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2006

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An abstract of

A thesis submitted to the Faculty of the
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Abstract

Impact of Nutrition Education and Counseling on Anemia Prevalence and Iron Status in Women of Reproductive Age: a Systematic Review

By Oluwafunke Olude

Background: Anemia affects 42% of pregnant and 30% of nonpregnant women of reproductive age. It is associated with hemorrhage, poor neonatal outcomes, reduced work productivity and increased risk of infections. Causes of anemia include infections, hemoglobinopathies and nutritional deficiencies. A commonly employed strategy to tackle anemia is nutrition education and counseling (NEC). NEC strategies focus on increasing heme and non heme iron intake, decreasing the intake of iron absorption inhibitors, encouraging iron-folic acid supplementation.

Objective: The objective of this review is to systematically evaluate the impact of NEC on indicators of anemia and iron status in pregnant and nonpregnant WRA in low/middle income (LMIC) and high income countries (HIC) and to identify current gaps in research.

Method: A systematic review of the impact of NEC delivered to pregnant and nonpregnant females 11-49 years on anemia and iron status was conducted using modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) and CHERG (Child Health Epidemiology Reference Group) approaches. Data from studies meeting inclusion/exclusion criteria were abstracted into a standardized form. Meta- analysis was conducted for outcomes with ≥ 3 studies by pregnancy status; sub group analysis was conducted according to country context and category of NEC intervention.

Result: Three categories of NEC delivery emerged, namely 1) NEC provided alone (7 studies); 2) NEC as part of a comprehensive package of health messages (3 studies); and 3) NEC with nutrition support (9 studies). Overall, NEC reduced the risk of anemia in pregnant ((RR=0.63 (0.48, 0.82)) and nonpregnant WRA (RR= 0.45 (0.24, 0.86)). NEC was most effective in LMIC and when provided with nutrition support. However, NEC did not improve mean Hb, mean hematocrit, iron deficiency, mean serum iron and ferritin.

Discussion: NEC decreased risk of anemia in WRA regardless of pregnancy status, in LMIC and when provided with nutrition support. The overall quality of evidence was judged to be moderate for anemia and mean Hb and low for mean hematocrit, iron deficiency, mean serum iron and mean serum ferritin. Better designed studies grounded in appropriate theories are needed to adequately estimate the effectiveness of NEC to improve anemia status and iron stores and identify best practices.

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Abbreviations

IDA: Iron Deficiency Anemia

IFA: Iron Folic Acid Supplementation

SD: Standard Deviation

Hb: Hemoglobin

DALYS: Disability Adjusted Life Lost

WHO: World Health Organization

NEC: Nutrition Education and Counseling

DALYs: Disability Adjusted Life Years

HIV: Human Immunodeficiency Virus

sTfR: soluble Transferrin receptor

sTfR /F: sTfR/ log ferritin index

ZPP/H: Zinc Protoporphyrin/Heme ratio

TIBC: Total Iron Binding Capacity

FAO: Food and Agriculture Organization

ACD: Anemia of Chronic Disease

NaFeEDTA : Sodium Iron Ethylenediaminetetraacetic Acid

LMIC: Low/ Middle income countries

HIC: High income countries

Introduction

It is estimated that about 25% of the world is anemic (McLean, Cogswell et al. 2009). While anemia prevalence is highest in low/ middle income countries (LMIC) of the world it continues to be a problem in high income countries (HIC) where other forms of malnutrition have been eradicated (Stoltzfus, Dreyfuss et al. 1998). Anemia is commonly high in pregnant and non pregnant women/ girls and preschoolers with global rates of 42%, 30% and 47% respectively (McLean, Cogswell et al. 2009). Thus anemia is one of the most widespread public health issues in the world.

Although other nutritional deficiencies contribute to anemia including vitamin A, riboflavin, folic acid and vitamin B_{12}, iron deficiency is the most prevalent cause of anemia (WHO and UNICEF 2004). An estimated 50% of anemia is attributable to iron deficiency and as a result the terms anemia and iron deficiency anemia are used interchangeably (McLean, Cogswell et al. 2009). The main causes of iron deficiency anemia include low intake of iron, poor bioavailability of dietary iron, and blood loss. Blood volume expansion and fetal requirements increase the risk of iron deficiency anemia during pregnancy. In addition to iron deficiency, parasitic and other infections contribute to anemia including intestinal worms, schistosomiasis, HIV infections and malaria (Sanghvi, Harvey et al. 2010).

The total global burden of anemia is an estimated 841000 deaths and over 35 million disability adjusted life years (DALYs) lost (Stoltzfus, Mullany et al. 2004). In pregnancy, anemia and IDA are linked to poor outcomes including preterm delivery, low birth weight infants and infants with poor iron stores (Lokeshwar, Mehta et al. 2010). As well, anemia, even mild anemia, is associated with blood loss during delivery and in the immediate postpartum period (Kavle, Stoltzfus et al. 2008). In fact it is estimated that a 1 g/dL increase in the population mean hemoglobin of pregnant women would reduce maternal mortality by 25% (Stoltzfus, Mullany et al. 2004). In addition to its effects on women during pregnancy, anemia may also impair women's and adolescent girls' concentration, attention span, and educational attainment, decrease work efficiency and physical stamina and increase the risk of infection (Lokeshwar, Mehta et al. 2010).

Some commonly employed strategies to tackle anemia include fortification, diet diversification, iron folic acid supplementation and nutrition education and counseling (NEC). NEC strategies to reduce iron deficiency anemia and improve hemoglobin and iron levels in pregnant and non pregnant women/ adolescents aged 11-49 focus on increasing heme and non heme iron intake from foods, decreasing the intake of iron absorption inhibitors, encouraging iron-folic acid supplementation compliance and educating about the importance of iron and the consequences of being deficient. NEC aims to promote healthy behavior change (healthy nutritional practices), increase iron folic acid compliance and diet modification in some cases.

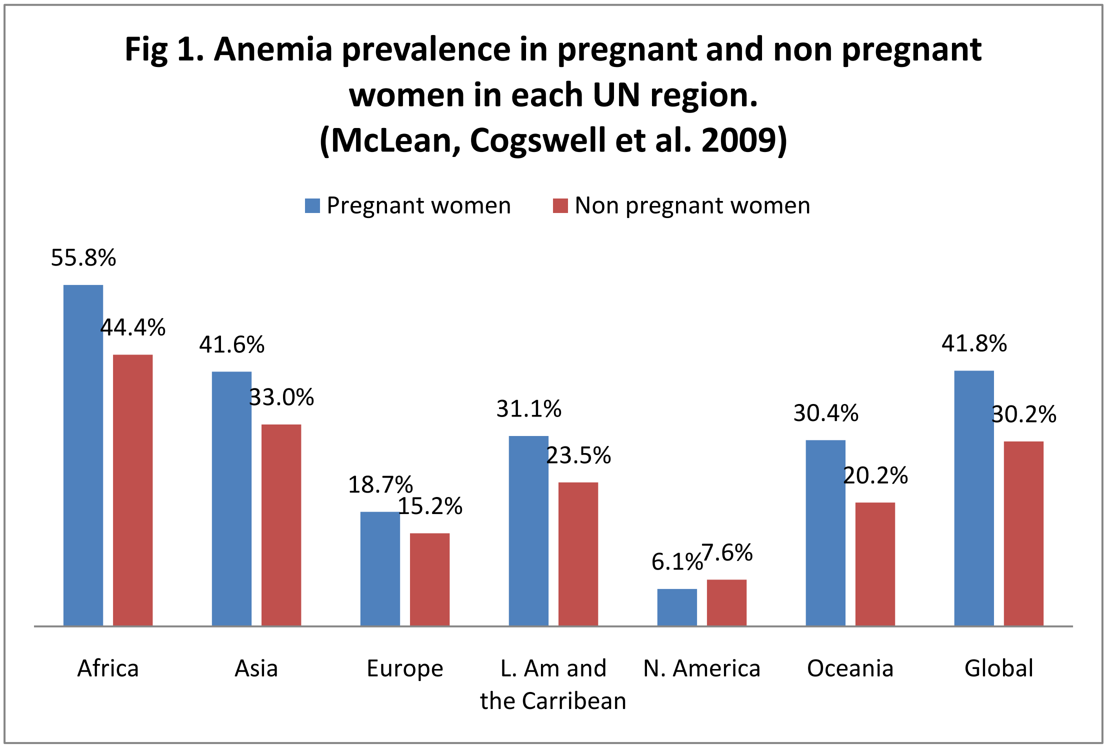
There is currently no known systematic review of the effects of nutrition education and counseling interventions specifically geared towards reducing anemia prevalence and improving iron and anemia status of both pregnant and non pregnant women and girls. The objective of this review is to systematically review the effect of NEC on anemia and iron status related outcomes in pregnant and non pregnant women aged 11-49 in HIC and LMIC countries and identify the gaps in research.

Chapter 1: Literature Review

1.1 Scope of the problem

Anemia is one of the most common public health issues in the world. Anemia arises from a range of issues including micronutrient deficiencies such as vitamin A, Riboflavin, vitamin B_{12}, folic acid and iron. Medical conditions such as chronic or repeated diarrhea, genetic disorders and malabsorption syndromes lead to anemia by impairing iron absorption and usage (Huma, Salim Ur et al. 2007). Infections and parasites such as HIV, helminths (hookworm, schistosomiasis) and malaria also contribute to anemia. Gastrointestinal bleeding from hookworm infestation contributes to anemia.

Iron deficiency is the most prevalent cause of anemia with an estimated 50% of anemia cases attributable to iron deficiency. As a result the terms anemia and iron deficiency anemia are used interchangeably (McLean, Cogswell et al. 2009). Iron deficiency is the one of the most common nutritional deficiencies, affecting more than 2 billion people in the world (Stoltzfus, Dreyfuss et al. 1998). Iron deficiency anemia (IDA) has been mentioned as one of the most important factors leading to the global burden of disease (Mathers, Bernard et al. 2003; McLean, Cogswell et al. 2009). Although anemia affects young and old, male and female, it is most prevalent in young children and women of reproductive age. It is estimated that 41.8% of pregnant women and 30.2% of non pregnant women globally are anemic (McLean, Cogswell et al. 2009) (Figure 1).



Anemia is highest in developing regions of the world but continues to be a problem in developed countries where other forms of malnutrition have been eradicated (Stoltzfus, Dreyfuss et al. 1998). In Africa alone, anemia prevalence is as high as 57.1% and 47.5% in pregnant and nonpregnant women, respectively. An estimated 18 and182 million pregnant and non pregnant women are affected by anemia in South East Asia while another 2.6 and 41 million pregnant and non pregnant women are affected in Europe (McLean, Cogswell et al. 2009).

An individual is considered to have anemia when hemoglobin (Hb) levels are less than 2 standard deviations (SD) of the mean of Hb in a normal population of the same gender and age living at the same altitude (WHO 2001). Anemia becomes a public health concern when more than 5% of the population has low Hb values (WHO 2001; Zimmermann and Hurrell 2007) as 2.5% of a normal population is expected to be below the 2SD threshold (WHO 2001) (See Table1.1a). The cut offs used to assess anemia severity differ for different sects of the population. Pregnant women with Hb levels less than 110 g/l and non pregnant women with <120 g/l are considered anemic (WHO 2001) (See table1.1b).

Table 1.1a: Anemia prevalence and estimated classification of public health significance.[1]	
Category of public health significance	Prevalence of anemia (%)
Severe	≥ 40
Moderate	20- 39.9
Mild	5- 19.9
Normal	≤ 4.9

Table 1.1b: Severity of anemia and cutoffs in pregnant and non pregnant women.[2]		
Categories of anemia	Cutoffs (g/l) / population	
	Pregnant	Non pregnant
Mild	100 to 109	110 to 119
Moderate	70 to 99	80 to 10
Severe	40 to 69	50 to 79

[1] WHO, U. (2001). "UNU. Iron deficiency anaemia: assessment, prevention, and control. A guide for programme managers. Geneva." World Health Organization.

[2] Mathers, C. D., C. Bernard, et al. (2003). "Global burden of disease in 2002: data sources, methods and results." Geneva, Switzerland, WHO.

1.2 Health consequences of anemia

Anemia contributes to unfavorable maternal and neonatal outcomes. In Asia, anemia (irrespective of severity) is the second leading cause of maternal death and accounts for 12.8% of maternal deaths independent of death due to postpartum hemorrhage (Khan, Wojdyla et al. 2006; Sanghvi, Harvey et al. 2010). Maternal mortality and morbidity due to anemia either directly or indirectly is associated with the presentation of anemia in its acute or chronic state (Brabin, Hakimi et al. 2001; Jamil, Rahman et al. 2008). For example, acute severe anemia during pregnancy leads to rapid cardiac decompensation and can be a primary cause of acute hemolysis resulting from an underlying disease such as sickle cell (Brabin, Hakimi et al. 2001; Jamil, Rahman et al. 2008). Chronic anemia on the other hand may contribute to maternal mortality indirectly through increased risk of hemorrhage and infections (Brabin, Hakimi et al. 2001). A recent study by Kavle et al found that moderate and severe anemia were each associated with blood loss during delivery and postpartum compared to no anemia (Kavle, Stoltzfus et al. 2008). Indeed it was recently estimated that a 1g/dl increase in population mean hemoglobin could reduce the risk of maternal mortality by 25% (Stoltzfus, Mullany et al. 2004).

In addition to poor outcomes for the mother, anemia contributes to neonatal complications such as small for gestational age, still births and neonatal deaths (Rohilla, Raveendran et al. 2010). IDA, specifically is also linked to poor pregnancy outcome such as preterm delivery, low birth weight infants and infants with poor iron stores (Eden 2005). Further, IDA increases maternal susceptibility to infections thus indirectly increasing the risk of maternal morbidity and mortality (Jamil, Rahman et al. 2008). In terms of global burden, iron deficiency is estimated to cause 591,000 perinatal deaths and 115,000 maternal deaths globally. This amounts to 3 and 19 million DALYS lost from maternal and perinatal causes respectively (Stoltzfus, Mullany et al. 2004). In all women, regardless of pregnancy status, anemia, including IDA, impairs concentration, attention span, and educational attainment (Lokeshwar, Mehta et al. 2010), decreases work efficiency and physical stamina, and increases the risk of infection, morbidity and mortality (Lokeshwar, Mehta et al. 2010).

1.4 Causes of anemia

The etiology of anemia is multifactorial. A variety of issues ranging from nutritional deficiencies to infections and hemoglobinopathies contribute to the development and perpetuation of anemia. Anemia can also occur in association with chronic disease and inflammation. In this case, anemia results because iron availability is reduced, erythropoietin and erythroid progenitor cell production is impaired and red blood cell life span is shortened (Smith 2010). In HIC, chronic diseases for example, chronic kidney disease, cancer, arthritis, inflammatory bowel diseases contribute to anemia (Smith 2010).

In developing countries, infections such as HIV, tuberculosis, intestinal helminths (ie. Hookworm), schistosomiasis and malaria contribute substantially to anemia (Semba and Bloem 2002). Hemoglobinopathies, or genetic disorders of hemoglobin, such as thalassaemias and sickle cell anemia are characterized by impaired or absent polypeptide chains or amino acid structures of the globin part of hemoglobin (Jamil, Rahman et al. 2008). Thus, these diseases cause anemia because they are associated with impaired hemoglobin formation. Socioeconomic factors such as access to adequate health care, food availability, environmental sanitation and personal hygiene in as much as they contribute to inadequate diet and substandard disease control and prevention also contribute to anemia (Huma, Salim Ur et al. 2007). For example, anemia prevalence in pregnant women in the US by trimester is 9%, 14% and 37% (Umbreit 2005) with higher rates among poorer, less educated and minority populations (Umbreit 2005; Zimmermann and Hurrell 2007). This is illustrated by the anemia prevalence among pregnant women in low income areas in the US which are 2%, 8% and 27% for each trimester (Scholl 2005).

Anemia also results from micronutrient deficiencies such as vitamin A, riboflavin, vitamin B_{12}, folic acid and iron. The contribution of each of these micronutrient deficiencies to anemia is discussed below.

Vitamin A deficiency: Vitamin A deficiency is common in pregnant women and children especially in LMIC (Muller and Krawinkel 2005). Although the exact biological mechanisms are yet to be elucidated, vitamin A is known to influence hematopoiesis (Fishman, Christian et al. 2000). The hypothesized mechanisms by which vitamin A deficiency leads to anemia are impaired red blood cell production (erythropoiesis), increased susceptibility to infections and impaired iron stores mobilization (Fishman, Christian et al. 2000; Semba and Bloem 2002; Muller and Krawinkel 2005).

Low vitamin A levels are associated with low serum iron, low total iron binding capacity and transferrin saturation levels (Semba and Bloem 2002; Oliveira, Michelazzo et al. 2008). Vitamin A deficiency is also associated with low hemoglobin levels while supplementation with vitamin A only or in combination with iron or other micronutrients increased Hb levels in women and children (Muhilal, Permeisih et al. 1988; Chawla and Puri 1995; Kolsteren, Rahman et al. 1999; Fishman, Christian et al. 2000; Semba, Kumwenda et al. 2001; Semba and Bloem 2002). In vitamin A deficient populations and HIV- positive women, vitamin A supplementation significantly reduced maternal anemia (van den Broek, Dou et al. 2010). Lastly, vitamin A supplementation can improve iron supply to hematopoietic tissue through the mobilization of iron stores in the liver (Fishman, Christian et al. 2000; Chen, Li et al. 2008).

Riboflavin (Vitamin B_2) deficiency: Riboflavin deficiency is common in pregnant and lactating women (Allen and Casterline-Sabel 2001). It is hypothesized that riboflavin deficiency contributes to anemia through impaired iron mobilization and globin production (leading to ineffective erythropoiesis), and decreased intestinal absorptive capacity for iron (Fishman, Christian et al. 2000; Powers 2003). Reversing riboflavin deficiency improves hematologic responses to iron supplements (Powers 2003). Several studies have demonstrated that riboflavin supplementation in children, adolescents and pregnant women either with iron alone or with other micronutrients reduced anemia, improved Hb concentration and decreased micronutrient deficiency compared to nothing or IFA supplementation alone (Ma, Schouten et al. 2008; Vinodkumar and Rajagopalan 2009; Ahmed, Khan et al. 2010).

Vitamin B_{12} deficiency: Though direct effects of vitamin B_{12} on anemia are not clear, vitamin B_{12} deficiency impairs folate metabolism which may contribute to ineffective erythropoiesis and subsequent anemia (Fishman, Christian et al. 2000).

Folic acid deficiency: Folic acid deficiency potentially contributes to anemia by impairing DNA synthesis which modulates erythropoiesis (Fishman, Christian et al. 2000). The magnitude of anemia due to vitamin B_{12}, folic acid, vitamin A and riboflavin deficiency is still unclear (WHO and UNICEF 2004).

Iron deficiency: Iron deficiency in women can be linked from infancy to adulthood. During pregnancy, the fetus stores approximately 250 mg of iron. A newborn has 80mg/kg which eventually drops to 60mg/kg; this is maintained by absorbing 0.5mg in excess of body losses (Umbreit 2005; Zimmermann and Hurrell 2007). About 1000mg is stored as ferritin or hemosiderin and another 2500mg is within hemoglobin. Women of childbearing age lose about 3000mg or iron due to menstrual losses and must absorb twice as much as men (Umbreit 2005; Zimmermann and Hurrell 2007) as a result non pregnant women/ adolescents are prone to IDA compared to men. For pregnant women, iron requirements increases from 1.25mg per day (nonpregnant women) to 6mg per day towards the end of pregnancy (Zimmermann and Hurrell 2007).

Iron deficiency can arise as a result of low iron intake through diet and increased iron requirements during pregnancy, menstruation, infancy and adolescence. Meat, liver and egg yolk are the best dietary sources of iron (Nojilana, Norman et al. 2007). They contain heme iron which is highly bioavailable; 15-35% of heme iron is absorbed (Zimmermann and Hurrell 2007). Plant foods, on the other hand, such as cereals, pulses, legumes, and green leafy vegetables contain non heme iron. Additionally, these plant foods are high in phytates, polyphenols and/or calcium which are strong inhibitors of iron absorption. Thus, plant based iron has poor bioavailability; only 2-5% of the iron in these sources is absorbed (Allen and Casterline-Sabel 2001; Nojilana, Norman et al. 2007). In developing countries, the intake of nonheme iron sources are very high ranging from 15 to 30 mg (Allen and Casterline-Sabel 2001), however because this form is low bioavailable iron, intakes are often insufficient to meet needs and iron deficiency anemia is common. While the inclusion of vitamin C improves the bioavailability of nonheme iron, its inclusion is less significant compared to including heme iron in the diet (Allen and Casterline-Sabel 2001; Zimmermann and Hurrell 2007). Also fermentation, soaking and germination can improve iron absorption in plant foods, however the effect is limited and not as effective as including heme iron or vitamin C in the meal (Allen and Casterline-Sabel 2001).

Based on these dietary characteristics, the FAO/WHO define three different types of diets based on their iron bioavailability: 1) high iron diets with 15% bioavailability, 2) intermediate diets with 10% bioavailability and 3) low iron diets with a bioavailability of 5% (Zimmermann and Hurrell 2007). Iron absorption from these different diets depends on the age, gender and iron status of an individual (Allen and Casterline-Sabel 2001) (Table 1.2).

Pregnant women are at risk of developing anemia especially if they were iron deficient prior to pregnancy. This is usually the case in developing countries. A study in Northwest Vietnam found 37.53% of non pregnant women anemic and 23.1% of anemic women were iron deficient (Pasricha, Caruana et al. 2008). In Cote d'Ivoire, of the 20-39% found anemic, approximately 50% were iron deficient (Asobayire, Adou et al. 2001). In 2000, 9-12% of pregnant women had IDA and 4.9% of maternal deaths were attributed to IDA (Nojilana, Norman et al. 2007). Increased iron requirements due to rapid growth in adolescent females accounts for IDA in this group of people. Twenty one percent of adolescents (11-18%) in the UK are iron deficient (Hercberg, Preziosi et al. 2001; Zimmermann and Hurrell 2007).

Other risk factors associated with pregnancy for anemia include short birth interval, multiple pregnancies, adolescent pregnancy and blood loss with the use of intrauterine devices for birth control (Allen and Casterline-Sabel 2001; Huma, Salim Ur et al. 2007). Also other medical conditions such as chronic or repeated diarrhea, genetic disorders and malabsorption syndromes may impair iron absorption and usage and thus contribute to iron deficiency anemia (Huma, Salim Ur et al. 2007)

Table 1.2: Recommended Daily Iron Intake (mg/day) by Estimated Dietary Iron Bioavailability.[3]

	Children (1-3 yrs)	Children (4-6 yrs)	Women (19-50yrs)	Pregnant women (second trimester)	Lactating women
15%	3.9	4.2	19.6	>50	10
10%	5.8	6.3	29.4	>50	15
5%	11.6	12.6	58.8	>50	30

1.5 Diagnostic indicators of iron deficiency, iron deficiency anemia and anemia.

A series of laboratory methods can be applied to test for anemia, IDA and iron deficiency. These are summarized in Appendix 1; Table 1.3).

[3] Zimmermann, M. B. and R. F. Hurrell (2007). "Nutritional iron deficiency." Lancet **370**(9586): 511-520.

1.6 Prevention and control of iron deficiency anemia and anemia

Four main strategies are currently implemented to deal with IDA. These include fortification, diet diversification, micronutrient supplementation, namely iron and folic acid (IFA) and nutrition education and counseling (NEC) (See Table 1.4).

1. Fortification: Fortification is the addition of nutrients to the diet. Fortification including iron fortification is known to be an effective national ID intervention strategy as it doesn't require the cooperation of the individual; it has an expensive start up cost but the cost of maintenance is lesser than supplementation (Walter, Olivares et al. 2001; Huma, Salim Ur et al. 2007; Gautam, Saha et al. 2008; Ma, Jin et al. 2008; Lokeshwar, Mehta et al. 2010). The cost per capita per year of food fortification in China was estimated to be as low as $0.06 compared to $11.4 for supplementation (Ma, Jin et al. 2008).

   Iron fortification is more difficult than other micronutrients because the bioavailable forms of iron are chemically reactive and produces color and odor changes in food (Walter, Olivares et al. 2001; Huma, Salim Ur et al. 2007). In developed countries, iron fortification has been successful as they are either mandatory (i.e. legislated/regulated by the law) or voluntary (Hercberg, Preziosi et al. 2001; Ramakrishnan and Yip 2002; Huma, Salim Ur et al. 2007). In the US, a decline in anemia and ID among infants and young children from 7.8% to 2.9% was achieved after the introduction of fortified infant formula and foods and the Women's, infants and children (WIC) program in the 1960s and 1970s respectively irrespective of SES group (Ramakrishnan and Yip 2002; Lynch 2005). In LMIC, foods such as wheat flour in Pakistan, India, Venezuela, sugar in Guatemala, curry powder in South Africa, soy sauce in China, fish sauce in Vietnam, maize flour in Kenya, rice in the Philippines, salt in Mexico amongst others are being fortified (Huma, Salim Ur et al. 2007; Gautam, Saha et al. 2008). The decline in anemia in some LMIC and HIC among schoolchildren and pregnant and non pregnant adolescents and women of childbearing age may be attributed to iron fortification (Lynch 2005). In Chile, anemia dropped from 27.3% to 8.8% after the institution of a program that provided children under 18 months with milk fortified with ferrous sulphate and ascorbic acid (Yip and Ramakrishnan 2002; Lynch 2005).

Although, these effects have been shown and numerous countries are currently fortifying foods especially wheat flour with iron, only 9 of these countries are expected to have the intended impact (Hurrell, Ranum et al. 2010). This is attributed to lack of compliance to wheat fortification guidelines, use of less effective fortificants and inadequate levels of added fortificant (Hurrell, Ranum et al. 2010). These also represent drawback to fortification. Other types of fortification include the use of iron sprinkles (Schauer and Zlotkin 2003) and instant noodles fortified with NaFeEDTA (Le, Brouwer et al. 2007).

2. Diet Diversification: Diet diversification strategies aim to increase the consumption of micronutrient rich foods through production strategies. Strategies can include both commercial agricultural programs and home production and processing of fruits and vegetables, large and small animal husbandry, and fish farming (Muller and Krawinkel 2005; Gibson and Anderson 2009). Diet diversifi-

cation strategies seek to improve dietary intakes through NEC (discussed separately in detail later); increase bioavailability of micronutrients through preservation, conservation and home processing techniques; food combinations; plant breeding strategies; and animal rearing strategies (Ruel and Levin 2000; Muller and Krawinkel 2005). Diet diversification empowers individuals and households to be responsible for their diet quality (Ruel and Levin 2000). It also works to empower women and increase household income (Boy, Mannar et al. 2009; Olney, Talukder et al. 2009). Diet diversification has the potential to be sustainable and very effective in the long run as it targets behavior change (Ma, Jin et al. 2008). In the case of iron, the production of small animal and fish production, use of cast iron pots (Kapur, Agarwal et al. 2002), fermentation and germination have been employed and in some cases observed to be effective (Tontisirin, Nantel et al. 2002). Indeed reviews of the literature indicate that diet diversification strategies improved vitamin A status, anemia status and zinc levels in children (Boy, Mannar et al. 2009; Gibson and Anderson 2009).

Although diet diversification is perhaps the most sustainable approach to addressing micronutrient deficiency (Tontisirin, Nantel et al. 2002; Muller and Krawinkel 2005), the startup and maintenance cost is considerably higher compared to other intervention strategies. In China, the estimated cost per capita per year of diet diversification was $1148 compared to $11.4 for supplementation and $0.06 for food fortification (Ma, Jin et al. 2008). Also, behavior change is complex and it is difficult to change dietary preferences (Lynch 2005). Overall, the degree of increase in micronutrient intake depends on the diet diversification strategies, habitual diet, and the inclusion of a behavior change/ nutrition education counseling component (Gibson and Anderson 2009).

3. Iron folic acid supplementation (IFA): WHO recommends 60mg iron with 400µg folic acid daily for 6 months during pregnancy (120mg/day iron if the 6 months duration cannot be reached), 3 months postpartum in areas where anemia prevalence is >40% and for severely anemic women, a daily dose of 120mg per day (WHO 2001). Iron supplementation has been predicted to have an effect size of 1.17g/dl increase in Hb concentration in women (Sanghvi, Harvey et al. 2010). Routine supplementation reduces anemia prevalence among women with moderate to severe anemia in late pregnancy (Kulier, de Onis et al. 1998; Sanghvi, Harvey et al. 2010). Iron supplementation alone or with folic acid has been shown to increase Hb levels in pregnant women at term and decrease the risk of having anemia or iron deficiency (Pena-Rosas and Viteri 2009) Weekly iron supplementation of adolescent girls and women of reproductive age improves iron status and reduces anemia (Casey, Phuc et al. 2009; Kotecha, Nirupam et al. 2009; Casey, Jolley et al. 2010). According to WHO, weekly IFA supplementation can be effective before pregnancy and during the first trimester of pregnancy especially in areas where food based strategies are not fully implemented or effective (WHO 2009).

Although IFA supplementation has been shown to have positive effects on anemia and most ANC programs worldwide require routine supplementation during pregnancy, IDA is still unacceptably high (Yip and Ramakrishnan 2002;

Mungen 2003). Adverse side effects such as nausea, diarrhea, constipation, heartburn and abdominal discomfort, lack of adequate anemia and supplementation knowledge and misconceptions has been implicated in low IFA compliance (Galloway, Dusch et al. 2002; Yip and Ramakrishnan 2002; Mungen 2003). Other programmatic issues abound including availability of iron tablets, access to these tablets, effective delivery channels and lack of clarity about policy goals (Allen 2002; Yip and Ramakrishnan 2002; Mungen 2003). A comprehensive strategy including fortification, diet diversification, infection control and nutrition education has been suggested has an ideal avenue to controlling IDA (Mungen 2003).

4. Nutrition education and counseling (NEC): An eight country study by Galloway et al indicated that women needed a better understanding of anemia, its causes and consequences as well as the understanding of the benefits of IFA supplementation to promote compliance (Galloway, Dusch et al. 2002). NEC strategies aims at addressing these issues in order to reduce iron deficiency anemia and improve hemoglobin and iron levels in pregnant and non pregnant women and girls It focuses on increasing heme and non heme iron intake, decreasing the intake of iron absorption inhibitors, encouraging iron-folic acid supplementation compliance and educating about the importance of iron and the consequences of being deficient. It aims at promoting healthy behavior change (healthy nutritional practices), increasing iron folic acid compliance and diet modification in some cases. It also promotes healthy feeding practices such as breastfeeding practices, use of iron fortified formula and infant cereals after 6 months of age, and oral iron supplement drops for pre term and low birth weight infants at 1 month of age (Eden

> 2005). A review by Baird et al found that interventions with an educational component were effective in resulting in positive changes in dietary behavior of women from disadvantaged backgrounds (Baird, Cooper et al. 2009). NEC interventions have been shown to significantly increase Hb levels, reduce anemia prevalence among pregnant (Adhikari, Liabsuetrakul et al. 2009) and non pregnant women (Amani and Soflaei 2006).

There is currently no known systematic review of nutrition education and counseling interventions specifically geared towards reducing anemia prevalence and improving iron and anemia status of both pregnant and non pregnant women and girls. The objective of this review is to systematically evaluate the impact of NEC on anemia and iron status related outcomes in pregnant and non pregnant women and girls in HIC and LMIC and identify the gaps in research.

Table 1.4: Summary Table of Strategies to Control IDA

Control strategy	*Description*	*Effectiveness*	*Drawbacks to implementation/ research*
Fortification	Addition of iron to the diet through staple foods on a large/ small scale (sprinkles) beyond the levels available in industrialized foods.	Consumption of iron fortified staple foods leading to increased iron levels. Decline in anemia among schoolchildren, pregnant and non pregnant adolescents and women of childbearing age in numerous countries including Chile. Considered the safest, most cost effective approach.	Chemically reactive bioavailable forms of iron, issues with color and odor changes in food. Selection of appropriate vehicle. Adequate amount of fortificant (threshold) to address deficiency. Mandatory vs. voluntary fortification. Private – public partnership.
Diet diversification	Agricultural programs (commer-	Increase in food diversity, increase in know-	Expensive start up cost. Relatively more expensive com-

Table 1.4: Summary Table of Strategies to Control IDA

	cial/ home) to increase production of micronutrient rich food such as fruits and vegetables, small animal and fish rearing.	ledge, attitude and practice towards usage of micronutrient rich foods, increase in household income, decrease in prevalence of micronutrient deficiency.	pared to other interventions. Behavior change is complex. Creation and implementation of food security policies. Community mobilization, provision of land and resources.
IFA Supplementation	Supplementation with iron folic acid.	Decrease in anemia prevalence, increase in Hb levels, increase in iron levels in pregnant and non pregnant women and children.	Availability of iron tablets, access to tablets, adverse side effects, compliance, daily versus weekly supplementation. Increased iron and malaria susceptibility in malaria endemic areas. Clarity of policy goals concerning target population and effective supplementation period.
Nutrition Education and Counseling	Promoting healthy behavior change through communication and education about iron, IDA and its consequences and IFA compliance.	Increase in knowledge about iron, IDA and consequences, appropriate measures to prevent and tackle IDA. Behavior change. Increase in IFA compliance	Use of theoretical frameworks to bring about behavior change. Adequate NEC delivery method and materials. Increase in knowledge may not necessarily facilitate practice. Incorporation with other programs.

Chapter 2: Methods

2.1 Literature Search Strategy

To assess the impact of nutrition education and counseling intervention on anemia prevalence and iron status among women and girls, a systematic review of literature was conducted. Pubmed, Population Information Online (Popline), Web of Science, Cumulative Index to Nursing and Allied Health (CINAHL), and Excerpta Medica Database (EMBASE) databases were searched for relevant publications. As well as journals JNutr, Soc Sci Med, AJCN, AFJAND, PHN, Nutr J, and hand searching of articles for relevant studies was conducted. The search terms used were anemia, iron, nutrition, dietary, non pregnant, pregnant, counseling, education, advice, women and adolescents. The search strategy used both keywords and MeSH terms. These keywords were also used in various combinations.

2.2 Inclusion / exclusion criteria

Nutrition education counseling interventions pertaining to improving anemia and iron status of pregnant and non pregnant women aged 11-49 in any country were systematically reviewed. Experimental studies published in English, including randomized controlled trials (RCTs); cluster RCTs (cRCTs), quasi-experimental studies were included.

Relevant interventions encompassed education on the importance and process of diet change or diet improvements and/or iron supplementation. Studies included for review included a concurrent control or comparison group that either did not receive nutrition education counseling or the system of delivery, number of sessions, and / or intensity differed between groups. Studies targeting women with rare or congenital diseases (i.e.

PKU, MSUD) or women with chronic diseases or conditions (i.e. obesity, diabetes type I or II) were excluded. As well, studies prescribing special diets were excluded.

Outcomes of interest included anemia prevalence, hemoglobin, hematocrit, iron deficiency, serum iron and serum ferritin.

2.3 Data collection and analysis

Titles and abstracts retrieved by the search were reviewed for relevance Studies with irrelevant titles / abstract were excluded. Potentially appropriate studies with abstracts containing insufficient information to justify exclusion were retained for additional review of the full text against inclusion / exclusion criteria. Discrepancies were sorted through discussion. Data from studies that met inclusion/exclusion criteria were abstracted into a standardized form for each outcome of interest. Key variables with regard to the study identifiers and context, study design and limitations, intervention specifics, and effects on outcomes were abstracted. Because the objective of this review was to compare nutrition education and counseling with none, data related to other intervention groups such as iron supplementation alone (without education) were not considered.

Meta- analysis

Meta- analyses were conducted for pregnant and nonpregnant women separately. Due to the heterogeneity of studies abstracted, especially with regards to the nutrition education and counseling exposure, missing values and data representation, meta- analyses were conducted for outcomes with at least 3 studies with complete data (i.e. reported all data including standard deviations) in pregnant and non pregnant women/ adolescents. In this case, meta-analyses were conducted for anemia prevalence and mean Hb in pregnant and non pregnant, iron deficiency and mean serum iron in pregnant women/ adolescents while a descriptive analysis was reported for other outcomes and population. The summary estimates are presented as relative risk (RR) or mean difference and their corresponding 95% confidence interval (CI) for dichotomous and continuous outcomes respectively. Statistical heterogeneity was assessed in the pooled data by using a chi square test and calculating the I^2 statistic. Heterogeneity was taken as significant if I^2 exceeded 50%. Fixed effects models were used for primary analysis and random effect models used when I^2 exceeded 50%.

Group (i.e. cluster) randomization of study subjects was taken into account. Preference was given to cluster adjusted values provided by the study. If results were not adjusted for cluster randomization, sample sizes were adjusted by using an estimate of the intra-cluster correlation co-efficient (ICC) inferred from literature (Table 2.1).

I conducted sub group analysis according to country status (LMIC and HIC) and category of nutrition education and counseling intervention. Summary tables of other outcomes were constructed with the same stratification. Country status was defined based on World Bank classification of countries as low, lower- middle income, upper- middle and high income countries. For simplicity sake, low and lower- middle income countries were collapsed into low/middle countries in this review. Meta analyses were conducted using Review Manager Software (RevMan version 5.1). Forest plots are presented for each sub group analysis.

Grading the evidence

The quality of the body of evidence for each outcome was assessed and graded according to the modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) and CHERG (Child Health Epidemiology Reference Group) approaches. To assess and summarize the evidence, the quality of individual studies and overall quality of evidence for each outcome were conducted. The GRADE and CHERG system categorizes the quality of evidence as *high, moderate, low* or *very low*. Randomized trials start out as high quality evidence but confidence in the evidence may decrease due to study limitations, inconsistency of results, and indirectness of evidence, imprecision and reporting bias. On the other hand, observational studies begin as low quality evidence and may be graded upwards if the magnitude of treatment effect is very large, if all plausible confounders are accounted for or if there is evidence of a dose response relation (Guyatt, Oxman et al. 2008; Walker, Fischer-Walker et al. 2010)

When the body of evidence for an outcome receives a rating of *high* this implies that additional evidence is unlikely to change our confidence in the estimate of effect. *Moderate* quality indicates that further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. *Low* quality indicates further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate and *very low* indicates any estimate of effect is uncertain (Guyatt, Oxman et al. 2008; Walker, Fischer-Walker et al. 2010).

To grade the quality of outcomes, heterogeneity of results (where applicable), consistency of effect, generalizability to population of interest and intervention of interest, biases and summary of findings were taken into consideration (Refer to Appendix 3;

Table 3a & 3b). While grading individual studies, information on sequence generation, allocation concealment, blinding, loss to follow up, intention to treat analysis, selective reporting, and other biases were taken into consideration (Refer to Appendix 3; Table 3c & 3d).

Table 2.1. NEC vs. no NEC: Cluster randomized trials

Study ID	Intervention	Control	Number of clusters and ICC
Anemia			
Kafatos 1989	47/232	30/133	20, ICC= 0.0052
Belizan	176/1009	174/1019	4, ICC= 0.0052
Creed Kanashiro 2000	8/65	16/42	8, ICC= 0.0052
Meenakshi 2008	140/133	104/177	2, ICC= 0.0052
Mean Hemoglobin			
Kafatos 1989	1.83±0.46/232	1.88±0.35/133	20, ICC= 0.000
Meenakshi 2008	10.46±1.31/133	10.74±1.07/177	2, ICC= 0.000
Iron deficiency			
Kafatos 1989	13/118	2/61	20, ICC= 0.05
Mean serum iron			
Kafatos 1989	115.14± 8.32/118	134.64 ±11.4/61	20, ICC= unknown

ICC anemia obtained from (Dowswell, Carroli et al. 2010).
ICC Hb obtained from (Wang, Zhan et al. 2008)
ICC iron deficiency obtained from Directly Observed Iron Supplementation to Treat Anemia (DOHBIT) http://clinicaltrials.gov/ct2/show/NCT01129843

Chapter 3: Results

The search yielded 1087 titles. Of these, articles in English conducted in any country during any time period that met the inclusion/ exclusion criteria were included for further review. Eighty-four articles were selected as relevant for inclusion/ exclusion review after careful assessment of each title/abstract. Two individuals reviewed all 84 full-text articles for inclusion independently. Articles agreed upon were automatically qualified to be included for or excluded from abstraction. Discrepancies were sorted through discussion.

Of these 84 articles, 39 studies were subsequently selected for abstraction. During abstraction an additional 20 articles were excluded for the following reasons (Refer to Appendix 2, Figure2): non-experimental designs (Rush 1981; Neeson, Patterson et al. 1983; Hardy, King et al. 1987; Kanani 1994; Callen 2000; Ishizaki, Koshimizu et al. 2006; Pawloski and Moore 2007; Vir, Singh et al. 2008; Kotecha, Nirupam et al. 2009; Moore, Pawloski et al. 2009); the target population was solely or included girls less than 11 yrs (Childs, Aukett et al. 1997; Faber, Jogessar et al. 2001); women older than 49 years (Jansen and Harrill 1977); statistical data were not reported for the outcomes of interest (Hassan, Kamal et al. 2005; Longfils, Heang et al. 2005; Gross, Gross et al. 2006; Ny, Dejin-Karlsson et al. 2006; Davies, Damani et al. 2009); or the NEC component was unclear or absent (Faber, Jogessar et al. 2001; Bodnar, Siega-Riz et al. 2004; Prosser, Heath et al. 2010).

Overall, there were 5 studies conducted in HIC and 14 in LMIC. Of these, 6 studies targeted non pregnant and 13 targeted pregnant women and adolescents. Three categories of NEC emerged from these studies. Category 1 provided nutrition education and counseling on iron status improvement and anemia prevalence reduction as the sole intervention (Kafatos, Vlachonikolis et al. 1989; Sun, Shao et al. 1990; Creed-Kanashiro, Uribe et al. 2000; Heath, Skeaff et al. 2001; Amani and Soflaei 2006; Garg and Kashyap 2006; Meenakshi, Vashisht et al. 2008; Alaofe, Zee et al. 2009). Participants did not receive nutritional support such as supplements or psychosocial support. The second type of NEC (Category 2) provided nutrition education as a component of a larger comprehensive package of health messages. Additional health messages included for example, education on smoking cessation, pregnancy danger signs, social / emotional support, stress/anxiety reduction in conjunction with anemia and iron status education (Olds, Henderson et al. 1986; Smoke and Grace 1988; Belizan, Barros et al. 1995). The third type of NEC (Category 3) provided nutrition education with nutrition support. Nutrition support included food supplements (Gopaldas 2002) and / or micronutrients (Senanayake, Premaratne et al. ; Hunt, Jacob et al. 1976; Sachdeva and Mann 1994; Abel, Rajaratnam et al. 2000; Gadallah, Rady et al. 2002; Adhikari, Liabsuetrakul et al. 2009; Ndiaye, Siekmans et al. 2009). Findings from the meta-analysis are summarized in Table 3.1; complete findings for the meta-analysis including estimates and forest plots for individual studies are presented in Appendix 4.

3.1 Anemia prevalence and anemia related outcomes

3.1a Anemia prevalence

Of the 19 studies included, 15 reported data on anemia prevalence. Studies conducted among pregnant women measured anemia as hemoglobin (Hb) level <11g/dl in the third trimester. The exceptions were Kafatos et al and Hunt et al where it was measured as <1.6mmol/l and <10.4g/dl in the third trimester respectively. Anemia was also represented by hematocrit <32% in two studies (Hunt, Jacob et al. 1976; Smoke and Grace 1988). In nonpregnant women, anemia was measured as Hb <12g/dl or <120g/l among non pregnant women. Overall, 11 studies were with pregnant and 4 with non pregnant women/girls.

Anemia among pregnant women/ adolescents

The overall meta-analysis of all the nutrition education categories and countries for pregnant women showed that nutrition education significantly reduced anemia by 30% compared to comparison groups (RR= 0.70 [0.58, 0.84] (Refer to Appendix 4; Figure3a). Eight studies were conducted in LMIC and three in HIC. Among studies conducted in LMIC, one was an NEC only intervention without any additional message or support (Sun et al), 1 study provided an NEC intervention as a component of a larger comprehensive package of health messages (Belizan et al) and 6 were NEC interventions with nutrition support (Abel et al, Adhikari et al, Garg et al, Gadallah et al, Ndiaye et al). Among the 3 studies conducted in HIC, Kafatos et al was an NEC only intervention study (without any additional message or support), Smoke et al provided an NEC intervention as a component of a larger comprehensive package of health messages and Hunt et al provided an NEC intervention with nutrition support.

A stratified meta-analysis by LMIC and HIC showed that NEC significantly reduced the risk of anemia in the LMIC studies (RR= 0.69 [0.56, 0.85]) (Appendix _Figure3b), but not in HIC studies (RR=0.80 [0.53, 1.19]) (Refer to Appendix 4; Figure3c). There was no association between reduction in anemia risk and NEC provided alone but it approached significance (RR=0.83 [0.69, 1.00]) (Refer to Appendix 4; Figure3d). Stratified analysis for NEC provided as a component of a larger comprehensive package of health messages was not conducted as there were not enough studies in this category. NEC interventions provided with nutrition support significantly reduced the risk of anemia (0.58 [0.44, 0.76]) (Refer to Appendix 4; Figure3e).

Anemia among non pregnant women/adolescents

All four studies conducted among non pregnant women/girls were in LMIC. The overall meta- analysis for non pregnant women showed a significant 55% reduction in the risk of anemia (RR= 0.45 [0.24, 0.86]) (Refer to Appendix 4; Figure3f). However, NEC only interventions were not associated with anemia risk reduction in meta-analysis (0.52 [0.21, 1.30] (Refer to Appendix 4; Figure3g). Additional stratified meta- analysis was not conducted for studies providing NEC with nutrition support due to an insufficient number of studies.

One study provided NEC with nutrition support (Gopaldas et al). Here, compared to those who received no intervention, there was a significant reduction in anemia prevalence in both intervention groups (iddli RR 0.42 (0.3, 0.59), gooseberry juice RR 0.33 (0.22, 0.48)). When compared to the supplementation only group, women in both intervention groups were at a higher risk of having anemia. No studies provided NEC as a part of a comprehensive package among non pregnant women.

3.1b Mean Hemoglobin

Twelve studies reported data on mean Hb. Eight studies were conducted among pregnant women and 4 among non pregnant women/adolescents.

Mean Hb among pregnant women/adolescents

Of the 8 studies in this population, 6 were in LMIC and 2 in HIC. Regardless of NEC category and country setting, NEC was not associated with mean Hb in pregnant women/adolescents (RR =0.54 [-0.07, 1.14]) (Refer to Appendix 4; Figure3h). This overall analysis included only four studies (Senanayake et al, Gadallah et al, Kafatos et al and Sun et al). The remaining studies were excluded from analysis due to insufficient study data. In stratified analysis, significant association between NEC and mean Hb in LMIC (RR= 0.69 [0.50, 0.88]) (Refer to Appendix 4; Figure3i) was observed.

Stratified analysis on HIC and on type of NEC was not possible due to an insufficient number of studies. Among the 2 studies conducted in HIC, one provided NEC as the sole intervention (Kafatos et al) and one provided NEC with nutrition support (NEC). Neither reported a significant effect of NEC on mean hemoglobin.

Mean Hb among non pregnant women/adolescents

Of the four studies in nonpregnant woman/girl reporting mean hemoglobin, only 3 reported sufficient data to be included in a meta analysis Overall, meta-analysis showed no association between NEC and mean Hb (RR=0.75 [-0.29, 1.79]) (Refer to Appendix 4; Figure3j).

3.1c Mean Hematocrit

Only one study, based in a HIC, reported on mean hematocrit in pregnant women (Olds et al). NEC provided with nutrition support had no effect on mean hematocrit.

3.2 Iron status related outcomes

3.2a Iron Deficiency

Four studies reported on iron deficiency in pregnant and two in non pregnant women/adolescents.

Iron deficiency among pregnant women/adolescents

The overall meta-analysis of all the nutrition education categories and countries for pregnant women showed that nutrition education did not reduce the risk of iron deficiency (RR= 0.99 [0.53, 1.86]) (Refer to Appendix 4; Figure3k). Due to limited number of studies stratified analyses were not conducted.

Iron deficiency among non pregnant women/adolescents

Due to an insufficient number of studies, meta- analyses was not conducted. As a result, descriptive analysis is reported. Although none of the studies (all LMIC) reported significant difference in iron deficiency between intervention and control groups, Alaofe et al reported a 50% decline in iron deficiency among the intervention group compared to a 32% decrease in the control. Similarly, Creed Kanashiro et al reported a 2.6% decrease in the intervention and an 11% increase in iron deficiency in the control group.

3.2b Mean Serum Iron

Three studies measured mean serum iron levels in pregnant women with 2 in LMIC (Sun et al and Sachdeva et al) and 1 in a HIC (Kafatos et al). Overall, NEC had no effect on mean serum iron in this population (RR=-1.98 [-26.32, 22.36]) (Refer to Appendix 4; Figure3l). No stratified analyses were conducted as there were less than 3 studies in each stratum. No studies measured serum iron in nonpregnant women/adolescents.

3.2c Serum Ferritin

Four studies reported on serum ferritin levels, 2 in pregnant and 2 in non pregnant women/girls. Due to a lack of sufficient studies, no meta- analyses were conducted. Among pregnant women, Abel et al provided NEC with nutrition support and reported a mean difference of 9.38±21.17, 2.17 ±17.23 and 3.16 ±19.86 in the 1^{st}, 2^{nd} and 3^{rd} trimesters respectively but did not report the significance of the differences. Conversely, Senanayake et al provided NEC with nutrition support but reported a significant difference of 9.9 ± 18.72 with a higher mean in the intervention group.

Neither of the two studies in non pregnant women reported a significant effect of NEC on serum ferritin irrespective of country context or type of NEC (Amani et al and Heath et al).

Table 3.1. Meta- analysis overall and stratification Effect Estimates for Each Outcome in Pregnant women			
	Total Population	RR (95%CI)[4]	I^2
Overall effect			
Anemia prevalence	2588	0.70[0.58, 0.84]	71%
Mean Hb	826	0.54[-0.07, 1.14][5]	88%
Iron Deficiency	746	0.99[0.53, 1.86]	73%
Mean Serum Iron	382	-1.98[-26.32, 22.36]	99%
In HIC			
Anemia prevalence	866	0.80[0.53, 1.19]	0%
In LMIC			
Anemia prevalence	1922	0.69[0.56, 0.85]	78%
Mean Hb	461	0.69[0.50, 0.88][6]	91%
NEC provided alone			
Anemia prevalence	554	0.83[0.69, 1.00][7]	43%
NEC provided as a component of a comprehensive package of health messages: No meta-analysis			
NEC provided with nutrition support			
Anemia prevalence	1359	0.58[0.44, 0.76]	69%

[4]Statistical method: Mantle-Haenszel, Random effect

[5]Statistical method: Inverse Variance, Random effect

[6]Statistical method: Inverse Variance, Random effect

[7]Statistical method: Mantle-Haenszel, Fixed effect

Table 3.1b. Meta- analysis overall and stratification Effect Estimates for Each Outcome in Non Pregnant women			
	Total population	RR (95%CI)[8]	I^2
Overall effect			
Anemia prevalence	599	0.45[0.24, 0.86]	93%
Mean Hb	682	0.75[-0.29, 1.79][9]	97%
In LMIC			
Anemia prevalence	1922	0.69[0.56, 0.85]	78%
Mean Hb	682	0.75[-0.29, 1.79]	97%
NEC provided alone			
Anemia prevalence	287	0.52[0.21, 1.30]	92%
NEC provided as a component of a comprehensive package of health messages: No meta-analysis			
NEC provided with nutrition support: No meta-analysis			

[8]Statistical method: Mantle-Haenszel, Random effect

[9]Statistical method: Inverse Variance, Random effect

Chapter 4: Discussion

The objective of this thesis was to conduct a systematic review of RCTs and quasi experimental studies that assess the impact of NEC on anemia prevalence and iron status in pregnant and non pregnant women/girls. Heterogeneity of studies, especially with regards to the nutrition education and counseling exposure, missing values, study design, number of studies and data reporting, limited the ability to conduct a meta- analysis for certain outcomes. As a result of heterogeneity and inconsistencies between studies, the overall quality of the body of evidence for effect of NEC on risk of anemia, mean Hb in pregnant women was judged to be moderate. For iron deficiency, mean serum iron and mean serum ferritin, the quality of the evidence was judged to be low while mean hematocrit was judged to be very low. In the non pregnant population, the overall quality of evidence for anemia prevalence and mean Hb, was judged to be moderate while iron deficiency and mean serum ferritin was judged to be low.

Overall, NEC, with or without additional interventions, reduced the risk of anemia in pregnant and non pregnant women/girls in LMIC but not in HIC. However when stratified on the type of NEC provided, it became evident that in pregnant women NEC was most effective when delivered with nutrition support (IFA or micronutrient). Due to increased nutritional demand during pregnancy, NEC delivered alone may not be ideal to meet the increased requirements and reduce anemia risk, especially in contexts where access to adequate foods or micronutrient supplements may be limited.

In studies with pregnant women, both the intervention and the control groups received iron supplementation making it possible to tease out the independent effect of

NEC on risk of anemia. As a result, the effect reported through meta- analysis can be attributed to NEC. NEC can be an additional component to supplementation and antenatal care during pregnancy to improve anemia status. It should noted that most studies (4) that provided nutrition support delivered NEC in groups/ classes and some studies (2) provided one on one education and gave additional materials such as pamphlets. This indicates that results did not differ by delivery method.

Overall NEC is associated with decreased anemia risk in non pregnant women but not when NEC was provided alone. This null result may be as a result of the small number of studies (3) included in meta- analysis. Also, one study compared NEC alone versus a supplemented group who did not receive NEC making for an inadequate comparison (Meenakshi, Vashisht et al. 2008). The effect of NEC with nutrition support on anemia risk reduction among non pregnant women couldn't be ascertained as there was only one study in this category (Gopaldas 2002). However, this study showed a significant improvement in anemia status compared to the control.

Overall, NEC (with or without additional interventions) showed no effect on mean Hb in pregnant or non pregnant women/girls. This may have been due to the small number of studies. Also, these studies were highly heterogeneous. Stratified analysis was not conducted due to a limited number of studies/ data available. The effect on mean hematocrit is inconclusive as there was one study reporting on this outcome (Olds, Henderson et al. 1986). However, it showed a significant improvement in intervention compared to control.

NEC did not have an effect on mean serum iron levels and iron deficiency among pregnant women. This null effect may have been due to a limited number of studies ($\leq$ 4 studies). NEC may have a positive impact on mean serum ferritin but more studies are needed to validate this. Since no meta- analyses were conducted for iron deficiency and mean serum ferritin levels in nonpregnant women, the effect of NEC on these outcomes is unclear and more studies are required to ascertain this.

Nutrition education methods that target behavior, practices and clearly defined issues have been shown to produce positive results compared to methods that are knowledge based and focused on disseminating information such as lectures and handouts (Cullen, Baranowski et al. 2001; WIC 2006; Contento 2007). It is important that interventions promoting dietary or other behavior change such as compliance to IFA utilize theoretical frameworks to characterize determinants of behavior such as personal or environmental factors, behavioral objectives and strategies to realize behavioral change (Cullen, Baranowski et al. 2001; Nielsen, Gittelsohn et al. 2006). A combination of several educational theories/ models has been shown to be the most effective nutrition education interventions regardless of the delivery method (WIC 2006). One of such strategies is goal setting; it involves a four step process aimed at recognizing the need for change, establishing a goal, adopting and monitoring goal related activities and self reward for goal attainment (Cullen, Baranowski et al. 2001). Another strategy uses the stages of change framework which involves precontemplation, contemplation, preparation, action, and maintenance.

Only one study in this review utilized a theoretical framework (positive deviance approach) in its design and delivery to encourage behavior change among pregnant women (Ndiaye, Siekmans et al. 2009). In this model, community health volunteers including women of childbearing age and elderly women were used to distribute iron supplements, educate and promote good practices identified among positive deviant women. There was a decreased risk of anemia in the positive deviant group at post intervention compared to baseline.

A variety of education methods were employed in the studies with pregnant women contributing to a high heterogeneity. Delivery ranged from home based visitations to facility based discussions. Some methods were individualized while others were group based. A number of studies had intensive follow up visits at home to encourage non compliant women. Finally, a number of studies gave out educational materials such as brochures, pamphlets to reinforce message. For non pregnant women studies, workplace and school based group lectures and discussions were employed. Two studies at a boarding school and community kitchen sought to improve their menus (Creed-Kanashiro, Uribe et al. 2000; Alaofe, Zee et al. 2009). Telephone checkups were used in one study to encourage compliance (Heath, Skeaff et al. 2001). A number of studies distributed additional educational materials such as pamphlets posters, recipe booklets, t-shirts and folders with iron related messages. These differences likely contributed to study heterogeneity and inconsistency in findings. No clear evidence for best practices emerged.

Strength and limitations of the review

Our search included several databases but with language restrictions which may have limited the number of studies included in this review. Also, authors were not contacted for additional information especially in the case of missing data. However, the likelihood of reviewers' error or bias was decreased as a result of the involvement of all reviewers in the search, abstraction and grading of evidence. In addition, there was also no indication of publication bias. Significant and null results were reported in all papers and all articles found and included in this review are published.

Strength and limitations of the evidence

Certain limitations abound in the quality of studies abstracted. There were 11 RCTs (Hunt, Jacob et al. 1976; Kafatos, Vlachonikolis et al. 1989; Belizan, Barros et al. 1995; Creed-Kanashiro, Uribe et al. 2000; Heath, Skeaff et al. 2001; Meenakshi, Vashisht et al. 2008; Adhikari, Liabsuetrakul et al. 2009) and 7 quasi experimental studies (Smoke and Grace 1988; Sun, Shao et al. 1990; Sachdeva and Mann 1993; Abel, Rajaratnam et al. 2000; Gadallah, Rady et al. 2002; Gopaldas 2002; Amani and Soflaei 2006; Garg and Kashyap 2006; Alaofe, Zee et al. 2009; Ndiaye, Siekmans et al. 2009; Senanayake, Premaratne et al. 2010). RCTs are considered high quality studies as such, there's a need for more RCTs to further test the efficacy of NEC in pregnant and non pregnant women. Of all the studies included, only 3 adjusted for potential confounding or tested for interactions (Heath, Skeaff et al. 2001; Adhikari, Liabsuetrakul et al. 2009; Alaofe, Zee et al. 2009).Only 2 RCTs indicated intent to treat analysis (Adhikari, Liabsuetrakul et al. 2009; Heath, Skeaff et al. 2001) and only 5 RCTS indicated allocation method and/ or allocation concealment (Kafatos, Vlachonikolis et al. 1989; Belizan, Barros et al. 1995; Creed-Kanashiro, Uribe et al. 2000; Heath, Skeaff et al. 2001; Adhikari, Liabsuetrakul et al. 2009). All included studies also varied in terms of duration and times of assessment.

In some cases, it is difficult to tease out the impact of NEC as in case of NEC provided as a component of a comprehensive package of health messages (Olds, Henderson et al. 1986; Smoke and Grace 1988; Belizan, Barros et al. 1995) and in situations where the intervention group received supplements and/ or antihelmintic and/ or anti malarial drugs but it was unclear if the control group received the same amount of additional materials at the same intensity (Sachdeva and Mann 1994; Abel, Rajaratnam et al. 2000; Garg and Kashyap 2006). One study used a control group in a different trimester (Garg and Kashyap 2006). Most articles did not compare post intervention versus control but compared pre post results within groups. In this case, I calculated the risk ratio or mean difference and SD of the difference which gives room for biased results due to human error. Some articles didn't report SD. There were differences in outcome definitions making summarized conclusions somewhat difficult.

Implications for public health practice and research

In a guide for World Bank task managers on communication for behavior change, Favin et al advices that formative research be done to ascertain barriers that may prevent change in nutrition practices as well as fine tune communication strategies to fit the intended audience (Favin and Griffiths 1999). Contento outlines a theory based step by step nutrition education process (Refer to box 1). This step wise procedure will help nutrition educators to hone in on specific behavior(s) or practice(s) and achieve intended impact while using theory based frameworks. NEC interventions to improve dietary practices and uptake of iron supplements should "increase public awareness of nutritional needs, train health workers or relevant health care provider to counsel more effectively, inform mothers about feasible, improved practices, negotiate specific practices with individual mothers, give important enabling information, motivate to adapt new practices, address fears and questions, inform recipients on how and where to get iron tablets and inform on appropriate use and how to minimize side effects" (Favin and Griffiths 1999). To date, none of the studies reviewed here followed these guidelines.

Box 1: Stepwise theory based procedural model for nutrition education[10]	
Step 1	Analyze health issue and intended audience. Identify behavior(s), practices(s) of concern and a clear definition of behavioral goals. Involve stakeholders as well.
Step 2	Use theory to identify personal psychosocial and environmental mediators for behavior change
Step 3	Use existing theory or newly created theoretical framework based identified models to guide program and determine channels and components of program.
Step 4	Identify objectives clearly
Step 5	Design theory based strategies to address personal psychosocial and environmental mediators.
Step 6	Design a theory based outcome and process evaluation

Nutrition education and counseling interventions to reduce anemia prevalence and improve iron status in general have achieved some positive results but better study designs, inclusion of behavioral frameworks and appropriate follow up periods especially for non pregnant women may further strengthen the evidence. Additionally, the timing of NEC interventions needs to be explored further to determine the most appropriate time to introduce NEC to observe optimal results. It is known that during pregnancy iron requirement increases and it's recommended to introduce supplementation early in pregnancy (WHO 2001) as a result the timing of NEC is equally important especially if its purpose is to increase IFA compliance; only three studies in this review indicated they began interventions exclusively at first or second trimester.

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[10] Contento, I. R. (2007). Nutrition education: linking research, theory, and practice, Jones & Bartlett Learning.

Further, anemia can be aggravated by parasitic infections especially LMIC where one- third of pregnant women are infected with hookworms (Gyorkos, Larocque et al. 2006). WHO recommends pregnant women receive anthelmintic treatment after the first trimester. Nine of the 13 pregnant women studies were in LMIC but only two studies indicated the administration of deworming drug. This lack of deworming especially in NEC only studies may have contributed to a small effect size observed although participants may have been exposed to treatments of infections as part of routine antenatal care.

Nutrition education is especially important to promote iron supplementation compliance during prenatal care as lack of understanding of the severity of anemia, advantages of supplementation and incorrect perceptions of the consequences of iron tablets has been implicated in low compliance (Galloway, Dusch et al. 2002). Interventions to improve the iron status of women of childbearing age which may include intermittent, preventative supplementation, food based approaches and nutrition education to improve dietary intake has been suggested as a way to ensure adequate iron stores during pregnancy (DeMeyer, Dallman et al. 1989; Bothwell 2000; Viteri and Berger 2005).

Thus future NEC research should:

1. Apply relevant theoretical frameworks to the selected behavioral objectives and intervention strategies.
2. Conduct formative research or baseline measurements of outcomes in the population of interest to ensure targeted and successful intervention delivery.
3. Ensure study designs that include adequate comparison groups and sample sizes.
4. Adjust for confounding and effect modification such as environmental and socio demographic factors that may affect iron status where necessary.

5. Adjust for sampling strategies especially if cluster randomized design.
6. Provision of antihelmintic and anti malaria drugs to both intervention and control groups especially in helminth and malaria endemic areas.

In conclusion, comprehensive NEC in conjunction with food or medicinal supplements (and anthelmintic treatment in low/ middle income countries) can be efficacious to decrease anemia prevalence in women of reproductive age.

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Appendix 1

Table 1.3: Diagnostic Indicators Related to anemia and iron status in Adults.

Laboratory test	Factors to consider	Normal	Anemia/ IDA	Comments
Serum ferritin (µg/l)	Levels are affected by infections, inflammation disorders, cancer and liver disease	40-160	<12-15, <30 in the presence of infection in <5yrs. ≥30% below threshold (ID in pregnant women in the absence of infection)	In an adult, 1µg/L of serum ferritin indicates about 8mg of storage iron while in children, 1µg/L indicates about 0.14µg/kg. Currently recommended by WHO as one of the best indicators of anemia and ID.
Total Iron Binding Capacity (TIBC) (µg/dl)	Levels are affected by inflammatory and neoplastic disorders	330±30	410	Inferior indicator compared to serum ferritin levels; it provides an estimate of plasma transferrin concentration
Serum Iron (µg/dl)		60-165	<40µg/dl	
Serum transferrin saturation	Levels are affected by inflammation disorder conditions	20-50%	<15%. <20% and ferritin <100ng/ml in the presence of inflammation indicates	Usually 30-35% saturated with iron. Transferrin saturation levels below 15% indicate insufficient iron delivery to sustain erythropoesis signifying iron deficiency.

Table 1.3: Diagnostic Indicators Related to anemia and iron status in Adults.				
			iron deficiency.	
sTfR (µg/mL)	Level increase during red cell production and/or turnover such as cases of haemolytic anemia and thalassemia	0.76-1.76 normal	>2.3 very high	Less affected by the presence of inflammation and doesn't vary by age, gender or pregnancy. Good indicator for assessing iron deficiency.
sTfR-F		<1	>1.8	Good indicator for assessing iron deficiency.
Hb (g/dl)	Low Hb may occur in other conditions such as anemia of chronic disease (ACD) and thalassemias	<12-16 (women)	<12 (non pregnant women) <11 (pregnant women)	
Hematocrit		>32%	<32%	
Reticulocyte Hb Content (pg)		28-35	<27.2	Found to be comparable to the use of serum iron, serum ferritin and Hb levels for assessing iron deficiency.
Erythrocyte protoporphyrin (µg/dl)	Levels increase in the presence of inflammation/ infections, lead	30	200µg/dl	Increased levels of erythrocyte protoporphyrin (EP) indicate inadequate iron supply for heme synthesis.

Table 1.3: Diagnostic Indicators Related to anemia and iron status in Adults.				
	poisoning and hemolytic anemia.			
Zinc protoporphyrin/heme ratio (ZPP/H)	Zn is influenced by inflammation and makes it difficult to distinguish between IDA and ACD.			Zinc utilization increases as iron supply decreases resulting in an elevated ZPP/H ratio. ZPP/H has been noted as a preferred method compared to bone marrow aspiration and compares satisfactorily to serum ferritin, Hb and mean cell volume (MCV) levels in diagnosing IDA and preanemic iron depletion
Hepcidin	Production is decreased in IDA and increased in the case of inflammation and iron loading			The measurement of hepcidin levels might be preferred in areas where ACD is prevalent as it may be more accurate in differentiating between IDA and ACD.
Source: (Brugnara, Schiller et al. 2006; Pasricha, Caruana et al. 2008; Clark 2009; Munoz, Garcia-Erce et al. 2010)				

Appendix 2

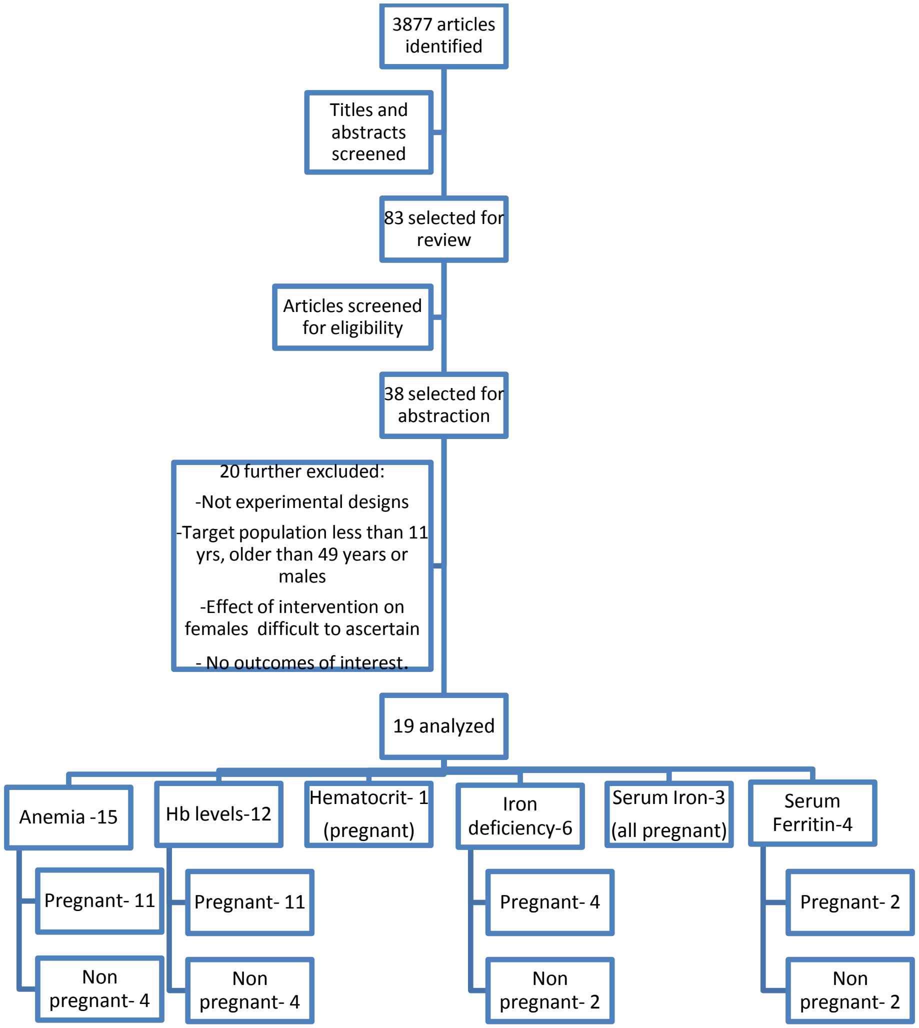


Figure 2. Methodological Flow chart of systematic review

Appendix 3

Table 3.1a. Quality assessment of studies of nutrition education and counseling strategies on Anemia and iron status related outcomes during pregnancy.								
Quality Assessment						Summary of Findings		
No of studies and study design	**Heterogeneity of results**	**Consistent size of effect**	**Generalizability to population of interest**	**Generalizability to intervention of interest**	**Other sources of bias (e.g., major limitations in study design)**	**No of events**		
						Statistical method	**Effect estimate**	**Sample size**
Anemia prevalence third trimester: Overall quality of evidence=moderate								
12 cRCT; RCTs, Quasi Experimental (QE)	Yes (I^2=71%)	Consistent and positive effect across studies.	Studies conducted in low/middle income countries (7) and high income nations (3) (one high income geared towards adolescents, another among Spanish speaking (mostly emigrants from Mexico))	One on one, group and home visits employed. One study used positive deviant approach; In some cases cannot distinguish effect of NEC from other health messages (category 2 NEC). Other studies were in category 1 NEC or 3 resulting in different exposures. Another study was a community based intervention program. Low attendance rate resulted in the reduction of the program from 12 classes to 5 in another case. Studies defined anemia in third trimester differently: Hb <11g/dl or <110g/l; <1.6mmol/l; 9-10.4g/dl while two studies measured anemia using hematocrit <32% in addition to these definitions.	One study self reported outcome; no adjusted for confounding. No randomization in QE; no adjusting for confounding; one study didn't follow same subjects pre to post	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.58, 0.84]	2588
Mean Hb third trimester: Overall quality of evidence=moderate								
10 RCT; cRCT; QE	Yes (I^2=88%)	Inconsistent	Studies in high income	One study had a low at-	QE no randomi-	Mean Difference	0.54 [-0.07,	826

Table 3.1a. Quality assessment of studies of nutrition education and counseling strategies on Anemia and iron status related outcomes during pregnancy.

Quality Assessment						**Summary of Findings**		
No of studies and study design	**Heterogeneity of results**	**Consistent size of effect**	**Generalizability to population of interest**	**Generalizability to intervention of interest**	**Other sources of bias (e.g., major limitations in study design)**	**No of events**		
						Statistical method	**Effect estimate**	**Sample size**
		effect across included studies. (only 4 studies qualified for meta analysis)	countries (2); 5 in low/middle income nations	tendance rate that resulted in the reduction of the program from 12 classes to 5. Varying Interventions employed including one on one and/ or home visits and group NEC sessions. Also different studies used NEC 1, 2 or 3. One study was a community based intervention program.	zation; No adjusting for confounding	(IV, Random, 95% CI) Meta-analysis included only 4 studies.	1.14]	
Mean Hematocrit third trimester: Overall quality of evidence=low								
1 RCT	N/A. meta analysis not conducted	0 of 1 show benefits	High income country: US	Cannot distinguish effect of NEC only from other health messages (NEC 2)		Mean Difference	N/A	308
Iron deficiency third trimester: Overall quality of evidence=low								
4 QE; cRCT, RCT.	Yes (I^2=73%)		Studies in low/middle income (1) and high income countries (2)	One study was a community based intervention program. Another intervention received one on one NEC. One study had low attendance rate which resulted in the reduction of the program from 12 classes to 5. Varying Interventions employed including one on one and/ or home visits and group NEC	No randomization, no adjusting for confounding, didn't follow same subjects pre to post	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.53, 1.86]	746

Table 3.1a. Quality assessment of studies of nutrition education and counseling strategies on Anemia and iron status related outcomes during pregnancy.								
Quality Assessment						Summary of Findings		
No of studies and study design	**Heterogeneity of results**	**Consistent size of effect**	**Generalizability to population of interest**	**Generalizability to intervention of interest**	**Other sources of bias (e.g., major limitations in study design)**	**No of events**		
						Statistical method	**Effect estimate**	**Sample size**
						1, 2 or 3 sessions. Iron deficiency defined as serum iron <10.74 µmol/l, serum iron <40µg/100ml; serum ferritin <12µg/l and <20ng/dL.		
Mean Serum Iron third trimester: Overall quality of evidence=moderate								
3 RCT; QE	Yes (I^2=99%)	Meta- analysis showed inconsistency of effect.	Studies in high income (1) and low/middle income (2) nations	Studies delivered intervention differently one on one NEC, group and home visits, NEC 1 and 3.	No randomization for QE	Mean Difference (IV, Random, 95% CI)	-1.98 [-26.32, 22.36]	382
Mean Serum Ferritin third trimester: Overall quality of evidence=low								
2 QE	N/A. meta analysis not conducted	1 of 2 show benefit	Low/middle income country	Study was a community based intervention program and in NEC 3 category.	No randomization, no adjusting for confounding, didn't follow same subjects pre to post	Mean Difference	N/A	404

Table 3.1b. Quality assessment of studies of nutrition education and counseling strategies on anemia and iron status related outcomes in non pregnant women and girls.								
Quality Assessment						**Summary of Findings**		
No of studies and study design	**Heterogeneity of results**	**Consistent size of effect**	**Generalizability to population of interest**	**Generalizability to intervention of interest**	**Other sources of bias (e.g., major limitations in study design**	**No of events**		
						Statistical method	**Effect estimate**	**Sample size**
Anemia prevalence measured as <12g/dl or <120g/l: Overall quality of evidence=moderate								
4 cRCT; QE	Yes (I^2=93%)	Consistent and positive effect	4 low/middle income countries (2 among adolescents)	For one study, intervention was through community kitchens. Another study in high school setting while another study was at boarding school setting receiving group NEC and menu improvement. Another study at workplace and workers received food supplements. Studies delivered NEC 1 or 3 interventions. Anemia defined as <12g/dl or <120g/l.	No adjusting for confounding and No randomization in QE	Risk Ratio (M-H, Random, 95% CI)	0.45 (0.24, 0.86)	255
Mean Hb: Overall quality of evidence=low								
3 RCT; cRCT; QE	Yes (I^2=97%)		2 in high income countries and 2 in low/middle income nations.	One study at high school setting. Another study received comprehensive iron education. One study at workplace and received food supplements, one at high school and received group/face to face NEC and pamphlets. Studies delivered NEC 1 or 3 interventions.	No adjusting for confounding; No randomization for QE	Mean Difference (IV, Random, 95% CI)	0.75 [-0.29, 1.79]	682
Iron deficiency: Overall quality of evidence=low								

Table 3.1b. Quality assessment of studies of nutrition education and counseling strategies on anemia and iron status related outcomes in non pregnant women and girls.								
Quality Assessment						Summary of Findings		
No of studies and study design	**Heterogeneity of results**	**Consistent size of effect**	**Generalizability to population of interest**	**Generalizability to intervention of interest**	**Other sources of bias (e.g., major limitations in study design**	**No of events**		
						Statistical method	**Effect estimate**	**Sample size**
2 cRCT ; QE	N/A. meta analysis not conducted	0 of 2 show benefit	Studies in low/middle income countries	One study Intervention through community kitchens, another intervention at boarding school setting and received group NEC and menu improvement. Studies delivered NEC 1 or 3 interventions. Iron deficiency defined as serum ferritin <20µg/l and two of the following values: serum iron <11umol/L, TIBC >68umol/L, Transferrin saturation <20%; serum ferritin <12µg/l	No adjusting for confounding; No randomization in QE	Risk Ratio	N/A	175
Mean Serum Ferritin: Overall quality of evidence=low								
2 RCT; QE	N/A. meta analysis not conducted	0 of 2 show benefit. P value not reported in one study	High income country: New Zealand	One study intervention received comprehensive iron education. The other study at high school and received group/face to face NEC. Studies delivered NEC 1 or 3 interventions.	No randomization; No adjusting for confounding	Mean Difference	N/A	101

Table 3.2. Grading the quality of individual trials included in the meta-analysis										
Author, year (ref.)	Trial design	Adequate sequence generation?	Adequate allocation concealment?	Blinding	Loss to follow-up	Intention to treat analysis?	Free of selective reporting?	Other bias (e.g., small sample size)?	Comments	Grade
Abel 2000 (6)	QE	No: lack of randomization	No	No blinding	N/A: study didn't follow same participants baseline to endline.	No	Yes	Lack of randomization, no control for confounding and sampling strategy, population at follow-up not same as baseline. No discussion of power calculations	Community based intervention. Mean differences and RR (95%CI) were not reported between groups so they were calculated by hand or using Open epi.	Low (no randomization or blinding)
Adhikari 2009 (7)	RCT	Yes: block of eight generated	Yes: concealed using numbered, sealed opaque envelope method overseen by an independent person.	Unclear	8.75% to 12.5% lost to follow up across the groups.	Yes	Yes	N/A	All study participants received daily iron supplementation from 2nd trimester. Study was for a period of 3 months.	High (Randomized trial, adequate sequence generation, allocation concealment, controlled for potential confounding).
Alaofe 2009 (12)	QE	No: lack of randomization	No: Not described explicitly	No	No lost to follow up in intervention, 15% eliminated from the control group.	No	Yes	No randomization, Schools not randomly selected. Analysis didn't adjust for sampling strategy (based on individuals not group sampling)	P values reported but RR (95%CI) not reported, they were calculated by hand. Post intervention measurement after 26 week of interventions. Deworming and antihelmiths provided to both groups.	Moderate (Adjusted for potential confounders, low loss to follow up).
Amani 2006 (14)	QE	No: lack of randomization	Unclear	No	None	No	Yes	Selection method for high schools not indicated but girls were	Study over 2 month period. Mean differences presented for	Low (no randomization or blinding

Table 3.2. Grading the quality of individual trials included in the meta-analysis

Author, year (ref.)	Trial design	Adequate sequence generation?	Adequate allocation concealment?	Blinding	Loss to follow-up	Intention to treat analysis?	Free of selective reporting?	Other bias (e.g., small sample size)?	Comments	Grade
								randomly selected within schools. No adjustment for confounding or interactions. No discussion of power calculations.	Hb and serum ferritin were calculated by hand as study did not report.	
Belizan 1995 (2)	cRCT	Yes: computer generated code for randomization within balanced blocks of 20 women and stratified by center.	Unclear	Single blinded: to participants	9% lost to follow up	Not reported	Yes	No adjusting for sampling strategy or confounders.	Self reported anemia prevalence among participants.	Moderate (randomized, low loss to follow up, blinded)
Creed Kanashiro 2000 (9)	cRCT	Yes: not reported but communities were randomly selected, one community kitchen (CK) randomly selected from each and adolescent girls randomly selected from each CK	Unclear	Unclear	11% and 12% lost to follow up in intervention and control 60espectively	No	Yes	No adjusting for sampling strategy or confounders. No discussion of power calculations.	Intervention over 9 month period. P values were reported but RR (95%CI) and mean differences were calculated by hand or using Openepi.	Moderate (randomized, low loss to follow up)
Gadallah 2002 (8)	QE	No: lack of randomization	Unclear	No	None	No	Yes	Lack of randomization, no control for confounding and sampling strategy, No discus-	Possible contamination amongst groups as the two clinics were in the same health	Low (no randomization and adjustment, possible

Table 3.2. Grading the quality of individual trials included in the meta-analysis

Author, year (ref.)	Trial design	Adequate sequence generation?	Adequate allocation concealment?	Blinding	Loss to follow-up	Intention to treat analysis?	Free of selective reporting?	Other bias (e.g., small sample size)?	Comments	Grade
								sion of power calculations	district. 2 month follow up period. P values were reported for pre post cpmarisons but RR (95%CI) and mean differences between groups were calculated by hand or using Openepi.	contamination between groups)
Garg 2006 (5)	QE	No: lack of randomization, inadequate group division	No	No	8% lost to follow up in intervention	No	Yes	Purposive sampling of pregnant women through domiciliary visits. Inadequate comparison group as participant were in different stages of pregnancy, intervention in the 5th -7th month of pregnancy and control in 8th to 9th as a result control group could not be studied parallel to the intervention group. No discussion of power calculations. No adjustment for potential confouders.	Pre-intervention data for control and intervention,post-intervention data for intervention only reported. It appears post-intervention, intervention group is compared with control baseline data. Follow up ranged from 2.5-4 months.	Low (inadequate control, no randomization or blinding)
Gopaldas 2002 (13)	QE	No: lack of randomization	Not reported	No	None	No	Yes	No discussion of power calculations. Group allocation strategy not reported. No adjust-	Four workplace units were selected. P values for pre post comparision reported but	Low (no randomization or blinding,

Table 3.2. Grading the quality of individual trials included in the meta-analysis

Author, year (ref.)	Trial design	Adequate sequence generation?	Adequate allocation concealment?	Blinding	Loss to follow-up	Intention to treat analysis?	Free of selective reporting?	Other bias (e.g., small sample size)?	Comments	Grade
								ment for potential confouders.	RR (95%CI) and mean differences between intervention and control calculated by hand or using Openepi.	
Heath 2001 (10)	RCT	Yes: stratified block design	Unclear	Yes: Double blinded placebo/ intervention packaged similarly	4% and 17% lost to follow up in intervention and control groups respectively.	Not reported	Yes	Allocation concealment not reported. Small sample size. No discussion of power calculations.	The strata used for balancing groups: recruitment serum ferritin (<12μg/L or 12-19 μg/L), menstral blood loss (<33.5 blood loss units or ≥ 33.5) and vegetarianism (yes/no). Adjusted for potential confounders.	High (Randomized trial, adequate sequence generation, controlled for potential confounding).
Hunt 1976 (15)	RCT	Not reported	Not reported	No	19% lost to follow up	Not reoprted	Yes	Strategy and allocation concealment not reported. Low attendance rate led to reduction in classes from 12 to 5. Possible 'contamination' via contact between women in two groups. No discussion of power calculations. No adjustment for potential confouders.	No adjustment for potential confouders. P values reported but RR (95%CI) and mean differences between intervention and control calculated by hand or using Openepi.	Low (no blinding, no report of allocation concealment and sequence generation)
Meenakshi 2008 (11)	cRCT	Not reported	Not reported	Not reported	4% lost to follow up	No	Yes	No discussion of power calculations. No	Nutrition education components not de-	Low (necessary informa-

Table 3.2. Grading the quality of individual trials included in the meta-analysis

Author, year (ref.)	Trial design	Adequate sequence generation?	Adequate allocation concealment?	Blinding	Loss to follow-up	Intention to treat analysis?	Free of selective reporting?	Other bias (e.g., small sample size)?	Comments	Grade
								adjustment for potential confounders and sampling strategy.	scribed. P values reported for pre post comparison within groups and not between groups so RR (95%CI) and mean differences between intervention and control calculated by hand or using Openepi.	tion not reported)
Kafatos 1989 (1)	cRCT	Yes: computer genenrated random numbers	Yes	No	Loss to follow up inconsistent for each outcome measured	No	Yes	No discussion of power calculations.	Analysis based on individual women, rather than clinic. Adjusted for potential confounders.	High (Randomized trial, adequate sequence generation, controlled for potential confounding)
Ndiaye 2009 (18)	QE	No	No	No	None but 12% excluded from analysis	No	Yes		Adjusted for potential confounders.	Moderate (Adjustment, power calculations)
Sachdeva 1993 (16)	QE	No	No	No	8% lost to follow up	No	Yes	No discussion of power calculations. No adjustment for potential confounders.		Low (no randomization, blinding, adjustment for confounding)
Senanayake 2010 (19)	QE	No	No	No	3% lost to follow up (control)	No	Yes	No discussion of power calculations. No adjustment for potential confounders. No	Routine IFA, Vit C supplementation and anthelminthic treatment to both groups	Low (no randomization, blinding, adjustments, no

Table 3.2. Grading the quality of individual trials included in the meta-analysis

Author, year (ref.)	Trial design	Adequate sequence generation?	Adequate allocation concealment?	Blinding	Loss to follow-up	Intention to treat analysis?	Free of selective reporting?	Other bias (e.g., small sample size)?	Comments	Grade
								discussion of process of group allocation	so its possible to tease out NEC effect.	report on allocation process)
Smoke 1988 (4)	QE	No: self selection	No	No	8% lost to follow up	No	Yes	No discussion of power calculations. No adjustment for potential confounders.		Very Low (no randomization, self selection)
Sun 1990 (3)	QE	No: using registration numbers- odd numbered participants to intervention and even numbered to control	No	No	Not reported	No	Yes	No discussion of power calculations. No adjustment for potential confounders.	P values reported but RR (95%CI) and mean differences between intervention and control calculated by hand or using Openepi.	L ow (no randomization, blinding, adjustment for confounding)

Table 3.3. Characteristics of studies included in the meta-analyses

Reference	Country	Study Design	Population	Intervention Details	Outcomes measured
Abel 2000	India	QE	All pregnant females and adolescent girls	Information on anemia, iron supplementation after 4 months of pregnancy, deworming, iron rich foods, iron enhancers, iron inhibitors disseminated by family care volunteers through flash cards for one-on-one teachings and by community officers, health aides and nurses for group teaching. Video on anemia shown at mass gatherings, and pamphlets on anemia for adolescent girls. Control: No specific intervention except usual Gov't prophylaxis program also available to intervention group.	Iron deficiency, serum Iron, hemoglobin, anemia, serum ferritin
Adhkari 2009	Nepal	RCT	320 pregnant women in their 2nd trimester who presented for their first prenatal visit.	Education only: Daily Iron supplementation and education of anemia, impact on maternal and fetal outcomes, importance of iron supplementation, clarification of misconceptions, handling side effects, ensuring good iron absorption/good diet. Education/pill count: Daily Iron supplementation and education of anemia, impact on maternal and fetal outcomes, importance of iron supplementation, clarification of misconceptions, handling side effects, ensuring good iron absorption/good diet. Compliance monitoring. Control: Daily iron supplementation but no nutrition education. Pill count: Daily iron supplementation and compliance monitoring.	Anemia, hemoglobin
Alaofe 2009	Benin	QE	68 adolescent non pregnant boarding school girls aged 12 to	Four nutrition education lessons lasting one hour each over a 4 week period. Lessons on functions of iron, prevalence and symptoms of iron deficiency, main sources of iron, definition of food iron bioavailability, dietary strate-	Serum ferritin, serum iron, hemoglobin, iron deficiency

Table 3.3. Characteristics of studies included in the meta-analyses

Reference	Country	Study Design	Population	Intervention Details	Outcomes measured
			17 years	gies to improve iron status, motivating session to encourage girls to adopt a balanced diet rich in iron. Discussion after a nutrition quiz. Menu improvement activities for 22 weeks. Girls were treated with antihelmintic and antimalarial drugs initially, monthly and when new infections occurred during the study. Control: No nutrition education or menu improvement but girls were treated with antihelmintic and antimalarial drugs initially, monthly and when new infections occurred during the study.	
Amani 2006	Iran	QE	60 adolescent non pregnant healthy high school girls aged 16 to 18 years.	Nutrition education on dietary sources of iron, iron availabilty, signs and consequences of iron deficiency and anemia via face to face group discussions and simple pamphlets. Control: no nutritional education.	Serum ferritin, hemoglobin
Belizan 1995	Argentina, Brazil, Cuba, Mexico	cRCT	2235 women 15 to 22 weeks pregnant.	Home visits to strengthen social support and reduce anxiety and stress; health education including nutrition a component of educational sessions during home visits. Health messages reinforced with the use of posters; pregnant women received a booklet of health education messages at the first visit. Control: Routine antenatal care.	Anemia

Table 3.3. Characteristics of studies included in the meta-analyses

Reference	Country	Study Design	Population	Intervention Details	Outcomes measured
Creed Kanashiro 2000	Peru	cRCT	121 adolescent non pregnant, non lactating girls aged 12-17 years.	Participatory training sessions with girls and community kitchen leaders. Development of iron rich menus, facilitation of increased accessibility to less expensive sources of heme iron. Educational materials promoting the relationship between consuming iron rich foods and iron enhancers and school performance. In the first 5 months, increased accessibility to less expensive sources of heme (chiken liver and blood) were facilitated at a cost price from a commercial chicken producer. Control: No intervention	Anemia, iron deficiency
Gadallah 2002	Egypt	QE	100 pregant women attending two antenatal clinics at rural primary health care units	Message on healthy nutrition, causes, symptoms, treatment and prevention of anemia, iron deficiency anemia and its impact on maternal and fetal health, balanced diet and daily caloric requirement for pregnant women and cheap ways to do so. messages on the importance of iron, proteins, vitamins, positive and negative traditional practices affecting iron absorption. iron supplements were provided Control: routine antenatal care only.	Anemia, hemoglobin
Garg 2006	India	QE	96 poor pregnant women in 5th to 7th month of pregnancy	Participants were educated on increasing quantitiy of food, improving food quality, promotion of IFA consumption, rest during pregnancy, tetanus toxiod injections, antenatal visits and use of iodized salt. Individual counseling, weekly home visits and group meetings. Control: No intervention (8th and 9th month pregnant)	Anemia, hemoglobin

Table 3.3. Characteristics of studies included in the meta-analyses

Reference	Country	Study Design	Population	Intervention Details	Outcomes measured
Gopaldas 2002	India	QE	302 non pregnant young working women aged 18 to 23 years	Intervention group 1: intense IEC related to iron deficiency anemia once a week, lectures on nutrition and reproductive heatlh twice a month, fermented steamed dumplings (iddlis) with relish and lentil soup 3 times a week @ 2pm when shifts changed. Intervention group 2: less intense IEC once a month, no lectures, 20 ml gooseberry juice to deliver 40mg of vit C 3 times a week. Positive control group 3: No IEC, no lectures, 400mg of albendazole once a week and 60mg of elemental iron as ferrous sulfate twice a week. Negative control group 4: no IEC, no supplements, no lectures	hemoglobin, anemia,
Heath 2001	New Zealand	RCT	57 non pregnant, non lactating, women with mild iron deficiency aged 18-40 years	Diet group: Diet counseling on increasing iron containing foods intake by eating at least one serving of iron high foods rich in heme iron, one serving of medium iron foods, intake of non heme iron foods with fortificant iron or vit c content. Cook tomato based sauce in a cast iron fry pan. inrease intake of enhancers of non heme iron absorption by consuming foods and beverages containg at least 50mg of vit C in each meal, table with quantities and recipes were provided. decrease intake of foods containg factors that inhibit non heme iron absorption and modiying eating patterns. Received placebo Supplement group: Usual diet (no nutrition education) and iron supplements.	Hemoglobin, serum ferritin

Table 3.3. Characteristics of studies included in the meta-analyses

Reference	Country	Study Design	Population	Intervention Details	Outcomes measured
				Control: Placebo and usual diet (no nutrition education).	
Hunt 1976	U.S	RCT	279 low income pregnant women of Mexican descent.	Nutrition education on how to plan nutritious meals using foods from the four basic food groups, how to buy, store and prepare these foods. Vitamin and mineral capsules (Vitamin A 4000 USP units, Vitamin D 400 USP units, thiamin mononitrate 3mg, riboflavin 2 mg, pyridoxine HCL 3mg, Vitamin B12 activity 2µg, nicotamide 10mg, folic acid 0.5mg, ascorbic acid 50mg, calcium carbonate 500mg, ferrous sulphate 100mg (iron deficient women were given ferrous gluconate in addition) given at initial visit. Control: No nutrition education. Vitamin and mineral capsules were also given to women in the control group.	Hemoglobin, hemotcrit, serum iron
Meenakshi 2008	India	cRCT	310 adolescent high school girls aged 13 to 16 years.	Nutrition education on anemia. Information on nutrition education not reported Control: supervised biweekly iron/folic acid supplemention (100mg elemental iron, 0.5mg folic acid) for 100 days.	Anemia, hemoglobin
Kafatos 1989	Greece	cRCT	300 Pregnant women	Nutrition education on the basics of nutrition during pregnancy including food sources and methods for selecting balanced diet; practical techniques for improving diet quality and encouraged to consume locally grown foods with high nutrient value; preparation and preservation techniques to reduce nutrient loss encouraged. Control: No nutrition education	Anemia, hemoglobin, iron deficiency, serum irom

Table 3.3. Characteristics of studies included in the meta-analyses					
Reference	Country	Study Design	Population	Intervention Details	Outcomes measured
Ndiaye 2009	Senegal	RCT	200 rural pregnant women	A positive deviance approach involving community health volunteers (elderly women, WCBA) trained to identify all pregnant women in each village and encourage them to attend ANC, distribute Iron supplements at a subsidized price during monthly sessions for promotion of healthy pregnancy including key messages on ANC, anemia, iron supplementation and nutrition during pregnancy. conducted food demostrations. conducted follow up visits for defaulters and encouraged them. Control: non positive deviant activities	Anemia
Olds 1986	US	RCT	374 pregnant (primiparas) women.	Nurse home visit during pregnancy once every 2 wks, (average of 9 visits) for 1hr and 15 mins including screening and transportaiton services. Education on fetal, infant development, to improve prenatal behavior and well being of newborn, improving diet by monitoring weight gain, eliminating use of cigarettes, alcohol, drugs. Other messages include enhancement of informal support grp, linkage of parents to community services., identifying signs of pregnancy complications, exercise, rest, good hygiene, labor, delivery and early care of newborn preparation. Nurses used a detailed curriculum. Control: No servies were provided.	Hematocrit
Sachdeva 1993	India	QE	61 low and lower middle income young pregnant women aged 18-28 years	Iron Folic Acid (folifer tablets) (60mg iron, 500µg folic acid) and calcium (500mg calcium gluconate, 15mg ascorbic acid, 1µg Vitamin B12 and 100IU Vitamin D3) supplements from the 5th month, pamphlets on diet during pregnancy. Individual and group visits to reinforce nutrition knowledge from pamphlets.	Serum iron

Table 3.3. Characteristics of studies included in the meta-analyses					
Reference	Country	Study Design	Population	Intervention Details	Outcomes measured
				Control: Medical supervision and folifer tablets as per Gov't practice. No nutrition education.	
Senanayake 2010	Sri Lanka	QE	115 pregnant women between 16- 20 weeks of gestation.	Detailed interactive educational session in small groups of 4-5 mothers. It focused on important aspects of iron deficiency and supplementation in pregnancy, improving the bioavailabilty of iron in the supplements (take iron tablet with Vit C, every night at least 2hr after night meal, avoid taking with calcium tablets, avoid taking with tea, coffee, milk of any food for at least 1 hr before or after the iron tablet). They also taught to identify the iron tablets. Instructions were reinforced at subsequent visits. women also received routine antenatal care and nutritional supplements including 60mg elemental iron as ferrous sulphate 200mg daily, vitamin C, folic acid and anthelmintic mebendazole. Control: Routine antenatal care including nutritional supplements (60mg elemental iron as ferrous sulphate 200mg daily, vitamin C, folic acid and anthelmintic mebendazole).	Hemoglobin, serum ferritin, anemia
Smoke 1988	U.S	QE	116 pregnant adolescents <18years.	Nutrition class included prenatal nutrition and nutritional needs for adolescents, food selection and substance abuse with other messages about pregnancy, familyplanning, baby nutrition, growth and development of newborn, labor delivery, anesthesia and hospital tours. Control:Attended regular obstetrical clinics, received prenatal care and were seen by a staff physician and registered/ licensed pratical nurse. Social workers and nutri-	Anemia, Hemotocrit <32%

Table 3.3. Characteristics of studies included in the meta-analyses

Reference	Country	Study De-sign	Population	Intervention Details	Outcomes measured
				tionist were available as needed with a minimum of one contact in the prenatal period.	
Sun 1990	China	QE	143 Primigravidas	Lectures on elementary knowledge of maternal nutrition, methods of proper cooking, explanation of harmful traditional dietary habits. Discussions on plans for improving eating habits and implementing new balanced diet recipes, complications of pregnancy and nutrient deficiencies. Participants were given booklet on guide to maternal nutrition. Control: No nutrition education	Anemia, mean hemoglobin, mean serum iron.

Appendix 4

Figure3a: Effect of Nutrition Education and Counseling on Risk of Anemia in Pregnant Women/Adolescents

	NEC		No NEC			Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
1.12.1 Overall: pregnant women						
Abel 2000	100	176	133	166	14.3%	0.71 [0.61, 0.82]
Adhikari 2009 1 (1)	13	73	27	70	6.4%	0.46 [0.26, 0.82]
Adhikari 2009 3 (2)	13	71	27	70	6.4%	0.47 [0.27, 0.84]
Belizan 1995 (3)	48	278	48	281	9.9%	1.01 [0.70, 1.45]
Gadallah	16	50	23	50	7.4%	0.70 [0.42, 1.15]
Garg 2006	36	41	33	35	14.5%	0.93 [0.81, 1.07]
Hunt 1976	1	117	3	98	0.7%	0.28 [0.03, 2.64]
Kafatos 1989 (4)	43	213	28	122	8.8%	0.88 [0.58, 1.34]
Ndiaye 2009	55	100	66	100	12.9%	0.83 [0.66, 1.04]
Senanayake 2010	15	107	52	111	7.3%	0.30 [0.18, 0.50]
Smoke 1998	2	70	3	46	1.1%	0.44 [0.08, 2.52]
Sun 1990	31	80	35	63	10.2%	0.70 [0.49, 0.99]
Subtotal (95% CI)		**1376**		**1212**	**100.0%**	**0.70 [0.58, 0.84]**
Total events	373		478			

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 37.34$, df = 11 (P = 0.0001); $I^2 = 71\%$

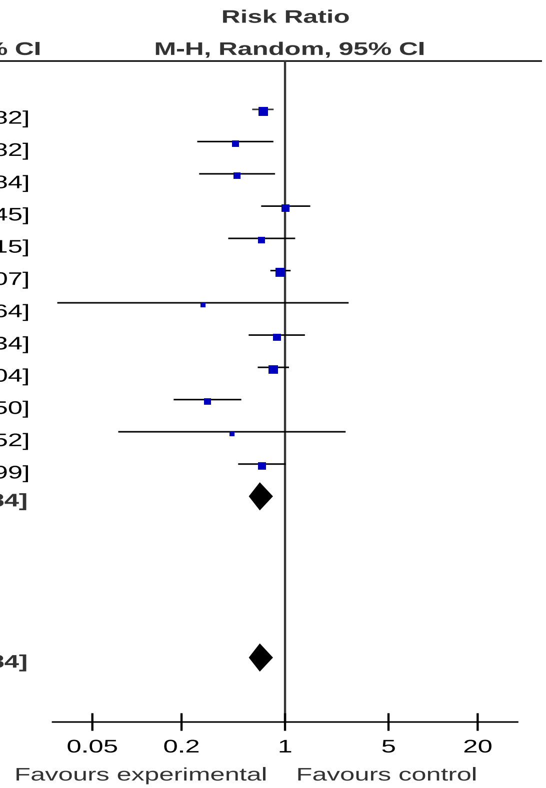
Test for overall effect: Z = 3.74 (P = 0.0002)

Total (95% CI)		**1376**		**1212**	**100.0%**	**0.70 [0.58, 0.84]**
Total events	373		478			

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 37.34$, df = 11 (P = 0.0001); $I^2 = 71\%$

Test for overall effect: Z = 3.74 (P = 0.0002)

Test for subgroup differences: Not applicable



(1) nutrition education/IFA compliance monitoring vs control

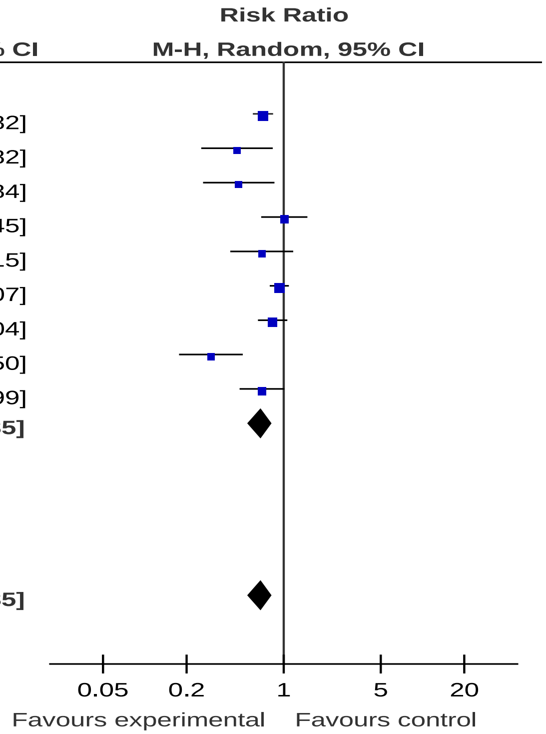
(2) nutrition education vs control

(3) Adjusted for clustering (DE= 3.6312, ICC= 0.0052)

(4) Adjusted for clustering (DE= 1.0897, ICC= 0.0052)

Figure3b: Effect of Nutrition Education and Counseling on Risk of Anemia in Pregnant Women/Adolescents in Low/Middle Income Countries.

	NEC		No NEC			Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
1.13.1 LMIC						
Abel 2000	100	176	133	166	15.5%	0.71 [0.61, 0.82]
Adhikari 2009 1 (1)	13	73	27	70	7.5%	0.46 [0.26, 0.82]
Adhikari 2009 3 (2)	13	71	27	70	7.5%	0.47 [0.27, 0.84]
Belizan 1995 (3)	48	278	48	281	11.2%	1.01 [0.70, 1.45]
Gadallah	16	50	23	50	8.6%	0.70 [0.42, 1.15]
Garg 2006	36	41	33	35	15.7%	0.93 [0.81, 1.07]
Ndiaye 2009	55	100	66	100	14.1%	0.83 [0.66, 1.04]
Senanayake 2010	15	107	52	111	8.5%	0.30 [0.18, 0.50]
Sun 1990	31	80	35	63	11.4%	0.70 [0.49, 0.99]
Subtotal (95% CI)		**976**		**946**	**100.0%**	**0.69 [0.56, 0.85]**
Total events	327		444			
Heterogeneity: Tau² = 0.07; Chi² = 36.69, df = 8 (P < 0.0001); I² = 78%						
Test for overall effect: Z = 3.51 (P = 0.0004)						
Total (95% CI)		**976**		**946**	**100.0%**	**0.69 [0.56, 0.85]**
Total events	327		444			
Heterogeneity: Tau² = 0.07; Chi² = 36.69, df = 8 (P < 0.0001); I² = 78%						
Test for overall effect: Z = 3.51 (P = 0.0004)						
Test for subgroup differences: Not applicable						



(1) nutrition education/IFA compliance monitoring vs control

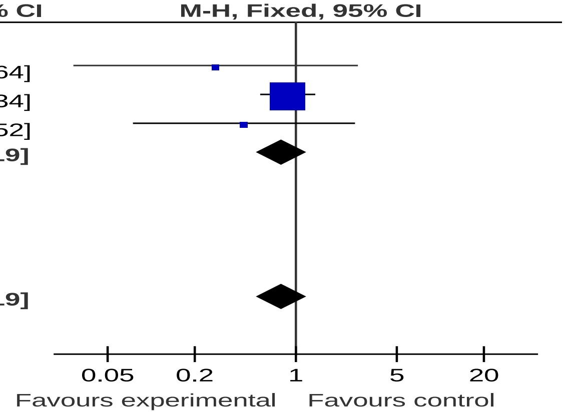
(2) nutrition education vs control

(3) Adjusted for clustering (DE= 3.6312, ICC= 0.0052)

Figure3c: Effect of Nutrition Education and Counseling on Risk of Anemia in Pregnant Women/Adolescents in High Income Countries.

	NEC		No NEC			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
1.9.1 HIC pregnant women						
Hunt 1976	1	117	3	98	7.7%	0.28 [0.03, 2.64]
Kafatos 1989 (1)	43	213	28	122	83.8%	0.88 [0.58, 1.34]
Smoke 1998	2	70	3	46	8.5%	0.44 [0.08, 2.52]
Subtotal (95% CI)		**400**		**266**	**100.0%**	**0.80 [0.53, 1.19]**
Total events	46		34			
Heterogeneity: Chi² = 1.50, df = 2 (P = 0.47); I² = 0%						
Test for overall effect: Z = 1.12 (P = 0.26)						
Total (95% CI)		**400**		**266**	**100.0%**	**0.80 [0.53, 1.19]**
Total events	46		34			
Heterogeneity: Chi² = 1.50, df = 2 (P = 0.47); I² = 0%						
Test for overall effect: Z = 1.12 (P = 0.26)						
Test for subgroup differences: Not applicable						

Risk Ratio
M-H, Fixed, 95% CI

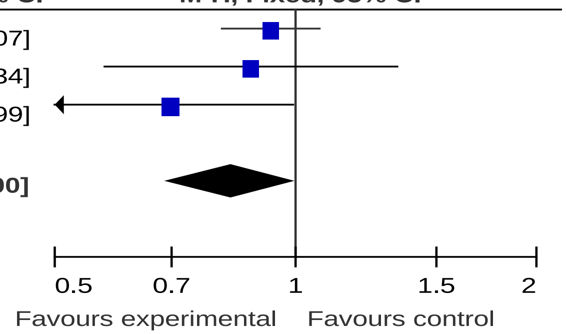


(1) Adjusted for clustering (DE= 3.6312, ICC= 0.0052)

Figure3d: Effect of Nutrition Education and Counseling Only on Risk of Anemia in Pregnant Women/Adolescents

	NEC		No NEC			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Garg 2006	36	41	33	35	32.3%	0.93 [0.81, 1.07]
Kafatos 1989 (1)	43	213	28	122	32.3%	0.88 [0.58, 1.34]
Sun 1990	31	80	35	63	35.5%	0.70 [0.49, 0.99]
Total (95% CI)		**334**		**220**	**100.0%**	**0.83 [0.69, 1.00]**
Total events	110		96			
Heterogeneity: Chi² = 3.52, df = 2 (P = 0.17); I² = 43%						
Test for overall effect: Z = 1.93 (P = 0.05)						

Risk Ratio
M-H, Fixed, 95% CI



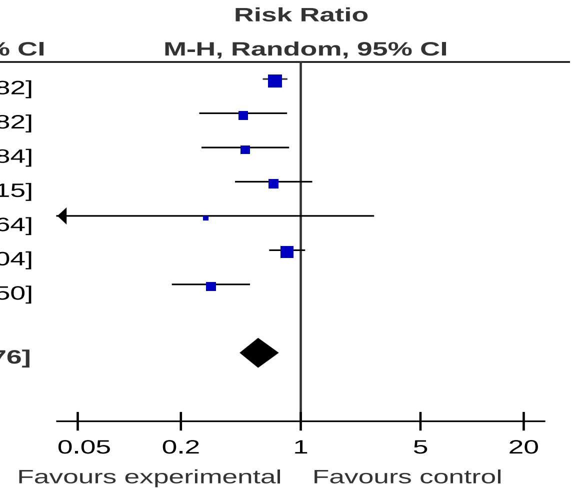
(1) Adjusted for clustering (DE= 3.6312, ICC= 0.0052)

Figure3e: Effect of Nutrition Education and Counseling with Nutrition Support on Risk of Anemia in Pregnant Women/Adolescents

	NEC		No NEC			Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Abel 2000	100	176	133	166	24.4%	0.71 [0.61, 0.82]
Adhikari 2009 1 (1)	13	73	27	70	12.2%	0.46 [0.26, 0.82]
Adhikari 2009 3 (2)	13	71	27	70	12.2%	0.47 [0.27, 0.84]
Gadallah	16	50	23	50	13.9%	0.70 [0.42, 1.15]
Hunt 1976	1	117	3	98	1.4%	0.28 [0.03, 2.64]
Ndiaye 2009	55	100	66	100	22.3%	0.83 [0.66, 1.04]
Senanayake 2010	15	107	52	111	13.7%	0.30 [0.18, 0.50]
Total (95% CI)		**694**		**665**	**100.0%**	**0.58 [0.44, 0.76]**
Total events	213		331			

Heterogeneity: Tau² = 0.07; Chi² = 19.46, df = 6 (P = 0.003); I² = 69%

Test for overall effect: Z = 3.89 (P < 0.0001)



(1) nutrition education/IFA compliance monitoring vs control

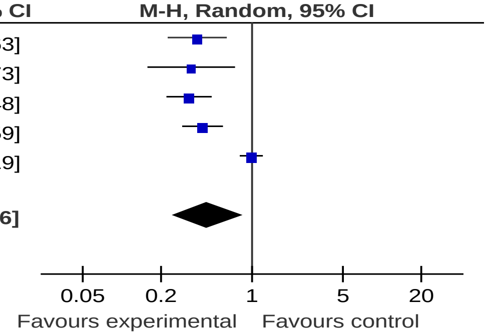
(2) nutrition education vs control

Figure3f: Effect of Nutrition Education and Counseling on Risk of Anemia in Non Pregnant Women/Adolescents

	Experimental		Control			Risk Ratio	Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**M-H, Random, 95% CI**
Alaofe 2009	11	34	29	34	19.6%	0.38 [0.23, 0.63]	
Creed-Kanashiro 2000 (1)	8	61	15	39	16.9%	0.34 [0.16, 0.73]	
Gopaldas 2002 GJ (2)	21	80	64	80	20.7%	0.33 [0.22, 0.48]	
Gopaldas 2002 iddli (3)	24	72	64	80	21.0%	0.42 [0.30, 0.59]	
Meenakshi 2008 (4)	40	51	54	68	21.9%	0.99 [0.82, 1.19]	
Total (95% CI)		**298**		**301**	**100.0%**	**0.45 [0.24, 0.86]**	
Total events	104		226				

Heterogeneity: Tau² = 0.47; Chi² = 58.08, df = 4 (P < 0.00001); I² = 93%

Test for overall effect: Z = 2.44 (P = 0.01)



(1) Adjusted for clustering (DE= 1.0, ICC= 0.000)

(2) GJ: Gooseberry juice

(3) Iddli

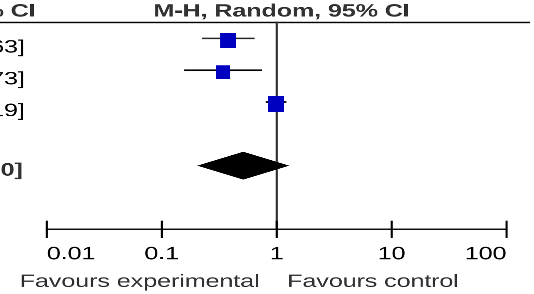
(4) Adjusted for clustering (DE= 1.0, ICC= 0.000)

Figure3g: Effect of Nutrition Education and Counseling Only on Risk of Anemia in Non Pregnant Women/Adolescents

	Experimental		Control			Risk Ratio	Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**M-H, Random, 95% CI**
Alaofe 2009	11	34	29	34	33.5%	0.38 [0.23, 0.63]	
Creed-Kanashiro 2000 (1)	8	61	15	39	29.7%	0.34 [0.16, 0.73]	
Meenakshi 2008 (2)	40	51	54	68	36.8%	0.99 [0.82, 1.19]	
Total (95% CI)		**146**		**141**	**100.0%**	**0.52 [0.21, 1.30]**	
Total events	59		98				

Heterogeneity: Tau² = 0.58; Chi² = 24.04, df = 2 (P < 0.00001); I² = 92%

Test for overall effect: Z = 1.39 (P = 0.16)



(1) Adjusted for clustering (DE= 1.0, ICC= 0.000)

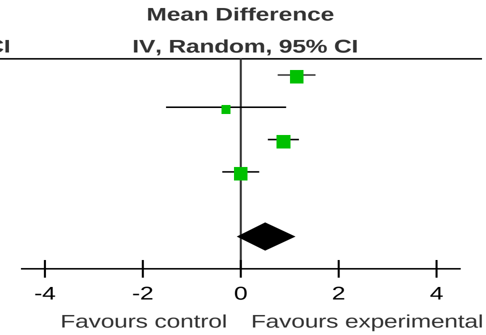
(2) Adjusted for clustering (DE= 1.0, ICC= 0.000)

Figure3h: Effect of Nutrition Education and Counseling on Mean Hb in Pregnant Women/Adolescents

	Experimental			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Gadallah	12.24	1.05	50	11.1	0.8	50	28.3%	1.14 [0.77, 1.51]
Kafatos 1989 (1)	11.4	8.9	232	11.7	2.2	133	14.0%	-0.30 [-1.50, 0.90]
Senanayake 2010	11.97	0.9	107	11.1	1.3	111	29.3%	0.87 [0.57, 1.17]
Sun 1990	10	0.9	80	10	1.2	63	28.4%	0.00 [-0.36, 0.36]
Total (95% CI)			**469**			**357**	**100.0%**	**0.54 [-0.07, 1.14]**

Heterogeneity: Tau² = 0.30; Chi² = 24.19, df = 3 (P < 0.0001); I² = 88%

Test for overall effect: Z = 1.74 (P = 0.08)



(1) Adjusted for clustering (DE= 1.0, ICC= 0.000)

Figure3i: Effect of Nutrition Education and Counseling on Mean Hb in Pregnant Women/Adolescents in LMIC

	Experimental			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Gadallah	12.24	1.05	50	11.1	0.8	50	27.9%	1.14 [0.77, 1.51]
Senanayake 2010	11.97	0.9	107	11.1	1.3	111	42.6%	0.87 [0.57, 1.17]
Sun 1990	10	0.9	80	10	1.2	63	29.5%	0.00 [-0.36, 0.36]
Total (95% CI)			**237**			**224**	**100.0%**	**0.69 [0.50, 0.88]**

Heterogeneity: Chi² = 21.67, df = 2 (P < 0.0001); I² = 91%

Test for overall effect: Z = 6.99 (P < 0.00001)

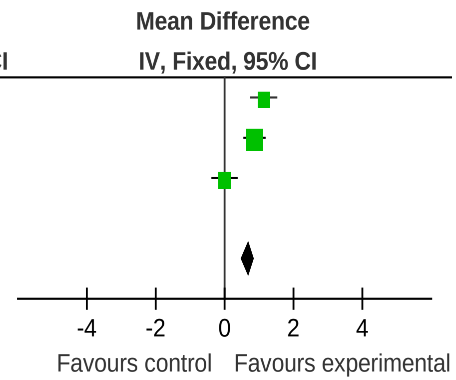
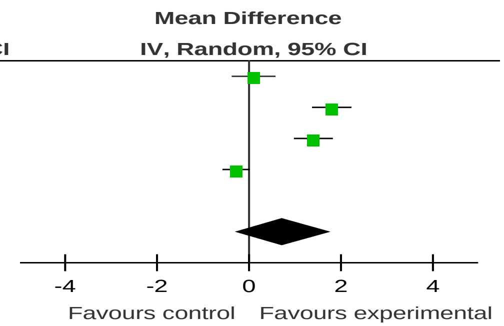


Figure3j: Effect of Nutrition Education and Counseling on Mean Hb in Non Pregnant Women/Adolescents

	Experimental			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Amani 2006	13.5	0.9	30	13.4	0.9	30	24.7%	0.10 [-0.36, 0.56]
Gopaldas 2002 GJ (1)	12.7	1.1	80	10.9	1.5	80	24.9%	1.80 [1.39, 2.21]
Gopaldas 2002 iddli (2)	12.3	1	72	10.9	1.5	80	24.9%	1.40 [1.00, 1.80]
Meenakshi 2008 (3)	10.46	1.3	133	10.74	1.1	177	25.5%	-0.28 [-0.55, -0.01]
Total (95% CI)			**315**			**367**	**100.0%**	**0.75 [-0.29, 1.79]**

Heterogeneity: $Tau^2 = 1.09$; $Chi^2 = 92.30$, $df = 3$ ($P < 0.00001$); $I^2 = 97\%$

Test for overall effect: $Z = 1.41$ ($P = 0.16$)



(1) GJ: Gooseberry Juice

(2) Iddli

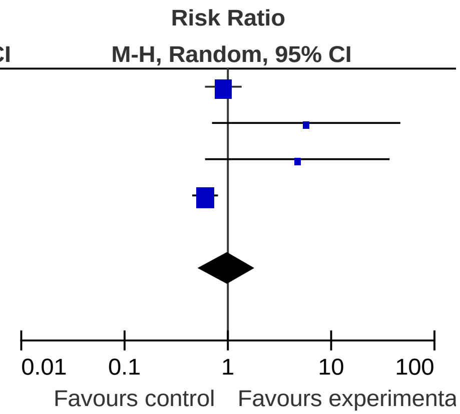
(3) Adjusted for clustering (DE= 1.0, ICC= 0.000)

Figure3k: Effect of Nutrition Education and Counseling on Iron Deficiency in Pregnant Women/Adolescents

	Experimental		Control			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Abel 2000	34	101	32	86	40.4%	0.90 [0.61, 1.33]
Hunt 1976	7	117	1	96	7.7%	5.74 [0.72, 45.87]
Kafatos 1989 (1)	9	84	1	44	8.0%	4.71 [0.62, 36.02]
Senanayake 2010	43	107	74	111	44.0%	0.60 [0.46, 0.79]
Total (95% CI)		**409**		**337**	**100.0%**	**0.99 [0.53, 1.86]**
Total events	93		108			

Heterogeneity: $Tau^2 = 0.22$; $Chi^2 = 11.09$, $df = 3$ ($P = 0.01$); $I^2 = 73\%$

Test for overall effect: $Z = 0.02$ ($P = 0.99$)



(1) Adjusted for clustering (ICC=0.05)

Figure3l: Effect of Nutrition Education and Counseling on Mean Serum Iron in Pregnant Women/Adolescents

	Experimental			Control				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Kafatos 1989	115.14	8.32	118	134.64	11.4	61	33.7%	-19.50 [-22.73, -16.27]
Sachdeva 1994	51.9	6.1	30	38.3	5	30	33.7%	13.60 [10.78, 16.42]
Sun 1990	140	30	80	140	20	63	32.6%	0.00 [-8.22, 8.22]
Total (95% CI)			**228**			**154**	**100.0%**	**-1.98 [-26.32, 22.36]**

Heterogeneity: $Tau^2 = 455.41$; $Chi^2 = 228.72$, $df = 2$ ($P < 0.00001$); $I^2 = 99\%$

Test for overall effect: $Z = 0.16$ ($P = 0.87$)