

The Puberty Nomogram and Transient Breast Budding in Healthy Girls



Marie Lindhardt Johansen¹, Casper Hagen¹, Mikkel G. Mieritz¹, Jørgen Holm Petersen¹, Anders Juul¹

¹Dept. of Growth and Reproduction, Rigshospitalet, University of Copenhagen, Denmark



INTRODUCTION

Little is known about normal progression of female puberty. Usually puberty is evaluated in terms of onset vs. lack of onset. Furthermore, intermittent breast budding (girls entering stage B2 and then subsequently regressing to B1) in healthy girls is a frequent phenomenon observed by most clinicians and has, to our knowledge, never been studied in detail.

AIMS

- To present and validate the female Puberty Nomogram indicating age specific SD scores for Tanner breast stages (based on Van Buuren *et al*'s stage-line diagram [1]).
- To evaluate pubertal progression, longitudinal reproductive hormone profiles, and genetic polymorphisms affecting FSH signalling in girls with transient breast budding.

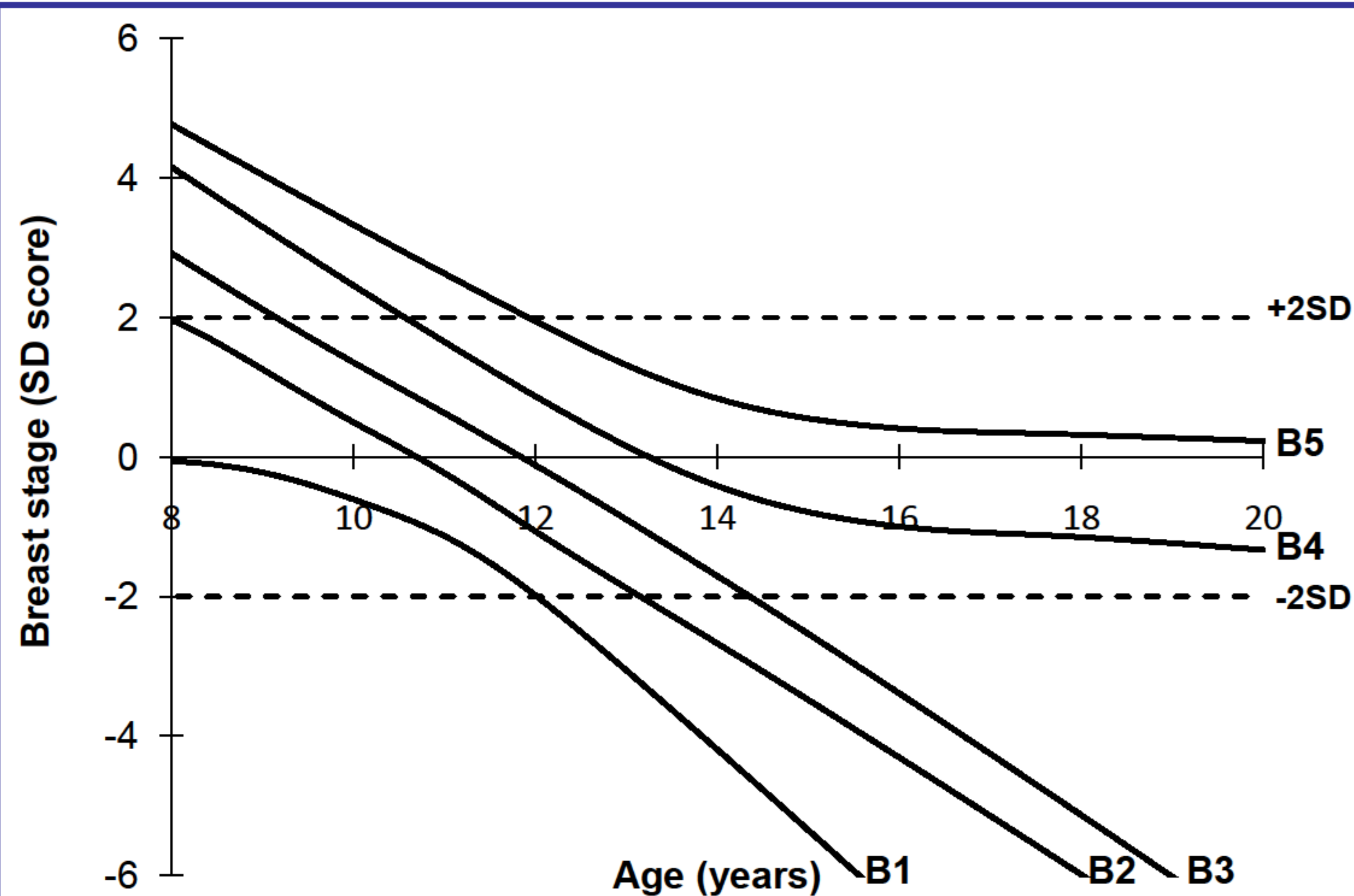


Fig. 1. The Puberty Nomogram: breast stage SDS is plotted against age and +/- 2SD are indicated with dotted lines.

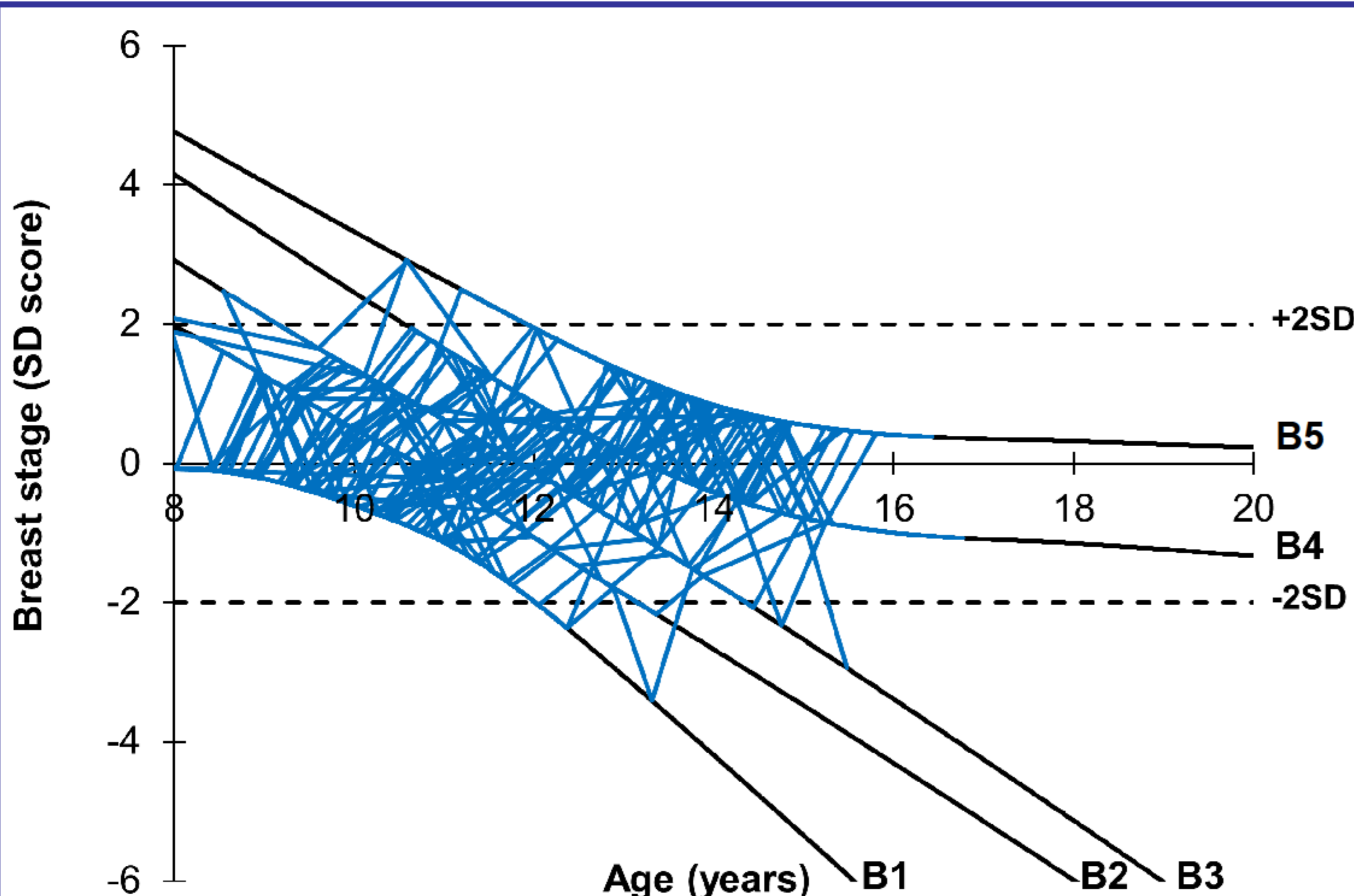


Fig. 2. The Puberty Nomogram validated by 98 healthy girls followed longitudinally (blue).

METHOD

The Puberty Nomogram was based on 1375 healthy, Caucasian girls from cross-sectional studies in Copenhagen and Randers, and was validated using data from 98 girls from the longitudinal part of the COPENHAGEN Puberty Study. DNA was isolated from blood and *FSHB* c.-211G>T, *FSHR* c.-29 G>A and *FSHR* c.2039 A>G were assessed by KASP™ genotyping assays.

RESULTS

Thirteen girls (13%) from the longitudinal cohort presented with transient breast budding. On the Puberty Nomogram it is apparent that after a variable period of time, pubertal development progresses normally in girls with intermittent breasts (median +1.7 years, range 1.14 to 4.29). Transient breast budding was associated with lower concentrations of hormones, significantly for inhibin B ($p=0.031$), at the time of the initial B2 compared to girls who initiated and progressed normally (inhibin B (pg/ml) (median (range)) 26.5 (14-47) vs. 34.5 (14-69)). The distributions of *FSHB* and *FSHR* SNPs were not associated with transient breast budding.

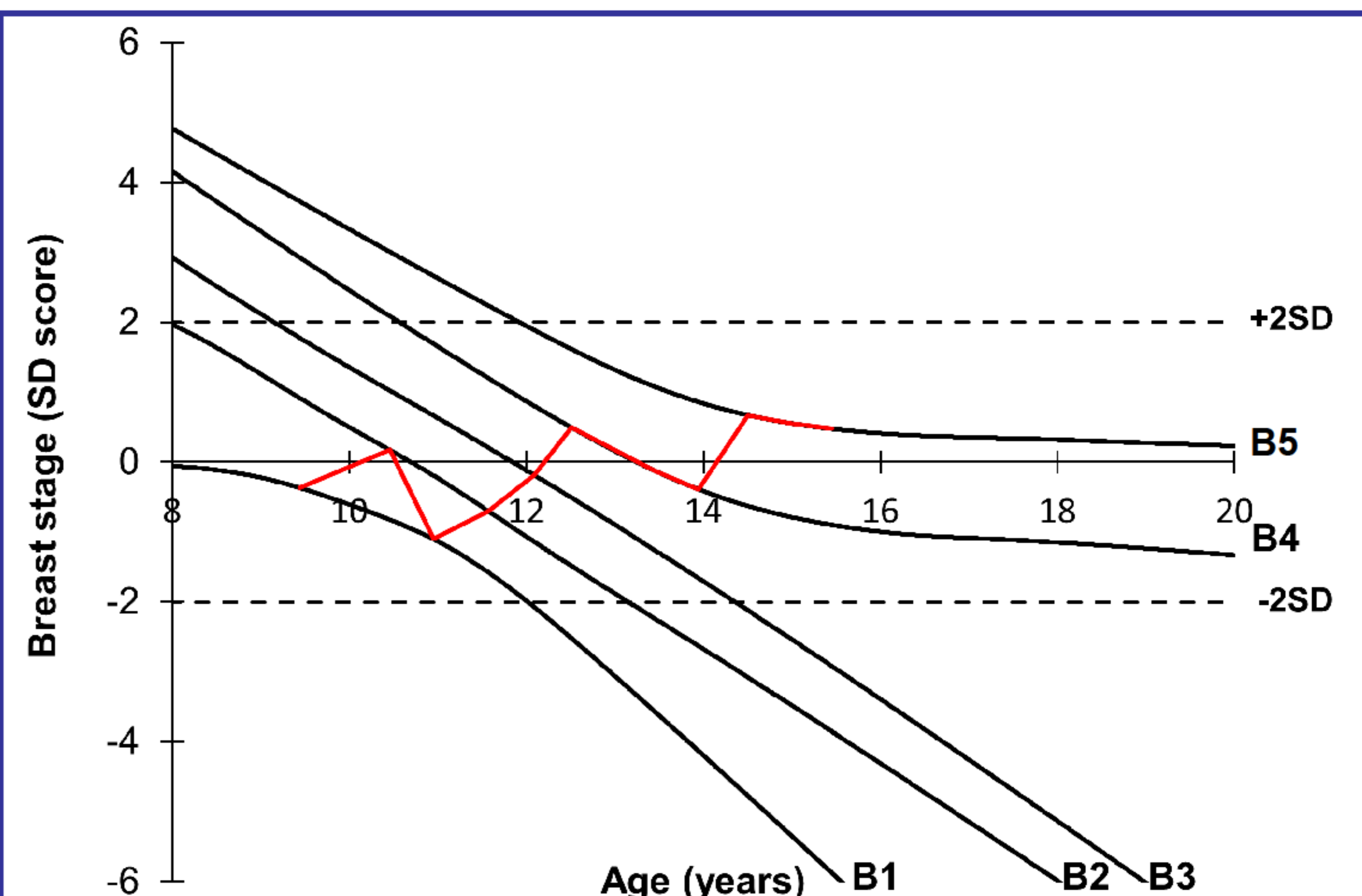


Fig. 3. An illustrative example of a girl (red) with transient breast budding that subsequently progresses normally through puberty.

CONCLUSIONS

We believe that the Puberty Nomogram is a useful clinical tool that allows for a meaningful distinction between abnormal and normal puberty by evaluating not only the onset but also the progression.

Transient breast development is a clinical phenomenon observed in 13% of healthy girls and is not associated with a pubertal rise in gonadotropins and reproductive hormone concentrations at the initial breast development. Genetic polymorphisms affecting FSH signalling did not appear to be associated with the phenomenon in this pilot study.

References: [1] van Buuren *et al.*, Stat Med 2009;28:1569-1579.

