

2023

## Staff Education to Promote Probiotic Breastfeeding Therapy

José Diaz  
*Walden University*

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# Walden University

College of Nursing

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José Diaz

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Walden University  
2023

Abstract

Staff Education to Promote Probiotic Breastfeeding Therapy

by

José Diaz

MSN, Walden University, 2014

Project Submitted in Partial Fulfillment  
of the Requirements for the Degree of  
Doctor of Nursing Practice

Walden University

January 2023

## Abstract

Preterm birth is the leading cause of death in children under 5. In addition, there are 22 million babies born underweight each year which also contributes to the infant mortality rate. Some reasons for the inability to thrive and survive are the infants' immature system, allostatic load inadaptability, and undiversified and underdeveloped microbiota. Human breast milk (HBM) provides lifesaving nutrients, which prevents necrotizing enterocolitis and mortality. In addition, probiotic supplementation helps reduce late-onset sepsis, morbidities, and mortality. A literature review provided substantial evidence that HBM and probiotics can improve an infant's microbiota, thus improving thrivability and survivability. Probiotics offset the infant's allostatic load, which may decrease the infant mortality rate. Furthermore, probiotics are involved in intestinal epithelium proliferation, nervous system maturity and function, and human life energy production. This Doctor of Nursing Practice (DNP) project addressed the medium-level knowledge gap of probiotics among healthcare professionals (HCPs). The educational empowerment model and the allostatic model assisted in educating HCPs on probiotics and probiotic breastfeeding therapy (PBT). A pretest and posttest measured the effectiveness of an in-service on probiotics, breastfeeding mothers and infants. The pretest had a 49% score, while the posttest resulted in an improved score of 95%. The posttest results answered the DNP project question of whether a probiotic staff educational program would improve the HCP's knowledge of probiotics and their use concerning PBT. The DNP project promotes positive social change by increasing the HCPs' knowledge of probiotics and PBT, while providing an appropriate recommendation that all HCPs undergo probiotic training.

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## Dedication

This DNP Project is dedicated to The Most High G\_D, and to all the souls of infants who never got the opportunity to experience a full life on Earth.

When considering the vast complexity of the Human Microbiome and the various Microbiotas, one cannot ignore the biblical writings of Genesis 2:7 where man was created from the dust, soil or bacterial microorganisms of the Earth, giving light to the idea if these biblical writings are nothing more than scientific codes waiting to be unraveled.

## Acknowledgments

I would like to acknowledge that this work would have never been possible without the tireless efforts and studies of scientific researchers before me who provided us with the knowledge and pathways needed to create this research project. If it were not for the “True Scientists” of this planet who sacrificed their lives, loves, families and freedoms for the discoveries of evolutionary facts, we future scientists and researchers would be faced with insurmountable challenges in finding G\_D and ourselves.

All the authors of the research articles in the reference list, who allowed me to discover, uncover, shape and reshape my goals and research, thank you all for your life commitment and works.

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Gloria Ester Morales who fought to keep me alive when illness plagued my dying childhood years.

Rubin Blades who once said: We are never alone as everyone plays a part in the greater good.

Author: If I am a success in any field, it was not solely due to my efforts and knowledge, but because of the gift the Most High G\_D blessed me with and the people HE placed in my path to propel me to the top.

Remember, it is never too late, to be great.

Thank you all for your contributions.

Praiseworthy and Blessed Is The Most High G\_D of Israel.



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## Section 1: Nature of the Project

### **Introduction**

According to the Center for Disease Control and Prevention (CDCP; 2021), infant mortality is the death of a child before its first year of life. The two categories of infant mortality are neonatal death, which occurs within the first 30 days after birth, and post-neonatal death occurring before the first year of life but after 2 months of birth (Chen et al., 2016). By the end of 2018, about 21,000 infants had passed away in the United States (CDCP, 2021). The five leading causes of death were congenital disabilities, maternal complications, injuries, sudden infant death syndrome, and low birth weight (CDCP, 2021). Low birth weight (LBW) falls into three main categories, the first being newborns under 2500 grams, very low birth weight (VLBW) weighing under 1500 grams, and extremely low birth weight (ELBW) under 1000 grams (Wolke, 2018; Abdallah et al., 2018; Tanaka et al., 2019). Maternal health complications contributing to infant mortality were hyperemesis gravidarum, infections, obesity, gestational diabetes, urinary tract infections (UTI), mental health issues, anemia, and hypertension (CDCP, 2020). There are over 383,000 annual preterm births (PTB) in the United States (CDCP, 2021). PTB falls into four categories, extreme preterm, those born under 28 weeks; very preterm between 28 and 32 weeks, moderate preterm 32 and 34 weeks; and late preterm, 34 to less than 37 weeks of gestation (World Health Organization [WHO], 2018; UpToDate [UTP], 2022).

The overall cost of PTB in the United States is over \$26 billion, while medical care alone surpasses \$17 billion annually (Waitzman et al., 2021). The cost of caring for a

healthy full-term child is about \$5,000, while the care and treatment of a preterm infant can easily exceed \$50,000 (National Healthy Start Association [NHSA], 2021). If they survive past the first year of life, many of these preterm children may need additional training and education to assist their development, surpassing 1 billion dollars (NHSA, 2021). In addition, parents, caregivers, and employers may endure a \$6 billion price tag from missing workdays (NHSA, 2021).

The US is one of the most medically advanced countries in the world and has one of the highest infant mortality rates (IMR). Some states have incredibly high infant death rates, as in the case of Ohio, which ranks 12th in the country and seventh in the top 10 states with the most infant mortalities (World Atlas [WA], 2018; Montgomery et al., 2020). The USA IMR is lowest within the first week of life, but after this period, it exceeds the death rate of peer countries (Chen et al., 2016). With birth weight playing a role in the IMR, it is not an accurate indicator as infants of average weight in the US have 2.3 deaths to 1000 births indicating that almost a third of the IMR occurs in infants with normal-birth weight (Chen et al., 2016). In the USA, the IMR is high among normal-weight babies with high APGAR scores (Chen et al., 2016). The USA IMR of 6.78 to 1,000 births occurs in American babies averaging 7.4 pounds, 38.8 gestation weeks, 51.2% are male, and the average mother's age is 27.4 (Chen et al., 2016). African Americans account for 15% of the IMR, which alludes that the IMR is not a result of racial disparity (Chen et al., 2016).

Probiotics promote the absorption of essential nutrients and proteins, indicating that they may improve the health function of the maternal and fetal microbiota,

improving survivability (Jäger et al., 2019). In addition, a deficiency in macronutrients and micronutrients can lead to LBW deliveries and adverse pregnancy outcomes (Rodríguez-Rodríguez et al., 2018). For this reason, there is a dire need to research the utilization of probiotics during pre-pregnancy, pregnancy, and post-pregnancy breastfeeding and determine if there is a correlation between the utilization of a strand-specific-probiotic and the reduction of PTB, LBW, and infant mortality or morbidity. Furthermore, studies that examine the most appropriate dosage, therapy duration, and type of probiotic strand are crucial to establishing efficacy and safety (Grev et al., 2018). Moreover, the analysis and mapping out of the maternal human microbiome may help predict infant mortality or morbidity as some pathogenic microorganisms appear to dominate the gut microbiota of PTB and LBW infants and the mother.

This Doctor of Nursing Practice (DNP) project created an educational presentation that educated healthcare professionals (HCPs) involved in prenatal and postnatal care about the potential evidence-based value of using probiotics with breastfeeding mothers and improving the knowledge practice-gap of probiotics among these providers. Providing the current evidence about probiotics and pregnancy will contribute to bridging the knowledge practice gap in medical providers' understanding of the potential use of probiotics with breastfeeding mothers to maintain and improve the outcome of LBW infants and PTBs.

### **Problem Statement**

More than 20 million infants are born underweight annually worldwide (Utami et al., 2020). In some countries, over 30% of these LBW infants die within the first year of

life, while others continue developing chronic and cognitive diseases well into their elder years (Utami et al., 2020). Furthermore, many of these infants experience underdeveloped organs and immune systems, making these LBW babies susceptible to infection and 20 times more likely to die than normal-weight infants (Utami et al., 2020). Prenatal care focusing on disease prevention and nourishment appears to be the fundamental approach in helping these LBW infants survive. Unfortunately, undernourishment, or modern-day famine, is one of the leading causes of death in children and is challenging to remedy (Million et al., 2017). Three leading preventers of malnutrition are clean water, viable food, and breastfeeding (Million et al., 2017). In life-threatening malnutrition, undigested foods were discovered in the intestinal tract, suggesting that an underdeveloped gut microbiota lacking diversity may be insufficient in digestive enzymes and friendly bacterial life forms to break down, ferment, or absorb food substances (Million et al., 2017). Many pathological conditions of underdeveloped gut microbiota are a result of unfriendly microflora, which can be tamed or removed through the use of specific probiotics as these friendly bacteria compete with unfriendly bacteria in absorbing available nutrients and attaching to intestinal epithelial, which alters the environment to prevent the viability of unfriendly microflora (Łubiech et al., 2020).

Considering the life values of probiotics and the current health literacy practice gap about probiotics and PBT among HCPs, the DNP staff educational in-service involved HCPs who are indirectly or directly involved in prenatal and postnatal care, especially with breastfeeding therapy or lactation consultation. The DNP Project was significant as registered nurses and advanced practice registered nurses (APRN) possess



medium-level knowledge of probiotics with inadequate awareness of the various strands (Fijan et al., 2019). The current nursing knowledge of probiotics is limited to only three strands of probiotics, *Lactobacillus rhamnosus*, *Lactobacillus acidophilus*, and *Bifidobacterium bifidum* (Fijan et al., 2019). Furthermore, knowledge of the utilization of probiotics among HCPs appears to be limited to the treatments of antibiotic-related diarrhea, constipation, and allergy prevention (Fijan et al., 2019). This lack of probiotic health literacy is critical, as knowledge gaps among HCPs can make the difference between saving a patient's life and causing injuries. Fijan et al. (2019) mentioned that 79% of HCPs have recommended probiotic supplementation but need sufficient knowledge of probiotics, prebiotics, or fermented foods to safely and effectively make such recommendations. Patients place their lives and well-being in the providers' hands, making it imperative that HCPs advising for or against a probiotic supplementation must be competent and knowledgeable of the product on which they are educating the patient. In addition, many HCPs are quick to reject complementary and alternative therapies which indicate a clinical bias of denying the patient access to a holistic approach and possible relevant treatment options.

### **Purpose Statement**

To my knowledge, no educational programs have focused on the health benefits of probiotics or PBT in either hospital or outpatient clinical environment. Considering that HCPs have an average knowledge of probiotics and their benefits, a widely-advertised and target-focused probiotic educational program would increase the

proficiency and familiarity of probiotics among healthcare practitioners (Fijan et al., 2019).

The practice-focused question guiding this DNP Project is: “Will implementing a probiotic staff education in-service training program improve the healthcare professional's knowledge of probiotics and their use concerning PBT?”

The DNP project provided in-service training focused on increasing the HCPs’ knowledge of the human microbiome and probiotics concerning maternal and infant microbiota and the health benefits of probiotic implementation during breastfeeding therapy, via breastfeeding mothers’ ingestion of probiotics and prebiotics. The PBT program provided a pretest, posttest, and in-service on the benefits, purpose, and definition of probiotics based on the International Scientific Association for Probiotics and Prebiotics (ISAPP).

According to the ISAPP, probiotics are living microorganisms that, when prescribed sufficiently, the host will experience beneficial health outcomes (Fijan et al., 2019). These live nonpathogenic microorganisms predominately consist of yeast derivatives such as *Saccharomyces boulardii* or lactic acid bacterium as in the case of *Lactobacillus* species and *Bifidobacterium* species (Wilkins & Sequoia, 2017). Probiotics are safe for infants and adults and effective in supporting the treatments involving gastrointestinal electrolyte absorption, restoring gastrointestinal permeability, *Clostridium difficile*, hyperintestinal epithelial permeability (leaky gut), antibiotic-associated diarrhea, traveler's diarrhea, hepatic encephalopathy, irritable bowel syndrome,

and several functional gastrointestinal disorders (Wilkins & Sequoia, 2017; Ahmadi et al., 2020).

In addition, probiotics decrease the development of obesity, diabetes, respiratory tract infections, hypercholesterolemia, necrotizing enterocolitis (NEC), colic, streptococcal tonsillitis, hypertension, ulcerative colitis, urinary tract infections, and various types of diarrhea. However, it also maintains optimal gastrointestinal function by breaking down carcinogens, fermenting undigested foods, and synthesizing and absorbing vitamins, trace substances, minerals, and electrolytes (Łubiech et al., 2020). Administering probiotics to pregnant mothers affects their mammary gland probiotic colonization by the increasing concentration of Lactobacilli and Bifidobacteria in both matured breast milk and the mother's colostrum (Łubiech et al., 2020). Mothers who ingest probiotics may have a more significant influence on the health of the infant as human breast milk (HBM) has been noted to increase the presence of Lactobacillus species, alter the infant's microbiota and promote microbiome diversity in the infant's feces (Shin et al., 2021). In addition, HBM favors infant growth through increased body length, weight gain, and cephalic perimeter (Morais et al., 2021). LBW babies are at a higher risk of death or developing lifelong neurological conditions, which indicates that the presence of an undeveloped intestinal microbiota is linked to malnutrition regardless of food intervention, which gives light to the importance of promoting PBT (Aceti et al., 2017; Million et al., 2017).

### **Nature of Doctoral Project**

The PBT is a staff education DNP project to promote knowledge of the human microbiome, prebiotics, probiotics, and the benefits of ingestion of probiotics by breastfeeding mothers. The DNP project conducted an in-service presentation for HCPs. In-service education plays a crucial role in professional knowledge expansion, improving healthcare quality, and propelling healthcare staff to meet the patients' and organizations' goals and needs (Chaghari et al., 2017). The in-service consisted of a pretest to determine the staff current knowledge, a lecture to build staff knowledge, and a posttest to verify retention and knowledge growth. Furthermore, the DNP project analyzed the results of the exams utilizing percentage calculation to determine the effectiveness of the staff education project.

The in-service focused on the allostatic model and empowerment educational approach as it decreases the incompatibility of educational-medical alignment (Chaghari et al., 2017). The empowering educational approach promotes engagement and problem-solving awareness and provides relevant result-oriented material (Chaghari et al., 2017). This approach also motivated the staff and taught them how to expand their knowledge of probiotics outside the in-service by developing analytical research probing skills (Chaghari et al., 2017).

In the case of the allostatic model, unlike homeostasis, allostasis understands that there are no fixed points in the human microbiome as everything is in a constant state of fluctuation, including the death of human tissue; this also extends to experiencing hunger, thirst, and requiring sleep or movement; these allostatic responses range from supportive

to defensive as they are there to protect life (Tonhajzerova & Mestanik, 2017). When considering allostasis, it is vital to understand that a newborn may overestimate a threat resulting in a more significant adverse risk reaction which can result in the development of other biological concerns (Tonhajzerova & Mestanik, 2017). For this reason, considering that "patterns lead to predictabilities," it is imperative to assess patterns and predict forthcoming events to decrease the potential risk of hidden stressors. This phase of prenatal care will assist the providers in determining the infant's pathological genetic predisposition by examining the maternal and parental medical history and considering administering probiotics that have been proven through evidence-based research to address specific biological concerns. Exposure to stressors in infants and children determines their development and clinical reactions, resulting in either standard or biological and behavioral dysfunctions (Tonhajzerova & Mestanik, 2017). The allostatic model allows us to remain conscious of the multidimensional responses of the human body to stressors, especially the reactions of a new being (newborn) in our medical-biological world. These sporadic reactions to stressors will affect the infant's development, survivability, and thriving throughout the first year of life, which can have positive outcomes considering the child can adapt biologically to the stressors (Tonhajzerova & Mestanik, 2017). The utilization of the allostatic model promotes a strong applicable awareness of science in nursing.

### **Significance**

This DNP staff education project may play a significant role in preventing infant mortality and morbidity worldwide. As to my knowledge, it is the first of its kind to

synthesize the concept of the allostatic biological event of an LBW or preterm newborn with consideration of the utilization of PBT to improve or diversify the infant's microbiota in order to improve the survivability and thriving of the first year of life. It is essential for medical evolution that HCPs understand the function and power of the neonatal microbiota and its involvement in the survival and ability of an infant to thrive. The human gut microbiota is a complex bacterial-dominated environment consisting of parasites, viruses, archaea, and fungi (George et al., 2022). There are at least 150 different species in the 100-plus trillion bacteria found in the intestinal tract, making the human microbiome a relatively untapped high-level science (George et al., 2022).

Breastfeeding helps develop the infant's microbiota as *Bifidobacterium* species, *Lactobacillus* species, and *Staphylococcus epidermidis* are in HBM (Simpson et al., 2018; George et al., 2022). Through direct breastfeeding (DBF), the infant's gastrointestinal microbiota will evolve and become one of the most significant health determinants in life, shaping the child's immunity, metabolism, neurological system, nutrient absorption, and the prevention of diseases throughout the adult years which include asthma, allergies, autism spectrum disorders, obesity, and attention deficit hyperactivity disorder (George et al., 2022). The importance here is that poor gut-microbiota diversity may result in the development of asthma and other respiratory conditions, which is an urgent pediatric concern as respiratory malfunction can lead to permanent respiratory failure (Moossavi et al., 2018). Better gut microbiota may explain why breastfed infants have a higher rate of survivability and a lower rate of acquiring an

infection (Bonner, 2019). HBM is the gold standard for LBW preterm babies as it provides the most lifesaving nutrients (Aceti et al., 2017).

Furthermore, probiotic supplementation helps reduce the development of late-onset sepsis and other pathological conditions (Aceti et al., 2017). It is imperative to mention that for probiotics to provide immunological equilibrium, the correct probiotic (family, genus, species), duration of therapy, disease-specific strand, and daily dosage of at least 5 billion colony-forming units (CFUs) is required (Wilkins & Sequoia, 2017). These key points were taught to stakeholders in the staff education in-service training.

During the research priority-setting phase, the stakeholders selected for this DNP project were HCPs. HCPs are essential stakeholders in this educational project as they are clinical providers, decision-makers, and life influencers who can guide the patient's healthcare and preventative practice decisions. In addition, by involving APRN stakeholders in the research project, we not only incited their curiosity about the topic of PBT but also allowed us to discover and meet their needs concerning their patients and practice needs (Grill, 2021). One key element as to why APRNs, high-level providers (nurse practitioners and midwives), and physicians are crucial stakeholders is because they will be involved in the prenatal and postnatal care of the patient, as well as provide education and guidance on breastfeeding therapy. Furthermore, HCPs tend to develop personal bonds with the patient, which allows HCPs to tailor their clinical approach to the community and the patient's health needs by identifying the most appropriate probiotic strands for the patient and community.

As a result of this acknowledgment of the HCPs' role, the potential contribution to nursing practice occurs by decreasing the knowledge gap and increasing the awareness and knowledge of the health benefits of utilizing probiotics during breastfeeding therapy and maternal postnatal care, as existing research shows that the consumption of probiotics confers health benefits, which includes preventing or improving certain pathological conditions which include PTB reduction, NEC, gestational diabetes, and bacterial vaginitis (Grev et al., 2018; Chen et al., 2019).

Furthermore, when considering the transferability of research results transitioning from paper to practice, it is essential to find a similar and relevant ground between the research environment and the natural world (Colorado State University [CSU], 2022). In the case of PBT, the research's most salient relevance and applicability are that the diversity of an infant's microbiota indicates disease resistance. By supplementing the breastfeeding mother's microbiota with probiotics, the mother can diversify and improve the infant's ability to resist the negative allostatic changes of its environment and possibly improve survivability and thriving. Although transferability cannot always provide a complete solution to a problem, it can support HCPs in modifying, reshaping, and discovering new best practices (CSU, 2022). In the case of probiotic and PBT training, it may help clinicians to understand the effects of probiotics and how to apply them to improve the overall health and microbiota of the mother and infant. By increasing and fortifying this knowledge, one can implement a positive social change that creates an opportunity to uphold and advance culture, organization, or in this case, the advanced practice of applied science of nursing (CSC, 2021). Furthermore, by increasing the



knowledge of probiotics and their safety among HCPs, I hope that it will lead to an increase in provider self-esteem, confidence, worth, support, and further research of probiotics and PBT to facilitate infant survivability and thriving.

### **Summary**

The implementation of PBT will provide newborns with probiotic-based HBM, which is one of the ideal approaches in helping an infant to live and grow as HBM contains hundreds of thousands of bioactive elements that protect the infant from developing many inflammatory and disease-causing conditions; probiotics also help build and diversify the infant gut microbiota to fight off illness, which allows it to adapt to stressors (Norarbartolo et al., 2021). Furthermore, PBT may help the survivability and thriving in an LBW or preterm infant as Lactobacilli and Bifidobacterium plays a vital role in the absorption of minerals, vitamins, and various nutrients, as well as promote infant growth (Radke et al., 2017; Aloisio et al., 2018). It is detrimental to acknowledge that nutrients play a significant role in the infant's microbiota, environmental adaptability, thriving, and survivability, a problem that affects the entire planet's wellbeing both financially and biologically, especially when tens of thousands of infant die each year in the United States alone (CDCP, 2021).

Section 2 illustrates the effects of infant mortality, LBW, and PTB. In addition, the concepts and science of the human microbiome and its relevance to infant mortality and nursing practice is detailed in Section 2. Furthermore, the rationale and function of the allostatic model's application towards PBT, infant mortality prevention and nursing science will be detailed, as well as the DNP student's role in increasing a higher scientific

awareness among current and future nurses and how this can improve and propel the nursing profession into a better future.

## Section 2: Background and Context

### **Introduction**

There are over 383,000 annual PTB in the US; worldwide there are 15 million annual PTB and over 20 million LBW, which is a clear indication of the health and future of our planet and species (Casavant et al., 2019; Utami et al., 2020; CDCP, 2021). Because in the US about 21,000 infants died in 2018, it is important to take an expansive view of these deaths; if these infants survived and grew up as healthy reproductive adults, they may have contributed not only to the existence of the human species but its technological advancement as well. The loss of one infant is the potential loss of multigenerational families. For this reason, medical science needs to change its perspective and approach on this issue.

In mid-1980, medical professionals believed that infants did not feel pain due to their underdeveloped nervous system; later, this proved untrue after the performance of countless surgical procedures on infants without administering anesthetic medication (Casavant et al., 2019). These assumptions inhibit the progression of medical science and endanger patients' lives. For this reason, the allostatic model was implemented in this DNP Project as it provides a better understanding of continuous multidirectional changes in probiotics, prebiotics, and the human microbiome. The classical homeostatic school of thought is outdated and unrealistic as nothing in existence ever stagnates but instead is in a continuous physical and psychological state of acclimation. Whether conceived, born, or dead, the human body is in a constant multidirectional biological seesawing event of allostasis.

Biological allostatic stress responses undergo three phases, the Alarm phase, the Resistance phase, and the Exhaustion phase (Tonhajzerova & Mestanik, 2017). According to Tonhajzerova and Mestanik (2017), at the alarm phase, the body will ignite the hypothalamus-hypophysis-adrenal axis, sympathoadrenal axis, and proopiomelanocortin system by releasing endorphins and affecting blood pressure, electrolytes, glycemia, cardiac rhythm, and circulation (Tonhajzerova & Mestanik, 2017). The resistance phase involves the body's compensatory mechanism involving the process of inhibition and control to lessen the damage, such as increasing the release of neutrophils, thrombocytes, and other mechanisms to decrease the inflammatory responses (Tonhajzerova & Mestanik, 2017). In the third phase, as the name implies, the body can no longer adapt to the changes of prolonged stressors and, as a result, enters the states of mechanical failure and pathological development, which may include death, as seen in the mortality of infants (Tonhajzerova & Mestanik, 2017). As a result, using probiotics may help improve the infant's resistance to stressors, as fermented foods reduce systemic inflammation and oxidative stress (Slykerman et al., 2017). In addition, the oral administration of probiotics both while pregnant and after birth transforms, adjusts, and develops the immunological genetic expression (Jagodzinski et al., 2019).

The following areas in this section will cover the relevance of how the allostatic model and PBT can improve postnatal care and HCPs' knowledge of probiotics, considering that this is an area lacking in the nursing practice (Fijan et al., 2019). In addition, the local background and context area will address evidence that supports the practice question, which will merge into the role of the DNP student in facilitating an in-

service educational program to improve clinicians' knowledge of probiotics and PBT. Furthermore, the role of the project team supported and helped guide this DNP project through its many challenges, which included resistance experienced from medical organizations, as well as universities and colleges of nursing and midwifery. This project provides valuable medical career insight into the workings of the human microbiome, probiotics, prebiotics, fermented foods, and PBT.

### **Concepts, Models, and Theories**

The human microbiome has opened the scholastic doors to question whether the uterus is a sterile environment considering that there are various bacterial life forms in the amniotic fluid, meconium, umbilical cord, and placenta in healthy births (George et al., 2022). The human gut microbiota is a complex bacterial-dominated environment that, as mentioned, consists of parasites, viruses, archaea, and fungi (George et al., 2022). Thus far, over 150 different species reside in the 100-plus trillion bacteria found in the intestinal tract (George et al., 2022).

The goal in the prevention of infant mortality begins with first understanding and attempting to help the infant adjust and adapt to both its internal and external stressors, as these stressors can result in shifting the body's attention from development, digestion, and cellular regeneration to a more metabolic taxing focus of cardiovascular, immunological, respiratory, or neurological compensation (Casavant et al., 2019). For this reason, the allostatic model is imperative to consider when approaching treatments with probiotics. The aim is to give the infant's microbiota the necessary organisms to support its biological system in appropriately responding to stressors.

A stressor is any event that threatens the infant's life, whether the threat is perceived or existent (Casavant et al., 2019). When the infant reacts to these stressors, she or he will respond by counteracting the event with continuous restful and non-restful responses, shutting down due to extended response and lack of adaptation, or developing a hyperactive compensatory mechanism due to an inability to adapt to the stressors (Casavant et al., 2019).

The allostatic load may be an appropriate framework for improving the thriving and survivability of PTB and LBW infants, as the transgenerational allostatic load is a genetic inheritance (Casavant et al., 2019). Similar to how an infant's microbiota is inherited from the parents, the infant's ability to adapt to stressors is also an inherited trait (Casavant et al., 2019). Furthermore, the maternal reaction to stressors will directly affect her neuropeptides and hormones such as oxytocin, progesterone, and prolactin levels, which can determine the stability of the pregnancy or whether the child becomes a PTB statistic (Casavant et al., 2019). In addition, the higher an infant's allostatic load, the more significant its risk of developing NEC, intraventricular hemorrhage, retinopathy, dysbiosis of the gut microbiota, neurodevelopment delays, feed intolerance, and bronchopulmonary dysplasia (BPD), which can proceed throughout adult life and increase its ability to develop many stress-related diseases (Casavant et al., 2019).

The motivating idea behind this doctoral project is to address the probiotic knowledge practice gap and promote PBT in order to help the infant gut microbiota adapt to its environment and potential stressors, which may decrease its allostatic load and improve survivability and thriving; this is in consideration that the gastrointestinal

microbiota has a protective mechanism of synthesizing cortisol, which decreases the allostatic load (Casavant et al., 2019). Casavant et al. (2019) suggest that feeding intolerance can result from the infant's gut microbiota and cortisol levels. A gap in practice is providing healthcare professionals and medical providers with training that would increase their knowledge of the human microbiome and the utilization of prebiotics and probiotics in breastfeeding mothers.

Considering that the body's regulatory systems under stressors abruptly affect the physiological processes of glucose regulation and metabolism, hydration balance, cardiovascular regulation, and thermoregulation, more research is needed to explore which probiotic strain may aid in building up the infant's resistance to internal and external stressors in order to improve survivability and thriving (Tonhajzerova & Mestanik, 2017).

The idea of homeostasis suggests that when the biological environment steers away from a tolerable function, the physiological systems initiate a reactive response to guide the body back to a viable baseline. However, once that threat is no longer present, the regulatory response is no longer active (Tonhajzerova & Mestanik, 2017). The limitation to this concept is that the body is ever-changing, just as no breaths, whether inhaled or exhaled, are equal, and not all cardiac pulses carry the same force or blood components. Everything in the human body and its microbiota is ever-changing, adjusting and adapting to its environments. It is this continuous adaptability that further limits the idea of homeostasis as it does not take into account the body's ability to learn and anticipate future anomalies, which prepares it for the demands of the environment by

activating protective systems in order to reduce or prevent damage, as patterns lead to predictability (Tonhajzerova & Mestanik, 2017).

### **Relevance to Nursing Practice**

The purpose of this study is to attend to the practice knowledge gap of probiotics by helping clinicians understand the function and appropriate use of probiotic supplementation in breastfeeding mothers and opening the door for future research on the utilization of probiotics in prenatal and postnatal care. Although over 70% of practitioners recommend probiotics supplementation to their patients, most medical providers possess no more significant than a medium level of probiotic knowledge, indicating that most allopathic medical providers are not qualified to recommend probiotics and possibly other complementary alternative approaches (Fijan et al., 2019). One strategy to remedy this knowledge gap is to offer probiotics in-service educational programs to increase the knowledge level in the healthcare field and improve probiotic recommendatory skills. To the researcher's knowledge, there are no proactive approaches currently available to promote complementary and alternative practices in probiotic knowledge among healthcare professionals and medical providers with prescriptive authority, especially among high-level providers such as nurse practitioners. The DNP project addressed this issue by developing and delivering a probiotic educational in-service focusing on PBT.

Probiotics given during pregnancy and postpartum have decreased gastrointestinal discomfort and the inflammatory process in mothers and support the immunological development of the infant (Bond et al., 2017). Probiotics help decrease the development



of mastitis caused by *Staphylococcus aureus*, which can result in early cessation of breastfeeding (Bond et al., 2017). This inflammation of the breast tissue occurs in as much as 21% of breastfeeding mothers, and 3% can develop breast abscesses (Bond et al., 2017). Furthermore, breastfeeding helps develop the infant's microbiota (Simpson et al., 2018). The infant's gastrointestinal microbiota will evolve and become one of the most significant health determinants in life, shaping the child's immunity, metabolism, neurological system, nutritional substance absorption, and the prevention of diseases throughout the adult years, which include asthma, allergies, autism spectrum disorders, obesity and attention deficit hyperactivity disorder (George et al., 2022). In addition, breastfed infants have a higher rate of survivability and a lower rate of acquiring an infection (Bonner, 2019).

Bifidobacteria species ferment human milk oligosaccharides (HMO), which in turn lowers the potential hydrogen of the large intestine and produces short-chain fatty acids, which decrease the growth of pathogenic bacteria and prevent the attachment of these harmful organisms to the intestinal wall, which further decreases the potential for colonization (Bonner, 2019). With a clear understanding of the human microbiome and its ever-changing state, we can fully appreciate the influence that probiotics, prebiotics, and fermented foods consumed by the mother, can have on an infant's microbiota.

Probiotics are live health-promoting microorganisms that come in various forms, such as cheeses, chewing gum, yogurts, fermented kinds of milk and juices, or manufactured tablets or capsules (Pujia et al., 2017). Probiotics are involved in intestinal

epithelium proliferation, nervous system maturity, function, and human life energy production (Pujia et al., 2017).

Probiotic development by Eli Metchnikoff was rooted in the idea that these microorganisms hold the key to human longevity (Pujia et al., 2017). Metchnikoff highlighted the new revolutionized notion that not all bacterial organisms cause disease but promote life (Pujia et al., 2017). Many conditions are a result of unfriendly microflora, which can be tamed or removed through the use of the probiotic microbiota as probiotics compete with unfriendly bacteria in absorbing available nutrients and attaching to intestinal epithelial, which alters the environment to prevent the viability of unfriendly microflora (Łubiech et al., 2020).

Breast milk provides an allostatic effect of adapting to the infant's biological and nutritional needs (Łubiech et al., 2020). Administering probiotics to pregnant mothers affects their mammary gland probiotic colonization by increasing the concentration of Lactobacilli and Bifidobacteria in both matured breast milk and the mother's colostrum (Łubiech et al., 2020). The incidence of gastrointestinal inflammation decreases through the ingestion of HBM (Anjum et al., 2020). The probiotics of *Bifidobacterium breve* and *Lactobacillus rhamnosus* help support cesarean birthed infant's microbiota (Korpela et al., 2018). Two main mechanisms that influence and help develop and proliferate the infant's intestinal microbiota are the mother's milk microbiota which contains the intelligence of her gut microbiota, and her natural prebiotic, the HMO (Moossavi et al., 2018). Preterm infants have poor diversified and maturation-deficient intestinal microbiota; this is a vital concern as postnatal microbiota influences an infant's growth (Younge et al., 2019). The

human microbiome is a genetic collection of protists, viruses, bacteria, fungi, archaea, and many other microorganisms (Jagodzinski et al., 2019). As the infant adapts to its environment, these microbes also proceed throughout life under an allostatic model as they are ever adapting, taking on temporary and permanent roles in connection with the human cellular body of which these organisms can outnumber human cells at a ratio of three to one (Jagodzinski et al., 2019). By educating HCPs on these workings, the PBT DNP project will not only improve the clinical staff's knowledge and safety of the use of probiotics in breastfeeding therapy but spark interest in further investigation of the use of probiotics in improving infants' survivability, thriving, and gut microbiota diversity, as well as disease prevention.

### **Local Background and Context**

In Ohio, for every 12 births, one is born underweight, which increases the infant's likelihood of developing morbidities or illnesses (March of Dimes [MOD], 2022). In addition, Ohio is ranked 12th in the nation's IMR (Montgomery et al., 2020). Probiotic supplementation reduces the occurrence of NEC, infection, and mortality (Bührer et al., 2020). Utilizing probiotics and breast milk promotes positive weight gain in infants (Chi et al., 2020; Morais et al., 2021). LBW infants are at a higher risk for mortality (Abdallah et al., 2018). As a result of Ohio's high LBW rate and the benefits of combined probiotics and breastfeeding, the DNP PBT staff education project provided an option to address this state issue and narrow the probiotic knowledge practice gap among APRNs and other HCPs.

When considering the institutional context of the issue, the PBT DNP project provided an educational probiotic-based in-service for HCPs. APRNs and physicians have an average knowledge of probiotics, which may deter them from correctly recommending probiotics. Probiotics improve infant weight gain and reduce mortality rate, NEC, sepsis, medical complications, and hospital stay in LBW infants (Jing Sun et al., 2017). Using probiotics in postnatal care may help the clinical environment and the community setting and reduce the rising occurrence of infections, morbidities, and infant mortality.

The Ohio Women, Infants, and Children program (O-WIC) attempted to reduce the infant mortality rate by reducing the incidence of LBW infants (Ohio Department of Health [ODH], n.d.). Healthy People 2030 indicate that the USA's preterm birth rate is worsening, even though the IMR has experienced a mild improvement of 0.2 per 1000 live births (Office of Disease Prevention and Health Promotion [ODPHP], 2020). The O-WIC program attempts to tackle this issue through increased education in nutrition and breastfeeding and by providing fortified foods (ODH, n.d.). Unfortunately, these remedies have not proven successful, and the nutrients in fortified foods are only sometimes well absorbed. In addition, the concern with this approach is that if the infant's microbiota is not well diversified or developed, its physiological system may be unable to efficiently break down and utilize nutrients (Younge et al., 2019). For this reason, the DNP PBT research project may play a significant role in helping reduce Ohio LBW issues and possibly support the fight against infant mortality, as probiotics can aid in metabolism and weight gain (Łubiech et al., 2020).

PBT is a new approach to promote social change in breastfeeding therapy as it aims to improve the probiotic practice knowledge of HCPs, increase the clinician's technical capacity of probiotics, and build on their current knowledge leading to a better quality of care and innovation (Chaghari et al., 2017). Because nurses, nurse practitioners, midwives, physicians, and other healthcare professionals, in general, can improve the standards of healthcare, it is vital to expose them to new information, updated research, and new best practices for the delivery of care and patient education (Chaghari et al., 2017). The staff education in-service training program will guide clinicians in reviving interest in their professional duties and improve learning and development in their chosen field and specialty (Chaghari et al., 2017). Furthermore, the authority to implement this new approach and force the creation of better research involving medical microorganism management remains in the hands of nurses, as this profession accounts for almost 60% of the medical industry's global workforce, making them a medical powerhouse (den Breejen-de Hooge et al., 2021). The significance is that conscious collaborative unification of all specialty nurses (License Practical Nurses, Registered Nurses, Advance Practice Registered Nurses, Certified Nurse Midwives, Certified Registered Nurse Anesthetists and Nurse Practitioners) can dictate the direction of human life care, especially considering that nurses have their own governing and licensing bodies independent from physician medical boards and other HCP organizations.

When providing in-service training, it is beneficial for the reception and retention of the staff that the material is relevant to the practice area (Chaghari et al., 2017). For

this reason, the empowerment education model (EEM) was used to deliver the PBT in-service to clinicians who encounter breastfeeding mothers, as in the case of high-level medical providers, such as nurse practitioners.

EEM allows for motivational learning and encourages a problem-solving approach to clinical practice (Chaghari et al., 2017). The EEM helps with practical learning, facilitates clinical task expertise, and meets the needs of adult learners (Chaghari et al., 2017). Staff development educators and college professors perform a vital role in an organization or industry as these educators help guide professionals in the direction the company or future requires in meeting its plans, as well as providing employees with career development and long-term job satisfaction and retention (Chaghari et al., 2017). Education plays a critical role in exposure to new evidence-based practices, ideas, and evolution.

The steps in EEM entail active participation, applying problem-solving skills, result-oriented material, transferable training, a motivational approach, encouraging research database searching skills and lifelong learning, and monitoring the training outcome (Chaghari et al., 2017).

The PBT in-service occurred at a midwifery clinic in northeast Ohio which provides lactation consultation services and is staffed by family nurse practitioners, physicians, registered nurses, medical assistants, lactation consultants, and certified nurse midwives. The clinic is in an area populated by over 46,000 residents and serves two cities. Most residents are unmarried, with about half females and half males. The racial demographic is 47% Caucasians, 25% Hispanic, and 23% American Americans, with the

remaining 5% being Asian, bi-racial, or Native American. The area's annual gross taxable income is \$29,000, \$25,000 less than the state's average. In regards to education, only about 30% have a college education.

Although the PBT program originated in Ohio, its aim is a global consideration. In Ohio, 12% of infant deaths occur within the first-hour post-birth and 28% within the first 24 hours after birth (Zeltner, 2020). In addition, over 30% of infant death occurred among babies born prematurely, less than 24 weeks gestation (Zeltner, 2020). Although there have been some reports of mild improvement in the infant mortality rate of only 0.2 per 1000 live births, the PTB continues to worsen (ODPHP, 2020).

For this reason, the PBT program was set in motion at a midwifery clinic due to its frontline focus on mothers and infants. The PBT in-service involved staff participation in a pretest conducted before the in-service presentation, followed by a posttest to determine the staff's understanding of the benefits of PBT and increase interest in probiotics. Both exams identify specific areas of the knowledge gap, discussed in section four of this DNP research project. The HCPs received relevant practice content that promoted knowledge of the various strains of probiotics and their utilization in the prevention of PTB and infant morbidities, as well as improved their problem-solving skills and the application of training (Chaghari et al., 2017). Moreover, staff understood how to search for updated information on probiotics and prebiotics, as well as interconnecting the human microbiome to the disease process, health, and infant mortality, which resulted in improved professional empowerment and knowledge growth.

### **Role of the DNP Student**

A doctoral research project is a vast endeavor. As the Doctor of Philosophy is an academic terminal degree, the DNP is the terminal degree for clinical practice, placing the DNP graduates in a clinical expert role which opens the doors for further research investigations, consultations, development of scientific writing, and a leader in their chosen field. The DNP student learns to cultivate and promote interprofessional and intraprofessional collaborating relations, create and educate on newer innovations, and help evaluate, revise, plan and implement newer ideas and practices in the clinical setting (Staffileno et al., 2019). The DNP research project aims to share one's scientific and clinical knowledge of probiotics, prebiotics, and PBT to increase HCPs' knowledge, competence, and confidence in the subject.

I am a family nurse practitioner (FNP) whose fundamental interest is to promote a more scientific approach to APRN training programs and nursing research, as well as increase knowledge among APRN medical providers in traditional, cultural or complementary and alternative medicine. Here, my relationship with the project has emerged as it implements all three areas of interest to help tackle a serious global problem. Furthermore, my FNP woman's health residency and DNP practicum were under a midwife's direction at an Ohio reproductive sexual health clinic. Throughout this training program and population exposure, I became aware of the ineffective solutions provided by the medical field to solve the ongoing problem in Ohio with infant mortality. Furthermore, when attempting to figure out a potential solution to the LBW, PTB, and infant mortality rate, it was noted that many of the peer countries that had a similar to



better infant survival rate as the United States also had an increase consumption of fermented foods or food products (CIA, 2022; Chilton et al., 2015). The consumption of fermented food gave rise to a curiosity about the possible connection between gut microbiota, probiotics, and the reduction of infant mortality. I hold no bias concerning the DNP project or its research focus.

### **Role of the Project Team**

The DNP practice mentors played a massive part in the success of the DNP student's future as these faculty members helped identify a student's disadvantage and assist the student in refining her or his research idea(s) to facilitate and successfully complete the project and doctoral degree requirements (Staffileno et al., 2019). These academic advisors or Project Team Members (PTMs) are successful due to their clinical and academic experience (Staffileno et al., 2019). The PBT DNP Project became a realization as a result of the mentor's ability and patience in helping refine the student's ideas and interests, examining the best approach for the project, overcoming barriers, maintaining an open line of communication, helping the student understand Walden University's requirements and providing clarity of roles (Staffileno et al., 2019). In addition, the PTMs rallied to advise and support the DNP student on various approaches when experiencing substantial professional resistance within the medical industry. Many clinical sites and universities rejected the DNP project, and some even challenged the topic with opposition and disagreeability.

The PTMs consisted of experienced doctoral-prepared members of the Walden University faculty. The PTMs assisted the DNP student in his role in completing the DNP

project. They supported the DNP student by ensuring that he followed the required Walden guidelines of the DNP project. The project team maintained the DNP student on track and guided him in refining his ideas and goals. The team played a significant role in helping the student gain ground on the subject and complete the degree requirements promptly; this is crucial, considering that this DNP project took over six years to complete. The support provided was significant as no one succeeds alone.

The PTMs communicated weekly with the DNP student, addressing background information, evidence, and discussions of conflicts and challenges. These discussions allowed the PTMs to provide their insight and experience.

The critical project team member, the DNP student's mentor, had a 2 week timeline to review and provide academic feedback upon each submitted project draft. These reviews and feedback were instrumental to the DNP project as they helped refine the gap in practice, the research-focused question, and the relevance of the human microbiome concerning the infant's microbiota, LBW, and PTBs.

### **Summary**

When contemplating the importance of the human microbiome, it is imperative to consider that the microorganism in the human vessel outnumbers the genetic cellular makeup (Pujia et al., 2017). These microbial or bacterial life forms are directly involved in developing and modifying immunological reactions and metabolism, as well as brain development and the utilization and production of micronutrients (Pujia et al., 2017). It is critical to know the function of the human microbiome and its influence on growth and development. The brain, for example, continues to develop until the age of 25 and

possibly longer, which places more emphasis on the need to understand how medications, foods, prebiotics and probiotics affect the human microbiota's function (Arain et al., 2013). The significance here is that the maternal microbiota is involved in the child's development and adult future.

Before being birthed, the mother's microbiota helps develop the fetus's gut microbiota in-utero, while vaginal birth, breastfeeding, and skin contact promote an increase in the infant's gut microbiota bifidobacteria and lactobacilli species (Million et al., 2017). In addition, gastrointestinal inflammation's incidence decreases through the ingestion of HBM (Anjum et al., 2020). These crucial pointers and the allostatic model will help HCPs understand the vital importance of PBT, and DBF as HBM is a natural symbiotic that contains both prebiotics and probiotics, which play a role in the health and safety of infants (Cukrowska et al., 2020).

The PBT program aims to educate HCPs on these benefits of breastfeeding mothers ingesting the correct probiotics, as the health benefits of HBM are most effective when combined with probiotics (Jing Sun et al., 2017). In addition to the education on probiotics and prebiotics, two separate studies mentioned fermented foods; pregnant mothers who consumed fermented foods birthed children with a lower incidence of atopic dermatitis and enhanced sleep duration within the first year of life (Celik et al., 2019; Sugimori et al., 2019). Two possible explanations concerning improved sleep hygiene are that some fermented foods, such as yogurt, have traces of the amino acid tryptophan and reinforces the gut microbiota, which correlates with better sleep patterns (Celik et al., 2019; Sugimori et al., 2019). Probiotics' sleep promotion is vital as inadequate sleep

increases mortality risk, mental illness, diabetes, obesity, behavior problems, and delayed cognitive development (Cole et al., 2020; CDCP, 2021). Furthermore, probiotics can reduce maternal stress, as in the case of *Lactobacillus reuteri*, decreasing an infant's crying time by 56 minutes daily (Sohn & Underwood, 2017).

In the case of reduced dermatological inflammation such as eczema, probiotics and fermented foods' ability to amplify the level of short-chain fatty acids (SCFA) stimulates the immunological response, contributes to the integrity of the mucosal, and improves metabolic function (Celik et al., 2019; Zhou et al., 2019). In addition, maternal ingestion of fermented foods provides a relevant tool for the delivery of probiotics for gut microbiota diversification and proliferation in mothers of different cultures unfamiliar with probiotics or prebiotics.

Section three addresses the importance of probiotics and gut microbiota, the source of evidence, research articles collected, how the evidence is collected, and the analysis and synthesis of the DNP project. In addition, section three will discuss how the articles of evidence apply to PTB, LBW, and infant mortality. Furthermore, probiotic strains and their application to microorganism medical management will be mentioned, including the thyroid's involvement in neonatal issues.

### Section 3: Collection and Analysis of Evidence

#### **Introduction**

Mechanisms that influence and develop the infant's intestinal microbiota are the mother's milk microbiota which contains her gut microbiota and natural prebiotic HMO (Moossavi et al., 2018). The mother's microbiota is a crucial factor in predicting the prematurity of birth. A full-term infant will have a gut microbiota dominated by *Lactobacillus* species, *Bifidobacterium* species, or *Streptococcus*. In contrast, a preterm infant will not have sufficient *Lactobacillus* species, *Bifidobacterium* species, or *Streptococcus* colonization (Łubiech et al., 2020). A preterm infant gut microbiota has a high presence of *Enterobacteriaceae* and *Clostridium*, which is why mothers of premature infants will produce HBM high in HMO, which contains over 200 oligosaccharides and promote probiotic growth as the mother's body acclimates to the child's needs (Łubiech et al., 2020). Upon analysis of the infant's gut microbiota, the superiority of HBM to formula milk is evident because formula-fed infants have a lower count of *Lactobacillus* and *Bifidobacterium* species (Aloisio et al., 2018). The introduction of *Lactobacillus acidophilus* and *Bifidobacterium bifidum* into pasteurized human donor milk significantly impacted the reduction of preterm infant mortality, feeding tolerance, and a decrease in central venous line usage and duration of the mechanical respiratory ventilator (Sharpe et al., 2018).

When considering the combined importance of HBM and probiotics and the practice gap in probiotic knowledge among HCPs, the DNP project-focused question asked if a probiotic in-service would increase the knowledge of probiotics among HCPs

and medical providers. The post-in-service test utilized determined this. The source of evidence for the test questions, as well as the information gathered for the in-service, were a result of an extensive analysis of peer-reviewed research articles which predominantly concentrated on the utilization of probiotics in the population of pregnant mothers, breastfeeding mothers, and infants. In addition, research articles were predominately collected and selected based on their review of previous studies or live experiments on human subjects. In the synthesis analysis, the articles included were selected based on their transferability or ability to transition from paper to practice. For this reason, the mentioned probiotics have already been tested on humans with safe outcomes, especially for mothers and infants.

When considering the research question, “Will implementing a probiotic staff education in-service training program improve the healthcare professional's knowledge of probiotics and their use concerning PBT?” the content in Table 1 provides insight into the evidence selected to teach the participants. The evidence collected provided the data to create a pretest, posttest, and PowerPoint presentation. Complete detail of the program and its results are in Section 4, with data collection tables and clarified results.

**Table 1***Research Connection to PBT*

Research Citation	Findings
Chi et al. 2020	Bifidobacterium assisted infants in weight gain.
Craighead et al., 2020	Probiotics have demonstrated an evidence-based risk reduction in VLBW infants with NEC.
Li et al., 2019	Lactobacillus Plantarum increases transformation growth factor- $\beta$ 2, and Lactobacillus species a decrease in Interleukin-6.
Aceti et al., 2017	Probiotics in HBM-fed infants demonstrated a significant decrease in developing late-onset sepsis.
Narbona-López et al., 2017	VLBW infants whom Lactobacillus acidophilus, Lactobacillus bifidum, or Lactobacillus rhamnosus GG experienced a decrease in NEC and fewer nosocomial infections and mortality.
Sharpe et al., 2018	The pasteurized human with Lactobacillus acidophilus and Bifidobacterium bifidum reduced the mortality of preterm infants and improved feeding tolerance.
Härtel et al., 2017	Probiotics therapy correlated with the infant's growth in length and improved weight gain and head circumference growth.
Fortmann et al., 2020	HBM with Lactobacillus acidophilus and Bifidobacterium infantis that was given to infants less than 29 weeks of gestation benefited the infants' growth and prevention of septic conditions.
Torkaman et al., 2017	Lactobacillus rhamnosus, Bifidobacterium lactis, Bifidobacterium bifidum, and Lactobacillus acidophilus decrease hospitalization in infants with hyperbilirubinemia.
Tanaka et al., 2019	Maternal colostrum colonizes infant gut microbiota.

### **Practice-Focused Question**

Although infant death can be a result of many maternal issues such as infection, obesity, gestational diabetes, UTIs, hypertension, mental illness, and birthing an underweight infant, documented findings provide evidence that probiotic supplementation helped improve these health conditions (Radke et al., 2017; Aloisio et al., 2018; Wu & Chiou, 2021; CDCP, 2021). Because there is a practice gap in probiotic knowledge among healthcare practitioners, the DNP project aimed to narrow this health literacy gap by providing a staff educational in-service focused on probiotics and PBT. The DNP project attempted to answer the following research-focused questions; “Will implementing a probiotic staff education in-service training program improve the healthcare professional's knowledge of probiotics and their use concerning PBT?”

I anticipate that this doctoral project can improve the outcome of probiotic knowledge and use among medical providers and HCPs, especially among high-level providers such as nurse practitioners. For this reason, the project aimed toward a scientific approach involving probiotics and the human microbiome. The project's utilization of the allostatic model allowed for a clearer understanding of the infant's microbiota and its physiological adaptation to internal and external environment life changes, thriving, and survivability. The countless sources of research articles reviewed provided evidence and exploration of a potential solution to increase the survivability and thriving of preterm and LBW infants through the use of PBT.



### **Sources of Evidence**

The articles in the following section will provide insight into the data that was collected to design the PBT educational program. Each research article provided knowledge of the health outcomes of specific probiotic strands. The purpose of the evidence collected was to demonstrate the benefits and safety of probiotics among infants and pregnant or breastfeeding mothers. The collection and analysis of these research articles have provided the foundation to build the doctoral project and design the probiotic educational in-service training program, both of which will offer a clear answer to the project research-focused question of whether a probiotic-based in-service training will supply the necessary tool to increase healthcare providers' knowledge of probiotics.

### **Articles of Evidence**

In the process of research article search, several databases were utilized, such as Cumulative Index to Nursing and Allied Health Literature, Pubmed, Cochrane, OVID, and Science Direct. All articles were within five years from the project's origin, with the exception of 18 articles written in 2011, 2012, 2013, 2014, 2015, and another in 2016 due to the essential information provided by the authors, which included the Sterling's Allostatic Model and prebiotic prevention of PTBs. Some of the terms implemented in the search were “Midwifery and Probiotics,” “Physician and Probiotics,” “Nurse Practitioners and Probiotics,” “Prebiotics and Probiotics,” “Probiotics and Infant Mortality,” “Probiotics and LBW,” “Probiotics and PTB,” “Fermented Foods and Culture,” “Fermented Foods and Infant Mortality,” “Fermented Foods and PTB” and “Fermented Foods and LBW.” Even though there were many valuable and insightful

articles in the literature search, due to the five-year timeline requirement, only the previously mentioned were allowed in the DNP project. Although researchers cited older articles in more recent research studies, the current researchers did not carry over some of the vital information from these older articles resulting in many lost treasures of knowledge.

According to Chi et al. (2020), LBW infants are at higher risk of developing an inflammatory condition due to their lack of diversity of gut microbiota. LBW is any infant weighing less than 2500 grams at the time of birth, which occurs in 15% of the babies born on the planet (Chi et al., 2020). The lack of intestinal microbiota diversity in infants results in microorganism shifting location from the gut to the blood; this can result in a systemic inflammatory reaction and potential development of a disease, which accounts for up to 40% of preterm infants developing severe medical complications and even death (Chi et al., 2020). Furthermore, an undiversified and imbalanced gut microbiota opens the doors for the development of diabetes, autism, late-onset sepsis, cerebral palsy, and NEC (Chi et al., 2020). In an observational study of 97 neonatal intensive care hospitalized infants, 56 received probiotics, and 41 did not. In the non-probiotic group, *Salmonella* and *Helicobacter pylori* were prominent. In contrast, the probiotic group had a higher presence of *Bifidobacterium*, which assisted infants in weight gain (Chi et al., 2020). Also, the non-probiotic group experienced a low level of tyrosine and alanine, which can increase the potential risk of developing future neurological conditions such as Parkinson's, schizophrenia, and encephalitis (Chi et al., 2020).

One common condition that has seen promising outcomes with integrated probiotic therapy is NEC, a gastrointestinal condition that affects both term and preterm infants. The condition can result in a severe inflammatory reaction which can result in hypoperfusion of the intestinal tissue allowing translocation of bacteria, intraventricular hemorrhage, neurodevelopmental injury, lung disease, and even death (Craighead et al., 2020). NEC occurs in 10% of VLBW babies weighing less than 1500 grams (Craighead et al., 2020). In addition, VLBW infants with NEC have a 28% probability of dying and a 35% likelihood of needing surgical interventions (Craighead et al., 2020). Probiotics have demonstrated an evidence-based risk reduction of 0.41 (95% CI 0.31–0.56) in VLBW infants with NEC (Craighead et al., 2020). According to Craighead et al. (2020), prophylactic probiotic therapy (PPT) is a cost-effective way to reduce the prolonged time experienced in clinical care interventions for VLBW infants. The implementation of PPT projects to prevent over 100 cases of neurodevelopmental impairment, more than 1800 cases of NEC, and over 700 deaths (Craighead et al., 2020). Unfortunately, although HBM and probiotics are superior to formula milk and no probiotics therapy in preventing NEC, according to Craighead et al. (2020), due to the various probiotic strains researched, new emerging strains under development, poor regulation, insufficient knowledge of dosage requirements, and having no standard approved clinical probiotic or postbiotic products, probiotics continue to experience difficulty in becoming part of the medical mainstream practice.

Li et al. (2019) randomized, double-blind control trial divided 32 VLBW infants into a probiotic and placebo group. The *Lactobacillus Plantarum* probiotic group

experienced an increase in transforming growth factor- $\beta$ 2, (TGF- $\beta$ 2) and the *Lactobacillus* species experienced a decrease in Interleukin-6 (IL-6). At the same time, there were no significant cytokine changes in the placebo group (Li et al., 2019). The probiotic group also experienced a decrease in alpha diversity as there was a drop in gut microbiota harmful pathogens (Li et al., 2019). Although the discovery was influential for a better understanding of the correlation between cytokines and probiotics, the limitation was its sample size which opened the door for the opportunity to pursue similar research with more participants.

The systemic review by Aceti et al. (2017) revealed that late-onset sepsis occurs in 20% of infants with LBW. LBW babies are at a higher risk of death or developing neurological conditions (Aceti et al., 2017). This neurological disruption links to an imbalanced microbiota. Infant intestinal dysbiosis is a direct result of various events such as whether the child experienced a cesarean or vaginal birth, the child's maternal flora exposure, the mother's dietary intake, microbes present in the hospital's environment, and whether the infant was breastfed or received formula nourishment (Aceti et al., 2017). HBM, unlike formula milk, provides a variety of nutrients, probiotics, intestinal-friendly bioactive factors, and prebiotics, which shape the infant's gut microbiota (Aceti et al., 2017). HBM is the gold standard for LBW preterm babies as it provides the most lifesaving nutrients (Aceti et al., 2017). Furthermore, probiotic supplementation helps reduce the development of late-onset sepsis (Aceti et al., 2017). Probiotics in HBM-fed infants demonstrated a significant decrease in the development of late-onset sepsis (RR 0.79 (95% CI 0.71–0.88),  $p < 0.0001$ ) (Aceti et al., 2017).

The study by Narbona-López et al. (2017) shows a significant reduction in late-onset sepsis, NEC, and mortality in infants between the ages of 27 weeks and 32 weeks. The study also identified that more research is needed for infants less than 27 weeks of gestational age (Narbona-López et al., 2017). NEC is the most common gastrointestinal disease among VLBW infants, which is linked to neurodevelopmental disorders and has a mortality risk of up to 30% (Narbona-López et al., 2017). Since VLBW infants have a lower presence of *Lactobacillus* and *Bifidobacterium*, breastfeeding is one of the most efficient methods to colonize the infant's intestinal microbiota with beneficial bacteria, decreasing the proliferation of pathogenic microorganisms and reduce the risk of developing NEC (Narbona-López et al., 2017). The study demonstrated that VLBW infants who received the combination of *Lactobacillus acidophilus* and *Lactobacillus bifidum* or *Lactobacillus rhamnosus* GG experienced a decrease in NEC, fewer nosocomial infections and mortality. In contrast, infants less than 27 weeks only experience a decrease in mortality (Narbona-López et al. (2017).

The study by Sharpe et al. (2018) revealed that the introduction of *Lactobacillus acidophilus* and *Bifidobacterium bifidum* into pasteurized human donor milk had a significant impact on the reduction of mortality of preterm infants, as well as feeding tolerance and a decrease in central venous line usage and duration on a mechanical respiratory ventilator. Although it is well-known that breastfeeding from an infant's mother provides many protective measures, including a decrease in mortality, the aim was to examine if a pasteurized donor's breast milk and probiotics would provide similar protective outcomes. According to Sharpe et al. (2018), the retrospective analysis

involving 1791 subjects divided into two cohorts of 457 post-donor probiotic milk feeds and 1334 pre-donor probiotic milk feeds utilizing *Lactobacillus acidophilus*, and *Bifidobacterium bifidum* showed that after the introduction of probiotics there was a 69% mortality rate reduction.

The study by Härtel et al. (2017) explored the effects of *Lactobacillus acidophilus* and *Bifidobacterium infantis* on VLBW infants. The study suggests that the use of probiotics positively correlated with the infant's growth in length and improved weight gain and head circumference growth (Härtel et al., 2017). As in many previous studies, the authors discovered that gut dysbiosis is associated with obesity, NEC, growth failure, and chronic inflammatory conditions (Härtel et al., 2017). As a result, preventive probiotic therapy or PPT would be beneficial for researching vulnerable populations (Härtel et al., 2017). The study revealed that after a five-year follow-up, there remained a sustained result of the positive effects of probiotic therapy on growth parameters (Härtel et al., 2017). The study proposes that many of the inconsistencies found in microbiome probiotic studies may be due to the various population studied, the current state of the subject's gut microbiota, whether researchers are administering a multi-strain or mono-strain probiotic, the type of microbes exposure in the subject's environment, the probiotic, and quality of the formulations (Härtel et al., 2017). The author also mentioned that formula-fed term infants might experience healthy growth with *Bifidobacterium lactis* (Härtel et al., 2017). Furthermore, *Bifidobacterium breve* has shown weight improvement and gastrointestinal tolerance, which plays a vital role in infants experiencing feed intolerance (Härtel et al., 2017).

In the study of Fortmann et al. (2020), the authors aimed at the hypothesis that the administration of *Lactobacillus acidophilus* and *Bifidobacterium infantis* with HBM given to infants less than 29 weeks of gestation would benefit an infant's growth and prevent septic conditions. The outcome of the observation yielded that infants who were given probiotics with HBM had an improvement in growth and a lower incidence of sepsis development than infants on the formula-milk diet (Fortmann et al., 2020). The authors emphasized that HBM is an ideal colonizer of the infant's gut microbiota to prevent dysbiosis (Fortmann et al., 2020). The authors also mentioned that PPT needs to be medically personalized as there is still a high mortality rate among ELBW infants weighing less than 1000 grams, even with probiotics as a preventer (Fortmann et al., 2020). Many conflicting finds result from the inconsistency of strains used, the formulation, the need for set protocols, and the development of set strains for specific target populations (Fortmann et al., 2020). Formula-fed infants may experience a higher weight gain than human milk-fed infants. However, there are no studies on the comparison quality and effects of body mass expansion of formula-fed versus HBM-fed. The study suggests a need for future research in identifying a complete HBM microbiome sequencing and a breastfed infant gut microbiota sequencing with probiotics (Fortmann et al., 2020).

In the study by Torkaman et al. (2017), the authors mentioned that hyperbilirubinemia is one of the most common reasons for infant hospital readmissions. The current estimation mentions that within the first week of life, premature infants have an 80% chance, and full-term infants have a 60% chance of being hospitalized due to

hyperbilirubinemia (Torkaman et al., 2017). In order to prevent neurological damage, hyperbilirubinemia receives phototherapy and, in severe cases, blood transfusions (Torkaman et al., 2017). Since probiotics decrease the transit times of intestinal substances, infants given probiotics have experienced a decreased therapeutic length of treatment with phototherapy (Torkaman et al., 2017). In addition, the utilization of *Lactobacillus rhamnosus*, *Bifidobacterium lactis*, *Bifidobacterium bifidum*, and *Lactobacillus acidophilus* in infants with hyperbilirubinemia has experienced a decrease in hospitalizations (Torkaman et al., 2017).

Colostrum is an immunoprotective agent that helps prevent the development of sepsis in infants (Tanaka et al., 2019). In the Tanaka et al. (2019) study, the earliest an infant receives its mother's colostrum, the sooner its gut microbiota will begin to colonize with lifesaving bacteria. Considering that early breastfeeding is detrimental to infants' survival and microbiota diversification, it is imperative to strategically initiate Kangaroo Mother Care (KMC) immediately after birth as it promotes early breastfeeding among preterm and LWB but also regulates an infant's emotional state and body temperature (Mekonnen et al., 2019). LBW babies who received immediate KMC versus post-birth stabilization embrace had a decrease in mortality (WHOIKMCSG et al., 2021). The reason behind the KMC and decreased IMR is due to a decrease in cross-contamination handling which decreases the risk of infection, the skin-to-skin microbiota colonization, and, as mentioned initiating early breastfeeding and colostrum ingestion helps promote the infant's microbiota growth (WHOIKMCSG et al., 2021). When considering the



epidemiological retro-analysis of KMC, KMC's historical result was not due to the practice of embracing, but rather the colonization of the human microbiome.

After two to three days of breastfed, the HBM Bifidobacterium species begin colonizing the newborn's gut, as detected in stool samples (Tanaka et al., 2019). The key here is that DBF is the superior method of nourishment delivery as infants fed with pump breast milk did not display the same level of protective Bifidobacterium gut microbiota colonization as infants who received DBF (Tanaka et al., 2019). In addition, Bifidobacterium bifidum decreased the incidence of late-onset sepsis development in VLWB (Tanaka et al., 2019). The rapid colonization of friendly bacteria is crucial as bacterial cell components, whether living or dead have been shown to affect the gut microbiota. However, there is insufficient evidence of how dead bacterial cells affect gastrointestinal colonization or bifidobacterial proliferation and function (Tanaka et al., 2019). The authors indicated that delay in reception of the first colostrum could result in maternal or infantile issues, which should involve staff intervention to limit or reduce these issues in order to ensure early reception of the mother's colostrum to speed up the infant's gut microbiota (Tanaka et al., 2019).

### **Evidence Generated for the Doctoral Project**

#### **Participants**

The purpose of the DNP project was to provide a staff education in-service program for HCPs. The location of participating organization resides in the Northeastern part of the United States. All the participants were HCPs.

Furthermore, the exclusion criteria included non-HCPs. The outline of the in-service is in Appendix I. The PowerPoint presentation is in Appendix J. The topics covered were probiotics, prebiotics, fermented foods, infant mortality, PTB, LBW, human microbiome, the benefits of HBM, and PBT. The development of the PBT program underwent extensive research reviews and extraction, including PowerPoint material, pretest, and posttest. Criteria for data selection involved relevance to the DNP Staff Education Research Project on Probiotics and PBT to address the knowledge practice gap among healthcare providers involving the understanding, utilization, and future contribution of probiotics in the healthcare field.

### **Procedures**

The project's purpose was solely educational. The organization's representative was able to help the DNP student gain access to the participants and receive permission to proceed with the educational project. The representative of the participating site offered insight and the best approach for the project delivery. The project occurred in one-morning session on-site. Upon completion, the data collected from the tests and participants' feedback was analyzed and provided to the DNP project as a suggestion for improving the program's future focus. The DNP student obtained an official site agreement from Walden University's Institutional Review Board (IRB). The Walden University IRB approval number is 08-01-22-0377505.

The DNP staff educational in-service project identified HCPs as critical stakeholders. Prior to the PowerPoint presentation, participants completed a pretest. After the presentation, the participants received a second test, where they provided feedback on

the in-service and graded the effectiveness of the PBT in-service to increase their knowledge and interest in probiotics. The pretest is in appendix D, and the posttest is in appendix E, while the comparison results are displayed in tables three, four and five, which can be located in section four.

### **Protection**

Under the United States Food and Drug Administration (USFDA) control, the IRB is a group active in protecting research subjects' rights, safety, and well-being (FDA, 2019). The following steps detail the method taken to ensure the safety and anonymity of the research participants:

- The project will be exclusively educational.
- There was no physical experimentation performed.
- No brand of probiotics products was included or mentioned in the research project.
- The participants' names were kept anonymous and excluded from the DNP final product or the collected tests.
- The name of the site was excluded from the final report.
- The site was required to sign a consent form; consent form for anonymous questionnaires was given to the participants.
- Participants were informed that the results of the survey were to remain anonymous.

- Participants were informed that the DNP project aimed to improve evidence-based knowledge on narrowing the health literacy practice gap among healthcare providers concerning probiotics and PBT.

Table 2 details the recruitment and consideration of all participants to ensure safety and anonymity. In addition, the table also reiterates the previous course taken to protect the safety of the participants and the IRB involvement.

**Table 2***Participants, Recruitment, and Procedures*

DNP Participants and Considerations	Practice and Procedures
Number of Participants	Nine participants were provided through volunteer recruits via the participating site.
Selection Process	The site representative sent out a memo of the presentation of which the participants were aware that the PBT presentation was part of a DNP project, and anonymity was assured. All participants were volunteers interested in learning about PBT.
Participants' Relevance to Practice Question	All participants were HCPs ranging from certified nurse midwives, family nurse practitioners, medical assistants, lactation consultants, and nurses.
Measurement of reliability and validity	All data collected from the pretest and posttest were graded on the accuracy of answers and tallied up through the use of percentage calculation.
Participants Ethical Protection	<ul style="list-style-type: none"> <li>• The project will be exclusively educational, with no physical experimentation</li> <li>• The names of all the participants and the site were kept anonymous and not included in the DNP project or the collected tests.</li> <li>• The site was required to sign a consent form; consent form for anonymous questionnaires was given to the participants.</li> <li>• Participants were informed that the survey results were to remain anonymous.</li> <li>• Participants were informed that the DNP project aimed to improve evidence-based knowledge on narrowing the health literacy practice gap among healthcare providers concerning probiotics and PBT.</li> </ul>
Recruitment strategies	The partnering site's representative solely did recruitment through email requests.
Walden IRB	The partnering site agreed to have completed IRB approval via the Walden IRB department.

### **Analysis and Synthesis**

The DNP project researched information is vital to the lifesaving knowledge of high-level primary care medical providers, such as nurse practitioners and certified nurse midwives. As a result, the outcome of the DNP project's educational questionnaire results was analyzed through percentage calculation to determine if the knowledge of probiotics had improved post-in-service training. Based on the percentage results of the descriptive statistical analysis, the test results determined if the in-service narrowed the probiotic knowledge gap among the participants. The data collected was organized and stored in Microsoft Word and Excel programs. All pretest and posttest were provided and collected by the DNP student, who monitors the testing process to ensure the integrity of the answers. All answers were then analyzed to determine if the PBT in-service improved the participating HCPs' knowledge of probiotics, the human microbiome, and PBT, based on the foundation of the research question, "Will the implementing a probiotic staff education in-service training program improve the healthcare professional's knowledge of probiotics and their use concerning PBT?"

### **Summary**

In conclusion, the human microbiome can be one of the leading identifiers of disease development and progression as it influences gut microbiota, colorectal cancer, atopic dermatitis, multiple sclerosis, lupus, breast cancer, diabetes, rheumatoid arthritis, obesity, inflammatory bowel disease, and asthma (Shin et al., 2021). The utilization of probiotics may provide a protective measure in these pathological conditions (Shin et al., 2021). When considering the vulnerability of an LBW or preterm infant's inability to

adapt to stressors, it is imperative to reflect on the potential of PBT, as HBM provides an allostatic effect of adapting to the infant's nutritional health and growing needs (Łubiech et al., 2020). The mother's breast milk microbiota contains *Corynebacteria*, *Lactobacilli*, *Lactobacillus salivarius*, *Enterococci*, *Lactobacillus vaginalis*, *Lactobacillus casei*, *Bifidobacteria* species, *Lactobacillus rhamnosus*, *Enterococcus faecium*, *Propionibacteria*, *Lactobacillus plantarum*, *Lactobacillus gastricus*, *Lactobacillus reuteri*, *Leuconostoc* species, *Lactobacillus fermentum*, *Lactococci*, *Lactobacillus gasseri*, and *Staphylococci* which directly builds the infant's intestinal microbiota (Łubiech et al., 2020). A well-balanced, stable, and diverse gut microbiota may determine the infant's future physical and mental health, as intestinal bacteria regulate and influence the function of human behavior and its cognitive-neurological processes (Jagodzinski et al., 2019). One way probiotics improve the life of the infant is that probiotics compete against pathogens by making pathogenic propagation challenging by occupying attachment sites that the pathogens would have dominated without the presence of a probiotic strain (Mantziari et al., 2020).

The newborn's intestinal microbiota is of extreme concern considering that it can make the difference between developing NEC and sepsis or surviving (Underwood et al., 2017). The human microbiome has 100 times more expressions than the human genome (Schepper et al., 2017). This complexity makes the intestinal microbiota an essential physiological regulator of the human multi-organ system (Schepper et al., 2017). When a microbial imbalance or dysbiosis occurs, the body will experience disease emergence in infants and adults, as well as skeletal breakdown, which in adults manifests as

osteoporosis (Schepper et al., 2017). The importance here is that some mineral deficiencies influenced by gut microbiota dysbiosis are zinc, selenium, and iron, which can promote thyroid dysfunction (Fröhlich et al., 2019). Of these minerals, zinc has Lactobacillus species-producing effect (Fröhlich et al., 2019). The thought here is that probiotic therapy may be beneficial to those infants experiencing thyroid malfunction (Fröhlich et al., 2019). The microbiota is involved in the uptake of iodine and may influence the effects on thyroid function and dysfunction (Fröhlich et al., 2019). The significance is that some ELBW and preterm infants have elevated thyroid-stimulating hormone (TSH) levels (Shin Ae Yoon et al., 2019). The critical implication of further researching probiotics and prebiotics is to determine how to improve the human microbiota of infants and mothers through the oral administration of maternal probiotics and infants experiencing PBT.

The research-focused question was positioned to guide the DNP research project and efficiently address the educational practice gap among HCPs. Probiotics offer a vast number of health benefits to both infants and mothers. The researchers believe that probiotics may provide a solution to improving the infant's microbiota to engage and resist environmental changes that can be detrimental to the allostatic load. The conduction of an extensive literature exploration to locate the most relevant articles has assisted with the potential transferability of the research finds from paper to practice. Since patterns lead to predictability, the researcher hopes clinicians will be more conscious and considerate of the patient's current health situation, parental medical history, lifestyle risk, and nutritional, physiological, and environmental stressors. By



understanding these factors and selecting the correct probiotic for breastfeeding, the DNP researcher anticipates that this project will improve the IMR throughout the planet.

Further data elaboration is discussed in section four. Section 4 will stress the DNP project's findings, limitations, and recommendations. The section details the utilization of probiotics and prebiotics in disease prevention and the importance of KMC and HBM in preventing PTB, LBW, and infant mortality. Lastly, the significance of the PBT research findings and interpretation of data collected will be discussed on the relevance to nursing in addressing the probiotic knowledge gap.

## Section 4: Findings, Discussion, and Implications

### **Introduction**

Ohio has the 12th highest IMR in the nation; for every 12 live births, there is one LBW infant, leading to an increase in mortality and morbidities (Montgomery et al., 2020; MOD, 2022). Probiotics help reduce morbidities and mortalities. However, HCPs only have a medium level of knowledge in the functional utilization of probiotics, which presents a clinical literacy knowledge practice gap. To my knowledge, there needs to be specific training geared towards improving the knowledge and recommendation of probiotics among HCPs and medical providers. In addition, the current nursing and medical school of thought places minimal attention on the human microbiome, especially involving the maternal and infant microbiota. The human microbiome is a new emerging organ and science. Some areas in which the human microbiome shapes life are the gut microbiota's multiorgan axes, the function, and development of the brain, nerves, intestines, behaviors, immune, lungs, skin, and liver (Cukrowska et al., 2020). The human microbiome is a genetic collection of protists, viruses, bacteria, fungi, archaea, and many other undiscovered microorganisms (Jagodzinski et al., 2019). The neonatal microbiota adapts to environmental stressors and develops microbes that will continue evolving and adjusting throughout life (Jagodzinski et al., 2019). Preterm infants have poor diversification and maturation and deficient intestinal microbiota (Younge et al., 2019). Even with efficiently delivered nutrition, growth failure may remain an issue, as malnutrition may result from intestinal microbiota immaturity (Younge et al., 2019). The infant may still fail to thrive in undeveloped microbiota even with sufficient nutrients. An

infant's microbiota which develops 1,000 days after birth, is influenced by several factors such as the number of siblings, method of birth, mother's microbiota, maternal dietary changes, nutrient absorption, intrauterine environmental conditions, hospital environment, genetics, contact with animals, inhaled air particles, infant's diet, and medications administered (Cukrowska et al., 2020; Jagodzinski et al., 2019).

Although various factors influence the introduction and development of the infant's microbiota, lactation plays a key role (Shin et al., 2021). HBM is the primary source of infant intestinal tract colonization with friendly bacteria (Shin et al., 2021). HBM, unlike formula milk, provides a variety of nutrients, probiotics, intestinal-friendly bioactive factors, and prebiotics (Aceti et al., 2017). Probiotics are prescribed during pregnancy and postpartum to decrease gastrointestinal discomfort and the inflammatory process in mothers and support the immunological development of the infant (Bond et al., 2017). Probiotics control and prevent periodontal disease, which may also indirectly prevent the development of vascular disease, atherosclerosis, PTB, LBW babies, and systemic inflammation (Pujia et al., 2017). The word probiotics is a Latin-Greek merger meaning "for life." In contrast, antibiotics (ATB) means "against life," as ATB may harm both nonpathogenic organisms and pathogenic organisms (Schepper et al., 2017).

Probiotics have existed for more than 10,000 years through the fermentation of beer, milk, wine, kumis, cheeses, olives, bread, kefir, and cabbage (Schepper et al., 2017). Many dessert travelers utilize animal stomachs and skin to store milk containing *Lactobacillus acidophilus* and *Lactobacillus bulgaricus*, which turn the milk in the hot dessert into yogurt (Schepper et al., 2017). Elie Metchnikoff believed that Bulgarian

people with an average lifespan of 87 resulted from high fermented food consumption (Schepper et al., 2017). This observation inspired Metchnikoff over 100 years ago to develop probiotics. Probiotics are live microorganisms found in various foods, such as cheese, chewing gum, yogurts, fermented milk, juices, or manufactured liquid drops, tablets, or capsules (Pujia et al., 2017). The utilization of probiotics in the development of an infant's gut microbiota is vital as disruption of the human microbiome, which can occur through the cesarean birthing process or formula feeding and ATB therapy can increase an infant's likelihood of inflammation, metabolic and immunological conditions (Korpela et al., 2018).

For this reason, the DNP research project endeavored to narrow the probiotic knowledge practice gap among HCPs and medical providers by offering a clinical presentation with a pretest and posttest that answered the research question; “Will implementing a probiotic staff education in-service training program improve the healthcare professional's knowledge of probiotics and their use concerning PBT?”

As previously mentioned, the Cumulative Index to Nursing and Allied Health Literature, Pubmed, Cochrane, OVID, and Science Direct databases were utilized to locate meaningful research with transferability potential. In addition, a serious attempt was made to select articles from the project's origin within 5 years, except for 18 articles written in 2012, 2013, 2014, 2015, and 2016. The older articles implemented in the project were due to the rare value of their findings to support evidence of probiotic utilization to improve thriving. Two such articles involved Sterling's allostasis model and prebiotic prevention of PTBs. In the case of word search, the following terms were

implemented in the literature investigation, “*Midwifery and Probiotics*,” “*Physician and Probiotics*,” “*Nurse Practitioners and Probiotics*,” “*Prebiotics and Probiotics*,” “*Probiotics and Infant Mortality*,” “*Probiotics and LBW*,” “*Probiotics and PTB*,” “*Fermented Foods and Culture*,” “*Fermented Foods and Infant Mortality*,” “*Fermented Foods and PTB*” and “*Fermented Foods and LBW*.” The strategy to utilize specific articles was determined by my focus on human subjects, namely pregnant and breastfeeding mothers and infants. Rarely was an animal study utilized, and only done so to determine if critical human research was needed in an area already studied in animals. For example, although not included in the DNP project due to insufficient data, vitamin E and selenium were utilized in the 1970s to decrease the occurrence of “sticky placental” in animals. In addition, the articles were probed for data on the human microbiome, probiotics, prebiotics, fermented foods, and the prevention of infant mortality, LBW, PTB, and morbidities.

### **Findings and Implications: Probiotics and Areas of Influence**

When considering the multi-aspects of infant mortality, PTB, LBW, and maternal complication, the focus of the DNP research project was to search out the science of current practice. For example, KMC, although not an exact science, is a clinical practice that has yielded some results in the care of infants. The goal was to trace the science and not just the prenatal routine, as science takes us to the epidemiological core of why certain practices work. By seeking the scientific explanation for a practice, one can further dive into the root of the cause and potentially discover a workable solution or cure. Clinical epidemiology is the highest level of medical thinking as it is the reverse

engineering of clinical technology and investigation. Through unrestricted retro-analysis, we can determine the origins of any condition and develop a program to stop the condition from developing and creating or re-creating other disease conditions in the body. When merging clinical epidemiology with the human microbiome, high-level providers such as nurse practitioners can retro-analyze events to seek the scientific source causing the condition or practice, allowing the opportunity to create personalized treatment plans to heal the patient or prevent infant mortality from occurring.

The significance here is that the prevention of infant mortality has been unsuccessful for decades through commonly utilized interventions such as parental education, paternal presences, KMC, smoke cessation, reproductive planning, birth spacing, and breastfeeding, as evidence of the inability of these programs to provide significant results or solutions (Cleveland Department of Public Health [CDPH], n.d.). Although these interventions have provided mild help, they have yet to strike the problem at the core and offer effective solutions. Root solutions occur when the science behind an issue or result is understood. For example, breastfeeding provides results because it uses the human microbiome's science of diversifying and developing the infant's microbiota. Another example is parental smoke cessation reducing an infant's exposure which decreases an infant's airway illness by reducing the development of nasopharyngeal *Streptococcus*. In addition, KMC, which was around thousands of years before the term was coined, aids the infant's survival as it is a microbiota colonization method. For the human species to evolve, thrive, and survive, we as nurse scientists must return to the father of invention, the human microbiome and the life sciences. Non-scientific

behavioral modifications can help alleviate many human concerns, but the core of the cure is the science behind the practice. In other words, when we discover a new practice that works, we as scientists have a responsibility to dig deep into the core of the discovery to unravel the scientific reason why it works. This process may help us as a species to solve countless planetary problems and, in this case, infant mortality.

Infant mortality is a complex problem that is personal for all as it reflects a nation's health status and is an indicator of the future survival of the human species. Data collected for this project focused on the current medical practice of salvation and the multiple conditions contributing to an infant's death. Probiotics influence dietary outcomes, HBM development, ATB effectiveness, oral and mental health, human microbiota, colonization, and prevent adverse health conditions. In addition, probiotics and prebiotics can improve maternal health and reduce preeclampsia, PTB, LBW births, and possibly IMR.

Unfortunately, the human microbiome and the utilization of probiotics are still in the infancy of research. The limitation of this science is the lack of extensive human and disease-related research. In addition, probiotic supplementation must establish a daily dietary recommended allowance, dosage, or universal pharmaceutical-grade supplementation. As a result of these limitations, the currently available research outcomes are inconsistent. Fortunately, in the case of NEC, infant mortality, and PTB, several articles ignite further need to research more strand-specific dosages and disease-resistant probiotics.

Based on the findings of this DNP research project, probiotics and PBT are available tools that help alleviate many of the health-related stressors and medical costs experienced by an individual and family of PTBs, as well as those endured at the institutional, community, systemic and global levels. In addition, *Lactobacillus* species, *Saccharomyces cerevisiae*, *Bacillus* species, and *Pediococcus pentosaceus* reduce the absorption of lead, which is a significant concern as currently there are thousands of communities throughout the USA suffering from toxic lead levels in their water supplies, which is negatively affecting the development and biological function of children (Bhattacharya et al., 2019; White, 2017). The utilization and research of probiotics is a health priority, considering that increased intestinal permeability occurs in progesterone, obesity, hyperglycemia, and insulin resistance, allowing harmful organisms to enter the bloodstream and produce systemic inflammation. Implementing probiotics and PBT in clinical practice will promote a positive social change in prenatal care and positively affect planetary health conditions. With this said, the following areas were addressed in the analysis and synthesis of the evidence as they play an essential role in preventing maternal mortality, PTB, LBW, and the IMR.

- ATBs and Probiotics
- Lung Microbiota
- Diet and HBM
- Human Microbiota and Colonization
- Probiotic Uses and Prevention
- Probiotic and Oral Care



- Prebiotics and Fermented Foods
- Prebiotics and Polyphenols
- Probiotics, MRSA and Neonatal Infection
- Probiotics, Uric Acid, Preeclampsia, PTB
- Probiotics, Precision Medicine and Medical Microorganism Management
- PTB and Probiotics
- HBM as a Golden Elixir of Life

### **ATBs and Probiotics**

Although ATB therapies such as Clarithromycin and Azithromycin have provided promising results in treating many conditions, including BPD, ATB therapy generally causes gut and lung microbiota disruption, which may result in asthma later in life (Permall et al., 2019). Infants who receive ATBs within the first six months of life demonstrated a decrease in the presence of Lactobacilli species, Bacteroides, and Bifidobacteria species which may explain why antibiotic exposure results in the development of allergies, behavioral problems, anxiety disorder, emotional problems, depression, lower cognitive abilities, and obesity, (Slykerman et al., 2019; Bond et al., 2017; Million et al., 2017). In addition, Infants who are given ATBs or are born to pregnant women who received ATBs experience decreased microbiome diversity and delayed colonization (Firmansyah et al., 2016).

In addition to ATB therapy, cesarean-born infants experience a reduction of Lactobacillus groups due to the biological effects of anesthesia usage (Łubiech et al., 2020). Furthermore, ELBW preterm infants with BPD exposed to chorioamnionitis

displayed a decreased level of *Lactobacillus* species which can further diminish with ATB therapy (Underwood et al., 2017; Permall et al., 2019).

Mothers administered ATBs had a decrease in *Bifidobacterium* species, and *Lactobacillus* species which is a concern as the birthing mother's microbiota plays a significant role in the infant's microbiota design and colonization, primarily through DBF (Cukrowska et al., 2020; Łubiech et al., 2020). Probiotics help decrease the development of mastitis caused by *Staphylococcus aureus*, which can result in early cessation of breastfeeding and weakening of the infant's microbiota (Bond et al., 2017). Mastitis occurs in as much as 21% of breastfeeding mothers, and 3% can develop breast abscesses (Bond et al., 2017). *Lactobacillus salivarius* and *Lactobacillus fermentum* are effective antibiotic alternatives in mastitis treatment (Bond et al., 2017). In addition, many *Lactobacillus* species play an essential antagonistic role against *Streptococcus pyogenes* (Anjum et al., 2020).

Probiotics can help the human microbiome resist the development of diseases; for example, according to Wastnedge (2021), in a study conducted in India of 400 infants who received *Lactobacillus Reuteri*, there was a 40% reduction in both sepsis and death. *Lactobacillus rhamnosus* had a 26% reduction in the development of atopic eczema, which lasted up to the age of 10 (Simpson et al., 2018; Wickens et al., 2018). Pediatric probiotic usage may contribute to lifelong health benefits.

In addition, probiotics may help with the prevention of fungal overgrowth. For example, *Lactobacillus casei*, *Lactobacillus rhamnosus*, *Lactobacillus paracaesi*, and *Lactobacillus fermentum* displayed anti-fungal activities while reducing the number of

*Candida albicans* (Mantziari et al., 2020; Manovina et al., 2021). *Lactiplantibacillus Plantarum* and *Leuconostoc mesenteroides*, found in kimchi, have anti-viral effects against certain influenza viruses (Mantziari et al., 2020). *Lactobacillus acidophilus* help decrease the frequency of rotavirus-related diarrhea (Mantziari et al., 2020).

*Bifidobacterium longum*, *Lactobacillus gasseri* A5, *Lactobacillus casei rhamnosus*, and galactooligosaccharides/polydextrose (GOS/PDX) improve lung function, decrease airway infections, and asthmatic occurrences (Permall et al., 2019). In addition, the implementation of probiotics into clinical practice may improve the survivability of asthmatic Puerto Rican children. Puerto Rican children have the highest morbidity, mortality, and occurrences of asthma compared to other Hispanic groups and have a 2.8 times higher rate of asthmatic events than other non-Hispanic groups (Brehm et al., 2015; El Burai-Félix et al., 2015; Weiler, 2018; American Academy of Allergy, Asthma and Immunology [AAAAI], 2022; Nazario et al., 2022). Furthermore, Puerto Rican children, due to a genetic design, experience a decreased therapeutic response to rescue inhalers and first-line anti-asthma drugs, which plays a contributing factor in their death rate (Brehm et al., 2015; El Burai-Félix et al., 2015; Weiler, 2018; AAAAI, 2022). Notably, some African American children also experience decreased responses to bronchodilators (Weiler, 2018; AAAAI, 2022). Furthermore, females have a 39% increased risk of dying from an asthmatic event (AAAAI, 2022). Moreover, Infants born to mothers who were positive for human immunodeficiency virus (HIV) experienced a positive growth outcome when given *Bifidobacterium lactis* (Schepper et al., 2017). Colostrum applied to

the buccal pouch of intubated infants experienced a decrease in the incidence of pneumonia (Underwood et al., 2017).

The human microbiota shapes the biological structure as 20% of blood metabolites are from bacterial composition (Fröhlich et al., 2019). About 30% of healthy infants less than 30 days old have *Clostridioides difficile* in their gut microbiota; after the first year of life, it decreases to about 10% (George et al., 2022). Furthermore, pregnancy amplifies intestinal permeability due to the release of progesterone (Shin et al., 2021). This increase in permeability results in the mother's intestinal microbiome entering the bloodstream, which reaches the mammary gland allowing the production of HBM with the mother's natural probiotics (Shin et al., 2021). In addition, as the gastrointestinal tract changes in pregnancy, hyperglycemia and insulin resistance in the presence of obesity results in increased intestinal permeability, which allows harmful organisms to enter the bloodstream and produce systemic inflammation (Wu & Chiou, 2021). Intestinal permeability and how it relates to the gut microbiota is critical when considering other conditions, such as autism spectrum disorder (ASD), as these children experience amplified intestinal permeability, which alters their microbiota and places them at risk for gut issues and infections (Ristori et al., 2018).

Probiotics such as *Bifidobacterium infantis* produce acetate and lactate, which attach to the intestinal wall decreasing inflammation by inhibiting pro-inflammatory cytokines and the attachment of unfriendly bacteria (Smilowitz et al., 2017). In addition, *Lactobacillus plantarum*, *Lactobacillus coryniformis*, *Bifidobacterium infantis*, *Bifidobacterium breve*, *Lactobacillus fermentum*, *Lactobacillus casei*, *Bifidobacterium*

longum, and *Lactobacillus gasseri* improves hypertensive conditions (Wu & Chiou, 2021). This may explain why a high-fiber diet from the indigestible probiotic-producing prebiotics improves cardiovascular health, aiding mother-baby cardiac health (Wu & Chiou, 2021).

Infants who receive ATBs months after ATB therapy have the presence of potentially pathogenic microorganisms in the respiratory tract, questioning the influence that ATB therapy may have on the health of the infant's airway (Gallacher & Kotecha, 2016). Although HBM can help colonize the respiratory tract, the maternal air exchange during KMC between the infant and mother may aid in the colonization of the lung microbiota of the infant. A previous study on mice showed that probiotics administered through nebulizers (nasal administration) might help with resistance to respiratory infection development (Gallacher & Kotecha, 2016). Early lung microbiota colonization is critical as most infant urgent events and terminal outcomes begin with respiratory distress.

### **Lung Microbiota**

Inhaled oxygen contributes to the formation of upper airway microbiota (Elgamal et al., 2021). Research on maternal-infant air exchange and the effects of medicated inhalers and nebulizers on the lung microbiota is needed to determine the extent that air-lung exchange colonizes the lung microbiota. Airway dysbiosis can lead to pulmonary disorders, inflammation, and life-threatening respiratory conditions (Elgamal et al., 2021). Upper airway infections are the leading cause of decreased quality of life, thriving, and death in some cases (Elgamal et al., 2021).

The airway system involves many survival aspects, such as temperature and humidity regulation, inhaled filtration, mucus secretion, potential hydrogen adjustment, and oxygen-concentrated bacterial colonization (Elgamal et al., 2021). Here we get a better appreciation of the allostatic effects of the airway system of the infant and her or his lung microbiota. HBM supports the infant microbiota, which takes about two years to acclimate fully, and in some cases three. Formula-fed infants have a higher presence of *Staphylococcus aureus* (Elgamal et al., 2021). The significance here is that the existence of nasopharyngeal *Streptococcus* is an asthmatic predictor (Elgamal et al., 2021). Furthermore, the detection of *Streptococcus* in passive tobacco smoke exposure may indicate why infants and children who live in homes of smokers may experience airway issues related to *Streptococcus pneumoniae* growth (Elgamal et al., 2021). These points are crucial to applied nursing science as they illustrate the importance of early breastfeeding and knowing the maternal and neonatal microbiota.

### **Diet and HBM**

Immediate breastfeeding is a valuable, potentially life-saving practice. Initiating breastfeeding within 24 hours of birth reduced neonatal mortality in India, Nepal, and Ghana (Wastnedge et al., 2021). HBM inoculates the infant's system with *Lactobacillus* species and *Bifidobacterium* species, regardless of the infant's term, preterm, LBW, vaginal, or caesarian birth, which is significant as the first 1000 days of existence will determine the infant's lifetime microbiome (Firmansyah et al., 2016). In addition, HBM influences the growth of body length, weight gain, and cephalic perimeter, as well as the growth, development, and function of the infant's lungs, decreasing asthma by 22% and

improving resistance to air pollution contaminants (Moossavi et al., 2018; Morais et al., 2021). This is critical when considering newborns living near airports, as the airline pollution produced can have detrimental effects on lung development and function as these children may experience higher incidents of asthma (Habre et al., 2018).

Breastfeeding is critical as HBM contains many components that contribute to the infant's thriving, including melatonin, oligosaccharides, Epidermal Growth Factor, leptin, insulin, Tumor Necrosis Factor- $\alpha$ , interleukin-6 and interleukin-10 (Norarbartolo et al., 2021). The maternal diet influences the growth, development, and availability of *Lactobacillus* species in her breast milk (Amezcuca López et al., 2019). DBF has a more substantial influence on the development of the infant's microbiota than indirect breast milk-pumped feeding (Norarbartolo et al., 2021). The school of thought is that indirect breast pump milk poses the risk of exposing the mother's milk to unfriendly environmental bacteria, which can develop asthma due to acquiring *Pseudomonadaceae* and *Stenotrophomonas* (Norarbartolo et al., 2021). DBF provided a more stable *Bifidobacterium* species in the infant gut microbiota, which played a role in the decrease in incidents of asthma in children when compared to indirect feeding (Smilowitz et al., 2017; Norarbartolo et al., 2021). This may indicate that some microorganisms in the HBM may need an anaerobic transmission. HBM provides a protective mechanism for at-risk infants by improving the immunological reactions to pathogens, developing the gut microbiota, and maturing the intestinal tract (Smilowitz et al., 2017). In the case of thawing HBM, the utilization of microwave machines is not recommended as the radiation exposure decreases the immunological function of HBM (Kim et al., 2019).

HBM consists of Streptococcus, Serratia, Staphylococcus, Bifidobacterium, Corynebacterium genera, Lactobacillus, and Pseudomonas; its prebiotic human milk oligosaccharides (HMO) promotes an internal environment dominated by Lactobacillus species and Bifidobacterium species which makes HBM superior to formula-milk as it protects against many pathogens including Staphylococcus aureus (Radke et al., 2017; Jagodzinski et al., 2019; Łubiech et al., 2020). Formula-fed infants may experience weight gain and growth; but may be at risk for the development of NEC, which places high emphasis and need on infants to receive Mother Own Milk (MOM) to ensure the best life outcome (Morais et al., 2021). One reason is that formula-fed infants had lower levels of Bacteroides and Bifidobacterium compared to breastfeeding infants who receive HMO, which promotes the growth of Bacteroides and Bifidobacterium (Morais et al., 2021). In addition, formula-milk-fed infants have a lower presence of oral Lactobacillus species and pathogen resistance than breastfed infants (Pujia et al., 2017). MOM-fed infants displayed increased alkaline phosphatase level (ALP) activity; a lack of intestinal isoform of ALP activity may place the infant at risk for developing NEC and systemic inflammation (Morais et al., 2021).

Staphylococcus aureus may play a role in the onset of NEC (Firmansyah et al., 2016). When the infant's gut microbiota consists of lower levels of Staphylococcus aureus and higher Collinsella and Bifidobacterium, the infant may experience normal-weight preservation (Firmansyah et al., 2016). Moreover, infants with lower levels of Bifidobacterium species such as Bifidobacterium Breve, Bifidobacterium infantis, and Bifidobacterium bifidum, had a higher likelihood of atopic diseases, especially in the



presence of fecal clostridia (Firmansyah et al., 2016). *E. coli* was linked to eczema, and *C. difficile* was seen in the occurrence of eczema, allergies, and wheezing, which improved through prebiotic consumption (Firmansyah et al., 2016). The presence of these and other microorganisms leads to the fact that the fetal environment is not sterile.

### **Human Microbiota and Colonization**

Contrary to popular clinical and academic belief, the human body is not sterile; microbes reside within the placenta, blood, umbilical cord, amniotic fluid, meconium, and fetal membrane (Pujia et al., 2017; Jagodzinski et al., 2019). The fact that urinary tract infections occur is evidence that bacterial life forms circulate throughout areas once thought to be sterile. These bacterial life forms are crucial for the colonization of the human microbiota.

The infant's tongue and tonsils have a similar microbiota as the placenta but are not identical to the vaginal microbiota (Pujia et al., 2017). Much of the infant's microbiota develops from its mother microbiome and skin contact resulting in the transferring of *Staphylococci*; at the same time, vaginal delivery will introduce *Lactobacillus johnsonii*, *Lactobacillus crispatus*, *Lactobacillus iners*, and *Lactobacillus jensenii* (Jagodzinski et al., 2019). Since the fluid in the amniotic sack is not sterile, this would indicate that bacterial colonization of the fetus's skin and intestines begins in the uterus (Underwood et al., 2017).

Cesarean birth microbiota forms by infant-to-mother skin contact and exposure to the microbes of the hospital environment (Jagodzinski et al., 2019; Łubiech et al., 2020). This raises the question of the benefits of hospital-based care in LBW infants,

considering that in Nepal, community volunteer base homecare of LBW infants provided a higher survivability rate (Neupane et al., 2017). Furthermore, this may explain why non-vaginal births have higher incidents of asthma, eczema, obesity, and allergic food reactions (Jagodzinski et al., 2019). Cesarean-born infants have lower maternal microbiota exposure, decreased microbiome diversity, and delayed colonization, which increases the risk of developing type 1 diabetes, allergic rhinitis, obesity, and celiac disease compared to infants born via vaginal deliveries (Firmansyah et al., 2016; Pujia et al., 2017). The probiotics of *Bifidobacterium breve* and *Lactobacillus rhamnosus* help support cesarean birthed infant's microbiota (Korpela et al., 2018). One procedure that assisted cesarean births in developing a microbiota similar to vaginal births was inserting a sterile gauze pad in the mother's vaginal canal. After the birth, the gauze pad is applied to the infant's body, oral cavity, and face. However, this procedure is unsafe due to potentially transmitting an undetected sexually transmitted infection (STI) (Jagodzinski et al., 2019). Considering the mother is freed of any STIs, this makes vaginal delivery superior to the cesarean section in introducing *Bifidobacterium* species to the infant, which assists in metabolizing complex carbohydrates found in HBM and aids in evolving the infant's immune system (Chichlowski et al., 2020). In addition, after eight hours of vaginal delivery, an infant's oral cavity is colonized with *Streptococcus salivarius* (Pujia et al., 2017). Furthermore, the infant's first meconium has a similar microbiome to the mother's oral cavity (Firmansyah et al., 2016).

*Bifidobacterium* species comprise 40% and 80% of an infant's gut microbiota (Chichlowski et al., 2020). *Bifidobacterium* species provide disease-resistance measures

to protect against asthma, obesity, autoimmune conditions, and the development of allergies (Chichlowski et al., 2020). Bifidobacterium species such as Bifidobacterium Infantis decrease the body's likelihood of rejecting or resisting vaccination medicine (Chichlowski et al., 2020).

The significance here is that probiotics may play a protective role against vaccination-related adverse events considering that in some subjects, the messenger ribonucleic acid (mRNA) transitioned into the infant, which may have unpredictable results as the Center for Diseases Control does not currently have a COVID vaccination recommendation schedule for infants under six months of age (CDCP, 2022; Hanna et al., 2022). Furthermore, Bifidobacterium longum and Bifidobacterium pseudologum are aerotolerant probiotics that play a vital role in the maturation of the infant's intestinal microbiota, which may provide immunological protection (Million et al., 2017).

Infant intestinal dysbiosis is a direct result of various events such as whether delivery occurred through a cesarean or vaginal pathway, maternal flora exposure, the mother's dietary intake, environmental exposures, cellular medication saturation, the presence of any pathological conditions, and whether the infant was breastfed or received formula nourishment (Aceti et al., 2017; Pujia et al., 2017). Furthermore, pregnancy results in a dysbiosis remodeling of the maternal microbiota (Firmansyah et al., 2016).

Bifidobacteria are the dominant intestinal bacteria in infants living in developing countries. However, lower levels of these bacteria are present in the gut of infants residing in developed nations, which may lend a clue to the obesity epidemic in developed nations (Smilowitz et al., 2017). Bifidobacterium infantis is a well-tolerated

probiotic, which produces fewer, but well-formed stools among infants (Smilowitz et al., 2017). Although the life of the infant's microbiota begins intrauterine and continues to evolve through a delivery method, it is not until the reception of the prebiotics and probiotics of HBM that it is adjusted to assist with the allostatic environment (Fröhlich et al., 2019). HBM supplies one-third of an ounce of HMO-Prebiotic for every quart produced (Firmansyah et al., 2016). Prebiotics provides a similar result as stool softeners without adverse effects, which is critical as almost 40% of pregnancies experience severe constipation (Firmansyah et al., 2016). The prebiotic inulin increases zinc's absorption and retention while promoting magnesium's absorption (Firmansyah et al., 2016). In addition, GOS enhances calcium absorption (Firmansyah et al., 2016). Moreover, overweight mothers experience a lower folate level, which puts the infant's neurological system at risk, which can be remedied by ingesting prebiotics such as inulin-type fructans (Firmansyah et al., 2016). Prebiotics may also help attenuate insulin resistance and control oxidative stress which results in high allostatic loads (Firmansyah et al., 2016).

### **Probiotic Uses and Prevention**

Women experiencing major depressive disorder supplemented with *Lactobacillus casei*, *Lactobacillus acidophilus*, and *Bifidobacterium bifidum* had a lower incidence of depression-related symptoms (Slykerman et al., 2017). Furthermore, postnatal women taking *Lactobacillus rhamnosus* reported lower incidents of anxiety and depression. Women suffering from postpartum depression can experience prolonged periods of fatigue, hopelessness, anxiety, insomnia, sleep disturbance, suicidal ideation, and feeling of guilt and inadequacy, which can result in neglectful infant care and feeding

(Slykerman et al., 2017). The utilization of probiotics is not only beneficial for the life of the infant but in improving the maternal experience as well. Mothers of infants suffering from colic had a higher rate of reported depression and anxiety (Slykerman et al., 2017). *Lactobacillus plantarum* and *Lactobacillus delbrueckii* have demonstrated potential colic treatment by inhibiting gas-forming coliform bacteria (Aloisio et al., 2018).

The maternal probiotic of *Bifidobacterium longum* supports the prevention of malnutrition (Million et al., 2017). Vitamin B-12 deficiency correlates to the maturity and efficacy of the gut microbiota (Million et al., 2017). Probiotics' ability to help with vitamin and mineral absorption is essential, especially when considering that folic acid and zinc supplementation reduce PTB, which may be explained by an animal study that showed the combined zinc and folic acid reduced uric acid, which is a predictor of preeclampsia and PTB (Wastnedge et al., 2021; Sun et al., 2022). Folate, essential in the fetus's development and health, is produced through the effects of bifidobacteria, including *Bifidobacterium breve* (Korpela et al., 2018). *Bifidobacterium breve* helps decrease the occurrence of gastrointestinal disorders, such as decreasing the occurrence of daily emesis and improving stool consistency and frequencies (Aloisio et al., 2018). Infants with gastrointestinal disorders, such as colic, experience more extended periods of crying, which, as mentioned, can contribute to maternal depression (Aloisio et al., 2018).

Furthermore, children with colic tend to have decreased microbiota diversity and may experience childhood migraines (Aloisio et al., 2018). In addition, vomiting, constipation, or regurgitation increases the frequency of pediatric visitations (Aloisio et al., 2018). *Bifidobacterium* assists in the prevention of food allergies, which is critical as

food allergies tend to begin after the second year of life and can result in an infant's failure to thrive, delayed growth, and life-threatening events, as well as disrupt the child's and family's quality of life (Wang et al., 2022).

### **Probiotic and Oral Care**

Although probiotics are live microorganisms, some do not need to be viable to provide benefits to the infant; in fact, inactivated probiotics can attach much more quickly to the intestinal mucosa than live organisms, protecting against infections (Mantziari et al., 2020). Probiotics supplementation decreases the incidents of sepsis, NEC, feeding times, and deaths of preterm infants, and in the case of *Bifidobacterium lactis*, it promotes infant growth (Radke et al., 2017; Underwood et al., 2017). In addition, ingesting probiotics can help reduce dental caries and halitosis and prevent periodontal disease and *Candida* (Pujia et al., 2017). Changes in the oral microbiota can contribute to several oral and dental diseases (Pujia et al., 2017). *Streptococcus mutans*, which promote the development of dental cavities, are known to be reduced by the probiotics *Lactobacillus paracasei* and *Lactobacillus rhamnosus* (Pujia et al., 2017). Periodontal disease increases the risk of delivering infants prematurely (Underwood et al., 2017). In addition, although over 600 species within the oral microbiota protect the human genome from pathogenic microorganisms, pregnancy disrupts the mother's natural microbiota, resulting in an imbalance between good and harmful bacteria (Butera et al., 2021). When health conferring microorganism becomes insufficient to resist pathogens, the maternal microbiota dysbiosis will result in the pregnant woman experiencing excessive weight gain, insulin resistance, inflammation, hyperglycemia, hormonal

imbalance, microthrombi formation, gestational hypertension, and vascular permeability (Butera et al., 2021). Furthermore, when there is a decrease in firmicutes, leptotrichia and an increase in proteobacteria, there will be an increased risk for GDM (Butera et al., 2021).

Another concern of these pathogenic microorganisms is that they are prone to utilize progesterone as a food (Butera et al., 2021). Pathogenic microorganism consumption of progesterone will decrease circulatory progesterone levels and increase the risk of preterm labor (PTL). *Prevotella intermedia*, *aggregatibacter actinomycetemcomitans*, *porphyromonas gingivalis*, *fusobacterium nucleatum*, and *tannerella* species are pathogens that contribute to gingival and periodontal diseases and tend to thrive in pregnant women due their ability to utilize progesterone as a food source (Butera et al., 2021). Prophylactic progesterone therapy reduces PTL (da Fonseca et al., 2020). Once progesterone begins to decline, the cervix begins to ripen, and inflammatory mediators increase (da Fonseca et al., 2020). This may clarify why vaginal progesterone therapy may reduce PTL, as progesterone is a hormone that protects the maintenance of pregnancy (Sykes, & Bennett, 2018; Norman, 2020; da Fonseca et al., 2020).

Furthermore, according to Di Renzo et al. (2018), placenta trophoblast cells experience a decrease in lipopolysaccharide inflammatory response with maternal ingestion of *Lactobacillus rhamnosus*, which explains why the ingestion of probiotics reduces episodes of preeclampsia and PTB.

The human microbiome, probiotics, and progesterone connection is significant as PTB is the leading cause of neonatal morbidity and mortality (Sykes & Bennett, 2018).

Although the factors involved in PTL and PTB include infections, uteroplacental ischemia, decidual hemorrhage, cervical pathology, maternal stress, fetus stress, and uterine overdistension, progesterone deficiency plays a vital role as this is a protective hormone that can deplete through pathogenic microorganism feeding, of which maternal probiotic ingestion may prevent this occurrence (Di Renzo et al., 2018).

### **Prebiotics and Fermented Foods**

Prebiotics are nondigestible nutrients that nourish the body's microbiota (Davani-Davari et al., 2019). There are several prebiotic types: fructans, Glucose-Derived Oligosaccharides, Non-Carbohydrate Oligosaccharides, pectins, resistant starches, and Galacto-Oligosaccharides (Davani-Davari et al., 2019). Although prebiotics production occurs with starches, lactose, and sucrose, many are found in Jerusalem artichokes, beet sugar, asparagus, bananas, barley, garlic, onions, wheat, honey, rye, HBM, HMO, animal milk, peas, legumes, seaweed, microalgae, chicory, tomatoes, apricots, raisins, dates, figs, spring onions, green tea, black tea, prunes, and oolong tea (Sun et al., 2018; Davani-Davari et al., 2019). One well-known and time-proven life-saving prebiotic treatment is the utilization of Lactulose in controlling hepatic encephalopathy by taming the presence of ammonia in the gut (Davani-Davari et al., 2019). This medical practice provides a better understanding of the direction future medicine will journey to understand the new emerging organ, the human microbiome.

Prebiotics and probiotics or symbiotic therapy have many benefits; for example, *Lactobacillus* species and Mannose or D-mannose, which in biblical times was a Monosaccharide found in Manna, prevents urothelium bacterial adhesion, which in turn



treats and prevents recurrent urinary tract infections (Pugliese et al., 2020; Kyriakides et al., 2021, De Seta, et al., 2022). LBW, preeclampsia, intrauterine growth restriction, and PTB can result in the presence of urinary and vaginal infections (Pugliese et al., 2020). Mannose creates a pathogenic reduction by binding to salmonella (Davani-Davari et al., 2019).

Prebiotics and probiotics help prevent diarrhea and inflammatory bowel disease (Wu & Chiou, 2021). Probiotics can help prevent various diarrhea types, including rotavirus-induced, ATB use, and traveler's diarrhea (Wu & Chiou, 2021). Prebiotics protect against colorectal cancer, especially in symbiotic therapy of inulin, *Lactobacillus rhamnosus*, and *Bifidobacterium Lactis* (Davani-Davari et al., 2019).

Fructans (inulin and fructo-oligosaccharide) and galactooligosaccharides (GOS) promote *Bifidobacterium* and *Lactobacillus* in infants, pectic oligosaccharide, resistant starches, and non-carbohydrate oligosaccharide which can be found in dark chocolate (Davani-Davari et al., 2019). Fructo-oligosaccharides (FOS) and GOS's abilities to reduce pathogenic organisms and increase gut microbiota growth and function provide infants with a protective mechanism against NEC (Davani-Davari et al., 2019).

*Bifidobacterium breve* helps prevent preterm NEC (Aloisio et al., 2018). FOS can be found in more than 36,000 plant life, which indicates that a maternal plant-based diet may provide the gastrointestinal microbiota with many prebiotic benefits (Davani-Davari et al., 2019).

Probiotics' survival occurs by the type of nutrients and prebiotics ingested (Pujia et al., 2017). Prebiotics are GOS, fructans, FOS, and maltodextrins, as well as various

foods such as honey, Jerusalem artichoke, dark chocolate, berries, goat milk, burdock, acai berry, oats, soya beans, and asparagus (Pujia et al., 2017). In addition, although green tea is rich in prebiotic properties, hot water utilized on chicory root can produce a prebiotic coffee brew rich in inulin (Whisner & Castillo, 2018). Oligosaccharides and polysaccharides are prebiotics that ferment in the gastrointestinal tract and promote the growth of beneficial *Bifidobacterium* species and *Lactobacillus* species (Sunu et al., 2019). Xylitol decreases pathogenic microorganisms, increasing *Lactobacilli* and *Bifidobacterium* (Whisner & Castillo, 2018). Today, several chewing gums are made with Xylitol.

The indigestible prebiotic oligosaccharides are the third largest element found in HBM, which promotes the growth of bifidobacterial strains in the infant's gut microbiota (Smilowitz et al., 2017). *Bifidobacteria* ferments HMO, which in turn lowers the potential hydrogen of the large intestine and produces SCFAs, which decrease the growth of pathogenic bacteria and prevent the attachment of these harmful microorganisms to the intestinal wall, which further decreases the potential for injurious colonization (Bonner, 2019). Trace amounts of HMO detected in blood and urine samples may be the reason for lower incidents of infections in the urinary and respiratory tract (Bonner, 2019). Although infant formula manufacturers have instilled FOS and GOS, these prebiotics are not as complex or bio-available as the mother's HMO (Bonner, 2019). However, HMO was superior to the synthetic GOS and FOS, infants who received these formulas still benefitted from decreased bronchitis and respiratory infections (Bonner, 2019). In addition, the prebiotic-laced formulas also resulted in infants needing fewer antibiotics

and antipyretics when compared to infants ingesting non-prebiotic or probiotic formulas (Bonner, 2019). Mothers of infants with NEC produced HMO with less disialyllacto-N-tetraose (DSLNT) (Bonner, 2019).

Although human gut microbiota accounts for less than half a percent of the human body mass, it houses over 9 million genes and is 450 times larger than the entire human genome (Wu & Chiou, 2021). Gut microbiota dysbiosis occurs in many pathological conditions, including heart failure, arterial hypertension, atherogenesis, atherosclerosis, and thrombosis (Wu & Chiou, 2021). A possible reason may be that the metabolites of specific microbiota can result in the development of harmful pathogens such as *Shigella*, *Enterobacteriaceae*, *Candida*, *Yersinia*, *Campylobacter*, and *Streptococcus* species (Wu & Chiou, 2021).

Although, on average, about 9% of healthy humans suffer from gastrointestinal (GI) disorder, in the case of autistic patients, there is a 70% occurrence, and in stroke patients a 50% occurrence of gut issues, and the greater the gastrointestinal disorder, the greater the symptom manifestation (Davani-Davari et al., 2019). One possible explanation is that autistic sufferers have lower *Bifidobacterium* species and a higher gastrointestinal permeability, allowing opportunistic pathogens to seep into the bloodstream (Ristori et al., 2018; Davani-Davari et al., 2019; Wu & Chiou, 2021).

Probiotics and prebiotics also help the human body adapt to its environment. For example, symbiotic treatment of *Bifidobacterium breve* and GOS provides a way to decrease water retention, which may help mothers experiencing higher episodes of blood pressure and edema (Davani-Davari et al., 2019). Inulin, Lactulose, Trans-galacto-

oligosaccharides (TOS), and oligofructose improve calcium absorption (Davani-Davari et al., 2019). *Lactobacillus casei* Shirota has fracture healing benefits, and kefir improved bone density (Schepper et al., 2017). In addition, calcium deficiency during pregnancy will negatively affect human genetic expression, leading to GDM, high blood pressure, preeclampsia, and PTB (Takaya, 2021). Fortunately, the prebiotics, Lactulose, GOS, oligofructose, FOS, soluble corn fibers, and inulin positively affect bone health by improving calcium absorption and retention, leading to more robust skeletons (Whisner & Castillo, 2018). In an animal study, *Bifidobacterium longum*, FOS, and *Bifidobacterium bifidum* increase calcium, phosphorus, and magnesium in bone content and strengthen bone-breaking force (Whisner & Castillo, 2018). Another benefit to the consumption of prebiotics is the improved reaction of antibodies in the presence of vaccination, which in turn reduces the adverse vaccine-induced systemic effects (Davani-Davari et al., 2019).

Prebiotics produce competitive probiotics that overpower other harmful organisms by inhibiting their proliferation and protecting the human microbiome (Wu & Chiou, 2021). The prebiotic properties of leeks, prunes, dates, apricots, onions, figs, raisins, spring onions, and garlic help decrease PTB (Myhre et al., 2013). Probiotics microorganisms are *Streptococcus*, *Lactobacillus*, *Saccharomyces*, *Bifidobacterium*, *Lactococcus*, and *Enterococcus* (Wu & Chiou, 2021). Some of these can be found yogurt, kombucha, kefir, sauerkraut, kimchi as well as other fermented foods (Wu & Chiou, 2021). Probiotics can also potentiate the effects of other elements, as in the case of diabetics with heart disease who are given selenium and Vitamin D in combination with

probiotics, resulting in improvements in mental health, oxidative stress, and cholesterol control (HMB) (Wu & Chiou, 2021). In addition, *Akkermansia muciniphila* provides a protective mechanism against diabetes and obesity (Wu & Chiou, 2021). The symbiotic use of *Lactobacillus Plantarum* and *Lactobacillus rhamnosus* reduces inflammation and metabolic endotoxins and improves vascular endothelial function (Wu & Chiou, 2021). *Bifidobacterium bifidum*, *Lactobacillus acidophilus*, and *Lactobacillus casei* may be a consideration for mothers with gestational diabetes as these probiotics increase HDL cholesterol and improve insulin sensitivity (Wu & Chiou, 2021).

### **Prebiotics and Polyphenols**

Prebiotics are substrates that can enhance host microorganisms, mineral absorption, satiety, pathogenic defense, metabolic and gastrointestinal function, and immunological response (Sanders et al., 2019). Strand-specific research is critical as not all probiotics perform the same task as where one reduces sepsis and NEC in infants; another may not (Sanders et al., 2019). In addition, probiotics affect not only the human microbiome but other areas of creation. *Lactobacillus* and *Bifidobacterium* species' lactic and acetic acid-producing effects can lower pH levels, promoting pathogenic microorganisms' reduced viability (Sanders et al., 2019). The cross-feeding effects achieved through probiotic ingestion can maintain the production of butyrates and SCFAs, which can have a positive, long-standing effect on cardiometabolic diseases and insulin resistance (Sanders et al., 2019). Probiotics can combat *helicobacter pylori* and the adverse events associated with ATB use (Sanders et al., 2019). These living

microorganisms' complex functions and purposes do not all interact with the human host identically.

For this reason, medical microorganism management is not aimed solely at the focus of probiotics and prebiotics therapies but at any organisms involved in the human body's development, design, and destiny. Probiotics can aid in the tolerance of foods that previously created gastrointestinal distress, such as using *Lactobacillus bulgaricus* and *Streptococcus thermophilus* to consume lactose products. In addition, although milk (casein and whey proteins) and milk products such as cheese should not be consumed with iron-rich foods as they inhibit the absorption of iron, probiotics have been noted to improve iron absorption (André et al., 2018; Vonderheid et al., 2019; Axling et al., 2020). A strategic maternal diet and beneficial food combination are critical to building HBM components of iron and zinc, which transfer to the fetus and infant, who will experience an improved in-utero developmental and birthing outcome (Bzikowska-Jura et al., 2021).

Polyphenols have an antioxidant (anti-rusting) role that exerts prebiotic effects which have anti-thrombotic, anti-inflammatory, anti-atherogenic, anti-mutagenic, and anti-allergic properties that can help the body resist cancer, as well cardiovascular and neurodegenerative disease development or progression (Gorzynik-Debicka et al., 2018; Halib et al., 2020; Sorrenti et al., 2020). Furthermore, cocoa high in polyphenol increases the production of *Lactobacilli*, butyrate, and bifidobacteria and decreases *Clostridium perfringens* (Sanders et al., 2019; Sorrenti et al., 2020). Polyphenols occur in thousands of edible plant foods, with cocoa and unfiltered olive oil being two of the highest in polyphenols.

Cocoa flavanol has an anti-obesity effect with cognitive and neuroprotective mechanisms that also helps produce nitric oxide, promoting microcirculation and lowering blood pressure (Halib et al., 2020; Sorrenti et al., 2020). If chocolate becomes one's probiotic/prebiotic of choice, the aim is to focus on dark chocolate, greater than 80% cocoa and soy-free. As with olive oil, it must be an unfiltered extra virgin from ripe olives, which still possess their natural scent, and stored in a dark glass container as this contains the highest polyphenol (Gorzynik-Debicka et al., 2018).

### **Probiotics, MRSA, and Neonatal Infection**

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a commonly known multidrug-resistant nosocomial pathogen that occurs in neonatal intensive care units (NICU) and is carried by 20% of the world's population (Jayashree et al., 2018; Lavie-Nevo et al., 2019). The transmission of MRSA to an infant can occur through paternal skin contact, healthcare worker cross-contaminated handling, maternal skin contact, HBM feeding, and from other MRSA-positive infants admitted to the NICU (Lavie-Nevo et al., 2019). Although the treatment of multi-drug resistant organisms has been limited due to pathogenic adaption to ATB therapy, there have been small studies that encounter probiotics inhibitory effects against MRSA. A study conducted in 2013 by Sikorska and Smoragiewicz mentioned that probiotic organisms' ability to attach to the intestinal wall prevented pathogenic organisms from settling. In addition, probiotics lower the gastrointestinal tract's potential hydrogen, which inhibits pathogenic thriving (Sikorska & Smoragiewicz, 2013; Jayashree et al., 2018). Furthermore, probiotics are resistant to bile salts, gastric acids, and pancreatic enzymes (Jayashree et al., 2018).

*Lactobacillus reuteri*, *Lactobacillus casei*, *Lactobacillus paracasei*, and *Lactobacillus rhamnosus* were probiotics that displayed resistance to MRSA (Sikorska & Smoragiewicz, 2013). *Lactobacillus rhamnosus* SHA113 isolated from the milk of women decreased the number of MRSA cells, restored neutrophil function, and repaired intestinal barriers which were damaged by infection (Liu et al., 2020). *Lactobacillus fermentum*, which can colonize the human gastrointestinal and urogenital tracts, has an immunomodulating mechanism that reduces the symptoms of respiratory and gastrointestinal infections (Jayashree et al., 2018). *Lactobacillus fermentum*'s antimicrobial effect may explain its ability to prevent MRSA organisms from adhering to the gastrointestinal tract (Jayashree et al., 2018).

Although MRSA is predominantly located on the nares, skin, gastrointestinal tract, and soft tissue, if it manages to infiltrate the bloodstream, it can infect any organ and bone tissue resulting in detrimental outcomes (Jayashree et al., 2018). In fact, biological infiltration from MRSA annihilates 35,000 humans each year in the United States (Møller et al., 2022). *Lactobacillus rhamnosus* and *Bacillus* bacteria were reported to overcome the presence of *Staphylococcus aureus* (Møller et al., 2022). This is significant as very LBW, and very PTB are at a high risk of contracting MRSA, which can severely burden the treatment illnesses within NICUs (Washam et al., 2017).

### **Probiotics, Uric Acid, Preeclampsia, PTB**

Preeclampsia is a multisystem disorder seen in the presence of hypertension and proteinuria after 20 weeks gestation, while eclampsia is a convulsive event that occurs in the presence of preeclampsia (Kumar & Singh, 2019; Paula et al., 2019). Preeclampsia



can lead to fetal distress, impaired renal function, intrauterine growth restriction, retinopathy, PTB, LBW, and infant and maternal mortality and morbidity (Le et al., 2019; Le et al., 2020). Sixteen percent of maternal deaths result from preeclampsia and eclampsia (Kumar & Singh, 2019). The severity of preeclampsia depends on the level of hypocalcemia ( $8.61 \pm 0.78$  mg/dl) and hyperuricemia ( $6.8 \pm 2.72$  mg/dl) (Kumar & Singh, 2019). In addition, the presence of hypocalcemia lowers iron and zinc levels, increasing the maternal risk of preeclampsia, while hypomagnesemia helps predict the occurrence of preeclampsia (Kumar & Singh, 2019; Čabarkapa et al., 2018).

Furthermore, high serum uric acid (SUA) and proteinuria simultaneously occur in eclamptic crises (Paula et al., 2019). SUA predicts preeclampsia complications, LBW, and fetal death (Le et al., 2019; Shakarami et al., 2020; Ayankunle et al., 2021). High SUA at weeks 13 and 18 in women older than 35 is associated with the development of GDM (Zhao et al., 2022). Probiotics and prebiotics play a role in taming SUA levels. Yogurt containing *Lactobacillus acidophilus* and *Bifidobacterium lactis* lower SUA levels and improves insulin sensitivity (Rezazadeh et al., 2021). *Lactobacillus gasseri* PA-3 also lowers SUA levels in humans (Yamanaka et al., 2019). In addition, Jerusalem artichoke has prebiotic properties that can reduce SUA and prevent constipation (Sawicka et al., 2020). *Lactobacillus rhamnosus* improves calcium and magnesium retention, which may reduce the severity of preeclampsia, while *Lactobacillus helveticus* and kefir improves hypertension and calcium reabsorption (Beltrán-Barrientos et al., 2016; Gohel et al., 2016; Suliburska et al., 2021).

The human gut microbiota plays a significant role in the thrivability and survivability of the specie as it helps form the immunological and metabolic systems and determines which nutrients becomes part of the absorption process (Miao et al., 2021). A prenatal gut microbiota analysis is crucial as mothers with preeclampsia were noted to have lower levels of Bifidobacteriaceae and Bifidobacterium than mothers without preeclampsia (Miao et al., 2021). In addition, high Blautia and Ruminococcus can negatively affect the maternal metabolic profile and lead to glucose intolerance, type-2 diabetes, or GDM (Miao et al., 2021). Moreover, a deficiency in Bifidobacterium negatively affects cardiovascular health through hypertension and hyperlipidemia (Miao et al., 2021). Preeclampsia may be prevented with Bifidobacterium supplementation (Miao et al., 2021). Fermented milk products containing *Lactobacillus acidophilus* LA-5, *Bifidobacterium lactis* Bb12, and *Lactobacillus rhamnosus* GG reduce the systemic inflammatory response, which contributes to preeclampsia (Brantsaeter et al., 2011). Lastly, anemic mothers with preeclampsia had extended hospitalizations (Smith et al., 2019). Anemia during pregnancy creates life-threatening conditions as an anemic mother is at higher risk of experiencing preeclampsia, cesarean delivery, LBW birth, PTB, delivering small for gestational age infants, perinatal deaths, and maternal death (Smith et al., 2019). Another problem with maternal anemia is that the placental is an iron highway for the fetus to accumulate 80% of its iron stores within the last trimesters, which determines its development, growth, and through its infancy, meaning that even if the infant makes it out alive, it may not necessarily remain alive or able to fully adapt to stressors (Cao & Fleming, 2016). For this reason, implementing probiotics in prenatal

care is essential, as *Lactobacillus Plantarum* improves iron absorption (Vonderheid et al., 2019; Axling et al., 2020).

### **Probiotics, Precision Medicine, and Medical Microorganism Management**

Precision Medicine (PM) is a newer approach to allopathic medicine which surpasses the traditional signs and symptoms approach and focuses on the effects of biomarkers, lifestyle, environment, and genetic makeup within an individual (König et al., 2019). Unfortunately, PM will remain lacking unless the human microbiome becomes part of this clinical investigative process.

The human microbiome remains in its infancy compared to the fact that many bacteria in the Planetary Microbiota are more than half a million years old, but can still provide vital aims to plan for the survival and thrivability of the human species (Molinari, 2019). This DNP project arrived at a critical time in human evolution, considering that some organizations such as NASA, European Space Agency, the Indian Space Research Organization, and Space X are determined to research or travel beyond our galactic home. This survivability on other planets will only be possible if humans adapt to other worlds' viral and bacterial life forms. In other words, the human microbiome must be able to adapt to the Microbiome of an extraterrestrial environment. This is critical as although humans have been exposed to extraterrestrial organisms through the many bacterial and viral life forms entering Earth, the species will only reach full evolutionary potential when a complete merge occurs (Wickramasinghe et al., 2018; Wickramasinghe et al., 2020). It is imperative for survival that exposure to pathobionts be tamed as it may have detrimental effects on the human microbiome as the microbiota is the first-line of defense

against life-threatening pathogenic microorganisms (Arora et al., 2022). Maintaining a functionally effective and diverse microbiota can be challenging and critical, especially for those residing outside their previously adjusted environment (Al et al., 2022). As an astronaut that departs from its native planetary environment, a fetus experiences an extreme allostatic load as a result of the emotional, physical and psychological stress of being separated from its native utero-environment (Al et al., 2022).

Evolution is the interconnectivity of human, bacterial, and viral genetics exchanges and reactions at a cosmological scale (Wickramasinghe et al., 2018). For this to occur, a species' advanced scientific studies must focus on the entire gamut of creation to proceed with generational survival and thrivability. Furthermore, although PM may prove a better approach to personalized human medical treatment, it will only fully experience the evolutionary process of life extension once it embraces the human microbiome. Medical Microorganism Management (3M) differs from PM as 3M, unlike PM, is aimed at researching and utilizing signs, symptoms, biomarkers, lifestyle practices, psychological analysis, environmental exposures, nutrient and herbal therapy, human genomics, prebiotic and probiotic therapy, and the human microbiome in the clinical treatment of individuals. PBT which was birth from 3M may improve the survivability and thrivability of PTB and LBW infants, as it implements strand-specific PPT with consideration of the infant's allostatic load and its biological and environmental stressors.

The survivability of infants birthed outside of a hospital environment needs further research. Hospital environments are exposed to many deadly pathogens and

circulating electromagnetic fields and radiations from computers, electronics, diagnostics machines, direct ultrasounds, televisions, phones, and radiological studies being conducted. Children exposed to microwave radiation have a 2.15 greater risk of developing leukemia (Moon et al., 2020). In addition, maternal cell phone usage places the infant at an increased risk of developing behavioral problems, as children's heads have a greater radioactive absorbability than adults (Moon et al., 2020). The bio-physics school of thought here is that humans are predominantly organic electrical vessel which may experience adverse changes from outside electromagnetic interference. Educating new mothers and pregnant women on decreasing cell phone usage and keeping phones away from the uterus or infant is essential. This is crucial as the neurological system is the core sensory mechanism of the human body and provides prompt defensive reactions in the presence of a stressor, which can be diminished in children when exposed to EMF (Moon et al., 2020). *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, and *Lactobacillus casei* under EMF exposure proceeded to proliferate, which may indicate that in harsh, threatening environments, some probiotics may remain functional (Amanat et al., 2020). In an animal study, the symbiotic therapy *Bifidobacterium longum* and GOS provided integumentary protection against ultraviolet B irradiation (Kim et al., 2021). Protecting infants and PTB against radiation is crucial as radiation exposure can alter genetic cells, decrease lymphocytes, and increase the risk of disease development in later years (Al et al., 2022). *Lactobacillus sakei*, found in fermented sausages and kimchi, not only has an anti-inflammatory effect but can protect against some radiation damage, as in the case of radiation-induced enteritis (He et al., 2018).

Although this science is in the nascent stages, the vital importance of understanding the function and manipulation of the human microbiome is that it can tip the symbionts scales in favor of human survival, especially when developing a solution for PTB, maternal mortality, LBW, stillbirths and the IMR. A microbiota that is well-developed and adaptive to the residing environment can produce interconnectivity between networks to allow the sharing of life-sustaining resources within several areas of the body to ensure unified survival (Al et al., 2022). When Joshua Lederberg coined the term “Human Microbiome” in 2001 as the body’s ecological community of commensal, symbiotic and pathogenic microorganisms, little attention was given by the scientific and medical community for two decades to realize later that it may possess the key to helping us understand pathological conditions and help the human species to thrive and in the case of this DNP project help us find effective solutions to the global IMR (Urbaniak & Reid, 2016). The human microbiome is involved in the vast scale of human physiological function. For example, vitamin and mineral deficiencies were historically taught as an issue with nutrient availability, storage, absorption, and hyper-excretion, but today it is understood to be a dysfunction of the human microbiome (Al et al., 2022). This is imperative as an ineffective microbiota can improperly utilize vital minerals such as vitamin K, Calcium, and Pro-hormone D. Instead of functionally implemented, they can fall into uncontrolled circulation, resulting in calcified deposits in the brain, kidneys and vascular system (Al et al., 2022). This is critical as fermented soy can provide vitamin K2 to help appropriately distribute calcium, as *Bacillus* species helps control calcium oxalate kidney stones (Al et al., 2022). This may benefit astronauts who experience bone loss,

fracture risk, and renal calculi (Urbaniak & Reid, 2016). In addition, some *Lactobacillus* species found in fermented Indian foods can supplement the body with B vitamins, which may decrease the need to purchase specific over-the-counter supplementation as some prenatal vitamins contain traces of arsenic and lead, which can have damaging effects on the fetus (Schwalfenberg et al., 2018).

The combine administration of *Lacticaseibacillus paracasei* DG and Vitamin D improves the maintenance of vitamin D levels, which is critical as vitamin D deficiency increases the risk for preeclampsia, bacterial vaginosis, GDM, PTB, small for gestational age, reproductive failure or pregnancy loss (Ota et al., 2014; Castagliuolo et al., 2021). *Lacticaseibacillus paracasei* DG promotes plant-based amino acid absorption (Castagliuolo et al., 2021). *Lactobacillus* is vital to monitor in women as a decreased colony in the gastrointestinal tract will also decrease in the vaginal canal, which may result in difficulty in conceiving (Urbaniak & Reid, 2016).

### **PTB and Probiotics**

PTB creates a damaging effect on families, communities, health care systems, and the global economy as these prematurely developed infants tend to experience respiratory distress syndrome, hearing impairments, disorders of executive functioning, cardiovascular disorders, visual impairments, intraventricular hemorrhage, sepsis, global developmental delay and necrotizing enterocolitis (Dibo et al., 2022). Some of the causes of PTB are infection, diabetes, cardiovascular conditions, uterine over-distention, inflammation, an endocrine disorder, uteroplacental ischemia, oral dysbacteriosis, and environmental-genetic factors (Andrikopoulou et al., 2018; WHO, 2018; Pausan et al.,

2020; Yin et al., 2021; Dibo et al., 2022). Most PTBs and PTL membranes rupture are due to infection (Dibo et al., 2022). In addition, pubertal pregnancies or maternal biological immaturity are linked to birth complications, PTB, LBW, and high mortality rates (Rahman et al., 2019). Furthermore, alcohol intake can damage the gut microbiota, which may contribute to PTBs (Dibo et al., 2022).

Inflammatory-producing behaviors and lifestyles such as smoking, alcohol, microbiota dysbiosis, obesity (poor nutrition), drug abuse, emotional stress, poverty-related stress, and low socioeconomic (unaffordable living) status contribute to PTB (WHO, 2018; Pausan et al., 2020). HMO has an immunomodulatory and anti-inflammatory effect that combats some behavioral lifestyle damages (Pausan et al., 2020). Oral microbiota dysbacteriosis plays a significant role in the PTB as porphyromonas detected in periodontal disease promotes fetal-maternal gut dysbiosis and tissue damage due to inflammation (Yin et al., 2021). The pathogen that contributes to dental cavities, fusobacterium, contributes to preeclampsia (Yin et al., 2021). Both pathogens were detected in the stools of PTBs, indicating that the oral microbiota translocates into the gut microbiota (Yin et al., 2021). The oral microbiota contributes to blood pressure (Hudek et al., 2022). Unfortunately, pharmaceutical treatment of hypertension during pregnancy increases the risk of neonatal teratogenicity (Willmott et al., 2020). Untreated or inefficiently treated hypertension can lead to increased rates of coronary artery disease, strokes, increase neutrophils, decrease saliva protein levels, ischemic heart disease, increased parathyroid hormone levels, decrease saliva flow, and a decrease in calcium and vitamin D levels and absorptions (Willmott et al., 2020; Hudek



et al., 2022). The effects of decreased calcium, saliva flow and vitamin D levels can lead to oral damage. Females have a high level of edentulism and dental prostheses when compared to men (Marchi-Alves et al., 2017). In addition, dental prostheses promote the colonization of *Candida*, which is significant as presence of *Candida*, streptococci, and staphylococci in the saliva promotes hypertension (Marchi-Alves et al., 2017). Probiotics and prebiotics have been reported to improve blood pressure, while *Lactobacillus reuteri* increases the concentration of vitamin D levels (Willmott et al., 2020; Hudek et al., 2022).

Furthermore, antenatal steroid therapy, ATB therapy, healthy pregnancy, midwifery-led care, and low-dose aspirin in nulliparous women with no significant health conditions have helped PTB and PTL (Andrikopoulou et al., 2018; WHO, 2018). Once a mother experiences early-onset labor, several drugs are initiated to delay the PTB, such as antibiotics, oxytocin antagonists, calcium channel blockers, magnesium, and progesterone (Dibo et al., 2022). Unfortunately, these treatments do not offer dependable solutions and lack long-term research on their effects on the infant's adult life (Dibo et al., 2022). In addition, these agents result in a maternal experience of hyperglycemia, hypokalemia, headaches, tachycardia, palpitation, shortness of breath, tremors, nausea, chest pain, vomiting, and nasal rigidity (Dibo et al., 2022). Although antibiotic can be given as a prophylactic, it does not prevent PTB or PTL and damages the protective microbiota of the mother and infant (Dibo et al., 2022). This is important as probiotics antimicrobial compounds have demonstrated preventative measures against infections

and the promotion of human cellular survival without the same adverse effects as antibiotics (Dibo et al., 2022).

Lactic acid production of *Lactobacillus* species reduces the vaginal pH levels, which decreases the development of infection, which is one reason why the low presence of *Lactobacillus* species increases the risk of PTB (Pausan et al., 2020; Dibo et al., 2022). *Lactobacillus casei*, *Lactobacillus rhamnosus*, and *Lactobacillus paracasei* have anti-apoptotic effects (Dibo et al., 2022). *Lactobacillus Plantarum* prevents pathogenic microorganisms from attaching to the lumen (Dibo et al., 2022). *Bifidobacterium infantis*, *Lactobacillus acidophilus*, *Lactobacillus lactis*, *Lactobacillus. helveticus*, *Lactobacillus kefir*, and *Lactobacillus rhamnosus* promote T cell growth and regulation while fighting inflammation (Dibo et al., 2022). In addition, some of the probiotics found in a healthy vaginal microbiota include, *Lactobacillus gasseri*, *Lactobacillus crispatus*, *Lactobacillus iners*, and *Lactobacillus jensenii* (Dibo et al., 2022). In the case of *Lactobacillus jensenii*, this strand was noted in the presence of PTL contractions and women with short cervix, while *Gardnerella* species were associated with PTB and short cervix (Pausan et al., 2020). In the case of bacterial vaginosis, in addition to vitamin D supplementation, the following strands were utilized to treat the condition, *Lactobacillus casei*, *Lactobacillus acidophilus*, *Lactobacillus reuteri*, *Lactobacillus gasseri*, *Lactobacillus crispatus*, *Lactobacillus salivarius*, *Lactobacillus fermentum* and *Lactobacillus rhamnosus* (Dibo et al., 2022).

Probiotic effects against bacterial vaginosis provided positive signs and symptoms after 14 days of ingestion of *Lactobacillus rhamnosus* and *Lactobacillus fermentum* twice

a day (Dibo et al., 2022). *Lactobacillus kefir*, *Bifidobacterium lactis*, *Lactobacillus rhamnosus*, and *Lactobacillus acidophilus* reduce the risk of PTB (Dibo et al., 2022). When kefir was drunk throughout the pregnancy, it reduced the risk of PTB (Dibo et al., 2022). It is imperative to reconsider the current approach to prevent PTL, PBT, LWB, and the IMR, as current measures have shown minimal improvements in the past decades (Dibo et al., 2022).

### **HBM: The Golden Elixir of Life**

HBM, when adequately produced, can provide all the needed nutrients for the first 6 months of an infant's life (Sánchez et al., 2021). In addition to building the infant's microbiota, HBM decreases the risk of mortality, otitis media, dental malocclusion, obesity, and asthma and enhances the child's intelligence and cognitive function (Sánchez et al., 2021). HBM is the true essence of functional food. HBM natural emulsification process allows nutrient-rich fat globules to be bioavailable in the infant's gut (Sánchez et al., 2021). Unfortunately, formula milk's fat compositions derived from vegetable oils do not provide the same benefits as a mother's milk, making HBM essential (Sánchez et al., 2021). Animal breast milk (ABM) substituted for HBM does not provide the same benefits, as ABM is a foreign species' body fluids and not biologically identical or created for the body of a human infant. Early production of HBM has the highest amount of disialoganglioside, which may contribute to the proliferation, activation, and discrimination of immune cells and immunomodulatory outcomes (Sánchez et al., 2021). HBM's lactoadherin, mucin,  $\beta$ -palmitate, linoleic acids,  $\alpha$ -linolenic and genetic HMO are all involved in gastrointestinal development, immunological brain growth and

maturation, microelement absorptions, and the microbiota's maintenance (Sánchez et al., 2021). HMO is superior to animal milk oligosaccharides (AMO) as HMO has more diverse and higher numbers of oligosaccharides. Some women may genetically carry 200 types, which may indicate one reason for human intelligence, consciousness, and advanced cognitive and linguistic function (Sánchez et al., 2021). In addition, HBM's genetic proteome carries over 1500 expressions and 700 bacteria species, which highlights the superiority of the human species (Sánchez et al., 2021; D'Alessandro et al., 2022). The female microbiota's influence and configuration on human life highlight the importance of aiding and protecting the maternal experience.

HBM's caseins are lower than those produced in ABM as human infants require a carefully titrated growth rate and, unlike animals, are incapable of walking and functioning as an immediately birthed animal. Furthermore, the HBM caseins produce a C12 peptide that assists the infant's cardiovascular system adapts to its allostatic load (Sánchez et al., 2021). HBM is rich in  $\alpha$ -lactalbumin, which has a prebiotic effect to fuel Bifidobacterium and helps with the binding and absorption of iron, zinc, and calcium (Sánchez et al., 2021). In addition,  $\alpha$ -lactoalbumin has an anti-cancer effect on about 50 different types of cancer cells. Furthermore, the HBM lactoferrin activity has an anti-parasitic and anti-viral effect, which helps protect the infant from coronaviral infections (Sánchez et al., 2021). ABM and formula milk are deficient in taurine, which is sufficient for HBM and essential to the infant's vision and hearing function (Sánchez et al., 2021). HBM provides the infant's microbiota with an average of 800,000 bacteria daily, which impacts human microbiome colonization (Sánchez et al., 2021). The impact of this

colonization occurs through the symbiotic presence of probiotics and prebiotics, as in the case of *Bifidobacterium infantis* and HMO.

*Bifidobacterium infantis* promote gut microbiota colonization through the metabolism of HMO. In addition, *Bifidobacterium infantis* decreases intestinal permeability, decreasing pathogenic microorganisms that can translocate into the bloodstream and improving leaky gut and gastrointestinal inflammation, which can contribute to the decrease in NEC occurrence (Chichlowski et al., 2020). The combination of HBM and *Bifidobacterium infantis* effectively normalizes the infant's fecal microbiota due to its ability to metabolize HMO (Chichlowski et al., 2020). In addition to the benefits of HBM on the infant's microbiota, HBM can also benefit other populations by isolating microorganisms. Some probiotic strains isolated from HBM are *Lactobacillus plantarum*, *Bifidobacterium animalis*, *Bifidobacterium longum*, and *Lactobacillus gasseri* (D'Alessandro et al., 2022). In addition, *Bifidobacterium* was first isolated from the stool of breastfed infants 123 years ago (Chichlowski et al., 2020). The origins of probiotics are critical to cultural acknowledgment and religious beliefs when recommending these life-promoting microorganisms. Although probiotics can be isolated from fermented foods and HBM, they can also be isolated from infant fecal matter, vaginal secretions, and oral saliva, which may not be considered acceptable or koshered for some (Srikham et al., 2021). Lastly, although the HBM microbiome originates in the gastrointestinal tract, it is influenced by the bacteria within the breast tissue pathways (Eslami-S et al., 2020). HBM is not just a composition of the maternal gut and breast

microbiota but a collection of her life, genetics, and environmental exposures and consumptions.

### **Probiotics, Antibiotic-Associated Diarrhea, Spontaneous Abortion**

Prescribing ATBs to a pregnant woman is a serious medical decision, as some ATBs can adversely affect tissue remodeling and promote DNA damage (Muanda et al., 2017). Furthermore, since ATBs do not differentiate between non-pathogenic and pathogenic microorganisms, these drugs may behave as fetal rejection drugs resulting in spontaneous abortion. For example, although nitrofurantoin and trimethoprim–sulfamethoxazole do not seem to increase the risk of spontaneous abortions, other ATBs such as Azithromycin, Clarithromycin, and Metronidazole amplify the risk of spontaneous abortion (Muanda et al., 2017). Although there are many causes of vaginal microbiota dysbiosis, such as menstruation, sexual relations, hormonal changes, vaginal douching, infections, and diabetes, ATB therapy appears to be the most abrupt method of microbiome change (Chee et al., 2020). Lactobacillus species decrease the transmission of STIs, including reducing HIV-1 infection adhesion and target cell entrances (Chee et al., 2020). In addition to infection transmission prevention, probiotics may protect the fetal and maternal microbiota, decreasing the risk of reproductive failure.

When recommending probiotics to offset the dysbiosis created by ATB therapy, it is imperative to prescribe a combination of Lactobacillus and Bifidobacterium species (Rowles, 2017). The combined recommendation of Lactobacillus and Bifidobacterium species decreases the adverse effects of ATBs, such as yeast overgrowth, intestinal inflammation, loss of friendly bacteria, antibiotic-resistant bacteria, diarrhea, and

disruption of the composition and function of the human microbiome, which results in better patient compliance to ATB therapy (Rowles, 2017). Over 20% of patients on ATBs develop diarrhea which results in not completing the course, resulting in recurrent infections, expensive diagnostic testing, prolonged hospital stays, ATB resistance, and increased medical costs (Neut et al., 2017; Rowles, 2017). ATB-associated diarrhea (AAD) can last ten days and result in dehydration and electrolyte imbalance, increasing the risk for arrhythmia and adverse events to the fetus (Neut et al., 2017). Broad-spectrum ATB places the patient at higher risk for microbiota dysbiosis (Neut et al., 2017). In addition, AAD increases the likelihood of opportunistic pathogenic microorganism colonization and susceptibility to *Clostridium difficile*-associated diarrhea (CDAD), which occurs in 20% of patients with AAD (Neut et al., 2017). *Saccharomyces boulardii* can help prevent CDAD. *Saccharomyces boulardii* and *Lactobacillus rhamnosus* GG prevents AAD in children (Neut et al., 2017). *Saccharomyces boulardii* is affected by anti-fungal, but not by oral ATB (Neut et al., 2017). In addition, a vaginal capsule containing *Bifidobacterium bifidum*, *Lactobacillus helveticus*, *Lactobacillus salivarius*, *Lactobacillus plantarum*, *Lactobacillus acidophilus*, and *Lactobacillus brevis* was able to help restore the vaginal microbiota (Chee et al., 2020).

Diversified vaginal microbiota plays a significant role in fertility (Fernández et al., 2021). Vaginal microbiota dysbiosis is associated with infertility, intra-amniotic infection, bacterial vaginosis (BV), PTB, and spontaneous abortion (Fernández et al., 2021). Furthermore, the presence of *Klebsiella pneumoniae*, enterococci, *Escherichia coli*, streptococci, and staphylococci, results in an increased risk of miscarriages and fertility

treatment failure (Fernández et al., 2021). The presence of Lactobacilli species improves the outcome of fertility treatment and natural fertility (Fernández et al., 2021).

Lactobacillus salivarius CECT5713, renamed Ligilactobacillus salivarius, has an antimicrobial inhibiting effect against Candida albicans, Streptococcus agalactiae, Candida glabrata, Gardnerella vaginalis, Ureaplasma urealyticum and Candida parapsilosis (Fernández et al., 2021). In addition, Ligilactobacillus salivarius CECT5713 increases the successful pregnancy rate in women who experienced spontaneous abortions (Fernández et al., 2021).

The human microbiome in the science of fertilization is critical as TGF- $\beta$  1, and TGF- $\beta$  2 which are involved in implantation, trophoblast differentiation, immunoregulation, and angiogenesis, are highly concentrated in seminal fluid, which creates an environment for the maternal immune-tolerant response, embryo implantation, and successful pregnancy (Fernández et al., 2021). Furthermore, research is needed to analyze the compatibility of the female-to-male microbiome, as the seminal fluid plays a significant role in ensuing pregnancy and causes miscarriages (Fernández et al., 2021). In addition, Lactobacillus salivarius increases the presence of TGF- $\beta$  1 and TGF- $\beta$  2, which may reduce the risk of reproductive failure (Fernández et al., 2021). Women who received daily supplementation of Ligilactobacillus salivarius CECT5713 for six months experienced a 56% improvement in successful pregnancy (Fernández et al., 2021). Overall, the combined use of probiotics with ABT can not only reduce the risk of ATB-related adverse events but reduce the risk of spontaneous abortions.



### Findings and Implications: DNP PBT Project Presentation

The DNP PBT project occurred at a midwifery clinic in Northeast Ohio. The staff was welcoming and eager to learn about the implication and research of probiotics and PBT. Nine participants took the pretest and posttest. The pretest had a mean score of 49%, which aligns with previous research on healthcare professionals with medium-level knowledge of probiotics (Fijan et al., 2019). Table 3 indicates where the most significant gap exists. Although most HCPs knew the textbook definition of a probiotic and the scientific benefits of KMC, most demonstrated a knowledge gap of what the human microbiome consists of, the health components of HBM, the application of probiotics in disease prevention, how HBM can benefit LBW and PTB infants and what probiotic research is currently available.

**Table 3**

*PBT Pretest Results*

Test Question	Correct	Incorrect	Purpose of Question
One (Interest Rating)	N/A	N/A	N/A
Two	8	1	Probiotic Definition
Three	1	8	Prebiotic/ Nutrient of HBM
Four	3	6	Probiotics in disease prevention
Five	3	6	HBM in PTB & LBW
Six	4	5	Probiotic research
Seven	5	4	Human Microbiome
Eight	6	3	Infant microbiota colonization
Nine	7	2	KMC science
Ten	3	6	Human Microbiome Makeup

*Note.* The total overall grade for all exams was 49%.

Table 4 reports the data results of the posttest, which had a mean score of 95%, attributed to the PBT presentation. Questions two, four, five, and seven, each received one incorrect answer. The areas of incorrect answers on the posttest dealt with the components of HBM, research of probiotics concerning infection, the benefits of HBM to LBW and PTB infants, and the colonization of infants' microbiome.

**Table 4**

*PBT Posttest Results*

Test Question	Correct	Incorrect	Purpose of Question
One	9	0	Probiotic Definition
Two	8	1	Prebiotic/ Nutrient of HBM
Three	9	0	Probiotics in disease prevention
Four	8	1	HBM in PTB & LBW
Five	8	1	Probiotic research
Six	9	0	Human Microbiome
Seven	8	1	Infant microbiota colonization
Eight	9	0	Probiotic - GDM
Nine	9	0	Neonatal Microbiome
Ten (Interest Rating)	N/A	N/A	N/A

*Note.* The total overall grade for all exams was 95%.

Table 5 displayed the participants' level of interest before and after the in-service. Overall, the staff was welcoming and willing to learn with the intent to understand better ways to benefit their patients and clinical knowledge. In addition, participants who were highly motivated and interested in the subject remained highly motivated and interested in the subject. Only one staff member remained moderately interested before and after the in-service. In addition, four participants achieved a higher rate of interest after the in-

service presentation, indicating that the PBT in-service provided a tool to increase clinicians' knowledge and interest in probiotics and PBT.

**Table 5**  
*Participants' Interest Level in PBT and Probiotics*

Participant Number	Pretest (Question 1)	Posttest (Question 10)
One	High	High
Two	Moderate	Moderate
Three	Moderate	High
Four	High	High
Five	Moderate	High
Six	High	High
Seven	Low	Moderate
Eight	Moderate	High
Nine	High	High

When considering the unanticipated outcomes or limitations of the DNP PBT project presentation, the critical factor was the need to increase knowledge on how probiotics can be utilized among vulnerable populations and specific health-related conditions or preventative measures. This unanticipated realization propels the need for a complete course on probiotics and the human microbiome. Although the in-service was successful in improving the knowledge practice gap, with the many strands available and continuous research on probiotics, prebiotics, and the human microbiome, an entire detailed course involving medical microorganism management would benefit both medical providers and patients. Narrowing the probiotic and prebiotic knowledge gap will help individual patients, communities, institutions, and healthcare systems in promoting better clinical practice and quality of life through adequate allostatic load management and disease prevention. In addition, considering that PTB is a global

epidemic, the PBT aspect of the training may provide a positive global social change to improve and effectively manage the current issues with PTB, LBW, and the IMR.

### **Recommendations**

Considering that the probiotic industry is a multi-billion-dollar business, with HCPs contributing a 79% recommendation rate with a medium level of knowledge, it is imperative for the safety of the patient-consumer that HCPs be provided with qualified in-service training and testing to address several areas of probiotics (Fijan et al., 2019). HCPs' knowledge gap of probiotics and PBT can improve with educational in-services on the various strands of probiotics and how to implement them in specific populations. It is imperative that the HCPs only recommend probiotics and prebiotics that have been researched on the population that their medical specialty treats and only after receiving training on the utilization of probiotics, prebiotics, and PBT.

HCPs recommending probiotics to mothers who are breastfeeding must only do so based on the dosage, duration, and strand utilized in this vulnerable population. In addition, the recommended probiotic must be a single dosage package containing expiration dates and more than five billion CFU (Wilkins & Sequoia, 2017). Furthermore, the strand must be linked to the prevention of a disease that the patient-consumer is at risk of developing or is currently diagnosed as having, such as prescribing researched probiotics strands to prevent GDM in at-risk mothers.

Lastly, as mentioned in the previous section, based on the findings, it is highly recommended that HCPs be offered a detailed course on medical microorganism management involving probiotics, prebiotics, and the human microbiome. A medical

microorganism management course would detail the function and benefits of probiotics and prebiotics and how it influences health and the human microbiome. In addition, the training program will detail how to safely and effectively prescribe strand-specific probiotics to improve health conditions and prevent the development of disease, as well as how to recommend probiotics to vulnerable populations, especially in the case of PBT. Considering the many issues that may arise from medication and ATB therapies, including microbiota dysbiosis, it is vital to educate HCPs on the correct probiotic to recommend with prescription medications. Furthermore, the implementation of the program will be most effective if provided during academic medical training, with post-prescriptive practice. The evaluation process will need to address the knowledge practice gaps involving HBM and HMO, probiotic research, neonatal microbiota, maternal microbiota, microbiota influence on disease, strand-specific probiotics in disease prevention, and the human microbiome. Moreover, taking into account Fijan et al. (2019) finding that 79% of HCPs with insufficient knowledge are recommending probiotics, it is critical that a probiotic-prebiotic practice guideline be developed to assist high-level medical providers such as NPs, advanced nurse midwives, and physicians to better understand and safely prescribe probiotics.

### **Contribution of the Doctoral Project Team**

The Doctoral Project Team (DPT) provided the DNP student support and encouragement during the project, as the DNP student received countless rejections from many organizations, including two midwifery universities. To the DNP student's surprise, the midwifery universities believed that the PBT to prevent LBW, PTB, and help reduce

the IMR "was not aligned with their views and mission." Fortunately, most practicing midwives and nurse practitioners, as well as physicians who encountered and learned of the project, did not share this view. Many were excited to learn that this could be a future option in the war to solve infant mortality and morbidities, as many previous preventative programs have been unsuccessful. With the help, encouragement, and guidance of the Walden University DPT, the DNP student was made aware and discovered many forward-thinking and scientifically encouraged high-level nurse practitioners and physicians willing to learn about probiotics and their implementation in medical practice.

When detailing the working relationship with the DPT, the team was forwarded thinking and even extremely encouraging. The mentor was highly involved in guiding and developing the DNP student to seek various alternatives to transmitting the vision into the project at hand. The DNP student was a plethora of raw knowledge, while the DPT was the guiding light in helping the DNP student to develop, shape, design, and transmit the DNP project effectively and with great purpose. In addition, considering that the DNP student's native tongue was not English, the DNP mentor played a significant role in helping the student obtain a better grasp of the English language in order to use more precise medical terminology in the project's narrative.

With this said, in order to further propel PBT doctoral project, the DNP student plans to convert the DNP research project (DRP) into a book and continue offering lectures throughout the country and hopefully internationally.

### **Strengths and Limitations of the Project**

The limitations of the DRP were as follows:

- Sample size: The DRP sample was a small group of providers and would benefit from a larger population.
- Population: Although the participants were HCPs within the midwifery clinic, the DRP would benefit from designing an expansion to programs that can build the knowledge of probiotics in several specialty areas such as gastroenterology, cardiology, family medicine, psychiatry, and pediatric providers.
- Disease-specific patient population: The current DRP focuses on PBT, but further research and in-service training involving the utilization of probiotics, fermented foods, and prebiotics in various patient populations, such as those with cancer, heart disease, and many others.
- Lack of practice observation: The DRP was a staff education project and would have benefited from having the opportunity or privilege to observe if the new onset knowledge of probiotics improved the safety and quality of care in patients seeking medical knowledge of the correct probiotic and its use.

The strengths of the DRP were as follows:

- Gain knowledge: The DNP project provided a positive correlation between offering a probiotic presentation and narrowing the knowledge practice gap.
- New Approach: The DNP project helped in surfacing an original body of knowledge involving the utilization of probiotics in PBT and disease prevention.

- Expansion: The project allowed for the expansion of existing knowledge involving probiotics.
- Synthesis: Data collection was precise and methodical, which reduced the presence of bias. The research findings were matched and translated into a theoretical but realistic and safe practice, allowing the project to be implemented in an academic setting.
- APRN Contact: The project provided an opportunity to receive feedback from HCPs, feedback that will allow better design of future probiotic in-services.

### **Literature Gap**

Although HBM and PPT are superior to formula milk in preventing NEC and other conditions, according to Craighead et al. (2020), due to the various researched probiotic strains, new emerging strains development, poor regulation, insufficient knowledge of dosage requirements, and no standard approved clinical probiotic products, or lack of prescriptive guidelines, probiotics continue to experience difficulty in becoming part of the medical mainstream practice. Other reasons HCPs have not implemented probiotic recommendations in their practice is due to the limited research on pro-inflammatory responses, the potential for septic-like responses, and the development of antibiotic-resistance strands (Deshpande et al., 2018; Davani-Davari et al., 2019).

These concerns are a result of the probiotic industry needing better regulations and educational programs. When purchasing probiotics, one cannot determine how many of the live organisms are alive as the dead particles may induce an adverse biological



response (Deshpande et al., 2018). For this reason, the development of post-probiotics, para-probiotics, or ghost-probiotics is being considered, as these are non-viable microbial cells that may theoretically decrease potential adverse reactions (Deshpande et al., 2018). Post-probiotics are inactive microorganisms or metabolites secreted after a bacterial breakdown during fermentation (Mantziari et al., 2020). These may provide immune support, as in the case of a heat-treated *Lactobacillus paracasei* post-probiotic, which may protect against the influenza virus by increasing IgA production in the small intestine (Mantziari et al., 2020). Post-probiotics are a growing interest due to the lack of standardized development and regulation of probiotics, which prevents predictive knowledge as to the reaction an immune-compromised person, such as cancer, HIV, or transplant patient, will experience upon the ingestion of a potentially dead organism within the probiotic which theoretically may result in the emergence of endocarditis, bacteremia or septicemia (Davani-Davari et al., 2019).

In addition, the study by Härtel et al. (2017) propose that many of the inconsistency found in probiotic microbiome studies may be due to the population being studied, the current state of the subject's gut microbiota, whether a multi-strain or mono-strain were administered, the microbes in the environment that the subject is exposed to, the type of probiotic, sample size, and quality of the formulations. Moreover, current research lacks a population-specific and disease-specific prebiotic and probiotic investigation (Davani-Davari et al., 2019). Similar to the aged argument on vaccination medicine, research is needed to determine the long-term effects of prebiotic use and how different dosages affect human health (Whisner & Castillo, 2018). Although probiotics

are associated with a decrease in preterm mortality, further studies into the long-term effects of probiotics should be considered (Singh et al., 2019). Probiotic dosing and beneficial bacterial strains need to be universally established to prophylactically colonize the infant's gut microbiota (Singh et al., 2019).

Many of the conflicting finds in probiotics therapy can be attributed to the inconsistency of the strains used, the formulation, the lack of set protocols, and the development of set strains for specific target populations (Fortmann et al., 2020). Future research must identify the maternal gut microbiota, the HBM microbiome sequencing, and breastfed infant gut microbiota sequencing with probiotics (Fortmann et al., 2020). In addition, although formula-fed infants may experience a higher weight gain versus HBM-fed infants, the quality, benefits, and effects of body mass expansion of formula-fed versus HBM-fed infants have not been studied.

Section 5 of this DNP project will provide personal insight into the DNP student's project experience, findings, and future aims to publicize this critical knowledge.

## Section 5: Dissemination Plan

### **Introduction**

The plan to publicize these findings will extend beyond the institutions experiencing this problem, as LBW, PTB, and infant mortality is a global problem that affects everyone, not just specific communities and nations. Although this project was utilized to gain credentials needed to gain access to specific professional settings, it remains my intellectual property, which indicates vast areas of mobilization will be utilized in order to spread the information through a research-book conversion, speaking events, workshops, field collaborations, and eventually allowing the data and its expansion to become part of the academic nursing science curriculum.

PBT, prebiotics, and strand-specific lectures on probiotics will benefit HCPs as it opens the doors to possibilities outside the pharmaceutical world of medicating patients. Although specific medical conditions are not managed with probiotics, the utilization of probiotics can play a significant role in disease resistance and prevention. Whether the human microbiome focuses on disease prevention related to cardiobiome, neurobiome, psychobiome, immunobiome, renalbiome, osteobiome, gastrobiome (gut microbiota), or the microbiota of the skin and remaining biological systems, it is without a doubt that even in micro-dosing of these live organisms, the human body has experienced symptomatic alleviation through the mechanics of bioactive metabolite emission, reducing pathogenic attachment, improving mucosal barriers, enzymatic formations, immunological development, organic acid production and central nervous system regulation (Liu et al., 2018; Sanders et al., 2019). Unfortunately, until medical

researchers begin to focus on strand and dosage-specific disease prevention effects of probiotics involving the human microbiome and human genome with pharmaceutical grade and dosage-specific supplementation, this minimally explored almost \$20 billion industry will remain an untapped potential for the prevention of disease and infant mortality (Liu et al., 2018).

### **Analysis of Self**

Although my background is not involved in infant mortality or prenatal care, all clinicians have a responsibility to address all issues, gaps in practice, or disparities that affect the living future of humans and the planet. This is an important objective to understand as many in the medical industry have a biased pattern of thinking that if a clinician or nurse does not have experience in a specific area, they are not qualified to perform a specific function at an expert level. However, this DNP project proves otherwise. Registered nurses and family nurse practitioners receive clinical training in all areas of medical care, which indicates that these groups should theoretically enter any field of nursing successfully. In addition, this DNP project further emphasizes the high-level function of the nurse practitioner (NP) as a medical provider, researcher, and agent of global clinical restructuring, as we see many dehumanizing and uneducated comments referring to NPs as midlevel providers. NPs are high-level medical providers who diagnose, treat, prescribe medication, order and interpret advanced medical diagnostics tests, and function as high-level primary medical and psychiatric providers. Not once has an NP been hired as a primary care provider for patients with mid-level conditions. NPs treat both acute and chronic disease patients of all age ranges.

Furthermore, this DNP project aimed to push the nursing field to embrace the human microbiome and the life sciences as nursing has struggled for decades to gain ground in creditability among other high-level scientific scholars due to the avoidance of involving themselves in complex scientific research that can be transferred into the field of nursing. Behavioral practices are essential when they provide alleviation of symptoms, such as KMC, but it is still our responsibility to search out the natural science propelling these benefits. It is no different from implementing a diagnostic algorithm versus having scientific knowledge. A diagnosis illustrates an occurrence but does not scientifically detail the clinical-biological function of the condition. This is why NPs and physicians can be excellent diagnostic algorithm implementers but are challenged by the depths of the science that causes the diagnosis. By returning to the science of facts, nursing will not remain a behavioral practice of hunches and theories. An old chemistry teacher of mine once said that if one cannot explain a complex scientific process or law in the simplest form, then they do not understand it themselves. We must aim to understand science to the level science requires to be understood.

In the case of the challenges faced during the attempt to complete the DNP project, the greatest obstacle was the lack of support from the medical and nursing stakeholders and organizations that employ them. I faced insurmountable opposition in the project's development, from delayed presentations, rejection, false promises, and even direct attacks from clinicians who felt that the DNP project would force the nursing field to change and NPs to gain higher ground in the medical industry. The process was similar to facing turtles that hid in their shells; most did not want to face this new pioneering

approach. Fortunately for me, these oppositions and professional attacks were enlightening and extremely helpful as they forced me to review the data and the project, which only created a realization that it was the right path to a trailblazing journey.

The DNP student intended to provide a different explorative approach to save the lives of children worldwide by questioning the old nursing and medical paradigm. As mentioned, two midwifery universities expressed that the DNP project, which focused on the human microbiota and PBT to aid the reduction of PTB, LBW, and infant mortality, did not align with their mission. Infant mortality is crucial as the IMR of an individual state is not a true reflection of the entire area. Kentucky, for example, has a PTB rating of 11, LBW rate of 8.5, and IMR of 6.43 per 1000 live birth, but if one reviews the rate per county, one will encounter even more disturbing statistics such as the case of Fulton County in the state of Kentucky carrying the burden of 17 per 1000 live births (FHK, n.d; CDCP, 2022; CDCP, 2022). This highlights the thought that the IMR is not an accurate indication of how astronomical the problem is but a generalized average. LBW is another dilemma, as it can lead to infant death. Some states, such as Mississippi, Louisiana, Nevada, Colorado, North and South Carolina, Georgia, Alabama, West Virginia, Wyoming, and Arkansas, are rated 9 per 1000 per birth or greater (CDCP, 2022). In the DNP's home state of Ohio, the IMR is 6.5, LBW 8.5, and PTB 10.3 (CDCP, 2022).

Overall it was a remarkable and enlightening experience, especially to be a nurse practitioner on the verge of entering an innovative science that researches and questions planetary life and the human existence of microbial and mammalian cellular body merger and function.

## Summary

It is vital to know that infant mortality is a true reflection of the health and future of the human species. The world's human population is affected by the IMR, maternal deaths, and an unexpected increase in the world mortality rate. Maternal death is the biological termination of a woman while pregnant or within 42 days postpartum (CDCP, 2020). In 2020 there has been as much as a 20% increase in maternal death and an increase in maternal death rate involving home births (CDCP, 2020; Johnson, 2022). Recent reports for the World Data and life insurance companies have reported an increase in non-COVID-related death worldwide (Giattino et al., 2022; MH, 2022; Scism, 2022). In addition, countries such as Scotland are experiencing an unexplainable surge in their IMR (BBC, 2022; NRS, 2022). Moreover, there are concerns that human fertility rates are dropping, which will contribute to a sudden population decline in industrialized regions, such as the USA (Skakkebaek et al., 2022). Nurses worldwide must begin utilizing the life sciences and the human microbiome in their practice and research to create global conditions that will help these infants and mothers to thrive and not just survive.

Although further studies are required, probiotics appear to have seminal protective qualities while increasing sperm motility and decreasing DNA fragmentation, which may improve fertility (Valcarce et al., 2017; Farahani et al., 2021). In addition, the research and implementation of probiotics, prebiotics, and PBT into clinical practice and academic curriculums may improve the outcomes of maternal health, PTB, LBW, infant mortality, and the mortality and morbidity of humans in general. With this said, the DNP

student anticipates that this project will pave the way for the nursing profession to take a proactive approach to further researching the human microbiome and probiotics while implementing PBT in the clinical arena.

Lastly, when considering the DNP student final though on the project, regional disease frequency (RDF) is another integral approach to the human genome, human microbiome, and the IMR. Exhaustible Big-Data collection is retrieved and categorized, but more research is needed to review the epidemiology patterns of these findings. Researchers must locate the anomalous occurrence of any data, as patterns lead to predictably. There is always a solution, even when faced with an impasse. If humankind expects to survive and thrive in the distant future, humankind must focus on methods to revolutionize medical science. We must begin to focus on a balanced, respectful, and humanistic approach to achieve a truthful, peaceful life with each other and our planet and universe. We do not need one world government or monopolies but rather one unified love and respect for each other, a unification that places us in a righteous mindset to protect and help each other to survive and thrive through conscious, meaningful support. This is the core motivation that keeps good scientists sacrificing with no expectation of being rewarded or known, to ensure all species are well and safe. This is the greatest gift any scientist from the past, present, and future can ever experience, the blessing of knowing that she or he made the Earth a better place to live, even if no one knew or heard of us.

It is critical that this research not be taken lightly or equated to "just" an academic student project, as the DNP student is a board-certified and licensed nurse practitioner



who held a 17-year clinical career at the bedside and training clinicians of all levels to provide competent and effective safe care. This DNP student also held positions in clinical resuscitation teams, education leadership, and critical project management. In addition, other effective created programs were the registered nurse intervention program to reduce hospital readmission rates, infection control investigations of blood culture procedures, and clinical investigations of medical errors and sentinel events. Furthermore, this DNP student has created and designed programs involving rapid response team development and clinical programs promoting medical knowledge into clinical practice.

This is essential to understand as although this DNP project was completed for an academic degree, the knowledge itself was generated from years of clinical exposure and experience from a highly seasoned and competent clinical practitioner and investigator who places astronomical importance on the value and safety of all human lives.

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## Appendix A: Probiotic Chart

Probiotics	Usage	Research
Lactobacillus Fermentum	Mastitis Immunomodulatory effect. Improves high blood pressure. Improved oxidative stress and memory Enhance cognitive function	Bond, et al., 2017 Łubiech, et al., 2020 Improves high blood pressure Wu & Chiou, 2021 Kumar et al., 2022
Lactobacillus delbrueckii	Inhibit gas-forming coliform bacteria Improved oxidative stress and memory	Aloisio, et al., 2018 Kumar et al., 2022
Lactobacillus Salivarius	Mastitis Anti-inflammatory effect. This probiotic can be decreased significantly in the presence of anesthesia administration. Prevents spontaneous abortion	Bond, et al., 2017 Łubiech, et al., 2020 Fernández et al., 2021
Lactobacillus plantarum	Inhibit gas-forming coliform bacteria. Increases transforming growth factor- $\beta$ 2 (TGF- $\beta$ 2). Decreases interleukin-6 (IL-6). Improves high blood pressure Increases iron absorption Decreases lead level	Aloisio, et al., 2018 Li, et al. 2019 Wu & Chiou, 2021 Hoppe, et al., 2017 Bhattacharya, 2019
Akkermansia muciniphila	Improves obesity and diabetes.	Wu & Chiou, 2021
Lactiplantibacillus Plantarum	Anti-viral effects against certain influenzas.	Mantziari, et al., 2020
Leuconostoc mesenteroides	Anti-viral effects against certain	Mantziari, et al., 2020

	influenzas.	
Kefir	Improved bone density. Heightens memory Improves spatial intelligence and executive function Improves mitochondrial dysfunction Aids DNA repair	Schepper, et al., 2017 Kumar et al., 2022
Lactobacillus Rhamnosus	Atopic Dermatitis Eczema, Reduces the dental cavity promoter Streptococcus Mutans. Support caesarian birth microbiota. Reduces postnatal maternal depression and anxiety Anti-fungal activities against Candida albican. Help decrease the risk of NEC, nosocomial infections and mortality. Decrease in length of phototherapy treatment and hospitalizations in infants with hyperbilirubinemia. Inhabits the absorption of mercury and arsenic. Decrease lead levels Improves calcium and magnesium retention	Simpson, et al., 2018 Wickens, et al., 2018 Pujia, et al., 2017 Korpela, et al., 2018 Slykerman, et al., 2017 Mantziari, et al., 2020 Narbona-López, et al. 2017 Torkaman, et al., 2017 Bisanz, et al., 2014 Bhattacharya, 2019 Suliburska, et al., 2021
Lactobacillus reuteri (chewing gum)	Decreases Streptococcus Mutans and promotes Lactobacillus paracasei concentration	Pujia, et al., 2017
Lactobacillus species	Lactose Metabolism	George, et al., 2022

Lachnospiraceae and Ruminococcaceae	Metabolism of complex carbohydrates	George, et al., 2022
Bifidobacterium breve	Supports caesarian birth microbiota. Decreases the occurrence of gastrointestinal disorders. Helps prevent NEC. Produces folate. Weight gain improvement and gastrointestinal tolerance. Improves high blood pressure	Korpela, et al., 2018 Aloisio, et al., 2018 Härtel, et al., 2017 Wu & Chiou, 2021
Bifidobacterium Infantis	Breakdown the complex carbohydrates found in the mother's milk. Helps develop and mature the immune system. Biological acceptance of vaccination medicine. Reduce stool frequencies and produce well form stools. Improves growth in length. Improve weight gain. Improves growth of head circumference. Lessens risk of NEC surgery intervention. Improve growth in human breast milk fed infants. Improves high blood pressure	Chichlowski, et al., 2020 Smilowitz, et al., 2017 Härtel, et al., 2017 Fortmann, et al., 2020 Wu & Chiou, 2021
Bifidobacterium lactis	Helps promote normal infant growth. Promotes growth in formula fed term	Radke, et al., 2017 Schepper, et al., 2017 Härtel, et al., 2017 Torkaman, et al., 2017

	<p>infants.  Decrease in length of phototherapy and hospitalizations in infants with hyperbilirubinemia.  Lowers uric acid levels  Improves insulin sensitivity</p>	Rezazadeh, et al., 2021
Lactobacillus acidophilus	<p>Reduces maternal symptoms of depression  Reduction of mortality.  Improved feeding tolerance.  Decrease in central venous line usage.  Decrease ventilator duration.  Decrease the frequency of rotavirus related diarrhea.  Help decrease the risk of NEC, nosocomial infections and mortality.  Improves growth in length.  Improves weight gain.  Improves growth of head circumference.  Improve growth in human breast milk fed infants.  Lessens risk of NEC surgery intervention.  Decrease in length of phototherapy treatment and hospitalizations in infants with hyperbilirubinemia.  Lowers uric acid levels  Improves insulin sensitivity</p>	<p>Slykerman, et al., 2017  Sharpe, et al., 2018  Mantziari, et al., 2020  Narbona-López, et al. 2017  Härtel, et al., 2017  Fortmann, et al., 2020  Torkaman, et al., 2017  Rezazadeh, et al., 2021  Kumar et al., 2022</p>

	Enhance cognitive function	
Lactobacillus bifidum	Help decrease the risk of NEC, nosocomial infections and mortality.	Narbona-López, et al., 2017
Bifidobacterium bifidum	Reduces maternal symptoms of depression Reduction of mortality. Improved feeding tolerance. Decrease in central venous line usage. Decrease ventilator duration. Prevents late on-set sepsis. Decrease in length of phototherapy treatment and hospitalizations in infants with hyperbilirubinemia. Enhance cognitive function	Slykerman, et al., 2017 Sharpe, et al., 2018 Tanaka, et al., 2019 Torkaman, et al., 2017 Kumar et al., 2022
Lactobacillus casei	Reduces maternal symptoms of depression. Reduction in anxiety. Anti-fungal activities against Candida albican. Improves high blood pressure Enhance cognitive function	Slykerman, et al., 2017 Mantziari, et al., 2020 Wu & Chiou, 2021 Kumar et al., 2022
Lactobacillus casei Shirota	Helps heal fractures	Schepper, et al., 2017
Lactobacillus casei rhamnosus	Decreases respiratory infections	Permall, et al., 2019
Oligosaccharides	Prebiotic (Indigestible) Promotes the growth of bifidobacterial strains	Smilowitz, et al., 2017



Galacto-oligosaccharide/polydextrose	Protects against respiratory infections	Permall, et al., 2019
Direct Breast Milk Feeding	Asthma prevention. Prevents necrotizing enterocolitis. Stabilizes Bifidobacterium Species in the gut microbiota	Norarbartolo, et al., 2021
Streptococcus Salivarius	Oral cavity colonization at birth	Pujia, et al., 2017
Xylitol (prebiotic)	Reduces the dental cavity promoter Streptococcus Mutans.	Pujia, et al., 2017
Lactobacillus paracasei	Suppress Streptococcus mutans growth Anti-viral effects against certain influenzas. Lower uric acid	Pujia, et al., 2017 Mantziari, et al., 2020
Lactobacillus gasseri	Improves high blood pressure Improves lung function and decreases asthmatic symptoms Lower uric acid	Wu & Chiou, 2021 Permall, et al., 2019 Yamanaka, et al., 2019
Bifidobacterium longum	Helps prevent malnutrition Improves high blood pressure Decrease asthma occurrence	Million, et al., 2017 Wu & Chiou, 2021 Permall, et al., 2019
Antibiotic Therapy in infancy	Decreases the infant gut microbiota of Lactobacilli species, Bacteroides and Bifidobacteria species. Promotes behavioral issues and depression in children	Slykerman, et al., 2019
Lactobacillus Reuteri	Reduction of newborn sepsis and death	Wastnedge, et al., 2021

Lactobacillus coryniformis	Improves high blood pressure	Wu & Chiou, 2021
Apple Polysaccharide	Decreases firmicutes and fusobacterium Increases Lactobacillus and Bifidobacterium	Zhou, et al., 2019
Lactobacillus helveticus	Lowers hypertension Improves cognitive function, memory and attention	Beltrán-Barrientos et al., 2016 Kumar et al., 2022
Lactobacillus fructivorans	Improved oxidative stress and memory	Kumar et al., 2022
Lactobacillus kefirifaciens	Improved oxidative stress and memory	Kumar et al., 2022

## Appendix B: Probiotic Terms

Term	Definition Match Test
Anti-Biotics	Synthetic medication utilized o fight infection whose name means Against-Life (Schepper, et al., 2017)
Pre-Biotics	Non-digestible nutrients that are metabolize to make probiotics (Davani-Davari, et al., 2019).
Pro-Biotics	Live organism that mean for life (Schepper, et al., 2017; Pujia, et al., 2017).
Post-Biotics / Post-Probiotics	Inactive microorganisms or metabolites secreted after bacteria (Mantziari, et al., 2020).
Para-Biotics / Para-Probiotics	Also referred to as Ghost-Probiotics, which are non-viable microbial cells or crude cell extracts (Deshpande et al., 2018)
Synbiotic	Combination of prebiotics and probiotics (Cukrowska, et al., 2020).
MOM	Mother's Own Milk
DHM	Donor Human Milk
Formula Milk	Milk that artificially created to substitute HBM
Human Microbiome	Collection of all the microbiota within a human
Human Genome	Genetic science of human genetic sequence / DNA (NHGR, 2018).
Microbiota	Microorganisms within a specific organism which can consist of viruses, bacteria, archaea, protists, fungi
Low birth weight (LBW)	1500–2500 grams (Tanaka, et al., 2019).
Very low birth weight (VLBW)	Less than 1500 grams (Wolke, 2018)
Extremely low birth weight (ELBW)	Less than 1000 grams (Wolke, 2018)
Term	Greater than 37 weeks gestational age (UTD, 2022)
Preterm	Between 33 and 37 weeks of gestation (WHO, 2018).
Moderate Preterm	Greater than 34 week, but less than 37 week (UTD, 2022)
Very Preterm	Between 28 and 32 weeks of gestation (WHO, 2018).
Extremely Preterm	Less than 28 weeks of gestation (WHO, 2018).
Neonatal death	Death occurring 30 days after birth (Chen et al., 2016).
Post-neonatal death	Death occurring 60 days after birth but before the first year of life (Chen et al., 2016).

Infant Mortality (<12)	Death prior to the first year of life (CDCP, 2021)
Protist	Eukaryotic organisms that are neither plants, animals nor fungi
Viruses	Infectious microbe
Bacteria	Single cell organisms
Fungi	Single or multi-cell heterotrophs eukaryotic organisms
Archaea	single-celled organisms that lack a nucleus such as prokaryotic
CFU	Colony Forming Unit
PUFA	Polyunsaturated Fatty Acids

## Appendix C: Fermented Foods and Probiotics

Probiotics and Prebiotics	Fermented and Non-Fermented Foods
<i>Lactobacillus fermentum</i>	Chocolate
<i>Lactobacillus Plantarum</i>	Chocolate, Dosa, Sauerkraut, Kefir
<i>Lactobacillus helveticus</i>	Chocolate
<i>Bifidobacterium longum</i>	Chocolate
<i>Bifidobacterium bifidum</i>	Kefir
<i>Bifidobacterium breve</i>	Fermented soymilk
<i>Leuconostoc mesenteroides</i>	Kimchi
<i>Lactobacillus acidophilus</i>	Yogurt
<i>Lactobacillus casei</i>	Shirota fermented milk
<i>Candida species</i>	Ogi
<i>Aspergillus oryzae</i>	Miso, Wheat, Soybeans
<i>Zygosaccharomyces</i>	Miso
<i>Haloanaerobium praevalens</i>	Surströmming
<i>Pediococcus species</i>	Miso, fermented sausage
<i>Bifidobacterium infantis</i>	Certain cheeses and yogurts
<i>Lactobacillus reuteri</i>	Sourdough
<i>Lactobacillus rhamnosus</i>	Yogurt
<i>Zymomonas mobilis</i>	Pulque
<i>Haloanaerobium alcaliphilum</i>	Surströmming
<i>Lactobacillus bulgaricus</i>	Yogurt
<i>Streptococcus thermophilus</i>	Yogurt
<i>Saccharomyces cerevisiae</i>	Kefir, Sourdough, Wine
<i>Lactobacillus species</i>	Kvass, Kaffir beer, Ogi, Garlic, fermented sausage
<i>Saccharomyces species</i>	Ogi
<i>Lactobacillus cremoris</i>	Crème fraîche
<i>Lactobacillus lactis</i>	Crème fraîche, Camel milk
<i>Gluconacetobacter</i>	Kombucha
<i>Zygosaccharomyces</i>	Kombucha
<i>Micrococcus</i>	Fermented sausage
<i>Penicillium roqueforti</i>	Cheddar cheese, Stilton cheeses
<i>Yarrowia lipolytica</i>	Cheddar cheese, Stilton cheeses
<i>Debaryomyces hansenii</i>	Cheddar cheese, Stilton cheeses
<i>Trichosporon ovoides</i>	Cheddar cheese, Stilton cheeses
Lactobacilli	Cortido Kraut
Inulin	Chicory root, Dandelion root
FOS / Oligofructose	Jerusalem artichoke, Chicory Blue agave, Barley, Wheat, Yucon, Jicama

GOS	HBM, HMO
Soluble Corn Fiber	Supplement
Lactulose	Found in heat treated dairy, promotes the growth of <i>Lactobacillus bifidus</i>
Bacillus	Rabadi and Kishk

## Appendix D: Staff Education Probiotic Pretest

1. Probiotic Self-Interest:
  - a. I have no interest in probiotics
  - b. I have little interest in probiotics
  - c. I am interested in probiotics
  - d. I am highly interested in probiotics
  
2. Probiotics are?
  - a. A living microorganism that yield health benefits
  - b. A vitamin that yields health benefits
  - c. A dead microorganism that yields health benefits
  - d. Not Sure
  
3. The third most abundant component of human breast milk is?
  - a. Lactobacillus species
  - b. Bifidobacterium species
  - c. Oligosaccharides Prebiotics
  - d. Not Sure
  
4. Which medical condition has been improved with the administration of probiotics among pediatric patients?
  - a. Autism
  - b. Necrotizing enterocolitis (NEC)
  - c. HIV
  - d. Not Sure
  
5. What is the dietary Gold Standard for low birth weight preterm infants?
  - a. Colostrum
  - b. Human breast milk
  - c. Formula-Milk
  - d. Probiotics
  - e. Not Sure
  
6. No research has proven that probiotics reduce the development of late onset sepsis?
  - a. True
  - b. False
  - c. Not Sure
  
7. The Human Microbiome is a new emerging science that is also referred to as an Organ?

- a. Yes
  - b. No
  - c. Not Sure
8. The Hospital environment influences the Infant's Microbiota?
- a. No
  - b. Yes
  - c. Not sure
9. Kangaroo Mother Care is a method for the infant's Human Microbiota colonization?
- a. Yes
  - b. No
  - c. Not Sure
10. The Human Microbiome is a genetic collection of Protist, viruses, bacteria, fungi, Archaea and many other microorganisms, which outnumber the cellular make-up?
- a. No
  - b. Yes
  - c. No Sure

**Answer Key for PBT Pretest:**

- 1. N/A
- 2. A
- 3. C
- 4. B
- 5. B
- 6. B
- 7. A
- 8. B
- 9. A
- 10. B



## Appendix E: Staff Education Probiotic Posttest

1. Probiotics are?
  - a. A living microorganism that yield health benefits
  - b. A Dead microorganism that yields health benefits
  - c. A mineral created by the body
  - d. Not Sure
  
2. The third most abundant component of human breast milk is?
  - a. Fructo-oligosaccharides
  - b. Galacto-oligosaccharide/polydextrose
  - c. Human Milk Oligosaccharides Prebiotics
  - d. Probiotic
  - e. Not Sure
  
3. Which medical condition has been improved with the administration of probiotics among pediatric patients?
  - a. Weight Gain
  - b. Necrotizing enterocolitis (NEC)
  - c. Decrease Length of Hospital Stay-Days
  - d. All the above
  
4. What is the dietary Gold Standard for low birth weight preterm infants?
  - a. Artificial Breast Milk (Formula)
  - b. Human breast milk
  - c. Colostrum
  - d. Not Sure
  
5. Probiotics reduces the development of late-onset sepsis?
  - a. No
  - b. Yes
  - c. Not Sure
  
6. The Human Microbiome is larger than the Human Genome?
  - a. Yes
  - b. No
  - c. Not Sure
  
7. The Hospital environment and maternal skin contact influences the microbiota of cesarean births?
  - a. No

- b. Yes
  - c. Not Sure
8. Probiotics may help reduce the complication of gestational diabetes?
- a. Yes
  - b. No
  - c. Not Sure
9. Probiotics can help the development and diversification of the infant's gut microbiota?
- a. No
  - b. Yes
  - c. Not Sure
10. After the In-Service on Probiotics and PBT, do you feel:
- a. Less to no interest in probiotics
  - b. My interest is the same as before
  - c. I feel more interesting in learning about probiotics
  - d. I am highly interested in learning more about probiotics

**Answer Key for PBT Posttest:**

- 1. A
- 2. C
- 3. B
- 4. B
- 5. B
- 6. A
- 7. B
- 8. A
- 9. B
- 10. N/A

## Appendix F: Recommendation Guiding Points

Conditions	Rational
Know the maternal and paternal health history and which strand help.	Knowing the family medical history allows one to determine the conditions the infant may be susceptible later in life and determine if any probiotic research was conducted on that condition.
Know which strand has been already researched on breastfeeding mothers and infants, as well as on health conditions.	It is crucial to never recommend anything that has not been research on a vulnerable population
Seek pharmaceutical grade probiotics, to improve Safety, Efficiency and Quality.	This prevents the likelihood of receiving an ineffective or cross-contaminated supplement.
Know which strands are in fermented foods.	This will allow one to cross match the correct foods with the health condition.
Teach the client the importance of identifying negative effects, stopping the probiotic immediately and reporting it to their Primary Care Provider at once	High focus on patient education is crucial to life safety.
Reinforce the importance of seeking qualified medical advice prior to initiating and new complementary and alternative therapies.	It is imperative to understand that most allopathic healthcare providers do not always possess an expertise level of knowledge in naturopathic medicine and as research demonstrates probiotics. Patients may ask providers about alternative health products and the provider may shunt the patient's request due to the provider's practice knowledge gap in naturopathic medicine. For this reason, it is imperative that providers refer patients to a more knowledgeable and qualified provider then to not address the patient's questions and risk the patient depending on blogs, laypeople and websites of no credibility which can place the patient at high risk for injury. There is no room for ego-mania in healthcare or when addressing the lives of others.
Supplements of five billion (live) or greater	Better chance of having therapeutic effects

## Appendix G: Antibiotics and Risk for Spontaneous Abortions (SA)

Increase Risk of SA	Decreased Risk of SA
Amoxicillin/potassium clavulanate	Nitrofurantoin
Phenoxymethylpenicillin	Trimethoprim–Sulfamethoxazole
Penicillins	Erythromycin
Azithromycin	Amoxicillin
Clarithromycin	Cephalexin
Clindamycin	Cefixime
Metronidazole	Cefuroxime
Ciprofloxacin	Cefaclor
Norfloxacin	Cefprozil
Levofloxacin	
Doxycycline	
Minocycline	
Tetracycline	
Demethylchlortetracycline	
Spiramycin	
Telithromycin	
Pivampicillin	
Ampicillin	
Cloxacillin sodium	
Moxifloxacin	
Ofloxacin	

## Appendix H: Probiotics Susceptibility and Resistance to Antibiotics

Antibiotics	Susceptible Probiotics	Resistant Probiotics	Citation
Oxacillin	Bifidobacterium lactis BB12 Lactobacillus helveticus Lactobacillus acidophilus Streptococcus thermophilus Bifidobacterium longum Bifidobacterium bifidum	Lactobacillus reuteri Saccharomyces boulardii Lactobacillus rhamnosus Bacillus clausii Lactobacillus paracasei	Neut et al., 2017
Amoxicillin) / Clavulanic acid	Lactobacillus acidophilus Bifidobacterium lactis BB12 Lactobacillus helveticus Lactobacillus acidophilus Streptococcus thermophilus Lactobacillus rhamnosus Bacillus clausii Lactobacillus paracasei Bifidobacterium longum Bifidobacterium bifidum	Lactobacillus reuteri Saccharomyces boulardii	Neut et al., 2017
Amoxicillin	Bifidobacterium lactis BB12 Lactobacillus helveticus Lactobacillus acidophilus Streptococcus thermophilus	Lactobacillus reuteri Saccharomyces boulardii	Neut et al., 2017

	Lactobacillus rhamnosus Bacillus clausii Lactobacillus paracasei Bifidobacterium longum Bifidobacterium bifidum		
Penicillin	Lactobacillus acidophilus Bifidobacterium lactis BB12 Lactobacillus helveticus Streptococcus thermophilus Lactobacillus rhamnosus Bacillus clausii Lactobacillus paracasei Bifidobacterium longum Bifidobacterium bifidum	Lactobacillus reuteri Saccharomyces boulardii	Neut et al., 2017
Azithromycin	Lactobacillus reuteri Lactobacillus acidophilus Bifidobacterium lactis BB12 Lactobacillus helveticus Streptococcus thermophilus Lactobacillus rhamnosus Bifidobacterium longum Bifidobacterium bifidum	Saccharomyces boulardii Bacillus clausii Lactobacillus paracasei	Neut et al., 2017
Cefuroxime	Lactobacillus reuteri Lactobacillus acidophilus	Saccharomyces boulardii Bacillus clausii	Neut et al., 2017

	Lactobacillus helveticus Bifidobacterium lactis BB12 Streptococcus thermophilus Lactobacillus rhamnosus Lactobacillus paracasei Bifidobacterium longum Bifidobacterium bifidum		
Cefpodoxime	Bifidobacterium lactis BB12 Streptococcus thermophilus	Lactobacillus reuteri Saccharomyces boulardii Lactobacillus helveticus Lactobacillus acidophilus Lactobacillus rhamnosus Bacillus clausii Lactobacillus paracasei Bifidobacterium longum	Neut et al., 2017
Cefixime	Streptococcus thermophilus	Lactobacillus reuteri Saccharomyces boulardii Lactobacillus acidophilus Bifidobacterium lactis BB12 Lactobacillus helveticus Lactobacillus rhamnosus Bacillus clausii Lactobacillus paracasei Bifidobacterium longum	Neut et al., 2017

Clarithromycin	Lactobacillus reuteri Lactobacillus acidophilus Bifidobacterium lactis BB12 Lactobacillus helveticus Streptococcus thermophilus Lactobacillus rhamnosus Bifidobacterium longum Bifidobacterium bifidum	Saccharomyces boulardii Bacillus clausii Lactobacillus paracasei	Neut et al., 2017
Clindamycin	Lactobacillus reuteri Bifidobacterium lactis BB12 Lactobacillus helveticus Lactobacillus acidophilus Streptococcus thermophilus Lactobacillus rhamnosus Lactobacillus paracasei Bifidobacterium longum Bifidobacterium bifidum	Saccharomyces boulardii Bacillus clausii	Neut et al., 2017



Ciprofloxacin	Streptococcus thermophilus Bacillus clausii Lactobacillus paracasei	Lactobacillus reuteri Saccharomyces boulardii Lactobacillus acidophilus Bifidobacterium lactis BB12 Lactobacillus helveticus Lactobacillus rhamnosus Bifidobacterium longum Bifidobacterium bifidum	Neut et al., 2017
Levofloxacin	Bifidobacterium lactis BB12 Streptococcus thermophilus Bacillus clausii Lactobacillus paracasei Bifidobacterium longum Bifidobacterium bifidum	Lactobacillus reuteri Saccharomyces boulardii Lactobacillus acidophilus Lactobacillus helveticus Lactobacillus rhamnosus	Neut et al., 2017
Doxycycline (tetracycline)	Lactobacillus acidophilus Lactobacillus helveticus Streptococcus thermophilus Lactobacillus rhamnosus Bacillus clausii Lactobacillus paracasei Bifidobacterium longum Bifidobacterium bifidum	Lactobacillus reuteri Saccharomyces boulardii Bifidobacterium lactis BB12	Neut et al., 2017
Metronidazole	Bifidobacterium lactis BB12 Bifidobacterium	Lactobacillus reuteri Saccharomyces boulardii Lactobacillus	Neut et al., 2017

	longum Bifidobacterium bifidum	acidophilus Lactobacillus helveticus Streptococcus thermophilus Lactobacillus rhamnosus Bacillus clausii Lactobacillus paracasei	
Cotrimoxazole	Bifidobacterium lactis BB12 Streptococcus thermophilus Bacillus clausii Bifidobacterium longum Bifidobacterium bifidum	Lactobacillus reuteri Saccharomyces boulardii Lactobacillus acidophilus Lactobacillus helveticus Lactobacillus rhamnosus Lactobacillus paracasei	Neut et al., 2017
Pristinamycin	Lactobacillus reuteri Lactobacillus acidophilus Bifidobacterium lactis BB12 Lactobacillus helveticus Lactobacillus rhamnosus Streptococcus thermophilus Bacillus clausii Lactobacillus paracasei Bifidobacterium longum Bifidobacterium bifidum	Saccharomyces boulardii	Neut et al., 2017

## Appendix I: PBT In-Service Module Plan

Probiotic Breastfeeding Therapy In-Service Module
Preterm Birth, Low Birth Weight and Infant Mortality
Cost of PTB
Preterm Birth, Low Birth Weight and Infant Mortality
What is the Human Microbiome (HMB)
What Influences the Infant's Microbiota?
What are Probiotics
Infants: Probiotics & Human Microbiome
Human Breast Milk: Probiotics & Human Microbiome
Disease: Probiotics & Human Microbiome
Probiotics and Health Conditions
Allostasis and The Infant
Practice Gap
Probiotics Manufacturing Issues
Probiotic Breastfeeding Therapy
How to Recommend Probiotics
Prebiotics
Fermented Foods
Open Question and Answers



# Probiotics and Probiotic Breastfeeding Therapy

José Diaz

## Objectives

At the end of the Probiotic Breastfeeding in-service program, participants will:

- Understand the health benefits of probiotics, prebiotics, and fermented foods.
- Understand the relation of the Human Microbiota and probiotic research to mothers, infants, and health conditions
- Understand how Probiotic Breastfeeding Therapy (PBT) mitigates the morbidity of Preterm Birth (PTB) and other contributors to infant mortality
- Articulate the best practice when recommending probiotics

## Empowering Education Model (EEM)

According to Chaghari, et al. (2017) the EEM will provide the following benefits:

**Participatory training:** First is the Pre-test which allows the participant to determine if their knowledge is at the same level of current research.

**Problem-solving approach:** Educating participants of the various types of probiotics and their use.

**Result-oriented content:** Discussion involving an allostasis frame of thinking which allows the participants understand the core of critical thinking of understanding the stressors and how the application of probiotics will work.

**Training implementation practices:** Discussion of how to re-consider current practice of probiotic recommendation.

**Focus on motivational factors:** Fueling the idea of being involved in new innovative approaches and technology and becoming a change agent for the profession and patient.

**Fostering the searching skills:** Educating the providers in understand the value of supporting new and better research to implementing complementary and alternative medicine (CAM). CAM is a diverse form of practice and products alternative to conventional medicine which is considered complementary when utilized to support conventional medicine. Most allopathic providers are unqualified to utilize or provide patient health-education on this health system in their practice. Presenting an even greater knowledge practice-gap and safety concern, then probiotics alone.

**Performance monitoring:** Post-Test results will allow for performance of knowledge acquired.

## Preterm Birth, Low Birth Weight and Infant Mortality

PTB is a global epidemic. Each year 15 million infants are born prematurely of which one million die, making PTB the leading cause of death in children under age five.

In addition, there are 22 million babies born underweight each year, which contributes to the rate of infant mortality.

Kangaroo Mother Care (KMC) has allowed LBW babies to experience early hospital release, but this has not provided a solution for survivability. An infant's ability to survive is a result of thrivability. Thrivability is affected by an immature biological system, allostatic load inadaptability, and the infant's microbiota. An undiversified or underdeveloped microbiota can result in late-onset sepsis in 20% of LBW infants, as well as many lifespan conditions.

Although KMC may not be a solution to determine early discharge, it does provide specific benefits to enhance the infant's Microbiota.

## Cost of PTB

The overall cost of PTB in the United States of America (USA) is over \$26 billion, while medical care alone surpasses \$17 billion annually.

The cost of caring for a healthy full-term child is about \$5,000, while the care and treatment of a preterm infant can easily exceed \$50,000. If they survive past the first year of life, many of these preterm children, may need additional training and education to assist their development, surpassing one billion dollars.

In addition, a loss of \$6 billion occurs from missing work days that the parents, caregivers, and employers may endure. The goal is not just to save the life of the New-Being (New Born) but to produce functional humans.

## Preterm Birth, Low Birth Weight and Infant Mortality

According to the Center for Disease Control and Prevention (2021), infant mortality occurs within the first year of life. Neonatal infant mortality occurs within the first 30 days after birth, and post-neonatal death, occurs two months after birth, but before the first year.

In 2018, about 21,000 infants had passed away in the United States. Although the USA is one of the most medically advanced countries in the world, it still has one of the highest infant mortality rates (IMR), with some states having extremely high IMR. Ohio, for example, ranks 12th in the country.

## IMR & Depopulation

- Maternal death is biological termination of a woman while pregnant or within 42 days postpartum (CDCP, 2020). In 2020 there has been as much as 20% increase in maternal death and an increase maternal death rate involving home births (CDCP, 2020; Johnson, 2022).
- Recent reports from the World Data and life insurance companies have reported an increase in non-COVID related death, worldwide (Giattino et al., 2022; MH, 2022; Scism, 2022).
- In addition, countries such as Scotland are experiencing an unexplainable surge in the IMR . (BBC, 2022; NRS, 2022).
- This provides a critical insight into the need to improve the IMR as the human population is dying out.

## What is the Human Microbiome (HMB)

The Human Microbiome is a new emerging science that is also referred to as an Organ as it is a genetic collection of protist, viruses, bacteria, fungi, archaea, and many other microorganisms, which is 100 times more expressive than the Human Genome.

Currently, of the 150-plus species identified, over 100 trillion bacterias reside in the intestinal tract. The five leading causes of infant casualties were congenital disabilities, maternal complications, injuries, low birth weight, and sudden infant death syndrome.

Some maternal health complications contributing to infant mortality were hyperemesis gravidarum, **infections**, **obesity**, **gestational diabetes**, **urinary tract infections** (UTI), **mental health issues**, **anemia**, and **hypertension**.

\* **Red** indicates areas of microbiota and probiotic research.

## What Influences the Infant's Microbiota?

The fetus's gut microbiota which begins in-utero is impacted by:

- Hospital Environment
- Vaginal-contact childbirth
- Breastfeeding: Human Milk Oligosaccharides, Colostrum
- Skin contact
- Mother-infant air exchange
- An infant's tongue and tonsils have a similar microbiota to the placenta
- The formation of the cesarean birth microbiota occurs via the hospital environment and contact with the mother's skin.
- A sterile gauge is employed to swab the mother's vaginal fluid upon the infant's body, oral cavity, and face. Still, this procedure has the potential to transmit a sexually transmitted infection.

## What are Probiotics

According to the International Scientific Association for Probiotics and Prebiotics (ISAPP), probiotics are living microorganisms that, when prescribed in a sufficiently, the host will experience beneficial health outcomes. These live non-pathogenic microorganisms predominately consist of yeast derivatives such as *Saccharomyces boulardii* or lactic acid bacterium, as in the case of *Lactobacillus* species and *Bifidobacterium* species. Probiotics are safe for infants and adults and effective in supporting treatments involving gastrointestinal electrolyte absorption, restoring gastrointestinal permeability, *Clostridium difficile*, antibiotic-associated diarrhea, traveler's diarrhea, hepatic encephalopathy, irritable bowel syndrome, and several functional gastrointestinal disorders.

Probiotic development by Eli Metchnikoff was rooted in the idea that these microorganisms hold the key to human longevity. Metchnikoff highlighted the new revolutionized notion that not all bacterial organisms cause disease but promote life. Many conditions result from unfriendly microflora, which can be tamed or removed through probiotic therapy. Probiotics compete with unfriendly bacteria in absorbing available nutrients and attaching to intestinal epithelial, then altering the environment to prevent the viability of unfriendly microflora.



## Infants: Probiotics & Human Microbiome

Probiotic is involved in intestinal epithelium proliferation, nervous system maturity and function, and the production of human life energy, as well as the prevention of late-onset sepsis.

Probiotics increase the absorption of essential nutrients and proteins, and may improve the health function of the maternal and fetal microbiota, improving survivability and thriving.

A full-term infant will have a gut microbiota dominated by *Lactobacillus* species, *Bifidobacterium* species, or *Streptococcus*. In contrast, a preterm infant will not have sufficient *Lactobacillus* species, *Bifidobacterium* species, or *Streptococcus* colonization.

Microorganisms found in the preterm infant's gut microbiota are *Enterobacteriaceae* and *Clostridium*, which is why mothers of premature infants will produce HBM high in HMO, which contains over 200 oligosaccharides and promote probiotic growth as her body adapts to the child's needs. This process is similar to how certain species eat specific foods to grow that other species reject; the Mother's HMO will produce prebiotics that human life-promoting bacteria eat to grow, survive and thrive.

Formula-fed infants have a lower count of *Lactobacillus* and *Bifidobacterium* species.

## Minor Insight Into The Microbiota of The Preterm Gut

### Enterobacteriaceae Contributes to:

- Gram-negative bacteria
- *Escherichia coli*, *Klebsiella pneumoniae*, ect.
- Multi-drug-resistant *Enterobacteriaceae* accounts for 60% to 80% of infection-related casualties (IDA, 2017).
- Nosocomial isolates - 21%
- Catheter-line-associated bloodstream infections - 11.4%
- Bloodstream infections - 12%
- Nosocomial urinary tract infections - 34%
- Surgical site infections - 18%
- 23% of ventilator-associated cases of pneumonia (IDA, 2017)

### Clostridium Contributes to:

- *C. perfringens*: food poisoning, necrotic enteritis, diarrhea, sudden infant death (Auwaerter, et. al., 2019).
- *C. difficile*: Colitis, antibiotic-associated diarrhea
- *C. septicum*: Intestinal myonecrosis
- Wound infection
- It impairs blood flow in the tissue and decreases oxygenation resulting in an anaerobic condition (UK, 2017).

## Human Breast Milk: Probiotics & Human Microbiome

Human Breast Milk (HBM) is the first medicine of life.

HBM is the gold standard for LBW and PTB babies.

HBM provides lifesaving nutrients and prevents necrotizing enterocolitis. Breastfed infants have a higher rate of survivability and a lower rate of acquiring an infection. Through direct breastfeeding (DBF), the infant's gastrointestinal microbiota will evolve and become a significant health determinant in its life.

DBF shapes the child's immunity, metabolism, neurological system, nutrient absorption, and the prevention of diseases throughout the adult years, decreasing the occurrence of asthma, allergies, autism spectrum disorders, obesity, and attention deficit hyperactivity disorder.

## Human Breast Milk: Probiotics & Human Microbiome

Administering probiotics to pregnant mothers affects their mammary gland probiotic colonization by increasing the concentration of Lactobacilli and Bifidobacteria in both matured breast milk and the mother's colostrum.

The incidence of gastrointestinal inflammation decreases through the ingestion of HBM. Probiotics and breast milk promote positive weight gain in infants.

The importance here is that LBW infants are at a higher risk for mortality. Mechanisms that influence and develop the infant's intestinal microbiota are the mother's milk microbiota which contains her gut microbiota and natural prebiotic HMO.

The mother's microbiota is a critical factor in predicting the prematurity of birth, indicating that qualified and credible maternal microbiota analysis should be part of the prenatal care plan.

## Disease: Probiotics & Human Microbiome

The Human Microbiome is one of the leading identifiers of disease development and progression throughout life.

Gut microbiota dysbiosis can lead to colorectal cancer, atopic dermatitis, multiple sclerosis, lupus, breast cancer, diabetes, rheumatoid arthritis, obesity, inflammatory bowel disease, mental health issues, PTB, and asthma. For this reason, a probiotic prescription is crucial as it improves the gut microbiota and may provide a protective measure against these pathological conditions.

Bifidobacterium species provide disease resistance measures to protect against asthma, obesity, autoimmune conditions, and the development of allergies, as well as help develop the infant's gut microbiota.

It is imperative to note that although probiotics and the gut microbiota of infants and mothers are the focus of this research, every area and organ of the human vessel has a specific microbiota, whether it is skin, sperm, vaginal cavity, skeletal, oral, or intestinal tract.

## Failure to Thrive vs. Failure to Survive

The medical mindset model of treatment is set on survivability and not thriving. The importance here is that the allopathic goal is to turn off the red light and help the sinking ship to sail until it can no longer navigate.

The Medical Microorganism Model (3M) utilization of probiotics aims to create and prepare conditions that will help the person to adapt, regenerate and flourish. Surviving past a crisis is not enough; we must be able to withstand our allostatic loads and resist any life-threatening situation to continue existing as a species.

PBT is crucial as it provides the most current research on the appropriate utilization of probiotics to help the infant adapt to internal and external stressors and assist in nourishing the body so that it can support the alternating physiological functions of life and grow abundantly. Furthermore, it is imperative for the safety and benefit of the patient that the correct probiotic and prebiotic foods are recommended based on the known, suspected, or expected condition.

## Defining Probiotic Breastfeeding Therapy

PBT is the process of maternal ingestion of probiotics.

These strands then become part of the mother's microbiota and the HBM, transferring its benefits to the infant and building its internal microbiota.

## Probiotics and Health Conditions

*Lactobacillus delbrueckii*: Inhibit gas-forming coliform bacteria

*Lactobacillus Salivarius*: Mastitis, Anti-inflammatory effect

*Lactobacillus Plantarum*: Inhibit gas-forming coliform bacteria, Increases transforming growth factor- $\beta$ 2 (TGF- $\beta$ 2). Decreases interleukin-6 (IL-6), Improves high blood pressure, Improves stress tolerance, Decreases lead absorption

*Akkermansia muciniphila*: Improves obesity and diabetes

*Lactiplantibacillus Plantarum*: Anti-viral effects against certain influenzas

*Leuconostoc mesenteroides*: Anti-viral effects against certain influenzas

Kefir: Improves bone density

*Lactobacillus Rhamnosus*: Atopic Dermatitis, Eczema, Reduces the dental cavity promoter Streptococcus Mutans, Supports caesarian birth microbiota, Reduces postnatal maternal depression and anxiety, Anti-fungal activities against *Candida albican*, Help decrease the risk of NEC, nosocomial infections and infant mortality, Decrease in the length of phototherapy treatment and hospitalizations in infants with hyperbilirubinemia.

## Probiotics and Health Conditions

*Lactobacillus* species: Lactose Metabolism

*Lachnospiraceae* and *Ruminococcaceae*: Metabolism of complex carbohydrates

*Bifidobacterium breve*: Supports caesarian birth microbiota, Decreases the occurrence of gastrointestinal disorders, Helps prevent NEC, Produces folate, Weight gain improvement, and gastrointestinal tolerance, Improves high blood pressure

*Bifidobacterium Infantis*: Breakdown the complex carbohydrates found in the mother's milk, Helps develop and mature the immune system, Biological acceptance of vaccination medicine (decrease adverse reaction), Reduce stool frequencies and produce well form stools, Improves growth in length, Improves weight gain, Improves growth of head circumference, Lessens the risk of NEC surgery intervention, Improve development in HBM-fed infants, Improves high blood pressure

*Bifidobacterium lactis*: Helps promote average infant growth, Promotes growth in formula-fed term infants, Decreases the length of phototherapy and hospitalizations in infants with hyperbilirubinemia.

## Probiotics and Health Conditions

*Lactobacillus acidophilus*: Reduces maternal symptoms of depression, Reduction of mortality, Improves feed tolerance, Decreases central venous line usage, Decreases ventilator duration, Decreases the frequency of rotavirus-related diarrhea, Helps decrease the risk of NEC, nosocomial infections, and mortality, Improves growth in length, Improves weight gain, Improves growth of head circumference, Improves development in HBM-fed infants, Lessens the risk of NEC surgery intervention, Decreases in the length of phototherapy treatment and hospitalizations in infants with hyperbilirubinemia

*Lactobacillus bifidum*: Help decrease the risk of NEC, nosocomial infections, and mortality

*Bifidobacterium bifidum*: Reduces maternal symptoms of depression, Reduction of mortality, Improved feed tolerance, Decreases central venous line usage, Decreases ventilator duration, Prevents late-onset sepsis, Decreases the length of phototherapy treatment and hospitalizations in infants with hyperbilirubinemia.

*Lactobacillus casei*: Reduces maternal symptoms of depression, Reduction in anxiety, Anti-fungal activities against *Candida albican*, and Improves high blood pressure.

## Probiotics and Health Conditions

*Lactobacillus casei* Shirota: Helps heal fractures

*Lactobacillus casei rhamnosus*: Decreases respiratory infections.

Oligosaccharides: Prebiotic (Indigestible), Promotes the growth of bifidobacterial strains, Galacto-oligosaccharide/polydextrose, Protects against respiratory infections

Direct Breast Milk Feeding: Asthma prevention, Prevents necrotizing enterocolitis, Stabilizes Bifidobacterium Species in the gut microbiota

*Streptococcus Salivarius*: Oral cavity colonization at birth

Xylitol (prebiotic): Reduces the dental cavity promoter *Streptococcus Mutans*

*Lactobacillus paracasei*: Suppress *Streptococcus mutans* growth, Anti-viral effects against certain influenzas

*Lactobacillus gasseri*: Improves high blood pressure, Improves lung function, and decreases asthmatic symptoms

*Bifidobacterium longum*: Helps prevent malnutrition, Improves high blood pressure, Decreases asthma occurrence

## Probiotics and Health Conditions

Antibiotic Therapy in infancy: Decreases the infant gut microbiota of *Lactobacilli* species, *Bacteroides*, and *Bifidobacteria* species, Promotes behavioral issues and depression in children

*Lactobacillus Reuteri*: Reduction of newborn sepsis and death

*Lactobacillus coryniformis*: Improves high blood pressure

*Lactobacillus Fermentum*: Mastitis, Immunomodulatory effect, Improves hypertension

*Lactobacillus helveticus*: Improves hypertension, Decreases anxiety, Improves calcium reabsorption, Decreases insomnia

## HBM and MRNA

Bifidobacterium species decrease the body's likelihood of rejecting or resisting vaccination medicine (Chichlowski et al., 2020).

Probiotics may play a protective role against vaccination-related adverse events considering that in some subjects the messenger ribonucleic acid (MRNA) has been reported to transition into the infant via HBM, which may have unpredictable results as the Center for Diseases Control does not currently have a COVID vaccination recommendation schedule for infants under six months of (CDCP, 2022; Hanna et al., 2022).

Furthermore, Bifidobacterium longum and Bifidobacterium pseudologum are aerotolerant probiotics that play a vital role in the maturation of the infant's intestinal microbiota, which may provide immunological protection (Million et al., 2017).

## Allostatic Model & The Infant

- The allostatic model, unlike homeostasis, understands that there are no fixed points in the Human Microbiome.
- Everything is constantly changing, including dead human tissue; this also extends to experiencing hunger, thirst, and requiring sleep or movement. Allostatic responses range from supportive to defensive as they are there to protect life. An equivalent idea is the belief of "Side-Effects" when there are no side effects, but rather "Systems-Effects" as one medication or treatment will influence the function of other organ systems.
- The Human Microbiome undergoes thousands of continuous enzymatic processes to ensure the reproductive survivability of our species.
- The allostatic model allows us to remain conscious of the multi-dimensional responses of the human body to stressors, especially the reactions of a New-Being in our medical-biological world, to ensure thriving. These sporadic reactions to stressors will affect the infant's development and survivability throughout the first year of life, which can have positive outcomes considering the child can adapt (thrive) biologically to the stressors.
- Probiotic Breastfeeding Therapy aims to help the infant and mother adapt to and tolerate stressors.

## Practice Gap

The probiotic-knowledge practice gap negatively affects High-Level Providers such as Nurse Practitioners (NP) and Certified Nurse Midwives (CNM), but 50% of physicians have a discrepancy in probiotic prescription/recommendations.

Forty percent of physicians leave the probiotic strand selection to patients with less medical knowledge, indicating that, in a general scope, physicians have an even more significant probiotic health literacy gap than NPs, who have a 79% recommendation rate with a medium rate of knowledge.

Sixty-three percent of health care providers felt that implementing electronic charting involving pop-up suggestions would improve their knowledge of correct probiotic prescribing. The concern with this approach would be that it would still not indicate proficiency in prescription, especially considering that there are no probiotic medical guidelines.

## Probiotics Manufacturing Issues

Studies that examine the most appropriate dosage, therapy duration, and type of probiotic strand are crucial to establishing efficacy and safety.

Since probiotics are classified as food or dietary supplementation instead of medicine, they are not as highly regulated. This is a significant issue as 1 in 16 probiotic products matched the manufacturer's claim, indicating that only about 6% to 7% are providing the consumer with a quality product.

Medical-grade probiotic supplementation must be developed to reduce the likelihood of contamination, as in an isolated case of an infant who died from receiving a contaminated probiotic containing a parasitic fungus.

Although probiotics are considered safe for general use, those prescribed to vulnerable populations should be high-quality bio-pharmaceutical-grade tested for purity, strand stability, and cross-contamination, and provided in single dosage packages with expiration date and storage instruction.



## Die (Death of) + Beta (Cells) = Diabetes

Diabetes is one of the worst diseases to acquire as it not only destroys the body's ability to function correctly but also opens the pathway to the developing other dangerous diseases (Manovina, et. al., 2021). Fortunately, until sugar and sugar products are either controlled or banned from the market, the supplementation of probiotics twice a day for three months has been noted to help reduce blood glucose levels (Manovina, et. al., 2021).

The management and profitability of diabetes exceed \$300 billion annually (ADA, 2022). Since the 1990's diagnosed and undiagnosed diabetic conditions have doubled, reaching almost 40 million Americans with 1.4 million new cases each year (CDCP, 2021; ADA, 2022).

Through a retro-analysis of a diabetic patient, we realize that conditions such as neuropathy, skeletal deterioration, bowel dysfunction, accelerated aging, premature deaths, heart attacks, strokes, retinopathy (blindness), and sexual dysfunction are preventable.

Probiotics may help prevent diabetic conditions from progressing, which is crucial as diabetes kills close to 100,000 diseased individuals each year (Tanne, 2022). In addition, 40% of all COVID-related deaths were of people with diabetes (Tanne, 2022).

## Gestational Diabetes

Gestational diabetes is a condition that pre-existed in the body prior to pregnancy but did not surface until the body exhausted its physiologic compensatory system.

Gestational diabetes can result in hypertension/preeclampsia, maternal stroke, infant seizure disorders, hypoglycemia, caesarian operation, and obese infants (CDCP, 2020). Considering the Human-Genome-Microbiome Memory (HGM), a mother with preeclampsia provides an infant with an HGM gear for developing a cardiac disease. Probiotics and PBT are of substantial value because it opens the probing epidemiological mind-mapping investigation into disease prevention.

Clinical Epidemiology is the highest level of medical thinking as it is the reverse-engineering of clinical technology and investigation. Through unrestricted retro-analysis, we can determine the origins of any condition and develop a program to stop the condition from developing and creating or re-creating other disease conditions in the body.

## Gestational Diabetes

Gestational diabetes plays a major role in infant mortality. If the mother can not utilize glucose effectively and efficiently, neither can the fetus (CDCP, 2020).

Some of the probiotics found in fermented foods and supplementation which help improve diabetic conditions are *Lactobacillus acidophilus*, *Bifidobacterium bifidum*, *Lactobacillus alivarius*, *Lactobacillus Plantarum*, *Bacillus coagulant*, *Bifidobacterium breve*, and *Lactobacillus casei* (Manovina, et al., 2021).

Famine-addressing foods are natural junk food that thrives in harsh growing conditions and consist of high carbohydrates, and is low in nutritional value and healing properties (Choi, et al., 2022). Also, these foods have fortified and artificial nutrients that are poorly digested.

*Bifidobacterium Bifidum*, *Lactobacillus Acidophilus*, and *Lactobacillus Casei* may be a consideration for mothers with gestational diabetes as these probiotics have increased HDL cholesterol and improve insulin sensitivity (Wu & Chiou, 2021).

## A Kangaroo Mother's Care

### Returning the Favor

## Colostrum and The Kangaroo Mother Care

Colostrum is an immunoprotective agent that helps prevent the development of sepsis in infants (Tanaka, et al., 2019). Tanaka et al. (2019) mentioned that the earliest an infant receives its mother's colostrum, the sooner its gut microbiota will begin to colonize with lifesaving bacteria. Early breastfeeding is detrimental to infants' survival and microbiota diversification and development.

Strategically initiating Kangaroo Mother Care (KMC) immediately after birth promotes early breastfeeding among preterm and LWB and regulates an infant's emotional state and body temperature (Mekonnen, et al., 2019). LBW babies who received immediate KMC versus post-birth stabilization embrace decreased mortality (WHOIKMCSG, et al., 2021).

KMC decreases IMR by decreasing cross-contamination handling, which decreases the risk of infection, the skin-to-skin microbiota colonization, initiating early breastfeeding, and colostrum ingestion help promote the infant's microbiota growth (WHOIKMCSG, et al., 2021). In addition, KMC provides thermoregulation, as heat is imperative to life and enzymatic processes.

## The Enzymatic Kangaroo

### Benefits of Kangaroo

- Immediate initiation of breastfeeding / three-day timeline for colostrum
- Skin and breath contact develops and improves the Human Microbiota
- Ingestion of Colostrum + HBM + HMO = Prebiotics and Probiotics colonization
- The emotional and psychological comfort of infant (Aiding with stressors)
- Decrease cross-handling (cross-contamination)
- Improves the Human Enzymatic Process through body heat contact.
- For every one-degree centigrade, enzymatic activity rises by 10% (Emerson, 2021). Chemical reactions that keep humans alive can not happen without an ideal control temperature of proteins called enzymes.
- Psychrotrophic bacteria are bacterial life forms that can thrive in cold environments of less than seven degrees Celsius and create psychrotolerant enzymes, such as refrigerated milk (Emerson, 2021). The body gets cold and can get hot, which is why we have a microbiota that can adapt to internal and external temperatures.

## ZAPP - PTB

### The Zinc, Arsenic, Probiotic and Preterm Birth Connection

Arsenic competes with zinc, which reduces the amount of zinc available to the fetus (Wei, et al., 2021). Zinc may help the allostatic load and oxidative stress, as well as reduce arsenic toxicity which as a result may reduce the occurrence of PTB and LBW deliveries as arsenic increases the risk of PTB and LBW (Almberg, et al., 2017; Rahman, et al., 2019; Wei, et al., 2021). In addition, water and soil contaminated with arsenic give rise to PTB, stillbirth, infant mortality, LBW, and spontaneous abortions (Rahman, et al., 2019).

Furthermore, arsenic causes depletion of folate (neural tube defects), increases manganese to unsafe levels, reduces fetal growth, and causes inflammation of the blood in the placenta and umbilical cord. In addition, arsenic negatively affects the fetal telomere, promotes congenital malformations, and alters angiogenesis, resulting in abnormal cellular growth in the placenta and placental abruption (Rahman, et al., 2019; Howe, et al., 2020; Khan, et al., 2022).

## ZAPP - PTB

### The Zinc, Arsenic, Probiotic and Preterm Birth Connection

Arsenic is a significant part of our daily lives and is in the following foods: white rice, infant cereal, asparagus, Brussels sprouts, well water, poultry feed, beer, wine, apple juice, pear juice, tap water (Almberg, et al., 2017; Nachman, et al., 2017; Signes-Pastor, et al., 2018). Moreover, many prenatal vitamins contain lead and arsenic (Schwalfenberg, et al., 2018).

Lactic acid bacteria species, namely yogurt-containing *Lactobacillus Rhamnosus*, can inhibit intestinal absorption of arsenic and mercury (Bisanz, et al., 2014).

Furthermore, the ingestion of zinc has *Lactobacillus* species-producing effect, which may help reduce serum arsenic (Fröhlich, et al., 2019). As mentioned, arsenic is in many of our foods, grains, drinking water, and the air of specific industrial communities. Promoting PBT and educating pregnant mothers on the importance of purified drinking water and metal-free liquid vitamins, especially zinc supplementation, may help reduce these risks.

## Probiotic Breastfeeding Therapy

Probiotic Breastfeeding Therapy may help in improving the survivability and thriving of PTB and LBW infants. According to Fleming, et al. (2019), the 2014 Cochrane Database of Systematic Reviews (CDSR) analyzed 24 probiotic-based randomized controlled trials (RCTs) of PTB and LBW infants concluding that probiotics were both safe and effective in reducing NEC.

No studies have reported the development of systemic infection or mortality due to probiotic administration (Fleming, et al., 2019).

Probiotic administration has a protective effect in potentially improving an infant's neurodevelopmental outcomes, which include mood and behavioral disorders (Fleming, et al., 2019).

If prescribing antibiotic therapy in the suspicion or presence of late-onset sepsis, it is imperative to recommend a probiotic strand that will not interfere with the antibiotic's function (Fleming, et al., 2019). Furthermore, probiotics should be taken two hours after the administration of oral ATB, as some strands can decrease the effectiveness of the ATB therapy.

## Probiotic Breastfeeding Therapy

LBW babies are at a higher risk of death or developing lifelong neurological conditions, which indicates that the presence of an undeveloped intestinal microbiota is linked to malnutrition regardless of food intervention, which gives light to the importance of promoting PBT (Aceti, et al., 2017; Million, et al., 2017).

The utilization of PBT may help develop or diversify the infant's Human Microbiota and improve survivability and thriving of the first year of life.

It is essential for medical evolution that healthcare professionals understand the function and power of the Neonatal Microbiome and the use of probiotics, and its involvement in the infant's survivability and thriving.

Analysis of the Maternal Microbiome may give light to the potential of PTB.

Breastfed infants have a higher rate of survivability and a lower rate of acquiring an infection. In addition, probiotic supplementation helps in reducing the development of late-onset sepsis, as well as other pathological conditions (Aceti, et al., 2017).

## Neonatal & MRSA

- Methicillin-resistant Staphylococcus aureus (MRSA) is a commonly known multidrug resistant nosocomial pathogen which occurs in neonatal intensive care unit (NICU) and is carried by 20% of the world's population (Jayashree et al., 2018; Lavie-Nevo et al., 2019).
- The transmission of MRSA to an infant can occur through the paternal skin contact, healthcare worker cross contaminated handling, maternal skin contact, via HBM feeding and from other infants who were admitted to the NICU (Lavie-Nevo et al., 2019).
- A study conducted in 2013 by Sikorska and Smoragiewicz mentioned that probiotics organisms' ability to attach to the intestinal wall prevented pathogenic organisms from settling. Lactobacillus reuteri, Lactobacillus casei, Lactobacillus paracasei and Lactobacillus rhamnosus were probiotics that displayed resistance to MRSA (Sikorska & Smoragiewicz, 2013). Lactobacillus rhamnosus SHA113 isolated from the milk of women decreased the number of MRSA cells, restored neutrophil function and repaired intestinal barriers which were damaged by infection (Liu et al., 2020).

## New Concept from the DNP: Critical Thinking Versus Allostatic Thinking

Critical Thinking (CT) is a meta-cognitive process involving the analysis of both subject and objective information and evidence, which is then matched with available resources and knowledge of the provider to immediately arrive at a definitive treatment or preventative measure (Nippold & Marr, 2022).

Allostatic Thinking (AT) is a new approach to treating and preventing clinical issues. Unlike CT, which is an "In The Now" mentality, AT merges CT, Concept Mapping, Scientific Knowledge, Clinical Comprehension, Human Intuition and Experience, Clinical Reasoning, Biological Retro-Analysis, Epidemiological Evaluation, Legal Scope of Practice, Systemic-Effect Awareness, and Medical Algorithms in order to embrace and effectively apply the ideological method of, "Patterns Leading To Predictability."

In other words, AT not only allows the clinician to address and treat the current issue(s) and permits her or him to push forward into the future by analyzing patterns, which can assist in predicting and preventing potential crises.

## New Concept from the DNP: Medical Microorganism Management

- **Friendly Bacteria:** A non-pathogenic microorganism (Probiotic/Bacteria) that is compatible with the human body and promotes resistance to allostatic changes, which can propel the development of negative health conditions.
- **Unfriendly Microorganism:** Pathogenic-disease causing microorganism
- **Medical Microorganism Management (3M):** This is a developing concept which utilizes the Allostatic Thinking Model to predict potential condition and reinforce the subjects natural resistance through probiotic and prebiotic therapy.
- **PBT & 3M:** The New Probiotic Breastfeeding Therapy is an example of the 3M application.
- **Difference between Conventional Medicine and 3M:** Allopathic medicine is Survival-Focused or Red-Light Medicine (RLM), while the 3M approach is Thrive-Centered. RLM is symptom control as an engines red light being shut off without addressing or treating the cause.

*Futuristic Scientifically Intense Research Will Be Required*

## Medical Microorganism Management Precision Medicine

- **Precision Medicine (PM):** A newer approach to allopathic medicine which surpasses the traditions signs and symptoms approach and focuses on effects of biomarkers, lifestyle, environment and genetic makeup within an individual (König et al., 2019).
- **Medical Microorganism Management:** Similar to PM, although is aimed at researching and utilizing signs, symptoms, biomarkers, lifestyle practices, environmental exposures and genetic makeup to diagnose and treat a person, it also takes into consideration the Microbiome.
- The **Human Microbiome** is an infant when considering that many bacteria in the Planetary Microbiota are more than half a million years old (Molinari, 2019). This is in addition to the many bacteria entering Earth from outer space (Wickramasinghe et al., 2018; Wickramasinghe et al, 2020). This indicates that as a species we need to focus on the entire gamut of creation in order to proceed with generational survival. Furthermore, although PM may prove a better approach to personalized human medical treatment it is not going to fully experience the evolutionary process of life extension until it embraces the Human and Planetary Microbiome.

## 3M & ATM: We Need Signs to Thrive

- **Positivity of Signs and Symptoms (PSS):** When utilizing ATM, the idea was to focus on the PSS. In this case the sign was the presence of an existing condition or disease and the symptom(s) was if the subject experienced an improvement in-lieu of probiotic therapy.
- **Negativity of Signs and Symptoms (NSS):** This is the common use of signs and symptoms. In NSS the sign is the manifestation of a disease or condition, while the symptoms are the physiological reaction to the disease or condition which allows the High-Level Provider to determine if the person is worsening.
- **PSS / NSS Focused Selection:** Research with PSS were reviewed for application and articles with mention of NSS were examined to determine the safety of probiotic administration to vulnerable population.

## How to Recommend Probiotics

As much as 79% of healthcare providers recommended probiotics to their patients. However, most NPs and Physicians have a medium knowledge of the subject.

*We are not saying to recommend, but rather take precautions and recommend with knowledge, wisdom, and understanding.*

*Know what you are doing, before doing it.*

- Know the maternal and paternal health history and which strand helps.
- Know the probiotic strands that have studies linked to breastfeeding mothers and infants and health conditions.
- Seek pharmaceutical-grade probiotics to improve Safety, Efficiency, Efficacy and Quality.
- Know which strands are in fermented foods. Before probiotic supplementation, consider food and lifestyle as thy medicine.
- Teach the client the importance of identifying adverse events, stopping the probiotic immediately, and reporting it to their Primary Medical Provider at once.
- Probiotic dosages greater than five billion strands are ideal.

*Play it safe and stick to what we know, until we know more.*

*Remember this is a vulnerable population*



## Prebiotics

Prebiotics are non-digestible nutrients broken down in the gastrointestinal tract and nourish the microbiota throughout the body (Davani-Davari et al., 2019).

There are several prebiotic types, fructans, Glucose-Derived Oligosaccharides, Non-Carbohydrate Oligosaccharides, pectins, resistant-starches, and Galacto-Oligosaccharides (Davani-Davari et al., 2019).

The survival of probiotics results from ingested nutrients and prebiotics (Pujia et al., 2017).

Trace amounts of HMO enter both blood and urine systems which may be the reason for lower incidents of infections in the urinary and respiratory tract (Bonner, 2019).

Although infant formula manufacturers have instilled the prebiotics FOS and GOS, they are not as complex or bio-available as the mother's HMO (Bonner, 2019).

## Prebiotics

Although prebiotics can be manufacture with the use of starches, lactose, and sucrose; many can be biologically extracted through the consumption Jerusalem artichoke, beet sugar, asparagus, bananas, barley, garlic, onions, wheat, honey, rye, HBM, HMO, animal milk, peas, legumes, seaweed, microalgae, chicory, tomatoes, apricots, raisins, dates, figs, spring onions, and prunes.

One well-known lifesaving prebiotic treatment is Lactulose helps patients suffering from hepatic encephalopathy by taming the presence of ammonia in the gut.

This provides a better understanding of the direction future medicine will journey to understand the New Emerging Organ, the Human Microbiome.

Prebiotic-laced formulas resulted in infants needing fewer antibiotics and antipyretics when compared to infants ingesting non-prebiotic or probiotic formulas.

## Fermented Foods

Probiotics microorganisms are Streptococcus, Lactobacillus, Saccharomyces, Bifidobacterium, Lactococcus and Enterococcus, many of which are in fermented foods, such as yogurt, kombucha, kefir, sauerkraut, kimchi as well as other fermented foods.

Fermented foods hold many values as in the case of chocolate. The following probiotics are in chocolate, Lactobacillus fermentum, Lactobacillus Plantarum, Bifidobacterium longum, and Lactobacillus helveticus.

Bifidobacterium longum and Lactobacillus helveticus improve cardiovascular health, indicating why many studies have reported chocolate's benefits to heart health.

Remember that not all foods sold as "fermented" are fermented but treated with vinegar to give them a fermented taste. Vinegar and chlorine-based water (tap water) can decrease probiotic effectiveness and health benefits.

## Fermented Foods

- Fermented Milk: Yogurt, Cheese, Kefir
- Fermented Fish: Jeotgal, Nam pal, Belacan
- Fermented Cereal: Tempeh, Sourdough, Natto
- Fermented Vegetable: Kimchi, Pickles, Sauerkraut
- Fermented Meats: Chorizo, Salami
- Fermented Alcohol: Beer, Wine, Kombucha, Sake

## Medicinal Food

### Is There an Ideal Food For Pregnancy?

**Sourdough Bread:** This bread has *Lactobacillus Reuteri* a bacteria that may prevent the likelihood of newborn sepsis and death.

**Lentil Soup:** May reduce arsenic absorption which may decrease the risk of PTB (Krohn, et. al., 2016). In addition, lentils provide naturally occurring zinc, iron and selenium. Zinc, as the prebiotic properties of garlic were noted to help prevent PTB due to their *Lactobacillus* species producing effects (Myhre, et. al., 2013).

**Purified Drinking Water:** May decrease the likelihood of ingesting toxic chemicals.

## Medicinal Food

### Is There an Ideal Food For Pregnancy?

*Lactobacillus paracasei* from pickled foods can degrade purine compounds in food, thus reducing uric acid.

## Maternal Serum Uric Acid and Preeclampsia

- Although an ongoing study, Serum Uric Acid (SUA) appears to be a predictor for preeclampsia complications and fetal death (stillbirth) (Le, et al., 2019).
- Preeclampsia can lead to fetal distress, impair renal function, retinopathy, intrauterine growth restriction, and PTB, LBW and infant mortality (Le, et al., 2019; Le et al., 2021). Mothers with high SUA and proteinuria have higher hypertensive readings and are at higher risk of caesarian operations and eclampsia (Paula et al., 2019; Le et al., 2021). In addition, the severity of preeclampsia can be determined by hypocalcaemia ( $8.61 \pm 0.78$  mg/dl) and hyperuricemia ( $6.8 \pm 2.72$  mg/dl) (Kumar & Singh, 2019). While high SUA at 13-18 week of gestation is associated with GDM.

### Probiotic / Prebiotic

- Yogurt containing *Lactobacillus acidophilus* and *Bifidobacterium lactis* lowers uric acid levels and improves insulin sensitivity (Rezazadeh, et al., 2021)
- Jerusalem artichoke has prebiotic properties that can reduce uric acid and help prevent constipation (Sawicka et al., 2020).
- *Lactobacillus gasseri* PA-3 lowers serum uric acid levels in humans (Yamanaka, et al., 2019).
- *Lactobacillus helveticus* and kefir improves hypertension and calcium re-absorption (Beltrán-Barrientos et al., 2016; Gohel et al., 2016; Schepper, et al., 2017)

## Medicinal Food

### Is There an Ideal Food For Pregnancy?

Fermented milk products containing *Lactobacillus acidophilus* LA-5, *Bifidobacterium lactis* Bb12, and *Lactobacillus rhamnosus* GG were noted to reduce the inflammatory systemic response which contributes to preeclampsia (Brantsaeter, et al., 2011).

## Medicinal Food

**Foods high in polyunsaturated fatty acids (PUFA) or omega-3 are helpful in preventing allergic conditions in children (Brosseau et al 2021).**

- Sesame seeds
- Walnut
- Pistachio
- Sunflower seeds
- Hemp Seeds
- Flax seeds
- Peanuts
- Brazilian nuts
- Paprika
- Cashews
- Pine nuts
- Hazelnuts
- Cayenne pepper fruit
- Pumpkin seeds
- Almonds
- Cod liver oil
- Chia seeds
- Pecans
- Sockeye Salmon
- Halibut
- Mackerel
- Egg yolk
- Avocado
- Green Plantain
- Sardines
- Kimchi
- Olives
- Trout

## Addendum

### Chemical Hydration:

**The Following Slides Reports The Chemicals Found in Tap Water Throughout the United States and Their Effects on the Human Body**

## Chemical Hydration

Could Tap Water be forcing the fetus to Tap-Out?

When applying a clinical, epidemiological approach to infant mortality, many states with the highest infant mortality are also the states with the most contaminated waters (WA, 2018; CAS, 2022).

Infants who consume tap water with nitrates can become ill (CAS, 2022). Some waters contain radiation.

Unclean water affects not only the health of a pregnant or fertile woman's future offspring, but that of the general population.

The Center for Accountability in Science (2022) reports that the following chemicals are in drinking water throughout the United States of America.

## Chemical Hydration and Health Effects

- Trihalomethanes: Cancer risk, hepatic/renal/nervous system issues
- Total Haloacetic Acids/ Haloacetic acids: Cancer risk
- Coliform: May not cause harm but may need to be tested for fecal coliforms/*Escherichia coli*
- 1,2-Dibromo-3-chloropropane: Cancer risk, reproductive issues
- Lead: Cognitive and physical developmental delays
- Asbestos: Intestinal polyps
- Mercury: Renal issues
- Benzo(a)pyrene: Reproductive issues, cancer risk
- Uranium: Renal issues, cancer risk
- Chlordane: Cancer risk, hepatic and neurological issues
- Carbon tetrachloride: Hepatic issues, cancer risk

## Chemical Hydration and Health Effects

- 1,1,2-Trichloroethane: Renal, hepatic, and immunological issues
- ortho-Dichlorobenzene: Circulatory, renal, hepatic issues
- 1,2-Dibromo-3-chloropropane: Cancer risk, reproductive issues
- Ethylene bromide: Cancer risk, hepatic/renal/reproductive /gastrointestinal issues
- Styrene: Hepatic, renal, circulatory issues
- 1,1,1-Trichloroethane: Circulatory, hepatic, nervous issues

## Chemical Hydration and Health Effects

- Barium: Hypertension
- Radium-226: Cancer risk (Homes in geographical areas that were under ice lands should be tested for radon gas).
- Hexachlorocyclopentadiene: Gastrointestinal and renal issues
- Trichloroethylene: Cancer risk, hepatic issues
- Copper: Gastrointestinal disorder
- Epichlorohydrin: Cancer risk, gastrointestinal issues
- Atrazine: Reproductive, hormonal, and cardiovascular issues
- cis-1,2-Dichloroethylene: Hepatic issues
- Simazine: Hematological issues
- 1,2-Dichloroethane: Cancer risk
- 1,2-Dichloropropane: Cancer risk
- Cadmium: Renal insufficiency
- Radium-228: Cancer risk
- Cryptosporidium: Single-celled protozoan parasite that causes gastrointestinal issues

## Chemical Hydration and Health Effects

- Chlorine dioxide: Neurological risk, anemia of children and infants
- Ethylene bromide: Cancer risk, hepatic/renal/gastrointestinal/reproductive issues
- Vinyl chloride: Cancer risk
- Trichloroethylene: Cancer risk and hepatic issues
- Antimony: Hypoglycemia, hyperlipidemia
- Chloramine: Gastrointestinal issue, anemia
- Tetrachloroethylene: Cancer risk, hepatic issues
- Chromium: Dermatological issues
- Ethylbenzene: Hepatic and renal issues
- trans-1,2-Dichloroethylene: Hepatic issues
- Bromate: Cancer risk
- Heptachlor epoxide: Hepatic issues, cancer risk
- Selenium: Circulation issues, peripheral numbness, hair and nail weakening and loss. Selenium, although needed for proper biological function in high blood concentration, becomes toxic (Majumdar, et. al., 2018).
- Turbidity: Cloudy presence of parasites, bacteria, and viruses that can cause headaches, nausea, vomiting, and diarrhea

## Chemical Hydration and Health Effects

- Haloacetic acids: Cancer risk
- para-Dichlorobenzene: Anemia, splenic/renal/hematological issues
- Beryllium: Intestinal issues
- Pentachlorophenol: Cancer risk, renal and hepatic issues
- Di(2-ethylhexyl) phthalate: Cancer risk, reproductive and hepatic issues
- Arsenic: Dermatological and circulatory issues, cancer risk
- Fluoride: Osteo pain and dental damage
- Nitrates: Infant illness and death, respiratory issues
- 1,1-Dichloroethylene: Hepatic issues
- Trichloroethylene: Cancer risk, hepatic issues
- Dichloromethane: Hepatic issues, cancer risk
- Thallium: Hair loss, renal / liver/ intestinal issues
- Toxaphene: Cancer risk, increased risk of renal, thyroid, and hepatic issues



## Chemical Hydration and Health Effects

- Endrin: Hepatic issues
- Heptachlor: Hepatic issues, cancer risk
- Cyanazine: Thyroid and nerve issues
- Diquat: Eye/visual issues
- Chlorite: Anemia and nervous systemic issues
- Chlorine: Gastrointestinal issues
- Methoxychlor: Reproductive issues
- Hexachlorobenzene: Cancer risk, hepatic/renal/reproductive issues
- Di(2-ethylhexyl) adipate: Weight loss, hepatic and reproductive issues
- Toluene: Renal / hepatic/nervous system issues
- Benzene: Cancer risk, anemia, platelet issues

Women who are pregnant or attempting to become pregnant should consider clean, purified water. Also, note that bathing and showering allows for integumentary or respiratory absorption, lessened with shower/water filters.

*Thank You All  
for  
Becoming Part of This New and Emerging Science*

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Once Again Thank You All

~ José Diaz ~