


Review

Advancing Precision Nutrition in Endometriosis Care: The Role of Nutrigenomics and Nutrigenetics

Maudlyn O Etekoachay, MPH¹, Devika Muraleedharan, MD², Subhasree Majumdar, PhD³, Mugisha Nsengiyumva, MPH⁴ 

¹ Inova Health System, Fairfax, Virginia, USA, ² Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia, ³ Zoology, Sonamukhi College, Sonamukhi, West Bengal, India, ⁴ Public Health and Scientific Research Center, Kigali, Rwanda

Keywords: Endometriosis, Nutrigenomics, Nutrigenetics, Personalized Diet, Precision Nutrition, Artificial Intelligence, Direct to Consumer Genetic Testing

<https://doi.org/10.62186/001c.124784>

Academic Medicine & Surgery

Endometriosis is a gynecological disorder that affects 10-15% of women of reproductive age. It is characterized as a chronic, inflammatory, and hormone-dependent disease in which the endometrial tissue is present on the external uterine lining, resulting in infertility and pelvic pain. Some research studies stated that about 97% of human diseases are monogenic diseases associated with genes. Thus, modifying dietary intake (personalized diet) can potentially prevent monogenic diseases.

Nutrigenomics and nutrigenetics have garnered substantial interest among researchers as potential avenues for managing chronic conditions like diabetes, cancer, obesity, and cardiovascular disorders. Nutrigenomics ascertains the effects of food and ingested nutrients on gene expression and regulation, tailoring nutritional needs to an individual's genetic makeup, thereby facilitating personalized diets. On the other hand, nutrigenetics investigates how an individual's genetic composition influences their response to dietary elements. Both fields could be beneficial in modifying various disease conditions. Furthermore, it explores the effects of precision nutrition, direct-to-consumer genetic testing, and the role of artificial intelligence in the nutrigenetics and nutrigenomics approach to managing endometriosis. This review aims to provide a comprehensive overview of potential treatment modalities for endometriosis through the lenses of nutrigenomics and nutrigenetics. It highlights the interplay between dietary interventions and gene expression, elucidating how personalized approaches could potentially modify the course of endometriosis.

1. INTRODUCTION

Endometriosis is a gynecological disorder in which the endometrial tissue is developed in the external uterine cavity, resulting in infertility and pelvic pain.¹⁻³ Endometriosis is often characterized as a chronic, inflammatory, and hormone-dependent debilitating disease.⁴ Endometriosis affects approximately 10-15% of women in their reproductive years, with about 70% of these women experiencing ongoing pelvic discomfort.⁵⁻⁷ The disease etiology is multifaceted and complicated involving hormonal, genetic, immunological, and environmental factors.⁸ Frequent indicators encompass intense pelvic discomfort, dysmenorrhea, dyspareunia, fertility challenges, fatigue, lower back pain, bloating, constipation, and diarrhea. Due to the potential lack of specific symptoms, diagnosis often faces delays.⁹ The delay in treatment may cause a decrease in fertility and reproductive function. Medical therapy aims to hormonally alter the menstrual cycle, inducing a pseudo-pregnancy, pseudo-menopause, or maintaining an anovulatory state. As of now, there are no definitive cures for endometriosis. The standard clinical approaches usually involve using hormonal therapies to inhibit estrogen produc-

tion, employing small-molecule drugs to alleviate pain, and conducting laparoscopic surgeries to eliminate endometriotic lesions.² However, hormonal therapy causes some severe side effects due to which some of the hormones like methyltestosterone and estrogen are phased out from the market. One extensively researched method involves administering estroprogestins and progestins for contraception, which has also been explored for delivering specific drugs targeting endometriosis.¹⁰ Various clinical strategies used for the treatment of vaginal infections include tablets, creams, vaginal rings, and vaginal suppositories.¹¹ Long-acting contraceptives that can be implanted, like Nexplanon®, and injectables such as Depo-Provera®, have been utilized in the treatment of endometriosis.¹² Likewise, extended-release GnRH products like Lupron Depot® are employed in the treatment of endometriosis. Endometriosis exhibits characteristics such as oxidative stress, angiogenesis, and matrix degradation. Consequently, directing drug therapy toward these specific targets may enhance therapeutic outcomes compared to presently employed methods.¹³

Diet is believed to influence the development of endometriosis, potentially impacting its onset and progres-

sion. Research suggests that certain dietary elements may contribute to an individual's risk of developing this condition.¹⁴ Moreover, Various lifestyle factors may affect endometriosis risk by potentially reducing inflammation. Physical activity and omega-3 fatty acids in the diet might lower levels of inflammatory markers e.g., interleukin6 (IL-6) and tumor necrosis factor-alpha (TNF α). Although the relationship between physical activity and endometriosis is not entirely clear, higher consumption of long-chain omega-3 fatty acids has been linked to a decreased risk of endometriosis.¹⁵ Some research studies stated that about 97% of human diseases are monogenic diseases associated with genes. Thus, monogenic diseases can potentially be prevented by modifying dietary intake (personalized diet) (Gaboony, 2011).

The research-focused approach of nutrigenetics and nutrigenomics emerges as a pivotal domain within precision nutrition, offering pathways to advance personalized nutritional interventions.¹⁶ They have garnered substantial interest among researchers as potential avenues for managing chronic conditions like diabetes, cancer, obesity, and cardiovascular disorders (Gaboony 2011). Nutrigenomics ascertains the effects of food and ingested nutrients on gene expression and regulation, tailoring nutritional needs to an individual's genetic makeup, and thereby facilitating personalized diets.¹⁷ On the other hand, nutrigenetics investigates how an individual's genetic composition influences their response to dietary elements (Gaboony, 2011). Both fields could be beneficial in modifying various disease conditions, for example, fish oil inhibits colonic tumor growth.

The exploration of a link between dietary factors and the onset of endometriosis has garnered significant interest, primarily driven by the observation that both normal bodily functions and the disease's pathological processes can be impacted by diet (Parrazzani, 2013). Here, in this review, we summarized the role of nutrigenetics, nutrigenomics, and precision nutrition in endometriosis treatment.

2. NUTRIGENOMICS AND NUTRIGENETICS IN ENDOMETRIOSIS

Sufficient and appropriate nutrient intake plays a vital role in averting the onset of chronic diseases.¹⁸ Dietary interventions have shown potential in both preventing and managing endometriosis as well as alleviating the associated pain.⁹ Maintaining an optimal equilibrium between the overall oxidation status and the body's antioxidant response is crucial for a balanced genomic system. Employing a nutrigenomic strategy involves bolstering the body's antioxidant levels by supplementing deficient antioxidants in individuals affected by such diseases.¹⁹ Nutrigenetics and nutrigenomics can be regarded as two distinct methodologies within the field of nutritional genomics.²⁰ Nutrigenetics examines the influence of genetic diversity, particularly in the form of a single-nucleotide polymorphism (SNP), on an individual reaction to dietary consumption e.g. An individual reaction to caffeine differs due to genetic variations in the CYP1A2 gene. This gene produces an enzyme in the liver responsible for breaking down caffeine, and

certain gene variants metabolize caffeine at different rates (Sadeghi et al., 2019). In essence, nutrigenetics explores how an individual's genetic makeup impacts their physical response to dietary consumption.²⁰ [Figure 1](#) depicts how dietary nutrition and nutrigenomics/nutrigenetics impact the overall health of an individual.

Several nutritional elements, such as folate, choline, methionine, selenium, and retinoic acid, have demonstrated the ability to influence alterations in DNA methylation patterns.²¹

Nutrigenomics and nutrigenetics play an evolving role in understanding endometriosis. They explore how individual genetic variations and dietary components interact, potentially influencing the development and progression of endometriosis. These fields examine how specific nutrients and dietary patterns might impact gene expression and biological pathways involved in the condition, offering insights into potential personalized dietary interventions or preventive strategies (Otero BMC and Bernolo LF, 2023). Nutrients significantly influence the vaginal microbiome diversity. Lacking of vitamins e.g., D, E, C, and A, in diet and high in sugar and fats may contribute to the infection of the vagina. Also, the presence of folate, calcium, and β -carotene in diet may decrease the chances of infection. These infections are associated with adverse outcomes like human immunodeficiency virus (HIV) transmission risk, preterm birth, high susceptibility to infection of human papillomavirus (HPV), as well as higher probabilities of developing cervical, endometrial, and ovarian cancers as shown in [Figure 1](#) (Ciberia et al., 2021). The different types of dietary supplements and their role in endometriosis are summarized in [Table 1](#).

In cases of endometriosis, CpG hypomethylation may result in the overexpression of steroidogenic factor 1 (SF1) or estrogen receptor β (ER- β). This overexpression can subsequently elevate the levels of estradiol and prostaglandin E2 (PGE2), promoting inflammation and facilitating cell growth. When diets lack these nutrients, it can lead to changes in lipid metabolism, increased oxidative stress, and abnormalities in epigenetic processes. Thus, giving proper food, diets, and nutrition can prevent the chances of endometriosis as discussed in [Table 2](#).²² A growing body of evidence indicates that extra virgin olive oil is rich in unsaturated fatty acids and phytochemicals could be used potentially for cardiovascular protection, cancer prevention, and anti-inflammatory properties.²³

Dietary elements could potentially impact the advancement and onset of endometriosis by influencing steroid hormone metabolism, the menstrual cycle, regulation of inflammation, oxidative stress, and muscle contraction.²⁴ Furthermore, incorporating nutrients possessing anti-inflammatory and antiestrogenic properties, such as antioxidants like curcumin, epigallocatechin gallate, quercetin, resveratrol, and inositol has been proposed to alleviate endometriosis-associated pain.^{24,25} The impacts of diet and nutrients on endometriosis and related symptoms e.g., pelvic pain and infertility, etc., are summarized herein and in [Table 2](#) and [Figure 2](#).

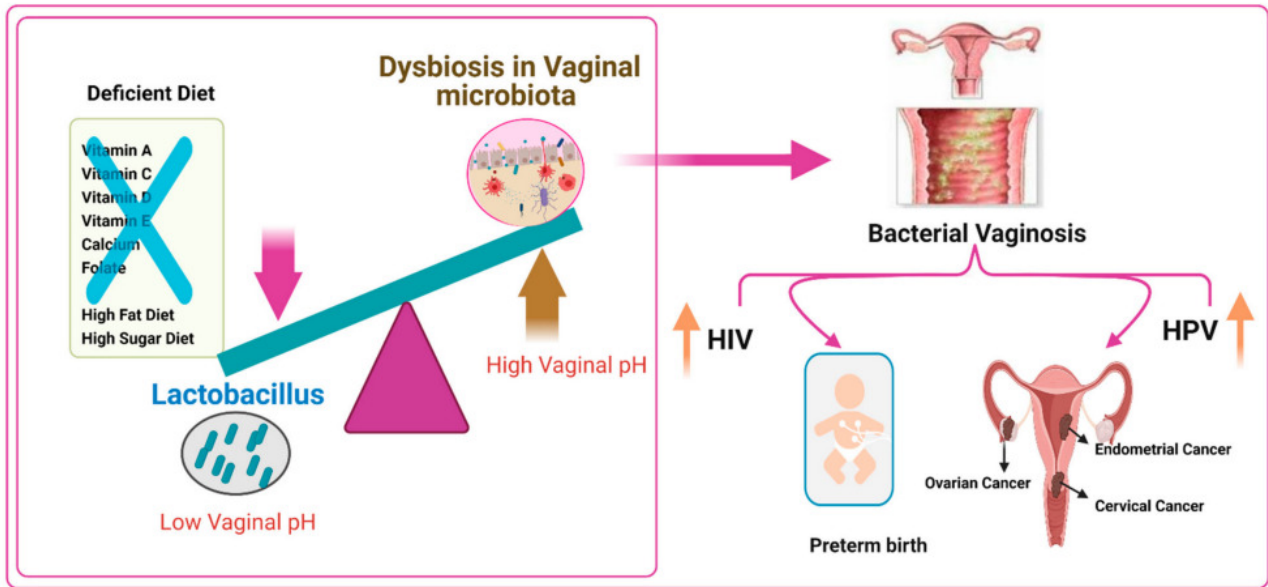


Figure 1. Diet and its Impact on vaginal microbiome. Deficiency of vitamins e.g., E,D,C, and A, and folate, calcium, and β -carotene in the diet but having high sugars and fats may alter vaginal microbiota and enhances the possibilities of bacterial vaginosis, and infections e.g., transmission risk of the human immunodeficiency virus (HIV), human papillomavirus (HPV), preterm birth, and cancer etc. Reproduced from an open-access journal under the term of Creative Commons Attribution (Ciberia et al., 2021). <https://doi.org/10.1038/s44222-023-00040-w>.

A meta-analysis conducted by Arab et al. in 2022 aimed to consolidate findings regarding the correlation between dietary intake of specific food groups and nutrients and the risk of developing endometriosis. Their research highlighted potential associations suggesting that an optimal intake of total dairy products, along with reduced consumption of red meat, trans fatty acids (TFA), and saturated fatty acids (SFA), might be linked to a decreased risk of developing endometriosis.¹⁴

A comprehensive review was conducted involving women diagnosed with endometriosis and those considered healthy. The aim was to investigate the potential correlation between diet and endometriosis. Ten studies were analyzed in total. The findings indicated that the intake of non-cruciferous vegetables, fruits, potatoes, legumes, dairy products, fish, vitamins (B12, C, D, and A), fatty acids-mono and polyunsaturated, as well as minerals like magnesium, calcium, potassium, appeared to lower the risk of developing endometriosis.²⁶

2.1. MEDITERRANEAN DIET

The Mediterranean diet, abundant in fruits, vegetables, whole grains, nuts, legumes, and olive oil has demonstrated multiple advantages for overall human health (Ciberia et al., 2021). Adopting a preconception Mediterranean diet by couples undergoing IVF/ICSI treatment contributes positively to the success of achieving pregnancy as evidenced by Vujkovic and associates (Vujkovic et al., 2010; Ciberia et al., 2021). A single-arm study conducted in Austria investigated the impact of the Mediterranean diet on pain associ-

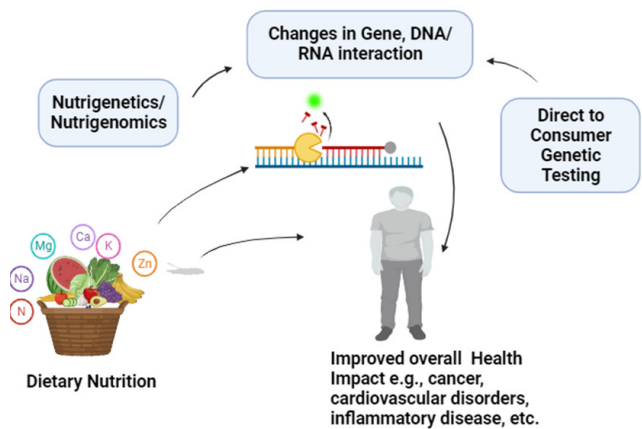


Figure 2. Dietary nutrition and Nutrigenetics/Nutrigenomics impacts on overall health.

ated with endometriosis. A particular dietary regimen comprising fresh vegetables, fruits, white meat, fatty fish, soy products, whole grain foods, magnesium-rich food sources, and cold-pressed oils was given to patients. The study revealed a notable alleviation in overall pain, including dysmenorrhea, dyspareunia, and dyschezia, along with enhancements in the general condition among participants.²⁷

In a case-control study conducted in Mexico, 82 infertile patients diagnosed with rASRM stages I–II endometriosis were randomly divided into two groups. One group adhered to a normal diet, while the other followed a high-antioxidant diet (HAD) for 4 months, tailored to each patient's energy requirements. Both groups demonstrated strong ad-

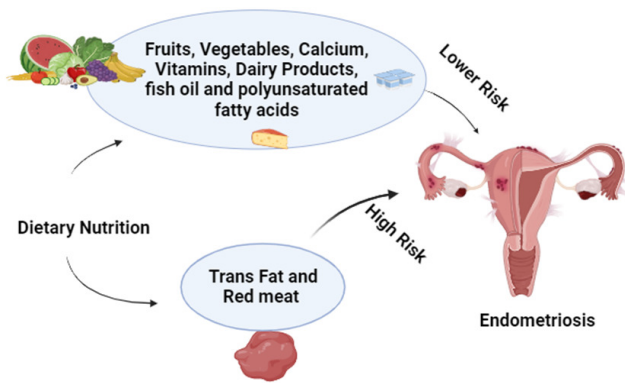


Figure 3. Nutrition and Endometriosis Risk.

herence, with 91.4% in the HAD group and 91.9% in the normal diet group completing the study. After 2 months of the intervention, the HAD group exhibited increased concentrations of vitamins (serum retinol, alpha-tocopherol, leukocyte, and plasma ascorbate), heightened activity of antioxidant enzymes (superoxide dismutase and glutathione peroxidase), and decreased levels of oxidative stress markers (malondialdehyde and lipid hydroperoxides).²⁷

2.2. DAIRY PRODUCTS

A cohort prospective study conducted by MD Nodler and associates among adolescent patients in Mexican female suggested that consuming dairy products, especially yogurt and ice cream, during adolescence might decrease the risk of being diagnosed with endometriosis later in life²⁸ as shown in [Figure 3](#).

A case-control study carried out among Iranian women between 2015-2016, involving 206 women without endometriosis and 207 with confirmed endometriosis through laparoscopy, revealed notable findings. The study suggested that the intake of green vegetables, red meat, dairy products (such as milk and cheese), fresh fruit, grains, and legumes lowers the risk of developing endometriosis. However, the consumption of carrots, green tea, fish, eggs, and oil did not show a significant relationship with the risk of endometriosis (M.D. Ashrafi et al., 2020).

A randomized controlled study was carried out by Sesti and associates in patients treated with hormones and dietary supplements. The study demonstrated that both hormonal suppression therapy and dietary supplementation have similar effectiveness in reducing non-menstrual pelvic pain.²⁹

2.3. FATS

Studies focusing on specific nutrients did not establish a significant association between saturated fat and animal fat intake and the risk of developing endometriosis.⁸

Long-chain polyunsaturated fatty acids (LC-PUFA) have positive effects on various physiological processes such as growth, neurological development, accumulation of lean and fat mass, reproduction, as well as both innate and ac-

quired immunity. Additionally, they impact the occurrence and severity of nearly all chronic and degenerative diseases, encompassing cancer, atherosclerosis, stroke, arthritis, diabetes, osteoporosis, neurodegenerative conditions, inflammatory diseases, and skin disorders (Gaboon, 2011). In xenograft models, dietary n-3 PUFAs effectively inhibited the growth of endometrial cancer cells (zheng et al., 2014). Omega-3 supplementation has demonstrated the potential to decelerate the expansion of endometrial implants, alleviate pain and inflammation, and enhance the quality of life for women diagnosed with stage III and IV endometriosis.²²

2.4. MULTIVITAMINS AND MINERALS

Selenium regulates the functions of numerous regulatory proteins involved in signal transduction, offering advantages in managing inflammatory diseases. Lowered selenium levels have been observed in both acute and chronic inflammatory conditions. In a study involving patients with endometriosis, simultaneous administration of vitamins E, C, selenium, and zinc showed an inverse correlation with the severity of the disease. Increased disease severity was noticed with reduced oral intake of antioxidant nutrients.²¹

Vitamin D might contribute to both the prevention and treatment of endometriosis. A meta-analysis conducted in 2020 revealed a correlation between low levels of vitamin D and a higher likelihood of being diagnosed with endometriosis, as well as a greater severity of symptoms.⁹

Four human studies, four animal studies, and four in vitro studies were done to assess the role of Vitamin D on endometriosis. While in vitro and animal studies indicated a potential regression of endometriotic implants and a reduction in invasion and proliferation following vitamin D supplementation, these outcomes were not mirrored in the findings of the meta-analysis.³⁰

In a significant and large cohort study, the correlation between vitamin consumption (C,E,B) and the occurrence of endometriosis was determined. Dietary habits were evaluated using a questionnaire of food frequency. Throughout a follow-up period encompassing 735,286 persons/years, 1,383 new cases of laparoscopically-confirmed endometriosis were identified among 70,617 women. The study confirmed an inverse relationship of vitamin C, E thiamine, and folate consumption with endometriosis.³¹

2.5. PROBIOTICS

Probiotics have been suggested as a potential strategy to improve reproductive health and mitigate the risk of diseases.³² Probiotic microorganisms like *Lactobacillus reuteri* and *Lactobacillus Plantarum*, naturally produce vitamin B (). They play a crucial role in endometriosis patients as vitamin B levels are often found to be lesser in the general population. Also, they enhance the effectiveness of the immune system and stimulate vitamin and mineral absorption. Additionally, these probiotic microorganisms might have the capability to generate specific enzymes such as esterase, lipase, coenzymes A, Q, NAD, and NADP.^{21,33}

Table 1. Different types of dietary supplements and their role in endometriosis treatment.

Nutrients	Role	References
Long-chain polyunsaturated fatty acids	Helpful in chronic and degenerative diseases e.g., skin diseases, atherosclerosis, cancer, diabetes, osteoporosis, neurodegenerative and inflammatory conditions	Gaboon, 2011
Omega-3 supplements	Enhance life quality in women diagnosed with stage III and IV endometriosis	Halpern et al., 2015
	Notable improvements in pain symptoms linked to endometriosis, including dyspareunia, dysmenorrhea, and chronic pelvic pain	Yalcin Bahat et al. ²¹
Zinc, Selenium	Shows inverse relationship with severity of endometriosis	Yalcin Bahat et al. ²¹
Probiotics	influence the microbial makeup of the human body	Thanaboonyawat et al. ³⁴ ; Feng and Liu. ³²
Lactobacilli	Protects the vaginal environment	Thanaboonyawat et al. ³⁴
Lactobacillus plantarum	Actively prevent the presence of sperm-agglutinating Escherichia coli (E. coli) bacteria	Yalcin Bahat et al. ²¹
Lactobacillus rhamnosus GR-1 and Lactobacillus fermentum RC-14	Help sustain and reestablish a healthy vaginal microbial balance in cases of vaginal dysbiosis	Yang et al. ³⁵
Vitamin D	Reduces pelvic pain and endometriosis risk by increasing antioxidant levels.	Barnard et al. ⁹
Zinc, Magnesium, Vitamin C and E	Can improve endometriosis risk as evidence from animal and human studies.	Yalcin Bahat et al. ²¹
Curcumin	In vitro, animal, and human studies evince a decrease in endometriotic lesion size preventing the recurrence of disease.	Yalcin Bahat et al., ²¹ ; Kizilay et al. ³⁶ ; Jelodar et al. ³⁷

Not only factors directly related to endometriosis but also individual patient factors can influence the choice of dietary interventions beneficial for women with endometriosis. For instance, in individuals diagnosed with irritable bowel syndrome (IBS), adopting a low-FODMAP diet has demonstrated efficacy in alleviating symptoms such as abdominal pain and bloating (Black et al., 2021). Consequently, for women dealing with both endometriosis and concurrent IBS, considering a low-FODMAP diet as a primary intervention might be advisable before exploring other dietary approaches (Black et al., 2021).

2.6. DIRECT-TO-CONSUMER NUTRIGENETICS TESTING

Genomic data holds a unique significance as it encompasses not just our genetic makeup but also that of our family and future generations, including our children. Lately, numerous companies have begun marketing DNA testing kits directly to consumers through the Internet to provide genetic testing to customers without medical oversight, offering predictions about personal risks for prevalent diseases like cancer, autoimmune conditions, or cardiovascular diseases.^{38,39} Generally, “direct-to-consumer genetic testing” is abbreviated as DTC-GT.³⁹ DTC-GT assesses inherited disease risks and has received recent approvals from the Food and Drug Administration as depicted in [Figure 5](#).⁴⁰

DTC-GT usually employs a technique known as SNP-chip genotyping, which examines specific variants across the genetic code, such as particular single nucleotide polymorphisms (SNPs) or small insertions or deletions. SNP-

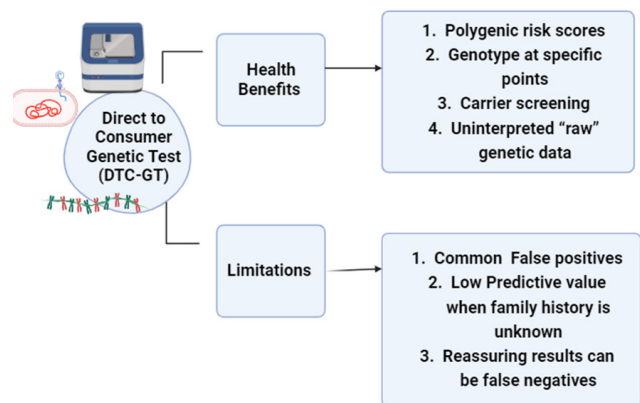


Figure 4. Health benefits and limitations of (DTC-GT).

chip genotyping is proficient at identifying common genetic variants. However, when it comes to detecting extremely rare variants, SNP chips often produce false positives, indicating the presence of variants that are not present in the individual’s DNA. Another increasingly employed method in DTC genetic tests is genome sequencing, which scrutinizes nearly the entire genetic code to identify its variants.⁴¹ The Food and Drug Administration (FDA), Medicare Centers, and Medicaid Services (CMS) offer some regulation of DTC-GT, but most genetic tests lack comprehensive federal oversight. [Figure 4](#) shows the health-related information/benefits and limitations of DTC-GT.

A study conducted by McGuire and associates among 1087 social networkers for their interest in personal genome testing (PGT) reported that about 6% of networkers have used PGT, 64% have an interest in its use, and 30% have no interest in attaining knowledge about diseases in their family.⁴²

It is remarkable to observe an increasing number of patients feeling empowered to make decisions regarding their reproductive choices and seeking support to achieve their family-building goals because of DTC testing. It was noticed that some individuals have already chosen a particular treatment, such as oocyte or embryo cryopreservation or IVF, relying on the interpretation of DTC results.⁴³ Thus, DTC testing could be an efficient approach to the diagnosis and treatment of endometriosis and related disorders.

As the demand for reproductive medicine rises and we grapple with a flood of misinformation from various media and online sources concerning fertility and reproductive health, it is crucial to ensure ethical and prudent practice of assisted reproductive technologies. Hence, we must receive education regarding the drawbacks of DTC testing, enabling us to offer optimal guidance and support to our patients on their reproductive journeys.

2.7. ARTIFICIAL INTELLIGENCE IN NUTRIGENETICS AND NUTRIGENOMICS

Experts anticipate that artificial intelligence (AI), deep and machine learning (ML) holds promise for diagnosing, managing, and treating an extensive range of medical conditions.⁴⁴ The most prevalent application of classical machine learning in healthcare is precision medicine, which forecasts the treatment procedures most likely to be effective for a patient by considering various patient characteristics and the context of the therapy (Kharb and Joshi). Few AI or machine learning applications aimed at enhancing women's health are currently in clinical practice, especially during pregnancy.⁴⁵ Leveraging a digital twin alongside AI provides the chance to create tailored and highly accurate recommendations that align with the patient's real-world circumstances. These recommendations can empower clinicians to make more precise, personalized, and effective decisions.^{44,46,47}

Davidson and associates conducted a study on novel methods e.g., artificial intelligence (AI), deep learning, and machine learning (ML) to improve pregnancy outcomes. Among 129 studies the prominent areas within the realm of pregnancy where AI and ML methods have seen extensive use comprise prenatal care, involving aspects such as fetal anomalies and placental functioning (73 instances); perinatal care, encompassing birth and delivery (20 instances); and addressing preterm birth (13 instances). Initiatives aimed at applying AI to clinical practice involve the development of clinical decision support systems (24 instances) and the creation of mobile health applications (9 instances).⁴⁸

LIMITATIONS

The major limitation is the integration of AI/ML into routine clinical practice, particularly concerning the regulation of these technologies.⁴⁴

3. PRECISION/PERSONALIZED NUTRITION

The ultimate objective of precision nutrition (PN) is to create personalized nutritional recommendations or prevent metabolic disorders by considering a blend of an individual genetic makeup, environmental influences, and lifestyle factors.⁴⁹⁻⁵¹ To achieve this objective, as depicted in the precision nutrition plate (Figure 4), factors extending beyond nutritional or genetic aspects—such as lifestyle choices like metabolomics, physical activity (PA) patterns, or gut microbiomics are increasingly recognized as substantial influencers deserving attention within the realm of precision nutrition.⁵⁰ The microbiota plays a crucial role in various biological functions of the host, including the development of the immune system, protection from harmful microorganisms, food breakdown during digestion, and production of micronutrients and bioactive compounds. Tailored intervention strategies could be formulated to “rebalance” an imbalanced microbiota or enhance the reaction to a particular diet. Probiotics, prebiotics, synthetic stools, and fecal transplantation have shown effectiveness in reducing weight in experimental obesity models, indicating the need for additional studies on human subjects.⁵² For an ideal assessment of the type, quantity, and frequency of food intake, real-time monitoring would be preferable over methods such as 24-hour dietary recalls or short-term measurements of food consumption. Table-embedded scales, automatic ingestion monitors with sensors, hand gestures, accelerometers, smartphone camera apps employing deep learning algorithms, and tooth-mounted sensors capable of recording various nutrients are devices designed to offer a more precise method for tracking and adjusting food consumption compared to dietary recalls.⁵²⁻⁵⁵

Improving the translation of PN (Precision Nutrition) science into products and services can be optimized by evaluating the equilibrium between advantages and drawbacks for both consumers and patients. Benefits encompass potential enhancements in specific health outcomes, the ease of utilizing user-friendly digital tools, and the effectiveness of a more tailored approach. Conversely, risks may stem from the expensive nature of recurrent omic testing, the time commitment required by intricate programs, and discrepancies between the scientific foundation and product assertions. These risks also involve apprehensions related to trust, privacy, and the management of data.⁵⁶ Figure 5 represents the precision nutrition plate where multifaceted aspects involved in tailoring personalized nutrition is summarized.

As per the Nutrigenetics/Nutrigenomics International Society (ISNN) three key dimensions should be addressed for the future direction of precision nutrition⁵⁷:

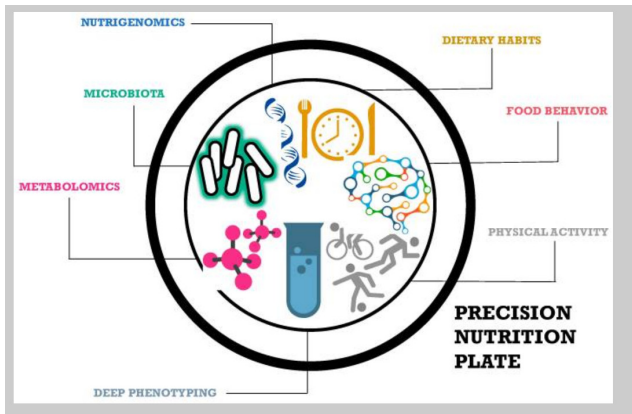


Figure 5. Precision Nutrition Plate represents the multifaceted aspects involved in tailoring personalized nutrition. Reproduced from an open-access journal under the term of Creative Commons Attributions.⁵⁰ DOI: 10.3390/nu9080913.

1. Refining conventional nutritional guidelines by segmenting them into population subgroups based on factors like gender, age, and social determinants.
2. Implementing individualized techniques derived from detailed and comprehensive phenotyping.
3. Integrating genetic-informed nutrition strategies that focus on rare genetic variations

In extensive studies, self-administered Food Frequency Questionnaires (FFQs) are typically favored for assessing food intake. However, all these methods demand thorough preparation before implementation, thus utilization of high-throughput omics tools facilitates a comprehensive and integrated exploration of nutrition.⁵⁸

3.1. MULTI-OMICS TECHNOLOGY

“Omics” encompasses scientific disciplines focused on high-throughput measurements of biological molecules, including DNA, RNA, proteins, and metabolites.⁵⁹ Several -omics technologies have been utilized in analyzing maternal urine and blood for pregnancy monitoring to identify potential diagnostic markers. However, these markers have not yet been integrated into clinical protocols. For example, the plasma concentration of ADAM-12 (A Disintegrin and Metalloproteinase-12) has exhibited changes in various pregnancy-related disorders. However, the effectiveness of ADAM-12 as a reliable marker for adverse outcomes remains uncertain.⁵⁹

Presently, many omics technologies offer comprehensive readouts at singular levels such as genomic, epigenomic, transcriptomic, proteomic, or metabolomic. Multi-omics, on the other hand, involves integrating two or more omics datasets for comprehensive data analysis, visualization, and interpretation. This approach aims to grasp the underlying biological mechanisms in various disease states. As multi-omics technologies advance, extensive genomic data, even at the single-cell level, is increasingly accessible (Atherine et al., 2022).

Functional genomic data, when combined with other omics data such as proteomics and metabolomics, provides a more comprehensive understanding of endometriosis. This integrated approach helps identify essential pathways and molecular signatures associated with the condition, offering potential benefits in diagnosis and the design of targeted therapies. CA-125, miRNA-200 family, miR-200b, HE4 (Human Epididymis Protein 4), and Circulating cell-free DNA are some key genetics and epigenetics biomarkers in endometriosis that affect the disease progression.⁶⁰

3.2. DIGITAL/ VIRTUAL TWIN TECHNOLOGY

In recent years, there has been an increasing demand for precise disease diagnosis and personalized treatment. The healthcare system is striving to tailor treatments to individual patients, aiming to maximize both effectiveness and efficiency.⁶¹ Digital twin technology is rapidly emerging as a game-changer in healthcare systems, fundamentally altering the delivery of patient care.⁶² Digital twins serve as a tool for patients to take an active role in their healthcare.⁶³ Also, digital twins have been employed in the industry since 2002 to enhance manufacturing processes and manage the entire product life cycle more effectively.⁶⁴ Through real-time monitoring of vital signs, physiological parameters, and other health-related data, digital twins possess the capability to detect early signs of deterioration or anomalies. This proactive identification allows healthcare providers to intervene early, preventing complications and fine-tuning treatment plans for optimal efficacy. Furthermore, digital twins foster communication and collaboration between patients and healthcare providers, fostering shared decision-making and a patient-centered approach to care.

The concept of a “virtual digital twin” aims to offer the most suitable, adaptable, efficient, and cost-effective dietary and lifestyle recommendations to an individual based on lifelong model and AI-driven models.^{46,52,65}

Moztarzadeh and associates introduce machine learning (ML)-driven methodologies for digitally replicating cancer, acknowledging certain constraints. The proposed methods encompass Decision Tree Regression (DTR), ML Linear Regression (ML LR), Gradient Boosting Algorithm (GBA), and Random Forest Regression (RFR). These technologies enable the system to process extensive patient data, constructing precise cancer progression models while effectively distinguishing between affected and healthy individuals. Leveraging a credible dataset, numerous machine-learning techniques have been created and simulated for breast cancer to illustrate the simplicity and feasibility of digital twin technology. This approach facilitates the simulation of cancer diagnosis and progression, providing insights into its future behavior. Such insights are invaluable in devising novel treatments, anticipating potential complications, and proactively addressing them.⁶⁵

A randomized controlled trial was conducted by Merlot and associates to assess the immediate and lasting effects, up to 4 hours, of a single 20-minute use of a digital therapeutic (DTx - Endocare) on pain levels in women enduring pelvic pain associated with endometriosis. Following treatment, both the Endocare and control groups exhibited a

significant reduction in clustered post-treatment pain compared to pre-treatment levels. Endocare consistently and significantly decreased pain perception up to 4 hours post-treatment, whereas the control group did not show significant differences. The mean perceived pain relief was notably higher for Endocare at 28% compared to the control group across all post-treatment assessments.⁶⁶

MAJOR CHALLENGES

(i) The data gathered and employed in crafting digital twins are presumed to be accurate and devoid of contradictions. However, one prevalent concern regarding data accuracy revolves around completeness, as incomplete data might introduce bias in predictions when utilized in the digital twin framework. (ii) Patient preferences often grapple with the balance between the quantity and quality of life. In certain scenarios, extended survival might coincide with a decline in the quality of life. Some patients prioritize a high quality of life even if it means acknowledging the potential shortening of their lifespan. (iii) A blending of real-world evidence and results sourced from randomized clinical trials. (iv) In healthcare, safeguarding data privacy and protection remains a critical concern, despite employing various forms of data encryption to manage data transfers.⁴⁶ Scientists are creating diets that might enhance how patients respond to cancer treatment by utilizing machine learning and genotyping to reveal the nutritional weaknesses of tumors thus paving new pathways for the treatment of disease using digital/ artificial technology.⁶⁷

4. PROSPECTS, CHALLENGES AND CONCLUSION

Endometriosis continues to be a substantial source of morbidity, significantly impacting the quality of life for women in their reproductive years.⁶⁸ Studies concluded a connection between genetic variations and endometriosis. However, the specific molecular pathways through which these

variations impact disease onset and progression remain unclear.⁶⁰

The integration of nutritionists into these teams might play a significant role in preventive and therapeutic outcomes in the future, contributing to the fight against endometriosis. Food and nutrients can impact both the development and advancement of the disease, opening the possibility of alternative or supplementary treatments for individuals affected by endometriosis. Further investigation is necessary to unravel the mechanisms of Nutritional genomics in improving the diagnosis of endometriosis. It is fundamental to design cost-effective interventional and clinical studies for PN, nutritional genomics, and AI/ML. Moreover, to attain the trust of policymakers and health professionals it is mandatory to design regulatory embodies.⁵⁸

A prominent limitation of Precision Nutrition (PN) is that most studies are observational rather than stemming from randomized controlled trials (RCTs) with evaluated clinical endpoints. Moreover, there is uncertainty about whether PN strategies can lead to improved endometriosis.⁵⁸

This review delves into various dietary supplements, nutritional genomics, and their influence on endometriosis and associated symptoms. Additionally, it elaborates on precision/personalized nutrition and the application of digital/virtual technology in addressing the progression of the disease. Furthermore, it explores the effects of direct-to-consumer genetic testing and the role of artificial intelligence in the nutrigenetics and nutrigenomics approach to managing endometriosis. Besides, more clinical approaches and research are needed to establish the accuracy and efficacy of this approach. Moreover, a nutritional approach to endometriosis management could be helpful for poor surgical candidates. As all are not easy to handle and operative procedure, nutritional approach can be a good alternative.

Submitted: September 03, 2024 EDT, Accepted: October 14, 2024 EDT



This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CCBY-4.0). View this license's legal deed at <http://creativecommons.org/licenses/by/4.0> and legal code at <http://creativecommons.org/licenses/by/4.0/legalcode> for more information.

REFERENCES

1. Becker K, Heinemann K, Imthurn B, et al. Real world data on symptomology and diagnostic approaches of 27,840 women living with endometriosis. *Sci Rep*. 2021;11(1):20404. [doi:10.1038/s41598-021-99681-3](https://doi.org/10.1038/s41598-021-99681-3)
2. Zondervan KT, Becker CM, Koga K, et al. Endometriosis. *Nat Rev Dis Primers*. 2018;4:9. [doi:10.1038/s41572-018-0008-5](https://doi.org/10.1038/s41572-018-0008-5)
3. Horne AW, Missmer SA. Pathophysiology, diagnosis, and management of endometriosis. *BMJ*. 2022;379:e070750. [doi:10.1136/bmj-2022-070750](https://doi.org/10.1136/bmj-2022-070750)
4. Gallagher CS, Mäkinen N, Harris HR, et al. Genome-wide association and epidemiological analyses reveal common genetic origins between uterine leiomyomata and endometriosis. *Nat Commun*. 2019;10:4857. [doi:10.1038/s41467-019-12536-4](https://doi.org/10.1038/s41467-019-12536-4)
5. Sugihara K, Kobayashi Y, Suzuki A, et al. Development of pro-apoptotic peptides as potential therapy for peritoneal endometriosis. *Nat Commun*. 2014;5:4478. [doi:10.1038/ncomms5478](https://doi.org/10.1038/ncomms5478)
6. Kim TH, Bae N, Kim T, et al. Leptin Stimulates Endometriosis Development in Mouse Models. *Biomedicines*. 2022;10:2160. [doi:10.3390/biomedicines10092160](https://doi.org/10.3390/biomedicines10092160)
7. Nazri HM, Greaves E, Quenby S, Dragovic R, Tapmeier TT, Becker CM. The role of small extracellular vesicle-miRNAs in endometriosis. *Human Reproduction*. Published online 2023:dead216. [doi:10.1093/humrep/dead216](https://doi.org/10.1093/humrep/dead216)
8. Parazzini F, Viganò P, Candiani M, Fedele L. Diet and endometriosis risk: A literature review. *Reproductive BioMedicine Online*. 2013;26(4):323-336. [doi:10.1016/j.rbmo.2012.12.011](https://doi.org/10.1016/j.rbmo.2012.12.011)
9. Barnard ND, Holtz DN, Schmidt N, et al. Nutrition in the prevention and treatment of endometriosis: A review. *Front Nutr*. 2023;10:1089891. [doi:10.3389/fnut.2023.1089891](https://doi.org/10.3389/fnut.2023.1089891)
10. Dowaidar M. Nanomedicine potential for endometriosis treatment. *Lat Am J Pharm*. 2023;42(1):1-28.
11. Swingle KL, Ricciardi AS, Peranteau WH, et al. Delivery technologies for women's health applications. *Nat Rev Bioeng*. 2023;1:408-425. [doi:10.1038/s44222-023-00040-w](https://doi.org/10.1038/s44222-023-00040-w)
12. Friend DR. Drug delivery for the treatment of endometriosis and uterine fibroids. *Drug Deliv and Transl Res*. Published online 2017:1-11. [doi:10.1007/s13346-017-0423](https://doi.org/10.1007/s13346-017-0423)
13. Garzon S, Laganà AS, Barra F, et al. Novel drug delivery methods for improving efficacy of endometriosis treatments. *Expert Opinion on Drug Delivery*. 2021;18(3):355-367. [doi:10.1080/17425247.2021.1829589](https://doi.org/10.1080/17425247.2021.1829589)
14. Arab A, Karimi E, Vingrys K, et al. Food groups and nutrients consumption and risk of endometriosis: a systematic review and meta-analysis of observational studies. *Nutr J*. 2022;21:58. [doi:10.1186/s12937-022-00812-x](https://doi.org/10.1186/s12937-022-00812-x)
15. Parasar P, Ozcan P, Terry KL. Endometriosis: Epidemiology, Diagnosis and Clinical Management. *Curr Obstet Gynecol Rep*. 2017;6(1):34-41. [doi:10.1007/s13669-017-0187-1](https://doi.org/10.1007/s13669-017-0187-1)
16. Di Renzo L, Gualtieri P, Romano L, et al. Role of Personalized Nutrition in Chronic-Degenerative Diseases. *Nutrients*. 2019;11(8):1707. [doi:10.3390/nu11081707](https://doi.org/10.3390/nu11081707)
17. Tuncel G, Hoti Q, Mocan G, Ergoren MC. A review of the Mediterranean diet and nutritional genomics in relation to cancer in women. *J Prev Med Hyg*. 2022;63(2 Suppl 3):E81-E86. [doi:10.15167/2421-4248/jpmh2022.63.2S3.2750](https://doi.org/10.15167/2421-4248/jpmh2022.63.2S3.2750)
18. Rajoka MI, Qadir MI, Pervaiz N, Ibrahim Z, Bukhari SA, Ahmad B. Nutrigenomics and Its Approaches for Control of Chronic Diseases. *Curr Biotech*. 2012;1(3):258-265. [doi:10.2174/2211550111201030258](https://doi.org/10.2174/2211550111201030258)
19. Da Costa LA, Badawi A, El-Sohemy A. Nutrigenetics and modulation of oxidative stress. *Ann Nutr Metab*. 2012;60 Suppl 3:27-36. [doi:10.1159/000337311](https://doi.org/10.1159/000337311)
20. Farhud D, Zarif Yeganeh M, Zarif Yeganeh M. Nutrigenomics and nutrigenetics. *Iran J Public Health*. 2010;39(4):1-14.
21. Yağın Bahat P, Ayhan I, Üreyen Özdemir E, İnceboz Ü, Oral E. Dietary supplements for treatment of endometriosis: A review. *Acta Biomed*. 2022;93(1):e2022159. [doi:10.23750/abm.v93i1.11237](https://doi.org/10.23750/abm.v93i1.11237)
22. Halpern G, Schor E, Kopelman A. Nutritional aspects related to endometriosis. *Rev Assoc Med Bras*. 61(6). [doi:10.1590/1806-9282.61.06.519](https://doi.org/10.1590/1806-9282.61.06.519)

23. Caradonna F, Consiglio O, Luparello C, Gentile C. Science and Healthy Meals in the World: Nutritional Epigenomics and Nutrigenetics of the Mediterranean Diet. *Nutrients*. 2020;12:1748. doi:10.3390/nu12061748
24. Mazza E, Troiano E, Mazza S, et al. The impact of endometriosis on dietary choices and activities of everyday life: a cross-sectional study. *Front Nutr*. 2023;10:1273976. doi:10.3389/fnut.2023.1273976
25. Sverrisdóttir UÁ, Hansen S, Rudnicki M. Impact of diet on pain perception in women with endometriosis: a systematic review. *Eur J Obstet Gynecol Reprod Biol*. 2022;271:245-249. doi:10.1016/j.ejogrb.2022.02.028
26. Zaragoza-Martí A, Cabrera-González K, Martín-Manchado L, Moya-Yeste AM, Sánchez-Sansegundo M, Hurtado-Sánchez JA. The importance of nutrition in the prevention of endometriosis: systematic review. *Nutr Hosp*. Published online November 27, 2023. doi:10.20960/nh.04909
27. Nirgianakis K, Egger K, Kalaitzopoulos DR, et al. Effectiveness of Dietary Interventions in the Treatment of Endometriosis: a Systematic Review. *Reprod Sci*. 2022;29:26-42. doi:10.1007/s43032-020-00418-w
28. Nodler JL, Harris HR, Chavarro JE, et al. Dairy consumption during adolescence and endometriosis risk. *Am J Obstet Gynecol*. 2020;222:257.e1-16. doi:10.1016/j.ajog.2019.09.010
29. Sesti F, Pietropolli A, Capozzolo T, Broccoli P, Pierangeli S, Bollea MR, et al. Hormonal suppression treatment or dietary therapy versus placebo in the control of painful symptoms after conservative surgery for endometriosis stage III-IV. A randomized comparative trial. *Fertil Steril*. 2007;88(6):1541-1547. doi:10.1016/j.fertnstert.2007.01.053
30. Kalaitzopoulos DR, Samartzis N, Daniilidis A, et al. Effects of vitamin D supplementation in endometriosis: a systematic review. *Reprod Biol Endocrinol*. 2022;20(1):176. doi:10.1186/s12958-022-01051-9
31. Darling AM, Chavarro JE, Malspeis S, Harris HR, Missmer SA. A prospective cohort study of Vitamins B, C, E, and multivitamin intake and endometriosis. *J Endometr*. 2013;5(1):17-26. doi:10.5301/je.5000151
32. Feng T, Liu F. Microorganisms in the reproductive system and probiotic's regulatory effects on reproductive health. *Computational and Structural Biotechnology Journal*. 2022;20:1541-1553. doi:10.1016/j.csbj.2022.03.017
33. Markowiak P, Ślizewska K. Effects of Probiotics, Prebiotics, and Synbiotics on Human Health. *Nutrients*. 2017;9:1021. doi:10.3390/nu9091021
34. Thanaboonyawat I, Pothisan S, Petyim S, et al. Pregnancy outcomes after vaginal probiotic supplementation before frozen embryo transfer: a randomized controlled study. *Sci Rep*. 2023;13:11892. doi:10.1038/s41598-023-39078-6
35. Yang S, Reid G, Challis JRG, et al. Effect of Oral Probiotic *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14 on the Vaginal Microbiota, Cytokines and Chemokines in Pregnant Women. *Nutrients*. 2020;12(2):368. doi:10.3390/nu12020368
36. Kizilay G, Uz YH, Seren G, et al. In vivo effects of curcumin and deferoxamine in experimental endometriosis. *Adv Clin Exp Med*. 2017;26(2):207-213. doi:10.17219/acem/31186
37. Jelodar G, Azimifar A. Evaluation of serum cancer antigen 125, resistin, leptin, homocysteine, and total antioxidant capacity in rat model of endometriosis treated with Curcumin. *Physiol Rep*. 2019;7(4):e14016. doi:10.14814/phy2.14016
38. Hauskeller C. Direct to consumer genetic testing. *BMJ*. 2011;342:d2317. doi:10.1136/bmj.d2317
39. Floris M, Cano A, Porru L, et al. Direct-to-Consumer Nutrigenetics Testing: An Overview. *Nutrients*. 2020;12(2):566. doi:10.3390/nu12020566
40. Apathy NC, Menser T, Keeran LM, Ford EW, Harle CA, Huerta TR. Trends and Gaps in Awareness of Direct-to-Consumer Genetic Tests From 2007 to 2014. *Am J Prev Med*. 2018;54(6):806-813. doi:10.1016/j.amepre.2018.02.013
41. Horton R, Crawford G, Freeman L, Fenwick A, Caroline F, Lucassen A. Direct-to-consumer genetic testing. *BMJ*. 2019;367:32. doi:10.1136/bmj.l5688
42. McGuire AL, Diaz CM, Wang T, Hilsenbeck SG. Social networkers' attitudes toward direct-to-consumer personal genome testing. *Am J Bioeth*. 2009;9(6-7):3-10. doi:10.1080/15265160902928209
43. Stanczyk FZ, Mandelbaum RS, Lobo RA. Potential pitfalls of reproductive direct-to-consumer testing. *F S Rep*. 2022;3(1):3-7. doi:10.1016/j.xfre.2022.01.007
44. Benjamens S, Dhunnoo P, Meskó B. The state of artificial intelligence-based FDA-approved medical devices and algorithms: An online database. *npj Digital Medicine*. 2020;3(1):118. doi:10.1038/s41746-020-00324-0

45. Lau AYS, Staccini P, Section Editors for the IMIA Yearbook Section on Education and Consumer Health Informatics. Artificial intelligence in health: New opportunities, challenges, and practical implications: Findings from the yearbook 2019 section on education and consumer health informatics. *Yearbook Med Inf.* 2019;28:174-178. doi:10.1055/s-0039-1677935
46. Kaul R, Ossai C, Mohammad Forkan AR, et al. The role of AI for developing digital twins in healthcare: The case of cancer care. Published online 2022. doi:10.1002/widm.1480
47. Angulo C, Gonzalez-Abril L, Raya C, Ortega JA. A proposal to evolving towards digital twins in healthcare. In: international work-conference on bioinformatics and biomedical engineering; 2020. doi:10.1007/978-3-030-45385-5_37
48. Davidson L, Boland MR. Towards deep phenotyping pregnancy: a systematic review on artificial intelligence and machine learning methods to improve pregnancy outcomes. *Brief Bioinform.* 2021;22(5):bbaa369. doi:10.1093/bib/bbaa369
49. Betts JA, Gonzalez JT. Personalised nutrition: What makes you so special? *Nutr Bull.* 2016;41:353-359. doi:10.1111/nbu.12238
50. de Toro-Martín J, Arsenault BJ, Després JP, Vohl MC. Precision Nutrition: A Review of Personalized Nutritional Approaches for the Prevention and Management of Metabolic Syndrome. *Nutrients.* 2017;9(8):913. doi:10.3390/nu9080913
51. Dumesic D, Chazenbalk G, Heber G. Chapter 13 - Precision Nutrition in Female Reproductive Health. In: Heber D, Li Z, Ordovas J, eds. *Precision Nutrition.* Elsevier; 2023:227-240. doi:10.1016/B978-0-443-15315-0.00002-X
52. Gkouskou K, Vlastos I, Karkalouso P, Chaniotis D, Sanoudou D, Eliopoulos AG. The “Virtual Digital Twins” Concept in Precision Nutrition. *Advances in Nutrition.* 2020;11(6):1405-1413. doi:10.1093/advances/nmaa089
53. Mattfeld RS, Muth ER, Hoover A. Measuring the consumption of individual solid and liquid bites using a table-embedded scale during unrestricted eating. *IEEE J Biomed Health Inform.* 2017;21(6):1711-1718.
54. Fontana JM, Farooq M, Sazonov E. Automatic ingestion monitor: a novel wearable device for monitoring of ingestive behavior. *IEEE Trans Biomed Eng.* 2014;61(6):1772-1779.
55. Mandracchia F, Llauro E, Tarro L, et al. Potential use of mobile phone applications for self-monitoring and increasing daily fruit and vegetable consumption: a systematized review. *Nutrients.* 2019;11(3):686.
56. Berciano S, Figueiredo J, Brisbois TD, et al. Precision nutrition: Maintaining scientific integrity while realizing market potential. *Front Nutr.* 2022;9:979665. doi:10.3389/fnut.2022.979665
57. Ferguson LR, De Caterina R, Görman U, et al. Guide and Position of the International Society of Nutrigenetics/Nutrigenomics on Personalised Nutrition: Part 1 - Fields of Precision Nutrition. *J Nutrigenet Nutrigenomics.* 2016;9:12-27. doi:10.1159/000445350
58. Tebani A, Bekri S. Paving the Way to Precision Nutrition Through Metabolomics. *Front Nutr.* 2019;6:41. doi:10.3389/fnut.2019.00041
59. Kharb S, Joshi A. Multi-omics and machine learning for the prevention and management of female reproductive health. *Front Endocrinol.* 2023;14:1081667. doi:10.3389/fendo.2023.1081667
60. Chiorean DM, Mitranovici MI, Toru HS, et al. New Insights into Genetics of Endometriosis—A Comprehensive Literature Review. *Diagnostics.* 2023;13:2265. doi:10.3390/diagnostics13132265
61. Sun Q, Lei Y, Zhang H, et al. A multifunctional nanoparticle for efferocytosis and pro-resolving-mediated endometriosis therapy. *Colloids Surf B Biointerfaces.* Published online 2022. doi:10.1016/j.colsurfb.2022.112893
62. Vallée A. Digital twin for healthcare systems. *Front Digit Health.* 2023;5:1253050. doi:10.3389/fdgh.2023.1253050
63. Syed-Abdul S, Li YC. Empowering patients and transforming healthcare in the post-COVID-19 era: the role of digital and wearable technologies. *J Pers Med.* 2023;13:722. doi:10.3390/jpm13050722
64. Venkatesh KP, Raza MM, Kvedar JC. Health digital twins as tools for precision medicine: Considerations for computation, implementation, and regulation. *npj Digit Med.* 2022;5:150. doi:10.1038/s41746-022-00694-7
65. Moztarzadeh O, Jamshidi M, Sargolzaei S, et al. Metaverse and Healthcare: Machine Learning-Enabled Digital Twins of Cancer. *Bioengineering.* 2023;10(4):455. doi:10.3390/bioengineering10040455

66. Merlot B, Dispersyn G, Husson Z, et al. Pain Reduction With an Immersive Digital Therapeutic Tool in Women Living With Endometriosis-Related Pelvic Pain: Randomized Controlled Trial. *J Med Internet Res*. 2022;24(9):e39531. [doi:10.2196/39531](https://doi.org/10.2196/39531)

67. Senior M. Precision nutrition to boost cancer treatments. *Nat Biotechnol*. 2022;40:1422-1424. [doi:10.1038/s41587-022-01502-z](https://doi.org/10.1038/s41587-022-01502-z)

68. Hansen KA, Eyster KM. Genetics and genomics of endometriosis. *Clin Obstet Gynecol*. 2010;53(2):403-412. [doi:10.1097/GRF.0b013e3181db7ca1](https://doi.org/10.1097/GRF.0b013e3181db7ca1)