CDPATH™

PERSONALIZED PROGNOSTIC TOOL

CDPATH is a validated* risk assessment tool that helps adult patients living with Crohn's disease (CD) understand their potential risk for developing serious complications† within three years.

A personalized risk profile, combined with a health care provider's (HCP) clinical assessment, can facilitate more collaborative discussions about disease management with patients. (Disease management considerations may include, but are not limited to, appointment cadence, diet modifications, exercise, supplements, medications, or other approaches.[1-3])

CDPATH is not affiliated or linked to any Crohn's disease treatments or drugs.

Model Development and Validation

CDPATH is a Laboratory Developed Test (LDT)* – a designation resulting from a multi-step process:

INDEPENDENT CLINICAL STUDY

first

THE MODEL WAS DEFINED

Through a Calibration Cohort[4]

The model was defined using a well-characterized calibration cohort of 243 adult patients (18 years and older) with Crohn's disease diagnosed within the last 15 years to identify statistically significant variables that predicted the potential of serious Crohn's disease-related complications within three years.†‡

next

CLINICAL RELEVANCE WAS ESTABLISHED

Through a Validation Cohort[4]

A well-characterized adult cohort of 109 patients with Crohn's disease who were within 15 years of diagnosis without a previous serious complication confirmed the clinical relevancy of the model.†‡

MODEL VALIDATION

finally

THE MODEL WAS DEVELOPED AND VALIDATED

By Prometheus Laboratories as a Laboratory Developed Test[5]

*The CDPATH risk assessment tool was developed and validated by Prometheus Laboratories Inc., a certified Clinical Laboratory Improvement Amendments (CLIA) laboratory and partner of Takeda, as a Laboratory Developed Test (LDT).

Prometheus Laboratories used calibration (N=106) and validation (N=32) cohorts of adult CD patients within 10 years of diagnosis without previous serious complications† to establish analytical and clinical validity in their validation process.

Prometheus Laboratories Inc. has received approval for CDPATH from the New York State Department of Health (NYS DoH) as an LDT.

†Serious complications are defined as bowel strictures, internal penetrating disease, or non-perianal surgery (bowel resection or stricturoplasty).

‡Patients were excluded if they had a complication at the time of diagnosis.

CDPATH COHORT DETAILS

The CDPATH model was tested in patient cohorts with varying characteristics, including but not limited to, age, disease duration, and disease location.[4]

INDEPENDENT CLINICAL STUDY

Patient Characteristics	Calibration Cohort (N=243)[4]	Validation Cohort (N=109)[4]
Age, median (range)	28 (18-76)	24.8 (10.5-52.0)
Proportion female, n (%)	118 (49)	N/A
Years of Crohn's disease, median (range)	6.1 (0.25-15)	9.1 (0.02-15.8)
Disease location, n (%) Small bowel only	55 (23)	11 (10)
Colonic only	37 (15)	37 (34)
Small bowel and colonic	149 (61)	57 (52)
Perianal	35 (15)	39 (36)
Disease phenotype, n (%) Stricturing	91 (38)	33 (30)
Internal penetrating	46 (19)	
Nonstricturing/nonpenetrating	118 (49)	76 (70)
Years to complication, median (range)	3.3 (0.3-15.7)	3.8 (0.02-11.3)
Underwent surgery (non-perianal), n (%)	121 (50)	24 (26)

MODEL VALIDATION

Patient Characteristics	Calibration Cohort (N=106)[5]	Validation Cohort (N=32)[5]
Age (mean ± SEM)	36 ± 1	29 ± 2
Years of Crohn's disease	Diagnosed with CD within 10 years	
Proportion female, n (%)	40 (38%)	N/A
Crohn's disease complication, n (%)	36 (34%)	15 (47%)
Years to complication (mean ± SEM)	2.7 ± 0.5	1.2±0.4
Disease location, n (%) Small bowel	82 (77%)	28 (88%)
Left Colon	63 (59%)	26 (81%)
Perianal disease	12 (11%)	11 (34%)

CD=Crohn's disease; SEM=standard error of the mean; N/A= not available but not required for model validation.

CDPATH MODEL VARIABLES

CDPATH analyzes patient characteristics, serologic factors, and a genetic factor to assess individual potential risk.[5]

PATIENT CHARACTERISTICS†	Capturing time from diagnosis is required to ensure CDPATH eligibility and serve as a baseline hazard function.	Time from diagnosis	Time between time of diagnosis and specimen collection (in months).
	Assessing an accurate disease location is required because where the disease occurs may determine the likelihood for complication(s) to occur.[6]	Small bowel disease	Describes CD located in the small intestine.
		Colonic disease	Describes CD located in the large intestine (right colon, transverse colon, left colon). Left colonic disease is the disease location element part of CDPATH.
		Perianal disease	Describes CD located at or near the anus.
		Upper GI disease*	Describes CD located in the stomach and esophagus
SEROLOGIC FACTORS	Measures of antibodies in the blood that may predict disease course.[7]	ASCA IgA ELISA ASCA IgG ELISA	A measure of antibodies in the immune system most often seen in patients with CD. There are two types of ASCA antibodies, IgG and IgA.
		pANCA IFA	A measure of antibodies against certain types of white blood cells most often seen in patients with UC.
		Anti-CBir1 IgG	A measure of antibodies that are produced by the immune system most often seen in patients with CD.
GENETIC FACTORS	A genetic factor may identify the likelihood of developing serious CD-related complications (defined as bowel strictures, internal penetrating disease, or non-perianal surgery (bowel resection or stricturoplasty).[6,8]	*NOD*2 SNP13 (1007fs)	A genetic factor that can be found in patients with CD.

*Upper GI disease is collected on the CDPATH test requisition but is not part of the CDPATH algorithm.

†Additional information collected on the test requisition but are NOT a part of the CDPATH algorithm: Crohn's diagnosis code, history of serious complications (defined as defined as bowel strictures, internal penetrating disease, or non-perianal surgery (bowel resection or stricturoplasty). gender, date of birth. This information is collected to verify CDPATH eligibility and contextualize report results.

ASCA=anti-Saccharomyces cerevisiae antibody; CBir1=anti-flagellin; CD=Crohn's disease; ELISA=enzyme-linked immunosorbent assay; GI=gastrointestinal; *NOD*2=nucleotide-binding oligomerization domain-containing protein 2; pANCA=perinuclear anti-neutrophil cytoplasmic antibody; SNP=single nucleotide polymorphism.

CDPATH ANALYSES USED

The CDPATH model was designed using Cox regression and Harrell's Concordance Statistic (C-Statistic) analyses.[4]

First, investigators determined which patient variables to include in the model using a Cox Proportional-Hazards Model (P Value).[4]

- Univariate Cox analysis was used to select statistically significant variables to potentially be included in the CDPATH model.
- Multivariate Cox analysis was used to understand the association between the identified variables and the time to first serious complication* of Crohn's disease.

Next, investigators assessed the predictive accuracy of those variables using a Harrell's Concordance Statistic (C-statistic)[4]

C-statistic predictivity scores explained:

- Value of 0.5 = no better than random chance
- Value of 1 = perfect prediction

THE RESULTS

The final CDPATH model demonstrated consistent, statistically significant performance results in both the independent clinical study and model validation.[5] The results suggest the model has good predictive accuracy.

	PATIENT POPULATION	*P* VALUE	C-STATISTIC
Independent Clinical Study	Calibration cohort (N=243)	P<0.001	0.73
	Validation cohort (N=109)	P<0.001	0.73
Model Validation†	Calibration cohort (N=106)	P<0.001	0.73
	Validation cohort (N=32)	P=0.015	0.70

*Serious complications defined as bowel strictures, internal penetrating disease, or non-perianal surgery (bowel resection or stricturoplasty).

†The CDPATH risk assessment tool was developed and validated by Prometheus Laboratories Inc., a partner of Takeda, and has received approval from the New York State Department of Health (NYS DoH) as a Laboratory Developed Test (LDT). Test results are provided via Prometheus Laboratories Inc. to health care providers.[5]

CDPATH Limitations

- Testing was conducted only with patients from North America; the results for patients from other regions have not been established.[4]
- Patients were recruited from large referral centers and may not be representative of all patients with Crohn's disease (CD).[4]
- The validity of the model after the first complication* or surgery has not been tested or established; therefore, CDPATH may only be used one time for each patient.[4]
- The model was built and established in patients who have had CD for up to 15 years. It is not understood whether the model is applicable to patients with long-standing CD beyond 15 years from diagnosis.[4]
- When the model was validated by Prometheus Laboratories as a Laboratory Developed Test (LDT)†, only patients who had been diagnosed within 10 years were included,[5] therefore CDPATH is only approved for patients diagnosed within 10 years.

References

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8. Ogura Y, et al. *Nature*. 2001;411:603-606.

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More information, including terms, conditions, and eligibility criteria available at www.CDPATH.com.

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