

THE SIGNIFICANCE OF CLINICAL AND INSTRUMENTAL INDICATORS IN PREDICTING MENSTRUAL DISORDERS IN ADOLESCENT GIRLS

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Background. Adolescent menstrual abnormalities may resolve with maturation or persist into adulthood. Distinguishing these trajectories requires evidence beyond a single abnormal test.

Objective. To evaluate the prognostic significance of clinical, hormonal and ultrasound indicators in adolescent girls with menstrual disorders.

Materials and methods. A targeted narrative review integrated longitudinal cohort studies, international clinical recommendations and prediction-methodology guidance. Associations, individual prediction and diagnostic criteria were assessed separately. No pooled estimates were calculated.

Results. Persistent cycle irregularity provides clinically relevant longitudinal information. Hyperandrogenism and anthropometric trajectories refine interpretation, but their usefulness depends on the population and outcome. Anti-Müllerian hormone and ovarian morphology have not demonstrated sufficient incremental value to justify routine adolescent prognostic screening. Available evidence predominantly concerns oligomenorrhoea and polycystic ovary syndrome; it cannot be generalised to every menstrual disorder. Cohort overlap, attrition and heterogeneous outcome definitions limit certainty.

Conclusion. Prognostic assessment should combine repeated menstrual history, developmental context and targeted investigations. Clinical risk features support follow-up but should not be converted into numerical probabilities without a validated model. Future research requires independent validation, calibration and evidence that prediction improves care.

Keywords: adolescent girls; menstrual disorders; prognosis; risk factors; hyperandrogenism; anti-Müllerian hormone; ultrasonography; polycystic ovary syndrome.

Introduction

A diagnostic assessment asks what explains the current menstrual abnormality; a prognostic assessment asks what is likely to happen next. These questions overlap but require different evidence. A test that separates patients with an established disorder from healthy controls may have little value for forecasting persistence, recovery or a later endocrine diagnosis. Treating diagnostic accuracy as prognostic accuracy risks giving adolescents an unjustifiably certain account of their reproductive future. The distinction is particularly relevant during puberty. International recommendations interpret menstrual irregularity according to time since menarche and require both ovulatory dysfunction and

hyperandrogenism for adolescent polycystic ovary syndrome (PCOS), after excluding other causes [1]. Longitudinal studies provide a separate basis for discussing future outcomes [2–5]. The objective of this review is to examine which clinical and instrumental indicators contribute useful prognostic information, identify their limitations and outline priorities for responsible prediction research.

Materials and methods

This targeted narrative review used web searches of indexed scholarly records, PubMed-linked publications and professional guidance. Search concepts included adolescent menstrual irregularity, prediction, longitudinal follow-up, hyperandrogenism, anti-Müllerian hormone, ovarian ultrasound and future PCOS. Primary studies were prioritised when adolescent measurements preceded a later outcome. Cross-sectional evidence was used only for contextual interpretation. The selected clinical evidence spans 2004–2025; older publications were retained when they supplied longitudinal observations unavailable from more recent cohorts. For each study, the review considered the baseline phenotype, follow-up horizon, outcome definition and whether an additional test improved prediction beyond clinical history. Publications from the same cohort were treated as related analyses rather than independent replications. The synthesis also distinguished spontaneous reproductive outcomes from outcomes influenced by subsequent treatment. Selected longitudinal evidence is summarised in Table 1 [2–6]. The search was not exhaustive, a review protocol was not registered, and independent duplicate selection was not undertaken. Formal risk-of-bias scores and pooled effect estimates were not calculated. Numerical findings retain their published outcome labels and uncertainty intervals. Figure 1 displays reported adjusted odds ratios from one study; it is not a meta-analysis. No original clinical dataset or simulated patient results were created.

Results

Table 1. Longitudinal evidence and its appropriate interpretation.

Study and horizon	Principal observation	Prognostic limitation
POMP; ages 15–18 [2]	Earlier cycle pattern was more informative for later oligomenorrhoea than isolated endocrine or ovarian findings.	Historical definitions and a specific cohort limit transportability.
Northern Finland; ages 16–26 [3]	Adolescent irregularity was associated with later menstrual irregularity, PCOS and infertility problems.	Associations do not establish individual absolute risk.
POMP; approximately two decades [4]	Adding high AMH to adolescent oligomenorrhoea did not improve prediction of adult PCOS.	Questionnaire follow-up; substantial non-participation.
POMP; 25-year follow-up [5]	Half of those with adolescent oligomenorrhoea reported regular adult cycles.	Shared cohort with [2,4]; fertility outcomes may reflect treatment.
Raine; adolescence to early adulthood [6]	Ovulatory dysfunction plus hyperandrogenism identified a phenotype with greater subsequent BMI gain.	Later BMI was the outcome, not future menstrual dysfunction.

AMH, anti-Müllerian hormone; BMI, body mass index; POMP, Pubertal Onset of Menstrual cycle abnormalities study. Repeated POMP publications are not separate validation cohorts.

Menstrual history and longitudinal outcomes

Repeated cycle records provide information on direction of change, not merely the presence of an abnormality. In the early POMP follow-up, cycle pattern at approximately 15 years predicted oligomenorrhoea at 18 years better than isolated luteinising hormone, androgen or ovarian ultrasound findings [2]. This supports careful history-taking while leaving open how much a modern, standardised laboratory assessment might add in another population. The Northern Finland Birth Cohort linked menstrual irregularity at 16 years to three outcomes at 26 years. The published adjusted odds ratios and 95% confidence intervals are reproduced in Figure 1 [3]. Their different magnitudes show why a single statement such as “increased reproductive risk” is insufficient: persistence of irregularity, PCOS and infertility problems are distinct endpoints.

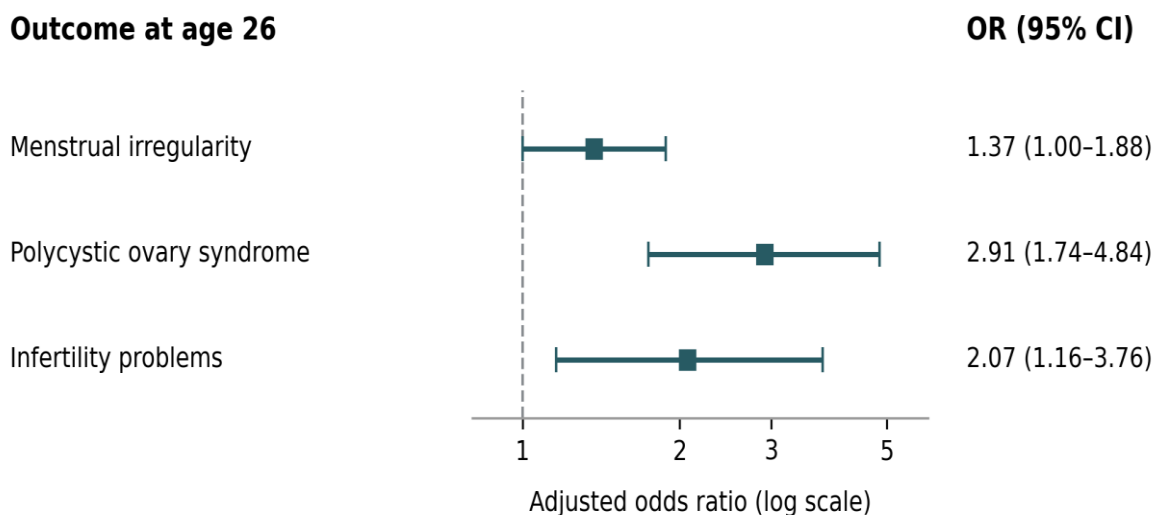


Figure 1. Associations between menstrual irregularity at age 16 and outcomes at age 26 in the Northern Finland Birth Cohort [3]. Squares indicate reported adjusted odds ratios; lines indicate 95% confidence intervals. The dashed line represents OR = 1. These are different outcomes in one cohort, without pooling or recalculation.

The estimate for later menstrual irregularity lies close to the null at its lower confidence limit. None of these odds ratios gives the probability that a particular adolescent will develop PCOS or experience infertility. Baseline outcome frequency, predictor distribution and model calibration would be needed for that purpose. Moreover, these observational associations do not show that treating an isolated adolescent marker prevents the corresponding adult outcome.

Persistence is not inevitable

In the 25-year POMP follow-up, 160 of 271 invited participants responded (59%). Half of those with adolescent oligomenorrhoea developed regular adult cycles [5]. These observations argue against deterministic fertility counselling. Attrition, retrospective adult reporting and intervening treatment complicate interpretation. The finding supports acknowledging both persistence and recovery, rather than describing every adolescent with irregular cycles as having an inevitable lifelong disorder.

Anthropometry and hormonal indicators

Anthropometry should describe a trajectory rather than a single weight category. The Raine analysis included 227 postmenarchal adolescents assessed at 14–16 years. The combination of ovulatory dysfunction and hyperandrogenism was associated with greater subsequent BMI gain [6]. Importantly, this direction of association does not prove that a specified BMI value predicts a later menstrual disorder. Reversing the exposure and outcome would create a claim the study did not test. Androgen measurements help characterise a hyperandrogenic phenotype. The 2023 international guideline recommends accurate methods for total and free testosterone assessment and recognises limitations of less reliable assays [7]. For prognosis, a result should also be interpreted in relation to sampling conditions, medication exposure and clinical progression. A reproducible abnormality may strengthen a diagnostic hypothesis; it does not by itself supply a validated probability of future disease. AMH illustrates the gap between biological association and clinical prediction. Caanen and colleagues reported an area under the receiver operating characteristic curve of 0.78 for adolescent AMH and adult PCOS. At the investigated 6 µg/L threshold, the positive predictive value was 22.3% and the negative predictive value 95.9%. Nevertheless, high AMH added no useful prediction among adolescents already identified by oligomenorrhoea [4]. This threshold is a research result, not a recommended adolescent screening cut-off.

Ultrasonography and other instrumental findings

Current adolescent recommendations do not endorse ovarian morphology or AMH for diagnosing PCOS during adolescence [1]. A prediction claim would require additional longitudinal validation, not relaxation of diagnostic safeguards. Pelvic ultrasonography can answer a targeted anatomical question, but the detection of multiple follicles should not be translated into a forecast of infertility. The early POMP findings also caution against assuming that ovarian imaging necessarily adds more information than menstrual history [2].

Table 2. Matching an indicator to the question it can answer.

Clinical question	Useful information	Inference to avoid
Is the pattern persisting?	Serial cycle dates, time since menarche and symptom trajectory.	One abnormal cycle equals chronic disease.
Is hyperandrogenism present?	Clinical examination and reliable androgen assays [7].	An abnormal concentration gives an individual future probability.
Does AMH improve prognosis?	Incremental performance beyond clinical history [4].	A significant group difference proves clinical utility.
Is an anatomical explanation suspected?	Targeted pelvic imaging interpreted in clinical context.	Ovarian follicle appearance predicts future infertility.

This table is a clinical interpretation framework, not a validated score. No points, probability bands or universal test thresholds are proposed.

Risk pathways beyond hyperandrogenic disorders

A PCOS-centred model cannot represent every adolescent with menstrual dysfunction. The Endocrine Society guideline on functional hypothalamic amenorrhoea highlights energy

deficit, weight loss, intensive exercise and psychological stress in the clinical assessment [8]. A normal BMI does not exclude inadequate energy availability. These exposures therefore require direct questioning rather than inference from body size alone. Their presence helps formulate a competing explanation for amenorrhoea but does not establish a numerical prognosis. This distinction changes how candidate predictors should be combined. Increasing adiposity and sustained energy deficit may both accompany menstrual abnormalities, yet they suggest different mechanisms. Adding them as interchangeable “risk factors” in a simple unvalidated score could obscure clinically important heterogeneity. A useful prognostic approach must first define the phenotype and the outcome, then examine whether the proposed variables improve prediction within that setting.

Discussion

The main contribution of this synthesis is a separation of three evidential levels: a feature associated with an outcome, a marker that adds information beyond routine assessment, and a prediction model that supports a clinical decision. These levels should not be treated as equivalent. The longitudinal studies support attention to menstrual trajectories, but they do not justify assigning universal probability categories to adolescents on the basis of an isolated hormone or scan. The AMH findings are especially instructive. Discrimination describes the ordering of individuals by risk; it does not establish that their predicted probabilities are accurate. Positive and negative predictive values also depend on the population in which the test is applied. Thus, an apparently informative marker can offer little practical improvement when a low-cost clinical variable already identifies the relevant group [4,9]. A proposed testing strategy must demonstrate added value over that clinical baseline. The review also identifies an endpoint problem. Persistence of oligomenorrhoea, development of PCOS, need for fertility treatment and failure to achieve pregnancy are not interchangeable. They occur over different horizons and are affected by different decisions and exposures. A model developed for one endpoint should not be relabelled as a general menstrual-health score. Fertility outcomes require particular caution because opportunity to conceive and access to treatment influence what is observed.

Practical implications for follow-up

A pragmatic application is to document cycle evolution, weight change, hyperandrogenic symptoms and relevant exposures in a consistent record. The purpose is to make change visible and support a reasoned reassessment. International guidance allows an “at risk” designation when adolescent PCOS features are incomplete, with subsequent review [1]. This is a follow-up category, not a quantified risk estimate or a reason to predict infertility. The proposed approach therefore gives longitudinal clinical information priority while reserving laboratory and imaging tests for questions they can answer. It is an interpretation of existing evidence, not a tested intervention. Its effects on patient outcomes, costs, unnecessary investigations and diagnostic delay remain to be evaluated. A future cohort should specify its target outcome and prediction horizon before model development. Persistence at the end of adolescence is a different objective from PCOS in adulthood or future fertility treatment. Baseline measurements must precede the outcome, and the definitions should distinguish menstrual patterns observed without hormonal treatment from treatment-induced bleeding patterns. Otherwise, apparent improvement or deterioration may reflect exposure to treatment rather than the underlying trajectory. The initial comparator should be an accessible clinical model

incorporating menstrual history and developmental context. Hormonal or instrumental variables should then be evaluated for incremental value. Useful reporting includes discrimination, calibration and uncertainty, followed by validation in an independent population [9]. Performance in the development sample alone is insufficient to justify clinical deployment. A model can separate higher-risk from lower-risk participants while systematically overestimating their absolute risk. Bias assessment must address participant selection, predictor measurement, outcome ascertainment and analysis [10]. Missing follow-up, small outcome counts and selective inclusion of specialist referrals can distort apparent performance. Any future local study should therefore report who was eligible, who was retained and how missing information was handled. Before applying a model in Uzbekistan, its calibration and clinical consequences should be assessed in the population and care setting where it will be used.

Strengths and limitations

The review compares clinical history with additional testing and explicitly recognises repeated analyses of the same POMP cohort. Its principal limitation is narrative source selection: relevant studies may have been missed, and no formal certainty grading was undertaken. Definitions and follow-up horizons vary, and most direct evidence concerns oligomenorrhoea and PCOS. The conclusions should not be extended to prediction of heavy menstrual bleeding, dysmenorrhoea or every cause of amenorrhoea. No validated multivariable model or locally calibrated risk estimate is presented.

Conclusion

Clinical and instrumental indicators have different roles in the prognosis of adolescent menstrual disorders. Repeated menstrual history provides the foundation for assessing persistence; anthropometric and hyperandrogenic features help interpret the phenotype. AMH and ovarian morphology should not be used as stand-alone forecasts of future PCOS or infertility. The appropriate clinical response is structured reassessment and targeted investigation, with uncertainty explained clearly. Progress requires prospective studies demonstrating that added tests improve prediction and that using the resulting model benefits patients.

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