBERTY (CPP)



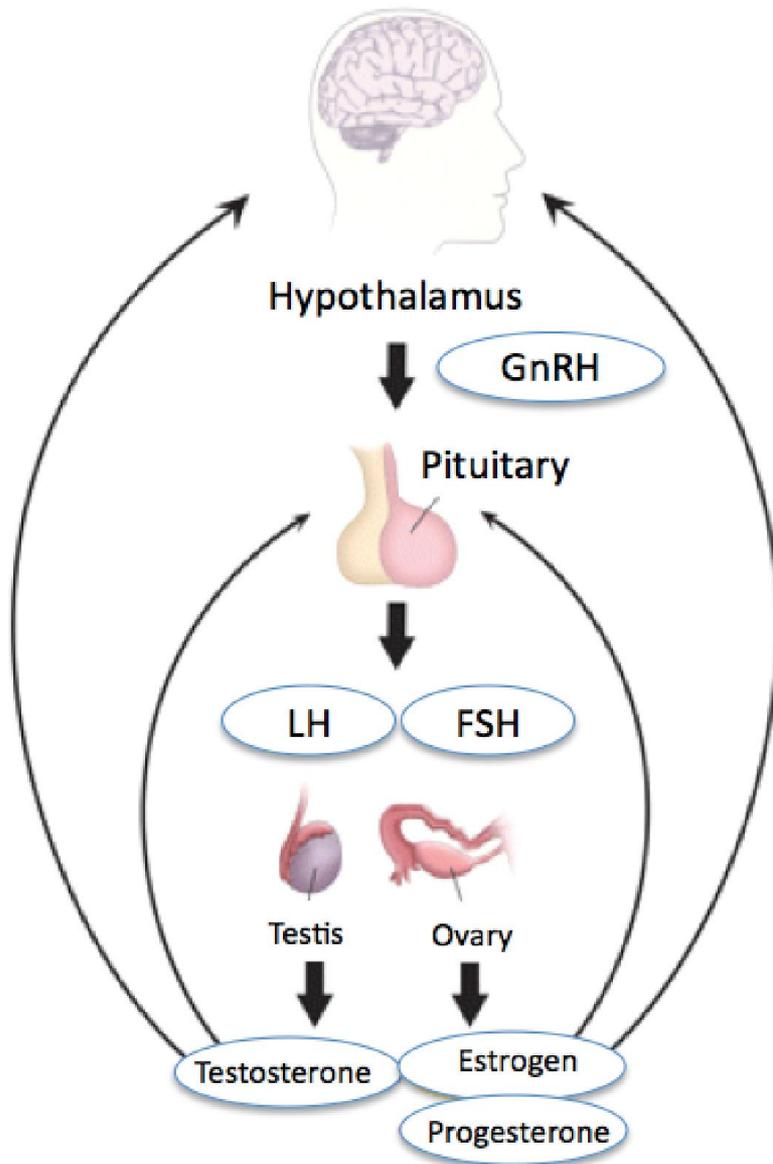
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  1. Roles of GnRH analogues in targeted adult height
  2. Available consensus
- Conclusion



# BACKGROUND



- Hypothalamic – Pituitary – Gonad Axis
- Puberty
- Precocious puberty – Problems

- The burst / continuously secretion of GnRH

**- DEVELOPMENT OF GnRH analogues (1986)**



## QUESTION 1

# ROLES OF GrRHA ON TARGET ADULT HEIGHT



**[Improvement of expected and final height in girls with central precocious puberty treated with gonadotropin releasing hormone analogues].**

[Article in Spanish]

Gómez F<sup>1</sup>, Picó AM, Vargas F, Mauri M.

- **Aim:** evaluate the effect of GnRHa on final height in CPP
- **Method:** prospective study for 3 years in 30 girls
- **Results:**
  - A **decrease** in growth speed and an **increase** in Chronological Age/Bone Age ratio ( $p= 0.034$ )
  - Predicted adult height increased significantly ( $p=0.041$ )
  - Final height: similar to and greater than predicted height



## **Two-year results of treatment with depot leuprolide acetate for central precocious puberty**

Neely EK<sup>1</sup>, Hintz RL, Parker B, Bachrach LK, Cohen P, Olney R, Wilson DM.

**-Method:** prospective study on 13 girls and 2 boys

**-Results:**

-Mean height increase:  $5.77 \pm 2$ cm/year

-Predicted adult height increased  $5.52 \pm 1.16$ cm at 18ms

**-Give evidence for:**

-Long-term treatment with depot GnRHa cause immediate, sustained laboratory & clinical suppression

-Predicted adult height progressive increase



## Efficacy of Leuprolide Acetate 1-Month Depot for Central Precocious Puberty (CPP): Growth Outcomes During a Prospective, Longitudinal Study

Peter A Lee<sup>1,2\*</sup>, E Kirk Neely<sup>3</sup>, John Fuqua<sup>2</sup>, Di Yang<sup>4</sup>, Lois M Larsen<sup>4</sup>, Cynthia Mattia-Goldberg<sup>4</sup> and Kristof Chwalisz<sup>4</sup>

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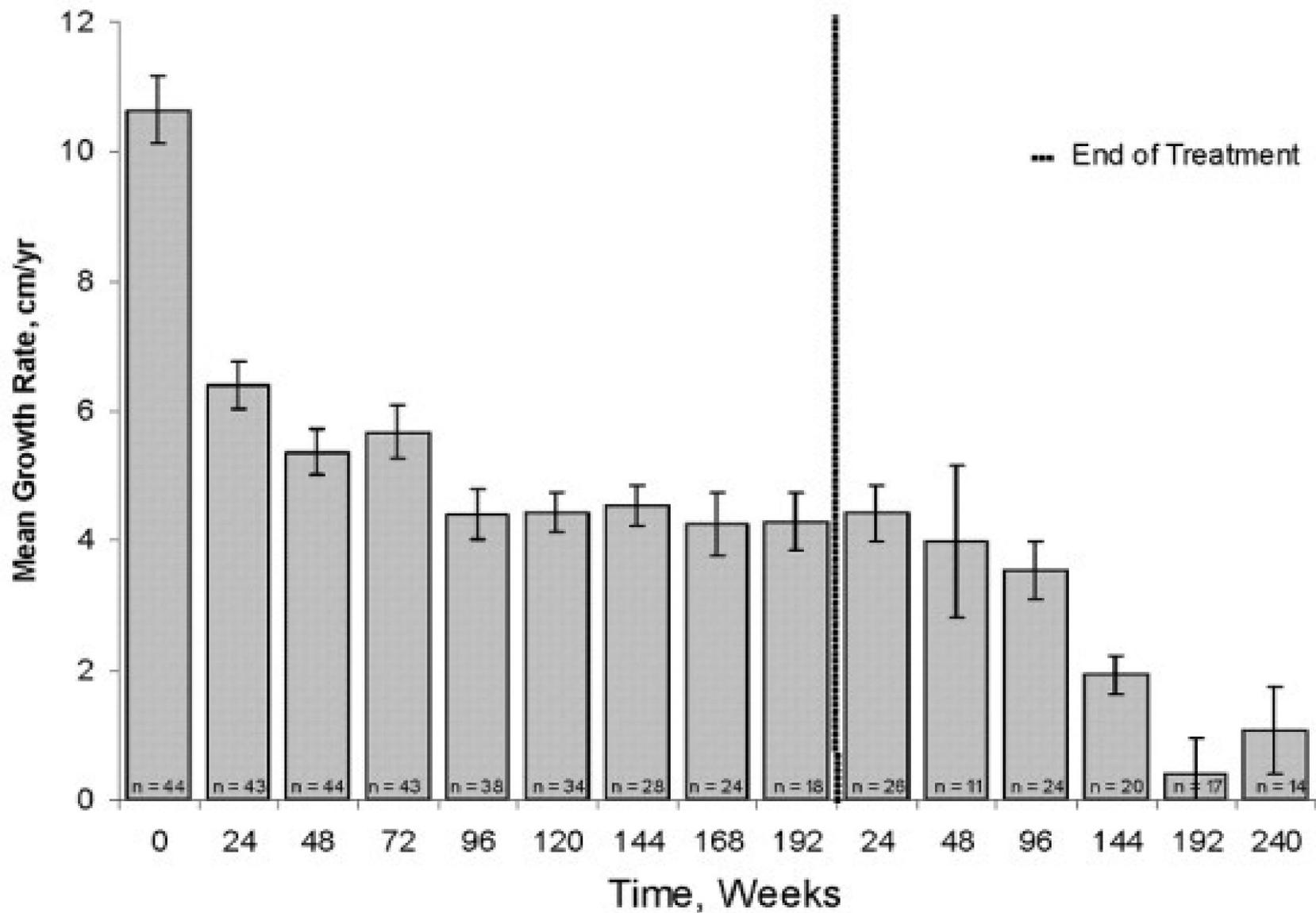
4 Abbott Laboratories, 200 Abbott Park Road, Abbott Park, IL 60064, USA

For all author emails, please [log on](#).

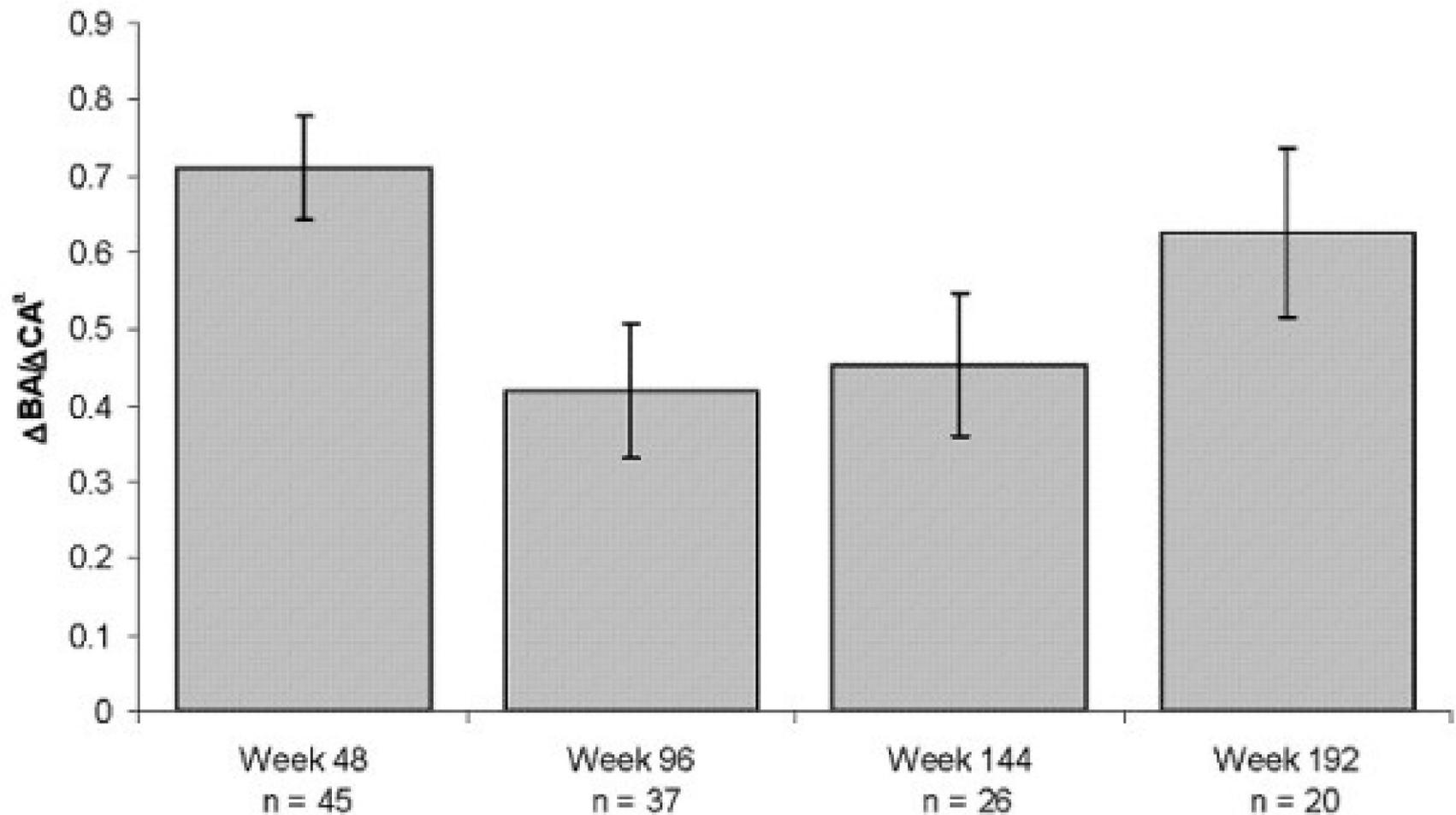
*International Journal of Pediatric Endocrinology* 2011, **2011**:7

doi:10.1186/1687-9856-2011-7

Prospective, longitudinal, multicenter (1991 to 2009)



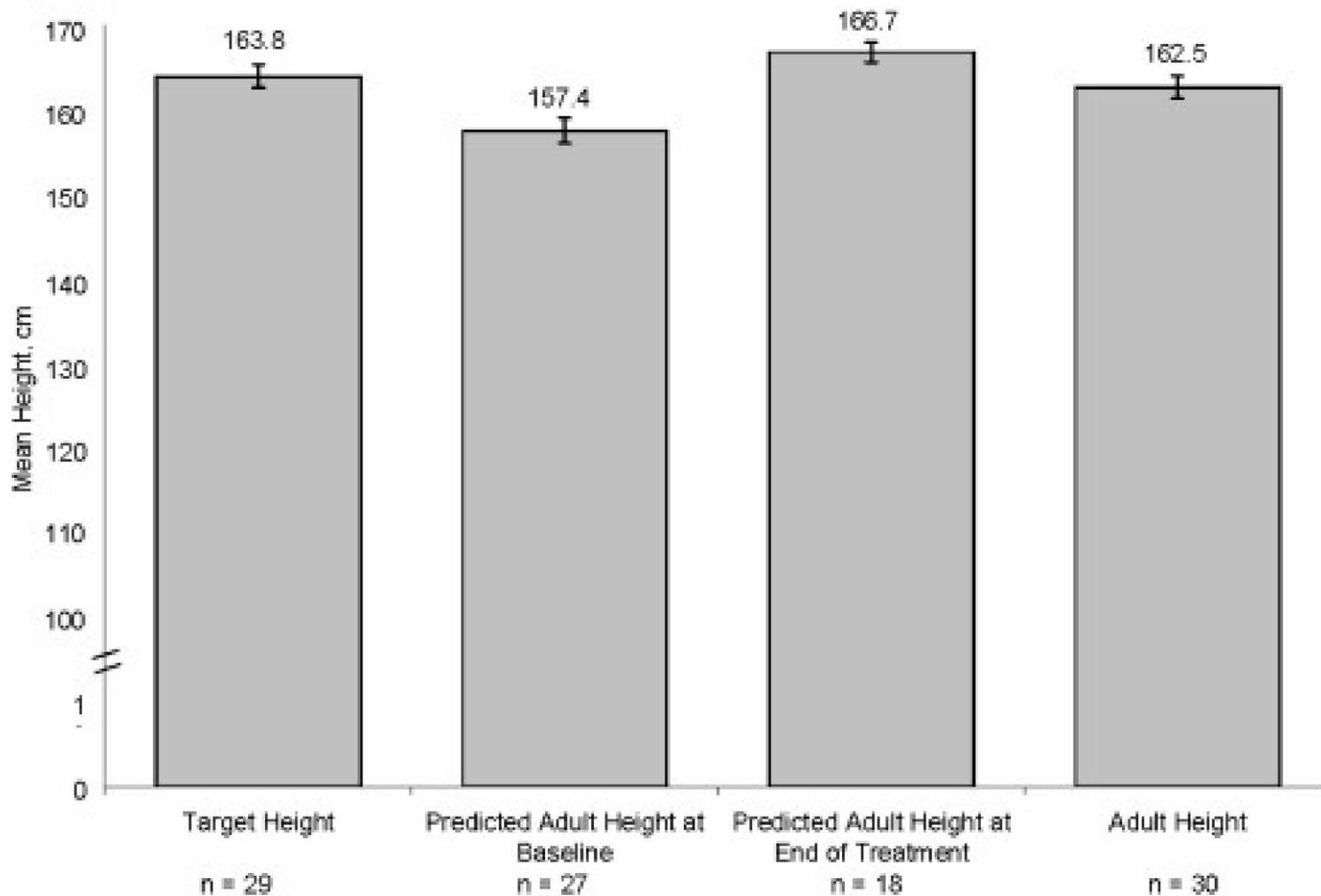
Mean Growth Rate (cm/year)



<sup>a</sup>BA=bone age, CA=chronological age. Change in bone age over the previous year/change in CA over the previous year.

$$\Delta BA / \Delta CA$$





Mean Height (cm)



## QUESTIONS 2

# AVAILABLE CONSENSUS



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## **Consensus Statement on the Use of Gonadotropin-Releasing Hormone Analogs in Children**

Jean-Claude Carel, Erica A. Eugster, Alan Rogol, Lucia Ghizzoni and Mark R. Palmert

*Pediatrics* 2009;123:e752; originally published online March 30, 2009;  
DOI: 10.1542/peds.2008-1783



# EVALUATION OF EVIDENCE

- The qualities of evidence
  - I: 1 properly randomized, controlled trial
  - II: other clinical studies
  - III: opinions of respected authorities
- The strengths of recommendation
  - A: good evidence to support use
  - B: moderate evidence to support use
  - C: poor evidence to support use
  - D: moderate evidence against use
  - E: strong evidence against use



# 1: INITIATION

- Clinical initiation: progressive pubertal development, Tanner stage III (breast), advanced skeletal maturation (CIII)
- Chronological age: Girl (6 yrs old) (BII), Boys (9 yrs old) (CIII)
- Hormonal criteria: Basal LH (BII), stimulated LH (BII)
- Pelvic ultrasound: differential diagnosis (BII)
- CNS imaging ((BII)
  - All Boys, Girls < 6 yrs old, (+/- Girl 6-8 yrs old)
  - Neurologic findings or Rapid pubertal progression



## 2: AVAILABLE GnRHa AND THERAPEUTIC REGIMEN

- Many formations: available and efficacious. The choice depends on patient, physician and local marketing (CIII)
- Monitoring
  - Tanner stage and growth / 3 – 6 months (BII)
  - Bone age: periodically (BII)
  - Random or stimulated LH, FSH, sex steroids: no consensus
  - Comprehensive reassessment if suboptimal response (CIII)
- Adverse events: headaches, hot flashes, local, anaphylaxis

# 3: DISCONTINUATION

- Based all many variables (CIII)
  - Chronological age (age at onset, age at initiation)
  - Bone age
  - Height, target height
  - Growth velocity
  - Parent/Patient preference



# 4: OUTCOMES

- **Reproductive function:** gonadal function is not impaired (BII)
- **BMI and Correlates of Metabolic syndrome:** not cause or aggravate obesity (BII)
- **Bone mineral density:** within the normal range for age (BII)
- Risk of **Polycystic Ovarian Syndrome:** not increase the eventual risk (BII to CIII)
- **Psychosocial** development: little or no evidence



# CONCLUSION

- GnRHa is the baseline therapy for CPP
- Increase the target adult height +/- psychosocial problems
- No significant short-term side effects
- No adverse event on long-term follow-up up to 5 years
- Few controlled prospective studies performed, need additional researchs



THANKS FOR YOUR ATTENTION

