A validated web-based tool to display individualised Crohn’s disease predicted outcomes based on clinical, serologic and genetic variables


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SUMMARY

Background
Early treatment for Crohn’s disease (CD) with immunomodulators and/or anti-TNF agents improves outcomes in comparison to a slower ‘step up’ algorithm. However, there remains a limited ability to identify those who would benefit most from early intensive therapy.

Aim
To develop a validated, individualised, web-based tool for patients and clinicians to visualise individualised risks for developing Crohn’s disease complications.

Methods
A well-characterised cohort of adult patients with CD was analysed. Available data included: demographics; clinical characteristics; serologic immune responses; NOD2 status; time from diagnosis to complication; and medication exposure. Cox proportional analyses were performed to model the probability of developing a CD complication over time. The Cox model was validated externally in two independent CD cohorts. Using system dynamics analysis (SDA), these results were transformed into a simple graphical web-based display to show patients their individualised probability of developing a complication over a 3-year period.

Results
Two hundred and forty three CD patients were included in the final model of which 142 experienced a complication. Significant variables in the multivariate Cox model included small bowel disease (HR 2.12, CI 1.05–4.29), left colonic disease (HR 0.73, CI 0.49–1.09), perianal disease (HR 4.12, CI 1.01–16.88), ASCA (HR 1.35, CI 1.16–1.58), Cbir (HR 1.29, CI 1.07–1.55), ANCA (HR 0.77, CI 0.62–0.95), and the NOD2 frameshift mutation/SNP13 (HR 2.13, CI 1.33–3.40). The Harrell’s C (concordance index for predictive accuracy of the model) = 0.73. When applied to the two external validation cohorts (adult n = 109, pediatric n = 392), the concordance index was 0.73 and 0.75, respectively, for adult and pediatric patients.

Conclusions
A validated, web-based tool has been developed to display an individualised predicted outcome for adult patients with Crohn’s disease based on clinical, serologic and genetic variables. This tool can be used to help providers and patients make personalised decisions about treatment options.

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BACKGROUND AND AIM
Crohn’s disease is a chronic inflammatory bowel disease that can cause a broad variety of clinical manifestations. Although Crohn’s disease is characterised as one disease entity, there are numerous phenotypic expressions that can translate to patients as a range of symptoms from intermittent nuisance to life altering and disabling.\(^1\) Over a long period of time, a majority of patients with Crohn’s disease develop complications such as a stricturing or internal penetrating disease that ultimately lead to surgery.\(^2\) Our current medications are very effective at treating active inflammatory disease and preventing these complications;\(^3\) however, once bowel damage occurs medical treatments are far less successful. Therefore, our goal of treatment is to offer appropriate and targeted therapy before complications develop.

Due to the high cost of biologic therapy and potential side effects, there is general hesitation of providers and patients to use immunomodulators, biologics or combination therapy early in the disease course before patients have declared themselves as having severe disease. This typically leads to a delay in starting effective therapy until patients feel sufficiently unwell, have inadequate responses to conventional therapies or until providers are concerned enough to feel that these treatments are required. It has been demonstrated that biologic therapy with or without the combination of an immunomodulator is more effective when used earlier in the disease course, before failing a standard ‘step up’ regimen.\(^4\) But, not all patients will require early aggressive ‘top down’ therapy, and we need to be able to stratify low risk patients from those who are at higher risk of rapid progression to Crohn’s disease complications. With recent advances in identifying serologic and genetic associations with Crohn’s disease, there is potential for these markers to add to clinical predictors in order to facilitate a more personalised approach to disease management. Furthermore, given the complexities of these data, clinicians need tools to be able to communicate this differentiation of high risk vs. low risk to patients so that they can participate in informed and shared decision-making process to choose an appropriate therapy for them as individuals.\(^5\)

Previously, we developed a tool for pediatric patients with Crohn’s disease to predict the risk of individual patients developing a complication of Crohn’s disease over time.\(^6\) As a prototype, it demonstrated that a combination of clinical and serologic variables could be used to create and display a personalised prediction of a patient’s natural history with Crohn’s disease. However, it was not validated or known if it could be extrapolated to adult patients. Now, to make this work applicable in the clinic, we developed a tool for adult patients with Crohn’s disease and validated the prediction model using external cohorts of both pediatric and adult patients. Then, a patient-facing web-based programme was created to allow both providers and patients to visualise individualised risk and facilitate personalised shared decision making.

METHODS
Calibration cohort

Patient population and data collection. The patient population for analysis included 695 well-characterised adult patients with Crohn’s disease at a single centre in Los Angeles, California (Cedars-Sinai Medical Center). Consecutive patients were included in the cohort and data were collected and entered into the Cedars-Sinai patient registry prospectively. Blood for serologic and genetic testing were drawn at the time of cohort entry. Additional chart review was performed for supplemental data acquisition relevant to our specific research question.

Model variables. Available data included demographics, clinical characteristics, dates of disease complications and medication exposure, serologic immune responses, and NOD2 status. Serologic markers were selected to include those that are most available commercially. Although over 100 genes have been associated with Crohn’s disease, only NOD2 polymorphisms were included in the analyses as these are the only genetic ‘prognostic’ parameters currently commercially available. Sera were analysed at Cedars-Sinai Medical Center quantitatively for anti-Saccharomyces cerevisiae antibody (ASCA) IgA and IgG, anti-flagellin (anti-CBir1), anti-outer-membrane porin C (OmpC) of Escherichia coli and perinuclear anti-neutrophil antibody.\(^7\) NOD2 genotyping was performed at Cedars-Sinai Medical Center using the Illumina Ichip Platform as previously described.\(^8\)

Main outcome of the model. The dependent variable of the model was the time from diagnosis to first complication of Crohn’s disease. Complication was defined as a bowel stricture, internal penetrating disease or non-perianal surgery (bowel resection or stricturoplasty).

Exclusion criteria. Patients missing key data were excluded. In an attempt to decrease the heterogeneity of
available treatments, patients diagnosed before 1998 were excluded based on the time when anti-TNF became widely available (the ‘biologic era’).

**Statistical analysis.** Cox’s proportional hazards model, univariable and multivariable analyses were used to model the association of patient characteristics and serologic and genetic markers with the time to Crohn’s disease complications within 10 years of diagnosis. Variables were considered for inclusion in the multivariate model if $P < 0.1$ in the univariate analysis (Table 2). An exception to this is perianal disease, which had a univariable $P > 0.1$, but was included based on strong historical data suggesting an association with complicated luminal Crohn’s disease. The multivariable model was parsed using backwards stepwise algorithm. Analyses were conducted in R. The predictive accuracy of the model was characterised using the C-statistics of Harrell and Zheng corrected for overfitting using bootstrap validation.

**Validation cohorts**

Two independent cohorts were used for validation of the calibration model. The first cohort included 612 adult Crohn’s disease patients from Mount Sinai Hospital in Toronto, Ontario. Identical data to the calibration cohort were captured in the Mount Sinai Hospital database. Data collection was a hybrid of prospectively enrolled patients and retrospective chart review. The second validation cohort included 409 pediatric patients with Crohn’s disease from a multicentre prospective patient registry, described in a previous publication. The ability of the model developed on the training cohort to discriminate events in the validation cohorts was characterised using Harrell’s Concordance (C) statistic.

Internal Review Board approval and inter-institutional data sharing agreements were obtained at Cedars-Sinai Medical Center, the University of Toronto, and Dartmouth-Hitchcock Medical Center.

**System dynamics analysis.** System dynamics analysis is a methodology that addresses the inherent dynamic complexity of interactions between variables. Used infrequently in medicine, it is typically used in the fields of engineering and economics to evaluate complex models. SDA provides a platform to provide a real-time individualised prediction of outcomes using a simple input/output format. Results are displayed graphically over time. Although other methods could effectively present the outcomes comparably, SDA allows flexibility for the future to layer data and relationships to the model outside of the original calibration dataset. This layering can enhance the Cox predictive ability to compare the effectiveness of different treatment options and expand the tool to assess other measures, e.g., cost effectiveness of therapeutic options.

The Cox model described above yields a prediction tool. The model is used to determine the Hazard Ratio (HR) for any patient (i.e., vector of risk factors) which in combination with the Breslow estimate of the cumulative hazard yields a predicted time-to-event curve. These results then drive the system dynamics model. The risk of an individual patient is calculated according to the HR of each variable. The overall unit hazard function is the risk of a complication at any given time. Equation 1 shows that it is the product of the baseline function and the expression derived from the calculated HR of each variable (HR) for the value of the variable, i.e.,

$$h(t|x) = \prod HR_i^{Value_i}$$

(1)

This expression is simplified as follows:

$$h(t|x) = h(t|0) \times \exp(\Sigma LN(HR_i) \times Value_i)$$

(2)

where $h(t|0)$ is the baseline hazard function and the expression LN(HR) yields the coefficient of each variable (Eqn 2). Model simulations run from month 0, i.e., when a patient enters the analysis, through 10 years. Model values are updated every 0.25 months. The model stores and can plot and print the output for every time step or for other time intervals, as desired. At each complication event, the risk is the number of patients with a complication relative to the number of patients remaining. The discrete time steps of the model require the time of each event to be rounded to a multiple of the time step. Accordingly, the risk of events that occur at distinct times that are rounded to the same time, but not actually occurring at the same time, are added together. For example, the risk of an event at 3 months and that at 3.07 months are added together; the sum is included in the baseline function as the risk at 3 months. The model underwent multiple iterations before arriving at the current model structure. The SDA platform is VENSIM (Harvard, MA, USA).
Web-based tool development
After the system dynamics model was finalised, a web developer created an interactive web design to include the graphical output of the predicted risk of the time to a Crohn’s disease complication. This SDA model graphical user interface was created using Forio Simulate, a web-based, Flash-dependent software platform (San Francisco, CA, USA). The web interface provides access for data entry to the underlying SDA programme by the clinical staff and visualisation of the resulting output from the SDA model analysis by provider and patient. The user interface is embedded within the encompassing web-based tool. Additional elements on the website include personalised identifiers for the patients, and other web pages that patients can view to display what variables they have and how these contribute to their risk. A page is also available so that patients could view different treatment options available for Crohn’s disease. This was developed from a previously created Option Grid, which is found at http://www.optiongrid.org/resources/crohndiseasetreatments_grid.pdf. The web-based tool was iteratively improved with provider and web-developer feedback in addition to cognitive patient interviews to ensure clear communication and accurate comprehension. In qualitative focus groups, patients expressed their preference to display the primary outcome as ‘complication’, which includes a composite endpoint of internal penetrating or strictureing disease, or surgery. Their reasoning was that these all were irreversible processes that required treatment prior to their occurrence, and therefore did not require presenting these complications separately. The prediction tool is named PROSPECT (Personalised Risk and Outcome Prediction Tool).

RESULTS

Patient population
Of the 303 adult patients diagnosed after 1998, 60 patients were excluded as NOD2 genotypes were incomplete, leaving a total of 243 for analysis. 142 patients (58%) experienced a complication of Crohn’s disease during follow up. Median duration of Crohn’s disease was 6.1 years (range 0.25–15 years) and approximately half were female. Other patient characteristics are displayed in Table 1.

Cox’s regression model
Cox’s (proportional hazards) regression was performed to model the probability of developing a CD complication over time (outcome of interest). Univariate analyses were performed with candidate variables and significant findings are shown in Table 2. The multivariable model was developed with variables with \( P < 0.1 \) in the univariate analysis, or other clinically relevant variables based on the literature. Exploratory analyses of associations between medication exposure and the primary outcome were performed, but these were not included in the model. The final multivariate model included disease

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of Crohn’s disease patients included in the calibration cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 243</td>
<td></td>
</tr>
<tr>
<td>Age (median, range)</td>
<td>28 (18–76)</td>
</tr>
<tr>
<td>Proportion female (%)</td>
<td>118 (49)</td>
</tr>
<tr>
<td>Years of Crohn’s disease (median, range)</td>
<td>6.1 (0.25–15)</td>
</tr>
<tr>
<td>Disease location (%)</td>
<td></td>
</tr>
<tr>
<td>Small bowel only</td>
<td>55 (23)</td>
</tr>
<tr>
<td>Colonic only</td>
<td>37 (15)</td>
</tr>
<tr>
<td>Small bowel and colonic</td>
<td>149 (61)</td>
</tr>
<tr>
<td>Perianal</td>
<td>35 (15)</td>
</tr>
<tr>
<td>Disease phenotype (%)</td>
<td></td>
</tr>
<tr>
<td>Strictureing</td>
<td>91 (38)</td>
</tr>
<tr>
<td>Internal penetrating</td>
<td>46 (19)</td>
</tr>
<tr>
<td>Non-stricturing/non-penetrating</td>
<td>118 (49)</td>
</tr>
<tr>
<td>Years to complication (median, range)</td>
<td>3.3 (0.3–15.7)</td>
</tr>
<tr>
<td>Underwent surgery (non-perianal) (%)</td>
<td>121 (50)</td>
</tr>
</tbody>
</table>

Crohn’s disease related variables evaluated but not added to the model include: upper tract disease, jejunal disease location, smoking history (dates of exposure not available), race, ethnic history, C-reactive protein at diagnosis, prior medication exposure. Results were either not significant or not included due to incomplete data.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Univariate analysis for the risk of Crohn’s disease complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>Hazard ratio (95% CI)</td>
</tr>
<tr>
<td>Small bowel disease</td>
<td>3.10 (1.65–5.82)</td>
</tr>
<tr>
<td>Left colonic disease</td>
<td>0.45 (0.31–0.63)</td>
</tr>
<tr>
<td>Perianal disease</td>
<td>0.86 (0.54–1.37)</td>
</tr>
<tr>
<td>LnASCA</td>
<td>1.42 (1.24–1.63)</td>
</tr>
<tr>
<td>LnC Bir1</td>
<td>1.47 (1.24–1.75)</td>
</tr>
<tr>
<td>LnANCA</td>
<td>0.68 (0.57–0.83)</td>
</tr>
<tr>
<td>NOD2 frameshift mutation</td>
<td>3.04 (1.92–4.80)</td>
</tr>
<tr>
<td>Perianal x log ASCA</td>
<td>0.96 (0.84–1.09)</td>
</tr>
</tbody>
</table>

CI, confidence interval; Ln = log; ASCA = highest value of anti-Saccharomyces cerevisiae antibody (ASCA) IgA or IgG, C Bir1 = anti-flagellin, ANCA = perinuclear anti-neutrophil antibody. Absolute value used for all serologic markers. NOD2 considered positive if 1 or 2 polymorphisms with frameshift mutation.
location (small bowel; left colonic disease, perianal disease), serologic markers (ASCA, CBir1, ANCA), the NOD2 frameshift mutation, and an interaction term between Perianal disease and ASCA (Table 3). This interaction term was created to make a better model fit because patients with both high ASCA and perianal disease had a clinically unrealistic predicted risk. The log of ASCA, CBir1 and ANCA were used to normalise these model variables. For patients who had a complication but no date was specified multiple imputation was used with imputation based on the distribution of the time-to-events. The Harrell’s Concordance (C) statistic for the calibration cohort was 0.73.

Model validation
The final model was applied to both the adult and pediatric external validation cohorts. Applying the same inclusion and exclusion criteria as the calibration cohort, of the 612 patients in the adult validation cohort, 109 patients were included in the analysis. Patients were excluded if they were diagnosed prior to 1998 (260 patients), had a complication at the time of diagnosis (53) or were missing some required data (190). Patient characteristics are described in Table S1. The second validation cohort included pediatric patients with Crohn’s disease from a multicentre prospective patient registry, described in a previous publication. Of the 579 patients with adequate follow-up time in this cohort, 392 were included in the analysis after excluding those diagnosed before 1998 and subjects with incomplete data. These patients are described in Table S2. The multivariate analyses for the risk of complication in the validation cohorts are shown in Table S3. The discriminatory ability of the model, as measured by Harrell’s C-statistic for the adult and pediatric validation cohorts were 0.73 and 0.75 respectively.

Web-based system dynamics model
Using SDA the results of the multivariate Cox model were transformed into a web-based tool to show patients their individualised probability of developing a complication over a 3-year period. After multiple iterations with feedback from providers, patients and a web developer, version 15.49 was used as the final programme. An individual patient’s characteristics are directly inputted online using radio buttons and slider bars (Figure 1). Then, a line is created and output shown on the patient results page. The model output shows the probability for that specific patient to have a complication of CD over the next 3 years. A sample ‘low risk’ patient is displayed in Figure 2, in contrast to a ‘high risk’ patient in Figure 3. As opposed to showing exact probability, the Y-axis is displayed as low, medium or high risk and colour coded based on strong patient feedback that the exact probability mattered less to them than a global interpretation of their risk. Patients could still see the exact predicted probability (0% at the bottom of the Y-axis to 100% at the top of the Y-axis) if desired by clicking on the percentage sign on the top right corner of the screen. Patients are able to view what variables they have and how these contribute to their risk by clicking on ‘Your Crohn’s Disease’ (Figure S1) and they can review a summary of benefits and risks of treatment options based on data from the literature by clicking on ‘Your Treatment Options’.

DISCUSSION
We have developed and validated a tool to predict an individual patient’s risk of developing a Crohn’s disease complication based on clinical, serologic, and genetic variables. All clinical input data are easily obtainable from standard Crohn’s disease evaluation and commercially available serologic and genetic tests. The model (PROSPECT) was transformed into an interactive, web-based tool that was pilot tested with providers and patients with excellent comprehension.

Our work builds on a prototype system dynamics model using pediatric data that had excellent model concordance (Harrell’s C = 0.81) with internal validation. Others have also explored risk factors for developing Crohn’s disease complications. However, as opposed to presenting a cohort derived survival curve, this current model is the first attempt to put these risk

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<td>Ln ASCA</td>
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Ln = log; ASCA = highest value of anti-Saccharomyces cerevisiae antibody (ASCA) IgA or IgG, CBir1 = anti-flagellin, ANCA = perinuclear anti-neutrophil antibody. Absolute value used for all serologic markers. NOD2 considered positive if 1 or 2 polymorphisms with frameshift mutation.
factors together in a validated adult predictive model that can be applied on an individual patient level and shared with patients. Validation in two external cohorts increases the confidence that this model is clinically relevant in different populations of patients with Crohn’s disease.

The use of system dynamics modelling is unique in medicine and gives the ability to adapt and improve the model over time as new data become available. These new data could be from additional datasets, literature, or new findings in clinical trials. We can use our current ‘baseline’ model, and enhance our predictive ability when new variables are identified and validated. Furthermore, when data on the influence of treatment on the time to complication are elucidated, this too can be added to the model to allow for a visual display of comparative effectiveness.

As with any predictive tool, this work has limitations. All of the patients included in the model were North American. It is not clear if patients from other regions in the world, with different genetics and disease phenotypes would be accurately represented by those in the calibration and validation cohort. Additionally, the cohorts included patients from large referral centres, so may not be representative of all patients. This is currently being evaluated. The model was built and validated looking at a maximum duration of disease of 15 years. We did not feel confident that we could accurately understand patients with long-standing disease. In addition, the model evaluated the time from diagnosis to first complication or surgery. The model is only validated in patients who have not yet had a complication; we did not assess time to a second or more complication or surgery, or as a tool for longitudinal prognostication over time. Therefore, this model is appropriate for patients earlier on in disease without complications, who we are trying to understand the pace of their disease and need for more intensive early intervention.

Ideally, for model development only patients with uncomplicated disease (B1 Montreal Classification)24 and

Figure 1 | Screenshot of the PROSPECT input page. On the right, patient characteristics, serologic markers and NOD2 results are entered. On the left is a representation of the personal risk curve generated for that patient.
serology drawn at the time of cohort entry would be included and followed prospectively until either a complication developed (progression to B2 or B3 Montreal Classification) or they remained with stable B1 disease. In this study, some patients were included who had complications previous to cohort entry, but the time from diagnosis to complication was well documented. In the calibration cohort, 59% of serologic markers were obtained prior to a complication developing. Although intuitively it seems important to have serology at baseline in all patients, a number of studies have shown that the serologic markers used in this study have little variation when following patients over time, including after surgical resection for a Crohn’s disease complication.28

Prospective inception cohorts following patients from diagnosis without any retrospective data collection would be preferable, but this model is the best possible with the currently available data. This is not without precedent. The most frequently used prediction tool in all of Gastroenterology and Hepatology is the The Model for End-Stage Liver Disease (MELD).29 MELD was developed initially for a completely different outcome (survival after TIPS) and validated with retrospective review of cohorts of patients from nearly 20 years prior to model development. Therefore, although imperfect,

Example Patient #1: Male DOB 11/30/1984; Dx 11/2013; Disease location: Left Colon only; ASCA IgA = 15; ASCA IgG-13; Cbir 1 = 28; ANCA = 47; NOD2 = negative

Figure 2 | Screenshot of a ‘low risk’ patient output in PROSPECT. This image shows a colour coded graph with an individual patient’s risk for a Crohn’s disease complication over the next 3 years. Patients can use their mouse to click on the percent sign to see their specific risk (from 0% to 100%), view their personal patient characteristics by selecting ‘Your Crohn’s Disease’, or view the ‘Option Grid’ to see side by side comparisons of Crohn’s disease treatment choices.
we believe that our predictive model for Crohn’s disease is strong enough to be used in clinically.

There are a number of other disease variables that likely play a role in predicting outcomes that were not included in this model. For example, endoscopic appearance, inflammatory markers (e.g., C-reactive protein) and imaging were not taken into account. This is because we did not consistently have these variables in our dataset, and could not include them at this time. Smoking is associated with worse Crohn’s disease outcomes, but smoking status was not appropriately collected in the data set to be able to analyse its impact on the time to complication. Specifically, current smoking status at the time of complication was not recorded. We explored the literature for an appropriate hazard ratio for smoking on our particular outcomes of interest, but robust data are not available. Impact of medications on the baseline predictions would strengthen this work, but due to the observational nature of medication exposure, and significant chance of bias by indication, we did not include therapeutic modification of risk in this model.

There are a number of clinical and policy implications to this work. Currently, there is evolving agreement that early intensive therapy is superior to a step-up approach for the management of Crohn’s disease. If the first step of clinical evaluation of a new or recent diagnosis was risk stratification and communication, more informed and shared decisions could be made between patient and pro-

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### Example Patient #2

**Gender:** Female  
**DOB:** 05/01/1958  
**Diagnosis:** Crohn’s disease  
**Date of Birth:** 5/1/1958

**Example Patient #2’s predicted risk of a complication from Crohn’s disease**

Based on the specific characteristics of your Crohn’s disease, the graph below shows your risk of developing complications such as fistulas and blockages, which often lead to surgery.

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**Figure 3** | Screenshot of a ‘high risk’ patient output in PROSPECT. This image shows a colour coded graph with an individual patient’s risk for a Crohn’s disease complication over the next 3 years. Patients can use their mouse to click on the percent sign to see their specific risk (from 0% to 100%), view their personal patient characteristics by selecting ‘Your Crohn’s Disease’, or view the ‘Option Grid’ to see side by side comparisons of Crohn’s disease treatment choices.
outcomes for patients with Crohn’s disease. High cost medications with potential side effects and algorithms using frequent evaluation and follow-up to prompt a therapeutic change could be used intensively in patients at high risk, where lower risk patients could be managed less aggressively. Payors and accountable care organisations will be very interested in risk stratification models. Cost effectiveness will become even more important in the future – and any technique to manage risk and cost will be valuable. We believe our model and models like PROSPECT can also be used by the pharmaceutical industry for proper patient selection for clinical trials. A high placebo rate is a frequent concern for trialists, and industry for proper patient selection for clinical trials. A high placebo rate is a frequent concern for trialists, and industry for proper patient selection for clinical trials. A high placebo rate is a frequent concern for trialists, and industry for proper patient selection for clinical trials. A high placebo rate is a frequent concern for trialists, and industry for proper patient selection for clinical trials.

PROSPECT is a tool to predict individualised disease outcomes for patients with Crohn’s disease who are early in their disease course and without known complications. It has been validated in two additional patient cohorts, and the web-based graphical display is easily interpreted by providers and patients. We are currently assessing how PROSPECT influences patient decision making and disease outcomes.

**SUPPORTING INFORMATION**

Additional Supporting Information may be found in the online version of this article:

**Table S1.** Characteristics of adult Crohn’s disease patients included in the validation cohort.

**Table S2.** Characteristics of pediatric Crohn’s disease patients included in the validation cohort.

**Table S3.** Multivariate analyses for the risk of Crohn’s disease complication in the validation cohorts.

**Figure S1.** Screenshot of the patient view of their personal characteristics that inform the PROSPECT model results. Patients can hover over the title of each category to see why these features are important for their personal risk.

**AUTHORSHIP**

Guarantor of the article: Corey A. Siegel.

Author contributions: CS, LS, MD, DM: study concept and design; CS, HH, LS, TM, SS, JS, SD, TH, AL, MB, RM, PD, ST, MS, MD, DM: acquisition and interpretation of data; CS: drafting of the manuscript; LS, KT, TM, PR, MS, MD, DM: critical review of the manuscript; LS, TM: statistical analysis.

All authors approved the final version of the manuscript.

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Declaration of personal interests: Dartmouth-Hitchcock Medical Center and Cedars-Sinai Medical Center have a patent pending for a System and Method of Communicating Predicted Medical Outcomes, filed 3/34/10. Dr Corey Siegel, Dr Lori Siegel and Dr Marla Dubinsky are inventors. CS, ST, MS, and MD are consultants to Prometheus Labs. CS, ST, and MD are consultants for Abbvie, Janssen, Takeda and UCB. MS is a consultant for Abbvie and Janssen. DM is a consultant for Genentech, Janssen, Ferring, Merck, and UCB.

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**REFERENCES**


