



UK IBD Twin and Multiplex Registry Newsletter

Spring 2015

Welcome to the first UK IBD Twin and Multiplex Registry Newsletter. The launch of the registry has been a busy and exciting time. We have not only recruited over 200 twins, but have expanded our resource to include multiplex families. We are also now enrolling children and young people.

Our work has gained recognition from the scientific and medical communities. We presented our initial findings at two international conferences. The abstract presented at the European Crohn's and Colitis Organisation was awarded "Best Abstract" and presented to an audience of thousands (have a look on the website www.ecco-ibd.eu and search "OP002 twin" to find it). As a result several international IBD experts are keen to work with us, with the ultimate aim of discovering new strategies for prevention, diagnosis and treatment of Inflammatory Bowel Disease.

This newsletter describes the progress we have made with our research to date, including our key presentations and publications. None of this would have been possible without you. Thank you so much!



Dr Marcus Harbord



Dr Hannah Gordon

Launching the Registry

Since the UK Twin and Multiplex Registry was launched at the end of 2013, almost 300 members have joined.

We began recruiting for the registry by retracing twins who took part in a study at the Royal Free Hospital in the mid 90s. 94 twin pairs who took part in this study have one or both twin enrolled in the current registry.

New members have also joined after responding to adverts on CCUK social media and newsletters. As well a very positive response from adults, we were approached by several parents of children with Crohn's Disease or Ulcerative Colitis who also wanted to help. Dr John Fell, a leading Paediatric Gastroenterologist, has been working with us to help us add a paediatric cohort to the registry.

Twin studies allow us to look at individuals who have

closely shared genetic information; this is very useful when looking at how environmental triggers influence disease. Families where several close members have Crohn's Disease or Ulcerative Colitis provide an avenue to look more closely about why IBD runs in some families and not in others. As such we are now also recruiting "multiplex" families with three or more close relatives diagnosed.

We have a sister registry in Asia, where the rates of IBD are lower yet rapidly rising. Twin pregnancies are very rare in Asia, however they have recruited several multiplex families. We will be comparing the patterns of disease behaviour in multiplex families from the East West.



Concordance and Environmental Risk Factors of Twins from the UK IBD Nixon Twin and Multiplex Registry

Our first analysis of the registry focussed on the first 100 twin pairs recruited. We looked at whether one or both twin have IBD, the disease type, and whether twin pairs are identical or non-identical. We also reviewed environmental exposure and lifestyle.

We found that within our registry there are more non-identical twin pairs who both have IBD than expected. This is particularly true of twins with Ulcerative Colitis. The rate of concordance, that is both twins being affected, was four times the likelihood of non-twin siblings both developing IBD after one was diagnosed. This may also be because twins grow up in a more similar environment than non twin siblings

When analysing specific environmental factors, a previous history of smoking was associated with Crohn's Disease, but not Ulcerative Colitis, which is consistent with other studies. There was a slightly higher report of previous cannabis use amongst people with Crohn's disease, although overall cannabis use was low so the numbers were not large enough to assess the statistical significance. It will be interesting to re-evaluate this trend as the registry grows.

The History of Twin Studies

It was first observed that diseases were sometimes shared between twins as far back as the ancient Greek philosophers in 5BC. Hippocrates attributed this to "shared maternal circumstance".

The first published twin study was written by Sir Francis Galton in 1876. The work describes the characteristics and behaviour of various twin pairs, some of which Galton realised were more alike than others. From this he concluded "nature is stronger than nurture". Galton was a cousin of Charles Darwin, who himself was troubled by a then mystery illness. Symptoms included

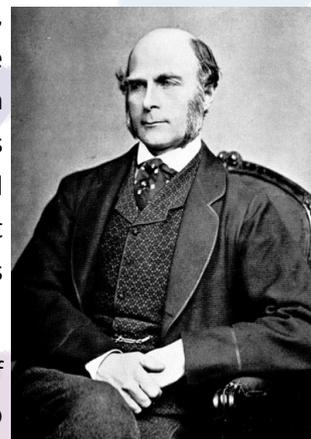
Our study showed an association with being a sickly child, or recalling being unwell more often than peers, and subsequently developing IBD. In twin pairs where only one developed IBD, the affected twin more frequently recalled gastrointestinal infection prior to diagnosis.

The vast majority of members of the registry described a normal, healthy diet prior to diagnosis. There was a slightly higher recall of eating "ready made" meals at least weekly in participants with Crohn's Disease. However, when the data was adjusted statistically to account for the multiple comparisons being made in environmental factors this association was lost. As with cannabis use, we will look at this again as the registry grows.

The slides of the presentations given at the European Crohn's and Colitis Organisation's International meeting in Barcelona can be found on our website www.ibdtam.org.uk. The video of the presentation will soon also be available. These first findings from the registry were also presented at United European Gastroenterologists' Week 2014 in Vienna.

abdominal pain, weight loss, mouth ulcers and fever. He shared this condition with several of his children; it is possible that Darwin and Galton were part of the first recorded "multiplex" Crohn's family.

There are various designs of twin study which are used to untangle the roles of genes



Sir Francis Galton



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The History of Twin Studies continued...

and the environment. The most common is the “classical twin design”. This type of study looks at twin pairs where one or both have a condition, and compares identical and non-identical twins. If it is more common for the identical twins to both have the disease, this implies the disease has a strong genetic component.

The classical twin study design was first used to assess the heritability of IBD by Professor Tysk in 1988. His study concluded that both Crohn’s Disease and Ulcerative Colitis were heritable, Crohn’s Disease more so. However, re-evaluation of this study, as well as review of other twin cohorts suggest that the initial underestimated the role of environment. Interestingly, it has also been shown that even non-identical twins are more likely to both have IBD than non-twin siblings.

Twin studies of IBD have also been used to investigate the ecosystem of bacteria within our gut – the microbiota – and changes to the packaging and regulation of our DNA which occur throughout our lives.

The studies to date have involved small sample sizes, but have shown distinct changes between “healthy” and “ill” twin pairs where one of the pair has Crohn’s Disease. It is hoped that as the UK IBD Twin and Multiplex Registry grows, we will be able to support larger scale studies of this nature.

The UK IBD TAM Registry gave a talk at the Wingate Institute entitled “The History of Twin Studies in IBD”. This is a meeting attended by academic gastroenterologists in London. The slides are available on our website www.ibdtam.org.uk.



The Heritability of Inflammatory Bowel Disease

Heritability is the extent to which a condition can be attributed to genetic factors. The heritability of Crohn’s Disease and Ulcerative Colitis is widely debated; family studies show that siblings and children of IBD sufferers are much more likely to develop IBD than those without a family history. However families are also more likely to share a similar environment. Interestingly, methods used to calculate heritability based upon the genes already known to be associated with IBD give strikingly different results.

To further complicate matters, the models for working out heritability were devised when it was thought that genes and environment acted independently of one another. This is now understood to be an

oversimplification; there are complex interactions between genetic and environmental factors, some of which are mediated by the ecosystem of bacteria within the gut, the microbiota. The packaging and regulation of genes is also known to change throughout our lifetimes, a phenomenon known as epigenetics.

The investigators of the IBD Nixon TAM Registry have worked with the Danish Twin registry in reviewing the methods used to calculate heritability. This work has been accepted to the journal Inflammatory Bowel Disease, and will be published this summer.



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Our Latest Research Study!

The IBD Nixon Twin and Multiplex Registry has just begun recruiting for a study of “Non-Genetic Factors in the Pathogenesis of IBD in Twins”. This study focuses on the bacteria within our gut and the changes to packaging and regulation of DNA which occur throughout our lifetime. It is believed these areas might mediate development of Crohn’s or Ulcerative Colitis in susceptible people.

Taking part in this study involves providing a sample of blood, urine and stool. This can be collected in a single visit which can be completed at home. Unlike the registry itself, we would need both twins of a pair to take part. If you would like more information about this study please let us know.

Coming Up

I am delighted to have been invited to speak at the Royal Society of Medicine and Crohn’s and Colitis Symposium on 6th June. I am talking about “Who gets IBD and why?”. I will also shortly be presenting a 20 year follow up of twins with IBD at the British Society of Gastroenterology Annual meeting. This presentation is based upon data collected from twin pairs who were members of both the old and current twin database. We will be working more closely with the Asian registry over the coming year, and hope to compare groups from the East and West.

Contact Details

Postal Address:

UK IBD Twin & Multiplex Registry

1st Floor St. Stephen’s Centre,
Chelsea & Westminster Hospital.
369 Fulham Road,
London,
SW10 9NH

To Contact Dr Hannah Gordon directly please use the email address below:

hannah.gordon@chelwest.nhs.uk

Or you can contact our research team on the phone number below:

+44 (0) 203 315 6322