MANCHESTER 1824
The University of Manchester

BIR
Biologics and Immunomodulators Register

2022

BADBIR
Annual Update

British Association of Dermatologists Biologics & Immunomodulators Register

Welcome

A reflection on the establishment of the register over the last 15 years. An ongoing success built by the UK and Ireland Dermatology Community.

It's hard to believe that BADBIR has been registering participants for 15 years, the first patient was recruited in Salford in September 2007. The register was established as biologics, namely efalizumab and etanercept, first started to be approved for psoriasis by the National Institute for Health and Care excellence (NICE). The primary reason for BADBIR being sited in Manchester was the in-house expertise of the British Society for Rheumatology Biologics Register (BSR-BR) set up by Professors Alan Silman and Deborah Symmons a few years earlier to monitor the safety of biologics for rheumatoid arthritis (RA). Their advice was instrumental to me and Professor Tony Ormerod as we worked with the BAD and its Biologics Sub-Committee to design BADBIR; their standout piece of advice was not to use a paper-based system but to be web-based from the start. We were aware from work on methotrexate that side-effects of drugs used for RA would not necessarily be the same in psoriasis, hence the need for a stand-alone psoriasis register. We designed and powered BADBIR to assess the risk of serious infections and cancer in the knowledge that real world evidence was more important to the practising clinician than data from clinical trials. Thus, BADBIR was, and always will be, a pharmacovigilance register.

The unique strengths of BADBIR: sophisticated database; 165 dermatology centre teams involved – large and small – across the UK and Ireland; the comparative cohort of patients on non-biologic systemic therapies; opportunities for research studies as exemplified by externally funded clinical research training fellows and PhD students; its independence from pharmaceutical companies; the dedicated operations team led by Ian Evans in Manchester; the hugely collaborative nature of British and Irish dermatology; and the invaluable portfolio support of the National Institute for Health and Care Research (NIHR). Indubitably, the envy of the world. The success of BADBIR has spawned other national initiatives including the MRC stratified medicine consortium PSORT, UK-TREND and the atopic dermatitis register ASTAR and in all likelihood will be the template for other registers.

Dry statistics don't tell the whole story but later in this newsletter we discuss BADBIR in numbers – 20,613 registrations, 140,000 patient years' follow up and 32 publications allied to the high quality of the entered data are world-leading and a gold standard for other registers worldwide. The long-term follow up of patients in BADBIR is crucial, particularly as we start to enrol more children, and this builds an invaluable and unique resource for research. BADBIR continues to evolve with the recent launch of the new Patient Portal, allowing study participants to record questionnaires directly into the register.

BADBIR is as relevant now as it was 15 years ago, new biologics, biosimilars and small molecules will continue to be approved for psoriasis and included in BADBIR, The long-term data on continuous biologic use provide new insights into safety and drug survival and effectiveness particularly as it is aligned to the Biomarkers and Stratification To Optimise outcomes in Psoriasis (BSTOP) biological resource run by Professor Catherine Smith. Later in this newsletter we will highlight important publications addressing safety, effectiveness and the value of Real World Data.

We have a fabulous BADBIR community and without the dedicated principal investigators and their teams the register simply wouldn't exist. It is your register please apply for data access and advice on how to analyse the data. For those of you interested in updates on BADBIR Dr Zenas Yiu and I will be talking about how to get involved in the register and our latest research at the upcoming 102nd BAD Annual meeting in Glasgow 4-7 July 2022. Please come along and listen to the talks and/or visit the BADBIR stand. It has been a privilege to have been the Chief Investigator for BADBIR over the years and to have played a role in the founding of what is now a flagship enterprise of the BAD.

With best wishes

Professor Chris Griffiths OBE
Chief Investigator BADBIR

BADBIR: The first fifteen years

BADBIR continues to receive data from dermatology departments across all of the UK and Ireland as we seek to answer important questions on the use, effectiveness and long-term safety of new treatments for psoriasis.

Here are some notable time points from the first fifteen years of the Register.

2006 – NICE provides approval for biologic treatments to be used for psoriasis.

2007 – BADBIR commences with pilot phase at eight hospital sites.

2008 – The Register fully launches with registrations accepted for **TNFi** products Humira (adalimumab), Enbrel (etanercept) and Remicade (infliximab).

2009 – **IL12/23** inhibitor Stelara (ustekinumab) launches in UK.

2010 – East Lancashire Hospitals NHS Trust registered **1000th BADBIR Participant**.

2012 – Kettering General Hospital NHS Foundation Trust registered **5000th BADBIR participant**.

2014 – **10,000th participant** joins from Great Western Hospital Swindon as BADBIR published study data in scientific journal for the first time.

2015 – Next wave of systemic psoriasis treatments launches as **IL-17** inhibitors Cosentyx (secukinumab), Taltx (ixekizumab) and Kyntheum (brodalumab).

2016 – Landmark paper published by BADBIR on Risk of Serious Infections in biologic-exposed psoriasis patients.

2017 – Huge increase in psoriasis treatments to the market with new **IL-23** inhibitors (Ilumetri, Skyrizi & Tremfya), new small molecule products (Otezla & Skilarance) and widespread use of new adalimumab biosimlars (including Amgevita, Hyrimoz & Imraldi).

2020 – **20,000th BADBIR participant** registered at the Churchill Hospital, Oxford.

2021 – Bimzelx (bimekizumab) launches in the UK with registrations accepted on BADBIR.

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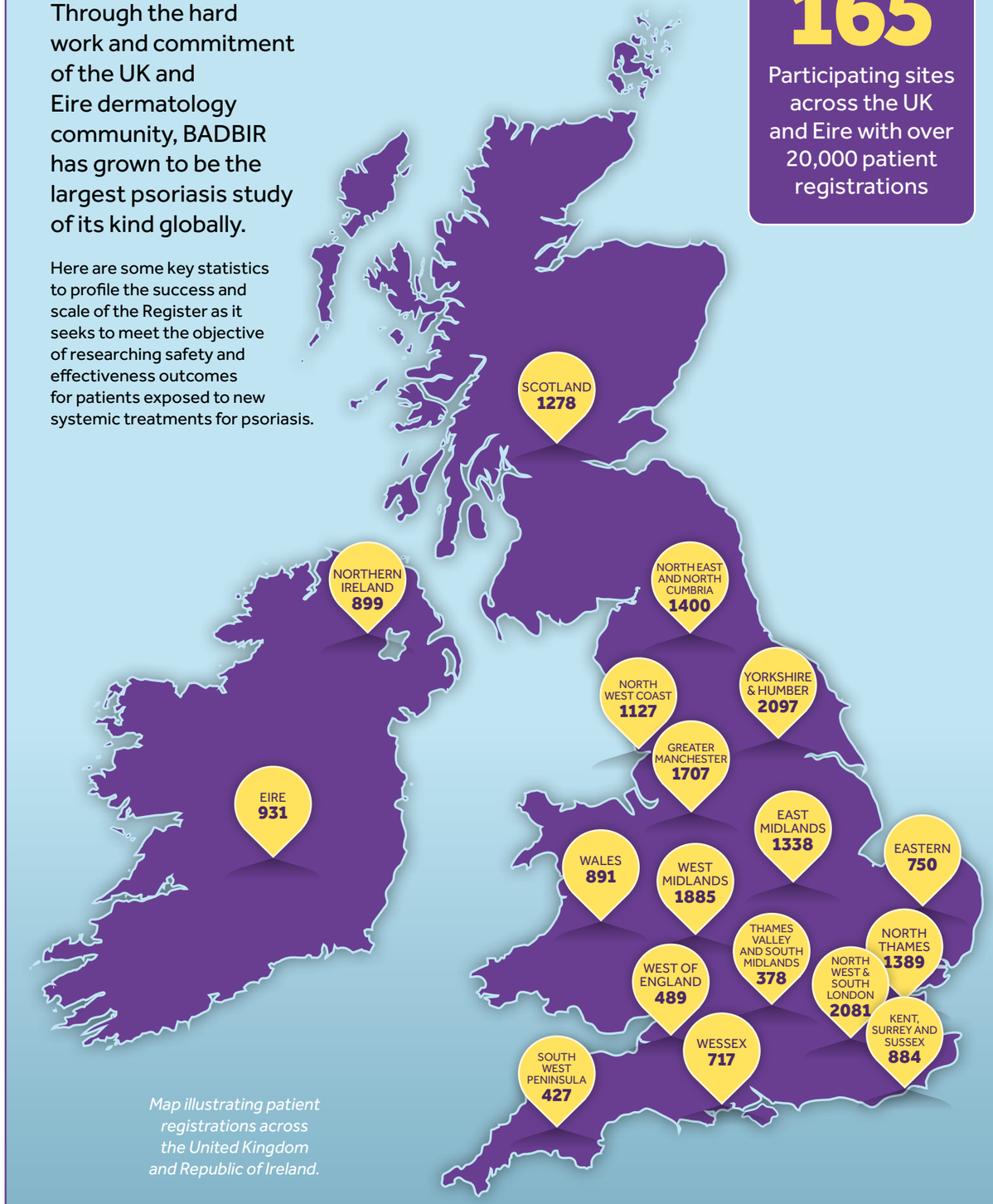
Key statistics

Through the hard work and commitment of the UK and Eire dermatology community, BADBIR has grown to be the largest psoriasis study of its kind globally.

Here are some key statistics to profile the success and scale of the Register as it seeks to meet the objective of researching safety and effectiveness outcomes for patients exposed to new systemic treatments for psoriasis.

165
Participating sites across the UK and Eire with over 20,000 patient registrations



Map illustrating patient registrations across the United Kingdom and Republic of Ireland.

20,613 total registrations

14,157
in Biologic Cohort

6,047
in the Conventional Comparison Cohort

409
in the Small molecule Cohort

100,000
Follow-up Visits recorded on BADBIR

Over
150,000
PASIs collected

Over
85,000
DLQIs completed

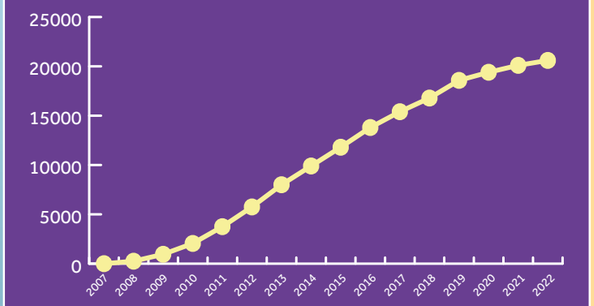
Over
75,000
Adverse events entered

350,000
Messages exchanged between study team and site research staff

32 Journal Articles Published Using Data from BADBIR

140,000+
Person Years Follow-up Collected in BADBIR and always increasing

Cumulative increase to recruitment continues...



Data held on
31
Different Systemic Treatments for Psoriasis

Largest Register Globally

Patient Portal

An alternative method for participants to record their BADBIR questionnaires launched in 2021. Here are some common questions.

Why has the Portal been developed?

With an increase in patients being seen by clinicians remotely, we have introduced the Patient Portal to provide another method for BADBIR participants to complete questionnaires. Previously the only method for questionnaires to be completed was on paper as part of routine appointments,

How do Participants use the Portal?

Patients can access the Portal via the BADBIR website (www.badbir.org) and can create an account using details already known to them (either their NHS number or BADBIR study ID number).

Newly registered patients can complete their baseline questionnaires through the Portal once they are entered onto the database by the clinical research team.

How do I inform patients of the Portal?

You are allowed to contact patients outside of their normal appointments to invite them to use the Portal. A BADBIR non-substantial amendment was approved on 15/07/2021 allowing you to make this contact. A copy of this amendment and the approval is available in section 3 of your site file to view.

You can contact patients however you wish (e.g. letter, phone, email, etc.) and advise them that more information is available on the BADBIR website on how to register and use the Portal.

To make it easier to direct patients to the Patient Portal, we've also added a feature to the database where you can email an invitation to a patient containing links to the Participant webpage and the Portal itself. You can access this feature by following the "Invite patient to Portal" link on your centre homepage.

Should all participants use the Portal?

There will be a study amendment in 2022 to alter the design to allow patient questionnaires to be completed at every follow-up. Currently the protocol requests questionnaires in the first three years of BADBIR participation only (baseline to follow-up 6). The amendment will allow collection of questions in line with the other data collected on the study (once annually from follow-up 7).

We hope this change in the study design will make the process clearer as all patients will be eligible to create a Patient Portal account, regardless of how long they have participated in the study.

Any data entered in the Patient Portal is automatically placed into the most appropriate follow-up based on the date it was completed.

Can the clinical research teams see the questionnaires responses entered by the patient?

On the View All Patients page within the database, they will have a phone symbol next to their study ID number. You can also filter this page to only view patients who have registered for the Portal.

There are several ways for you to track if patients have completed questionnaires through the Patient Portal:

- Any follow-up that contains data entered by a patient through the Portal will have a green phone symbol next the follow-up number on the Patient Summary page.
- If a patient has registered for the Portal, they will also have a 'Patient Portal activity log' below any queries/ feedback on their Patient Summary page. This gives you a full history of which questionnaires they have entered through the Portal – it tells you when they completed any questionnaires and which follow-up they were assigned to.
- On your centre homepage you will find the 'Manage patient questionnaires' link. Here you will see whether or not the questionnaires have already been entered into the patient's current follow-up either by a clinician at your centre or through the Patient Portal.

Will participants be reminded when to enter questionnaire data?

Patients who are set-up on the Portal will receive an email prompt when their next questionnaires are due and receive reminder emails if the questionnaires were not completed after the first prompt.

Where can I find more information on the BADBIR portal?

Further information about the Portal is available on the BADBIR website (**www.badbir.org**). The BADBIR team can also be contacted directly with any queries on **badbir@manchester.ac.uk** or **0161 306 1896**.

Benefits of the Portal

Save time in clinic by using the BADBIR Patient Portal

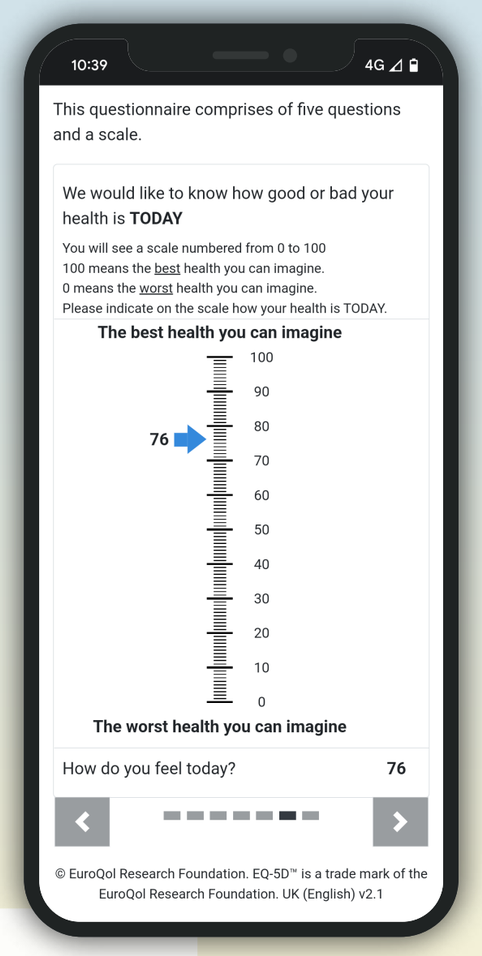
No need to print questionnaires for patients complete

No data entry required – patient responses are saved directly into the BADBIR database

Participants will be prompted automatically when questionnaires are due

Time required to file, scan or archive questionnaires is not needed with the Portal

Android and iOS App versions
LAUNCHING IN 2022



Portal Security

The BADBIR team at The University of Manchester is committed to process all data securely. Full details of how we explain data security to patients can be found in the Patient Information Sheet, study Transparency Notice and the University of Manchester Privacy Notice for Research Participants (all available at www.badbir.org).

The email address and password participants use to register with the Patient Portal are only used for the Portal and are not shared anywhere else.

Clinical Research Teams at sites cannot see these email addresses or passwords. Participants are informed that the local teams will be able to tell once they have registered for an account. Participants themselves will not be able to view any of the data entered by the local Research team separately – data flow is only in one direction with Participants recording questionnaires only with no access to wider data.

Patient Follow-up

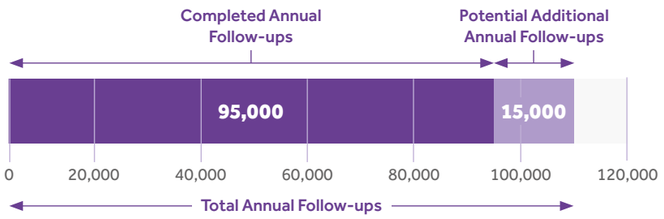
Obtaining follow-up data for our recruited patients remains our highest priority to ensure that we meet the primary purpose of the study.

The primary purpose is to establish if there is an increased risk of serious adverse events following the exposure of biologic and small molecule treatments compared to patients treated with conventional treatments who have a comparable disease severity. Long term follow-up of PASI and DLQI scores are required to determine the long-term efficacy of these treatments.

Every follow-up entered helps BADBIR get closer to powering analysis and answering important research questions

We also collect long term information on patient's exposure to concomitant therapies, photo therapy, smoking and alcohol consumption along with their weight and waist measurements to understand how these factors affect the safety of these patients and the severity of their psoriasis.

Figure 1 shows the proportion of annual follow-up data currently entered and the total annual follow-ups available to enter.



With currently ~95,000 follow-ups of annual data per patient, we already have a large amount of data entered. However, this could increase to ~110,000 follow-ups of annual data per patient once the backlog of empty follow-ups due to COVID have been completed.

Table 1 shows the top ten centres who have entered the most follow-up data within the last 12 months (1st May 2021 – 30th April 2022).

Centre	Follow-ups entered
Northern Care Alliance NHS Foundation Trust (Salford)	983
Nottingham University Hospitals NHS Trust	742
University Hospitals Bristol & Weston NHS Foundation Trust (Bristol Royal Infirmary)	480
County Durham and Darlington NHS Foundation Trust	444
Belfast Health & Social Care Trust	429
NHS Greater Glasgow and Clyde	425
Newcastle upon Tyne Hospitals NHS Foundation Trust	424
Portsmouth Hospitals University NHS Trust	400
Liverpool University Hospitals NHS Foundation Trust (Broadgreen Hospital Liverpool)	282
University Hospitals Birmingham NHS Foundation Trust (Heart of England)	268

Tips on Completing BADBIR Follow-ups

- The Follow-up Summary is useful to check what treatment the patient was on at their last BADBIR follow-up – this can be printed and taken to clinic.
- Speak to the Dermatology Team and Pharmacy as they may have a more accessible way to find out therapy start and stop dates as it can often not be clear from clinic letters.
- The most accurate adverse event data is obtained from checking hospital notes and speaking to the patient – some medical occurrences patients don't deem important enough to mention.
- If patient has multiple follow-ups outstanding all data can be entered in latest follow-up to save time.
- If you are struggling to catch-up, email us and a member of our team will contact you to arrange the appropriate support: **BADBIR@manchester.ac.uk**

We are hugely grateful for the support we receive from the staff collecting the follow-up data at the 166 centres contributing to BADBIR across the UK and the Republic of Ireland.

Centre Profile: **Worthing Hospital**

Linda Folkes is a Clinical Trials Nurse at Worthing Hospital which is under the University Hospitals Sussex NHS Foundation Trust.

We had a chat with Linda to find out how BADBIR is run at Worthing Hospital:

Left-Right: Chloe Hoskins – Clinical Research Practitioner Apprentice, Linda Folkes – Clinical Trials Nurse, Sarah House – Clinical Research Practitioner

What do you believe makes BADBIR a success at your hospital?

It is vital that we have good working relations with our Dermatology team. Without communicating with the Dermatology Team they are not aware what is required for BADBIR and how much work goes into collecting and inputting the data.

The study has benefited a great deal since the Dermatology Team understands what data is collected as they can make their clinic letters clear so that it makes the information easy for us to find.

What information would you like to see in a clinic letter?

It makes our job much more efficient if there are clear start and stop dates in the clinic letters.

This includes start and stop dates for:

- Psoriasis Therapy
- Concomitant Therapy
- Adverse Events

If dates aren't clear it can take us such a long time to try and work out what date we should enter in the database as we want to be as accurate as possible.

It is also helpful if the clinician completes a PASI for the patient. Sometimes a PASI isn't completed if the patient has minimal psoriasis or if the patient is not currently on treatment or receiving a conventional therapy and this has a negative impact on the BADBIR finance that we receive.

What functions on the database do you find helpful?

Preview Data Queries is helpful and we use this each time we enter a follow-up to make sure we haven't accidently missed any data. This minimises the queries that will be generated so it will save us time.

Each patient has a **Follow-up Summary** which lists all the data that has been entered onto the database for that patient - this is really helpful to print out and take to the clinic. Then I can check with the patient if stop dates can be added for their concomitant therapies or ongoing adverse events. I find this also prompts the patient to mention new therapies they have been taking.

It is also helpful to have on screen when looking through the patients notes so I can see what has already been entered.

Do you have any advice on how you work together as part of the Research Team?

We make sure that we communicate as much as possible and work together as a team. We have created our own tracker system to ensure we are not working on the same patient follow-ups.

Do you have communication with the BADBIR Team?

Yes, we find the BADBIR team really supportive. They are friendly and are always on hand to provide training on the register. We also find that the team are open to suggestions on how to make the database work for us.

We'd like to thank Linda and the rest of the team working at Worthing Hospital for all their hard work on BADBIR.

There are many centres which are working really hard to keep on top of their follow-ups. To show our gratitude we are choosing a centre each month to be our 'BADBIR Centre of the Month' these centres will receive some BADBIR goodies in the post and will feature on our website and our Twitter Feed.

The Importance of **Paediatric recruitment in BADBIR**

Dr Tess McPherson and Dr Sabrina Khan – Oxford University Hospitals NHS Foundation Trust


Psoriasis is not uncommon in children: one third of adult patients start their journey in childhood and 10% of patients with chronic plaque psoriasis present before the age of 10.

Psoriasis can have a huge impact on many aspects of life in these age groups and is known to have a long-term life impact.

BADBIR has included recruitment of children (under 16) since 2015. The inclusion of children and young people in this database, which enables monitoring of use of medication, efficacy, short and longer-term safety, is vital for various reasons.

Children are NOT little adults and there are many important differences across age including lifestyle, co-morbidities (and potential future co-morbidities), immunology, infection exposure and psychological impact. These factors are crucial when considering, for example, the impact of immunosuppressive therapy on an immature immune system and ongoing effects of cytokine blockade in children as they develop into adults. Additionally, lifetime exposure times are inevitably longer in younger patients (due to the chronic nature of the disease), possibly resulting in a different safety profile than that seen in adults and a potentially higher risk of malignancy and infection.

Data has previously shown variable management of paediatric patients and poor monitoring of medications in this age group. Over the past decade treatment options are rapidly expanding and there is a need for better guidance on what to use, when and how. Many treatments are unlicensed in children but are nonetheless important options and often used as first line medications, such as methotrexate. New(er) medications including biologics have been licensed in children since 2009, based on trials which show excellent efficacy and short-term safety. However, they remain expensive and without long term data, particularly in younger age groups. A real need persists for real world data, longer term follow-up and robust health economics for all medications.

We have commenced work to examine paediatric patients registered on the BADBIR database. There are 132 patients who were <18 years at registration in March 2021. Patients were registered to different cohorts and some to more than one. 90 (55.6%) patients were registered in the biologic cohort and 72 (44.4%) in the conventional cohort. In the biologic cohort, the mean age was 16.1 years (64% female, 36% male) and mean psoriasis area severity index (PASI) at registration was 15.2. The most common treatment at registration was adalimumab (52%). Others include ustekinumab (27%), etanercept (20%), representing licensed biologics at the time. Since 2021, IL-17 inhibitor Secukinumab has been licensed for this age group. In the conventional cohort, the mean age was 13.4 years (61% female, 39% male) and mean PASI at registration was 17.6. The most common therapies prescribed at registration were methotrexate (40%), ciclosporin (47%), acitretin (10%) and fumaric acid esters (3%).

Our ongoing work will include descriptive analyses of other patient characteristics such as patient reported outcomes, body mass index and co-morbidities. We will also analyse data on the development of any adverse effects of systemic therapy.

Registries such as BADBIR highlight the importance of real-world data in treatments for psoriasis and we are fortunate to have this database in the UK. Through the BADBIR group we are liaising with colleagues managing paediatric psoriasis patients (including European colleagues and PsoNET) to combine data sets. This work and engagement with international partners is a very encouraging collaboration. However, we are sure that there are many eligible paediatric patients in the UK who have not been registered with BADBIR and would really like this to change.

Recent evidence suggests that whereas previously children and young people may have been relatively undermanaged, there is a move to more effective control of psoriasis. As use becomes more frequent, the need for pharmacovigilance for systemic medications in this cohort becomes even more urgent. BADBIR is a fantastic initiative and few other countries have such good prospective data sets including children, thus allowing their seamless follow-up as they move into adulthood.
Please include your patients on the database and encourage colleagues to do so too. This is vital for our understanding of the risks and benefits of treatment in younger patients.

Recruitment Reminder

Anyone seeing young people with moderate/ severe psoriasis

Reminder: ANY systemic or biologic is eligible for peadiatric registration

Please inform colleagues who are managing paediatric patients.

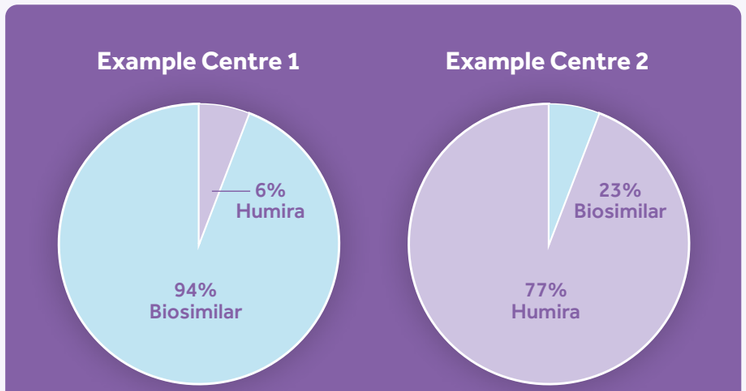
Biosimilars: **What is the importance of using brand names in BADBIR?**

Dr Zenas Yiu NIHR Clinical Lecturer in Dermatology, The University of Manchester

The availability of biosimilar drugs for our patients with psoriasis has vastly reduced the cost of treatment and is a very welcome development.

However, did you know that makers of biosimilars only need to show that the active substance of the biosimilar is similar in molecular and biological terms between their product and the reference product? In terms of clinical studies, if no clinically meaningful difference has been demonstrated in one licensed indication for the reference product the biosimilar could then be approved for all the other licensed conditions. This means that sometimes there can be no randomized clinical trial testing for the use of these biosimilars in skin conditions such as psoriasis prior to marketing authorisation.

It is vitally important that pharmacovigilance studies such as BADBIR are conducted to ensure that this extrapolation is sound, and that the differences in cell lines and glycosylation patterns between biosimilars and the reference product do not result in poorer treatment effectiveness or worse safety profile in the clinic. It is neither a trivial nor a purely theoretical concern: a specific biosimilar epoetin product was associated with an increased incidence in antibody-mediated pure red cell aplasia. Accurate documentation of the drug brand name is a critical pre-requisite for BADBIR researchers to test the effectiveness and safety of biosimilars. Mislabelling of a biosimilar, for example Imraldi for Humira, is an important drug safety issue as this would mean that any potentially important differential treatment effect or safety signal gets buried, and analysis results become biased towards the null. In the worse-case scenario, it could introduce avoidable harm to patients.



We urge all clinicians and researchers working in BADBIR recruiting centres to do the following:

1. Make sure you document the brand name of the biosimilar in your clinic notes and letters;
2. Double check that the right brand name is entered into BADBIR during follow-up;
3. Look back and check that the reference product was not entered incorrectly in past follow-up BADBIR data entries.

If your centre has switched over completely to a biosimilar for adalimumab or etanercept, a nice trick to know whether data from your centre is reliable is to look at your biosimilar to reference product ratio. We also use this ratio to help us flag these problems to your attention.

Centre Experience:
Taking the Role of Principal Investigator as a Nurse

Teena Mackenzie, Research Nurse and BADBIR PI for Royal Berkshire NHS Foundation Trust

Historically nurses have assumed the role of coordinator or research nurse rather than Principal Investigator.

Predominately Consultants and medical staff have led on this important role. Not any more, an increased number of nurses have now established themselves as Principle Investigators (PI).

The following article will focus on why all nurses should be seeking further opportunities in research, even if they are clinical nurse specialists. The Royal College of Nursing (2020) states Advanced Nurse Practioners must be recognised at the level of practice they are working at. This includes the four pillars of clinical practice, leadership, education and research. Incorporated within the British Dermatology Nursing Group (BDNG) Nursing Role descriptors are knowledge in research, and the role of a Principle Investigator at levels of 8a and above (BDNG 2020). Therefore nurses must recognise research and the importance of becoming a PI. I am proud to say I have personal experience of being a PI although I am clinical and not in a research role. The opportunities are there for nurse specialists to establish these roles alongside their clinical practice. In addition Research nurses should be encouraged to establish themselves in the PI role, as they have vast experience in this field.

The rewards to both nurse and patient speak for themselves. Raising awareness to take part in BADBIR can be incorporated into your consultation. Through collaborative working, an increased number of patients can be given the opportunity to participate in research. Having built rapport and trust with my patients, they are very receptive to enrolling onto BADBIR. They feel important and have an extra level of care when recruited and seen by the research nurse. The National Institute for Health Research (2022) explains encouraging a research positive culture is important to give patients access to research, improving patient care and improves positive outcomes. Establishing my PI role I provide my patients with opportunities to participate and often they feel they are giving something back to the NHS. They feel important and heard, that as clinicians we are taking an interest in their skin disease.

The support you receive from the BADBIR team is excellent when taking on the PI role as often nurses are feeling overstretched and concerned about taking on yet more work. The BADBIR team oversee much of the data, hence minimal work for the nurse taking on this role. Seeing your name as PI, the excitement of recruitment and knowing you are doing the very best for your patients make this role rewarding. The data and resources you can obtain through BADBIR ensures you are up to date with the latest evidence. I would encourage any nurse to take a step forward and become a PI for BADBIR.

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National Institute for Health and Care Research. (2022). Embedding a research culture. **nihr.ac.uk/health-and-care-professionals/engagement-and-participation-in-research/embedding-a-research-culture.htm**

Royal College of Nursing. (2020). RCN Credentialing for Advanced Level Nursing Practice. RCN Professional Services. **rcn.org.uk**

Publications

Data from BADBIR has now been used in 32 published journal articles and many other posters and talks across the globe.

Contribution of data from all participating sites has been integral to this huge achievement. BADBIR data is available to be accessed if you have a research question of interest. For full details please visit www.badbir.org/publications

There is lots more to come from BADBIR with data maturing rapidly as more follow-up data is recorded. To profile the research ouputs, we will concentrate on three key themes of Real World Data, Effectiveness & Safety.

Spotlight on Real World Data

BADBIR is the largest observational study of long-term outcomes for moderate-to-severe psoriasis patients globally.

Using the data generated by the study, BADBIR researchers are able to check the Real World experience of patients exposed to new therapies for psoriasis and compare this to outcomes from other studies including pre-marketing clinical trials .

BADBIR is providing Real World Evidence of clinical population, individual patient data, capacity for data linkages and flexibility in study designs. Another strength in observational studies is they provide real world effectiveness of medication that has granted marketing authorisation this is because in clinical trials individuals are randomly assigned to receive treatment, a process that is rarely the case in clinical settings. BADBIR is contributing significantly to our understanding of therapeutic options for psoriasis.

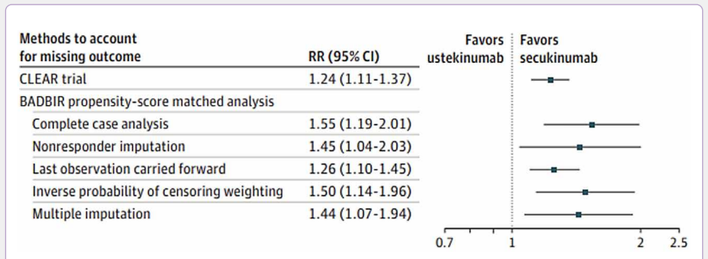
Key Publication

Randomized Trial Replication Using Observational Data for Comparative Effectiveness of Secukinumab and Ustekinumab in Psoriasis
Dr Zenas Yiu et al. JAMA Dermatology, 2021

Question: What is the effectiveness of secukinumab compared with ustekinumab for the treatment of psoriasis in an everyday clinical setting?

Findings: In this comparative effectiveness research study of 1231 patients receiving either secukinumab or ustekinumab for psoriasis, both drugs had lower treatment effectiveness in a real-world clinical setting than in a trial setting. Secukinumab had superior effectiveness compared with ustekinumab, and the estimate of this relative effect using observational data met regulatory and estimate agreement with trial data.

Meaning: Results of this study found a gap between the efficacy of biologic therapies in an idealized trial setting and the effectiveness of biologic therapies in the real-world clinical setting in the treatment of psoriasis; however, a target trial emulation approach can provide robust estimates of relative effectiveness that can be.



Abridged Forest Plot of the Risk Ratio (RR) Estimates for Participants Achieving PASI ≤2 at 12 Months. For full analysis please refer to article.

FUTURE WORK
Look out for upcoming work on trial replication studies in the IL-23 treatmeant sphere.

ALSO SEE
Comparison of Drugs Discontinuation, Effectiveness, and Safety Between Clinical Trial Eligible and Ineligible Patients in BADBIR from Dr K. Mason et al. in JAMA Dermatology, 2018

Publications

Spotlight on **Effectiveness**

Randomised clinical trials provide evidence for how well new treatments for psoriasis work in a selected group of people and are typically available before a new product for psoriasis is launched.

As an observational study with fifteen years of data collection, BADBIR is well-placed to assess effectiveness, in other words how well these treatments work when taken outside of the controlled trial settings to routine healthcare environments, of treatments in a real world population.

Within BADBIR the Psoriasis Area and Severity Index (PASI) is provided by clinicians. Patients participating in the study report the Dermatology Life Quality Index (DLQI). Both severity measures are important tools for assessing effectiveness of clinical interventions over time. In addition, BADBIR has also been interested in measuring persistence (also known as drug survival) of therapies used for psoriasis. This analysis looks at time between treatment initiation to discontinuation in a large number of patients. It is a useful proxy measure for overall effectiveness with the results from BADBIR adding to the knowledge available to clinicians and patients.

The latest drug survival article from BADBIR is summarised in the Key Publication.

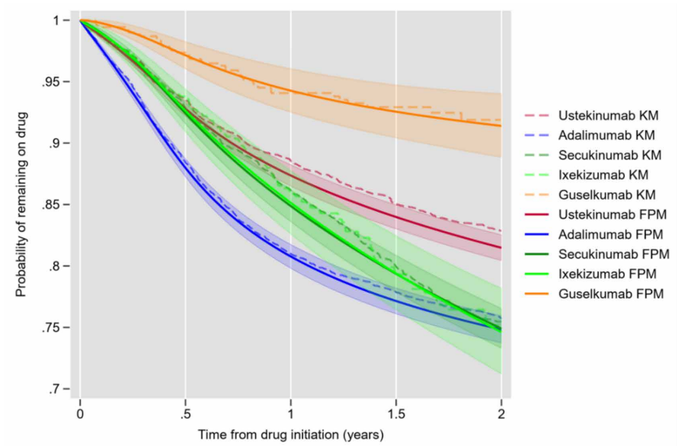
Key Publication

Drug Survival for Effectiveness and Safety of Guselkumab, Ixekizumab, Secukinumab, Ustekinumab, and Adalimumab in Patients with Psoriasis
Dr Zenas Yiu et al., JAMA Dermatology, 2022

Question: What is the drug survival defined as treatment discontinuation of adalimumab (Humira), ustekinumab (Stelara), secukinumab (Cosentyx), guselkumab (Tremfya), ixekizumab (Taltz) for effectiveness and safety in patients with psoriasis in the UK and Ireland? Are there any patient factors that affect survival of each biologic differently which could help treatment stratification?

Findings: In this study of 16,122 treatment courses in patients with psoriasis, guselkumab had the highest overall drug survival for effectiveness and safety out of the included biologics. Psoriatic arthritis, nail involvement, previous biologic exposure, and ethnicity were effect modifiers for biologics and their survival due to effectiveness.

Meaning: These results on longer term treatment effect, safety, and tolerability will be important for patients and their clinicians when making an informed decision to start a particular biologic therapy.



Kaplan-Meier plot reproduced from publication.
For full analysis please refer to article.

FUTURE WORK
As data matures, Drug Survival analyses will be completed on other new psoriasis treatments launched in recent years.

ALSO SEE
Drug survival of adalimumab, ustekinumab and secukinumab in patients with psoriasis
from Dr Z. Yiu et al. in BJD, 2020

Spotlight on **Safety**

The primary objective of BADBIR relates to drug safety. The Register was established by the BAD in 2007 to assess the long-term safety of biologics and other new psoriasis therapies by following a real-world population of patients from all areas of the UK and Republic of Ireland.

Observational studies are particularly important in safety surveillance by capturing serious adverse events associated with the use of medications due to the long term follow-up in an unselected group of people coupled with the continuous update of information on demographic, clinical and disease characteristics using routinely collected clinical data. This data allows BADBIR researchers to answer questions on whether different adverse event outcomes are associated with treatment exposure, and the inclusion of medical history and potential confounding factors allow for robust and reliable analyses to improve patient care.

Key Publication

Risk of Serious Infection in Patients with Psoriasis Receiving biologic Therapies: A prospective Cohort Study from the British Association of Dermatologists Biologic Interventions Register (BADBIR)
Dr Zenas Yiu et al., Journal of Investigative Dermatology, 2018

Question: Does treatment with etanercept, adalimumab or ustekinumab elevate the risk of serious infection more than non-biologic systemic therapies in patients with psoriasis?

Findings: Overall, 1,352; 3,271; and 994 participants were included in the etanercept, adalimumab, ustekinumab cohorts, respectively, and 3,421 participants were in the non-biologic cohort. A total of 283 patients had a serious infection; the incidence rates with 95% confidence intervals (CI) per 1,000 person-years were as follows: non-biologic, 14.2 (11.5-17.4); etanercept, 15.3 (11.6-20.1); adalimumab, 13.9 (11.4-16.6); and ustekinumab, 15.1 (10.8-21.1). No significant increases in the risk of serious infection were observed for etanercept (hazard ratio [HR] = 1.10, 95% CI = 0.75-1.60), adalimumab (HR = 0.93, 95% CI = 0.69-1.26), or ustekinumab (HR = 0.92, 95% CI = 0.60-1.41) compared with non-biologic systemic therapies or methotrexate-only (etanercept: HR = 1.47, 95% CI = 0.95-2.28; adalimumab: HR = 1.26, 95% CI = 0.86-1.84; ustekinumab: HR = 1.22, 95% CI = 0.75-1.99)..

Meaning: The risk of serious infection should not be a key discriminator for patients and clinicians when choosing between non-biologic systemic therapies, etanercept, adalimumab, and ustekinumab for the treatment of psoriasis.

FUTURE WORK
With more years of data collection BADBIR can answer important questions in other Safety areas including risk of cancer.

ALSO SEE
Risk of Major Cardiovascular Events in Patients With Psoriasis Receiving Biologic Therapies
from Dr W. Rungapiromnan et al. in JEADV, 2020

BADBIR **Publication Directory**

32 articles in scientific journals have used data from the Register.

The British Association of Dermatologists Biologic Interventions Register (BADBIR): Design, Methodology and Objectives, Burden *et al.*, BJD, 2012.

Biological therapies for the treatment of severe psoriasis in patients with previous exposure to biological therapy: a cost-effectiveness analysis, Sawyer *et al.*, PharmacoEconomics, 2014.

Differential Drug Survival of Biologic Therapies for the Treatment of Psoriasis: A Prospective Observational Cohort Study from BADBIR, Warren *et al.*, JID, 2015.

Demographics and disease characteristics of patients with psoriasis enrolled in BADBIR, Iskandar *et al.*, BJD, 2015.

Generating EQ-5D-3L Utility Scores from the Dermatology Life Quality Index: A Mapping Study in Patients with Psoriasis, Davison *et al.*, Value in Health, 2017.

Intentional and Unintentional Medication Non-Adherence in Psoriasis: The Role of Patients' Medication Beliefs and Habit Strength, Thorneloe *et al.*, JID, 2017.

Patterns of biologic therapy use in the management of psoriasis: cohort study from BADBIR, Iskandar *et al.*, 2017, BJD.

Comparative effectiveness of biologic therapies on improvements in quality of life in patients with psoriasis, Iskandar *et al.*, BJD, 2017.

Identification of Factors That May Influence the Selection of First-Line Biological Therapy for People With Psoriasis: A Prospective, Multicentre Cohort Study, Davison *et al.*, BJD, 2017.

Differential drug survival of second-line biologic therapies in psoriasis patients: observational cohort study from BADBIR, Iskandar *et al.*, JID, 2018.

Risk of Serious Infection in Patients With Psoriasis Receiving Biologic Therapies: A Prospective Cohort Study From BADBIR, Yiu *et al.*, JID, 2018.

Comparison of Drug Discontinuation, Effectiveness, and Safety Between Clinical Trial Eligible and Ineligible Patients in BADBIR, Mason *et al.*, JAMA Derm, 2018.

Cumulative exposure to biologics and risk of cancer in psoriasis patients: a meta-analysis of Psonet studies from Israel, Italy, Spain, UK and Republic of Ireland, Garcia-Doval *et al.*, BJD, 2018.

HLA-C*06:02 genotype is a predictive biomarker of biologic treatment response in psoriasis, Dand *et al.*, Journal of Allergy and Clinical Immunology, 2018.

Identifying demographic, social and clinical predictors of biologic therapy effectiveness in psoriasis: a multicentre longitudinal cohort study, Warren *et al.*, BJD, 2018.

Infliximab Is Associated With an Increased Risk of Serious Infection in Patients With Psoriasis in the U.K. And Republic of Ireland: Results From BADBIR, Yiu *et al.*, BJD, 2019.

Development and Validation of a Multivariable Risk Prediction Model for Serious Infection in Patients With Psoriasis Receiving Systemic Therapy, Yiu *et al.*, BJD, 2019.

Persistence and effectiveness of non-biologic systemic therapies for moderate-to-severe psoriasis in adults: a systematic review, Mason *et al.*, BJD, 2019.

Association of Serum Ustekinumab Levels With Clinical Response in Psoriasis, Tsakok *et al.*, JAMA Derm, 2019.

A Standardization Approach to Compare Treatment Safety and Effectiveness Outcomes Between Clinical Trials and Real-World Populations in Psoriasis, Yiu *et al.*, BJD, 2019.

Using Real-World Data to Guide Ustekinumab Dosing Strategies for Psoriasis: A Prospective Pharmacokinetic-Pharmacodynamic Study, Pan *et al.*, Clinical & Translational Science, 2020.

Risk of Major Cardiovascular Events in Patients With Psoriasis Receiving Biologic Therapies: A Prospective Cohort Study, Rungapiromnan *et al.*, JEADV, 2020.

Psoriasis treat to target: defining outcomes in psoriasis using data from a real-world, population-based cohort study, Mahil *et al.*, BJD, 2020.

BADBIR: a centenary celebration of research collaboration in British dermatology, Yiu *et al.*, BJD, 2020.

Drug survival of adalimumab, ustekinumab and secukinumab in patients with psoriasis: a prospective cohort study from BADBIR, Yiu *et al.*, BJD, 2020.

Randomized Trial Replication Using Observational Data for Comparative Effectiveness of Secukinumab and Ustekinumab in Psoriasis: A Study From BADBIR, Yiu *et al.*, JAMA Derm, 2020.

Characteristics and skin cancer risk of psoriasis patients with a history of skin cancer in BADBIR, Mason *et al.*, JEADV, 2021.

Defining Trajectories of Response in Psoriasis Patients Treated with Biologic Therapies, Geifman *et al.*, BJD, 2021.

Risks of basal cell and squamous cell carcinoma in psoriasis patients after treatment with biologic vs non-biologic systemic therapies, Mason *et al.*, JEADV, 2021.

Differences in Clinical Features and Comorbid Burden between HLA-C*06:02 Carrier Groups in >9,000 People with Psoriasis, Douroudis *et al.*, JEADV, 2021.

Application of information theoretic feature selection and machine learning methods for the development of genetic risk prediction models, Jalali-Najafabadi *et al.*, Scientific Reports, 2021.

Drug Survival for Effectiveness and Safety of Guselkumab, Ixekizumab, Secukinumab, Ustekinumab, and Adalimumab in Patients with Psoriasis, Yiu *et al.*, JAMA Derm, 2022.

For links to all articles please visit **www.badbir.org/publications**

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