**PARTICIPANT INFORMATION SHEET**

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| Version | 1.1 | Date | 2nd July 2021 |

Study Title: Micronutrient interventions to improve infant neurocognitive development and growth in early infancy

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| LEO/Protocol No: | 25071 |
| King’s College London Ethical Clearance Reference Number |  |

**Sponsor & Funder**: King’s College London (Sponsor) and Wellcome Trust (Funder)

## What is informed consent?

You are invited to take part in a research study, and to let your infant take part once they are born. Participating in a research study is not the same as getting regular medical care. The purpose of normal medical care is to improve one’s health. The purpose of a research study is to gather information that may be useful in the future for the whole population. Your choice to participate, and to allow your infant to participate, or not will be respected. It is your decision, and if you do choose to participate you can stop any time without giving any reason.

Before you decide you need to understand all about the study and what will happen in it. Please take time to read the following information or get the information explained to you in your language of understanding. Listen carefully. You can ask questions if there is anything that you do not understand. Ask for it to be explained until you understand it. You may also wish to discuss with your husband/wife, family members or others before deciding to take part in the study.

If you decide to join the study, you will need to sign or thumbprint a consent form saying you agree to be in the study. You will receive a copy of the consent form.

## Why is this study being done?

As you may know, many infants struggle to grow well across the first year of life and become smaller or not as heavy as other infants. This “growth failure” is very common in The Gambia and is also thought to effect other areas of an infant’s development, including their ability to fight infections and the development of their brain. One of the causes of this poor growth is not being able to get enough of the right foods in their diet all of the time. Foods contain many important building blocks for good health, including small amounts of what we call “micronutrients”. These micronutrients (which are also known as vitamins and minerals) are only needed in very small amounts, but if they are not available from the foods you are eating then health may be affected. For very young infants, these micronutrients are important for their developing brains and so if there are not enough micronutrients available from diets, then there may be a need to provide additional micronutrients in the form of a supplement. This is like the supplements that women in The Gambia receive during pregnancy (called “iron-folic acid” supplements) to prevent them from getting anaemic during the pregnancy.

For young infants who only receive breast milk, all of their nutrition comes from this milk. Breast milk is the best source of nutrition for young infants, and exclusive breast feeding (that is giving only breast milk) to infants until they are six months of age is recommended and encouraged in The Gambia. However, it is possible that some infants may need additional micronutrients at the same time they are receiving breast milk and that – by giving extra micronutrients – we might be able to help with their growth and development.

We hope that the study we are planning will help us to understand whether we can support breast fed infants by giving extra micronutrients to mothers, or to mothers and their infants. We hope that this research will help us to ensure that all infants get the right amount of micronutrients for them to grow and development well.

We will tell the results of this study to your community.

## What is the new vaccine/drug?

In pregnancy and after pregnancy, we will use pills (“capsules”) containing a mix of 15 micronutrients. This is called a “multiple micronutrient” capsule. This capsule has been used in many studies in pregnancy around the world and is safe and recommended for use in pregnancy and during the period after pregnancy when a woman is breast feeding her infant.

In infants, we will give a small amount of a syrup (a liquid medicine) containing a similar mix of micronutrients as given to mothers in pregnancy. Micronutrient syrups are often given to young, breast fed infants (such as infants born too early, or “preterm”) to help them grow.

## What does this study involve?

We are looking for pregnant women to take part in this study. If you are pregnant, and agree to participate, we will follow up you and your infant until your infant is one-year of age.

The first stage will be to measure how many weeks pregnant you are. To do this, we will use a process called “ultrasound” where we shine a light into your tummy so we can get a picture of the baby and measure their size. If you are less than 20 weeks pregnant, we will then invite you to enrol into the main study. At this visit, we will also measure your height and weight. These assessments should take about 30 minutes at the clinic in Keneba, and we will provide transport for you.

After enrolment, when you reach 20 weeks of pregnancy you will be invited to come to the clinic in Keneba again for a health check. At this visit, we will check your baby’s growth by using the same method of ultrasound as used before and we will also measure how much you weigh. We will also take a small quantity of your blood (7.5mL, about 1½ teaspoons) and ask you to provide us with a small amount of your urine. This visit to Keneba will take between 1-2 hours.

After this visit, we will ask you to start taking a daily capsule. This capsule contains micronutrients and also includes the iron and folic acid that you normally get given in pregnancy in The Gambia. Because it is important you take this capsule each day, we will arrange for a field assistant to visit you in your village each day to record whether you have taken the capsule. Each week after you start taking the capsules we will also ask you some questions on whether you have felt well in the previous week. The daily visits will take no more than 5 minutes, and the weekly questionnaires 10 minutes.

When you are 28 and 36 weeks pregnant, we will invite you back to Keneba for two further visits, again taking between 1-2 hours. At these visits, we will make the same measurements and collect the same samples as we did when you were 20 weeks pregnant. At the point you go into labour, we will ask you to let a member of the study team know so they can be close by when the baby is born. We will then ask whoever helps deliver your baby (nurse, midwife, doctor) to pass them the placenta as we would like to collect a small amount of blood (10mL, about two teaspoons) from the cord. We will then either return the placenta to you, if that is your wish, or dispose of it for you.

After the delivery of your baby, we will arrange for a midwife or nurse from the study team to visit you at home to check on your health and the health of your new baby. At this visit, they will also measure your baby, including their weight, length, and the size of their head (“head circumference”) and the size of their upper arm (“mid-upper arm circumference”). This visit will take no more than 30 minutes.

Following the naming ceremony for your infant, we will then visit you again to start giving daily supplements to your infant. This will be in the form of a syrup (liquid medicine) which we will drop directly into your infant’s mouth between breastmilk feeds. Your infant will be randomly put into one of three study groups:

Group 1: Micronutrient drops

Group 2: Micronutrients drops, with extra micronutrients compared to Group A

Group 3: Placebo drops (the same syrup as A and B but without micronutrients)

A member of the field team will then visit your infant daily, until they reach six months of age, to give these drops. These visits will take no longer than 10 minutes. From birth to seven months of age we will also ask you questions once a week about your infant’s health and how they are being fed. From when they are seven until 12 months of age these questions will become monthly, and each visit will last about 10 minutes. Each month, we will also measure your child’s size, using the same methods as before (weight, length, head circumference and mid-upper arm circumference) and ask you to collect a sample of your child’s stool, which we will then pick up from you. These monthly visits will take about 10 minutes.

From after delivery until your infant reaches six months of age, we will also ask you to continue taking daily capsules. You will be randomly put into one of two groups:

Group 1: Multiple micronutrient capsules, the same as you received in pregnancy.

Group 2: Placebo capsules (which will look and taste the same as the capsules you took in pregnancy, but do not contain the micronutrients)

At the weekly visits when we ask about your infant’s health, we will continue to also ask about your own health.

When your infant is one, six and 12 months of age, we will invite you and your infant to come to the Keneba field station for a study visit. At these visits will measure your infant’s brain development in a number of ways; we will ask your infant to do simple tasks to see if they can do things that are normally expected at their age. We may also ask you questions about things your infant may have done before at home. This may be videorecorded. At each visit we will also measure your infant’s brain development using a special hat containing lights and light sensors that are linked to a computer. The lights are harmless and will not hurt your infant. The lights will measure the activity in your infant’s brain when they see pictures on a screen, hear sounds, or sleep. This will be recorded using a small camera in the screen called an “eye tracker” which lets us see what your baby looks at. We will also measure the size of your infant (weight, length, head circumference and mid-upper arm circumference) at each of these visits and, at the six- and 12-month visit, collect a small amount of blood (5mL, equivalent to one teaspoon). When your infant is one, three, six and 12 months of age we will ask you to provide a small sample of your breast milk (10mL, equivalent to two teaspoons). At the 3 month time point, this will be at your home. These visits to Keneba will take between 3- 4 hours. Transport and refreshments will be provided for you at these visits.

We will also ask to visit your home when you infant is six and 12 months of age to do one more assessment. This involves a field assistant visiting your home to see what your compound is like and what you and your infant do on a normal day. The field assistant will observe you and other people who look after your child as you care for your child and take some notes on these relationships. They will also look at your home, and take some notes, such as where your kitchen is located This assessment in your home will take about 1.5 hours.

If we find out that you or your child are sick and cannot join the study, you and your child will receive the care routinely available in The Gambia. You may be treated at the study site and if necessary, you will be referred to a health facility that can manage the condition better.

If the research study needs to be stopped for any reason, we will tell you and you and your child will have normal medical care if you need it.

## What will happen to the results of this study?

The results from the study will be shared in The Gambia (for example at MRC meetings with the Gambian Government, or at public presentations) and also shared internationally through published reports. Copies of these will be available freely on the internet or can be provided by the MRC on request. Anonymised copies of the data will be made available for public use once the final results have been published, but this will not include any details that can link the information back to you or your infant as individuals.

## What will happen to the samples taken in this study?

The collected blood, urine and stool samples from you and your infant will be processed in the Keneba laboratory. Here we will measure the levels of certain micronutrients in the collected blood samples, but most samples will then be stored for further analysis of other micronutrients and measures of infection. Some of these samples will be transferred to laboratories overseas for analysis because we don’t have the equipment required for measuring all the factors we are investigating in The Gambia.

Samples will also be stored for possible genetic testing in the future, on questions directly related to the research focus.

## What harm or discomfort can you expect in the study?

Collection of blood can cause discomfort, but it will not cause any harm to you or your infant. There is a chance that a small bruise will be left where we took the blood, but this will disappear with time. There is also a small chance that the capsules we give to you or the syrups we give to your infant may cause diarrhoea or other tummy discomfort. This will be closely monitored by our daily visits.

Sometimes infants become upset when the hat used to look at brain development is put on their head, but the hat is soft and will not hurt them. Some infants do not like watching the screen or being asked to do tasks like play with toys. If they become scared or upset, we will stop or try again later when they are feeling better.

As the Covid-19 pandemic continues, all study visits and assessments will be performed in line with government advice at the time and in line with MRC guidance to ensure your safety and the safety of the staff performing the assessments.

## What benefits can you expect in the study?

We anticipate that the extra nutrients we give you during pregnancy and after delivery and those we give to your infant will help support your infant’s growth and development. If this study does show benefits of these extra nutrients, this will be important information for The Gambia and for other countries across the world that also suffer from poor diets and will help us to develop programmes to support women and infants at particular risk of micronutrient deficiencies.

## Will you be compensated for participating in the study?

You will not get paid by the study, but MRC will provide transport or give you back the money for your transport.

## Are there other products or treatment?

No.

## What happens if you refuse to participate in the study or change your mind later?

You are free to join the study, and to let your infant join the study, or not and you have the right to stop being in the study at any time without giving a reason. You and your infant will still get the normal medical care. If you need to miss a study visit because, for example, you have travelled to a family celebration, this will just be recorded.

If you do not want to continue in the study, we will use only the samples and information already collected from you.

A member of the study’s clinical team may ask to do an additional health check if needed for the safety of you or your infant.

If we find any new information during the study that may change if you or your infant can be in the study, we will tell you as soon as possible.

## If you are injured in the study what compensation will be available?

We will provide medical care if you or your infant get any medical problems from the study through insurance. If you or your infant have an unwanted reaction, we will treat you or refer you as needed.

If it is an emergency, please go to your nearest health centre or clinic and call immediately the research team or field worker who gave his/her telephone number to you or contact Dr Ousman Jarjou on 2461563 or 9825431.

## How will personal records remain confidential and who will have access to it?

All information that is collected about you in the study will be kept strictly confidential. Your personal information will only be seen by the study team members, the sponsor’s monitor and if necessary, the Ethics Committees and Government authorities.

Because this study is being led by King’s College London (a University in the United Kingdom) your data will be processed under the terms of UK data protection law (including the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018). This will further ensure your records are protected.

Data may be sent to other study staff in MRC Unit The Gambia at LSHTM, but this will be pseudonymised. This means that any information about you which leaves the clinic will have your personal details (your name and any other information that may identify you), removed so that you cannot be recognised, and your data will have the code number we use for your during the study instead.

Some of your information will be sent to the United Kingdom and to other countries, but they will not have any personal information about you only the study identifier. They must follow our rules about keeping your information safe.

Your personal details will be kept in a different safe place to the other study information and will be destroyed within 10 years of the end of the study.

At the end of the project, the study data will be archived at MRC Unit The Gambia at LSHTM. The data will be made available to other researchers worldwide for research and to improve medical knowledge and patient care. Your personal information will not be included and there is no way that you can be identified.

You can find out more about how we use your information

* At https://www.lshtm.ac.uk/files/research-participant-privacy-notice.pdf
* by asking one of the research team
* by sending an email to DPO@lshtm.ac.uk

## Who should you contact if you have questions?

If you have any questions or worried you can call Dr Ousman Jarjou on 2461563 or 9825431, the Research Clinician leading the study in The Gambia or email Dr Sophie Moore at Sophie.moore@kcl.ac.uk the lead investigator from King’s College London in the UK. You can also always call the personal numbers of the study staff given to you. If you have any concerns, you can also call staff at your health centre or hospital.

Please feel free to ask any question you might have about the study.

## Who has reviewed this study?

This study has been checked by scientists at the Medical Research Council and by the Gambia Government/MRC Joint Ethics Committee. The Ethics Committee protects your rights and wellbeing and has given permission for it to take place. It has also been checked by the Ethics Committee at King’s College London.

Consent Form

Participant Identification Number: |\_\_|\_\_|\_\_|\_\_|\_\_|\_\_|\_\_|\_\_|\_\_|\_\_|\_\_|\_\_|

 (Printed name of participant)

[ ]  I have read the written information **OR**

[ ]  I have had the information explained to me by study personnel in a language that I understand

and I

* confirm that my choice to participate is entirely voluntarily,
* confirm that I have had the opportunity to ask questions about this study and I am happy with the answers that have been provided,
* understand that I allow access to the information about me by persons described in the information sheet,
* had received enough time to think about whether I want to take part in this study,
* agree for me and my infant to take part in this study.

*Tick as appropriate*

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| I agree to have ultrasound measurements made on me at each clinic visit during my pregnancy |  Yes **[ ]**  No **[ ]**  |
| I agree to provide 7.5mL (about 1 ½ teaspoons) of my blood at three timepoints in pregnancy |  Yes **[ ]**  No **[ ]**  |
| I agree to provide a sample of my urine at three timepoints in pregnancy and also when my infant is 1, 6 and 12 months old |  Yes **[ ]**  No **[ ]**  |
| I agree to provide 10mL of breast milk (about 2 teaspoons) whenmy infant is 1, 3, 6 and 12 months old  |  Yes **[ ]**  No **[ ]**  |
| I agree for some cord blood (10mL, about 2 teaspoons) to be collected, after delivery |  Yes **[ ]**  No **[ ]**  |
| I agree for blood from my infant to be collected when they are 1month of age (fingerprick sample) and 6 and 12 months (5mL, about one teaspoon) |  Yes **[ ]**  No **[ ]**  |
| I agree for monthly stool samples to be collected from my infant |  Yes **[ ]**  No **[ ]**  |
| I agree for my samples and those of my infants to be shipped outside of The Gambia |  Yes **[ ]**  No **[ ]**  |
| I agree to further research on my samples and those of my infants including genetic testing | Yes **[ ]**  | No **[ ]**  |
| I agree for that some of the assessments made on my infant may be recorded  | Yes **[ ]**  | No **[ ]**  |
| I agree that information collection about me and my infant may be shared anonymously with other researchers in the future, for their ethically approved projects | Yes **[ ]**  | No **[ ]**  |

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| Participant’s signature/thumbprint\* |  |  |  |  |
|  |  |  | Date Time  |
| Printed name of impartial witness\* |  |
| Signature of impartial witness\* |  |  |  |  |
|  |  |  | Date Time  |
| Print name of person obtaining consent  |  |
| **I attest that I have explained the study information accurately in \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ to, and was understood to the best of my knowledge by, the participant and that the participant has freely given consent to participate *\**in the presence of the above named impartial witness (where applicable).**  A copy of this ICF has been provided to the participant. |
| Signature of staff obtaining consent |  |  |  |
|  |  |  | Date (dd/mmm/yyyy) Time (24hr) |

*\* Only required if the participant is unable to read or write.*