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ZINC SUPPLEMENTATION IN THE CASE OF DIARRHEAL DISEASE

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ABSTRACT

In this extensive literature review, the micronutrient zinc and its efficacy in treating and preventing diarrheal disease in children under the age of five was reviewed. With diarrheal disease being the second leading cause of death in the developing world, this paper hopes to reveal the gaps in not only the research, but in practice and policy as well. After further investigation, it seems that zinc plays a significant role in the treatment and prevention of diarrheal diseases in children over six months of age; however, this micronutrient appears to be ineffective in both treating and preventing diarrhea in infants younger than six months. The implications of this study also highlight the importance of zinc implementation programs and research within each country, wide acceptance of the effectiveness of zinc among healthcare providers and families, a change in behavioral practices as well as the improvement of other sectors of health, including water sanitation and hygiene.

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Chapter 1

Introduction to Diarrheal Disease

Although perhaps thought to be inconsequential in countries such as the United States, diarrheal disease remains the second leading cause of death in the developing world for children under five.[1] Therefore, in order to see an overall reduction in child mortality rates, the prevention and treatment of this deadly disease proves to be paramount. In recent years, these numbers have fortunately declined with diarrhea causing 9% of deaths for children under five, but with this number still equating to over half a million per year, the issue remains critical.[2]

Diarrheal diseases cause the body to become dehydrated, leaving it without sufficient levels of salt and water to continue everyday bodily functions. Diarrhea is usually a sign of infection in the intestinal tract and is characterized by the passage of at least three liquid stools per day. Clinicians have defined three types of diarrhea including: acute watery diarrhea lasting several hours or days, acute bloody diarrhea or dysentery, as well as persistent diarrhea, lasting 14 days or longer. Persistent diarrhea can then evolve into a chronic issue when lasting longer than 4 weeks (Figure 1). However, this paper will focus on the acute and persistent stages of diarrheal disease.

Figure 1: Cycle of diarrhea

Both acute and persistent cases can be attributed to issues of water sanitation and hygiene, which spread the viral, bacterial and parasitic sources of disease; however, rotavirus is the top cause of acute diarrhea in children worldwide.[3] Rotavirus causes gastroenteritis, with symptoms leading not only to diarrhea, but vomiting, fever and dehydration as well. Without proper treatment, diarrheal disease kills more children than AIDS, malaria and measles combined. [4]

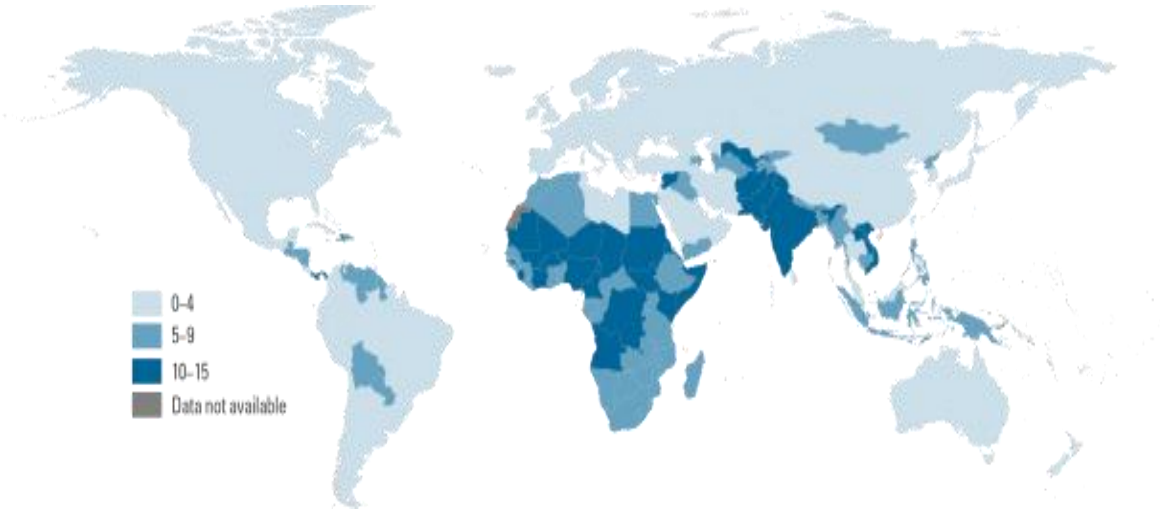

Figure 2: Percentage of deaths among children under age 5 attributable to diarrhea sourced from UNICEF (http://data.unicef.org/child-health/diarrhoeal-disease.html)[2]

In order to reduce the incidence rate of diarrhea, reformation of sanitation practices, vaccination for rotavirus, increased breastfeeding to reduce exposure to contaminated water, rehydration with oral rehydration salts (ORS) solution and micronutrient supplementations, such as vitamin A and zinc, should be considered. Although all these measures may be effective, this paper will delve deeper into the supplementation of the micronutrient zinc as it has become a recent topic of interest in the prevention and treatment of diarrhea.

Chapter 2

Zinc

One micronutrient that has found success in the treatment and prevention of diarrheal disease is the essential mineral zinc. Zinc, crucial during development and growth, requires a daily intake due to an absence of a specialized storage system within the body. To meet this requirement, zinc can be found in a variety of foods including lean red meat, poultry, whole-grain cereals, nuts and legumes. It is important to note that zinc is more bioavailable, or best absorbed through meat consumption.

Occurring in the small intestine, absorption of zinc is concentration dependent; however, under normal physiological conditions, uptake is continuous. Soluble, organic substances including hydroxy and amino acids assist in the absorption of zinc while insoluble compounds weaken this process. Additionally, competitive interactions with other similar ions can impair the uptake and absorption of this micronutrient, which has been observed in the usage of high dosage supplements and in aqueous solutions. Other major determinants of absorption are the amount of inositol hexaphosphate or phytate present, as well as the source and level of dietary protein. Phytates can be found in legumes, whole-grain cereals and other vegetables; they have a strong aptitude for bonding divalent cations, such as zinc, and diminishing its absorption. Conversely, animal proteins enhance the absorption of zinc, which explains why this micronutrient is more bioavailable in meat than grain-based food sources.[5]

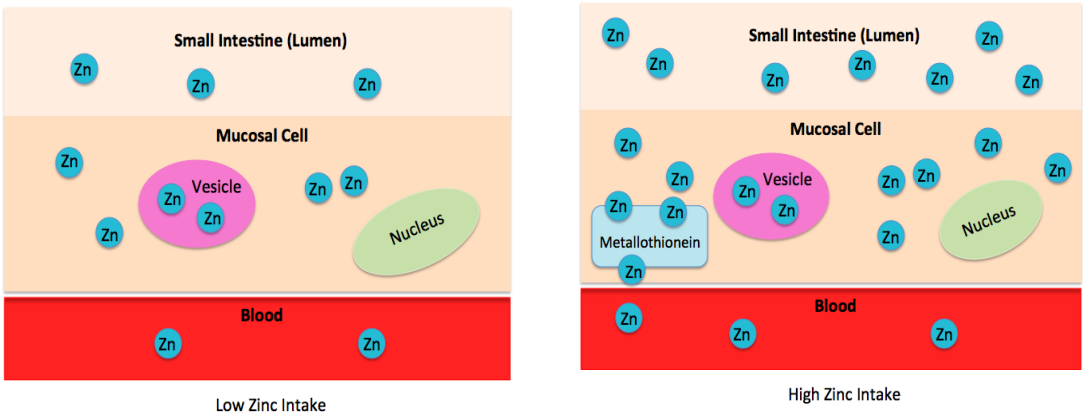

Figure 3: Zinc absorption in the body (adapted Gropper, S.)[6]

Proper and adequate zinc absorption shows to be important for the continuation of several processes at the cellular level including the catalyzation of approximately three-hundred enzymes involved in DNA and RNA synthesis, protein synthesis, immune function and cell division. Zinc also provides structure for cellular membranes, contributing to the upkeep of cell and organ integrity. It plays a part in the activation and repression of gene expression through polynucleotide transcription by allowing transcription factors to bind to the DNA helix.[7] But in order to properly conduct these cellular level bodily functions, intake must be achieved.

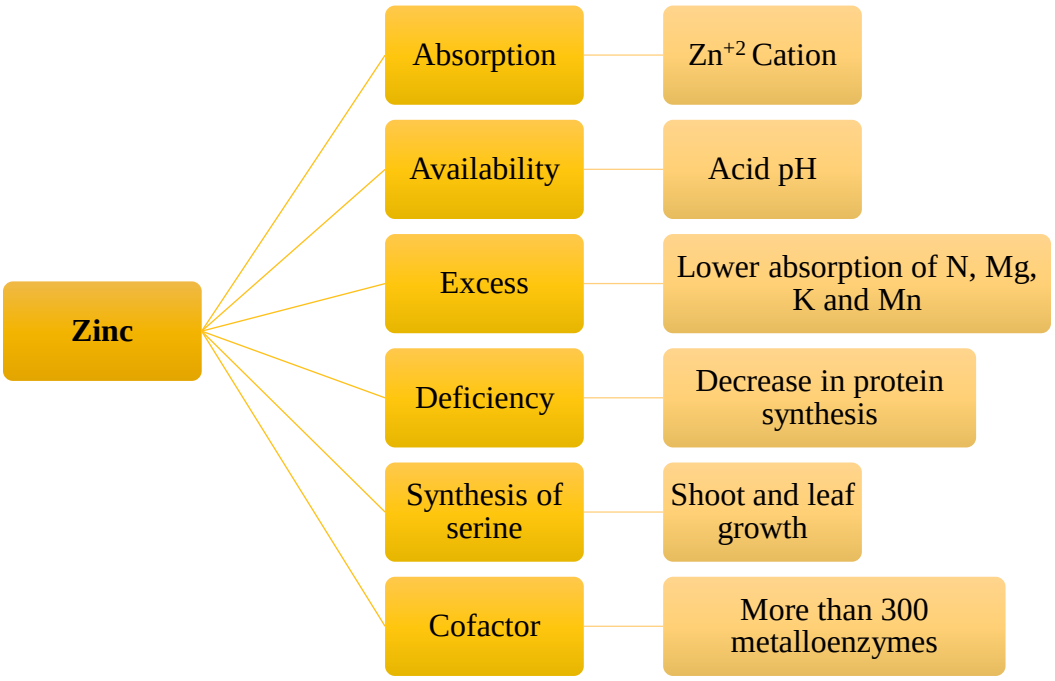

Figure 4: Zinc in the body (adapted from Escudero-Almanza, D. J. *et al.*)[8]

A proper amount of zinc consumption depends on stage of life and dietary behaviors. If this requirement is not met, it can lead to a series of complications including, but not limited to, a compromised immune system, growth retardation and loss of appetite. With a more severe deficiency, problems can involve hair loss, delayed sexual development, eye and skin lesions, weight loss and diarrhea. Groups of people who are at risk for zinc inadequacy are those who are malnourished, have gastrointestinal disorders, vegetarians, pregnant and lactating women, older infants that are not exclusively breastfed and people with sickle cell anemia. When these groups are zinc deficient, their immune systems become compromised, which can lead to bacterial and viral infections, such as diarrhea. In 2015, zinc deficiency was specifically responsible for approximately 4.4% of diarrheal diseases in Africa, South America and South Asia.[9] This illustrates the cycle between malnutrition, zinc deficiency, diarrheal disease and child mortality.

Table 1: Recommended dietary allowances (RDAs) for zinc[10]

Age	Male	Female	Pregnancy	Lactation
0 to 6 months	2 mg	2 mg		
7 to 12 months	3 mg	3 mg		
1 to 3 years	3 mg	3 mg		
4 to 8 years	5 mg	5 mg		
9 to 13 years	8 mg	8 mg		
14 to 18 years	11 mg	9 mg	12 mg	13 mg
19+ years	11 mg	8 mg	11 mg	12 mg

Note: mg = milligrams

Chapter 3

Diarrhea and Malnutrition

As described in chapter 2, malnutrition, zinc deficiency and diarrheal disease are intertwined into what becomes a vicious cycle. Malnutrition, defined as underweight, encompasses protein and micronutrient deficiencies, with zinc deficiency being a prime example. It is the number one risk factor in disease, but can be a result of illness as well. For example, diarrhea, which rids the body of proper nutrients, has led to higher rates of malnutrition, but diarrhea has also been an observed symptom of malnourishment, due to a weakened immune system and higher susceptibility to infection. This bidirectional relationship causes for difficulty when it comes to treatment and prevention of both diarrhea and malnutrition[11].

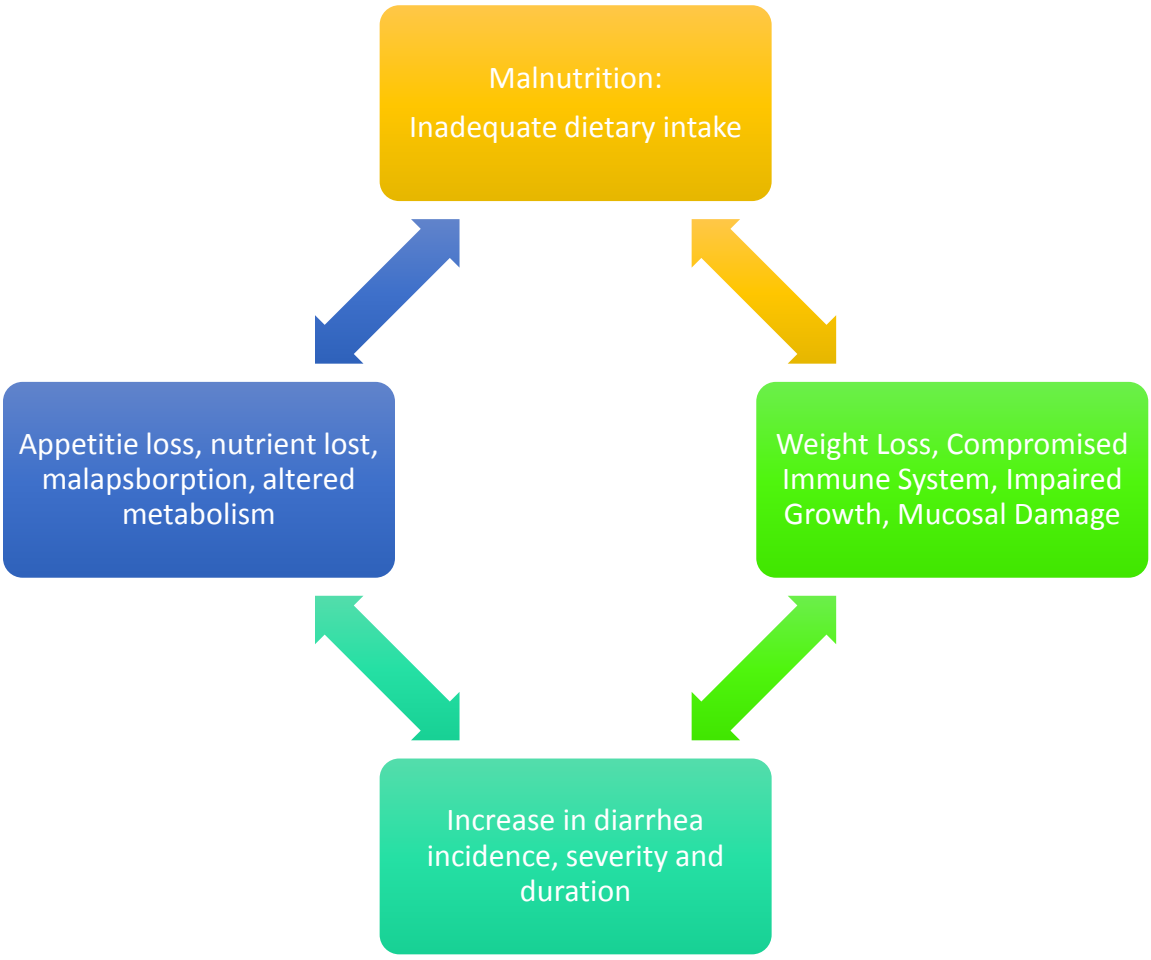

Figure 5: Cycle of malnutrition and disease (adapted from Müller, O. & Krawinkel, M.)[11]

Zinc may be considered the answer to diarrheal disease, which in turn may have a positive effect on malnutrition as well.

Chapter 4

Zinc as a Treatment

Glucose-electrolyte oral rehydration therapy (ORS), or the giving of fluids by mouth, has been widely successful in treating cases of acute and persistent diarrhea by preventing or correcting dehydration of the body. However, ORS cannot be considered the sole treatment, as it really only addresses dehydration and not the other symptoms associated with diarrheal disease. With accessibility of the rotavirus vaccine limited in parts of Africa and much of Asia, other methods, such as dietary supplements, have been introduced to decrease the mortality and morbidity rates of childhood diarrhea. Zinc supplementation has been at the forefront of these dietary approaches, being used in conjunction with ORS therapy, as well as a standalone treatment for acute diarrhea. Numerous studies conducted in hospitals and communities have proven that zinc therapy does in fact reduce stool output and duration of disease, but the physiological mechanisms of zinc remain unclear.

Kazi Mirajul Hoque *et. al.* presents several possible physiological processes that explain zinc therapy as an effective treatment for acute diarrheal disease.[12] Some possible mechanisms include the better absorption of sodium, which would prevent the body from losing an excess of water. The inhibition of second messenger (cAMP, cGMP, Ca2+)-induced Cl- secretion, enhanced regeneration of intestinal epithelium, and as mentioned earlier, the improved immune status of an individual are also ways zinc has been useful in treating diarrhea.[13] Researchers have also found that zinc promotes the absorption of ions in the gut when they were secreted due to the *Vibrio cholerae* toxin, a common virus that causes diarrhea.[14]

According to this research, zinc should indeed be effective in treating diarrheal disease, but now we will delve deeper into the studies that have tested this notion in order to see if zinc works as well in practice.

Chapter 5

Methods

In order to conduct this literature review, specific search parameters were made for the PubMed and Google Scholar databases. Separate searches were conducted for the following initial categories: zinc treatment in acute diarrhea, zinc treatment in persistent diarrhea and preventative zinc supplementation. After limited research reports were found on the effects of zinc in infants younger than 6 months of age, another search was made for this category.

Search criteria included: clinical trials or reviews written in English with full text availability, a publication date of 1996 – 2016 and human subjects ages 0 to 6 years. Under these parameters, 72 articles were found for the treatment of acute and persistent diarrhea. After further reading, articles that included children with comorbidities, emphasized other micronutrient supplementations over zinc or that did not specifically mention diarrhea were excluded. The sources of these articles were then examined to make certain the publication was of the highest quality, which included journals such as Lancet, CMAJ, Pediatrics, Journal of Health, Nutrition and Population, BMC Public Health and BMC Medicine, among others. Then, to more easily compare these studies, articles that illustrated the outcome measures of interest including: duration of diarrhea, severity and incidence were chosen. This provided us with 10 articles for acute/persistent diarrhea treatment and prevention in a range of ages. Under this criterion, 54 articles were found on zinc as a preventative measure in the case of diarrheal disease, 11 of which were deemed appropriate for this review. The same criteria was applied to the last

category of zinc supplementation in children <6 months, with age of participant corrected to 12 months or younger. Only 4 studies were found, all of which were included in this review.

Table 2: Database search criteria

Database Search Criteria	
Publication Date	1996-2016
Language	English
Article Type	Clinical Trials Reviews
Text Availability	Full Text
Subject	Human
Age	0 – 6 years

Table 3: Search word

Word Search
• **Diarrhea AND** • **zinc AND** • **supplementation AND** • **treatment AND** • **prevention AND** • **age affect AND** • **acute AND** • **persistent**

Chapter 6

Zinc Treatment Studies

Numerous studies have been performed in order to test the efficacy of zinc supplementation as a treatment of acute diarrheal diseases in children under the age of five. The World Health Organization (WHO) recognizes the effectiveness of zinc in the cases of diarrheal disease and has established guidelines for treatment as "routine use of zinc supplementation, at a dosage of 20 milligrams per day for children older than six months or 10 mg per day in those younger than six months, for 10–14 days" in addition to ORS therapy. With these established treatments, one may question why diarrheal diseases still cause over half a million deaths per year. WHO believes this to be the case due to lack of an implementation strategy in countries where doctors do not fully accept the benefits of zinc supplementation. In the doctors' defense, there have been studies that do contradict the belief that zinc has any positive effect on diarrheal disease. Numerous studies were reviewed to find the possible cause of this discrepancy, some of which are described below.

In a double blind, randomized, placebo study conducted in the Dhaka Hospital of Bangladesh, 179 children ages 3-14 years of age presenting symptoms of cholera or acute diarrhea were observed. Those who had a negative dark field examination, a systematic illness requiring antibiotics, bloody mucoid diarrhea, or had received antibiotics within 24 hours before coming to

the hospital, as well as those who were unconscious or considered medical emergencies, were excluded from this study. In order to test the effectiveness of zinc supplementation in treating cholera, 179 children were either given 30 mg of zinc or a placebo treatment, while everyone received erythromycin. Observing diarrheal stool output and time to resolution of diarrhea, the study showed that the group of children that were given zinc had less diarrheal stool output (1.6 v 1.8 kg/day, p=0.039) as well as a shorter duration of the illness (64.1 v 72.8 h, p=0.028).[15]

In a similar 2001 hospital study in Kolkata, India, a double blind, randomized, placebo-controlled, clinical trial was conducted in order to compare a mono-therapy of zinc to a combined therapy of zinc plus vitamin A in addition to other micronutrients and vitamins. In the 167 male participants age 6 to 24 months with acute watery diarrhea, the mono-therapy appeared to be the most effective with little significant difference among the supplemented groups. This trial also noted the importance of a suitable dosage of zinc for a successful outcome, which they found to be 20 mg. Along with appropriate dosages, the results of this study brought up the question of competitive absorption among nutrients when more than one supplement is introduced to the body at the same time. [16]

With competitive absorption in mind, the next double blind, randomized, controlled clinical trial was conducted in the Department of Pediatrics at Indira Gandhi Government Medical College Nagpur, India with a sample size of 808 children from 6 months to 6 years. Each child was given either a placebo, only zinc, or zinc and copper. For both groups, there was no significant difference in prior nutritional status and home sanitation practices. After the intervention, they made note of diarrhea duration and stool output during the child's hospital stay, but found that

zinc only or zinc/copper supplementations did not have the therapeutic effect usually observed. Possible reasons for this outcome could be that a lower dose was given with only 70% of the recommended dose actually received by participants, varying disease etiology or that baseline serum levels were significantly higher in the placebo groups compared to the treatment groups.[17] Having a group that received both zinc and copper could also have impacted the results. In order to see the effect of zinc alone, further researchers directed studies that only observed zinc.

Instead of comparing various micronutrients, a 2008 study in Iran used zinc as an adjunct therapy to ORS. Of 379 patients, 191 children with acute moderate diarrhea and dehydration received ORS plus a placebo syrup while 188 received both zinc and ORS therapy. The intervention group received their zinc in a split dose of 1mg/kg/day of syrup, unlike the usual zinc tablet. They found that those who received the zinc supplementation had shorter hospital stays (2.5±0.7 vs. 3.3±0.8 days; p=0.001) and less frequent diarrheal episodes (4.5±2.3 vs. 5.3±2.1; p=0.004). However, it is important to note that this study did not measure baseline zinc serum levels, but that Iran is at high-risk for zinc deficiency, making the dosage critical once more. This study also highlighted the possible change in outcomes when choosing between syrup and tablets.[18]

For the majority of these studies, zinc did in fact help to resolve diarrheal disease in children. Severity of illness, therapeutic approaches, patient demographics, duration and dosage appeared to be significant factors in determining the success of zinc as a treatment. However, the largest gap in findings was apparent in infants younger than six months.

Sub-Chapter 6: Zinc Treatment for Children Under 6 Months

A described above, zinc has been proven to be effective in children older than 6 months, but little to no effect has been observed in infants less than 6 months. With a sizeable amount of diarrheal patients falling in this age range, it is crucial to find why zinc seems to be ineffective during this time of development.

Effectiveness of zinc supplementation plus ORS for diarrhea in infants aged less than 6 months was studied in Haryana state, India. In addition to zinc supplementation and ORS, this study also provided education to parents on the importance of zinc. Results were mixed when it came to the effectiveness of zinc in children < 6 months, which indicates the need for further investigation, so other studies were conducted. [19]

In Pakistan, Ethiopia and India, infants aged 28 days to 5 months were registered for a randomized, placebo, controlled trial where 554 subjects received 10 mg of zinc and 556 received a placebo for 14 days. Prior health history, including diarrheal episodes, breast-feeding status and socioeconomic indicators were evaluated at baseline in this study. If signs of dehydration were present, this was corrected with the use of ORS solutions. Although not highly significant, the study showed unusual results where those infants who were given the zinc supplement experienced the diarrheal episode 0.21 days longer than those given the placebo. There was also no difference observed in the number of stools per day and vomiting rates were similar in the zinc supplemented (8.7%) and placebo groups (6.2%).[20]

With zinc efficacy studies in children 6 months and younger seemingly scarce, a more recent study was conducted in rural Bangladesh to test the benefits of zinc in children ages 3-5 months, 6-11 months and 12-59 months using the parameters of incidence and duration of diarrhea as well as rate of hospitalizations. Unlike the previous Fischer and Brooks et al. study where no benefits were observed, a small upward trend was seen in children less than 6 months treated with zinc and a shorter duration among infants. Unfortunately, the sample size of the 3-5 month age range was very small, leaving its findings not statistically significant ($p<0.001$ and hazard ratio=0.77, 95% confidence interval: 0.68–0.87 if >12 months). What is worth noting about this study is that even with a WHO recommendation of 10mg of zinc for this age group, this study administered 20 mg, which might make a case for increasing the dosage in order to see significant results for child 6 months and under. Although 20 mg appeared to be a safe amount, more studies need to be conducted for further proof that zinc is beneficial for all ages in the case of diarrheal disease.[21]

Sub-Chapter 6: Zinc Treatment in Persistent Diarrhea

Most studies have observed the effectiveness of zinc therapy in the case of acute diarrheal diseases, but zinc as a treatment for persistent diarrhea must also be assessed. Reports indicate that more severe cases of diarrhea such as persistent diarrhea and dysentery are the cause for 65% of diarrhea-related deaths in India, with similar findings also in Bangladesh, Brazil, Peru and Senegal.[22] Here is examined the effectiveness of zinc as a treatment for more enduring diarrheal diseases.

In New Delhi, India a recent double blind randomized placebo controlled trial was conducted in children from 3 months to 5 years to test the efficacy of zinc therapy in the case of persistent diarrhea. Thirty children received the zinc treatment while the other 30 children received a similar tasting placebo. Improvement was marked by the passage of the first formed stool. The study showed that in the treatment group, the duration of diarrhea (38.69 ± 13.94 hours) was almost cut in half compared to those given the placebo (71.50 ± 22.05 hours).[23]

Furthermore, in an analysis of randomized controlled trials on the therapeutics effects of oral zinc treatment in persistent diarrhea, those given zinc were 24% less likely to continue having diarrhea and 42% had a lower chance of treatment ending in failure or death. This pooled analysis controlled for baseline plasma zinc levels, sex, age and weight-for-height. With these controls, they observed a greater effect in persistent diarrhea male participants who were younger than 1 year of age and had very low baseline zinc levels.[24] This review pooled all published and unpublished studies pertaining to persistent diarrhea, giving us a comprehensive representation of zinc supplementation in persistent type diarrhea.

Consequently, in the studies reviewed in both persistent and acute diarrheal disease, therapeutic zinc appears to be effective in children 6 months and older. Now, we will look at zinc as a preventative measure for disease.

Table 4: Zinc treatment in acute diarrhea studies

Zinc Treatment in Acute Diarrhea					
Country	**Year**	**Outcome Measures**	**Design**	**Age/ Sample Size**	**Findings**
Bangladesh[15]	2008	Duration of diarrhea and stool output	Double blind, randomized, placebo study	3 -14 years n = 179	Zinc supplemented patients had 12% shorter duration (64.1 v 72.8 h, p = 0.028) and 11% less stool output (1.6 v 1.8 kg/day, p = 0.039)
India[16]	2011	Duration, volume of diarrhea and consumption of oral rehydration	Double blind, randomized, placebo-controlled clinical trial	6 - 24 months n = 167	Group 1 (zinc and vitamin A), Group 2 (Zinc, Vitamin A and other micronutrients), Group 3 (zinc plus Vitamin A) all illustrated significant reduction in outcome variables (p < .0001)
Iran[18]	2008	Frequency and consistency of diarrhea, duration of hospitalization and change in patients' weight	Double blind, randomized, placebo-controlled trial	9 months - 5yrs. n = 176	Diarrhea frequency was lower in zinc group (4.5±2.3 vs. 5.3±2.1; p=0.004) weight remained similar (10.5±3.1 vs. 10.1±2.3; p =0.14), Zinc group also had a shorter duration in hospitalization (2.5±0.7 vs. 3.3±0.8 days; p = 0.001

India[17]	2009	Mean duration of diarrhea and mean stool weight	Double-blind, randomized, controlled clinical trial	6 months -59 months n = 808	The mean duration (63.7 hours) and stool weight (940 grams) did not vary significantly across treatment groups

Table 5: Zinc treatment studies in children < 6 months

Zinc Treatment in Children < 6 months					
Country	**Year**	**Outcome**	**Study Design**	**Age/ Sample Size**	**Findings**
India[19]	2006	2 cross-sectional surveys	Cluster-randomized trial	< 6 months n = 11,881	Insignificant benefits of zinc was found in < 6 months
Ethiopia, India and Pakistan[20]	2006	Mean duration of diarrhea	Randomized, placebo, controlled trial	28 days – 5 months n = 1,110	Mean duration of zinc group was .21 days longer than placebo
Bangladesh[21]	2008	Duration of diarrhea	Cluster-randomized comparison	3-5 months 6-11 months 12-59 months n = 11,772	Positive trend in zinc groups 3 – 5 months, but only statistically significant among older children p <0.001 and hazard ratio=0.77, 95% confidence interval (CI): 0.68–0.87 if >12 months

Table 6: Zinc treatment in persistent diarrhea studies

Zinc Treatment in Persistent Diarrhea					
Country	**Year**	**Outcome**	**Study Design**	**Age/ Sample Size**	**Findings**
India[23]	2015	Mean duration of diarrhea	Double-blind, randomized, placebo controlled trial	3 months – 5 years n = 60	38.69 ± 13.944 hours (mean ± standard deviation (SD)) with range of 11-76 hours as compared with placebo group where duration was 71.50 ± 22.045 hours (mean ± SD) with range of 46-144 hours
Various Countries[25]	2000	Pooled analysis	Randomized controlled trial	<5 years n = N/A	Zinc-supplemented children 15% lower probability in acute diarrhea (95% CI: 5%, 24%) 24% lower probability in continuing diarrhea in persistent-diarrhea (95% CI: 10%, 63%)
Notes: SD = Standard Deviation CI = Confidence Interval					

Chapter 7

Zinc Prevention Studies

An intriguing detail about the micronutrient zinc is that not only has it been used as a treatment in diarrheal disease, but as a preventative measure as well. Studies have shown that prophylactic zinc has been successful in reducing both the prevalence and incidence of diarrheal diseases in children. As mentioned previously, due to zinc's role in the immune system, appropriate levels of consumption can keep the immune system at high functionality while preventing future infections, such as diarrhea. But for children not receiving proper nutrition, this could easily lead to a zinc deficiency and in turn, a compromised immune system and increased susceptibility to disease.[26] This is why it is crucial to study the nutritional aspects that lead to malnutrition and in turn, diarrhea. *(To read more about the effects of diet and zinc deficiency in India, refer to Appendix A)* The studies below illustrate the effectiveness of zinc as a preventative measure in both acute and persistent diarrhea.

Sub-Chapter 7 Preventative Zinc Supplementation in Acute and Persistent Diarrhea

A literature review was conducted in 2011 to reveal the impact that zinc supplements had on all cause mortality as well as specific mortality from diseases such as diarrhea, pneumonia and malaria. This review concluded that zinc supplementation alone was statistically insignificant in

the case of all cause mortality and only had an 18% reduction on diarrhea-specific events.[27] This could suggest that a micronutrient supplement alone is not effective enough in combatting diarrheal disease, but the following studies seem to read otherwise.

In a community-based, randomized, double blind intervention completed in Guatemala, 89 children aged 6 to 9 months were randomly assigned to receive a 4 mL drink that contained 10 mg of zinc sulfate each day for a 7-month duration. High rates of diarrheal infections were observed in the placebo group, but a 22% reduction in acute diarrhea occurred in the supplement group. An even larger reduction was seen in male participants and a 67% reduction in incidents of persistent diarrhea.[28]

Another study in Bangladesh that observed the effects of zinc on multiple disease burdens, including diarrhea, pneumonia and malaria, provided a weekly supplement of 70 mg to 1,665 children age 30 days to one year. In the group of 809 that received the zinc supplement, a large decrease was seen in pneumonia but not in diarrheal disease. The study also observed a problem with adherence to the weekly zinc supplements, which could foreshadow complications with a supplement intervention outside of the parameters of research.[29]

In Kenya, 16 villages were provided a 10-day course of zinc supplements and two oral rehydration solution packets every two months at their homes while the other 17 villages still received ORS at home, but were only able to obtain zinc from a healthcare facility. This study wanted to see the effects of a family having an optional zinc treatment in the home on community-wide prevention of diarrhea. Unfortunately, no differences were observed on the

incidence of diarrhea between the two groups of villages and only 60% of families provided with zinc actually used it in treatment.[30] A similar study in Delhi, India also provided an urban colony with a 14-day course of zinc or placebo syrup to see if this would decrease the incidence of diarrheal disease for the next 5 months. Unlike the Kenyan study, it was made certain that the 14-day zinc treatment was consumed, rather than being an option for if diarrhea occurred. To ensure compliance, visits were made on days 7 and 14 of treatment and then biweekly for the next 5 months. At the conclusion of 5 months, a significant reduction was observed in those who took the short-course of prophylactic zinc.[31]

Researchers in Turkey somewhat combined the methods of the previous two studies. Each child who currently had acute diarrhea was provided with 15-30 mg of elemental zinc daily for two weeks; they would then look to see if there was an incidence reduction in the next 2-3 months. As one would expect, plasma levels of zinc increased after two weeks, but there was no significant difference noticed in the prevalence and incidence of diarrhea between the control and treatment group. There was also no decrease in duration or severity of diarrhea.[32] A study in Bangladesh also used children from 4 – 59 months to detect the incidence of diarrhea after an initial treatment of zinc for an acute episode. The efficacy of a 5- and 10-day course of treatment was observed in 1,622 children of a rural community. Female field workers made daily visits to record the duration of the initial episode and any subsequent diarrhea occurrences. After 90 days, researchers concluded that either a 5 or 10 day treatment of zinc was equally effective in treating and preventing diarrhea for the next 3 months.[33]

Investigators in Dhaka, Bangladesh took this type of study a bit further by looking at the effects of zinc supplementation on the incidence of diarrhea over a 9-month period with weekly follow-ups. All 353 subjects were given a 10-day course of treatment at the time of the initial acute infection, but then 2 groups were randomly assigned either 20 mg of zinc per day for the next three months or a placebo supplementation. After 3 months, they observed a 28% reduction in disease and 21% after 9 months.[34] Another study that had a long follow-up period was again in Bangladesh and extended to two years. This study, similar to the methods of Feikin, D. R. et al[30] and Malik et al[31], provided daily zinc supplements for 14 days, but observed longer term effects. Interestingly enough, they did see a shorter duration and incidence of diarrhea.[35]

Other studies, such as the one conducted in the Peruvian Amazon examined a much longer supplement period by providing a daily zinc supplement for 7 months. Children of 6 months to 15 years in the single supplementation zinc group saw a 23% reduction in morbidity. What was especially interesting of this study though is the age effect. Children 5 years and under saw a 30% reduction in diarrheal disease but those older than 9 years of age who received iron or zinc experienced a significant increase in diarrhea.

Sub-Chapter 7 Preventative Zinc Supplement for Diarrhea for Children Under 6 Months

Analogous to the findings for therapeutic zinc, there appears to be a lack of research on the effects of preventative zinc supplements in children less than 6 months. In the few studies above that included children from birth, the sample sizes were either too small or no significant results were found for the exception of one. A community-based clinical trail in Nepal assessed the

effects of a daily zinc supplement in 20,968 children aged 1 – 35 months. Children older than one year received 10 mg tablets while those under 12 months received a half tablet or 5 mg for one year, with twice-weekly visits from study personnel. This study concluded that there was no significant effect in mortality rates between the zinc and placebo group. More specifically, no benefits were observed in children 0 to 12 months of age.[36]

Table 7: Preventative zinc in acute and persistent diarrhea studies

Preventative Zinc in Diarrhea					
Country	**Year**	**Outcome Measures**	**Study Design**	**Age/ Sample Size**	**Findings**
Guatemala[28]	1997	Incidence of diarrhea	Community-based, randomized, double blind	6 – 9 months n = 89	Zinc-supplemented children observed a 22% reduction in diarrhea incidence, 67% reduction in persistent diarrhea
Various Regions[27]	2011	Mortality	Literature Review	3 months – 5 yrs. n = 8 trials	Sole zinc supplementation in the reduction of all-cause mortality was associated with a statistically insignificant 9% (RR = 0.91; 95% CI: 0.82, 1.01) as well as an insignificant 18% reduction in diarrheal-related mortality.

Bangladesh[28]	2005	Rate of diarrhea	Randomized, placebo controlled trial	2 - 12 months n = 1665	Zinc-supplemented groups observed a small but significant effect in fewer incidents of diarrhea. (1881 cases vs. 2407; 0.94, 0.88-0.99)
Turkey[32]	2006	Mean duration of diarrhea, number of stools, and severity	Randomized, non-placebo controlled trial	6 – 60 months n = 280	Mean duration of diarrhea in zinc group was 3.02±2 days in comparison with control group/3.67±3.2 day which was insignificant ($p>0.05$)
Kenya[30]	2014	Incidence of diarrhea	Village-randomized clinical trail	n = 1,903	No differences were observed between zinc villages and comparison villages.
India[31]	2013	Incidence and duration of diarrhea	Randomized, double-blind, placebo-controlled trial	6 – 11 months n=272	There was a 39% reduction in diarrheal episodes and a 36% reduction in duration.
Bangladesh[33]	2011	Incidence and duration of diarrhea	Randomized, double-blind placebo controlled, community trial	4 – 59 months n = 1,622	A 5 and 10-day course of zinc treatment were both found to be effective in reducing the incidence and duration of diarrhea.

Bangladesh[34]	2010	Incidence of diarrhea	Randomized, double-blind field trial	6 – 23 months n = 353	The incidence of acute diarrhea was reduced by 28% by (2.64 vs.3.66 episodes/p-y follow-up) over the 3 month follow up and by 21% over 9 months.
Bangladesh[35]	2002	Duration, incidence of diarrhea, acute lower respiratory infections, admission to hospital for diarrhea or acute lower respiratory infections and child mortality.	Cluster randomized comparison	3 months – 59 months n = 8070	Reduction in duration (hazard ratio 0.76, 95% confidence interval 0.65 to 0.90) incidence of diarrhea (rate ratio 0.85, 0.76 to 0.96) was observed in the zinc-supplemented group.
Peru[37]	1998	Incidence of diarrhea	Randomized, placebo-controlled clinical trial	6 months – 15 years n = 855	Supplementation with only zinc reduced diarrhea morbidity by 23% in all children.
Bangladesh[38]	2001	Incidence and prevalence of diarrhea	Randomized, double blind placebo controlled trial	12 – 35 months n = 800	The incidence and prevalence of diarrhea were lower in the zinc and vitamin A groups than in the placebo group.

Notes:
RR: Relative Risk
CI: Confidence Interval

Table 8: Preventative zinc studies in children < 6 months

Preventative Zinc in Children <6 Months					
Country	**Year**	**Outcome Measures**	**Study Design**	**Age/Sample Size**	**Findings**
Nepal	2007	Frequency and duration of diarrhea, and mortality	Community-based, cluster-randomized, double-masked, placebo-controlled, 2x2 factorial trial	1-35 months n = 41,276	No significant difference was found in mortality between the zinc and placebo groups (316 vs. 333 deaths; hazard ratio 0.92, 95% CI 0.75-1.12) Zinc also had no effect on mortality in children younger than 12 months (181 vs. 168 deaths; 1.04, 0.83-1.31);

Chapter 8

Research Implications

The bi-directional relationship between zinc and diarrhea has led to much interest in the public health sector. Diarrhea causes a decrease in zinc absorption due to lower levels of dietary intake and higher intestinal nutrient loss. Vice-versa, a zinc deficiency can leave a child with an impaired immune system, increasing his or her susceptibility to infection, such as diarrhea. This is why we have chosen to further study zinc as a preventative measure and treatment for this deadly disease.

After reviewing numerous studies conducted on zinc, we can conclude that as a treatment, zinc appears to be effective in reducing the duration of diarrhea as well as its severity given that a proper dose is received. However, there seems to be a gap in the literature when it comes to children 6 months of age or younger. In the studies reviewed, zinc did not prove effective for these young infants and further study has yet to be conducted. As for the use of zinc in diarrheal disease prevention, this measure also proved to be successful, but even with these successes, some studies illustrated that perhaps the proposal of zinc supplements alone is not enough to end all cases of diarrheal diseases; which leads to the question, what else can be done in order to prevent diarrhea? We will now go more in depth into the questions raised after conducting this review.

Sub-Chapter 8: Preventative Zinc Supplement for Diarrhea for Children < 6 Months

In the literature evaluated, it was apparent that zinc supplementation in children younger than 6 months of age did not have significant benefits in the case of diarrhea. One study conducted by Fischer Walker et. al even revealed that zinc supplementation in this age category was associated with somewhat longer bouts of diarrhea and increased vomiting, although not very significant.[21] Conversely, other studies that showed improvement in infant health outcomes often had small sample sizes, leaving their findings not statistically noteworthy.

A lack of results could possibly be due to a difference in pathogens seen in this age group. As noted in our introduction to zinc, this micronutrient has been observed to hinder the ion secretion prompted by the cholera toxin, but not by other pathogens, such as the *Escherichia coli* heat-stable toxin. It is possible that the *Escherichia coli* heat-stable toxin is found to be cause of diarrhea in this age group more than the cholera toxin, but further investigation would be needed. Another reason for this outcome could be the varying in immune function between the age groups. As an infant, immune protection is provided through the mother who delivers immune factors through the practice of breastfeeding, whereas an older child relies on its own acquired immunity. Therefore, with a weakened immune system from a zinc deficiency, greater effects may be seen in the age where immune factors are passive rather than active.

Additionally, in children who display other health complications, the benefits of zinc may be concealed. Likewise, when infants are malnourished or have innate low levels of zinc, baseline zinc levels, appropriate dosages, and exclusive breastfeeding become crucial variables in zinc

studies. Although the positive effects of zinc supplementation remain to be seen in this age group, numerous studies attested to its efficacy in older children, yet cases of diarrhea continue.

Sub-Chapter 8: Supplementation Issues

One possible cause for the staggering extent of diarrheal disease could be due to the fact that the plan for zinc supplementation alone is not enough. Even though the World Health Organization recommends zinc supplements to children in the developing world, is this feasible for all families to adhere to and if so, will they? In 2008, UNICEF reported that in India, only 1% of prescriptions included the use of zinc.[19] This could be attributed to a lack of awareness and knowledge of the benefits of zinc by not only the general population, but by healthcare providers as well. We can see this disconnect clearly displayed with the continued prescribing of antibiotics by doctors in the case of diarrhea. With the most common form of diarrhea considered to be viral, families are asked to use the little resources they have on ineffective treatments, while also contributing to the rise of antibiotic resistance.[39] Zinc supplements could be utilized in place of useless and over-prescribed antibiotics in order to combat an array of diseases, including diarrhea, but this idea must first be accepted by health leaders around the world.

Sub-Chapter 8: Behavior

If healthcare providers do not recognize the importance of zinc, it is unlikely that the general population of low-income countries will either. Furthermore, even if a health professional recognizes the significance of this micronutrient, we still must consider the role of behaviors and

beliefs in a community who seek counsel from these professionals. We would first need to address the perceptions of the disease before we could consider a successful treatment plan. For example, if a community does not perceive diarrhea as a life threatening illness, treatment from a doctor will often not be sought. In many low-income countries, diarrhea is treated in the home by the primary caregiver, who is usually the mother. A study conducted in Ethiopia found that the knowledge of mothers on the causes, transmission and prevention of diarrhea was only 37.5%. Using a five-point Likert scale, it was also determined that mothers either did not have an adequate knowledge on how to prevent diarrheal disease or they did not have a positive attitude towards taking the necessary precautionary measures. From these results, it was concluded that only 62.4% of mothers would seek a licensed professional for their children in the case of diarrhea.[40] Perhaps a visit to the physician would be unnecessary if mothers were knowledgeable on proper home treatments, but unfortunately studies show otherwise.

In another analysis of 75 Indian mothers, each participant was asked to complete a questionnaire. From this survey, it was concluded that only 5.3% of mothers were aware that diarrhea led to dehydration and for those who used ORS in the home, almost one-third used an incorrect proportions of ingredients. More than 90.7% of mothers were aware of ORS, which was easily accessible, but even with this knowledge only two-thirds utilized the therapy to its full potential. Additionally, nearly half of the mothers did not practice effective hand washing behavior, and 32% chose bottle-feeding over exclusive breastfeeding.[41]

Mothers in Mirzapur, Bangladesh were also evaluated for patterns of health-care seeking behavior in 2007. Of 1,128 children, 7.4% of mothers reported signs of persistent type diarrhea

in their children, but only 12.2% received ORS, 27.6% received homemade fluids and none of these children received zinc in the home. Although a majority of caretakers sought care outside of the home, only 22.1% received care from a hospital. It was stated that the primary reason for not seeking care was that the illness was not perceived as severe (74%) and the high cost of treatment (21.9%).[42]

Here we can see that not only is knowledge on the disease and its treatment important, but so is a positive attitude towards behavior change when seeking treatment. In Anderson's three-pronged Behavioral Model of Health Services Use, we see that predisposing factors such as education, occupation, socioeconomic status, cultural norms and mental aspects in terms of health beliefs play a crucial role in utilizing health care. The second component of this model is need factors, which at an individual level can be defined as a person's perceived need for health services. Both of these determinants are clearly observed in low-income mothers with children that have diarrhea, but with an affirmative outlook on the proposed solution of zinc supplementation and confirmation on the effectiveness of ORS therapy, this could improve adherence and desire for treatment, but only if the treatment is available. Anderson's third model component of enabling factors, address the access and affordability of health care services.[43]

The Anderson Model of Health Care Utilization

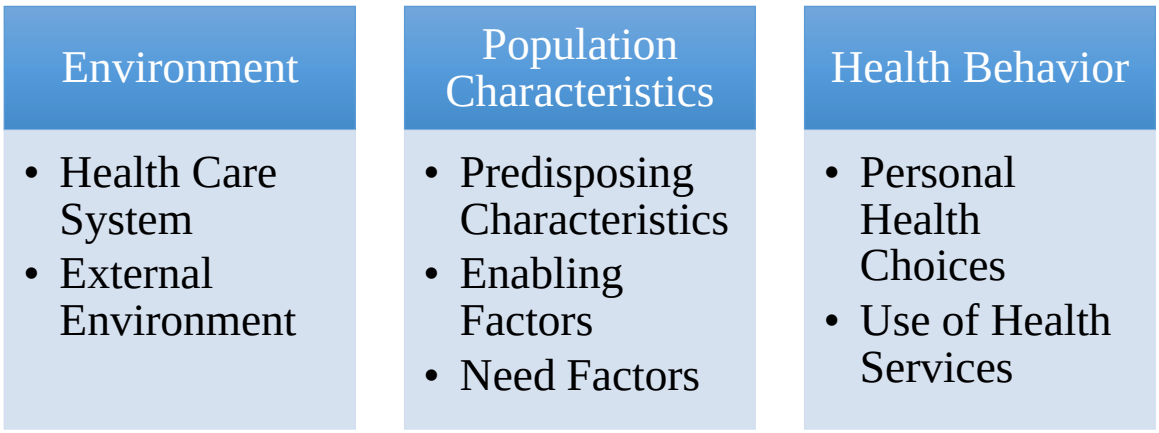

Figure 6: Anderson's model of behavior (adapted from Babitsch *et. el*)[43]

Sub-Chapter 8: Cost Effectiveness

After a community has the knowledge on the issue at hand as well as an open mind and positive attitude towards behavior change, we then ask, is this treatment feasible and cost effective? In the case of acute diarrhea, a study in Columbia performed over 1 month found that therapeutic zinc was less costly and more effective than other means of treatment, but the most effective method of delivery is yet to be determined. Keeping in mind that these results reflect the Columbian healthcare system, researchers found an average case of diarrhea in Colombia costs 42.5 USD. With the use of zinc supplementation, this cost would be reduced to 34.36 USD. Having this information, Columbia has incorporated routine zinc treatment in the case of acute diarrheal disease in children under 5, but the implementation of zinc has been slow to catch on in other developing countries. Several reasons could contribute to this slowed progress. For

example, heath care providers did not have a satisfactory pharmacological presentation of only the micronutrient zinc until very recently. Additionally, other countries could gather that the results of one study cannot also be directly applied to all other countries due to the varying cost of hospitalization, the consumption of competing micronutrients and the availability of zinc within the country. The Columbia study was also the first of its kind to be conducted on the cost effectiveness of zinc in a Latin country to this level of quality, which illustrates the further need for research on the cost and availability within each country considering the utilization of zinc supplementation. Although it is estimated that zinc would be the most wide spread cost effective option, depending on the disease burden in that area, costs could be sizable to either the individual household or the private/public sector. Expectantly, the investment into preventative zinc would compensate for other health care expenditures, but until this is illustrated, countries may be hesitant to invest in a zinc implementation program.

Sub-Chapter 8: Scale-Up and Delivery

Once funds are secured though, in order to scale up zinc programs one still faces the problem of access and delivery. To reach the most children, zinc supplements would need to be delivered not only through the government, but through the private sector and nonprofit organizations as well. In 2003, the International Centre for Diarrheal Disease Research in Bangladesh began to make plans for the scale up of 20 mg tablets of zinc operating under private sector health care providers, a pharmaceutical laboratory and a marketing agency. This study was based upon the theory of 'diffusion of innovation.'[44] This theory illustrates that the adoption of a new behavior occurs through a series of groups including innovators, early adopters, early majority, late

majority and laggards. Essentially, this means that through innovate education systems and a mass media campaign, the study expected a trickle down effect in scale up of the micronutrient zinc.[45]

In order to test the reach of this diffusion, three outcomes were monitored including: caretaker awareness of zinc treatment in the case of childhood diarrhea, the use and adherence to zinc, as well as ORS therapy. Over the course of three years, over 90% and 70% of urban and rural caregivers were aware of zinc therapy, but those who actually utilized the treatment were few. This discrepancy could be attributed to continued poor access to treatment and inefficient methods of awareness for rural-lower income areas. For example, with the use of a mass media campaign, this would favor families of higher income, but would still be inefficient in reaching more remote regions. The study also experienced difficulty in educating such a diverse population of licensed and non-licensed health care providers in the private sector. Additionally, to have such a high dose of zinc classified this treatment as a drug in Bangladesh, making it harder to approve and market.[44] Although increasing access to zinc by making it an over-the-counter product may lead to an increased use of the micronutrient, will mothers still seek medical attention in more serious cases? And how often will zinc be misused? When scaling zinc projects, these are important factors to consider.

Sub-Chapter 8: Adherence and Proper Use

When the micronutrient finally reaches the home, this brings us back to the question of adherence and proper use. With financing and access established, we may still see high rates of

diarrhea due to a lack of adherence in the home. In the same scale-up study, we saw that in order for the intervention to be effective, one must understand how to dissolve the 20 mg tablet in water or breast milk. The child must receive this fluid only once per day. Ninety percent of mothers were able to report understanding of this delivery method, but "only 56% of caregivers adhered to the full 10-day course of treatment."[44] Another 2015 study in Uttar Pradesh, India also saw that for a 14-day course of treatment, only 47.8% of caregivers completed it fully. Furthermore, only 30.8% and 67.3% of children received the proper dose of zinc syrups and tablets, respectively.[46]

Due to this lack of adherence, it is crucial that implementation programs stress the importance of completing a full course of zinc therapy at the proper dosage. Through health care provider and patient behavior change, increased accessibility, affordability as well as proper adherence and use, zinc supplementation may gain more success in the developing world. We cannot forget the over-arching factor of proper water sanitation and hygiene practices in low-income homes.

Even if a mother makes certain that her child consistently receives and consumes a zinc supplement, poor water supply, sanitation and hygiene can undo the work of zinc. This is why access to clean water and the observance of good hygiene practices are also essential in order to combat diarrheal disease. According to the WHO, diarrheal disease could be largely reduced through an improved water supply.[47] Perhaps a lack of infrastructure and the extensive reach of poor sanitation practices would be more challenging to quickly implement, which is why this paper focuses on the execution of zinc supplementation in the case of diarrheal disease.

Sub-Chapter 8: Recommendations for Stakeholders

With this knowledge, we would like to make recommendations for the following groups: families, healthcare professionals, training programs and the government. From a health professional's stand point, educating your patient on zinc and its benefits on immune function, wound healing, common colds and diarrheal diseases can be a way to reduce the incidence of diarrhea. Recommendations for health professionals include using a low-osmolality ORS AND zinc supplements. Fluid and supplements should be prescribed for a duration of 10-14 days with 10 mg/day for infants under 6 months and 20 mg/day for children over 6 months. This will address both dehydration and nutrient loss contributed to diarrhea in the patient. It is still not clear if other micronutrient supplements should be taken in conjunction with zinc as this might create a competitive absorption environment, nullifying the benefits of each micronutrient.

Since zinc is safe to provide without the consent of a physician, volunteers or other community leaders should also receive training on zinc. This training would include information on correct dosages, proper use, methods of delivery and the identification of more serious cases that should be referred to a doctor. With an increase in trained individuals, perhaps there would be a rise in zinc supplementation and in turn, a lower prevalence of diarrhea. However, these training groups would likely be established through government action.

Before clinician recommendation and training, we recommend governments to determine the best course of action within their own nation due to the varying nature of disease burden and zinc availability. As a broader recommendation, we suggest that countries that have not yet conducted

their own research on the cost effectiveness and efficacy of zinc supplements to prepare the region with a framework in order to take on this type of research. WHO and United Nations Children's Emergency Fund have issued a joint statement on zinc supplementation, but many countries of yet to decide what this will look like within their own borders. With this, there are a number of decisions each nation will have to make when it comes to creating a policy on zinc. For example one must first decide which formulation will be used, whether it will be included on the nation's essential drug list, its procurement, cost and budget, distribution, revision of clinical guidelines and an established monitoring method. With zinc sulphate utilized in less than 1% of diarrheal illnesses, Kenya has become an example for this implementation strategy and has made strides to improve access to the micronutrient and ORS at the community level by using an already existing program called Community Health Workers. With increased access to zinc, even the most marginalized of children can benefit from zinc supplementation.

Table 9: Recommendations for zinc supplementation by stakeholder

Recommendations	
Patient	Seek education on disease, cause, transmission and treatment Adhere to full course of zinc supplementation Have a positive attitude towards behavior change
Trained Community Leaders	Seek education on disease, cause, transmission and treatment Provide counsel to community members on treatment Recognize severe cases that require professional medical attention
Health Professionals	Educate and inform patients on disease, cause, transmission and treatment Use zinc in conjunction with ORS therapy to treat diarrheal disease
Government	Prepare country for zinc research Decide on zinc form to National Essential Drug List Procurement, Cost and Budget Revision of Clinical Guidelines Choose Monitoring Method

From this comprehensive review, we ask for further research to be conducted in zinc treatment and supplementation for children under 6 months of age in order to find a suitable dosage or more appropriate method of treatment. For zinc supplementation in child older than 6 months, this treatment must first gain wide acceptance from physicians worldwide. With this reception, health care professionals should then educate their community on the benefits of zinc, as well as

the gravity of diarrheal disease in young children. Special attention should be given to rural regions and how these areas will receive adequate education and access to zinc. Further research should also be conducted on the misuse of zinc and on what kind of education will more effectively illustrate the importance of full adherence and proper use. A cost analysis should also be completed in more countries considering zinc programs in order to have a more accurate representation. We must also not forget the influence of poor water sanitation and hygiene practices on diarrheal disease. With the collaboration of each nation's government, community leaders and residents, the implementation of zinc can become an actuality that leads to a dramatic decrease in diarrheal disease rather than an idea.

Appendix A

A Case Study: Zinc Deficiency in India

After conducting research on the micronutrient zinc, India became a place of interest due to the high prevalence of zinc deficiency in children. With 47% of children suffering from malnutrition and a culturally influenced plant-based diet, we were curious to see if this had any effect on the bioavailability of zinc in the country's adolescents.[48]

As we mentioned in our introduction, zinc can be found in a variety of foods, including vegetables and meat, but is best absorbed through animal proteins rather than phytates, which can be found in large quantities in vegetables. With 31% of the Indian population practicing vegetarianism, the highest number of vegetarians in a country, perhaps this cultural tradition has led to such a high occurrence of zinc deficiency.[49] In a study that observed the zinc consumption of adolescent Indian girls, the intake was 40-75% less than the recommended daily intakes.[50] To address this concern, a Biometry & Nutrition Group of Agharkar Research Institute in Pune, Maharashtra, India attempted to find suitable, zinc filled recipes for vegetarians and to create a nutrient quality index to measure the micronutrient sufficiency of vegetarian diets. It was stated that more extensive studies would need to be directed to find if these recipes would be successful in reducing zinc deficiency in larger populations.[51] We think it would also be of interest to study the rate of behavior change in changing one's diet to meet micronutrient needs in India.

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51. Kawade, R. Zinc status and its association with the health of adolescents: a review of studies in India. *Glob. Health Action* **5,** 7353 (2012).

Academic Vita: Sarah Kidder

EDUCATION

The Pennsylvania State University, Schreyer Honors College
The College of Health and Human Development
Bachelor of Science in Biobehavioral Health
Minors in Biology and Global Health
Concentration in Spanish
Honors in Biobehavioral Health **2012-2016**

AWARDS AND SCHOLARSHIPS

Dean's List **2013 – 2015**
Inter-Collegiate Horse Association All-Academic Award **2014 – 2015**
Gateway Scholars Program Scholarship **2014 – 2016**
Global Health Minor HHD Department Scholarship **2015**
2nd Place Information Literacy Award at the
Penn State Undergraduate Research Exhibition **2016**

RELATED EXPERIENCE

Penn State University, University Park, Pennsylvania
Donor Relations Chair, Raw Aesthetic Movements **Current**
Generates promotions, communicates with sponsors, strengthens partnerships, initiates sponsorship proposal and secures donations for mid-Atlantic region dance competition, Rhythm Spotlight.

Penn State University, University Park, Pennsylvania
Raw Aesthetic Movements THON Vice President **Current**
Hip-hop dance organization's THON chapter vice president plays a vital role in fundraising as the head of alternative fundraisers. Also works to secure corporate and private donations, plan events, complete administrative tasks, network with other organizations as well as manage a committee - on track to double monies raised from previous year.

Penn State University, University Park, Pennsylvania
Her Campus Writer and Marketing Chair **Current**
Published writer for #1 global online community for college women, written by the countries top college journalists from 230+ campus chapters. Promotes sponsors and the Her Campus brand.

Penn State University, University Park, Pennsylvania
Research Assistant in Dr. Knapp's Lab **Current**
Assist Dr. Knapp in writing a systematic review of the causes, treatments and policies of diarrheal diseases affecting children in India, Southeast Asia, and South Africa. Will also be conducting honors thesis under the advisement of Dr. Knapp.

The Malini Foundation, Colombo, Sri Lanka
Remote Health and Research Intern/ Intern Manager **2014-2015**
Malini Foundation is a non-profit organization that empowers orphans through the promotion of education in order to combat child labor, child marriage, domestic violence and trafficking. Worked on graphic design projects, outreach development programs, fundraising efforts, women's nutrition and health research, helped coordinate events, etc.

Penn State University, University Park, Pennsylvania
USEED Crowdfunding Team Leader for Global Health Minor Funding **Spring 2015**
Provision of leadership and direction for a crowdfunding campaign to raise over $8,000 in donations for Pennsylvania State University's Global Health Minor. Funds used to support student's individual fieldwork experiences in Senegal, Tanzania, and South Africa for the summer of 2015.

Muhimbili University of Health & Allied Sciences, Dar es Salaam, Tanzania
Global Health Field Work **2014 – 2015**
Selected to the 2014 Global Health Minor cohort who are required to complete coursework aimed at understanding world health issues, as well as a field site placement of 6 weeks in Tanzania.

Penn State University, University Park, Pennsylvania
Research Assistant in Dr. Danielle Down's Lab **Summer 2015**
Healthy Mom Zone Project: Control systems engineering to optimize a prenatal weight gain intervention. Assists with participant intake, data analysis and entry, as well as food and exercise test preparation etc.

Penn State University, University Park, PA
Research Assistant in Dr. Sonia Cavigelli's Lab **2013 – 2015**
Asthma/Anxiety Study: Looks to determine how differences in physiological and behavioral responses to stress affect the susceptibility to certain diseases and rates of aging. Conducted behavioral testing and examined post necropsy tissues. Additionally, presented and participated in discussion on relevant topics and similar studies each week.

TEACHING EXPERIENCE

Penn State University, University Park
Teacher's Assistant for Biology Recitation **Fall 2013**
Conducted class once per week and administered all grades for attendance, projects, and presentations

Mid-State Literacy Council, State College, PA
Health Literacy and English Tutor **Fall 2014**
Tutored a low literacy student of Centre County each week for four hours to advance their English and Health Literacy

Schreyer Honors College, University Park
SHOTIME Schreyer Honors College Student Mentor **2015**
Mentor to incoming honors students and leader of 3 day orientation

ORGANIZATIONS/VOLUNTEER

RAM Squad Member: Student led hip-hop dance organization at Penn State
HER Campus Writer
Penn State Equestrian Team Member/Webmaster/Newsletter Copy Editor: English Hunter/Jumper team competing at the regional and national level
State of State Student Speaker: 2015 selected student speaker for mental health issues on the college campus
Penn State IFC/PanHellenic Dance Marathon: THON Rules and Regulations committee member, Alternative Fundraising Chair, special interest org member, and RAM Squad THON Vice President
Horses with Hope Non-Profit Organization Volunteer: Therapeutic riding organization for children with various cognitive and motor impairments
Mount Nittany Medical Center Emergency Department/Patient Floors Volunteer

LANGUAGES

English – native language
Spanish – Proficient in reading and writing
German and Swahili – Speak with basic competency

SKILLS

Sales, Fundraising, Illustration, Photography, Photo Editing, Spanish, Microsoft Office, Social Media, Writing/Editing, Public Speaking