

# Carrying Alpha Zero Thalassaemia

## **A carrier can use this booklet to...**

- *help explain carrying alpha zero thalassaemia to their partner, blood relatives and others.*
- *show to any health professional (doctor, nurse or midwife) they see about having a family, or pregnancy, or carrying alpha zero thalassaemia.*

# Contents

Introduction .....	1
What does it mean to carry alpha zero thalassaemia? .....	2
Can carrying alpha zero thalassaemia affect your health?.....	3
Is it a bad thing to carry alpha zero thalassaemia? .....	4
Implications for a carrier's children... ..	5
What is alpha thalassaemia major? .....	7
What is haemoglobin H disease?.....	9
Can serious haemoglobin disorders be prevented? .....	10
Asking a partner to have a blood test .....	11
Telling the family about alpha zero thalassaemia.....	11
Alpha zero thalassaemia world-wide.....	12

## **Introduction**

Alpha zero thalassaemia is one of a range of variations in the blood called *haemoglobin gene variants*. Here we call them *haemoglobin variants* for short.

Carriers of alpha zero thalassaemia are also sometimes said to *have alpha zero thalassaemia trait*, or to *have alpha-1 thalassaemia trait*.

Alpha zero thalassaemia is inherited. That is, it is passed on from parents to their children, like height, hair colour or eye colour. It is passed on equally by men and women. It is present at birth, and it remains the same for life.

It is important to distinguish clearly between people who *carry alpha zero thalassaemia* and people who *have a haemoglobin disorder*.

### **Carriers of alpha zero thalassaemia...**

... inherited alpha zero thalassaemia from one of their parents. Carrying alpha zero thalassaemia does not affect their own health. However, if their partner also carries alpha thalassaemia, they could have children with a haemoglobin disorder.

### **People who have a haemoglobin disorder ...**

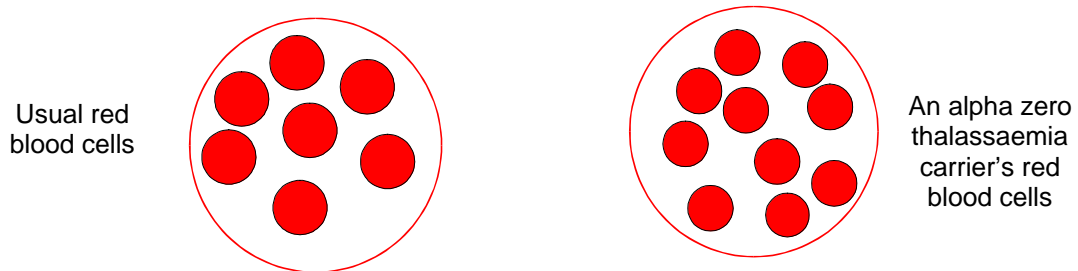
... inherited two haemoglobin variants, one from each of their parents. Together, the two variants cause a serious inherited anaemia that can lead to life-long health problems.

This document is about carrying alpha zero thalassaemia.

## What does it mean to carry alpha zero thalassaemia?

Blood is made up of millions of *red blood cells* floating in a fluid called *plasma*. Red blood cells are full of haemoglobin, which is red. This is why blood is red. The heart pumps blood round the body through the blood vessels. The body needs oxygen to function. Haemoglobin picks up oxygen as blood passes through the lungs, and carries it to the rest of the body as the blood circulates.

Carriers of alpha zero thalassaemia have smaller red blood cells, but more of them than other people. You can see the difference between other peoples' red blood cells and a thalassaemia carrier's red blood cells by looking down a microscope.



Alpha zero thalassaemia is *inherited* - it is handed on from parents to their children, it is present at birth, and it remains the same for life.

### How is alpha zero thalassaemia inherited?

It is inherited through *genes*. Every human characteristic, such as eye colour, or height, or type of haemoglobin is controlled by genes that parents pass on to their children. A child inherits two genes for every characteristic, one from each parent. Most people inherit two genes for the usual type of haemoglobin, *haemoglobin A*. Each gene is responsible for making half of the haemoglobin A in each red blood cell.

A carrier of alpha zero thalassaemia has inherited a gene for haemoglobin A from one parent and a gene for alpha zero thalassaemia from the other. The alpha zero thalassaemia gene cannot make any haemoglobin. As a result people who carry alpha zero thalassaemia have red blood cells that contain less haemoglobin than usual, and are smaller than usual. They make up for this by making more red blood cells. Their blood functions normally, and carrying alpha zero thalassaemia does not cause them any health problems.

### How do people find out that they carry alpha zero thalassaemia?

By having a special blood test "for haemoglobin disorders". This usually involves two steps.

- The first step is to measure the size of their red blood cells. This shows that they have smaller red blood cells than usual.
- The second step is to analyse the types of haemoglobin in their blood. This shows that their blood contains no unusual haemoglobin.

A DNA test is needed to show that they definitely carry alpha zero thalassaemia.

## **Can carrying alpha zero thalassaemia affect your health?**

Carriers of alpha zero thalassaemia are not ill, and are no more likely to get ill than other people. Carrying alpha zero thalassaemia does not make them weak, and they can do any kind of work they choose.

Some carriers have a mild anaemia. Anaemia means having a lower haemoglobin level than usual. Anaemia due to carrying thalassaemia has no effect on health or length of life.

The commonest type of anaemia is iron deficiency anaemia. It occurs in people whose diet contains too little iron, or who lose blood for some reason. People with iron deficiency anaemia may also have small red blood cells.

Occasionally a doctor thinks a person who carries thalassaemia must be short of iron because they have small red blood cells. If the doctor prescribes iron medicine, in the long run this could do more harm than good. A carrier should take iron medicine only if a special blood test (serum iron or serum ferritin) shows that they are short of iron.

### **Can a carrier of alpha zero thalassaemia also get iron deficiency anaemia?**

They can. They should have a diet with enough vitamins and iron to make sure that this does not occur.

### **What about pregnant women?**

Like other pregnant women, women who carry thalassaemia can become iron deficient and may need extra iron.

Anaemia due to carrying thalassaemia can become more severe during pregnancy, and sometimes a pregnant carrier can need a blood transfusion. The anaemia gets better after the baby is born.

### **Is there any treatment to get rid of alpha zero thalassaemia?**

No, a person who is born carrying alpha zero thalassaemia will always carry it.

### **Can carrying alpha zero thalassaemia turn into a serious form of thalassaemia?**

It cannot.

### **Can people catch alpha zero thalassaemia from a carrier?**

They cannot.

### **Can a carrier of alpha zero thalassaemia be a blood donor?**

They can give blood like other people, provided they are not anaemic.

The blood transfusion service tests donors for anaemia before each blood donation. This test will exclude a thalassaemia carrier with mild anaemia.

## **Is it a bad thing to carry alpha zero thalassaemia?**

It is not. Carriers of alpha zero thalassaemia are healthier than other people in several ways. For example, they have some natural protection against severe forms of malaria.

Malaria parasites live inside red blood cells, and are most comfortable in the red cells of people who do not carry any haemoglobin variant. Thalassaemia carriers can be infected with malaria like anyone else, but the parasites cannot grow well in their small red blood cells. Therefore they have less severe infections and less chance of dying from malaria than other people.

In countries where it was common malaria used to kill many children. Children who carried thalassaemia survived better than other children and passed thalassaemia on to their children in turn. As time passed carrying thalassaemia became very common in such areas, and that is why there are now so many carriers in the world.

Malaria has been eradicated in many countries, so being a carrier is less advantageous than it used to be. Thalassaemia does not go away when malaria is eradicated, or when a carrier moves to a different part of the world, because it is inherited.

*Carriers of alpha zero thalassaemia should not rely on their natural protection against malaria when they visit a malarious country. Their protection is limited. They should take antimalarial tablets like everybody else.*

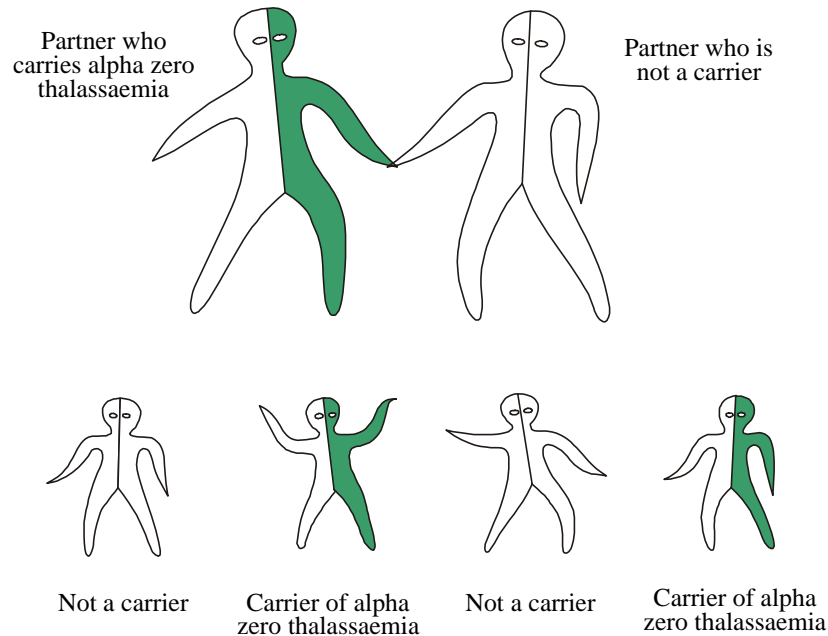
## **Does carrying alpha zero thalassaemia have any other health advantage?**

Recent research shows that alpha zero thalassaemia carriers are less likely than others to suffer from heart attacks. In the modern world, this is an important advantage.

*Carriers have a limited natural protection against heart disease. To benefit from it they also need to adopt a healthy life-style, with no smoking, adequate exercise and a balanced diet.*

## Implications for a carrier's children...

**If one partner carries alpha zero thalassaemia and the other does not carry any haemoglobin variant, their children could not have a serious haemoglobin disorder**



In each pregnancy, there are two possibilities.

- The child may not carry any haemoglobin variant.
- The child may carry alpha zero thalassaemia. This is harmless.

This couple has the same chance of a healthy family as other couples do. .

**There is also no risk of a serious haemoglobin disorder if one partner carries alpha zero thalassaemia and the other carries any of the following:**

beta thalassaemia (including unusual forms such as delta-beta thalassaemia and haemoglobin Lepore)

haemoglobin C

haemoglobin D

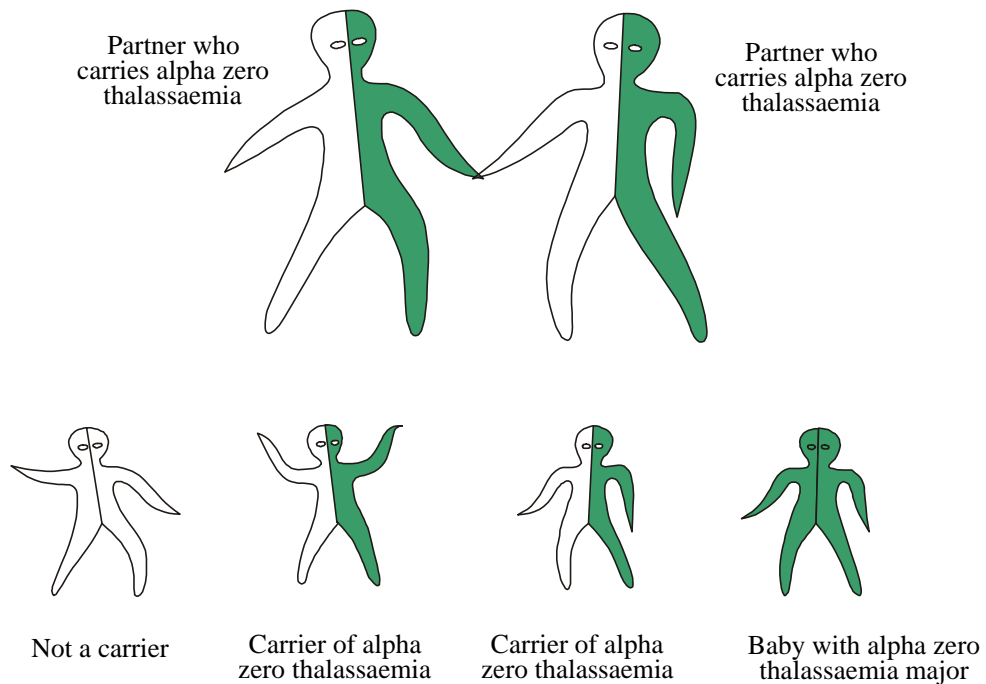
haemoglobin E

haemoglobin S

hereditary persistence of fetal haemoglobin (HPFH)

one of a range of possible rare haemoglobin variants

**If both partners carry alpha zero thalassaemia, their children could have alpha thalassaemia major**



In each pregnancy, there are three possibilities.

- The child may not carry any haemoglobin variant.
- The child may carry alpha zero thalassaemia. This is harmless.
- The child may inherit alpha zero thalassaemia from both parents. This child would have a serious haemoglobin disorder called alpha zero thalassaemia major.

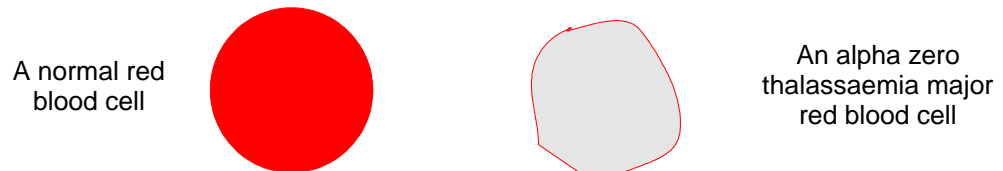
In each pregnancy there is a 3 in 4 chance of a healthy child and a 1 in 4 chance of a child with alpha thalassaemia major.



## What is alpha thalassaemia major?

(This is also known as *alpha thalassaemia hydrops fetalis*, or *haemoglobin Bart's hydrops fetalis*.)

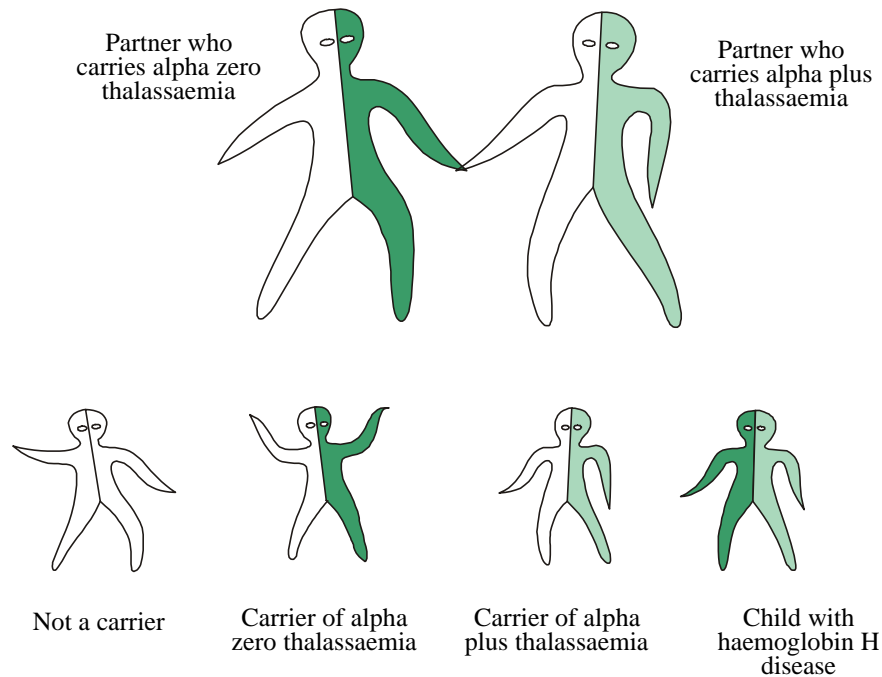
Unborn babies and new-born babies make mainly haemoglobin F (fetal haemoglobin). Usually this is replaced by haemoglobin A (adult haemoglobin) in the first few months of life. An unborn baby with alpha zero thalassaemia major cannot make haemoglobin F normally. Instead it makes *haemoglobin Barts*, which cannot carry oxygen properly. It cannot make normal red blood cells, and those it does make are nearly empty. This causes a serious anaemia while the baby is still in the womb.



When a baby has alpha zero thalassaemia major the pregnancy usually seems to continue normally. An ultrasound scan at around 5 months of pregnancy often shows that the baby is not growing properly, and is puffed up with water. The mother usually develops high blood pressure, and may have other problems during pregnancy or while the baby is being delivered. The baby is often born prematurely, and is usually dead or dying when it is born.

A few babies born with alpha zero thalassaemia major have been “rescued” by giving them regular blood transfusions from birth. Most such babies had suffered damage from the severe anaemia during pregnancy, and proved to have serious physical and/or mental handicap. It is thought that these problems might be avoided by starting transfusions before birth.

**If one partner carries alpha zero thalassaemia and the other carries alpha plus thalassaemia, their children could have haemoglobin H disease**



In each pregnancy, there are four possibilities.

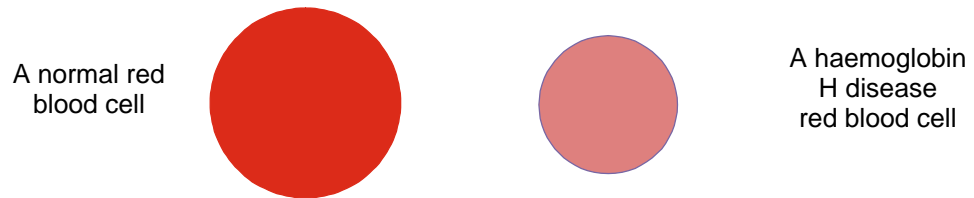
- The child may not carry any haemoglobin variant.
- The child may carry alpha plus thalassaemia. This is harmless.
- The child may carry alpha zero thalassaemia. This is harmless.
- The child may inherit alpha plus thalassaemia from one parent and alpha zero thalassaemia from the other. This child would have a mild inherited anaemia called haemoglobin H disease.

In each pregnancy there is a 3 in 4 chance of a healthy child and a 1 in 4 chance of a child with Haemoglobin H disease.

## What is haemoglobin H disease?

This is also known as *mild alpha thalassaemia intermedia*.

People with haemoglobin H disease cannot make the usual amount of haemoglobin, and so cannot make normal red blood cells. Their red blood cells are much smaller than usual and also contain a small amount of an unusual haemoglobin, *haemoglobin H*. They have a moderate anaemia that is present from birth.



People with haemoglobin H disease grow up normally, have a normal education, work, find a partner and have a family of their own. They are expected to live a normal length of life.

They can have some medical problems. Their spleen may become enlarged, they may develop gallstones, or their bones may become thin when they get old. These problems can all be corrected.

### What is the treatment for haemoglobin H disease?

People with haemoglobin H disease should take folic acid daily and have regular check-ups, so that any problem can be detected early and treated appropriately.

## Can serious haemoglobin disorders be prevented?

Carrier couples who know of the risk for their children have a number of choices. They can take steps to make sure that they have healthy children, and can make sure that affected children have the best possible care from birth. Their choices are not simple. They need to know their risk early, so that they have enough time to make the decisions that are right for them.

In the UK, it is national policy to identify and inform as many carriers as possible before they have children, so that they can have an informed choice. The NHS is expected to take the following steps.

- *Offer carrier testing.* At present this is usually offered by midwives to pregnant women. In some districts it is offered to all pregnant women, and in others only to pregnant women with ancestors from areas where haemoglobin variants are common.
- *Inform carriers.* They need information on (a) the possible risk to the health of their children, and (b) the need for their partner to have a carrier test.
- *Inform carrier couples.* Couples who are both carriers need to see a specialist counsellor for haemoglobin disorders. The counsellor will find out whether they are “at risk” for having children with a serious haemoglobin disorder, and inform them of the exact nature of the risk and the possibilities for avoiding it.

All at risk couples should be offered both *prenatal diagnosis* and *neonatal diagnosis* (new-born diagnosis).

- Prenatal diagnosis means testing an unborn baby to see whether it has a serious disorder. DNA tests are done on a tiny amount of tissue taken from the developing placenta. This can be done as early as 11 weeks of pregnancy. If the baby is affected, the parents can decide whether to continue the pregnancy and plan the best possible care for the baby, or to terminate the pregnancy and try again for a healthy child.
- Neonatal diagnosis is done after the baby is born, using blood taken from the umbilical cord or by pricking the baby’s heel a few days after birth. Neonatal diagnosis for thalassaemia is done by DNA tests. When there is a risk of a sickle cell disorder, early diagnosis and treatment can be life-saving for the child.

It is now recognised that screening during pregnancy often identifies at risk couples too late. Carrier testing should be offered by family doctors either before pregnancy, or as soon as a pregnancy has started.

## **Asking a partner to have a blood test**

A carrier who is thinking of having children needs to tell their partner that they carry alpha zero thalassaemia, and ask him or her to have a blood test “for haemoglobin disorders”.

### **Is it difficult for a carrier to ask their partner to have a blood test?**

It can be easy in some cases and difficult in others. It is easier if both the carrier and their partner know that:

- Carrying a haemoglobin variant is common.
- The test will probably show that the partner does not carry a haemoglobin variant.
- If they do carry a haemoglobin variant it will not affect their health or lifestyle in any way.
- A couple who are both carriers can have a healthy family, with medical help.
- Expert counselling is available.
- No-one will try to tell the couple what to do: all the choices are theirs.
- The results of blood tests, and the couples’ decisions, are completely confidential.

### **If a couple are both carriers, can it interfere with their relationship?**

It is unusual for a relationship to suffer because one or both of a couple carry a haemoglobin variant. On the contrary, many couples draw closer together to deal with their problem. This is true whether they are just starting their relationship or have been together for a long time.

### **When is the best time for a carrier to ask their partner to have a blood test?**

Ideally as early as possible, because it can take time to arrange a blood test, and a couple who are both carriers need time to decide what to do. Of course, the best timing depends on the couple’s relationship with each other. It may also be influenced by their families’ views, and the culture they belong to.

In practice a carrier might suggest a blood test to their partner at one of the following points.

- Before they settle down together.
- After they settle down together but before they start a pregnancy.
- As soon as they have started a pregnancy.

## **Telling the family about alpha zero thalassaemia**

A carrier inherited alpha zero thalassaemia from one of their parents, so their brothers and sisters and other blood relatives could also be carriers. For example a brother or sister has a 1 in 2 chance of being a carrier.

If a carrier has brothers or sisters, or already has children, they need to know that they may carry alpha zero thalassaemia. They should ask their GP or practice nurse for a blood test “for haemoglobin disorders”.

## Alpha zero thalassaemia world-wide

- Alpha zero thalassaemia major is the commonest serious inherited disorder in Southern China, Northern Thailand and many parts of South East Asia.
- At least one in 250 human beings carry alpha zero thalassaemia (0.4%). World-wide there are over 25 million carriers.
- World-wide, at least 6,000 babies are born each year with alpha zero thalassaemia major, and 12,000 children are born with haemoglobin H disease.
- In the UK there are at least 10,000 carriers of alpha zero thalassaemia, and at least 4 babies with alpha zero thalassaemia hydrops fetalis are conceived per year. (Estimates at the beginning of the year 2000.)
- Alpha zero thalassaemia is common among people who originate from South East Asia or the Eastern Mediterranean area. It is found in the native population of Northern England and Northern Ireland. It is uncommon among other North Europeans.

The table shows the carrier frequency in selected population groups.

Population group and area of origin	Frequency of alpha zero thalassaemia carriers	% of alpha zero thalassaemia carriers
South-East Asia		
<i>Southern China</i>	1 in 17	6
<i>Thailand</i>	1 in 10 - 1 in 30	3 - 10
<i>Malaysia</i>	1 in 100	1
<i>Laos, Cambodia, Vietnam</i>	1 in 30 - 1 in 100	1 - 3
<i>Philippines</i>	1 in 30 - 1 in 100	1 - 3
The Mediterranean		
<i>Cyprus</i>	1 in 50 to 1 in 100	1 - 2
<i>Southern Turkey</i>	around 1 in 100	1
Northern Europe	less than 1 in 1,000	< 0.1

## **DNA diagnosis:--Carrying alpha zero thalassaemia**

**(also known as having alpha zero thalassaemia trait, or alpha-1 thalassaemia trait)...**

... is not an illness, and will never become an illness. It was passed to you by one of your parents and you could pass it on to your children.

There is nothing to worry about, unless your partner is also a carrier.

- If your partner is also a carrier, together you could have children with a serious inherited illness. However, with medical help, a couple who are both carriers can have healthy children.
- If you are thinking of having children, your partner should have a blood test “for haemoglobin disorders”.
- If you have children or brothers and sisters, they could carry alpha zero thalassaemia like you. Encourage them to have the same blood test.

To find out more, see your GP or a specialist counsellor.