

Postbiotic Strategies for the Prevention of Polycystic Ovary Syndrome in Adolescence: Butyrate, Gut Microbiome, Timing and Delivery

Dr V. Ariarasudhan^{1,2*}, Jayavardhini S.³¹M.D, Department of Pharmacology, Sri Ramachandra Medical College and Research Institute, Porur, Chennai 600 116, Tamil Nadu, India²ThirdBiome and Aeon Formulations Pvt Ltd, India³Department of Biomedicine, Manchester Metropolitan University, Manchester, United KingdomDOI: <https://doi.org/10.36347/sajp.2026.v15i10.004>

| Received: 15.08.2026 | Accepted: 06.10.2026 | Published: 14.10.2026

*Corresponding author: Dr V. Ariarasudhan

M.D, Department of Pharmacology, Sri Ramachandra Medical College and Research Institute, Porur, Chennai 600 116, Tamil Nadu, India

Abstract

Review Article

Polyendocrine metabolic ovarian syndrome (PMOS, formerly polycystic ovary syndrome) commonly declares itself during adolescence, and its metabolic trajectory is substantially established by the time adult criteria are met. Depletion of short-chain fatty acid-producing gut bacteria is a reproducible feature of the adult syndrome, and butyrate acts on several of the pathways that define it, including insulin sensitivity, enteroendocrine signalling, intestinal barrier function and ovarian granulosa-cell inflammation. Whether restoring or preserving these organisms early can alter the course of the syndrome has not been examined. This review sets out the case for treating adolescence as the intervention window and documents how little evidence exists within it: a systematic review of the gut microbiome in youth with PMOS screened 178 records and included four studies. We summarise what those and adjacent studies show, including the finding that microbiota alterations are present in adolescent girls independently of obesity, and that an insulin-sensitising combination normalised a microbiota feature that an oral contraceptive did not. We then set out the principal preclinical result supporting a preventive strategy, in which a sustained-release butyrate preparation given from weaning prevented the development of the phenotype in prenatally androgenised mice, and the contrasting result in which bolus sodium butyrate given to animals with established disease was not protective. Together these define timing and delivery as the variables that matter. We conclude with the design requirements for a prevention trial and the diagnostic caveats that constrain it. We situate butyrate delivery within postbiotic and microbial-metabolite strategies and argue that formulation, not dose, is the variable that separated the one preventive success from the one harmful result.

Keywords Adolescence - butyrate - gut microbiome - polyendocrine metabolic ovarian syndrome - postbiotics - prevention - short-chain fatty acids – tributyrin.

Copyright © 2026 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

1. INTRODUCTION

Polycystic ovary syndrome was renamed polyendocrine metabolic ovarian syndrome (PMOS) in May 2026 by international consensus; diagnostic criteria were unchanged, and a transition period extends to the 2028 guideline update. We use PMOS throughout, retaining PCOS where citing work published under the former name.

PMOS is not a disorder of adult onset. Symptoms typically begin at or shortly after menarche, and the metabolic phenotype that determines long-term risk is largely established before the syndrome is formally diagnosed. The burden in adolescence is

substantial: a meta-analysis of 12 Indian studies comprising 4,473 participants estimated a pooled prevalence among adolescent girls of 17.7 per 100 (95% CI 11.8-23.7) by Rotterdam criteria [1], and a community-based study in Mumbai found 22.5 per cent prevalence among girls aged 15 to 24 years, of whom 71.8 per cent were non-obese [2]. The national adult study reports comorbidity that is already advanced by diagnosis, including dyslipidaemia in 91.9 per cent and non-alcoholic fatty liver disease in 32.9 per cent [3]. If any of that trajectory is modifiable, the modification has to begin earlier than it currently does.

This review asks a question that has not been asked directly: whether the gut microbial contribution to PMOS constitutes a preventable exposure in adolescence, and specifically whether preserving or restoring butyrate-producing bacteria during this window could alter the course of the syndrome. We are explicit that no clinical evidence exists for this proposition in humans. The purpose is to establish whether the question is worth the trial it would require.

2. Search strategy

We searched an academic literature aggregator indexing PubMed, Scopus, Semantic Scholar and arXiv between 23 and 25 September 2026, using combinations of *polycystic ovary syndrome, polyendocrine metabolic ovarian syndrome, adolescent, youth, gut microbiome, butyrate, short-chain fatty acids, prevention, early life and prenatal androgen*. Both disease names were searched. No language or date restriction was applied, and reference lists of retrieved reviews were hand-searched. This is a narrative synthesis.

3. Relationship to companion reviews

This review is one of four by the same author group examining a single question -- whether colonic butyrate supply is a modifiable determinant of disease -- in two clinical domains where the evidence is incomplete in different ways. Because the four share a mechanistic core, the boundary between them is stated here explicitly.

This review addresses the adolescent window and the design of a preventive trial within it. The companion review addresses the adult Indian phenotype and asks whether fermentable substrate supply has diverged from the fermentative capacity of a *Prevotella*-dominant community, ending in a measurement rather than an intervention agenda [4]. The relationship between the two is directional: the population baseline that article identifies as missing is a prerequisite for interpreting any endpoint in the trial this one specifies, and the two should be read in that order.

Two further reviews by this group apply the same butyrate-supply question in the infection domain, to the intestinal uropathogen reservoir in recurrent urinary tract infection [5] and to the iatrogenic depletion of butyrate-producing bacteria by antimicrobial therapy [6]. The second is directly relevant here: adolescent girls are among the most heavily antibiotic-exposed groups in Indian practice, and if that exposure depletes the taxa this review argues should be preserved, then the preventive window described below is being narrowed by routine care. That interaction has not been studied and is noted as a research priority.

4. How little is known

The evidence base in the target population is close to empty, and this has been documented rather than merely asserted. A systematic review of the gut microbiome in youth with PMOS identified 178 records

by database search, assessed 68 at full text, and included four studies [7]. Its findings were correspondingly limited: a change in alpha diversity in adolescents with PMOS, no significant alteration in beta diversity, and abundance of Firmicutes, Bacteroidetes and Actinobacteria in both groups with differences at family level. The authors concluded that further data are required to clarify these changes and to build a strategy to prevent the syndrome⁷. A separate narrative review of probiotics in adolescents with obesity and PMOS reached a similar position, describing the supporting evidence as suggestive and calling for studies in adolescent patients specifically [8].

This scarcity is itself the argument for the review. The adult literature now comprises meta-analyses of tens of studies [9], while the population in whom prevention would have to occur has four.

5. What the adolescent studies show

Three findings from adolescent and young adult samples are worth stating precisely. First, in a randomised comparison in girls with PMOS without obesity (mean age 15.8 years), the gut microbiota showed decreased alpha diversity and an altered taxonomic profile with greater abundance of Family XI and less abundance of Prevotellaceae, *Prevotella* and *Senegalimassilia* relative to age-matched controls; Family XI abundance correlated positively with hepato-visceral fat, and one year of spironolactone-pioglitazone-metformin normalised Family XI abundance whereas an oral contraceptive did not [10]. That dissociation between a treatment that addresses metabolic substrate and one that addresses symptoms is instructive, and is rarely discussed in these terms.

Second, microbiota alterations in PMOS appear to be associated with the syndrome rather than simply with adiposity: changes have been observed in adolescent girls with PMOS and obesity compared with body mass index- and age-matched females without the disorder, and in women of normal weight as well as those with obesity [11]. Third, and providing the likeliest explanation for why diversity findings disagree between studies, hyperandrogenism itself tracks with microbial diversity. In 163 women, hyperandrogenism, total testosterone and hirsutism were each negatively correlated with alpha diversity, and hyperandrogenism also correlated with beta diversity [12]; an independent study found indices of bacterial diversity correlating positively with serum androgens and negatively with oestradiol [13]. Diversity in PMOS may therefore be tracking severity rather than diagnosis, which matters when recruiting adolescents whose androgen status is still evolving.

6. Early-life programming and the case for an early window

The rationale for intervening early does not rest on adolescent data alone. Androgen exposure shapes the

gut microbiota, and the resulting community is itself pathogenic: microbiota shaped by dehydroepiandrosterone and transplanted into pseudo-germ-free recipients produced disturbances of hepatic glucolipid metabolism and reproductive hormone balance [14]. Transfer in the human direction produces the same conclusion: faecal microbiota from women with PMOS, transplanted into recipient mice, caused ovarian dysfunction, insulin resistance and infertility [15]. The microbial contribution is therefore transmissible and, in principle, modifiable, and the period during which the community is being established is the period in which modification should be most effective.

7. The preventive proof of concept, and its counterpart

One study addresses prevention directly. Butyric acid-based self-assembling nanoparticles, designed to release butyrate in a sustained manner in the intestine, were administered in drinking water to prenatally androgenised mice from immediately after weaning until 20 weeks of age. Administration normalised irregular oestrous cyclicity, improved polycystic ovarian morphology with fewer atretic follicles, and improved adipocyte hypertrophy and insulin resistance, with an increase in certain butyrate-producing bacteria supporting the proposed mechanism [16]. The design is preventive rather than therapeutic: the intervention began before the phenotype had developed [16].

The counterpart study is essential to cite and easy to misread. Sodium butyrate given by daily oral gavage to mice with pre-established diet-induced obesity and androgen excess was not protective; treated animals showed greater weight gain and adipose expansion, higher visceral interleukin-6 and tumour necrosis factor- α , reduced adiponectin and impaired glucose tolerance, and the authors concluded that butyrate effects are context-dependent [17]. The two studies differ in three respects that plausibly account for the divergence: timing (before versus after phenotype establishment), delivery (sustained intestinal release versus bolus gavage) and host state (androgen exposure alone versus androgen excess with established obesity). Given that only about 2 per cent of colonically administered butyrate reaches the systemic circulation [18], bolus and sustained-release administration are pharmacologically distinct interventions rather than the same intervention at different doses. Neither study is sufficient on its own; together they identify timing and delivery as the variables a preventive trial must control.

8. Mechanisms that make prevention plausible

Butyrate acts on the principal axes of the PMOS phenotype, which is why an early intervention might plausibly alter trajectory rather than merely symptoms. Short-chain fatty acids stimulate glucagon-like peptide-1 secretion through free fatty acid receptor 2, and

receptor-knockout animals show impaired secretion and impaired glucose tolerance [19]. In the ovary, butyrate suppresses METTL3-mediated m6A modification of FOSL2 in granulosa cells with downstream reduction of NLRP3, interleukin-6 and tumour necrosis factor- α , and serum butyric acid was lower in women with obese PMOS [20]. A lipid-coated sodium butyrate preparation restored oestrous cycles and ovulation in a rat model with reductions in testosterone, insulin and luteinising hormone and increases in colonic GPR41 and peptide YY [21]. Substrate-directed intervention shows the same pattern: inulin improved hyperandrogenism and glucolipid metabolism in both a patient cohort and mice, with verified enhancement of short-chain fatty acid biosynthetic capacity, and the benefit was transferable by faecal transplantation from treated patients [22].

9. What has been tested in humans, and in whom

Human intervention evidence exists but almost entirely in adults. A randomised placebo-controlled trial of inulin-type fructans at 10 g daily for 12 weeks in overweight and obese women with PMOS reduced waist circumference, total testosterone and free androgen index, raised sex hormone-binding globulin and reduced the number of women with irregular menses [23]. Pooled across 17 trials of gut-derived metabolite interventions comprising 1,214 women, total testosterone, the luteinising-to-follicle-stimulating hormone ratio, fasting insulin and HOMA-IR all improved, with certainty rated moderate for insulin-related outcomes and low for sex hormone outcomes [24]; a larger synthesis of 26 randomised trials of prebiotics, probiotics and synbiotics reported reductions in weight, body mass index, waist circumference, insulin, HOMA-IR and total testosterone [25]. None of these trials recruited adolescents, and none was designed to test prevention rather than treatment.

10. The diagnostic problem

Any adolescent prevention study confronts a difficulty that is not incidental. Diagnosis of PMOS in adolescence is contested because the diagnostic features overlap with normal pubertal variation: menstrual irregularity, acne and multifollicular ovarian morphology are common in the years after menarche in girls who will not develop the syndrome [7]. This creates two risks in opposite directions. A trial recruiting on diagnostic criteria will enrol girls who would have resolved, diluting any effect. A trial recruiting on risk factors instead, such as maternal PMOS, early adrenarche or central adiposity, avoids that problem but must then justify intervening in girls without a diagnosis. Our view is that the second design is preferable provided the intervention is a dietary substrate rather than a drug, since the risk-benefit threshold for increasing fermentable fibre intake in an adolescent is low.

11. Ethical constraints specific to adolescence

A prevention trial in adolescents is not a scaled-down adult trial, and three constraints shape what is permissible. The first concerns who would be recruited.

Because the diagnostic features of PMOS in adolescence overlap normal pubertal variation [7], a prevention trial must recruit on risk rather than on diagnosis, which means enrolling girls most of whom will never develop the syndrome. The acceptable risk threshold for such a cohort is correspondingly low. A fermentable dietary substrate or a food-grade short-chain fatty acid donor can meet it; a pharmacological agent with appreciable systemic exposure cannot. This is a constraint on the choice of intervention, not merely on the wording of the consent form.

Second, the counterpart animal experiment is a warning about harm and not only about efficacy. Bolus sodium butyrate given to animals with established diet-induced obesity and androgen excess produced greater weight gain, greater adipose expansion and higher visceral inflammatory cytokines than no treatment at all [17]. A trial recruiting on risk will inevitably enrol some participants in whom the metabolic phenotype is already established, so the possibility that one intervention helps before and harms after a phenotypic threshold must be handled prospectively: by stratifying at randomisation on adiposity and androgen status, by pre-specifying stopping rules on weight and insulin resistance, and by reporting the strata separately whatever the pooled result shows.

Third, labelling. Recruiting adolescents into a study organised around a syndrome they do not have risks conferring an anticipatory illness identity, a recognised harm of screening in this age group and a particular concern for a condition carrying reproductive and cosmetic connotations [3,7]. Study documentation should be framed in terms of dietary fibre and metabolic health rather than PMOS risk; results should be returned to participants and guardians with explicit statements of what they do and do not predict; and no participant should leave the study carrying a diagnosis she did not have on entry. None of these constraints is prohibitive. Together they argue that the first human study in this window should be a substrate-supply trial with metabolic endpoints in a risk-defined cohort, and that pharmacological butyrate delivery in adolescents should wait for adult efficacy data stronger than the pooled surrogate endpoints presently available [24,25].

12. Design requirements for a prevention trial

Five requirements follow from the evidence above and are set out in Table II. The intervention must deliver butyrate or its substrate to the distal colon in sustained rather than bolus form, because the two are pharmacologically different [16-18]. Recruitment must occur before the metabolic phenotype is established, which in practice means peri-menarcheal. Stratification by androgen status and body mass index is essential, since both modify the microbial phenotype and plausibly modify response [12,17,26]. The mediator endpoint should be plasma butyrate together with metagenomic butyrate-producing gene abundance rather than faecal

short-chain fatty acid concentration, which does not reflect production rate [27]. And the primary clinical endpoint should be metabolic rather than reproductive, since insulin resistance is measurable over a trial horizon whereas ovulatory outcome in adolescents is not.

13. Translational perspective: emerging postbiotic and butyrate-delivery strategies

Interest in microbiome-derived intervention has expanded beyond live probiotics to include postbiotic preparations and strategies designed to deliver microbial metabolites, or their precursors, to defined intestinal sites. Precision about the category is necessary before proceeding. A postbiotic was defined by international consensus as a preparation of inanimate microorganisms and/or their components that confers a health benefit on the host [28], and isolated or purified metabolites fall outside that definition [29]. Glycerol tributyrin (tributylin), a triglyceride ester of butyric acid, is therefore not a postbiotic in the consensus sense: it contains no microbial cells or cell components. It is a butyrate precursor, and it is discussed alongside postbiotic approaches here because the two act on the same host pathway and are being developed for the same clinical purpose, not because they belong to the same regulatory or definitional category.

The divergence between the two animal experiments central to this review turns on delivery as much as on timing. Sustained intestinal release from weaning prevented development of the phenotype [16]; bolus gavage to animals with an established phenotype did not, and was associated with harm [17]. Because approximately 2 per cent of colonically administered butyrate reaches the systemic circulation [18], a preparation that releases its payload in the stomach or proximal small intestine is not a lower dose of the same intervention but a different intervention with a different target organ. This is why formulation belongs among the primary design variables of a preventive trial rather than among its implementation details, and the human data available on butyrate precursors reinforce the point: the only published pilot study of a tributyrin complex, in healthy adults, reported decreased faecal acetate and propionate and was interpreted by its authors as small-intestinal release with hepatic activity [30]. A preparation with that profile would not test the hypothesis this review advances, whatever dose were given.

Aeon Formulations Pvt Ltd has developed a patented technology, designated GTB, comprising a microencapsulated powder form of glycerol tributyrin, and this technology is used in the development of the ThirdBiome platform. Microencapsulation is intended to alter where in the gastrointestinal tract the ester is hydrolysed, and therefore how much butyrate reaches the distal intestine; whether it does so in humans is an empirical question that has not been answered for this or, with the single exception noted above, for any

comparable preparation. Microencapsulated glycerol tributyrates technologies, including the patented GTB technology developed by Aeon Formulations Pvt Ltd and used in the development of the ThirdBiome platform, represent one approach to the sustained-delivery requirement identified above. The appropriate next step for any such preparation is characterisation against that requirement, in pharmacokinetic and colonic-exposure studies in adults, and then adult efficacy studies, before an adolescent trial is contemplated. No data of either kind

exist in adolescents, no efficacy claim is made here for this or any preparation, and the conclusion of this review is unchanged: the first human study in this window should be a substrate-supply trial with metabolic endpoints in a risk-defined cohort, and pharmacological butyrate delivery in adolescents should not occur outside a trial. The authors' commercial interest in this technology is declared in the competing interest's statement.

Table I: Studies of the gut microbiome in adolescents and young women with polyendocrine metabolic ovarian syndrome

Study	Population	Principal finding	Limitation
Tsinopoulou <i>et al</i> ^[7]	Systematic review; 178 records screened, 4 studies included	Altered alpha diversity; no significant beta diversity change; family-level differences	Four studies; heterogeneous methods; authors call for prevention strategy data
Garcia-Beltran <i>et al</i> ¹⁰	30 girls with PMOS (mean 15.8 yr), 31 age-matched controls	Reduced alpha diversity; Family XI increased and correlated with hepato-visceral fat; normalised by SPIOMET but not by oral contraceptive	Small randomised subgroups; post-treatment samples in 23 of 30
Calcaterra <i>et al</i> ⁸	Narrative review, adolescents with obesity and PMOS	Probiotic and synbiotic supplementation may improve hormonal, inflammatory and lipid profiles	Narrative; adolescent-specific trials lacking
Rizk & Thackray ¹¹	Review of human and rodent studies	Microbiota changes present in adolescent girls with PMOS independently of obesity	Review; adolescent primary data limited
Torres <i>et al</i> ¹²	73 women with PCOS, 42 with polycystic ovarian morphology, 48 controls	Hyperandrogenism, testosterone and hirsutism each negatively correlated with alpha diversity	Adult sample; cross-sectional

Table II: Design requirements for a trial of butyrate-directed prevention in adolescence

Domain	Requirement	Rationale
Formulation	Sustained intestinal release rather than bolus administration	Prevention succeeded with sustained-release nanoparticles ¹⁶ and failed with bolus gavage ¹⁷ ; systemic availability of colonic butyrate is ~2% ¹⁸
Timing	Peri-menarcheal recruitment, before the metabolic phenotype is established	Comorbidity is already advanced at adult diagnosis ³ ; the successful preventive model began at weaning ¹⁶
Stratification	Stratification by androgen status and body mass index	Both modify the microbial phenotype and plausibly modify response ^{12,17,26}
Mediator measurement	Plasma butyrate and metagenomic butyrate-producing gene abundance as mediator endpoints	Faecal concentration does not reflect production rate ²⁷
Primary endpoint	Metabolic rather than reproductive primary endpoint	Insulin resistance is measurable over a feasible trial horizon; adolescent ovulatory outcome is not
Eligibility	Recruitment on risk factors rather than adolescent diagnostic criteria	Diagnostic features overlap normal pubertal variation ⁷ ; acceptable only for a dietary-substrate intervention

14. Limitations

The central limitation is that this review argues for a hypothesis on which no human preventive data exist. The adolescent microbiome evidence comprises four studies [7]; the preventive evidence is a single rodent experiment [16]; and the human intervention evidence comes from adults with established disease and cannot be extrapolated to prevention in youth [23-25]. Regional variation adds further caution, since the microbial phenotype of PMOS differs between populations and the single Indian study available examined adult women in one region [31]. We name one formulation category in the translational perspective section for completeness, but propose no specific

preparation for use, and no conclusion here supports the use of a butyrate supplement in adolescents outside a trial.

15. CONCLUSIONS

Adolescence is the period in which the metabolic trajectory of PMOS is set and the period in which the gut microbial contribution has been least studied. Four studies exist in the target population. The one preventive experiment available shows that sustained intestinal butyrate delivery from weaning prevented phenotype development in an androgenised animal model, while bolus delivery to animals with established disease did not, identifying timing and

formulation as the decisive variables. Whether the same holds in adolescent girls is unknown and is answerable. Given the prevalence in this age group and the comorbidity already present at adult diagnosis, the question merits the trial.

16. Acknowledgements

The authors thank colleagues at ThirdBiome and at Aeon Formulations Pvt Ltd, whose work on the microencapsulation of glycerol tributyrates informed the discussion of delivery form in the translational perspective section. Neither organisation had any role in the literature search, in the selection or appraisal of evidence, or in the decision to submit this manuscript.

17. Declarations

Competing interests. The authors are founding members of ThirdBiome and are associated with Aeon Formulations Pvt Ltd, which has developed a patented microencapsulated glycerol tributyrates (GTB) technology used in the development of the ThirdBiome platform. These relationships constitute a financial interest in the subject matter of this review and are the reason for the disclosure that follows. The GTB technology and the ThirdBiome platform are named once, in the translational perspective section, as one example of a butyrate-delivery formulation approach. No efficacy claim is made for either, no unpublished or proprietary data from either organisation are reported, and no recommendation for clinical use is given anywhere in this article. Neither organisation funded this review, had any role in its design, conduct, literature identification, evidence appraisal or reporting, or reviewed the manuscript before submission. The authors confirm that every evidence assessment in this review reflects the published literature independently of these commercial interests.

Funding. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Author contributions. V.A.: conceptualisation, methodology, investigation, writing - original draft, writing - review and editing, supervision. J.S.: investigation, formal analysis, writing - review and editing. Both authors approved the final manuscript.

Ethical clearance. Not applicable. This is a narrative review of published literature. No human participants, human material or human data were involved, and no institutional ethics committee approval was required.

Data availability. No new data were generated. The search strategy is described in the manuscript; the full list of retrieved records is available from the corresponding author on reasonable request.

REFERENCES

1. Sharma M, Khapre M, Saxena V, Kaushal P. Polycystic ovary syndrome among Indian adolescent girls - a systematic review and meta-analysis. *Nepal J Epidemiol* 2021; 11: 1063-75. doi: 10.3126/nje.v11i3.38460
2. Joshi B, Mukherjee S, Patil A, Purandare A, Chauhan S, Vaidya R. A cross-sectional study of polycystic ovarian syndrome among adolescent and young girls in Mumbai, India. *Indian J Endocrinol Metab* 2014; 18: 317-24. doi: 10.4103/2230-8210.131162
3. Ganie MA, Chowdhury S, Suri V, Joshi B, Bhattacharya PK, Agrawal S, *et al.*, Prevalence, phenotypes, and comorbidities of polycystic ovary syndrome among Indian women. *JAMA Netw Open* 2024; 7: e2440583. doi: 10.1001/jamanetworkopen.2024.40583
4. Ariarasudhan V, Jayavardhini S. Butyrate, postbiotic strategies and the Indian polycystic ovary syndrome phenotype: dietary fibre, gut microbiome and the capacity-substrate mismatch hypothesis. Companion narrative review by the same author group; under consideration.
5. Ariarasudhan V, Jayavardhini S. Postbiotic strategies and the gut-bladder axis in recurrent urinary tract infection: the butyrate-oxygen hypothesis, epithelial hypoxia and the intestinal uropathogen reservoir. Companion narrative review by the same author group; under consideration.
6. Ariarasudhan V, Jayavardhini S. Postbiotic strategies after antibiotic exposure in recurrent urinary tract infection: the antibiotic paradox, butyrate-producing bacteria and microbiome recovery. Companion narrative review by the same author group; under consideration.
7. Tsinopoulou VR, Bacopoulou F, Fidani S, Christoforidis A. The role of the gut microbiome in youth with polycystic ovary syndrome: a systematic review. *Children (Basel)* 2023; 10: 1872. doi: 10.3390/children10121872
8. Calcaterra V, Rossi V, Massini G, Casini F, Zuccotti G, Fabiano V. Probiotics and polycystic ovary syndrome: a perspective for management in adolescents with obesity. *Nutrients* 2023; 15: 3144. doi: 10.3390/nu15143144
9. Li P, Shuai P, Shen S, Zheng H, Sun P, Zhang R, *et al.*, Perturbations in gut microbiota composition in patients with polycystic ovary syndrome: a systematic review and meta-analysis. *BMC Med* 2023; 21: 302. doi: 10.1186/s12916-023-02975-8
10. Garcia-Beltran C, Malpique R, Carbonetto B, Gonzalez-Torres P, Henares D, Brotons P, *et al.*, Gut microbiota in adolescent girls with polycystic ovary syndrome: effects of randomized treatments. *Pediatr Obes* 2021; 16: e12734. doi: 10.1111/ijpo.12734

11. Rizk MG, Thackray VG. Intersection of polycystic ovary syndrome and the gut microbiome. *J Endocr Soc* 2021; 5: bvaa177. doi: 10.1210/jendso/bvaa177
12. Torres PJ, Siakowska M, Banaszewska B, Pawelczyk L, Duleba AJ, Kelley ST, *et al.*, Gut microbial diversity in women with polycystic ovary syndrome correlates with hyperandrogenism. *J Clin Endocrinol Metab* 2018; 103: 1502-11. doi: 10.1210/jc.2017-02153
13. Insenser M, Murri M, Del Campo R, Martinez-Garcia MA, Fernandez-Duran E, Escobar-Morreale HF. Gut microbiota and the polycystic ovary syndrome: influence of sex, sex hormones, and obesity. *J Clin Endocrinol Metab* 2018; 103: 2552-62. doi: 10.1210/jc.2017-02799
14. Han Q, Wang J, Li W, Chen ZJ, Du Y. Androgen-induced gut dysbiosis disrupts glucolipid metabolism and endocrinal functions in polycystic ovary syndrome. *Microbiome* 2021; 9: 101. doi: 10.1186/s40168-021-01046-5
15. Qi X, Yun C, Sun L, Xia J, Wu Q, Wang Y, *et al.*, Gut microbiota-bile acid-interleukin-22 axis orchestrates polycystic ovary syndrome. *Nat Med* 2019; 25: 1225-33. doi: 10.1038/s41591-019-0509-0
16. Sakaguchi N, Yoshida M, Kawai K, Harada M, Osuga Y, Hirota Y, *et al.*, Butyric acid-based self-assembling nanoparticles: a potential strategy to prevent development of polycystic ovary syndrome. *Mol Hum Reprod* 2026; 32: gaag013. doi: 10.1093/molehr/gaag013
17. Ferreira M, Silva AR, Costa MM, Pereira SS, Monteiro MP. Impact of sodium butyrate supplementation on insulin resistance and adipose tissue modulation in murine models of polycystic ovary syndrome. *Gynecol Obstet Invest* 2026; online ahead of print. doi: 10.1159/000551076
18. Boets E, Gomand SV, Deroover L, Preston T, Vermeulen K, De Preter V, *et al.*, Systemic availability and metabolism of colonic-derived short-chain fatty acids in healthy subjects: a stable isotope study. *J Physiol* 2017; 595: 541-55. doi: 10.1113/JP272613
19. Tolhurst G, Heffron H, Lam YS, Parker HE, Habib AM, Diakogiannaki E, *et al.*, Short-chain fatty acids stimulate glucagon-like peptide-1 secretion via the G-protein-coupled receptor FFAR2. *Diabetes* 2012; 61: 364-71. doi: 10.2337/db11-1019
20. Liu K, He X, Huang J, Yu S, Cui M, Gao M, *et al.*, Short-chain fatty acid-butyric acid ameliorates granulosa cells inflammation through regulating METTL3-mediated N6-methyladenosine modification of FOSL2 in polycystic ovarian syndrome. *Clin Epigenetics* 2023; 15: 86. doi: 10.1186/s13148-023-01487-9
21. Feng X, Xiao H, Wang X, Fu W, Gao J, Jiang Y, *et al.*, Butyric acid ameliorates PCOS-related reproductive dysfunction through gut-brain-ovary axis signaling and ovarian steroidogenic factor activation. *Front Endocrinol (Lausanne)* 2025; 16: 1604302. doi: 10.3389/fendo.2025.1604302
22. Geng L, Yang X, Sun J, Zhao Y, Zhang J, Wang W, *et al.*, Gut microbiota modulation by inulin improves metabolism and ovarian function in polycystic ovary syndrome. *Adv Sci (Weinh)* 2025; 12: e2412558. doi: 10.1002/adv.202412558
23. Ziaei R, Shahshahan Z, Ghasemi-Tehrani H, Heidari Z, Ghiasvand R. Inulin-type fructans with different degrees of polymerization improve insulin resistance, metabolic parameters, and hormonal status in overweight and obese women with polycystic ovary syndrome: a randomized double-blind, placebo-controlled clinical trial. *Food Sci Nutr* 2024; 12: 2016-28. doi: 10.1002/fsn.3899
24. Maddirevula MK, Nelson SM, Soliman AT, Alanazi AH, Hegazy N, Baig M, *et al.*, Effect of probiotic-derived metabolites on hormonal and metabolic profiles in women with polycystic ovary syndrome: a systematic review and meta-analysis. *Front Cell Infect Microbiol* 2025; 15: 1680840. doi: 10.3389/fcimb.2025.1680840
25. Yin T, Zhang Y, Shen S, Wang Y, Liu M, Zhao Y, *et al.*, Gut microbiota, a new approach to management of polycystic ovary syndrome: a systematic review, meta-analysis and meta-evidence of 26 randomized controlled trials. *J Ovarian Res* 2026; 19: 12. doi: 10.1186/s13048-025-01959-x
26. Su BS, Cao Y, Ma J, Huang W. BMI-stratified phenotypes of polycystic ovary syndrome: advances in gut microbiota research and personalized management strategies. *Front Endocrinol (Lausanne)* 2026; 17: 1734041. doi: 10.3389/fendo.2026.1734041
27. Sakata T. Pitfalls in short-chain fatty acid research: a methodological review. *Anim Sci J* 2019; 90: 3-13. doi: 10.1111/asj.13118
28. Salminen S, Collado MC, Endo A, Hill C, Lebeer S, Quigley EMM, *et al.*, The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. *Nat Rev Gastroenterol Hepatol* 2021; 18: 649-67. doi: 10.1038/s41575-021-00440-6
29. Vinderola G, Sanders ME, Cunningham M, Hill C. Frequently asked questions about the ISAPP postbiotic definition. *Front Microbiol* 2024; 14: 1324565. doi: 10.3389/fmicb.2023.1324565
30. Smith M, Lelah M, Goggans M, Tunio S, Naqib A, Burton-Freeman B, *et al.*, Investigation of the tolerability and potential health benefits of a novel butyrate generating supplement in a pilot human study. *Nutr Healthy Aging* 2024; 9: 133-44. doi: 10.3233/NHA-240005
31. Khade K, Kulkarni A, Sonawane S, Kaur G, Mangoli V, Joshi B, *et al.*, Gut microbiota dysbiosis in Indian women with PCOS may be linked to metabolic and hormonal dysregulation. *Future Microbiol* 2026; 21: 153-65. doi: 10.1080/17460913.2026.2634572