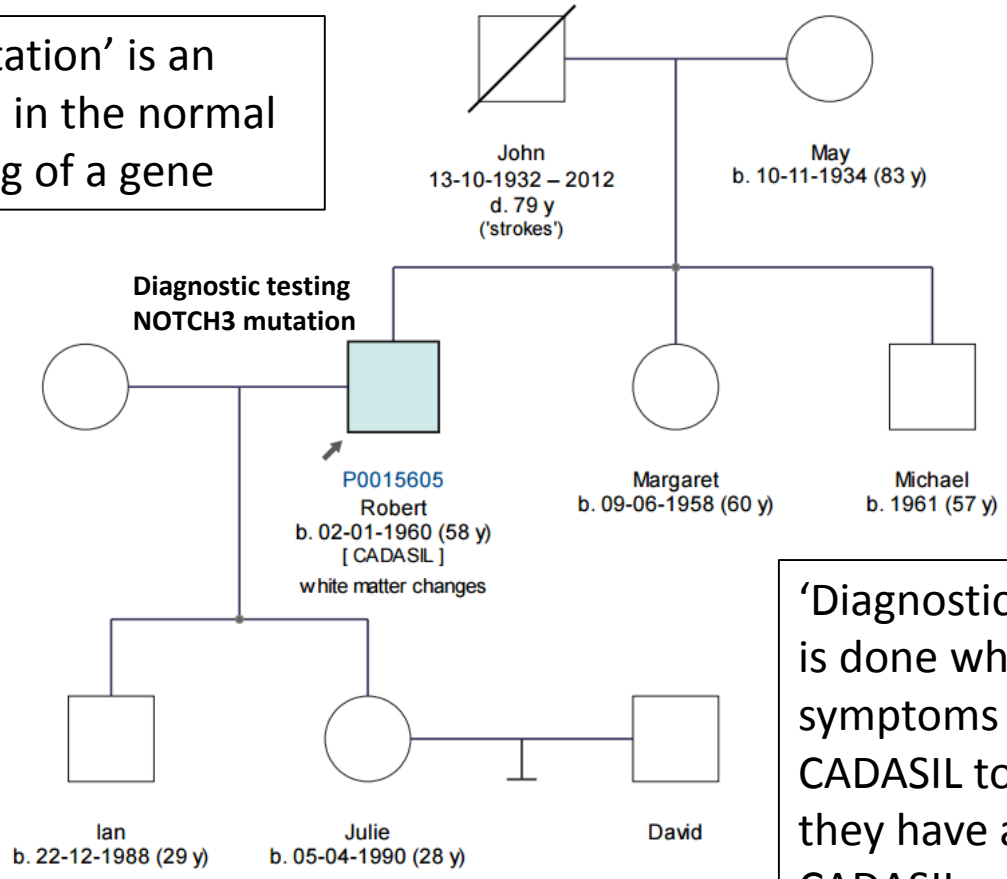
CADASIL and Genetics: Prenatal Testing, Insurance Issues

Heather Pierce, PhD, MS

Registered Genetic Counsellor
Clinical Genetics, Addenbrooke's

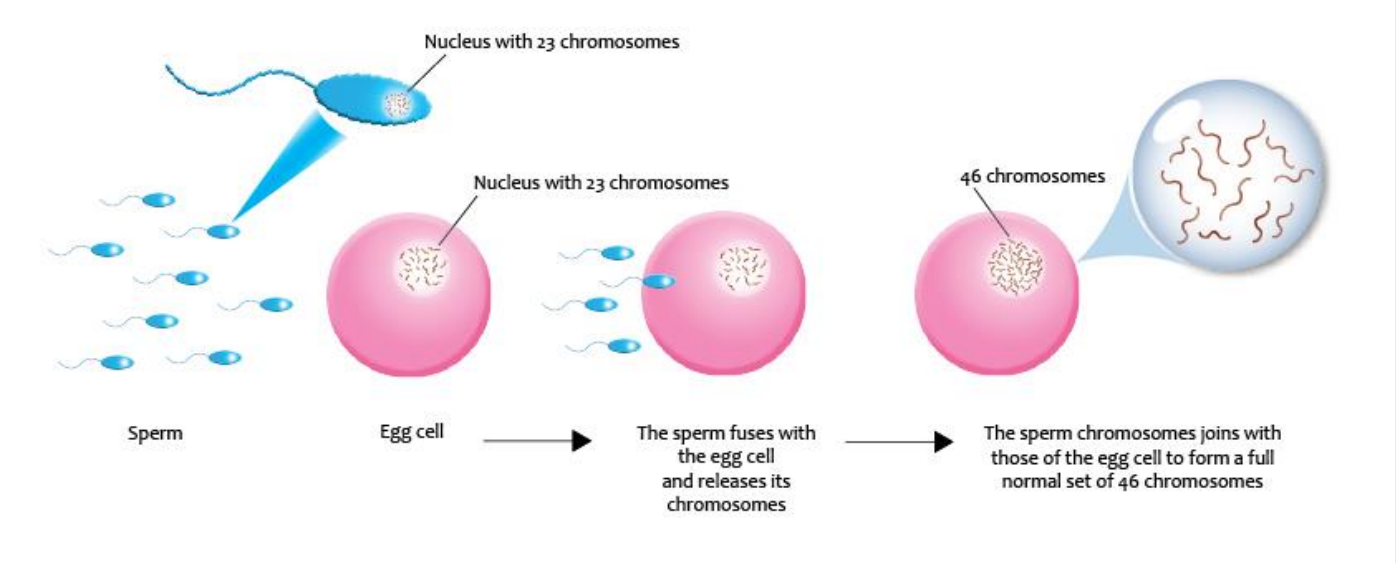
CADASIL Diagnostic Genetic Testing

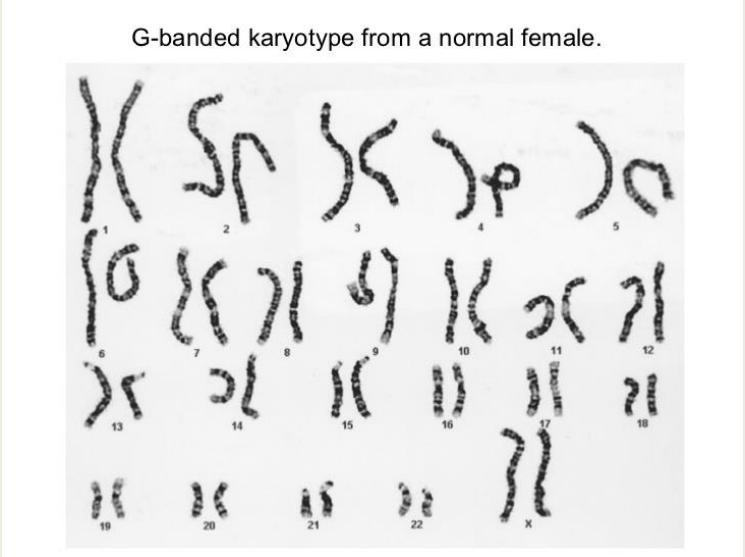
A ‘mutation’ is an alteration in the normal spelling of a gene



‘Diagnostic genetic testing’ is done when a person has symptoms suggestive of CADASIL to confirm that they have a diagnosis of CADASIL

CADASIL Inheritance



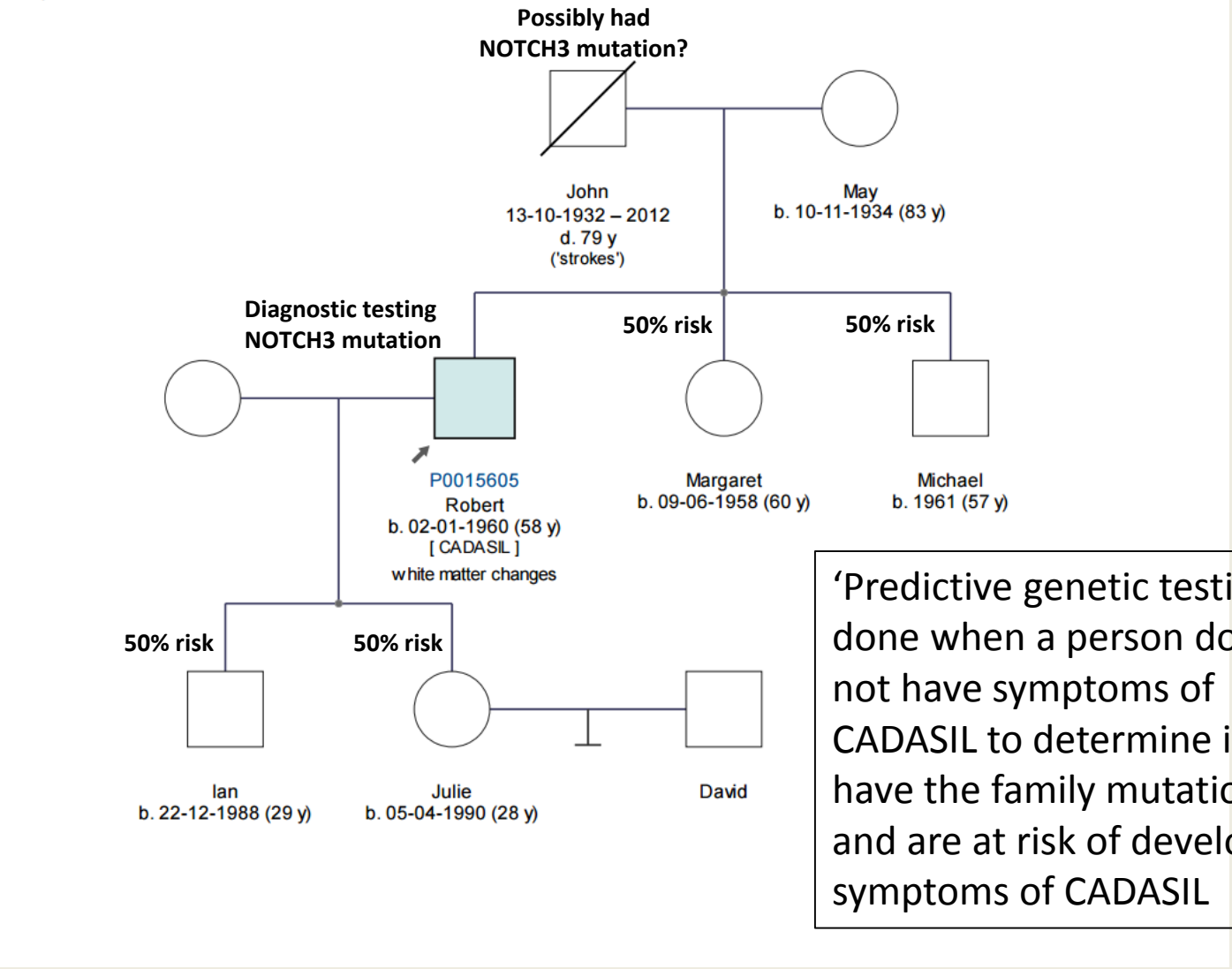


We inherit one copy of each chromosome from Mum and one copy from Dad

CADASIL Inheritance

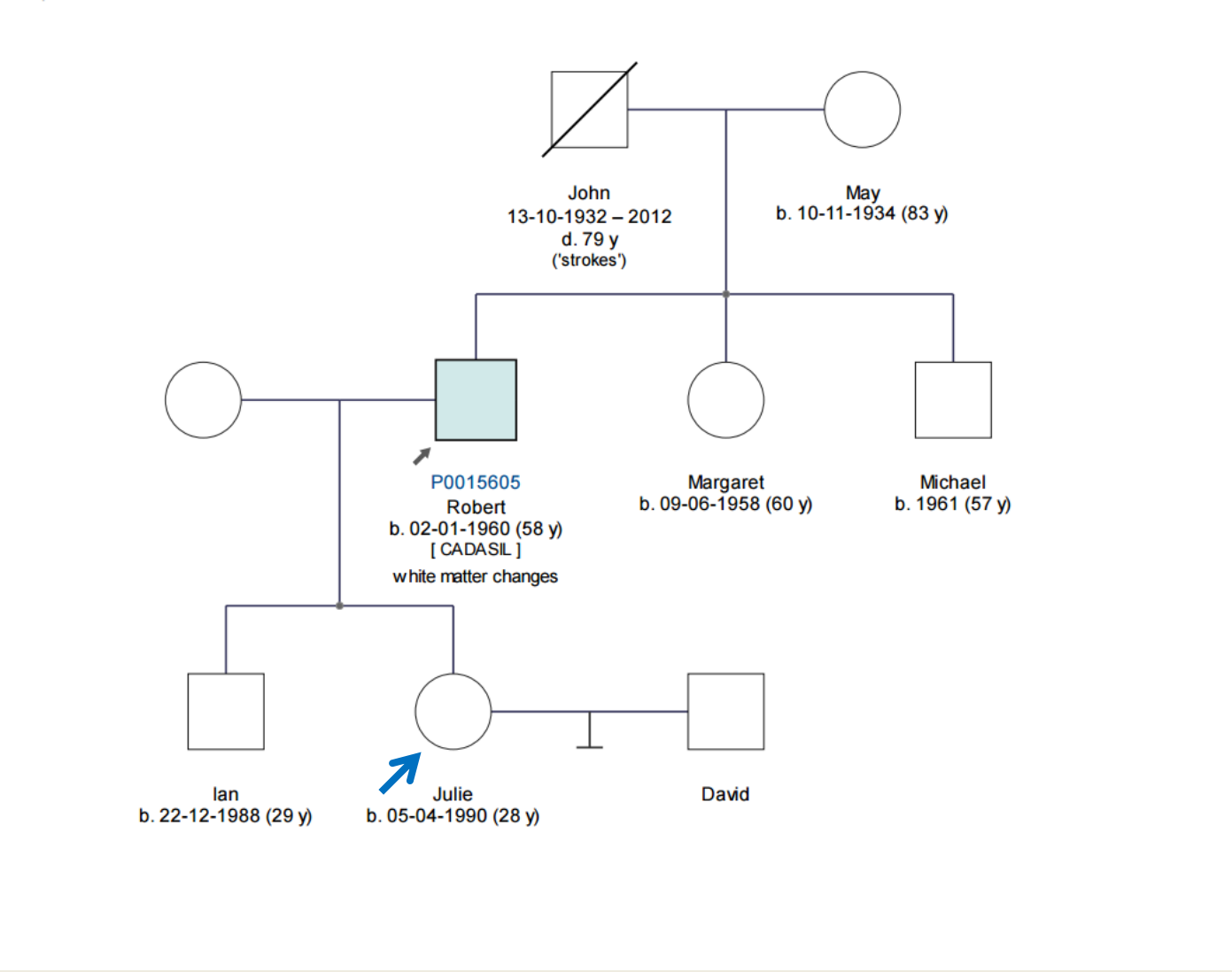
- CADASIL risk is inherited in a ‘dominant’ manner
  - A person only has to have a mutation (spelling change) in *one* copy of the NOTCH3 gene to be at risk of developing symptoms of CADASIL
- In someone with a NOTCH3 gene mutation, each of their children has a 50% (1 in 2) chance of inheriting the copy of the gene with the mutation

CADASIL Predictive Genetic Testing



'Predictive genetic testing' is done when a person does not have symptoms of CADASIL to determine if they have the family mutation and are at risk of developing symptoms of CADASIL

CADASIL Predictive Genetic Testing



Accessing Genetic Testing

- GP referral to local Genetics Service
- We do not offer predictive testing to anyone under the age of 18
- Appointment with a Genetic Specialist (Genetic Counsellor, Consultant, or Specialist Registrar)
- Usually, first appointment is discussion only
- If you wish to proceed with testing, a second appointment is made

I am at 50% risk of CADASIL
Things I need to consider…

Why be tested?

Why now?

Insurance issues
Life cover
Mortgages
Health cover
www.abi.org.uk

Coping
If I get tested
how will I cope with
the results?
How will those closest
to me cope?

Risks to my children?
Telling adult children
Tests in pregnancy?
-Prenatal
-Pre-implantation

Who can I talk to?
Family, friends, others
who have gone through
testing ,Clinical Genetics
my GP

Choice
I don't have to test.
I can take all the time
I need to make a
decision that is right
for me & my family

Working
Will getting tested affect
my job?
Should I tell my boss?
What plans do I have for my
future career?

Insurance and Genetic Testing

- Concordat and Moratorium on Genetics and Insurance
  - Voluntary agreement between the government and insurance companies, currently effective until 01/11/19, ongoing 3-yearly review since 2001
  - Allows patients who have taken a predictive genetic test to obtain significant levels of insurance cover without disclosing the results to the insurance company
    - Up to £500,000 of life insurance
    - £300,000 for critical illness insurance
    - Paying annual benefits of £30,000 for income protection insurance

Insurance and Genetic Testing

- What information do I have to disclose to my insurance company?
  - Your current health and any previous health problems
  - If a genetic condition runs in your family
  - Your family medical history
- What *can't* my insurance company ask?
  - Your predictive genetic test results
    - However, you may wish to inform them if your results show that you are *not* at risk (aka a 'negative' result)
  - Family members' predictive genetic test results

Pregnancy Options

- Not to test
- Prenatal genetic testing
  - Test after becoming pregnant
    - Direct testing
    - Exclusion testing
- Pre-implantation genetic testing
  - Test very early embryo, only implant embryo without the mutation
- Donor egg or sperm
- Adoption
- Not to have children

Prenatal Genetic Testing

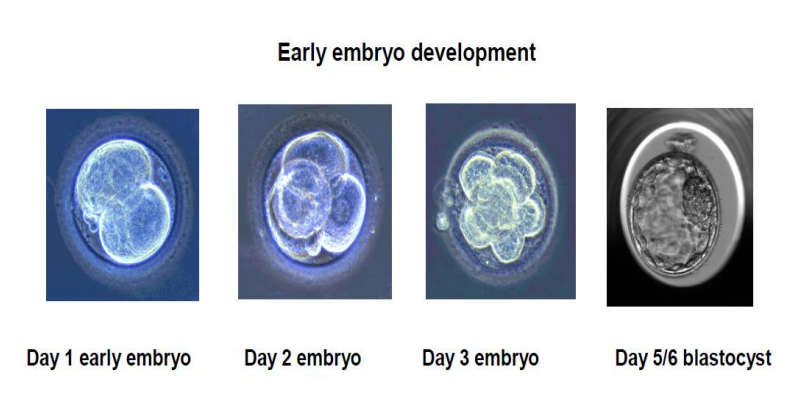
- Direct testing
  - At-risk parent knows that they have the mutation, existing pregnancy is tested to see if the fetus has the mutation
- Exclusion testing
  - At-risk parent does not have predictive testing, existing pregnancy tested to see if it has inherited a copy of the gene from the grandparent with CADASIL

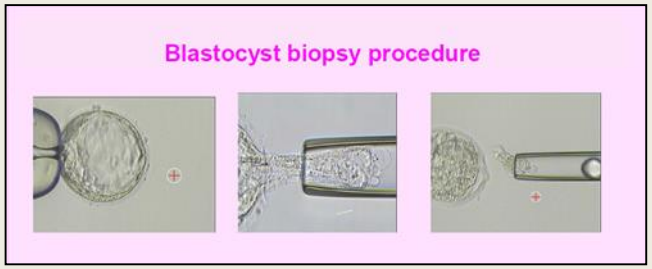
Pre-implantation Genetic Diagnosis (PGD)

- IVF to produce early embryos, biopsy and test embryos, freeze all biopsied embryos

Embryo biopsy:

1) Fertilisation —5 days→ blastocyst.





2) A few cells are removed from the trophectoderm (outer layer of cells surrounding the blastocyst) and sent to the lab for testing
3) All biopsied embryos are then frozen very quickly

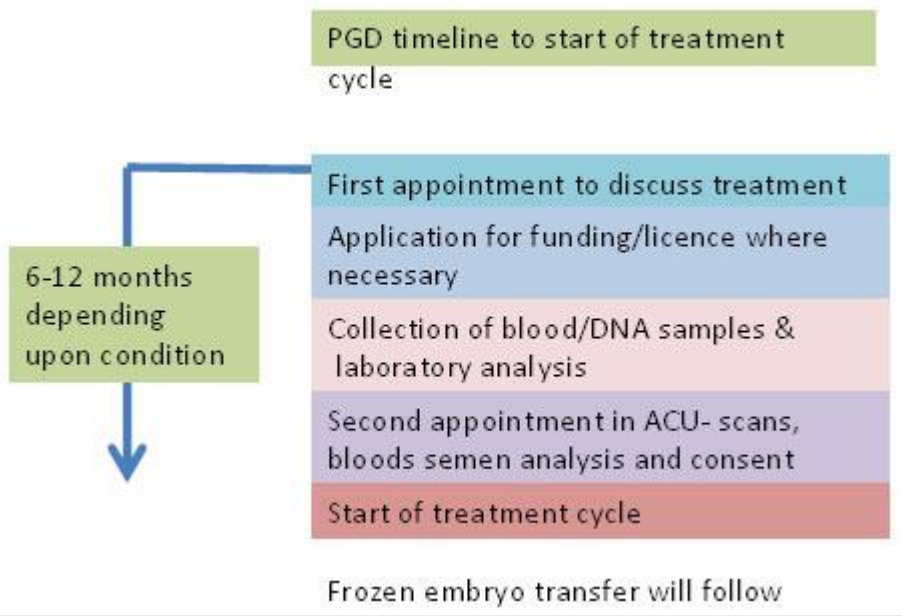
How do I access PGD?

- Referral to PGD Centre by your local Genetics Service

Criteria
Patients must be: <40 yrs at start of treatment. It may therefore not be possible to offer PGD to women over 39yrs
Female BMI must be over 19 and under 30
Couple must have been in a stable relationship for at least 1 year and living at the same address.
Molecular diagnosis **must** have been confirmed in a **CPA accredited NHS laboratory** * *this will need to be completed before we can start the PGD process*
Pathogenicity of mutation **must** have been determined by referring centre
Couple must be non smokers or be willing to complete an NHS Smoking Cessation programme
Couples with healthy children (from this union) will be accepted but must understand they will not be eligible for NHS funding
Parents of **de novo** cases **must** have been tested where possible to exclude gene carrier status

- NHS Funding of PGD
  - If a couple meets the NHS criteria, they can currently access UP to 3 cycles of NHS-funded PGD

PGD Other Considerations



- Self-funding of PGD
  - For self-funded couples the total cost of one cycle is approximately £10,000

For more information…

- Genetic testing
  - Have your GP refer you to the local Genetics Service
- Insurance issues
  - www.abi.org.uk
- Pre-implantation genetic diagnosis
  - www.pgd.org.uk
- Any other questions
  - Heather Pierce, Genetic Counsellor 01223 216 446