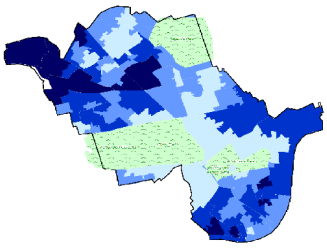
Westminster's

Joint Strategic Needs Assessment

Vitamin D Deficiency in Pregnant and Postnatal Women and Children aged 0-5 Years

Anna Varela-Raynes, January 2011



Westminster City Partnership

This document contributes to Westminster's JSNA

Acknowledgements

Thank you to all those who assisted in the preparation of this report:

Mandeep Butt, Colin Brodie, Lyne Coventry, Lauren Dias, Eva Hrobonova, Paul Lindars, Tanya McKay, Ami Patel, Gayan Perera, Sinan Rabee, Bethan Searle, Heather Wadsworth, Stephan Worrell.

Contents Page

1. Key Findings

Westminster has high numbers of pregnant women and children under five who are at high risk of vitamin D deficiency:

- Overweight or obese pregnant women are at high risk of being vitamin D deficient. Infants rely upon their mother's vitamin D stores for their own. Thirty percent of women presenting to St Mary's in 2008/9 were overweight and a further 13% were obese. These figures are likely to rise as the obesity trend increases nationally.

- Fifty-one percent of children under five are from a Black Minority Ethnic (BME) community. They are therefore included in the high risk category for vitamin D deficiency based upon their ethnicity.

- The ethnicity of pregnant women is not collected, but Westminster has high levels of BME communities who will all be at increased risk of being vitamin D deficient. Local evidence shows that women from BME communities have a higher prevalence of vitamin D deficiency during pregnancy than Caucasian women.

Although the exact prevalence of vitamin D deficiency for Westminster is unknown as regular testing is not common, there is evidence that it is likely to be wide spread.

- National data shows that the average national prevalence in women aged 19-64 is 15%. If applied to Westminster this equates to 13,335 women being vitamin D deficient.

- The prevalence of known vitamin D deficiency amongst children aged zero to four in one Westminster GP practice is 3%. If applied to Westminster as a whole this suggests, at a minimum, around 360 children under 5 years of age have vitamin D deficiency (including rickets) in Westminster. This is likely to be large under estimation.

The cost of treating vitamin D deficiency is far more expensive than preventing it. Should vitamin D deficiency go untreated and a person's vitamin D levels drop very low, rickets in children or osteomalacia in adults can result. The cost of treating these conditions to the NHS and the costs to the patients is very high.

- The cost of treating vitamin D deficiency (3 month course) in a child is variable, however it can cost NHS Westminster as much as £700.

- Two months vitamin supplementation (preventative dose) for a child costs the NHS as little as £1.61 (for Healthy Start vitamins).

- The cost of providing a child with vitamin supplementation (preventative dose) from age 6 months to 5 years is £43.47 (for Healthy Start vitamins).

2. Vitamin D

Vitamin D is an important vitamin which helps with the development of bones by controlling 'calcium absorption in the small intestine and works with parathyroid hormone to mediate skeletal mineralization and maintain calcium homeostasis in the blood stream' (Kulie et al., 2009. p698). There are two forms of vitamin D, ergocalciferol (vitamin D_2) is found in plants and some fish and cholecalciferol[1] (vitamin D_3) is synthesized in the skin by sunlight (Kulie et al., 2009). Unlike other vitamins which are derived mainly from food, the sun is the main source of vitamin D.

The history of vitamin D is linked directly to the disease rickets. This was first identified as a rare disorder in the early 17th century with initial descriptions of rickets written by Daniel Whistler and Francis Glisson in England. By the start of the twentieth century the disease had become endemic. In the early part of the twentieth century it was discovered that exposure to sunlight and cod liver oil could both prevent and treat rickets. By the 1930s the chemical structures of vitamin D had been determined and following easy ways to supplement foods were developed, nutritional rickets almost disappeared from industrialized countries. In the 1940s the British government started vitamin D supplementation through the Food Welfare Programme (Misra et al, 2008).

In recent years vitamin D deficiency has reappeared in industrial countries such as the United Kingdom. There is evidence that some groups of people are at increased risk of being vitamin D deficient, and certain life experiences such as pregnancy and breastfeeding, increase the risk for the whole population. Those most at risk of becoming vitamin D deficient include people with darker skin, people who cover themselves for cultural reasons, those who are housebound, obese people and older people and children. Women should try to maintain good levels of vitamin D during pregnancy to ensure their own needs are met and adequate stores are built for their baby for early infancy.

Deficiency occurs when the body is unable to process enough vitamin D due to limited sun exposure and a vitamin D poor diet leading to the body's stores becoming depleted.

2.1. Why is vitamin D important for Westminster?

Local clinicians have raised concern about seeing increasing cases of rickets and vitamin D deficiency in children and pregnant and breastfeeding women. It has also been identified that that the vitamin distribution element of Healthy Start[2] in Westminster was being under utilised and due to low national stock levels the vitamins were often unavailable. The Healthy Start vitamins include

[1] Also known as colecalciferol.

[2] Healthy Start is a benefit available for pregnant women, new mothers and families with children aged under 4 who are in receipt of certain benefits and all pregnant women under 18 years of age. It provides beneficiaries with vouchers to purchase fresh fruit and vegetables, cows' milk and baby formula. Vouchers are also provided for children and maternal vitamins.

vitamin D and have been especially formulated for pregnant women and young children.

Westminster has sizable Black Minority Ethnic (BME) communities and women and children from these communities are at high risk of being vitamin D deficient (Appendix A). However, local studies have also shown that white pregnant women are also vitamin D deficient in Westminster, though not in the same numbers as women from BME communities.

This needs assessment will focus on pregnant women and new mothers with children up to the age of 1 and children from birth to 5 years of age. It focuses on nutritional vitamin D deficiency[3] and excludes vitamin D deficiency which is a result of a medical condition or treatment which would predispose the person to vitamin D deficiency such as renal and liver disease and anticonvulsant therapy.

2.2. Sources of Vitamin D

Natural Sources

Over 90% of vitamin D is generated from exposure to ultraviolet B sunlight (Pearce and Cheetham, 2010. p 142). Some foods also provide limited amounts of vitamin D. These include oily fish (which are the main food source) and egg yolks and mushrooms which have smaller amounts.

To obtain enough vitamin D, a fair skinned person needs to spend 20-30 minutes in the midday sun with the sun on their face and forearms, two to three days a week during summer (Pearce and Cheetham, 2010. p142).

In the UK, people with darker skin need to extend the time they spend in the sun (either exposure time or frequency) between 2-fold to 10-fold to get the same level of vitamin D.

It is not possible to get vitamin D from the sun during the winter months (October-April) in the UK. However, vitamin D is stored in the liver and if appropriate stores have been built up during the summer months these will last through the remaining five months of the year. Life events such as pregnancy and breastfeeding deplete the vitamin D stores quicker and therefore supplementation is recommended.

Vitamin Supplements

Vitamin D can be taken as a dietary supplement. Though, as section 2.4 outlines, taking the correct amount can be complicated.

Vitamin D supplements can be purchased from supermarkets, pharmacies, health food stores etc though these can be expensive. The Healthy Start vitamins, available through the NHS, are specifically designed for pregnant women and new mothers and 0-4 year old children. These are available to Healthy Start beneficiaries for free or at a much cheaper price for non-beneficiaries than similar products on the high street.

[3] This includes deficiency due to lack of sunlight.

Some foods in the UK are fortified with vitamin D, this includes breakfast cereals (mainly supermarket 'own brands' in the UK) and margarine and infant formula milk which are required by law to be fortified (Pearce and Cheetham, 2010. p142). In other countries cows' milk is often fortified with vitamin D but this is not the case in the UK.

2.3. How much vitamin D do you need?

The recommended dose of vitamin D differs depending upon age and life events (e.g. pregnancy and breast feeding).

The Department of Health recommends that pregnant and breastfeeding women take 10µg of vitamin D daily[4]. Women should also take 400µg of folic acid daily whilst trying to conceive and until the twelfth week of pregnancy. There is also an increased need for folate in late pregnancy in order to maintain serum and red cell folate at pre-pregnancy levels (Department of Health, 1991. p30). The women's Healthy Start vitamins include the exact reference nutrient intakes (RNIs) for pregnant and breastfeeding mothers of vitamin D, folic acid and vitamin C.

Studies have shown that the standard 10µg vitamin D supplement given to breastfeeding mothers does not increase the vitamin D concentrations of the baby because breast milk is a poor conductor of vitamin D (Kovacs, 2008. p525S). Studies have found that a maternal dose 100µg per day was needed to see an increase in the infant's 25(OH)D concentrations to a sufficient level (>75nmol/L) (Kovacs, 2008. p525S). Instead, the UK recommendation is that babies are supplemented directly with smaller doses of vitamin D which produces normal vitamin D levels in the infants.

The Department of Health recommends a daily dose of 7µg/day of vitamin D for children aged 6 months to 5 years (Department of Health, 2009. p5) unless they are drinking 500ml (a pint) or more of infant formula a day at any time during this age range. The Department of Health recommendation states that younger infants aged 0–6 months may not need supplements as they should get adequate amounts from breast milk or infant formula milk. However, if there is any doubt about the mother's use of vitamin supplements during pregnancy and/or breastfeeding, breastfed infants will benefit from vitamin D supplements from 1 month ((Department of Health, 2009. p5).

Based on this recommendation, some areas in the UK recommend vitamin supplementation for all babies from one month. In some areas the PCT also provides supplements through Healthy Start for their whole population (e.g. Heart of Birmingham) as there is concern about the vitamin D levels in the maternal and young children population.

Recommended Daily Amounts & Reference Nutrient Intakes

The recommended daily amounts (RDA) which are required to be displayed on all vitamin supplement products including those for children, are based on adults and have no relevance to children. The RDA applies to the whole

[4] Vitamin D doses are normally expressed in units. 10µg of vitamin D is equal to 400 units; 1µg of vitamin D is equal to 40 units.

population in general and is set by a European committee. Parents will often buy the products which show they contain 100% RDA of vitamins thinking this will best provide for their children, but in fact this could be providing harmful amounts of a vitamin, risking toxicity levels, or too little meaning the supplements are ineffective (More, 2007).

In the UK, reference nutrient intakes (RNIs) have been developed by the Department of Health for different age groups and life events. There are several age bands for children so their changing needs as they grow and develop are met.

Table 1 - RDA & RNI for Children and Pregnant and Breastfeeding Women

Active Ingredient	100% RDA	Healthy Start Vitamins (Maternal)	Healthy Start Vitamins (Children)	RNIs for different age groups/life stages					
				0-6 months	7-12 months	1-3 years	4-6 years	Pregnant women	Breastfeeding women
Vitamin A	800 µg	-	233 µg	350 µg	350 µg	400 µg	400 µg	0	
Vitamin C	60 mg	70 mg	20 mg	25mg	25mg	30mg	30mg	50mg	70mg
Vitamin D	5 µg	10 µg	7.5 µg	8.5 µg	7 µg	7 µg	-	10 µg	10 µg
Folic Acid	200 µg	400 µg	-	0	0	0	0	400 µg	400 µg

Source: Department of Health & Healthy Start Vitamins

Toxicity Levels

Although this needs assessment is looking at vitamin D, it is important to consider vitamin A and C also as these two vitamins are included in the Healthy Start vitamin drops for children.

Vitamin A in high doses taken over a long period of time can be dangerous. Large amounts of retinol (preformed vitamin A) can cause liver and bone damage, hair loss, double vision, vomiting, headaches and other abnormalities (Department of Health, 1991. p87). Single doses of 100mg in children are harmful[5] and daily intakes for children should not exceed 900µg in infants; 1,800µg between 1 and 3 years of age and 3000µg from 4 to 6 years old (Department of Health, 1991. p87). Therapeutic doses may exceed these amounts but only under medical supervision.

High levels of vitamin C and D are not as dangerous as vitamin A; however they can have adverse effects. Intakes of vitamin C at 20 times the RNI or more (500µg for 0-12 month olds; 600 µg for 1-6 year olds) has been associated with diarrhoea and increased risk

[5] There are 1000 µg in 1mg (therefore the toxic dose of vitamin A is 100,000 µg).

of developing oxalate kidney stones in susceptible people (Department of Health, 1991. p32). Also, in people taking high levels of vitamin C (1g or more) if they suddenly revert to 'normal' intakes they may develop signs of scurvy.

Excessively high levels of vitamin D are more dangerous for infants than for adults. Intakes of 50µg per day have been associated with hypercalcaemia[6] in children.

As Table 1 shows, it is important that parents are advised not to give young children vitamin supplements which include 100% of the RDA for vitamin A or vitamin C as this is, at a minimum, double the daily dose they should take. For vitamin D the opposite is true as the 100% RDA does not provide enough of the vitamin for infants and young children. It is also recommended that parents should be advised not to give their children two supplements containing vitamin A.

A combination of fortified formula milk and Healthy Start vitamins would mean infants have higher than recommended vitamin intakes (RNI levels) for vitamins A, C and D. However, for vitamins C and D the levels do not reach those at which infants would be at risk of adverse effects. For vitamin A however, the levels seen in babies from 2-4 months who are formula fed and supplemented with Healthy Start vitamins does put them slightly over the recommended upper limit of 900ug per day. Infants on either side of this age range (0-2 months and 5-12 months) do not exceed this upper limit. Therefore, caution must be taken if recommending the supplementation of babies on formula milk with vitamins containing vitamin A. Full details of the work done to calculate these daily intakes can be found in Appendix B.

Vitamin A should not be taken by pregnant women as a link has been found between vitamin A and birth defects in infants. Women who are, or might become, pregnant are therefore recommended not to take supplements containing vitamin A or eat foods high in vitamin A such as liver.

2.4. How are vitamin D levels measured?

Plasma 25(OH)D concentration is used to assess vitamin D status. This reflects the sum of vitamin D from both endogenous synthesis (vitamin D_3) and from dietary intake (vitamin D_2) (Peterlik et al, 2009). This is obtained through a blood sample. GPs would request a vitamin D test and possibly a full blood count test so the level of calcium in the blood is also reported.

The Scientific Advisory Committee on Nutrition (SACN) report highlights that different units of measurement are used to describe plasma 25(OH)D concentration; 2.5nmol/l is equivalent to 1ng/ml (SACN, 2007. p8). The SACN report also highlights that 'different methods can be used to measure the serum or plasma 25(OH)D concentrations but comparisons are complicated by a lack of standardization' (p8). There is evidence that different

[6] Hypercalcaemia is a condition when there is too much calcium in the blood. Untreated severe hypercalcaemia can result in coma, cardiac arrest or death.

laboratories and methods have yielded different results from the same samples.

In an attempt to monitor the performance around vitamin D laboratory tests, the international Vitamin D Quality Assessment Scheme (DEQAS) was established in 1989 and now has over 100 registered members in 18 countries including the UK (SACN, 2007. p8).

Some of the older tests provide different results depending on the type of vitamin D concentration being measured ($25(OH)D_2$ or $25(OH)D_3$). DEQAS reported in 2004 that results were highly operator and laboratory dependent, but for samples containing only $25(OH)D_3$ most commercial methods available in 2004 were capable of giving results close to the target value (SACN, 2007. p8). However, new high performance liquid chromatographic methods and mass spectrometric methods may offer more robust and reliable measurements.

A number of studies have suggested alternative ways to obtain the blood needed for the vitamin D deficiency tests which may be more acceptable to the patient and more cost effective than the normal venipuncture sample method. These are considered in Appendix C.

It is agreed nationally and internationally that vitamin D deficiency occurs when the plasma 25(OH)D concentration is lower than 25nmol/l.

The SACN report highlights that there are no agreed limits for vitamin D insufficiency and sufficiency. However, it outlines that it has been suggested that 'vitamin D insufficiency or hypovitaminosis D, without clinical signs or symptoms, occurs at a plasma 25(OH)D concentration of less than 40nmol/l' (p. 8). And that an appropriate definition of vitamin D sufficiency can be measured as a 'plasma 25(OH)D concentration of greater than 75nmol/l' (p. 9).

3. Vitamin D Deficiency Risk Factors

There are a number of factors which increase the risk to a person of becoming vitamin D deficient.

Limited Sunlight
The main reason for vitamin D deficiency developing is not getting enough sunlight and therefore not processing enough of the vitamin to replenish the body's stores.

Britain's northern latitude location (50-62^{O}N) means that between October and April the ultraviolet B wavelengths do not reach 90% of the UK. Therefore it is not possible for the majority of the country to process adequate sunlight to maintain healthy vitamin D levels and it falls to dietary sources to make up the shortage. As there are limited food stuffs available which are rich in vitamin D, it is unsurprising that vitamin D deficiency peaks during the winter and spring months in the UK.

Darker Skin
Numerous studies have highlighted that individuals with darker skin are at high risk of vitamin D deficiency. People with darker skin need additional time or frequency, compared to someone with paler skin, in appropriate sunlight to process adequate levels of ultraviolet B sunlight to maintain a healthy level of vitamin D.

Covered Skin
Sunscreen with a sun protection factor 15 or more blocks more than 99% of dermal vitamin D synthesis Pearce and Cheetham, 2010. p144). Strict adherence to applying sunscreen places individuals with fair skin at a similar risk of vitamin D deficiency as those with darker skin.

Since 1992 reducing skin cancer has been a government priority in public health strategy (Hedges and Scriven, 2008). A consequence of these campaigns is increased knowledge about sun safety by the general public which has in turn negatively impacted vitamin D levels across the UK.

Concealing clothing, such as veils, headscarves, long sleeves etc also act like sunscreen and block the ultraviolet B sunlight from reaching the skin. Studies from Muslim countries have shown that even in very sunny conditions, observant Muslim women are likely to be at increased risk of being vitamin D deficient.

Limited Access to Outdoors
Another barrier to obtaining adequate levels of sunlight is being indoors. This may relate to people who are housebound, but could also apply to office or shop workers who are unable or choose not to go out at lunchtime.

3.1. Maternal Risk Factors for Vitamin D Deficiency

Pregnancy is one of the life events that increase a woman's risk of being vitamin D deficient. A woman's risk (and therefore her child's risk) of being vitamin D deficient is further increased by having multiple short interval pregnancies and obesity prior to and during pregnancy.

Multiple Short Interval Pregnancies

Women who have pregnancies with short intervals between them, will be at increased risk of being vitamin D deficient, especially if they breastfeed. They will not allow their body time to replenish the vitamin D stores ahead of the next pregnancy and without supplementation are putting themselves and their children at risk of being vitamin D deficient (Pearce and Cheetham, 2010).

Obesity

Obesity (BMI >30) prior to and during pregnancy increases the likelihood that women will be vitamin D deficient. An American study (Bodnar et al, 2007) identified a difference in vitamin D status between women who had been obese prior to pregnancy and those who had been a healthy weight. Obese pregnant women had lower adjusted mean serum 25(OH)D concentrations at 4–22 weeks (56.5 vs. 62.7 nmol/l; P 0.05) and a higher prevalence vitamin D deficiency (61 vs. 36%; P 0.01). Also, the study identified that the babies born to obese mothers had poorer vitamin D status than neonates of healthy weight mothers (adjusted mean, 50.1 vs. 56.3 nmol/l; P, 0.05).

NICE guidance (CG62, PH11) highlights that women with a pre-pregnancy BMI >30 are at increased risk of being vitamin D deficient. The guidance recommends that these women, along with other at risk groups, are encouraged to take a daily vitamin D supplement.

Recently published NICE guidance (PH27) encourages obese women to lose weight ahead of trying to conceive to reduce the risks associated with obesity in pregnancy for themselves and their baby. It also recommends postnatal support for women to lose weight as this will provide protection for future pregnancies as well as improve the mother's health in the interim.

3.2. Infants' Risk Factors for Vitamin D Deficiency

Infants' vitamin D status is based upon their mother's. If their mother has low vitamin D levels they will inherit this. Two specific factors relating to their mother increases their risk further.

Maternal Vitamin D Deficiency

Being born to a mother who is vitamin D deficient increases the likelihood that the baby will have sub-optimal vitamin D levels at birth. This is particularly important for babies born in the winter months when it is not possible to 'top up' vitamin D levels from sunlight. If a child is found to be vitamin D deficient it is likely that their mother is and also any siblings (Pearce and Cheetham, 2010. p145).

Exclusive, Extended Breastfeeding

Breast milk is the best food for a baby. It is recommended that babies are exclusively breastfed until 6 months when solid foods can be introduced. Breast milk is however a poor source of vitamin D and the levels found in breast milk reduce even further when the mother is vitamin D deficient. In cases of rickets it is frequently found (Sharma et al, 2009 & Modgil et al, 2010) that the baby has been breastfed exclusively for an extended period of time, well over the recommended 6 months.

4. Westminster's At Risk Population

As outlined in chapter 3, there are certain groups which are at greater risk of being vitamin D deficient than the general population. Whilst it is not possible to confirm exactly who is at risk, certain groups are highlighted here. There is likely to be cross-over between the groups.

4.1. Mothers and Infants

In 2009 in Westminster, there were 3,012 births to mothers residing in Westminster.

Ethnicity

It is known that Westminster has a diverse population with 51% of the population born outside of the UK. (ONS Annual Population Survey for 07/08). As Westminster has a highly mobile population ethnicity data collected in the 2001 Census is likely to be highly out of date. Ethnicity data collected through more recent hospital visits (PHAR, 2007-08) has shown that 19.7% of those attending described themselves as coming from a non-white ethnic group[7]. If this is applied to the number of births in Westminster, approximately 600 births would be to mothers' who maybe at risk of vitamin D deficiency due to their ethnicity. A further 11.7% described themselves as from 'any other ethnic group'. In Westminster, this has group has previously been shown to include people who self-report as North African or Middle Eastern ethnicity (also including categories of Arab, Israeli, Iranian, Kurdish and Moroccan) (Ethnic write-in (80 categories) by religion (9 categories), 2001 Census). This group may be at risk of vitamin D deficiency due to cultural and/or religious dress. This would equate to approximately 360 further mothers and children who could at risk of vitamin D deficiency.

As there is limited data on the ethnicity of pregnant women or their babies locally (ethnicity is not recorded at birth registration), these estimates are the best suggestions we have on this population.

Obesity

A large study of maternal Body Mass Index (BMI) in the London region (Sebire, NJ et al, 2001) found that 10.9% of women having singleton births were obese (BMI ≥ 30). A further 27.5% of the women in the study were found to be overweight (BMI 25 - 29.9). If this prevalence was applied to Westminster's births, 331 women would be obese (BMI ≥ 30) and a further 843 would be over weight (BMI 25 - 29.9) during pregnancy.

The upward national trend in obesity suggests that the numbers of women presenting to maternity services either overweight or obese will increase. Data from St Mary's Hospital would support this. Between April 2008 and March 2009, of all patients booked at St Mary's (of any gestation age) with

[7] African (Black or Black British), Any other Asian background, Any other Black background, Bangladeshi (Asian or Asian British), Caribbean (Black or Black British), Indian (Asian or Asian British), Pakistani (Asian or Asian British), White and Asian (Mixed), White and Black African (Mixed), White and Black Caribbean (Mixed).

BMI recorded, 13.5% were obese (BMI ≥ 30) and a further 30.4% were overweight (BMI 25 - 29.9). In both cases, the numbers recorded at St Mary's were higher than the national study (CMIS, data extracted 24/06/2009; extracted from Early Years JSNA). These figures would suggest that around two fifths of pregnant women seen at St Mary's Hospital would be at risk of being vitamin D deficient during pregnancy and by extension their babies at birth and during infancy.

Deprivation
There is evidence from a UK study that women on benefits, compared to other women, are more likely to be vitamin D deficient (12.1% versus 4.9%, p=.03) (Mahon et al, 2010. p16). Being on benefits themselves is not a risk factor, but increases the likelihood of being vitamin D deficient probably due to wider determinants of health such as obesity, poor housing etc. This study also highlighted, of the vitamin D deficient women, 72% were not in receipt of benefits (Mahon et al, 2010. p16) so vitamin D deficiency crosses socio-economic divisions.

The Department of Health reports that 9% of Healthy Start beneficiaries nationally are pregnant women. In Westminster this equates to approximately 200 women.

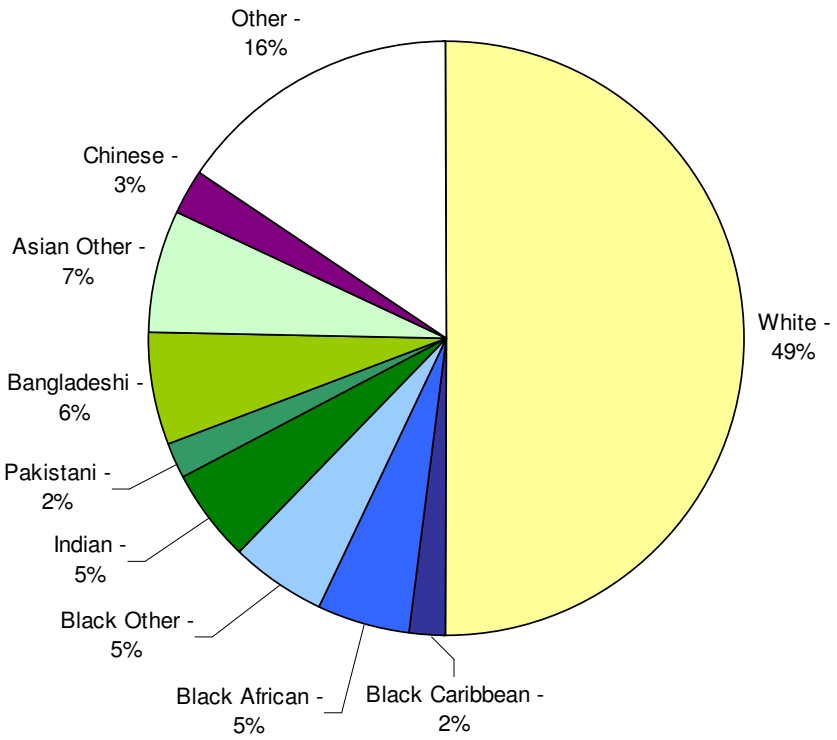
There is no local data on **Multiple Short Interval Pregnancies** or **Exclusive, Extended Breastfeeding** and therefore it is not possible to provide information on the numbers of women and infants who form these at risk populations. However, a number of studies have suggested that women who maintain exclusive breastfeeding longer than 6 months are often from BME communities rather than the white population.

4.2. Children Up to Age Five

It is estimated that Westminster has 12,300 children aged zero to four living in the borough (ONS population figures for 2009).

Ethnicity
The Greater London Authority estimates that just over a half of the children aged under five in Westminster are from BME groups (Figure 1). Thus, based on ethnicity alone, 51% (n=6,273) of the under fives population in Westminster would be at high risk of being vitamin D deficient.

Figure 1. The ethnic profile of the population aged under 5 years in Westminster



Source - GLA 2007 Round Ethnic Group Projections - PLP Low – for 2008

The North West and North East localities are more ethnically diverse than the South of Westminster. In the North West and North East localities, 51% and 59% respectively of the 0-4 year olds are white. This compares to 76% in the South locality (Westminster City Council).

Deprivation

Westminster is the eight most densely populated borough in the country (PHAR, 2007-08). Many families reside in flats and will have limited outdoor space. This may restrict the mother and children's exposure to the sun and increase their risk of becoming vitamin D deficient without vitamin supplementation.

The Early Years JSNA considered the housing types and areas in which families with children under five live. This identified that the largest proportion of children under five were concentrated in the north of the borough and in areas of highest deprivation such as Queen's Park (10%), Church Street (8%), Westbourne (8%) and Harrow Road (8%) (p12). The housing in these wards is often overcrowded; for houses that are occupied with dependent children 45% are overcrowded in Westminster (p27).

The Early Years JSNA has shown that the North West of the borough (especially Harrow Road, Queens Park and Westbourne wards), with pockets in the South and North East (particularly Church Street ward), is the most deprived. Patterns of deprivation and income deprivation in Westminster map

closely to areas with the highest proportion of children aged up to five years. Nearly one in three children lives in one of the four most deprived wards in the Borough.

As Healthy Start is a benefit for women and families on low incomes it can be expected that the majority of beneficiaries would be found in the poorest wards in Westminster. As these are more ethnically diverse than other wards it can therefore be assumed that the Healthy Start beneficiaries will include some of those who are at higher risk of becoming vitamin D deficient due to their ethnic background.

5. The Symptoms of Vitamin D Deficiency

There are a range of symptoms associated with vitamin D deficiency. These include:

- delayed growth
- bone pain
- muscle weakness
- skeletal problems

Only very severe cases of vitamin D deficiency will result in rickets. Children who do develop it will likely have the above symptoms but may also have:

- **Skeletal deformities** – such as soft skull bones, bowed legs, curvature of the spine, thickening of the ankles and wrists and knees. The breastbone can also stick out, which is sometimes called 'pigeon chest'.
- **Fragile bones** – bones become weaker and more prone to fractures.
- **Dental problems** – such as a delay in teeth coming through and weak tooth enamel.

In both adults with osteomalacia (soft bones) and children with rickets symptoms may also include:

- waddling when walking
- bending bones
- muscle weakness and pain

Rickets occasionally causes low levels of calcium in the blood, called hypocalcaemia. This can make the symptoms of rickets worse, as well as causing muscle cramps, twitching, tingling in the hands and feet, and fits.

A table adapted from Wagner et al (2008) in Appendix D shows the progression of symptoms through the various levels of vitamin D deficiency.

6. Vitamin D Deficiency Prevalence

Vitamin D deficiency often goes unreported and therefore prevalence data is mostly based upon estimates or known vitamin D deficiency cases. Neither of these provides the full picture for vitamin D deficiency prevalence and it is likely that many more people are vitamin D deficient.

6.1. National Data

The National Diet and Nutrition Survey (2004) reports that for women aged 19 to 64 years the mean concentration of plasma 25(OH)D was 49.6nmol/l (Ruston et al, 2004. p 55). This is in the 'normal' range slightly higher than the suggested insufficient cut off of 40nmol/l but considerably lower than the optimum level of 75nmol/l. Overall, 15% of women aged 19 to 64 years had a plasma 25-OHD concentration lower than 25nmol/l (p55).

As Table 2 shows the levels of deficiency amongst younger women, aged 19-24, is nearly double the average rate for women in the UK. For the other ages in women of childbearing age the levels of deficiency are similar to the average.

Table 2. Vitamin D levels in UK women of childbearing age

Women by Age	Vitamin D Level			
	Deficient Level (< 25nmol/l)	**Insufficient Level (>25nmol/l - 40nmol/l)**	**Sufficient Level (>40nmol/l - 70nmol/l)**	**Optimum Level (>70nmol/l)**
19-24	28%	26%	29%	13%
25-34	13%	27%	36%	19%
34-49	15%	28%	41%	14%

Source: The National Diet and Nutrition Survey Volume 4, p82 (Ruston et al)

As outlined previously, vitamin D levels are affected by seasonal variation due to the inadequate levels of sunlight in the UK during the winter months. Vitamin D levels are at their lowest in spring (January-March).

Women providing a sample of blood between July to September were significantly less likely to have a 25(OH)D concentration below 25nmol/l compared to a sample collected between January to March or April to June. Of the samples collected between January to March when vitamin D are at their lowest, 23% of them for women had a 25(OH)D concentration below 25nmol/l (p55). This is higher than the average samples for women.

6.2. Local Data

In 2007 a study was conducted at St Mary's Hospital (Yu et al, 2009) which documented vitamin D levels in pregnant women from four different ethnic groups[8]. The study confirmed that locally, pregnant women from BME groups were more likely to be vitamin D deficient than Caucasian pregnant women (Table 3). The study also recorded secondary hyperparathyroidism (PTH)[9] levels and found this was significantly higher in Asian women (27%), Middle Eastern women (49%) and Black women (24%) compared to Caucasian women (2%) ($P<0.05$) (p 688).

Table 3. Maternal Vitamin D Status at 27 weeks gestation

Ethnic Group	Vitamin D Status (%)		
	Deficient (<25nmol/l)	**Insufficient (≥25-50 nmol/l)**	**Sufficient (>50 nmol/l)**
Indian Asian	47	51	2
Middle Eastern	64	33	3
Black	58	16	6
Caucasian	13	60	27

Source: Yu et al, 2009

A local GP audit also confirmed that women and children under five years of age from BME communities dominated those who had been confirmed as being vitamin D deficient.

The audit of the opportunistic measurement of vitamin D levels and treatment of insufficiency and deficiency undertaken between 1 October 2008 and 30 September 2009 was conducted at a local GP practice in the North West of the borough[10]. A total of 347 patients were identified as having had Vitamin D levels measured between these dates.

Fifty-nine percent of the patients' audited were vitamin D deficient (n=204) and a further 22% had insufficient levels (n=76). There were 13 cases of rickets in children aged 0-14.

Twenty-one women aged 15 to 49 were diagnosed with unspecified vitamin D deficiency. The majority were from BME groups; only one in five of the

[8] The study looked at women from the following ethnic populations: Indian Asians, Middle Eastern, Black and Caucasian. Ethnicity was self-reported (p 686).

[9] Secondary hyperparathyroidism can result from low calcium levels which can occur with vitamin D deficiency. Raised parathyroid hormone (PTH) levels are harmful to bone and confirms that the vitamin D deficiency to be clinically significant.

[10] The practice population includes large numbers of BME patients at higher risk of vitamin D deficiency than the general population which might bias the results slightly. However, the population is likely to be comparable to other Inner London GP practices.

women were white. The largest ethnic group was 'Any Other Ethnic Group' which in Westminster includes the Arab population. Also, there were 5 children under 5 years of age who had vitamin D deficiency and 10 with active cases of rickets.

Similar to the women, in the under 5s, 53% (8/15) were from 'Any Other Ethnic Group' followed by African (Black or Black British). As expected, this suggests that at risk groups form a larger part of those patients who are vitamin D deficient in Westminster.

A London based study (Sharma et al., 2009) of children who had attended secondary care and were vitamin D deficient supports these numbers. The children entered secondary care either through accident and emergency or referred by their GP with acute clinical symptoms including hypocalcaemic seizures, failure to thrive, bone bowing etc. The study found that 54% of the children had vitamin D concentration levels <25 nmol/l (Sharma et al., 2009. p1679). They used this to estimate the prevalence of symptomatic vitamin D deficiency as 1.6 per 1000 deliveries based on the number of births in London during the audit period (Sharma et al., 2009. p1679). The audit excluded children who had a condition which may impact their vitamin D levels and so this estimated prevalence only applies to nutritional vitamin D deficiency. The study suggests that as many children may have asymptomatic vitamin D deficiency, the true prevalence is likely to be higher. The authors also hypothesise that the mothers of the children in the study would have 'almost certainly' been vitamin D deficient during their antenatal period (Sharma et al., 2009. p1679).

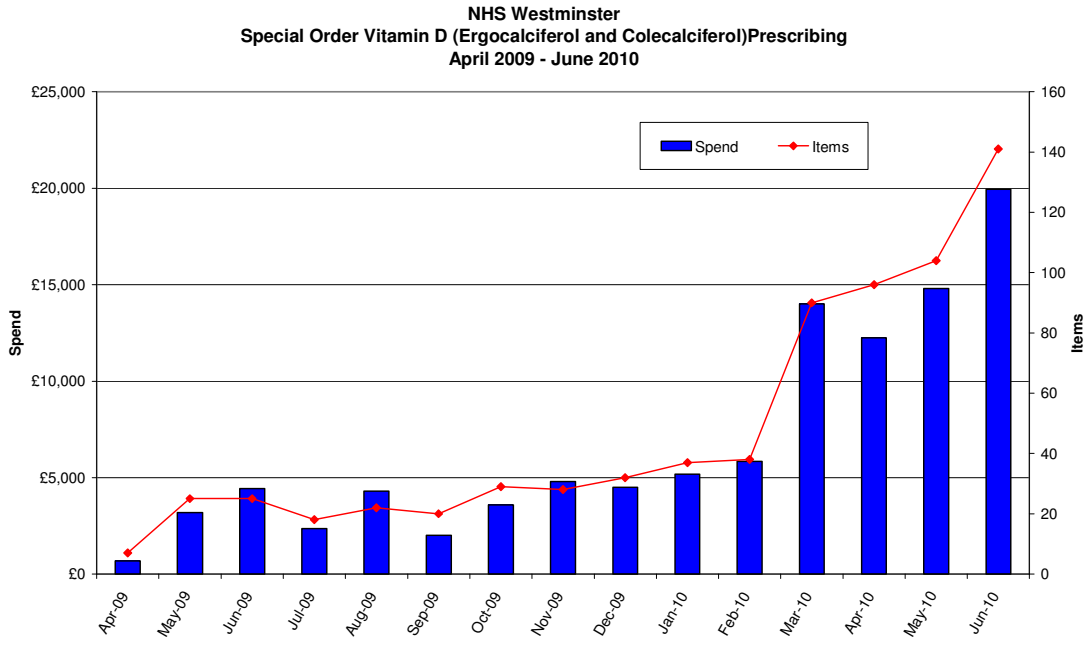
Hospital admissions data for Westminster residents due to vitamin D deficiency shows admissions are low. Between 1 April 2005 and 31 March 2010 there were 19 admissions to hospital for vitamin D deficiency in the 0-5 year old population and 26 admissions for women aged 15-44 years. In addition there were 7 admissions for adult osteomalacia in women aged 15-44 during this time period (SUS data).

It will be the most severe cases of vitamin D deficiency that are treated in hospital. Therefore, these numbers provide a very small part of the vitamin D deficiency picture in Westminster.

The other available local data is prescribing data. In 2009/10 Westminster GPs issued prescriptions for 273 single vitamin D treatment items. Some of these will be multiple scripts for the same patient as treatment is normally completed over 3 months, but as

Figure **2** shows, prescribing to treat vitamin D deficiency, has increased over the last year. This is due in part to greater awareness, amongst Westminster's GPs, of vitamin D deficiency and its associated poor health and therefore more patients are being diagnosed and treated. However, compared to the likely size of the problem, diagnosis and treatment remains low.

Figure 2. NHS Westminster Special Order Vitamin D Prescriptions April 2009-June 2010



Source: NHS Westminster, Medicines Management Team

6.3. Estimated Prevalence of Vitamin D Deficiency in Westminster

These estimates are likely to be an under representation of the true number of people with vitamin D deficiency in Westminster. This is because knowledge of vitamin D deficiency amongst the general public is low and therefore many people will not present to their GP as they are either asymptomatic or are self managing and may be unaware their symptoms are due to vitamin D deficiency and therefore do not seek treatment.

6.3.1. Women

The NDNS reported that 15% of women aged 19-64 in the UK are vitamin D deficient. If this prevalence is applied to Westminster's population[11], 13,335 women aged 20-64 years would be vitamin D deficient.

6.3.2. Children

There is no national average prevalence for vitamin D deficiency in children. The local GP audit data demonstrates the prevalence of known vitamin D deficiency (including those with rickets) in children aged under 5 years in that practice as 3%. If this percentage was extrapolated Westminster wide, this would suggest around 360 children aged under 5 would be vitamin D deficient.

Between January and June 2009 there were 1,494 births in Westminster. Using the estimated prevalence for vitamin D deficiency reported in (Sharma et al., 2009) of 1.6 per 1000 births, two babies in every thousand would be

[11] 88,900 2009 ONS estimate for female population (20 years to 64 years).

born vitamin D deficient. Westminster had 3,012 babies born to mothers resident in the borough in 2009. Therefore approximately 6 babies annually would be born vitamin D deficient. This appears to be a large underestimation.

Yu et al (2009) reported that only 8% of all babies in their study were born vitamin D sufficient (>50nmol/l). When extrapolated to Westminster's total births this equates to 240 babies in 2009 being born vitamin D sufficient. To follow this assumption through, the remaining 2,771 babies would have a vitamin D level under 50nmol/l and therefore be vitamin D insufficient or deficient. If the vitamin D insufficiency rate is calculated for this study population it is very much higher than that reported in (Sharma et al., 2009) at 944 per 1000 births.

It should be remembered that infant formula fed babies will not require vitamin D treatment or supplementation as the milk is legally required to be fortified with vitamin D. For breastfed babies whose mother's vitamin D supplementation during pregnancy is unknown vitamin D supplementation should start at 1 month otherwise supplementation should start at 6 months. At the 6-8 week check in Westminster[12] 49% of mothers continue to exclusively breastfeed their babies. A further 34% fed their babies with a mixture of breast milk and formula milk. Only 15% exclusively fed their babies with formula milk.

Based on the annual number of births in Westminster and the exclusive breastfeeding rate at 6-8 weeks, 1,476 babies should be given vitamin D supplementation from 6 months of age (a percentage of these will need supplementation from one month). If the rate is expanded to include all babies either exclusively or partially breastfed at 6 to 8 weeks, 2,530 children should receive supplementation from 6 months of age.

[12] Quarter 2, 2010-11

7. Consequences of vitamin D deficiency

Vitamin D deficiency is linked to a number of serious health conditions. The one most commonly associated with it is rickets in children and osteomalacia in adults. However, in recent years the evidence base linking vitamin D deficiency with other conditions and illnesses has been growing. The full literature review on these conditions can be found in the relevant appendixes. A general overview is included here. As this shows, the costs of not preventing vitamin D deficiency for both the patient and NHS services are high.

All these conditions, with the exception of asthma and lower respiratory infections and heart disease, are linked to the vitamin D status of the mother during pregnancy. Some of the conditions or illnesses affect the woman either during or after pregnancy and the remainder relate to the child.

Table 4. Conditions with a link to Vitamin D deficiency and when they occur

Conditions / Illnesses	Timeframe			
	Pregnancy	Postnatal	Infancy / Childhood	Other
Gestational Diabetes	✓			
Preeclampsia	✓			
Caesarean Sections	✓			
Bacterial Vaginosis	✓	✓		✓
Cancers		✓		
Low birth weight			✓	
Rickets			✓	
Osteomalacia		✓		✓
Skeletal problems in children (excluding rickets)			✓	
Diabetes			✓	✓
Allergies in children			✓	
Asthma and lower respiratory infections			✓	
Heart disease				✓
Multiple Sclerosis				✓

7.1. During Pregnancy and the Postnatal Period

The following conditions affect women during or after pregnancy. The evidence suggests a link between these conditions and vitamin D deficiency.

7.1.1. Gestational Diabetes

Gestational diabetes is a type of diabetes that affects women during pregnancy. Diabetes is condition caused by too much glucose (sugar) in the blood. It is estimated that in the UK gestational diabetes affects up to 14 in every 100 pregnant women (http://www.nhs.uk/conditions/gestational-diabetes/pages/introduction.aspx accessed on 24/8/10 at 15.00).

A link between vitamin D deficiency during pregnancy and an increased risk of developing Gestational Diabetes Millitus (GDM) has been identified by Zhang et al (2008). This study found that women with vitamin D deficiency had a 3.7-fold risk of developing GDM compared to women who were not vitamin D deficient. The study also highlighted that the risk was greatest for women who were overweight and vitamin D deficient. Further details of the studies are available in Appendix E.

7.1.2. Preeclampsia

Preeclampsia is a condition that can develop during the second half of pregnancy (around week 20). Preeclampsia occurs when the placenta is not getting enough blood. In the mother this can cause high blood pressure (hypertension), protein in her urine (proteinuria), and fluid retention (oedema). In the unborn baby, preeclampsia can cause growth problems (intrauterine growth retardation). The only way to prevent preeclampsia is to induce labour and deliver the baby. Depending on the gestation of the pregnancy this maybe done, but being born prematurely (before 37 weeks) can be dangerous for the baby (http://www.nhs.uk/Conditions/Pre-eclampsia/Pages/Introduction.aspx accessed on 24/08/10 at 14.55).

Two studies (Bodnar et al, 2008 & Haugen et al, 2009) have shown that there is a link between low vitamin D levels during pregnancy and the development of preeclampsia. Haugen et al's study (2009) also demonstrated that vitamin D supplementation of at least 10µg per day (the recommended amount in the UK) had the most protective effect and that women who took vitamin D supplements before pregnancy, in early pregnancy and late pregnancy had a 29% reduced risk of preeclampsia compared with those never taking vitamin D supplements' (Haugen et al, 2009. p723). Further details of the studies can be found in Appendix F.

7.1.3. Caesarean Section

A caesarean section delivery is usually carried out if a vaginal birth will put the mother or baby or both at risk. Approximately one baby in four born in the UK is delivered by caesarean section (http://www.nhs.uk/conditions/caesarean-section/Pages/Introduction.aspx accessed on 24/08/10 at 15.40). The reasons for caesarean sections vary, but this method of delivery may be a planned procedure if a medical risk has been identified, or an emergency procedure if during labour conditions mean it

is vital to deliver the baby quickly, or an elective procedure where the mother has chosen this as her preferred method of delivery.

An American study (Merewood et al, 2009) identified an association between vitamin D deficiency and caesarean sections. The study found that women with vitamin D deficiency (reported in the study as <37.5 nmol/l) were almost four times as likely to have a primary caesarean section as women without deficiency (OR 3.84, 95%CI 1.71-8.62) (Merewood et al, 2009. p942). Also, women who had caesarean sections had a lower median 25(OH)D level than women who delivered vaginally (Merewood et al, 2009. p941). The study also found that women who had caesarean sections were also more likely to be Caucasian/non-Hispanic white than black and/or Hispanic, to be US born and to have used alcohol in pregnancy.

It is unclear why a link may exist between vitamin D deficiency and caesarean sections. The authors suggest it may be related to the known link between vitamin D and smooth muscle function in early labour[13]. They hypothesise that vitamin D deficiency, through its link to maintaining calcium homeostasis, may play a role in initiation of early labour. They suggest that vitamin D deficiency may therefore be relevant for certain types of caesarean section deliveries (cephalopelvic disproportion or failure to thrive) rather than others (such as breech). The authors conclude that further research in the form of an RCT is needed to consider the link identified in their study.

7.1.4. Bacterial Vaginosis

Bacterial vaginosis (BV) is a vaginal infection that affects nearly one in three women of reproductive age. BV is 'an imbalance of the usual bacteria found in a woman's vagina. It causes an abnormal vaginal discharge which can smell fishy and unpleasant' (http://www.nhs.uk/conditions/bacterialvaginosis/Pages/Introduction.aspx accessed on 24/08/10 at 15.05). It is reported that BV is strongly associated with the risk of preterm birth (Bodnar et al, 2009. p1157).

Two American studies (Bodnar et al, 2009 & Williams et al, 2010) identified a link between low vitamin D levels and BV. The lower a woman's vitamin D levels the risk of having BV increased; this was shown both during pregnancy and when not pregnant. Further information on these studies can be found in Appendix G.

7.1.5. Cancer

Levels of vitamin D during pregnancy has been associated with ovarian and breast cancers in both a protective and negative way.

Insufficient vitamin D levels (<75 nmol/L serum 25(OH)D) during pregnancy has been found to increase a women's risk of ovarian cancer nearly three

[13] Serum calcium status, which is regulated by vitamin D, plays a role in smooth muscle function in early labour ((Merewood et al, 2009. p942). Other studies have shown higher levels of serum calcium in pregnant women at the time of vaginal delivery compared to term women not in labour or women who did not labour but delivered by scheduled CS.

times compared to women who have sufficient levels of vitamin D during pregnancy (Toriola, et al, 2009). Another study (Agborsangaya et al, 2010) found that there was no apparent link between vitamin D status during pregnancy and a woman's risk of breast cancer over time. However, this study did observe the possibility that higher levels of vitamin D during pregnancy may be associated with an increased risk of pregnancy-associated breast cancer (diagnosed within one year of delivery). Further details of these studies can be found in Appendix H.

7.2. During Infancy or Childhood

Though the following conditions affect infants or children the evidence shows that they are due to the maternal levels of vitamin D during pregnancy. The strength of the evidence for the different conditions differs and for some there is only a suggestion of a link.

7.2.1. Low Birth Weight

Low birth weight (<2500g) is associated with premature delivery and/or lower socio-economic groups, where maternal smoking and poor diet during pregnancy can play a determining role. Multiple births and certain ethnic origins are also associated with lower birth weights. Low birth weight is associated with childhood morbidity and can cause serious consequences for health in later life.

There is evidence that a low maternal vitamin D level can influence birth weight. An Australian study identified that maternal vitamin D deficiency increases the risk of neonatal vitamin D deficiency and lower birth weight (Bowyer et al, 2009). A study from London identified that mothers in the placebo group (no treatment) had more small-for-gestational age babies (8 vs. 13; P0.042) than treatment mothers (receiving multiple-micronutrient supplementation from the first trimester) (Brough, et al, 2010). Similarly, an audit conducted in London found that of the children presenting to acute care with vitamin D deficiency who had a documented birth weight (52/74), 58% of them were under 3kg at birth (Sharma et al, 2009.p1679).

There is evidence that low birth weight influences bone health and of a link between maternal nutrition and long-term bone health including osteoporosis as an adult (Williams et al, 2009). Low-weight babies, and children who fail to thrive, experience poor bone health later in life (Cooper, 2009 & Williams et al, 2009). Low birth weight is linked to a reduced bone density at peak during early adulthood and in older age, thus increasing the likelihood of developing osteoporosis in old age (Williams et al, 2009). Children who show a failure to thrive especially in their first year, have significantly lower bone size and mineral content at age 60 to 75 years (Cooper, 2009) and an increased risk of hip fracture in later life (Williams et al, 2009).

7.2.2. Rickets

Rickets is a disease which affects bone development in children. Children with a vitamin D status of <12.5nmol/l are at certain risk of developing rickets.

This is lower than the cut off for vitamin D deficiency (<25nmol/l) (ref ID 1956 p234). In adults rickets is known as osteomalacia (soft bones).

Rickets causes the softening and weakening of bones, which can lead to deformities, such as bowed legs and curvature of the spine. Children with rickets may experience pain in their bones, skeletal deformities, fragile bones (which maybe more prone to fracture), failure to thrive, and dental problems (http://www.nhs.uk/Conditions/Rickets/Pages/Introduction.aspx - accessed on 22/09/10 at 16.22). Vitamin D deficiency and rickets if left untreated can have serve consequences including seizures.

The vitamin D status of the mother has been identified as a causal factor in relation to rickets in infants. Whilst neontatal rickets is an uncommon consequence of vitamin D deficiency during pregnancy, low vitamin D exposure in utero combined with limited exposure postnatally (due to a lack of vitamin D in breast milk) can cause rickets in very young children (Yu et al, 2009. p685). Observational studies have found that up to 95% of children with vitamin D deficient rickets had been breastfed (Kovacs, 2008. p525S). An audit conducted in London between 2006-2008 found that the vast majority of children seen in hospital for acute vitamin D deficiency were breastfed (n=44/59) (Sharma et al, 2009. p1679).

7.2.3. Skeletal Problems in Children

Neonatal vitamin D stores are completely reliant on the mother's vitamin D supply. One study (ref ID 630) has shown that the bones of infants of mothers with low vitamin D levels at 19 and 34 weeks gestation already showed signs similar to childhood rickets. Another study (Viljakainen et al, 2009) found that newborns whose mother had low vitamin D levels had poorer bone mineral content and cross section area of their tibia at birth.

There is also increasing evidence that maternal vitamin D status impacts the bone development of the fetus not just in utero but also longer term. Two studies (Javaid et al, 2006 & Sayers & Tobias, 2009) found that children's bone size at 9 years of age was related to the mother's vitamin D levels during pregnancy. The latter study also found a link between exposure to sunlight and reduced risk of bone fracture. Another study (Ryan et al, 2010) has suggested a link between vitamin D deficiency in children with fractures, though according to (Perez-Rossello et al, 2010) maternal vitamin D level does not increase fractures in the child. Further details on these studies can be found in Appendix I.

7.2.4. Diabetes

Diabetes is a long-term condition that affects the body's ability to process sugar or glucose. It can have serious health consequences. In people with diabetes, the level of glucose in the blood is too high. This is because a hormone called insulin is either absent from the body or not working properly. Left untreated, diabetes can lead to heart disease, stroke, nerve damage and blindness. (http://www.nhs.uk/livewell/diabetes/pages/diabetesthefacts.aspx - accessed on 30/09/10 at 14.55).

There is evidence from a number of studies that the risk of developing type 1 diabetes[14] was significantly reduced in infants who were supplemented with vitamin D. There is evidence also that the more frequently the vitamin D supplementation is taken the lower the risk of developing type 1 diabetes. Further details are available in Appendix J.

7.2.5. Allergies in Children

The research evidence relating to vitamin D and allergies is small and conclusions cannot yet be drawn from it; details of these studies have been included for information only.

There is evidence that maternal vitamin D status in pregnancy and also the child's own vitamin D status can influence sensitivity to allergens. It would appear that maternal vitamin D intake during pregnancy can have a protective effect in relation to sensitisation to food allergens in the infant (Nwaru et al, 2010). However, a small study (Bäck et al, 2009) has found a suggested link between vitamin D supplementation during infancy and the development of atopic allergy later in childhood (up to age 6).

7.2.6. Asthma & Lower Respiratory Infections in Children

Asthma is a long-term condition that can cause a cough, wheezing and breathlessness. The severity of the symptoms varies from person to person. Asthma is caused by inflammation of the airways which makes it difficult to breathe and causes wheezing and coughing and also a tight chest. A severe onset of symptoms, known as an asthma attack or an 'acute asthma exacerbation', may require hospital treatment and can sometimes be life-threatening. There is currently no cure for asthma, but a number of treatments can help control the condition very effectively (http://www.nhs.uk/conditions/asthma/Pages/Introduction.aspx - accessed on 30/09/10 at 15.07).

In recent years, it has been hypothesised that the increase in the prevalence of asthma may in part be due to a change in diet. It is suspected that the maternal diet (including vitamin D intake) during pregnancy influences childhood asthma (Devereux, 2008).

Two studies have identified that higher maternal vitamin D intakes during pregnancy is associated with decreased wheezing symptoms in children at 3 years of age (Camargo Jr et al, 2007) and 5 years of age (Devereux et al, 2007). Camargo Jr et al (2007) reported that the method of obtaining vitamin D (through sunlight or by supplementation) did not matter, it was simply important that maternal vitamin D levels were sufficient. Further details can be found in Appendix K.

[14] Type 1 diabetes is the most common form of childhood diabetes. The body cannot produce any insulin. This type of diabetes usually occurs before age 40, and accounts for only around 10% of all cases (http://www.nhs.uk/livewell/diabetes/pages/diabetesthefacts.aspx - accessed on 30/09/10 at 14.55).

7.3. General

There is also evidence that vitamin D deficiency may be linked to conditions that can manifest themselves in early adulthood or at any stage during a person's life.

7.3.1. Heart Disease

There is a growing body of evidence that suggests there is a possible association between vitamin D deficiency and many cardiovascular disorders including hypertension, peripheral vascular disease, metabolic syndrome, coronary artery disease and heart failure (Vanga et al, 2010).

A large and increasing body of evidence suggests that poor vitamin D status is associated with poor cardiovascular outcomes. A number of studies have highlighted that vitamin D deficiency was more common amongst those who suffered cardiovascular disease. Also, a number of studies have shown that good vitamin D levels appear to have a protective effect against developing cardiovascular disease for those with no histories of cardiovascular disease. However, the little evidence there is of vitamin D supplementation on the risk of cardiovascular mortality found no significant effect (Vanga et al, 2010. p802). Further information can be found in Appendix L.

7.3.2. Multiple Sclerosis

Multiple sclerosis (MS) is the most common neurological condition in young adults in the UK, affecting around 85,000 people. MS is a condition of the central nervous system (the brain and spinal cord) which controls the body's actions and activities, such as movement and balance. Women are more than twice as likely as men to develop MS (http://www.nhs.uk/Conditions/Multiple-sclerosis/Pages/Introduction.aspx - accessed on 30/09/10 at 18.16).

Vitamin D deficiency during infancy has been identified as a risk factor in developing MS. Walker & Modlin (2009) report a study which used season of birth as a surrogate marker of vitamin D concentrations during pregnancy. This study found that season of birth was associated with familial cases of MS in a population based study conducted in several countries. An American study reported in Walker & Modlin (2009) found that among white adults a high vitamin D level had a protective effect in relation to an MS diagnosis[15]; this was not the case for African- Americans or Latinos (p109R).

[15] 'Those in the highest quintile of measured vitamin 25D before diagnosis had less of a risk for developing multiple sclerosis than those in the lowest quintile (odds ratio, 0.59). The inverse relationship...was strongest in subjects before their reaching 20 years of age' (Walker & Modlin, 2009. p109R).

8. Treating Vitamin D Deficiency

A number of different formulations are available for treating vitamin D deficiency in different population groups. The treatments listed here are approved and recommended by the Medicines Management Team at NHS Westminster as the most appropriate for patients. Figure 3 outlines optimum clinical care for vitamin D deficiency treatment in primary care.

As awareness of vitamin D deficiency within infants, children and young people has increased locally, Imperial College Healthcare NHS Trust, NHS Kensington and Chelsea and NHS Westminster have jointly produced local guidance on treating and preventing vitamin D deficiency in this population for primary care clinicians. This document entitled *Treatment and Prophylaxis Guidelines for Vitamin D Deficiency in Infants, Children and Adolescents* recommends the following treatment doses for children:

- Infant 1 to 6 months: 3,000 units daily
- Children 6 months to 12 years: 6,000 units daily
- Over 12 years to adult: 6,000 – 10,000 units daily

The recommended drugs for treatment are colecalciferol or ergocalciferol which can be used interchangeably. This is supported by recently released guidance from the NHS East & South East England Specialist Pharmacy Services on available products to treat vitamin D deficiency and insufficiency. This also outlines that all children should receive daily treatment for 8-12 weeks at the recommended dose for their age. The treatments may have a maximum shelf life once opened of 28 days, therefore children will need three bottles to complete a three month course.

Due to increasing treatment of vitamin D deficiency, NHS Westminster's Medicines Management Team has done a lot of work to ensure cost effective prescribing. This is largely due to variation in cost of colecalciferol and ergocalciferol special order liquid which are used to treat deficiency in children. The cost of a three month course has ranged from £479 to £940 depending on where the liquid was sourced from. Currently, colecalciferol 3,000units/ml sourced from Cardinal Health Martindale is recommended at a cost of £75 per 100ml, which totals £225 for a three month course.

Treatment doses for adults are different to those of children. Adults should be on 60,000IU once a week for 8-12 weeks (Pearce & Cheetham, 2010). Dekristol (colecalciferol) capsules of 20,000IU[16] are the current first line choice for adults (these are unlicensed in the UK however they can be imported through certain import companies). Local ICHT clinicians also believe that 20,000IU once a week may be suitable particularly in older people. If poor compliance with capsules is anticipated, the first choice treatment is the calciferol intramuscular injection of 300,000-600,000IU. The injection is given once every 8-12 weeks. If poor compliance with the

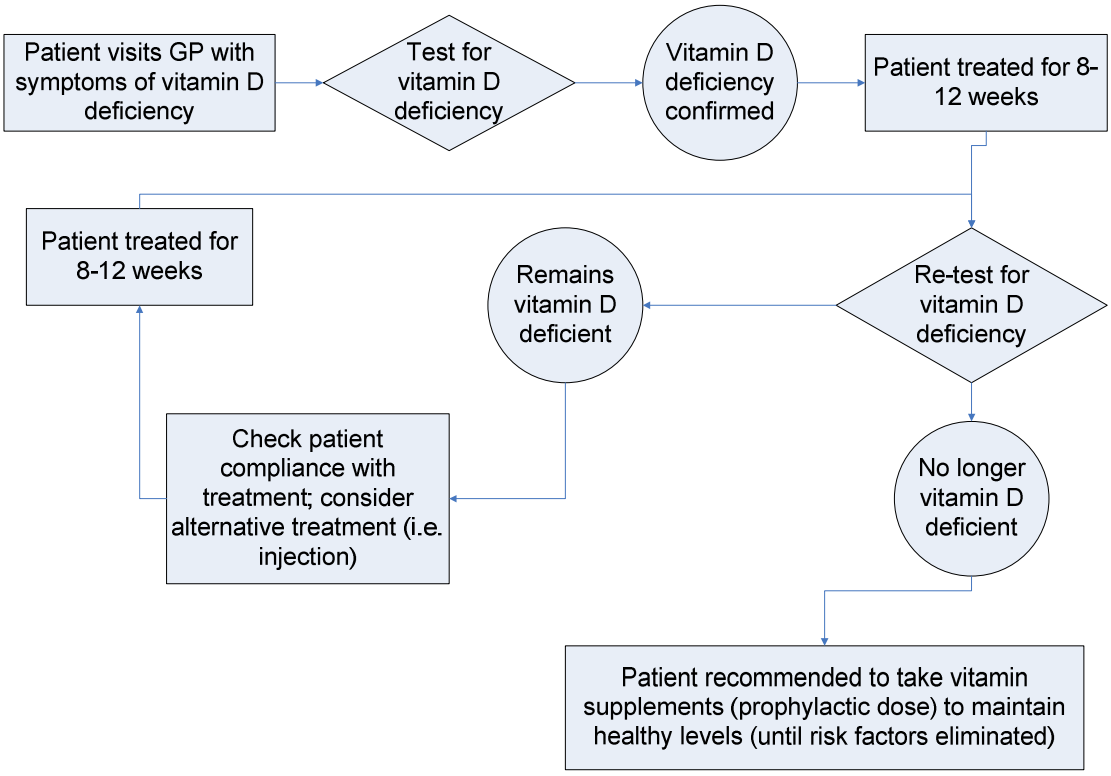
[16] Three tablets to be taken once a week.

capsules is identified after re-testing at three months, the injection may be considered as an alternative treatment.

Though the injection is more expensive than the capsules (£85 compared to £14.75 for 50 capsules) if a patient is unlikely to take the capsules the injection is the most clinical effective and cost effective method of treatment.

The local GP audit on vitamin D deficiency reported that 79% of patients who were vitamin D deficient and 65% of patients who were vitamin D insufficient were on treatment. However, compliance with treatment was poor. The audit report notes that many patients had only requested repeat prescriptions once or twice and thus without dietary and lifestyle changes and supplementation it was unlikely that vitamin D levels had been corrected or maintained.

Figure 3. Vitamin D Treatment in Primary Care Flowchart



9. Preventing Vitamin D Deficiency

The Department of Health recommends that at certain points in life such as early childhood or old age or during a specific life event such as pregnancy, the person should take supplementation to prevent vitamin D deficiency (see section 2.3 for further details).

There is evidence from a local study that supplementation during pregnancy either with a daily dose or a large single dose resulted in both the mother and baby having significantly higher 25-hydroxyvitamin D levels at delivery compared to the no treatment group (Yu et al, 2009. p687). Supplementation for vitamin D is recommended by the Department of Health throughout pregnancy.

The study supplemented women from 27 weeks gestation; only 30% of the mothers and 8% of the babies in the treatment groups achieved vitamin D sufficiency (p688). The authors suggested that the duration of supplementation and compliance with the treatment was important. The study found that overall the average percentage of tablets taken was 60% for the daily vitamin D dose (p688). The national recommendations are for supplementation throughout pregnancy. Though it should be noted, if a woman is vitamin D deficient prior to pregnancy, the prevention dose alone will not raise her vitamin D levels sufficiently; a treatment dose is required.

The Healthy Start vitamins are specially formulated for pregnant and lactating women. The cost of the Healthy Start vitamins to the NHS is £0.82 for 56 tablets (2 month supply). Alternative pregnancy multi-vitamins are available to purchase from pharmacies etc.

For children aged 6 months to 5 years, the Healthy Start multi-vitamin drops are available. Healthy Start vitamin drops cost the NHS £1.61 for 10ml. Alternative products include Dalivat® (£2.98 for 25ml) and Abidec® (£2.20) multi-vitamin drops.

10. Information Gaps

There is limited evidence around the extent of vitamin D deficiency in Westminster. If the following information gaps could be rectified, local knowledge on vitamin D deficiency and the at risk groups would be greatly furthered:

- Regular reporting of BMI measurements for women at first booking from the main maternity providers for Westminster.
- Regular reporting of ethnicity recorded at first booking.
- Testing of at risk women at first booking for vitamin D deficiency. Regular reporting of results.
- Testing of new borns for vitamin D deficiency. Regular reporting of results.
- Regular reporting from general practice on vitamin D testing, confirmed vitamin D deficiency and cases of rickets or osteomalacia.

11. Recommendations

Testing High Risk Pregnant Women for Vitamin D Deficiency at First Booking

Women from high risk groups (BME groups and women with a body mass index >30 at first booking) should be tested for vitamin D deficiency at first booking. If they are vitamin D deficient or insufficient they should then be treated accordingly. For women with sufficient levels of vitamin D they should be recommended to take a vitamin D supplement such as Healthy Start vitamins for the duration of their pregnancy and whilst breastfeeding to maintain their healthy levels of vitamin D.

Promoting Healthy Start to Pregnant Women & Families

The Healthy Start programme should be recommended to all pregnant women and families with young children. Eligible women and families should be encouraged to apply and make use of the programme.

Professional Training on Vitamin D Deficiency

Education and training on vitamin D deficiency and vitamin supplementation (including Healthy Start) should be provided for healthcare professionals and early years staff working directly with pregnant women and young families. The importance of cost effectiveness when prescribing vitamin D treatments should be reiterated to GP practices to ensure the most appropriate treatments are provided and unnecessary costs are not incurred.

Universal Healthy Start

Levels of vitamin D deficiency are likely to be quite high within Westminster due to the large BME communities within the borough and high numbers of pregnant women being overweight or obese at first booking. It is therefore recommended that to promote the importance of taking vitamin D supplements all women and babies should be provided with, at a minimum, one bottle of free Healthy Start vitamins. The optimum solution would be to provide to all women, infants and young children (up to age 5) their complete supply of Healthy Start vitamins.

Vitamin Supplement Safety

Health care professionals need to have a sound understanding of the difference between RDAs and RNIs and be able to explain these to parents. Parents must be advised not to supplement their children with any products that contain 100% RDA of vitamin A as this is dose is too high for young children and puts them at risk of toxic levels.

Vitamin A

Formula fed babies aged 2-4 months should not take Healthy Start vitamins along with their formula milk. The intake of vitamin A from these two separate sources totals more than the daily maximum intake recommended for infants.

12. Conclusions

The full extent of vitamin D deficiency remains hidden within Westminster. However, the identification of the at risk groups in the borough in this needs assessment highlights that large parts of the community are at high risk of developing vitamin D deficiency or may already be suffering from it.

This needs assessment has highlighted the wide ranging impact that vitamin D deficiency can have. The costs to the individual and the NHS of vitamin D deficiency are high.

Increased knowledge of vitamin D deficiency and how to prevent it or treat it is needed both within the community generally and amongst healthcare professionals. It is important that people understand why preventing or completing treatment for vitamin D deficiency is important and are supported to do this.

A consequence of increased testing for vitamin D deficiency would be an increase in vitamin D treatments. However, in the longer term by treating the deficiency at an earlier stage costs to the NHS and the individual will be reduced. Further, if appropriate recommended treatment is provided, unnecessarily high costs to the NHS for treatment can be avoided.

Promotion of methods to prevent vitamin D deficiency and maintain a healthy level of vitamin D should be encouraged and improved. It is important that all professionals that work with pregnant women and young families understand the importance of vitamin D and are trained to promote it. This extends beyond healthcare to those working in Early Years.

Glossary

Vitamin D_2	Vitamin D (ergocalciferol) found in plants and some fish
Vitamin $D_{3`}$	Vitamin D (cholecalciferol) synthesized in the skin by sunlight
25(OH)D	25-hydroxyvitamin D: the combined level of vitamin D3, from sunlight and vitamin D2, from dietary (including supplementation) sources.
mg	milligram or 10^{-3} g or one-thousandth of 1 g
µg	microgram or 10^{-6} g or one-millionth of 1 g (1000 micrograms are found in 1 milligram)
RDA	Recommended Daily Amounts of Food Energy and Nutrient for Groups of People in the United Kingdom (DH, 1991)
RNI	Reference Nutrient Intake for protein or a vitamin or mineral. An amount of the nutrient that is enough, or more than enough, for about 97% of people in a group. If average intake of a group is at RNI, then the risk of deficiency in the group is very small (DH, 1991).
BMI	Body mass index

Appendix A – Vitamin D Deficiency in Immigrant Groups

It is well known that people from certain cultural and religious backgrounds and those with darker skin are more at risk of being vitamin D deficient. This is because longer exposure is needed for darker skin to process adequate levels of vitamin D from the sun, and also due to the wearing of concealing clothing such as veils which block sunlight.

A local study (Yu et al, 2009) highlighted that women from BME groups had higher levels of vitamin D deficiency that Caucasian women (Table 3). This study found that locally 64% of Middle Eastern women were vitamin D deficient. A study conducted in the Hague found similar levels in women of Moroccan and Turkish origin with 56-66% having 25(OH)D levels <25 nmol/l compared with 8% of women of western origin (van der Meer et al, 2006).

A German study (Hintzpeter et al, 2008) compared immigrant children with native born children. It found that 'vitamin D concentrations were consistently lower among immigrants compared with nonimmigrants in both sexes' (Table 5) (Hintzpeter et al, 2008. p1484). The authors suggest that higher supplementation may be needed for immigrant children as despite a higher vitamin supplement use in infancy (Germany supplements all infants up to age 1) they go onto have higher vitamin D deficiency prevalence than non-immigrant children.

Table 5. Vitamin D levels in 3 to 17 year old children in Germany by Immigrant Status

Children	Percentage with vitamin D level <25 nmol/l
Immigrant boys	29%
Immigrant girls	31%
Non-immigrant boys	18%
Non-immigrant girls	17%

Source: Hintzpeter et al, 2008. p1484

This study also identified that children of immigrants from certain countries of origin had an increased risk of having low vitamin D concentrations (Table 6). Also, girls whose mothers came from an Asian (OR 6.7; [95%CI] 2.2-19.8) or African (OR 7.8; [95%CI] 1.5-40.8) background also had an increased risk of low vitamin D concentrations (Hintzpeter et al, 2008. p1484).

Table 6. Child's Risk of Low Vitamin D Concentrations by Mother's Country of Origin

Child's Gender	Country of Mother's Origin	
	Turkey	**Arab-Islamic[17]**
Boys	OR 2.3; [95%CI] 1.4-3.8	OR 7.6; [95%CI] 3.0-19.1
Girls	OR 5.2; [95%CI] 2.9-9.6	OR 5.9; [95%CI] 2.5-14.0

Source: Hintzpeter et al, 2008. p1484

Other studies have focused on the vitamin D status of immigrant children in a variety of different climates (Australian, McGillivray et al, 2007 & Northern Europe, Stellinga-Boelen et al, 2005 & Hintzpeter et al, 2008). The Australian and Dutch studies both identified that seasonality played a part in the vitamin D status of immigrant children. In the Australian study McGllivray et al (2007) found that being tested in winter or spring was the greatest independent risk factor associated with vitamin D deficiency (OR 9.0 95%CI 3.7 to 22.0) (McGillivray et al, 2007. p1090) in the population they studied (East African[18] immigrant children and adolescents). The Dutch study found that the 'improvement of 25(OH)D levels of African children during the summer without supplements was incomplete' (Stellinga-Boelen et al, 2005. p205). It also reported that the 'values of 25(OH)D in mid spring were significantly higher in children from Eastern Europe than in children from Central Asia ($p<0.05$) and Africa ($p<0.01$) respectively' (Stellinga-Boelen et al, 2005. p203).

The prevalence of vitamin D deficiency in the Australian study was reported at nearly half with 44% of the children being vitamin D deficient (McGillivray et al, 2007. p1089). The Dutch study found that in mid spring 13% of children had vitamin D deficiency and 42% were vitamin D insufficient (hypovitaminosis D) (Stellinga-Boelen et al, 2005. p 201).

All three studies found that girls were more likely to be vitamin D deficient than boys (with the exception of Turkish and Arab-Islamic background where both sexes were found to be high risk by Hintzpeter et al, 2008).

[17] The study defined these as 'Lebanon, Morocco, Algeria, Iraq, Egypt, Pakistan, Syria, Jordan, Senegal, Tunisia, Brunei, Indonesia, Iran, Kuwait, Bangladesh, Guinea and Gambia' (Hintzpeter et al, 2008. p1483)

[18] East African was defined in the study as 'Somalia, Sudan, Ethiopia, Kenya, Egypt, Eritrea or Djibouti' (McGillivray et al, 2007.p1088)

Appendix B – Vitamin A

The formula feed information has been calculated using the information from SMA First Infant Milk. This was chosen as it provided an 'average' amount of the three vitamins. The Cow & Gate and Aptamil brands both contained lower amounts of the vitamins. Hipp Organic first milk had higher amounts of vitamin A (70 µg compared to 66 µg per 100ml) and vitamin C (16.6mg compared to 9mg per 100ml) but lower amounts of vitamin D (1.1 µg compared to 1.2 µg per 100ml).

SMA First Infant Milk contains 66 µg of vitamin A, 1.2 µg of vitamin D and 9mg of vitamin C per 100ml of prepared feed. The total vitamin amounts in the feeds per 24 hours have been calculated based on the number of feeds recommended by SMA for the different ages listed and the amounts of the feeds; both differ with age.

As can be seen from the table, for all three vitamins, the RNI is exceeded when infants are formula fed and receive Healthy Start vitamin supplementation. However, it is only for babies aged 2-4 months that the level of any one vitamin exceeds the upper limit of the daily amount. Between 2 and 4 months, the daily feeds with the Healthy Start vitamins takes the vitamin A levels over the safe daily upper limit of 900 µg**.**

Age of Baby	Total Feeds Vitamins			Healthy Start Vitamins			Total Vitamin Intake with HS			RNI		
	Vitamin A µg	Vitamin D µg	Vitamin C mg	Vitamin A	Vitamin D	Vitamin C	Vitamin A µg	Vitamin D µg	Vitamin C mg	Vitamin A µg	Vitamin D µg	Vitamin C mg
birth - 2 weeks	356	6.4	49	233 µg	7.5 µg	20 mg	589	13.9	69	350 µg	8.5 µg	25mg
2 - 4 weeks	475	8.6	65				708	16.1	85			
2 months	795	8.9	68				1028	16.4	88			
4 months	693	12.5	95				926	20.0	115			
6 months	634	11.4	86				867	18.9	106			
7-12 months	416	7.5	57				649	15.0	77		7 µg	

Appendix C – Alternative Blood Sample Methods for Vitamin D Testing

The current method for obtaining the blood sample for vitamin D testing is the venipuncture sample method. Alternative methods are considered by the following studies.

One study (Dayre McNally et al, 2008) investigated whether a fingerprick blood test provided an adequate sample to test for vitamin D levels. The authors compared the fingerprick test to a normal venipuncture sample (blood test); the results demonstrated a highly significant relationship between 25(OH)D levels in serum derived from venous and capillary (fingerprick) blood samples. The authors, however, suggested a note of caution as the fingerprick samples had statistically higher 25(OH)D levels compared with venipuncture samples, but they did not feel this was enough not to recommend fingerprick samples as an alternative method to venipunture samples. Instead, they suggested for clinical application a correction factor may need to be included in the assessment of insufficiency and that research studies should not use the two methods interchangeably.

A study published in two articles (Eyles et al, 2009 & Eyles et al, 2010) considered the use of dried blood spot to test for vitamin D status. Blood spots are taken from babies shortly after birth as part of the routine screening programme. The authors (Eyles et al, 2009) outlined that both $25(OH)D_3$ and $25(OH)D_2$ can be reliably quantified in archived 3.2mm dried blood spots. They used samples that had been stored for up to 22 years. The dried blood spots also showed seasonal variation, with significantly higher concentrations of $25(OH)D_3$ found in dried blood spots taken in summer compared to winter ($p<0.0001$). Although, the authors note that they cannot be sure that the levels measured from the dried blood spots were the same as when they were collected, the fact that seasonal variation is seen allows them to conclude that dried blood spots are 'a useful tissue repository for testing a range of hypotheses linking developmental hypovitaminosis D and adverse health outcomes' (Eyles et al, 2009. p145).

The second paper published by Eyles et al (2010) aimed to 'validate the use of dried blood spots to estimate perinatal vitamin D status and to determine whether inter-group differences in cord serum $25(OH)D_3$ are reflected in dried blood spots' (Eyles et al, 2010. p303). They compared 4 year old frozen cord sera and matched dried blood spots from neonates. The study found that not only were $25(OH)D_3$ concentrations in both samples highly correlated ($r = 0.85$, $P<0.0001$), but that a seasonal difference was seen between babies born in winter and summer. The authors suggested therefore that dried blood spots could be used for case-control studies investigating the association between perinatal vitamin D status and later health outcomes.

Appendix D – Vitamin D Deficiency: Stages and Clinical Signs

Table 7. Vitamin D Deficiency: Stages and Clinical Signs

Stages of vitamin D deficiency		Clinical Signs of Vitamin D Deficiency	Potential latent disease processes associated with vitamin D deficiency
Stage 1	25-OH-D level decreases, resulting in hypocalcemia and euphosphatemia; 1,25-OH_2-D may increase or remain unchanged	▪ Dietary calcium absorption from the gut decreases from 30%–40% to 10%–15% when there is vitamin D deficiency ▪ Low concentrations of 25-OH-D trigger the release of PTH in older infants, children, and adolescents in an inverse relationship not typically seen with young infants; the increase in PTH mediates the mobilization of calcium from bone, resulting in a reduction of bone mass; as bone mass decreases, the risk of fractures increases ▪ Rickets: Enlargement of the skull, joints of long bones, and rib cage; curvature of spine and femurs; generalized muscle weakness ▪ Osteomalacia and osteopenia ▪ Abnormal immune function with greater susceptibility to acute infections and other long-latency disease states (see right)	▪ Dysfunction of the innate immune system is noted with vitamin D deficiency. ▪ Immunomodulatory actions may include: – Potent stimulator of innate immune system acting through Toll-like receptors on monocytes and macrophages – Decrease threshold for long-latency diseases such as cancers (including leukaemia and colon, prostate, and breast cancers), psoriasis, diabetes mellitus, and autoimmune diseases (e.g., multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosis)
Stage 2	25-OH-D level continues to decrease; PTH acts to maintain calcium through demineralization of bone; the patient remains eucalcemic and hypophosphatemic and has a slight increase in the skeletal alkaline phosphatase level		
Stage 3	Severe 25-OH-D deficiency with hypocalcemia, hypophosphatemia, and increased alkaline phosphatase; bones have overt signs of demineralization		

Source: Wagner et al, 2008

Appendix E – Gestational Diabetes

One American study (Zhang et al, 2008) identifies a link between vitamin D deficiency during pregnancy and an increase risk of developing Gestational Diabetes Mellitus (GDM). The study found that women who went onto develop GDM had at 16 weeks gestation lower levels of vitamin D that proved statistically significant compared to the control group (24.2 vs. 30.1 ng/ml, $P<0.001$).

The study reported that 'approximately 33% of GDM cases, compared with 14% of controls ($P<0.001$), had plasma 25-[OH]D concentrations consistent with a diagnosis of vitamin D deficiency (<20 ng/ml) (Zhang et al, 2008. p2). In addition to this, 'women classified as being deficient for vitamin D had a 3.7-fold increased subsequent risk of GDM…after adjustment for maternal age, race/ethnicity, first-degree family history of type 2 diabetes' (Zhang et al, 2008. p3). The study highlighted that the risk was greatest for overweight women who were vitamin D deficient.

The authors conclude that it is possible by treating vitamin D deficiency or preventing it in the first place with supplementation or lifestyle changes it may help to protect pregnant women from developing GDM.

Appendix F - Preeclampsia

These studies have been briefly reported in 7.1.2:

A study conducted in the USA (Bodnar et al, 2007) first identified a possible link between low vitamin D levels during pregnancy and the development of preeclampsia. Bodnar et al reported that 'maternal serum levels of 25(OH)D below 37.5 nmol/litre in early pregnancy were associated with a 5-fold increase in the risk of developing preeclampsia, independently of race/ethnicity, season of the year, gestational age at sampling, prepregnancy body mass index and educational level' (p3517).

A second study conducted in Norway (Haugen et al, 2009), based on the findings of Bodnar et al (2007) found similar results. This was a large study of 23,423 mothers which considered vitamin D intake from total diet and from vitamin supplements. Supplementation appeared to have a greater protective effect as limited vitamin D intake was achieved via total diet despite fortification of some foods in Norway (milk and margarine). The study reported that 'women reporting supplementary intake of vitamin D at all 3 points (before pregnancy, in early pregnancy, and in late pregnancy) had 29% reduced risk of preeclampsia compared with those never taking vitamin D supplements' (Haugen et al, 2009. p723).

The study highlighted that 'a protective effect from vitamin D supplements seemed to be most evident at doses of at least 10 µg/d' (Haugen et al, 2009. p725). The study also identified that season of birth had a slight influence on preeclampsia risk and this risk remained unchanged after adjustment for vitamin D intake.

Both studies identify that vitamin D deficiency may influence preeclampsia. Whilst neither study provides definitive proof, the evidence suggests that pregnant women adhering to the recommended daily amount of vitamin D supplementation throughout their pregnancy would have a reduced risk of developing preeclampsia.

A third study (Hyppönen et al, 2007) suggested a longer term protective effect of vitamin D supplementation in relation to preeclampsia. This study concluded that there may be 'a reduced risk of preeclampsia in the first pregnancy in women, who had received vitamin D supplementation during infancy' (Hyppönen et al, 2007. p1139). Using participants within a longitudinal study (Northern Finland Birth Cohort 1966) the authors were able to identify that the 'prevalence of preeclampsia was lower among women who had received vitamin D supplementation regularly during their first year of life compared to those who had received supplementation irregularly or not at all' (Hyppönen et al, 2007. p1138).

This study may add weight to the supplementation of infants during their first year as it appears to identify a longer term protective effect of vitamin D. However, it should be noted that the level of vitamin D supplementation

recommended in Finland at the time (1966) was 2000IU/day. This is significantly higher than the recommended daily amount for infants (8.5 µg/day up to 7 months and 7µg/day for babies aged 7-12 months). Thus, the daily recommended amounts are unlikely to be enough to replicate similar results.

Appendix G – Bacterial Vaginosis

An American study (Bodnar et al, 2009) identified a link between BV and vitamin D deficiency during early stages of pregnancy. It is reported that BV is strongly associated with the risk of preterm birth (Bodnar et al, 2009. p1157). The study sample came from a low socio-economic area in Pittsburgh PA with a 55% black and 44% white population; overall the population served by the ANC clinics used in the study were uninsured and on low incomes.

The authors reported that 41% of all women included in the study had BV. Women with BV had 'lower unadjusted mean 25(OH)D concentrations compared with women with normal vaginal flora…these associations remained after adjusting for race' (Bodnar et al, 2009. p1159). The prevalence of BV decreased as vitamin D status improved: 'approximately 57% of the women with a serum 25(OH)D concentration <20 nmol/L had BV compared with 23% of women with a serum 25(OH)D concentration >80 nmol/L' (Bodnar et al, 2009. p1159).

The authors also reported that BV was more common as vitamin D status worsened among black women but not among white women. They highlighted that this disparity maybe due to the overrepresentation of black women in the lower range. They were also not able to properly assess BV and vitamin D sufficiency as there were very low numbers of women in this group. However, the authors concluded that their findings 'suggest that vitamin D deficiency is associated with BV at <16 weeks of pregnancy' (Bodnar et al, 2009. p1161).

A second American study (Williams et al, 2010) also identified a link between vitamin D deficiency and BV. This study was conducted in non-pregnant women aged 20-49 years and found low vitamin D levels were associated with BV particularly the symptomatic form; this association was seen in white and black women, but not Hispanic women.

Appendix H - Cancer

A Finnish study (Toriola et al, 2010) looking into vitamin D deficiency and ovarian cancer risk found that women with insufficient vitamin D levels (<75 nmol/L serum 25(OH)D) during pregnancy were nearly 3 times as likely to be at risk of ovarian cancer compared to women who during pregnancy had sufficient levels of vitamin D (>=75 nmol/L serum 25(OH)D). However, the authors also reported that despite these findings, the study had not observed a significant association between serum 25(OH)D concentrations and the risk of ovarian cancer.

A Finnish study (Agborsangaya et al, 2010) looked at the risk of breast cancer relating to vitamin D level during the first and second pregnancy using a prospective nested case-control study within the Finnish Maternity Cohort. This study considered both the risk of breast cancer associated with vitamin D over time and the relationship between vitamin D levels and pregnancy-associated breast cancer (PABC, diagnosed within one year of delivery). This study found that there was no apparent link between vitamin D status during pregnancy and a woman's risk of breast cancer over time. However, the authors did observe the possibility that higher vitamin D levels during pregnancy may be associated with an increased risk of PABC (OR=2.7; 95% CI 1.04-6.8) (Agborsangaya et al, 2010. p468).

Appendix I – Skeletal Problems in Children

These studies are briefly reported in 7.2.3:

A number of studies have looked at maternal vitamin D status and bone development in the womb. A British study (Mahon et al, 2010) found that the fetuses of mothers who had lower vitamin D concentrations during pregnancy showed distal femoral metaphyseal splaying at both 19 weeks and 34 weeks gestation. This is what is seen in childhood rickets and there authors' suggest it could therefore act as a marker for children at risk of developing rickets. Whilst the study outcomes remain observational, another paper argues they 'are provocative on several levels' particularly the skeletal development link to vitamin D as early as 19 weeks gestation (Hewison & Adams, 2010). This is important as maternal levels of the active form of vitamin D rise in early pregnancy and therefore this research may support increased supplementation of vitamin D early in pregnancy (Hewison & Adams, 2010).

Another study (Viljakainen et al, 2009) found that newborns whose mother had low vitamin D levels had an average 13.5% lower bone mineral content and 15.6% smaller cross section area in tibia compared to newborns whose mother had higher levels of vitamin D (Viljakainen et al, 2009). There is also evidence that children born to mothers' with deficient or insufficient levels of vitamin D during pregnancy, show deficits in bone mineral content at 9 years of age (Javaid et al, 2006). A subsequent, larger trial, found similar results (Sayers & Tobias, 2009). The authors' measured children at 9 years of age (mean age 9.9) and identified that the children's bone size, independently of height and lean mass, were related to maternal vitamin D exposure during pregnancy. The authors' suggest that vitamin D status during pregnancy exerts a 'direct influence on periosteal bone formation' during childhood (Sayers & Tobias, 2009. p770). The study also observed a link between increased levels of UVB sunlight (vitamin D exposure) and a reduced risk in bone fractures in the child (for every $_{SD}$[19] increment in maternal UVB exposure, there is an approximate 5% decrease in fracture risk of the offspring' (Sayers & Tobias, 2009. p769)).

An American study looking at fractures in African American children (Ryan et al, 2010) found an association and recommended that children who had suffered fractures should have their vitamin D levels tested. However, contrasting evidence in one study found maternal vitamin D status during pregnancy does not increase fractures (Perez-Rossello et al, 2010).

[19] The authors' liken 1 $_{SD}$ increase in background UVB to being approximately equivalent to a 4 week holiday in winter to a destination where UVB levels are similar to those in summer (Sayers & Tobias, 2009. p768).

Appendix J – Diabetes in Children

A systematic review and meta analysis found that there is evidence from observational studies that vitamin D supplementation in infancy might be protective against the development of type 1 diabetes[20] (Zipitis & Akobeng, 2007). Meta analysis of data from case-control studies found that the risk of type 1 diabetes was significantly reduced in infants who were supplemented with vitamin D compared to those that were not; this was supported by the results of the cohort study.

The review found that there was some evidence of a dose-response effect. The Stene et al (2003) study found that as the frequency of supplementation increased from one to four times per week to more than five times per week the odd ratio of developing type 1 diabetes decreases (OR 0.81, 95% CI 0.55 to 1.19 and OR 0.74%, 95% CI 0.56 to 0.99 respectively) (Zipitis & Akobeng, 2007. p515). The review also found that those who took the recommended dose of 2000 IU regularly had a relative risk of 0.221 (95% CI 0.05 to 0.89) compared with those who regularly took less than the recommended dose (Zipitis & Akobeng, 2007. p515).

The review did not find any statistical difference between those who were supplemented for more or less than a year. However, there was some evidence that infants supplemented from 7-12 months had more protection and were less likely to develop type 1 diabetes compared to infants supplemented from 0-6 months (Zipitis & Akobeng, 2007. p515). However, these results should be interpreted with care as supplementation from 7-12 months may imply a longer supplementation. Also, babies being supplemented early in life (before 6 months) may be due to being born to a vitamin D deficient mother. This may explain earlier supplementation and the increased risk of type 1 diabetes which was also found to be the case in children who had suspected rickets, though this result was not statistically significant (Zipitis & Akobeng, 2007. p515).

The review acknowledges some limitations due to recall bias in the retrospective studies. It goes on to recommend that randomised control trials are needed to establish causality and the best formulation, dose, duration and period of supplementation (Zipitis & Akobeng, 2007. p516). However, this review does provide some evidence that vitamin D supplementation in infants does appear to have a protective effect against developing type 1 diabetes in later life.

[20] Type 1 diabetes is the most common form of childhood diabetes. The body cannot produce any insulin. This type of diabetes usually occurs before age 40, and accounts for only around 10% of all cases (http://www.nhs.uk/livewell/diabetes/pages/diabetesthefacts.aspx - accessed on 30/09/10 at 14.55).

Appendix K – Asthma & Lower Respiratory Infections

Two studies have identified that higher maternal vitamin D intakes during pregnancy is associated with decreased wheezing symptoms in children at 3 years of age (Camargo Jr et al, 2007) and 5 years of age (Devereux et al, 2007). In both studies the results were independent of confounding factors (fish intake, fruit and vegetable intake, early use of vitamin supplement and child's intake of vitamin D at age 2 years (Camargo Jr et al, 2007)) and maternal smoking status and maternal intakes of vitamin E, zinc, calcium and vitamin D by the 5 year old children (Devereux et al, 2007)).

The American study (Camargo Jr et al, 2007) found an association was present for vitamin D from either foods or supplements and that in children born in the autumn months when sunlight does not provide enough vitamin D the inverse association between maternal vitamin D intake during pregnancy and recurrent wheeze was stronger (p792).

Both study authors' recommend appropriate supplementation during pregnancy as a low cost and safe way to reduce the risk of children developing asthma or other respiratory problems.

Other studies support these findings including a 2009 study which also reports that maternal vitamin D intake from foods during pregnancy may be negatively associated with risk of asthma and allergic rhinitis in children aged 5 years (Erkkola et al, 2009).

A Turkish study (Karatekin et al, 2009) found that in infants admitted to the neonatal intensive care unit who had acute lower respiratory infection (ALRI) without rickets, had lower levels of vitamin D than the control group who were healthy newborns. This link was especially relevant for infants with vitamin D levels <10ng/ml (Karatekin et al, 2009. p475). The authors also found that there was a direct correlation between the vitamin D status of the mothers and of the babies in both groups, though it was slightly more pronounced in the study group ($r=0.79$, $P<0.05$ compared to $r=0.53$, $P<0.05$ in the controls). The authors' concluded that 'subclinical vitamin D deficiency in newborns may increase their risk of suffering from ALRI' (p476) and that the high correlation between maternal and infant vitamin D status highlights the importance of maternal supplementation during pregnancy.

However, a Finish study (Hypponen et al, 2004) looking at vitamin D supplementation in infancy reported that regular vitamin D supplementation in the first year of life increased the risk of developing atopy, allergic rhinitis and asthma by the age of 31 years. However, other studies have criticised this piece of research as it collected no information on maternal or childhood (>1 year) intake of vitamin D and there was limited control for major confounding factors. In addition, recall bias may have affected the ascertainment of early life asthma and allergies (Camargo Jr et al, 2007. p793 & Devereux et al, 2007. p857).

Appendix L – Heart Disease

These studies are briefly reported in 7.3.1:

There is some conflicting evidence around the role vitamin D deficiency plays in hypertension. A number of studies, reported in a systematic review, have shown a link between vitamin D deficiency and high blood pressure while others have documented a decrease in blood pressure with exposure to vitamin D either through sunlight or supplements (Vanga et al, 2010. p799). However, a recent meta-analysis reported by Vanga et al (2010) provided little support for a positive effect of vitamin D supplementation on blood pressure (p801).

Vanga et al (2010) also highlight that there is a growing body of evidence linking vitamin D deficiency with higher prevalence of peripheral arterial disease (p801). Studies have also suggested that one third of the excess risk for peripheral arteral disease in an African American population was attributed to racial difference in vitamin D status (p801).

Vanga et al (2010) report that observational studies have shown that osteporosis, osteopenia and low levels of vitamin D are common in patients with congestive heart failure (p802). There is also evidence of an ethnic variation in the incidence of heart failure and serum vitamin D levels. The implication being that that this is due to certain populations (those discussed in Vanga et al are African Americans) being at greater risk of being vitamin D deficient than others. There is also some evidence of poor vitamin D levels being associated with poor outcomes in patients with end-stage heart failure awaiting heart transplants (p803).

References

Agborsangaya, C, B., Surcel, H-M., Toriola, A, T., Pukkala, E., Parkkila, S., Tuohimaa, P., Lukanova, A & Lehtinen, M. “Serum 25-hydroxyvitamin D at pregnancy and risk of breast cancer in a prospective study.” European Journal of Cancer 46 (2010): 467-470

Bäck, O., Blomquist, H, K., Hernell, O & Stenberg, B. “Does vitamin D intake during infancy promote the development of atopic allergy?” Acta Dermato-Venereologica 89.1 (2009): 28-32

Bodnar, L. M., Catov, J, M., Roberts, J, M & Simhan,H, N. "Prepregnancy obesity predicts poor vitamin D status in mothers and their neonates." Journal of Nutrition 137.11 (2007): 2437-42.

Bodnar, L M., Catov, J M., Simhan, H N., Holick, M F., Powers, R W & Roberts, J M. “Maternal Vitamin D Deficiency Increases the Risk of Preeclampsia.” Journal of Clinical Endrocrinology & Metabolism 92 (2007): 3517-3522.

Bodnar, L, M., Krohn, M, A & Simham, H, N. “Maternal Vitamin D Deficiency Is Associated with Bacterial Vaginosis in the First Trimester of Pregnancy.” The Journal of Nutrition 139 (2009): 1157-1161

Bowyer, L., et al. "Vitamin D, PTH and calcium levels in pregnant women and their neonates." Clinical Endocrinology 70.3 (2009): 372-77

Bridges, N, Coren, M & Fletcher, P. Vitamin D deficiency in children and adolescents - Treatment and prophylaxis guidelines Imperial College Healthcare NHS Trust, 2010 (Local Guidelines, unpublished)

Brough, L., Rees, G, A., Crawford, M, A., Morton, R, H & Dorman, E, K. “Effect of multiple-micronutrient supplementation on maternal nutrient status, infant birth weight and gestational age at birth in a low-income, multi-ethnic population.” British Journal of Nutrition 104.3 (2010): 437-445

Brown, R. Audit of the opportunistic measurement of vitamin D levels and treatment of insufficiency and deficiency. Unpublished audit conducted at The Mintz Practice, Lisson Grove Health Centre, Gateforth Street London NW8 8EH (24 February 2010)

Camargo Jr, C, A., Rifas-Shiman, S, L., Litonjua, A, A., Rich-Edwards, J, W., Weiss, S, T., Gold, D, R., Kleinman, K & Gillman, M, W. The American Journal of Clinical Nutrition 85 (2007): 788-795

Cooper, C. “Early life influences on skeletal health.” Bone 45.S2 (2009): S48

Dayre McNally, J., Matheson, L, A., Sankaran, K & Rosenberg, A, M. "Capillary blood sampling as an alternative to venipuncture in the assessment of serum 25 hydroxyvitamin D levels." Journal of Steroid Biochemistry & Molecular Biology 112.1-3 (2008): 164-168

Department of Health. Dietary Reference Values - A Guide London: HMSO, 1991

Department of Health. Vitamin D: An essential nutrient for all...but who is at risk of vitamin D deficiency? NHS Leaflet, 2009

Devereux, G., Litonjua, A, A., Turner, S, W., Craig, L, CA., McNeill, G., Martindale, S., Helms, P, J., Seaton, A & Weiss, S, T. "Maternal vitamin D intake during pregnancy and early childhood wheezing." The American Journal of Clinical Nutrition 85 (2007): 853-859

Devereux, G. "Maternal diet during pregnancy: An emerging risk factor for childhood asthma." Expert Review of Clinical Immunology 4.6 (2008): 663-668

Erkkola, M., Kaila, M., Nwaru, B. I., Kronberg-Kippilä, C., Ahonen, S., Nevalainen, J., Veijola, R. , Pekkanen, J., Ilonen, J., Simell, O., Knip, M & Virtanen, S. M. "Maternal vitamin D intake during pregnancy is inversely associated with asthma and allergic rhinitis in 5-year-old children." Clinical and Experimental Allergy 39.6 (2009): 875-882

Eyles, D., Anderson, C., Ko, P., Jones, A., Thomas, A., Burne, T., Mortensen, P, B., Nørgaard-Pedersen, B., Hougaard, D, M & McGrath, J. "A sensitive LC/MS/MS assay of 25OH vitamin D3 and 25OH vitamin D2 in dried blood spots." Clinical Chimica Acta 403.1-2 (2009): 145-151

Eyles, D., Morley, R., Anderson, C., Ko, P., Burne, T., Permezel, M., Mortensen, P, B., Nørgaard-Pedersen, B., Hougaard, D, M & McGrath, J, J. "The utility of neonatal dried blood spots for the assessment of neonatal vitamin D status." Paediatric and Perinatal Epidemiology 24.3 (2010): 303-308

Haugen, M., Brantsœter, A L., Trogstad, L., Alexander, J., Roth, C., Magnus, P., Meltzer, H M. "Vitamin D Supplemenation and Reduced Risk of Preeclampsia in Nulliparous Women." Epidemiology 20.5 (2009): 720-726

Hedges, T. and Scriven, A. "Sun safety: What are the health messages?" Journal of The Royal Society for the Promotion of Health 128.4 (2008): 164-69

Hewison, M & Adams, J, S. "Vitamin D Insufficiency and Skeletal Development In Utero." Journal of Bone and Mineral Research 25.1 (2010): 11-13

Hintzpeter, B., Scheidt-Nave, C., Müller, M, J., Schenk, L & Mensink, G, B, M. "Higher Prevalence of Vitamin D Deficiency Is Associated with Immigrant

Background among Children and Adolescents in Germany." The Journal of Nutrition 138 (2008): 1482-1490

Hyppönen E, Sovio U, Wjst M, et al. "Infant vitamin D supplementation and allergic conditions in adulthood: northern Finland birth cohort 1966." Annals of the New York Academy of Sciences 1037 (2004): 84-95

Hyppönen, E., Hartikainen, A-L., Sovio, U., Järvelin, M-R & Pouta, A. "Does vitamin D supplementation in infancy reduce the risk of pre-eclampsia?" European Journal of Clinical Nutrition 61 (2007): 1136-1139

Javaid MK, Crozier SR, Harvey NC et al. "Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years: a longitudinal study." Lancet 367 (2006): 36-43

Karatekin, G., Kaya, A., Salihoğlu, Ö., Balci, H & Nuhoğlu, A. "Association of subclinical vitamin D deficiency in newborns with acute lower respiratory infection and their mothers." European Journal of Clinical Nutrition 63 (2009): 473-477

Kovacs, C. S. "Vitamin D in pregnancy and lactation: Maternal, fetal, and neonatal outcomes from human and animal studies." American Journal of Clinical Nutrition 88.2 (2008): 520S-8S

Kulie, T., et al. "Vitamin D: An evidence-based review." Journal of the American Board of Family Medicine 22.6 (2009): 698-706

Mahon, P., Harvey, N., Crozier, S., Inskip, H., Robinson, S., Arden, N., Swaminathan, R., Cooper, C., Godfrey, K. & the SWS Study Group. "Low Maternal Vitamin D Status and Fetal Bone Development: Cohort Study." Journal of Bone and Mineral Research 25.1 (2010): 14-19

McGillivray, G., Skull, S, A., Davie, G., Kofoed, S, E., Frydenberg, A., Rice, J., Cooke, R & Carapetis, J, R. "High prevalence of asysmptomatic vitamin D and iron deficiency in East African immigrant children and adolescents living in a temperate climate." Archives of Disease in Childhood 92 (2007): 1088-1093

Merewood, A., Mehta, S, D., Chen, T, C., Bauchner, H & Holick M, F. "Association between Vitamin D Deficiency and Primary Cesarean Section." The Journal of Clinical Endocrinology & Metabolism 94 (2009): 940-945

Misra, M., et al. "Vitamin D deficiency in children and its management: review of current knowledge and recommendations." Pediatrics 122.2 (2008): 398-417

Modgil, G., et al. "High prevalence of Somali population in children presenting with vitamin D deficiency in the UK." Archives of Disease in Childhood 95.7 (2010): 568-69

More, J. “Who needs vitmain supplements?” Journal of Family Health Care 17.2 (2007): 57-60

National Institute for Health and Clinical Excellence. Antenatal care: routine care for the healthy pregnant woman - Clincial Guideline 62 London: NICE, 2008

National Institute for Health and Clinical Excellence. Improving the nutrition of pregnant and breastfeeding mothers and children in low-income households - Public Health Guidance 11 London, NICE: 2008

National Institute for Health and Clinical Excellence. Dietary interventions and physical activity interventions for weight management before, during and after pregnancy - Public Health Guidance 27 London: NICE, 2010.

NHS Westminster. Annual Report of the Director of Public Health 2007-08: Tackling Obesity in Westminster London: NHS Westminster, 2009

Nwaru, B. I., Ahonen, S., Kaila, M., Erkkola, M., Haapala, A-M., Kronberg-Kippilä, C., Veijola, R., Ilonen, J., Simell, O., Knip, M & Virtanen, S, M. “Maternal diet during pregnancy and allergic sensitization in the offspring by 5 years of age: A prospective cohort study.” Pediatric Allergy and Immunology 21.1 Part 1 (2010): 29-37

Office of National Statistics. Annual Population Survey for 2007/08

Pearce, S. H. S., Cheetham, T. D., “Diagnosis and management of vitamin D deficiency.” BMJ 340 (2010): 142-147

Perez-Rossello, J. M., et al. "Is there an increase of fracture risk in healthy infants and toddlers with vitamin D deficiency?" Pediatric Radiology 40.4 (2010)

Peterlik, M., et al. "Vitamin D and calcium insufficiency-related chronic diseases: An emerging world-wide public health problem." International Journal of Environmental Research and Public Health 6.10 (2009): 2585-607

Ruston, D., Hoare, J., Henderson, L., Gregory, J., Bates, C., Prentice, A., Birch, M., Swan, G., Farron, M. The National Diet & Nutrition Survey: adults aged 19 to 64 years – Volume 4. London: TSO, 2004

Ryan, L. M., et al. "Prevalence of vitamin D insufficiency in African American children with forearm fractures: A preliminary study." Journal of Pediatric Orthopaedics 30.2 (2010): 106-09

Sayers, A & Tobias, J. H. “ Estimated Maternal Ultraviolet B Exposure Levels in Pregnancy Influence Skeletal Development of the Child.” The Journal of Clinical Endocrinology & Metabolism 94 (2009): 765-771

Scientific Advisory Committee on Nutrition (SACN), Update on Vitamin D – Positiion statement by the Scientific Advisory Committee on Nutrition. United Kingdom: TSO, 2007

Sebire, NJ and Jolly, M and Harris, JP and Wadsworth, J and Joffe, M and Beard, RW and Regan, L and Robinson, S (2001) "Maternal obesity and pregnancy outcome: a study of 287 213 pregnancies in London." International Journal of Obesity 25.8 (2001): 1175 - 1182

Sharma, S., Khan, N., Khadri, A., Julies, P., Gnanasambandam, S., Saroey, S., Jacobs, B., Beski, S., Coren, M & Alexander, S. et al. "Vitamin D in pregnancy-time for action: A paediatric audit." BJOG: An International Journal of Obstetrics and Gynaecology 116.12 (2009): 1678-82

Stellinga-Boelen, A, M., Wiegersma, P, A., Storm, H., Bijleveld, C, M, A & Verkade, H, J. "Vitamin D levels in children of asylum seekers in The Netherlands in relation to season and dietary intake." European Journal of Pediatrics 166 (2007): 201-206

Toriola, A, T., Surcel, H-M., Agborsangaya, C., Grankvist, K., Tuohimaa, P., Toniolo, P., Lukanova, A., Pukkala, E., Lehtinen, M. "Serum 25-hydroxyvitamin D and the risk of ovarian cancer." European Journal of Cancer 46.2 (2010): 364-69

Vanga, S, R., Good, M., Howard, P, A & Vacek, J, L. "Rose of Vitamin D in Cardiovascular Health." The American Journal of Cardiology 106 (2010): 798-805

van der Meer, I, M., Karamali, N, S., Boeke, A, J., Lips, P., Middelkoop, B, J, C., Verhoeven, I & Wuister, J, D. "High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands." American Journal of Clinical Nutrition 84.2 (2006):350–353

Viljakainen, H, T., Saarnio, E., Hytinantti, T., Miettinen, M., Surcel, H., Andersson, S., Laitinen, K. & Lamberg-Allardt, C. "Maternal vitamin D status determines volumetric bone mineral density of the newborn." Bone 44.S2 (2009): S240

Wagner, C.L., Greer, F, R & the Section on Breastfeeding and Committee on Nutrition. "Prevention of Rickets and Vitamin D Deficiency in Infants, Children and Adolescents." Pediatrics 122 (2008): 1142-1152

Walker, V, P & Modlin, R, L. "The Vitamin D Connection to Pediatric Infections and Immune Function." Pediatric Research 65.5 Part 2 (2009):106R-113R

Williams, E. L., et al. "Maternal nutrition and bone health in the offspring." International Journal of Clinical Rheumatology 4.2 (2009): 133-45

Williams, B., et al. “Vitamin D and lower reproductive tract infections in women: National health and nutrition examination survey (NHANES) 2001-2004.” HIV Medicine 11 (2010)

Wright, K. Early Years Joint Strategic Needs Assessment London: NHS Westminster Public Health Department, 2009

Yu, C. K. H., Sykes, L., Sethi, M., Teoh, T.G & Robinson, S. “Vitamin D deficiency and supplementation during pregnancy.” Clinical Endocrinology 70 (2009): 685-690

Zhang, C., Chunfang, Q., Hu, F, B., David, R, M., van Dam, R, M., Bralley, A & Williams, M, A. “Maternal Plasma 25-Hydroxyvitamin D Concentrations and the Risk for Gestational Diabetes Mellitus.” PLoS ONE 3.11: e3753 (2008): 1-6

Zipitis, C, S & Akobeng, A. K. “Vitamin D supplementation in early childhood and risk of type 1 diabetes: a systematic review and meta-analysis.” Archives of Disease in Childhood 93 (2008): 512-517