The UK IBD Registry as a platform to support an efficient randomised clinical trial of e-Health interventions to enhance the monitoring of long term biological therapy

Abstract

Introduction: Biological therapies have had a major impact on the management of Inflammatory Bowel Diseases (IBD) but there are challenges in providing safe, effective, appropriate use in the NHS. A number of candidate electronic health interventions (e-Health) exist (e.g. apps and portals) to address these problems, but none has been evaluated formally in a pragmatic clinical trial. The UK IBD Registry has established itself as a viable platform to support point-of-care data collection for local service delivery, audit participation and prospective post-marketing observational studies. A consent model captures local consent for future research participation, which offers the potential for the platform to support investigator-led trials by identifying centres with local cohorts of cases that might participate in registry-enabled studies of interventions. This project aimed to create a prototype for a web-based tool to interrogate the registry to provide a functionality to provide rapid responses to investigator queries

Methods: Source datasets were CSV files containing pseudonymized IBD Registry data, hosted on a secure server at the University of Liverpool. A prototype system was written in C# .Net 4.5 using the MVC5 framework, with the database built on MS SQL Server 2017 using Stored Procedures. An open source front-end framework (Bootstrap CSS) was used to create a 'web site' prototype with iterative development. The analysis is restricted to patients with an electronic record of consent for future research.

Results: The tool comprises a series of screens, with user-applied filters, which provide the ability to run queries on aggregated patient numbers and generate descriptives for phenotype and treatment history for the registry 'overall' and at the level of individual hospital sites. The prototype exists on an internal URL, allowing investigator queries to be executed rapidly by approved personnel.

Conclusions: The system focuses on the sub-group of IBD Registry cases with a record of consent for future research and establishes a capability for independent investigators to explore the feasibility of future Registry-enabled RCTs. The prototype provides a functionality to respond rapidly to queries relating to site identification and potential numbers of research participants for future studies. Further dissemination and access will form part of the IBD Registry's revision of infrastructure and data governance in early 2020 as a partner to the recent HDR UK IBD Hub (*Gut Reaction*).

Introduction:

Biological therapies have had a major impact on the management of Inflammatory Bowel Diseases (IBD) and their use continues to expand with availability of biosimilars and agents with new modes of action. Increasing numbers of IBD patients are receiving long term scheduled maintenance therapy. NICE recommends formal annual review of all such patients to ensure safe prescribing and to determine whether treatment should continue. The extent to which NICE guidance is followed in practice is unknown but limited evidence suggests significant deficiencies in long term supervision. One UK centre reported that 20% of cases lacked an annual review despite efforts to re-design local services. Larger scale attempts to audit compliance with annual biologics reviews across the NHS have proven challenging. Only 12% of 4,718 patients registered for National Clinical Audit of Biological Therapies (2015) had data submitted for twelve month review. Of the cases audited at this time-point, one third of patients with Crohn's disease lacked a formal record of disease severity and only a fifth of cases had a PROM captured (https://www.rcplondon.ac.uk/projects/outputs/national-clinical-audit-report-biological-therapies-adult-report-2015).

System-wide interventions are needed to increase the implementation of NICE guidance and ensure the safe and cost-effective use of these agents. Service pressures place major challenges on achieving this through traditional models of face-to-face follow-up. Current NHS IT systems fail to identify and track patients effectively over time. Patient-facing e-Health interventions (e.g. 'apps'/mobile technologies or other electronic interventions like portals, linking to ePROMs) offer opportunities to empower patients and support clinical teams to develop better ways to monitor long term treatment. A number of candidate interventions exist but none has been evaluated formally in a pragmatic clinical trial.

The UK IBD Registry – a potential vehicle to support efficient trials

Disease-specific registries offer opportunities to improve the efficiency of pragmatic clinical trials at various stages including hypothesis generation, study design and feasibility assessment, identification of sites and eligible patients, prospective recruitment and capture of baseline and follow-up data using established registry datasets and data collection systems that may be embedded into routine care. The UK IBD Registry (https://ibdregistry.org.uk/) has established itself as a viable platform to support point-of-care data collection for local service delivery, audit participation and prospective post-marketing observational studies (e.g. VEST study; https://clinicaltrials.gov/ct2/show/NCT03257345). Although routine reporting and audit activity is currently covered by s251 exemption from consent, the Registry has implemented a consent model which includes specific options relating to research participation. Patient preferences and consent to research options are captured electronically within quarterly data returns.

The current project was intended to explore the feasibility of using the UK IBD Registry as a future platform to support efficient, pragmatic clinical trials of interventions for IBD patients receiving biological therapies. The aim was to allow candidate inclusion and exclusion criteria for trial participants to be modelled using the available registry data items and generate outputs of case numbers by site for those with a record of consent status for research. In future, this could be deployed as a researcher-facing live website to allow IBD investigators to run near-real-time queries to support trial planning. The output was to be a working demonstrator of the website with analyst-only access, allowing responses to be generated to investigator requests.

Methods:

Development of the prototype 'website' (Search Tool)

To conform to current data processing permissions at UoL, the prototype tool functionality was focussed on data items that are included in site level reports, with the application of a top level filter to restrict analyses to the sub-population of the IBD Registry population with an electronic record of consent for research. The complete list of data items covers descriptions of total patient registrations (e.g. counts according to diagnosis, categorised as ulcerative colitis, Crohn's disease or IBD unspecified; demographics; disease duration; disease distribution based on the Montreal phenotype classification system; and smoking status) and additional data items for the sub-group of patients with a record of treatment with a biological drug (e.g. assessments of disease activity at initiation, post-induction and twelve months). The tool specification was to establish a prototype for a user-friendly search tool (in the format of a 'web site') to provide more rapid, flexible interrogation of the dataset in real time to allow response to external queries relating specifically to the population of patients with consent for research.

The source datasets are CSV files containing pseudonymized Registry data, which formed the tables for creating the database. These files contain structured, standardised data in a format conforming to the Registry's data submission framework. The files are generated quarterly after data submissions from participating sites (https://ibdregistry.org.uk/data-submission-framework/).

The prototype system was written in C# .Net 4.5 using the MVC5 framework, with the database built on MS SQL Server 2017 using Stored Procedures. An open source front-end framework (Bootstrap CSS) was used to create a 'web site' prototype. At the prototype stage, the URL is accessible only within the secure university network and by named analysts with password protection (http://ctrc5.liv.ac.uk/Tools/IBD/). The proof-of-concept tool enables the authorised user to run Registry-approved queries within the secure environment. Filters allow the user to create aggregated summaries of selected characteristics of patients for each participating hospital site. The 'use case' was to create a way to identify sites with local cohorts of potential research participants, providing an estimate of numbers of eligible patients with consent for research and descriptions of demographics and clinical characteristics.

Results: The prototype search tool provides a new capability for real-time queries to be run on request in response to external questions. The system interrogates only the sub-set of data relating to patients with a local record of consent for research, providing an intuitive interface to allow the user to rapidly generate aggregated data. Examples of outputs from the tool are shown in **Figures 1**, **2** and **3**.

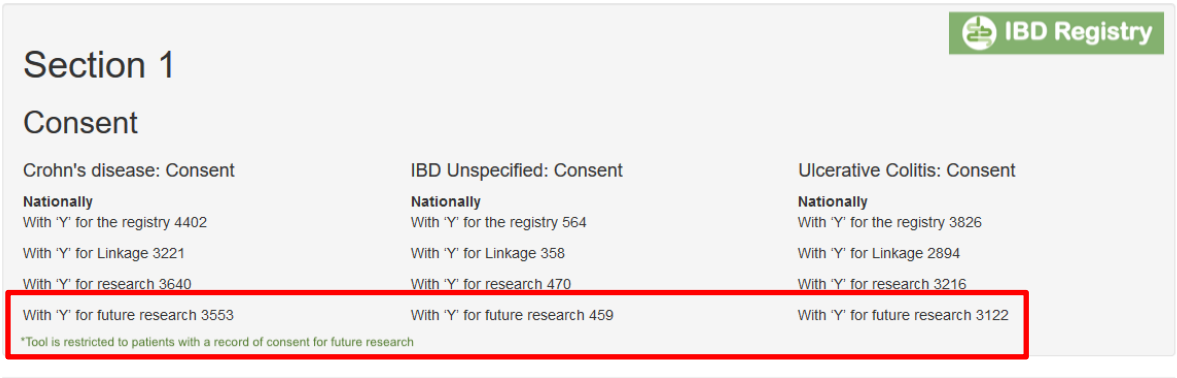

Figure 1 *– Screenshot of "**Consent**" section of prototype webtool, which displays the proportion of registered cases with a record of consent for each of the four-stage consent model, categorised by phenotype (IBD diagnosis). The final tool focuses on the sub-set of patients with a record of '**consent for future research**'. This screenshot shows that the total cohort with a local record of consent for research was 7,134 patients (red box).*

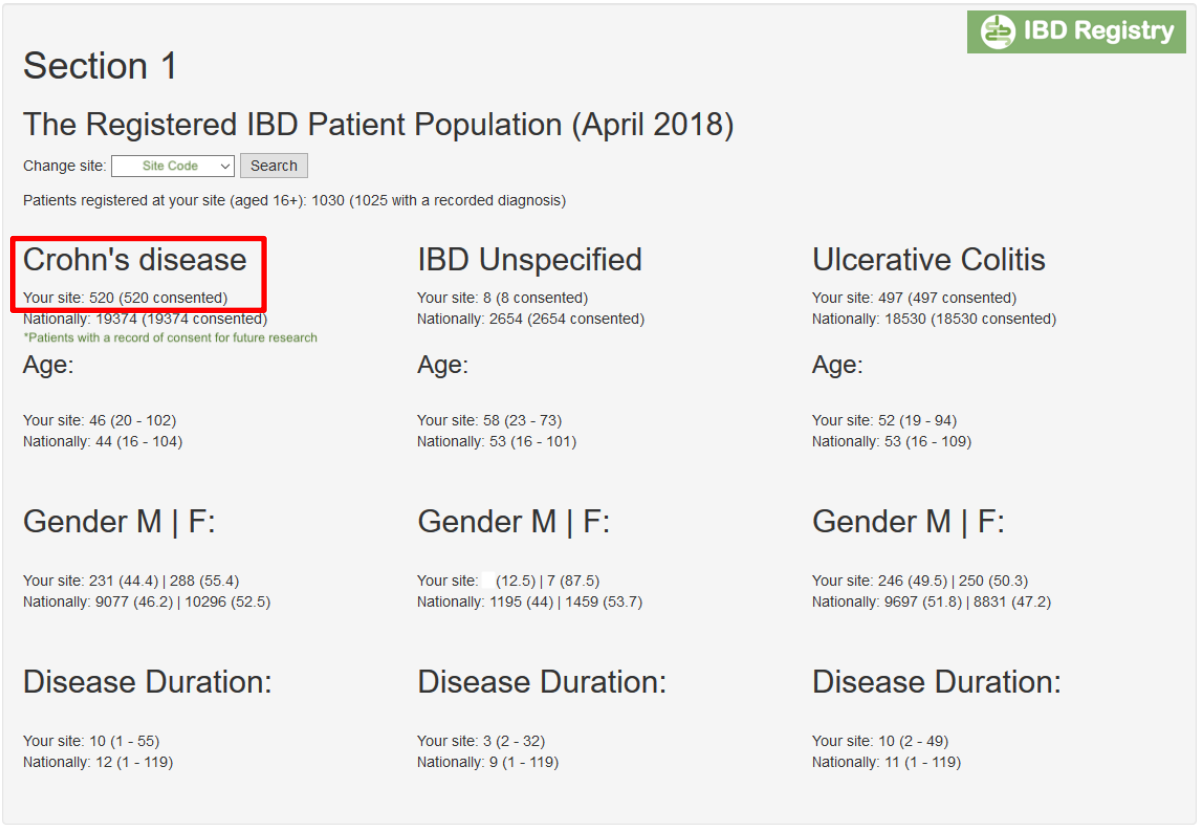

Figure 2 *– Screenshot of "**Registered IBD Patient Population**" section, which includes a hospital '**site-level filter**' to generate a display of the demographic and clinical characteristics of the sub-group of registered patients with a local record of consent for future research. As an example, this would address the following question: "How many patients with a diagnosis of Crohn's disease are registered and consented for future research at St Elsewhere hospital?". This particular site had 520 cases (red box).*

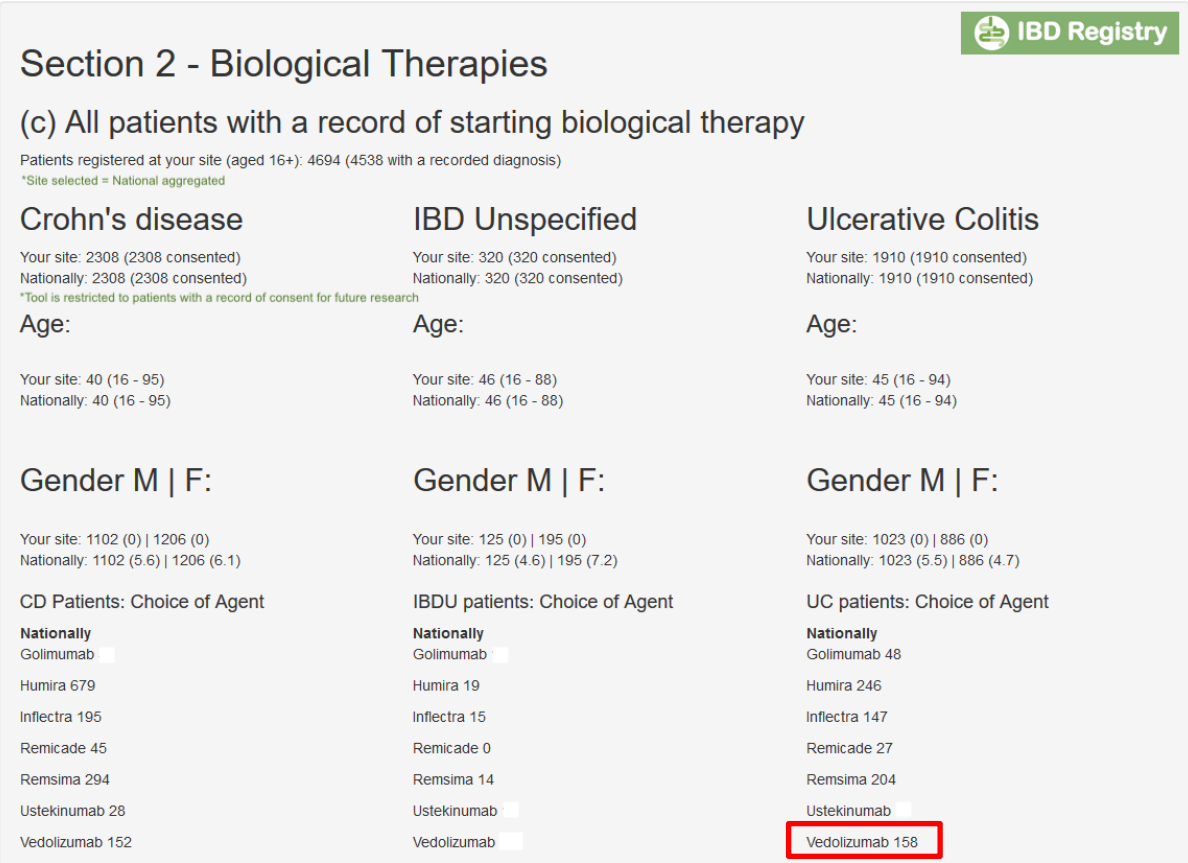

Figure 3 *– Screenshot of '**Biological Therapies**' section, which generates 'national' (i.e. Registry wide) or individual hospital site-level summaries of patients with a record of starting treatment with a biological drug. This provides an estimate of the size of cohorts of cases exposed to specific agents. As an example, this would address the following investigator question: "What is the current size of the national cohort of registered and consented patients with a diagnosis of ulcerative colitis and a record of starting treatment with vedolizumab?". The output illustrates 158 cases were in the system at that time (red box).*

Dissemination Plans:

During the course of this project, the UK IBD Registry became a partner in a successful bid led by the University of Cambridge to establish a Health Data Research Hub for Inflammatory Bowel Disease, or '*Gut Reaction*' (https://www.hdruk.ac.uk/infrastructure/the-hubs/gut-reaction/). The Hub collaboration includes plans for data linkage between the IBD Registry and IBD Bioresource cohorts, extraction and linkage of local hospital clinical and laboratory data from ten pilot sites, linkage to HES data and exploration of e-Consent and e-PROMs collection. This has resulted in imminent changes to the infrastructure, data warehousing, data flows and governance framework for the IBD Registry and UoL. Hence, the future deployment and use of the prototype search tool is being planned as part of these wider developments for early 2020. At this point, the tool's functionality allows a Registry-approved, university-based analyst to run queries on request from investigators (**Figure 4**). This is an interim measure, pending establishment of permissions to establish more direct access to the query tool. The Registry plans to create a link to the UoL-based team on the Registry website, allow incoming queries from investigators to be processed in the meantime.

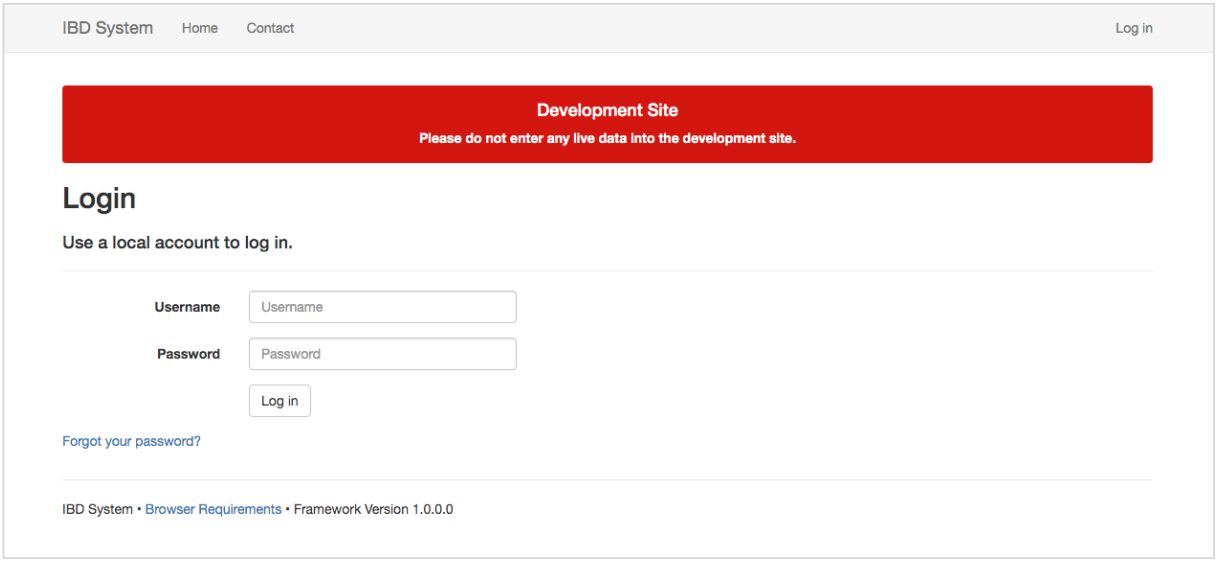

Figure 4 *Log-in page for web tool*

Collectively, these developments significantly enhance the opportunities for independent investigators to explore the feasibility of future Registry-enabled RCTs, not only in terms of identifying potential participating sites and patients but also in providing a data collection infrastructure, governance and consent framework to support research studies.

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None declared

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