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Iodine nutrition among pregnant women in B.M.C

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IODINE NUTRITION AMONG PREGNANT WOMEN IN B.M.C

by

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IODINE NUTRITION AMONG PREGNANT WOMEN IN B.M.C

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ABSTRACT

Iodine is an essential nutrient for thyroid hormone production. Due to inadequate public health measures, mild-moderate iodine deficiency has become a re-emerging problem in many developed countries in the past decades. Insufficient consumption of iodine in pregnancy may lead to brain damage and a lower Intelligence Quotient (IQ) in children in comparison to children of mothers with adequate intake. Recent National Health and Nutrition Examination Surveys (NHANES) data have shown that even though the non-pregnant United States (U.S) population has adequate iodine intake, U.S pregnant women are currently mildly iodine deficient, with median urinary iodine concentrations (UIC) being 129 μg/L. In 2004 pregnant women who attended the Boston Medical Center (BMC) Antenatal Clinic were also mildly iodine deficient, with median UIC of 149 μg/L. These values were higher than the NHANES median UIC (129 μg/L) Due to national trends of mild-moderate iodine deficiency among pregnant women, and since in 2011 the American Thyroid Association recommended that prenatal vitamins contain 150 μg of iodine, in this study we aimed to determine if the iodine status among the BMC pregnant women has changed. We also aimed to assess consumption of iodine-containing foods, knowledge regarding iodine nutrition, and frequency of use of iodine-containing prenatal vitamins.

We conducted a cross-sectional study targeting 125 women living in the Boston area attending the BMC Antenatal Clinic. To date, 61 women have been enrolled.

Participants provided urine samples, and completed questionnaires about their recent food intake and demographic characteristics. The participants' mean age was 31 ± 6.7 years and their median UIC was 145.5 µg/L (range 17.5 µg/L- 886 µg/L). As expected, UIC was positively associated with iodine supplement intake and recent consumption of iodine-rich foods (milk cheese) ($p \leq 0.0001$ for each), although these associations were not significant in multivariate analysis. No associations were observed between UIC and other factors such as age, race, education, use of multivitamins containing iodine in the past 24 hours, and whether health providers discussed iodine nutrition, possibly due to a small sample size.

Our results indicated that the iodine status of pregnant women attending B.M.C remained mildly iodine deficient in the past decade despite the recommended measures to increase the iodine content in multivitamins. In our sample, 52.5% of the pregnant women who attended BMC were mildly iodine deficient with median UIC <150 µg/L. Thus half of the pregnant women are at risk of brain damage occurring to their infant. It is important that follow up studies are done to determine the neurodevelopment of these children, as they grow older. Also since the intake of multivitamins containing iodine and consumption of dairy foods was positively associated with higher UIC levels, further measures need to be undertaken to ensure that all prenatal vitamins have 150 µg of iodine, and that pregnant women have higher dairy consumption, in order to increase their iodine intake. As well, larger regional and national studies should be undertaken to better understand current iodine status and sources of iodine among pregnant women.

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INTRODUCTION

Iodine deficiency, a Major Public Health Problem

Iodine is an essential nutrient that is necessary for the synthesis of thyroid hormone, which is necessary for many metabolic processes and for development of the central nervous system.[1] With few exceptions, most foods contain little iodine, unless iodine has been added during processing. Some foods that are naturally high in iodine are seafoods, such as fish, shellfish, and seaweed. In the United States (U.S), due to iodine fortification of animal foods and iodine added in food processing, milk, eggs, and some bread products are good sources of iodine nutrition.

Iodine deficiency is a major public health problem in many regions.[2] Iodine deficiency occurs when iodine intake falls below recommended levels. This occurs in many parts of the world due to erosion of soils in riverine areas, from to loss of vegetation, overgrazing by livestock, or tree cutting. All these processes lead to a loss of iodine in soil, and foods grown in these areas lack iodine.[4] When iodine intake falls below recommended levels, the thyroid may no longer synthesize sufficient amounts of thyroid hormone. The resulting low levels of thyroid hormone in the blood may damage the developing brain and cause other harmful effects known as "iodine deficiency disorders." Goiter is a frequent manifestation of iodine deficiency. Globally, iodine deficiency is the most common preventable cause of intellectual impairment.[3] Severe iodine deficiency in pregnancy causes spontaneous abortion, stillbirth, congenital anomalies, and perinatal mortality. Severe maternal iodine deficiency may result in cretinism in offspring, a syndrome of mental deficiency with mutism, spastic diplegia, squint, hypothyroidism, short stature, and increased infant mortality. In adults, iodine deficiency causes impaired mental function and greater susceptibility to iodine-induced hyperthyroidism, while in children and adolescents it also causes delayed physical development.[4]

Even though severe iodine deficiency does not occur in developed countries such as the United Kingdom (UK), U.S, and Australia, mild-moderate deficiency has reemerged as an important public health concern. This is due to insufficiently cohesive public health policies to eradicate iodine deficiency. In the U.S starting in the 1920's, iodine deficiency was eliminated through voluntary salt iodization. Later, the use of iodophors by the dairy industry in the U.S, UK, and Australia, and the use of iodate conditioners in bread manufacturing in the U.S ensured adequate iodine intake.[5] Since the iodization of these foods is not a required or regulated process, there is no assurance that the population will continue to obtain adequate iodine from these processed foods.[1] In past years there has been a reemergence of mild-moderate iodine deficiency due to changes in the use of iodophors in dairy production in Australia, decreases in the use of iodate conditioners by U.S bread manufactures, and decreases in iodized salt and milk consumption.[5,6,3] This reemergence of mild-moderate iodine deficiency is of greatest concern to populations that are at highest risk, for example pregnant and lactating women.

Variation in Iodine Requirements and in Iodine Status in the U.S Population.

The Food and Nutrition Board (FNB) of the Institute of Medicine (IOM) have developed age-specific recommended dietary allowances (RDA) for iodine intake for specific age groups and for pregnant and lactating women. The average daily uptake and release (turnover) of iodine in the body is used to estimate the average requirement of iodine, provided that the subjects have adequate iodine status and are euthyroid. Turnover studies are based on the intravenous administration of ^{131}I, and the calculation of thyroid iodine accumulation from measurements of thyroidal and renal radioiodine clearances, urinary iodine excretion, and fractional thyroidal release rate.[13] Based on these measurements the IOM set the RDA for iodine at 90 µg/day for children 6-11 years and 150 µg/day for adults. For pregnant women, the RDA increases to 220 µg/day.[15] The World Health Organization (WHO) recently increased the recommended iodine intake for pregnant women from 200 to 250 µg/day, and suggested that a median urinary iodine concentration (UIC) of 150–249 µg/L indicates dietary iodine sufficiency in this group.[13]

National Health and Nutrition Examination Surveys (NHANES) data showed that the general U.S population in 2007–2008 was nutritionally iodine sufficient based on a median UIC of 164 µg/L, and that 8.8% of individuals had a UIC < 50 µg/L.[19] These findings suggested that the dietary intake of the general population has remained stable since 2000. Nevertheless, there are variations in the status of dietary iodine sufficiency among different groups in the population. For example, children aged 6–11 years are slightly above the requirement for adequate iodine nutrition, with a median UIC of 239 µg/L. There are also differences in iodine status among different races. Non–Hispanic black Americans continue to have a lower median UIC (137μg/L) than non–Hispanic white (168 μg/L) and Mexican-Americans (174μg/L).[19] These differences among racial/ethnic groups are likely due to variations in their dietary intake.

Pregnant Women have Higher Iodine Requirements.

Fetal thyroid hormone production does not occur until mid-gestation. Thus, in early pregnancy the fetus is dependent on maternal thyroxine for normal brain development, and the fetus continues to benefit from maternal iodine throughout gestation. Therefore, maternal iodine intake is a critical factor for fetal neurodevelopment. Maternal iodine deficiency can range from severe iodine deficiencies, which can cause cretinism, to mild-moderate iodine deficiencies, which is associated with lower brain function in children in comparison to children of mothers with adequate gestational iodine intake.[7, 8]

Pregnant women require more iodine than non-pregnant adults because maternal thyroid hormone production increases by 50% starting early in the first trimester of pregnancy. Increased levels of estrogen during pregnancy reduce the hepatic clearance of thyroxine-binding globulin (TBG), which results in increased serum levels of TBG. Higher levels of TBG lead to an increase in the amount of bound thyroid hormone, which, in turn, increases total triiodothyronine (T3) and T4 levels in comparison to those found in non-pregnant women.[11] In addition, human chorionic gonadotropin (hCG) stimulates thyroidal TSH receptors, and when hCG levels are high in the first trimester of pregnancy they increase thyroid hormone synthesis and release.[10] Another reason for increased iodine requirements in pregnancy is the increase in maternal glomerular filtration rate (GFR). Because iodine is passively excreted, increased renal GFRs in pregnancy result in increased losses of ingested iodine in the urine.[11] During normal pregnancy, GFR increases within the first month after conception, peaking by the end of the first trimester at approximately 40-50% above pre-pregnant levels.[34] Thus urinary iodine excretion in the 2nd and 3rd trimester is lower than the first trimester. Finally, during the second half of pregnancy fetal thyroid hormone production requires iodine as well.[12] For these reasons the FNB of the IOM and the WHO have recommended higher intakes of iodine for women who are pregnant than for non-pregnant adults (Table 1).[13]

Effects of Mild-Moderate Iodine Deficiency in Pregnant Women

When pregnant women do not meet recommended iodine intake requirements there may be deleterious results for fetal development. Even mild-moderate iodine deficiency in pregnant women is associated with mental impairments in offspring. Bath et al. assessed the effects of inadequate iodine status among pregnant women in UK, a mildly iodine deficient country, on cognitive outcomes in children. After adjustment for confounders, children of women with an iodine-to-creatinine ratio of less than 150 μg/gm creatinine during gestation were more likely to have scores in the lowest quartile for verbal Intelligence Quotient (IQ), reading accuracy and reading comprehension, compared to children of mothers with ratios of 150 μg/g or more.[14] In another longitudinal follow up study done by Hynes et al. in Australia, children whose mothers had UIC <150 μg/L during gestation had reductions of 10.0% in spelling 7.6% in grammar and 5.7% in English-literacy performance compared with children whose mothers' UICs were ≥150 μg/L.[8] Therefore, even mild-moderate iodine deficiency should be treated as an important public health issue.

Table 1. WHO and IOM Daily Iodine Daily Consumption Recommendations.

Institute of Medicine[15]		World Health Organization Council [13]	
Age	µg/day	Age	µg/day
1-8 years	90	0-5 years	90
9-13 years	120	6-12 years	120
>13	150	>12 years	150
Pregnancy	220	Pregnancy	250
Lactation	290	Lactation	250

Urinary Iodine Concentrations are used to Assess Iodine Status

UIC can be used to assess iodine nutrition in populations. The WHO recommends a desirable median UIC for non-pregnant populations within the range of 100- 199 µg/L. It defines nutritional iodine sufficiency for a population by median UIC as follows: excessive iodine intake, >300 µg/L; more than adequate intake, 200–299 µg/L; adequate intake, 100–199 µg/L; mild iodine deficiency, 50–99 µg/L; moderate iodine deficiency, 20–49 µg/L; severe iodine deficiency, <20 µg/L (Table 2). The median UIC during pregnancy should range between 150 and 249 µg/L, whereas median UIC values greater than 250 µg/L are considered more than adequate those above 500 µg/L are considered excessive, and those below 150µg/L are considered insufficient. Ranges for mild, moderate, and severe iodine deficiency has nor been defined for pregnancy (Table 2).[16]

Because more than 90% of dietary iodine eventually appears in the urine, UIC is a sensitive indicator of recent iodine intake (hours). Due to substantial day-to day variability, UIC cannot be used as an individual biomarker.[17] Because it is impractical to collect 24-h samples in field studies, UIC can be measured in spot urine specimens from a representative sample of the target group and expressed as the median in µg/L. Although the median UIC does not provide direct information on thyroid function, a low value suggests that a population is at higher risk of developing thyroid disorders.[17] This method of assessing iodine status has been used in the U.S NHANES surveys for the past 40 years.[18]

Table 2: WHO's Recommendations on Population Urinary Iodine Values and Iodine Nutrition[16]

Median Urinary Iodine Concentration µg/L	Iodine Nutrition	Median Urinary Iodine Concentration µg/L	Iodine Nutrition
Non- Pregnant		**Pregnant**	
<20	Severe deficiency	**<150**	Insufficient
20-49	Moderate deficiency		
50-99	Mild deficiency		
100-199	Optimal	**150-249**	Optimal
200-299	More than adequate	**250-499**	More than adequate
>300	Possible excess	**>500**	Possible excess

UIC in U.S Pregnant and Non-Pregnant Women over the years has declined.

NHANES data have shown that the iodine status of the U.S population has changed over the past four decades. In NHANES I, performed in the years from 1971-1974, the median UIC for non-pregnant women was 293 ± 10 µg/L. These values were above WHO-recommended levels. However, by the time of NHANES III in 1988-1994, the median UIC dropped to 127 ± 4 µg/L for non-pregnant women, a value in the optimal range (Table 2),[18] In the NHANES survey from 2005-2010, the median UIC value remained at an optimal level, 164 μg/L, for non- pregnant adults (Figure 1).

Although dietary iodine intake in the U.S has remained sufficient overall, there have been growing concerns in recent years about mild iodine deficiency among U.S. pregnant women, whose UIC has recently fallen below optimal levels. [20] In NHANES I, pregnant women had a median UIC of 373 ± 35 μg/L. This value exceeded the WHO recommended levels. At the time of NHANES III, the median UIC for pregnant women had fallen below recommended levels, to 141 ± 14 μg/L.[18] The most recent NHANES data from 2005-2010 demonstrated that median UIC for pregnant women was 129 μg/L, which is less than adequate.[24] (Figure1). The first study to demonstrate marginal iodine nutrition in pregnant U.S. women was published by our group in 2004.[21] Among 100 pregnant patients from Boston Medical Center (BMC), the median UIC was 149 μg/L. Based on national data presented above, we suspect that the iodine status of BMC pregnant women may have worsened in the past decade.

Further Measures need to be Taken to Ensure Adequate Intake of Iodine

Ensuring adequate iodine intake is an important public health goal. The American Thyroid Association (ATA), together with other medical societies, recommends 150 μg daily iodine supplementation during pregnancy and lactation.[22] The ATA also recommends that all prenatal supplements should contain 150 μg iodine and that the iodine nutrition of the U.S population should be monitored at an ongoing basis.[35] Based on these recommendations, in January 2015, the Council for Responsible Nutrition, the U.S trade group for dietary supplement manufacturers, advised their constituents that all prenatal vitamins should contain 150 μg of iodine and that this should be implemented within 12 months.[36] It is not yet known how broadly these recommendations have been adopted.

Study Aims: Assess Current Iodine Nutrition in Pregnant-women in the Boston Area.

In light of national trends and likely increases in the iodine content of U.S prenatal multivitamins, the current iodine status of Boston-area pregnant women is unknown. In our study, we sought to determine whether the iodine status of patients at the BMC antenatal clinic has changed in the past decade. We aimed to target a more diverse population and a larger regional sample in comparison to previous studies done in pregnant women. While there are many national studies looking at iodine status, it is also important to conduct studies capable of identifying local and regional differences among pregnant women's iodine nutrition.

In order to assess the current urinary iodine status of BMC pregnant women, we planned a cross-sectional observational study in 125 pregnant women seeking routine prenatal care from the BMC Obstetrics Clinic. We aimed to determine their iodine status by measuring median UIC. We hypothesized that there may be educational gaps regarding iodine nutrition in pregnancy and that pregnant women may not be receiving enough information regarding the importance of iodine. We also hypothesized that participants with a higher consumption of foods with high iodine content and use of multivitamins with iodine would have higher median UIC values. This study was intended to inform future regional and national efforts to ensure adequate iodine nutrition for pregnant U.S. women.

Figure 1: NHANES UIC data 1971-2010.[18,19,24] National trends over the years of the median Urinary Iodine Concentrations (UIC) among pregnant women and non-pregnant women. Median UIC in Non-Pregnant Women: NHANES I (1971-1974) = 293 ± 10 μg/L, NHANES III (1988-1994)= 127 ± 4 μg/L, NHANES (2005-2010)= 164 μg/L. Median UIC in Pregnant Women: NHANES I (1971-1974) = 373 ± 35 μg/L, NHANES III (1988-1994)= 141 ± 14 μg/L, NHANES (2005-2010)= 129 μg/L.

METHODS

This study targeted 125 pregnant women who attended the antenatal clinic at BMC and were age 18 years or older. To date, 61 subjects have been recruited and the study is currently ongoing. We targeted a sample size of 125 because Andersen et al. have determined that this is the number of spot urine samples needed to estimate the iodine level in a population with 95% confidence within a precision range of ± 10%.[29]

Participants in this study must speak Spanish or English and must be able to provide informed consent. Participants can be of any gestational age, but must be carrying a singleton pregnancy. Carrying more than one fetus influences the physiological iodine requirements and other hormonal changes in the mother that could affect the UIC. Participants with a history of thyroid disease or who are taking thyroid hormone, anti-thyroid medication, or amiodarone were also excluded. In addition, participants who have undergone radiologic studies with iodinated intravenous contrast agents within the previous 6 months were excluded, because the iodine could still be present in their system, affecting the UIC.

Participants were asked to provide information including maternal age, race/ethnicity, and family history of thyroid disorder. Gestational age was determined from the electronic medical record, defined by the last menstrual period or by second trimester ultrasound dating if the two estimates differed by >10 days. Participants were asked if they were taking iodine-containing dietary supplements, and were asked to provide the brand and frequency of use of any prenatal or other multivitamins. If a participant did not know how much iodine her multivitamin contained, she was contacted within 24 hours so that she could verify the iodine content of her supplements. The survey also included questions to investigate the previous 24- hours' intake of foods known to have high iodine content.

Laboratory Methods

Spot urine iodine samples were obtained from all participants. Laboratory measurements were performed at the Boston University Iodine and Thyroid Function Test Research Laboratory. All urine samples are stored at -30° Celsius prior to iodine analysis. UIC was measured spectrophotometrically by modifying the method of Benotti et al.[23] Urinary iodine was measured by utilizing the reduction-oxidation reaction between ceric and arsenite catalyzed by iodide.[32]

All the urinary samples and control materials were thawed at room temperature. The urinary samples were mixed well before measurement. With every 12 urinary samples, 2 urinary controls (UICs of 70 μg/L and 238 μg/L) were also measured together with 4 potassium iodate standards (0.02 μg/ml, 0.04 μg/ml, and 0.06μg/ml, and one blank, 0.0 μg/ml). Aliquots of 0.2 ml of the urine sample were transferred to centrifuge test tubes to which 3.0 ml of chloric acid was added. Using a sand bath heater, the urinary samples, controls, and standards were digested for approximately 1 hour at 105-110° Celsius. After the formation of chromium trioxide crystals, digestion was complete and the test tubes were allowed to cool to room temperature. After cooling 2.1 ml of arsenious acid was added to each test specimen. From each test prepared specimen 2.0 ml were transferred to the autoanalyzer sample cups. These were then measured spectrophotometrically with a Technicon Autoanalyzer instrument. The UIC of the specimens were calculated from the slope and the Y-intercept of the standard curve, and the final UIC was expressed as µg/L. This procedure was run twice for each urinary sample with an inter coefficient of variation of 8.0%.

Statistical Analysis:

Statistical analysis were performed using SAS (SAS Institute, Cary, NC). ANOVA, with Tukey post-hoc comparisons, was used to assess for between-group differences in median UIC levels. Spearman's rank correlation coefficient was used to assess univariate associations between continuous variables. Multivariable linear regression models were used to determine significant predictors of UIC adjusted for important covariates: gestational age and race. These covariates were selected either because they were associated with UIC in univariate analysis in this data set or because they had been associated with UIC in NHANES analysis.

RESULTS

Demographic Data

Subjects' mean age was 31.0 ± 6.9 years, ranging from 18 to 45 years. The mean gestational age was 182.2 ± 64.3 days, ranging, from 58 days to 275 days. The majority of the participants in the study were Black, Non- Hispanic accounting for 24 (39.3%) of the women, while 13 (21.3%) of the participants were white, 15 (24.6%) were Hispanic, and 6 (9.8%) were Asian. A total of 25 (41.0%) of participants had a high school degree, while 13 (21.3%) had attended a 2-year college, 10 (16.4 %) had a 4-year college degree, and 7 (11.5%) had a graduate degree. A total of 32 (53.5%) of participants were single.

The majority of the participants (49, 80.0%) had no family history of thyroid disease. A total of 49 (80.0%) reported taking multivitamins/prenatal vitamins, with only 30 (62.5%) of them having taken the vitamins in the past 24 hours. Nevertheless, 88.0% of women reported that they did not consider iodine content when selecting their multivitamins. Almost half of participants (29, 48.0%) were in their 3rd trimester of pregnancy, 38 (46.7%) were in their 2nd trimester, and only 3 (5.0%) were in their 1st trimester. The majority of the participants (44, 84.0%) reported that their physician did not discuss iodine nutrition with them either prior to or during their pregnancies (Table 2).

Consumption of High-Iodine Food

The questionnaire contained questions regarding the participants' intake of iodine rich foods in the past 24-hours, and the quantity of these foods (see Appendix). This was not a validated FFQ. In response to survey questions, 24 (67.0%) of women reported using iodized salt for cooking, but 40 (65.6%) of them did not specifically look for iodized salt when purchasing table salt. Most subjects reported eating relatively few high-iodine foods. None of the participants ate any seaweed, and the majority did not consume any frozen yogurt (98.4%), freshwater fish (96.7%), shellfish (88.5%), bagels (91.8%), or ice-cream (70.5%). Iodine-containing foods that were frequently consumed included milk, cheese, eggs and bread (Table 3).

UIC Measurements

The median UIC for the 59 urine samples collected was 145.5 µg/L (range 17.5 µg/L to 886 µg/L). Ten percent of the participants had UICs <50µg/L, while 32.2% had UICs <100µg/L, 52.5% had UICs <150µg/L, and 28.8% had UICs >250µg/L (Figure 3). The median UIC falls just below the recommended range for pregnant women. UIC values with each trimester of pregnancy did not achieve statistical significance (p = 0.62) most likely due to the small sample size, especially in the 1st trimester: in the 1st trimester (n=3) the median UIC was 55.5 µg/L, while in the 2nd trimester the median UIC was 135.7 µg/L (n= 26), and in the 3rd trimester the median UIC was 169.5 µg/L (n=31). Nevertheless when looking at gestational age, considered a continuous variable, an increasing trend with UIC was observed even though the correlation did not reach statistical significance (p=0.09, r=0.22). The UIC distribution in the 1st trimester was highly variable (inter -quartile range IQR of 269.5 µg/L), while for the 2nd trimester the IQR was 137.5 µg/L, and for the 3rd trimester it was 88.5 µg/L (Figure 4). No correlation was observed between maternal age and UIC (p=0.99, r=0.0001).

Univariate ANOVA analysis

In order to observe if any of the variables affected UIC, Univariate ANOVA analysis was used. UIC did not vary by educational level (p=0.6) or race (p= 0.3). UIC did not vary based on whether women's health care providers had discussed iodine nutrition prior to or during pregnancy (n=59, p=0.4). Having a family history of thyroid disease was not associated with UIC values (p=0.9). We wanted to see if taking prenatal vitamins containing iodine affected UIC, and univariate analysis showed that the iodine content of prenatal multivitamins was significantly positively associated with UIC values (p<0.0001). The six participants taking multivitamins without any iodine content had a median UIC of 64.8 µg/L, while those taking multivitamins containing 150 µg iodine (n=35) had a median UIC of 138.5 µg/L, and the single participant taking a daily multivitamin containing 370 µg iodine had a UIC of 886 µg/L. Nevertheless UIC did not vary significantly with self-reported consumption of the multivitamin within 24 hours (p=0.16). We also wanted to know if consumption of food high in iodine affected UIC, and if so how much. Through ANOVA analysis UIC did not vary with iodized salt use (p=0.95), nor did it vary with the consumption of eggs (p=0.6) or bread (p=0.7). UIC was associated with both milk and cheese intake (p<0.0001 for each (Figure 2)).

Multivariable Analysis

In order to see how multivitamins with iodine content, and milk consumption were predictors of UIC, the multivariate analysis was adjusted for gestational age and race known to be variables that influence UIC. In adjusting for these variables use of multivitamins with iodine content (p=0.87), and milk consumption (p=0.59) were not predictive of UIC.

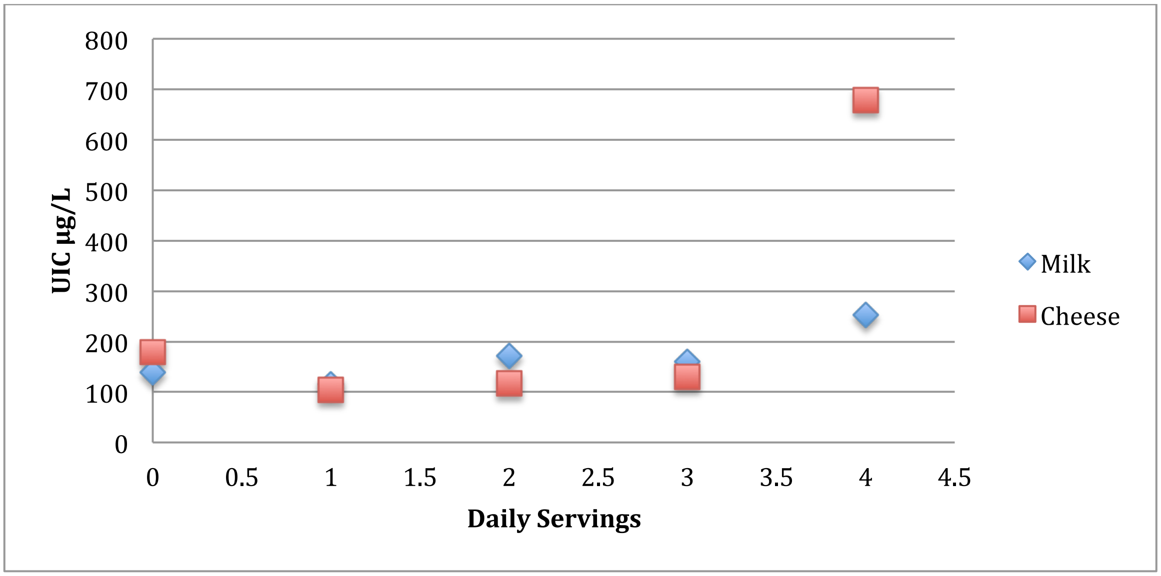

Figure 2: Median UIC by dairy consumption (p=0.0001). Post-hoc Tukey analysis comparisons, was used to assess for between-group differences in median UIC levels for each serving of milk and cheese.

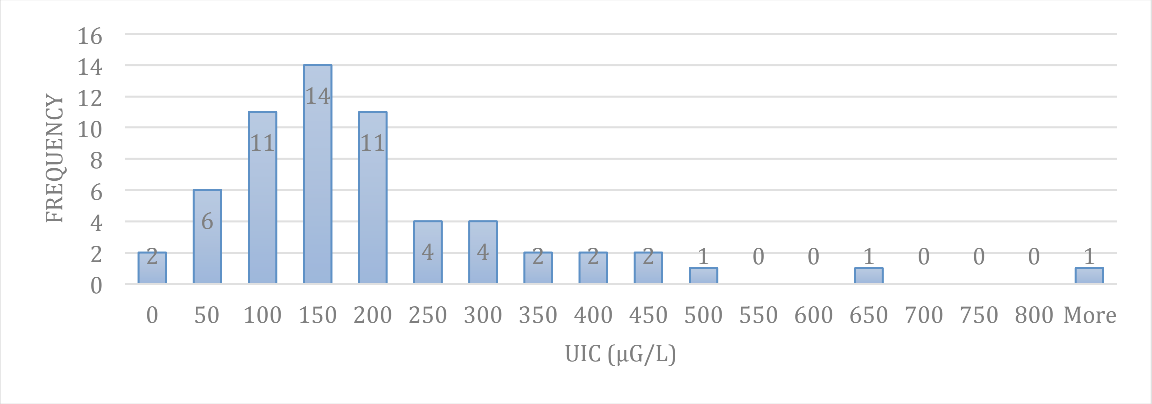

Figure 3: Frequency of Urinary Iodine Concentrations among Participants. Histogram analysis of UIC on BMC pregnant women (n=59). 10% of the participants UICs <50µg/L, 32.2% had UICs <100µg/L, 52.5% had UICs <150µg/L, and 28.8% had UICs >250µg/L.

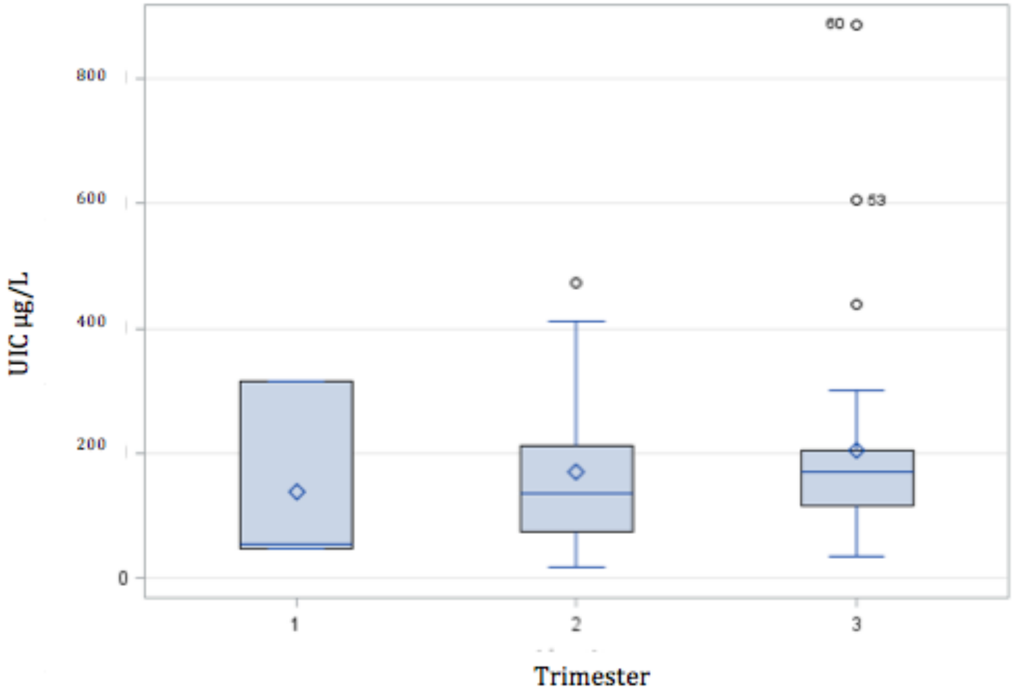

Figure 4: UIC distribution across Trimesters. Box-plot analysis looking at inter-quartile ranges (IQR) among trimesters: 1st trimester IQR=269.5 µg/L, 2nd trimester IQR =137.5 µg/L, and 3rd trimester IQR=88.5 µg/L.

Table 3. Participant Characteristics (n= 61)

Age, years (mean ± SD)	**31.03 ± 6.7**
Ethnicity/Race n(%)	
White (non- Hispanic)	13 (21.3%)
Black (non-Hispanic)	24 (39.3%)
Hispanic	15 (24.6 %)
Asian	6 (9.8 %)
Other	3 (4.9%)
Education level n (%)	
Less than high school	3 (4.9 %)
High School	25 (41%)
Vocational Trade School	3 (4.9%)
2-year college	13 (21.3 %)
4- year college	10 (16.4 %)
Graduate school	7 (11.5 %)
Marital Status n (%)	
Single	32 (52.5 %)
Married,	28 (45.9 %)
Other	1 (2 %)
Family History of Thyroid Disease n (%)	11 (18.3%)
Yes	49 (80.3%)
No	1 (1.6 %)
Don't know	
Multivitamins/ Prenatal Vitamins n (%)	
Yes	49 (80.3%)
No	12 (19.7%)
Iodine Content Present in Vitamins n (%)	
0 mcg	6 (13.6 %)
150 mcg	37 (84.1%)
370 mcg	1 (2.3%)
Vitamin taken in past 24 hours n (%)	
Yes	30 (62.5%)
No	18 (37.5%)

Look for Iodine Content when taking Vitamin n (%)	
Yes	6 (12.0 %)
No	44 (88.0 %)
Regular Salt Use n (%)	
Yes	42 (68.9%)
No	19 (31.1%)
Salt use in the previous 24 hours n (%)	
Yes	36 (59.0%)
Iodized	24
Non Iodized	3
Unknown Iodine Content	9
No	25 (41.0%)
Doctor discussed iodine n (%)	
Yes	10 (16.4%)
No	51 (83.6%)
Knowledge of why iodine is added to salt? n (%)	
Yes	18 (29.5%)
No	43 (70.5%)
Do you Look for Iodized salt? n (%)	
Yes	20 (32.8 %)
No	40 (65.6 %)
Don’t buy Salt	1 (1.6%)

Table 4. Participants' Self Reported Food Consumption in the past 24 hours (n=61)

Daily Servings	**0 (n,%)**	**1**	**2**	**>3**
Food				
Milk	22(37.7)	12	20	7
Cheese	28 (45.90)	15	8	10
Yogurt	38 (62.3)	17	5	1
Ice Cream	43 (70.5)	9	5	4
Frozen Yogurt	59 (98.3)	1	0	0
Eggs	28 (45.9)	12	15	6
Bread	16 (26.2)	8	24	13
Bagels	56 (91.8)	2	2	1
Other Bread type	50 (82)	7	1	3
Freshwater fish	57 (93.4)	1	1	2
Saltwater fish	49(80.3)	9	2	1
Shellfish	54 (88.5)	5	2	0
Seaweed	61 (100)	0	0	0

DISCUSSION

Iodine deficiency is an important global public health problem. Although the U.S population overall has been iodine sufficient for decades, in the last 10 years several surveys, including one conducted at BMC, have demonstrated that mild iodine deficiency has re-emerged among U.S pregnant women. Our preliminary data in 61 pregnant women indicate that they are mildly iodine deficient, with a median UIC of 145.5 μg/L. These results are similar to the results of a 2004 study in 100 pregnant women at BMC who had a median UIC of 149 μg/L.[21] The median UIC in our cohort was higher than the national median from NHANES 2005-2010, which was 129 μg/L.[24] Nevertheless, our cohort was mildly iodine deficient (Table 2).

There is a different racial distribution in NHANES 2005-2010 data in comparison to our study. While in NHANES the majority of the participants, 45.6%, were non-Hispanic white, 20.3% were non-Hispanic black, and 34.1% were Hispanic,[24] the majority of our participants are non-Hispanic black. In NHANES non-Hispanic blacks has lower median UICs in comparison to other races. Thus, having a majority of non-Hispanic black participants may have influenced the median UIC of our study. In the ANOVA analysis UIC did not vary significantly with race, but the small sample limits our ability to obtain accurate results due to insufficient power.

The distribution of our UIC values was right-skewed, similar to distributions in the NHANES data.[24] Among the participants surveyed there were a number of participants that were outliers, presumably due to high iodine intake within few hours of sample collection. When recommending and implementing changes to shift the curve to the right so that U.S pregnant women are no longer mildly iodine deficient, policymakers also need to ensure that these implemented measures don't adversely affect the participants in the far right tail of the distribution. Shifting average population iodine intake to the right could raise the iodine intake of this subgroup, potentially making their iodine intake more excessive.

Median UIC levels increased with each trimester, but it did not achieve statistical significance, possibly due to the small number of first-trimester women enrolled. There were no similar characteristics between the 3 pregnant women who were in their 1st trimester of pregnancy, nor were they any different from the rest of the study population. A similar trend was also recently observed in pregnant women from the U.S National Children's Study, which reported a median UIC of 109 µg/L in the first trimester, a median UIC of 128 µg/L in the second trimester, and a median UIC of 172 µg/L in third trimester.[24] The reasons for the increasing UIC across gestation are not clear. One reason could be due to higher GFR rates during the third trimester of pregnancy.[34] This increase across gestation could also be because women do not begin consuming iodine-containing supplements until later in gestation, or because diet may change during the pregnancy. NHANES showed a different trend across the trimesters: among pregnant women in the 2003–2004 and 2005–2006 survey periods, the median UIC in the 1st trimester was 182.4 µg/L (n =10) in the 2nd trimester, 154.6 mg/L (n=21); and in the 3rd trimester median UIC was 135.9 µg/L (n= 16).[19] However pregnant women are not oversampled in NHANES and numbers are small. Larger studies are needed to understand what is happening to the iodine status of these pregnant women over the course of gestation.

As expected, women in our study who took iodine-containing prenatal vitamins had higher UICs in comparison to women who did not take iodine-containing vitamins. This reinforces the current recommendations of the ATA and other medical societies regarding the need for 150 µg/day iodine content in all prenatal vitamins marketed in the U.S.[35] The one woman in our study who took supplements containing a higher-than-recommended iodine amount had a high UIC level of 880 µg/L, which suggests excessive intake. Excessive, as well as inadequate, iodine intake in pregnancy can cause thyroid dysfunction.[31]

While an important and useful step, iodine supplementation during pregnancy has some limitations.[22] The iodine content of prenatal vitamins in the U.S is not mandated, and until recently, many of the prenatal multivitamins marketed in the U.S did not contain any iodine. In 2009 Leung et al. reported that only half of the prenatal multivitamins marketed in the U.S contained any iodine, and that many of those preparations which did include iodine had measured iodine content discordant from that listed on product labels.[30] It is important that manufacturers of prenatal vitamins ensure that all prenatal vitamins actually contain 150 µg/day of iodine. In our study, most women (79.0%) reported taking prenatal vitamins with the recommended iodine content of 150 µg/day. When checking the iodine content of the prenatal vitamins in the major pharmacies located in the Boston area, all of them currently contain 150 µg of iodine.

Additional studies are needed to determine the proportion of U.S prenatal multivitamins that currently contains iodine.

Another limitation of reliance on supplements is that many pregnant women do not use supplements on a regular basis. In examining the utilization of folic acid supplementation, the Centers for Disease Control and Prevention (CDC) has reported that 37.5% of pregnant women surveyed had not taken their supplement in the past 24 hours.[26] Because much of the damage caused by iodine deficiency occurs early in pregnancy,[27] by the time a woman realizes she is pregnant and seeks prenatal care, damage may have already occurred. It is important for women and their providers to be educated regarding the importance of starting iodine supplementation pre-conception. Even so, relying only on prenatal vitamins for iodine intake could still be a problem since up to 50% of pregnancies are unplanned.

Few of the women in our study reported consuming foods that are naturally high in iodine content, such as seaweed and seafood. The majority did report consumption of milk, eggs, and bread, which contain iodine due to agricultural and manufacturing practices. As predicted, UIC levels increased with higher reported consumption of dairy products, such as milk and cheese, similar to results seen in NHANES.[24] U.S women who do not ingest milk or other dairy products (54.0% of our sample) may be at risk for iodine deficiency. The iodine fortification of dairy foods is currently not mandated or well regulated in the U.S. In the absence of further measures to ensure the constant presence of iodine in food, it remains critical to ensure that all the U.S women who are pregnant, lactating, or planning pregnancy receive iodine-containing prenatal vitamins. It is also important to ensure that pregnant-women and their providers are educated regarding the importance of iodine nutrition.

Only 16.4% of study subjects reported that their health care providers had discussed iodine nutrition with them either during or prior to pregnancy. The majority of them, 71.0%, did not know why iodine is added to salt and did not report looking for iodized salt when buying table salt. Thus, the majority of the participants regardless of their race, age, or education level, were lacking important knowledge regarding iodine nutrition.

A strength of this study was its diverse study population, and it is specifically looking at a large population in local region. NHANES only look at national trends and do not provide regional breakdowns. Since iodine content in food differs based on climate and region, it is important to perform local and regional studies as well as national surveys. Although these data are preliminary and current conclusions are based on a small sample size, this study was designed to be adequately powered.

This study also has some limitations. Although the survey instrument is based on U.S foods known to be high in iodine, and has been used in several prior published studies,[11] there is currently no validated food frequency questionnaire (FFQ) for iodine in the U.S. Since this is not a validated instrument there is a probability for misclassifications. Thus it is important that future efforts should be undertaken to develop a FFQ that accurately assesses the iodine intake of individuals. FFQs are typically based on national food tables, but in the U.S national food tables that contain iodine content are not available. Future studies could use a biomarker to validate dietary iodine. This would require collection of multiple 24- hour urine specimens from participants, and with participants eating a diet where all food is measured. This would allow for more accurate assessment regarding correlations between the participant's reported and actual iodine intakes. Nevertheless, this study would be difficult to conduct since participant compliance would likely be difficult, and collecting multiple 24-hour urine specimens from these participants would be a challenge.

Another limitation of our study was the fact that questionnaire data were based on self- report and recall, which can lead to misclassification. In addition median UIC data cannot be used to identify the iodine status of individuals, since 10 or more urinary spot specimens from each individual are required in order to provide individual status.[17] Therefore, although we can use these data to assess population iodine nutrition, we are unable to diagnose individuals who are deficient.

In conclusion, this study demonstrates that BMC pregnant women may still be mildly iodine deficient, and are inadequately informed about the importance of iodine nutrition. Important sources of iodine included iodine-containing prenatal multivitamins, milk, and cheese. To date no large surveys of UIC have been conducted on pregnant women.[24,19] Larger studies could better assess how race and other potential predictors such as education and social economic status influence median UIC. Given the knowledge gaps revealed in this study, efforts to educate pregnant women and obstetric providers regarding the importance of iodine should be expanded. Further studies are also needed to determine current availability of iodine in U.S prenatal vitamins. Finally, optimal national efforts to guarantee constant iodine content in foods should be undertaken in order to ensure that pregnant women in the future are able to achieve adequate iodine intake without the need for supplements.

APPENDIX

Subject ID__________

Subject Questionnaire: Urinary Iodine Concentrations of U.S. Pregnant Women

Today's date:

________/________/____________
mm dd yyyy

A1. What is your race?
- ☐ White, non-Hispanic
- ☐ Black, non-Hispanic
- ☐ Hispanic
- ☐ Asian
- ☐ Native American
- ☐ Other____________

A2. Where were you born?
- ☐ United States
- ☐ Other country: ________________

A3. What is your age? _______ years old

A4. What is your marital status?
- ☐ Single, never married
- ☐ Married
- ☐ Divorced
- ☐ Widowed
- ☐ Other ________________

A5. What is your highest level of education?
- ☐ Less than high school
- ☐ High school
- ☐ Vocational/trade school
- ☐ 2-year college
- ☐ 4-year college
- ☐ Grad school

A6. Does anyone in your family have thyroid disease?
- ☐ Yes
- ☐ No
- ☐ Don't know

A7. Do you take any multivitamins including prenatal vitamins?

❒ Yes (answer question A8)
❒ No (go to question B1)

A8. If yes, is it prescription?
❒ Yes (answer question A9)
❒ No (go to question A10)

A9. If yes, from which pharmacy do you get your multi vitamin?

____

A10. If the vitamin is not obtained with a prescription, what is the name of the brand?

____

A11. How much iodine is in one daily serving of the vitamin? __________ mcg

A12. Have you taken the vitamin in the last 24 hours?
❒ Yes
❒ No

A13. Did you consider iodine content when choosing a prenatal vitamin?
❒ Yes
❒ No

B1. Do you use ordinary table salt at least once a week? This is salt that is used in cooking and/or seasoning, but not kosher or sea salt.

☐ Yes
☐ No

B2. In the last 24 hours, have you added any ordinary table salt to your food (cooking and/or seasoning)?

☐ Yes (answer question B3)
☐ No (go to question B4)

B3. If yes, what kind of salt? (*Check ALL that apply).*

☐ Iodized
☐ Non-iodized
☐ Don't know

B4. In the last 24 hours, have you had any cow's milk?

☐ Yes (answer question B5)
☐ No (go to question B6)

B5. How many cups of <u>cow's milk</u>?

I've had _____cups of cow's milk.

B6. In the last 24 hours, have you had <u>cheese</u>? Include all types of milk-based cheese, such as cow's milk and goat's milk, etc.

☐ Yes (answer question B7)
☐ No (go to question B8)

B7. How many ounces of <u>cheese</u>? One ounce is about the size of your thumb.

I've had _____ ounces of cheese.

B8. In the last 24 hours, have you had any <u>yogurt</u>? Include all types of milk-based yogurt, such as cow's milk and goat's milk.

☐ Yes (answer question B8)
☐ No (go to question B9)

B8. How many servings of <u>yogurt</u>?

I've had _____ servings of yogurt.

B9. In the last 24 hours, have you had any <u>ice cream</u>?

☐ Yes (answer question B10)
☐ No (go on to question B11)

B10. How many scoops of <u>ice cream?</u>

I've had _____ scoops of ice cream.

B11. In the last 24 hours, have you had any <u>frozen yogurt</u>?

☐ Yes (answer question B12)
☐ No (go to question B13)

B12. How many scoops of <u>frozen yogurt?</u>

I've had _____ scoops of frozen yogurt.

B13. In the last 24 hours, have you had any whole <u>eggs (not just egg whites)</u>?

☐ Yes (answer question B14)
☐ No (go to question B15)

B14. How many eggs?

I've had ____ eggs.

B15. In the last 24 hours, have you had any bread that was not homemade?

☐ Yes (answer question B16)
☐ No (go to question B17)

B16. How many slices of bread that was not homemade?

I've had ____slices of bread that was not homemade.

B17. In the last 24 hours, have you had any bagels?

☐ Yes (answer question B18)
☐ No (go to question B19)

B18. How many slices of bagels?

I've had ____ bagel halves.

B19. In the last 24 hours, have you had any other types of breads or rolls?

☐ Yes (answer question B20)
☐ No (go to question B21)

B20. How many servings of other types of breads or rolls?

I've had ____ servings of other types of breads or rolls.

B21. In the last 24 hours, have you had saltwater fish?
Common saltwater fish are salmon, cod and haddock.

☐ Yes (answer question B22)
☐ No (go to question B23)

B22. How many servings of saltwater fish? One serving is 4 ounces, which is about the size of your palm.

I've had ____ servings of saltwater fish.

B23. In the last 24 hours, have you had freshwater fish?
Common freshwater fish are catfish and trout.

☐ Yes (answer question B24)
☐ No (go to question B25)

B24. How many servings of <u>freshwater fish?</u> One serving is 4 ounces, which is about the size of your palm.

I've had ____servings of freshwater fish.

B25. In the last 24 hours, have you had any <u>shellfish</u>?
Common shellfish are lobsters, clams, and scallops

☐ Yes (answer question B26)
☐ No (go to question B27)

B26. How many servings of <u>shellfish?</u> One serving is 4 ounces, which is about the size of your palm.

I've had ____servings of shellfish.

B27. In the last 24 hours have you had any <u>seaweed</u>? Common types of edible seaweed are kelp, kombu, dulse, and nori.

☐ Yes (answer question B28)
☐ No (go to question C1)

B28. How many servings of seaweed?

I've had ____ servings of seaweed.

C1. Has any of your healthcare providers ever discussed iodine nutrition with you?

☐ Yes (answer question C2)
☐ No (go to question C4)

C2. Did they discuss iodine nutrition before your pregnancy?

☐ Yes
☐ No

C3. Did they discuss iodine nutrition during your pregnancy?

☐ Yes
☐ No

C4. Do you know why iodine is added to some salts?

☐ Yes
☐ No

C5. Do you look for iodized salt when buying table salt?

☐ Yes
☐ No
☐ I do not buy salt

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Professional Experience

MEDITECH
Westwood, MA
Application Specialist
February 2014 – August 2014
Provided software support to 40 hospital client sites, exceeding the expectation of overseeing 5 sites.
Triaged urgent requests from hospitals via email/phone while completing regular intake of work tasks.
Acted as primary contact for resolving customer software/system problems, and for processing product enhancement requests.
Produced content for Physician Care newsletter distributed internationally to all MEDITECH sites. Readership in the thousands.
Traveled to company sites across MA to deliver product demo presentations.

Companion Referrals
Needham, MA
Home Health Care Aide
January 2012- Present
Administer vital medicine on precise schedule to maintain patient health.
Deliver adaptive support of daily routine based on the condition of patient.
Provide emotional support and comfort during waking hours.

Education

Boston University, Bachelors of Arts in Biology with Specialization in Neurobiology
September 2013
Activities: Secretary for Albanian United Club

Boston University, Candidate for Masters in Nutrition and Metabolism
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Research Experience

Boston University School of Medicine: Endocrinology Department
Boston, MA
Research Coordinator
June 2015- Present
Involved in the Recruitment of subjects at the Antenatal Center at BMC .
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Translated the IRB consent form and protocol in Spanish, in order to assure the recruitment of the Spanish Speaking Population.

Harvard University: Snedeker Lab of Language of Developmental Studies.
Cambridge, MA
Research Assistant
January 2012- July 2012
Designed study on language development in children and adults by creating experiment materials, recruiting/compensating participants, and running experiment with subjects. Summarized and analyzed research data collected in Excel.

Technical Skills

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