9TH ANNUAL CROHN'S & COLITIS PATIENT EDUCATION SEMINAR

SGH GASTROENTEROLOGY & HEPATOLOGY
2020
CELEBRATING
25 YRS

National IBD Registry: Research and Clinical Trials

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What is IBD?

- A chronic idiopathic relapsing and remitting inflammatory conditions of the gastrointestinal tract
- Two types
  - Crohn’ disease
  - Ulcerative colitis

Epidemiology

The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017

GBD 2017 Inflammatory Bowel Disease Collaborators. Lancet Gastroenterol Hepatol. 2020 Jan;5(1):17-30.

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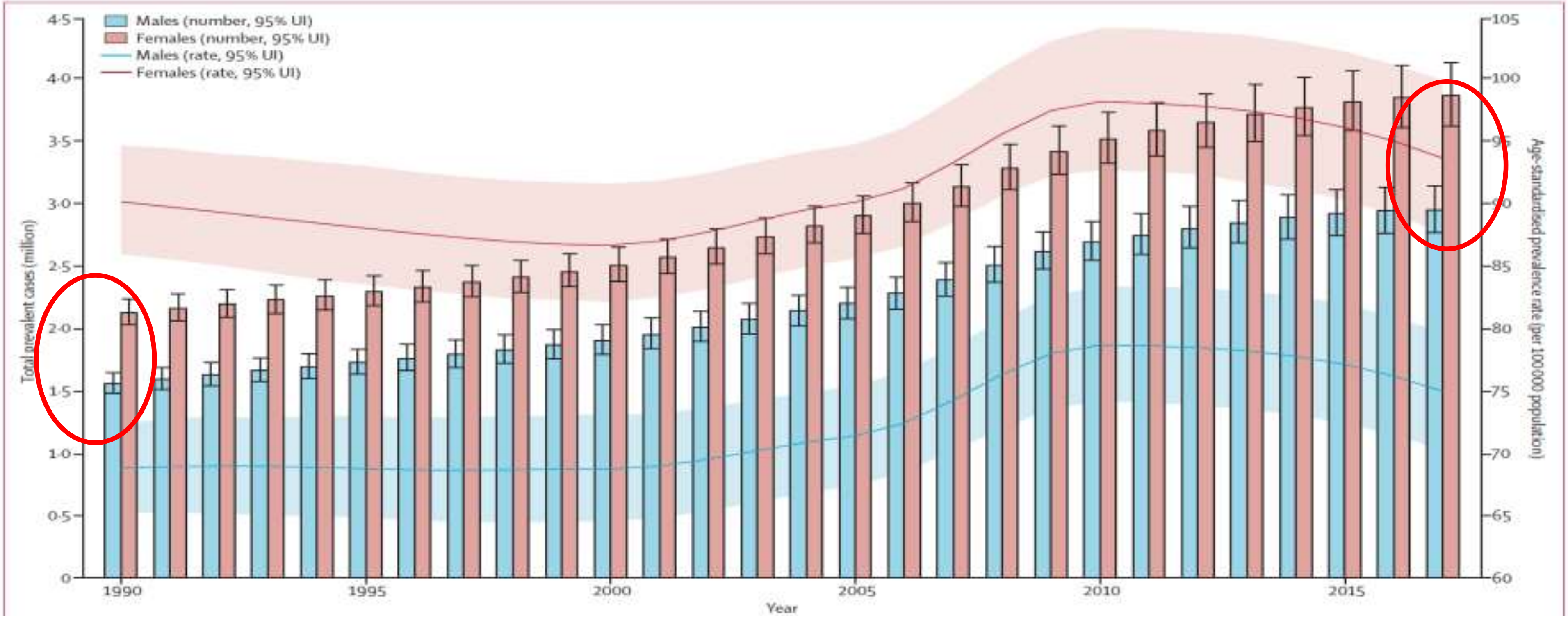
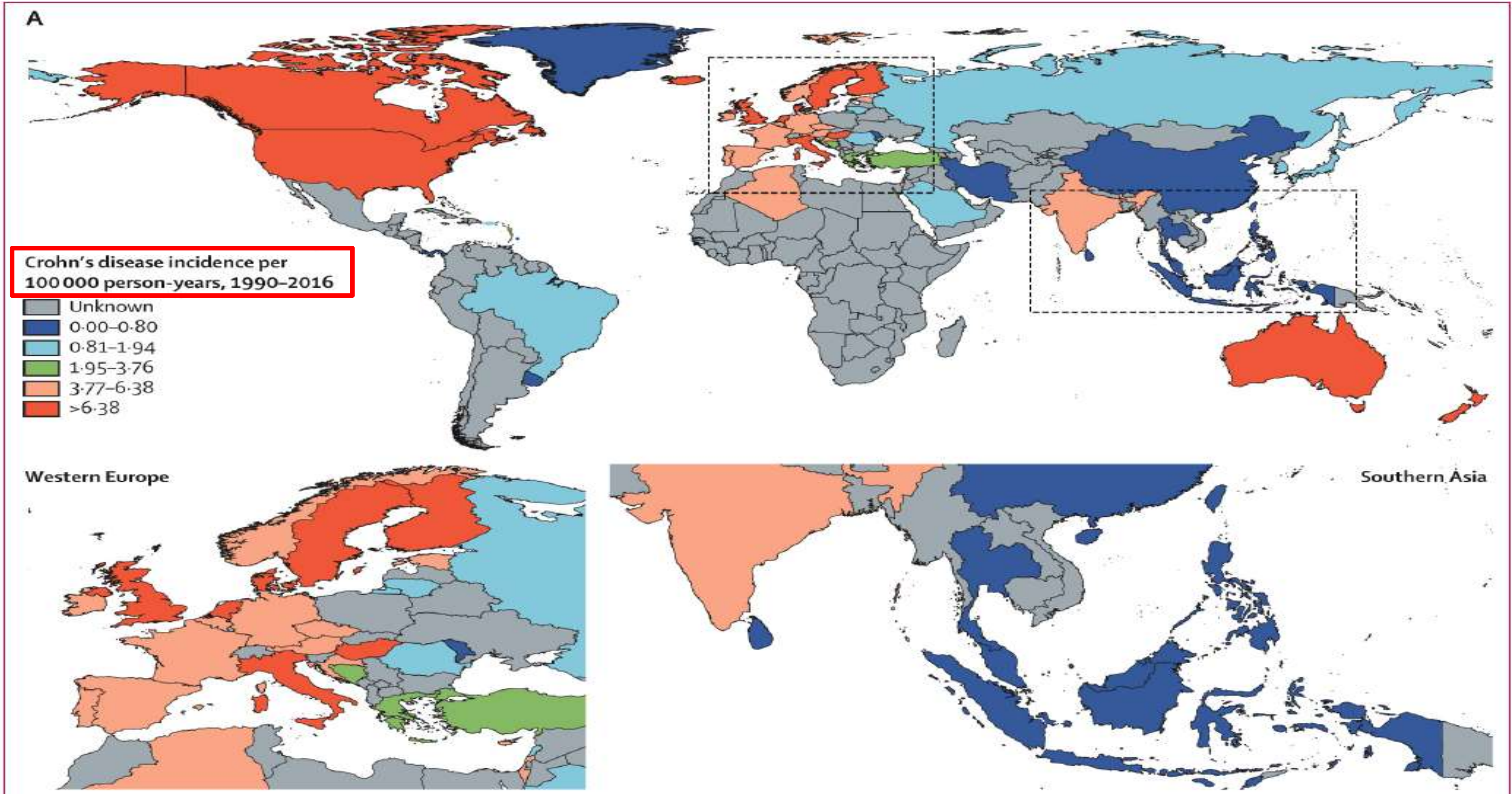


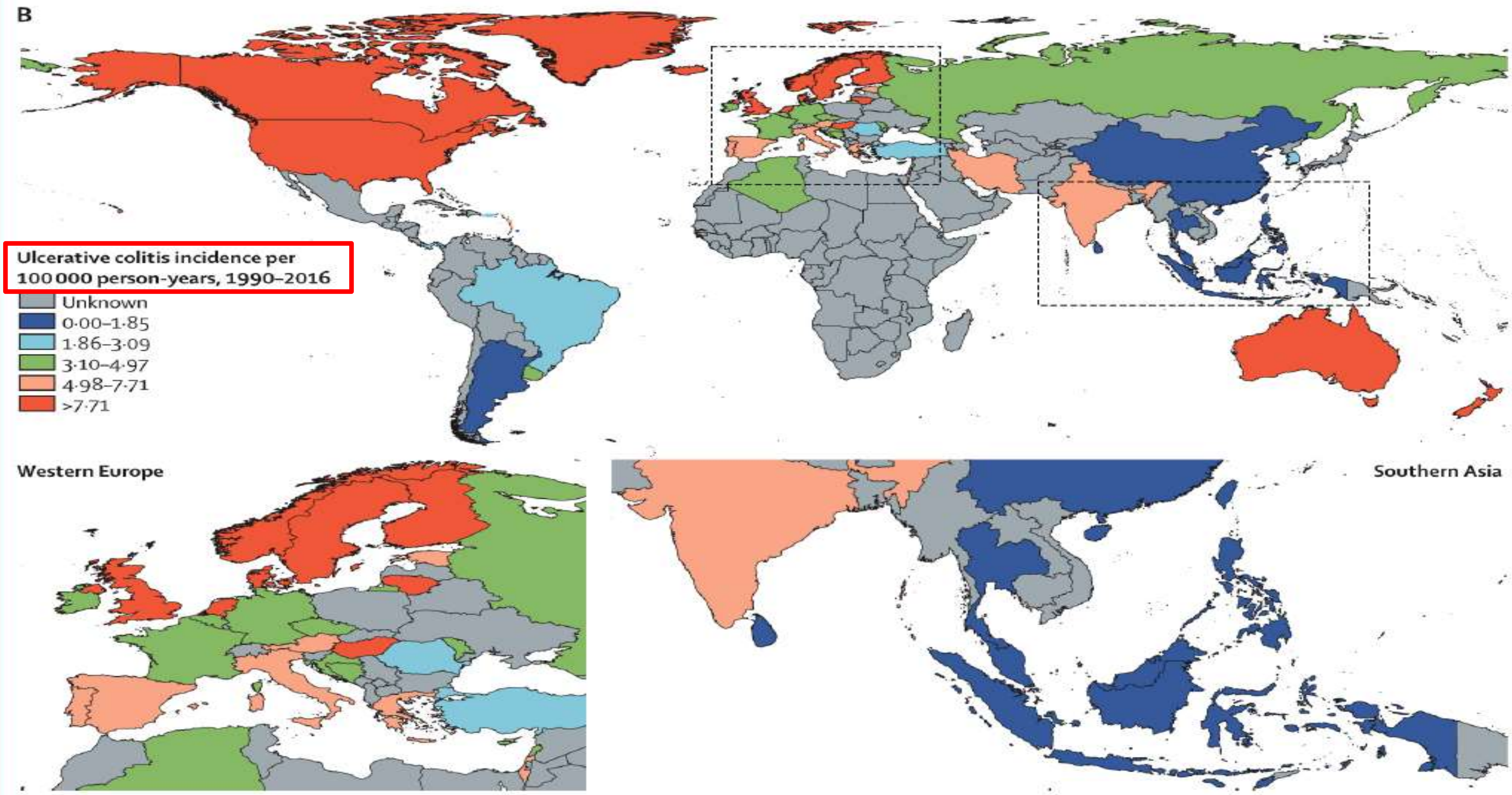
Males (number, 95% UI)
Females (number, 95% UI)
Males (rate, 95% UI)
Females (rate, 95% UI)
Total prevalent cases (million)
4·5
4·0
3·5
3·0
2·5
2·0
1·5
1·0
0·5
0
1990
1995
2000
2005
2010
2015
Year
Age-standardised prevalence rate (per 100 000 population)
105
100
95
90
85
80
75
70
65
60

Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies

Ng SC. Lancet. 2017 ;390(10114):2769-2778

- Stable or decreasing incidence of IBD in North America and Europe.
- Burden remains high, with prevalence surpassing 0·3%
- Since 1990, incidence has been rising in newly industrialised countries in Africa, Asia, and South America, including Brazil


A
Crohn's disease incidence per
100 000 person-years, 1990–2016
Unknown
0·00–0·80
0·81–1·94
1·95–3·76
3·77–6·38
>6·38
Western Europe
Southern Asia


B
Ulcerative colitis incidence per 100 000 person-years, 1990–2016
Unknown
0·00–1·85
1·86–3·09
3·10–4·97
4·98–7·71
>7·71
Western Europe
Southern Asia

Where does epidemiology data come from?

What is a Registry?

- A file of documents containing uniform information about individual persons, collected in a systematic and comprehensive way, in order to serve a predetermined scientific, clinical or policy purpose[1]

1. **Brooke EM. The Current and Future Use of Registers in Health Information Systems. Geneva, Switzerland: World Health Organization; 1974. Publication No. 8.**

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IBD Registry

- Collects and analyses data from patients with IBD in a particular population
- Supports better understanding by people, hospitals and other health-related organizations in about IBD in general, how IBD is treated, and about medications that are used
- Supports research into the causes of IBD and treatments that improve patients’ lives
- Helps hospitals to deliver their services more effectively
- Improves society’s understanding of how people’s lives are affected by IBD.

UK IBD Registry – https://ibdregistry.org.uk

Sources of data for IBD Registry

- Health insurance data – national or private
- Collection of electronic medical records from e.g. general practices
- Prescription drug dispensations
- Linking recruitment of participants at tertiary referral centers

Bernstein CN. Large Registry Epidemiology in IBD. Inflamm Bowel Dis. 2017 Nov;23(11):1941-1949.

What type of data in the IBD Registry?

Adapted from ECCO UR-CARE: United Registries for Clinical Assessment and Research

Examples of Databases and Registries in Use to Explore Epidemiology and Outcomes in IBD

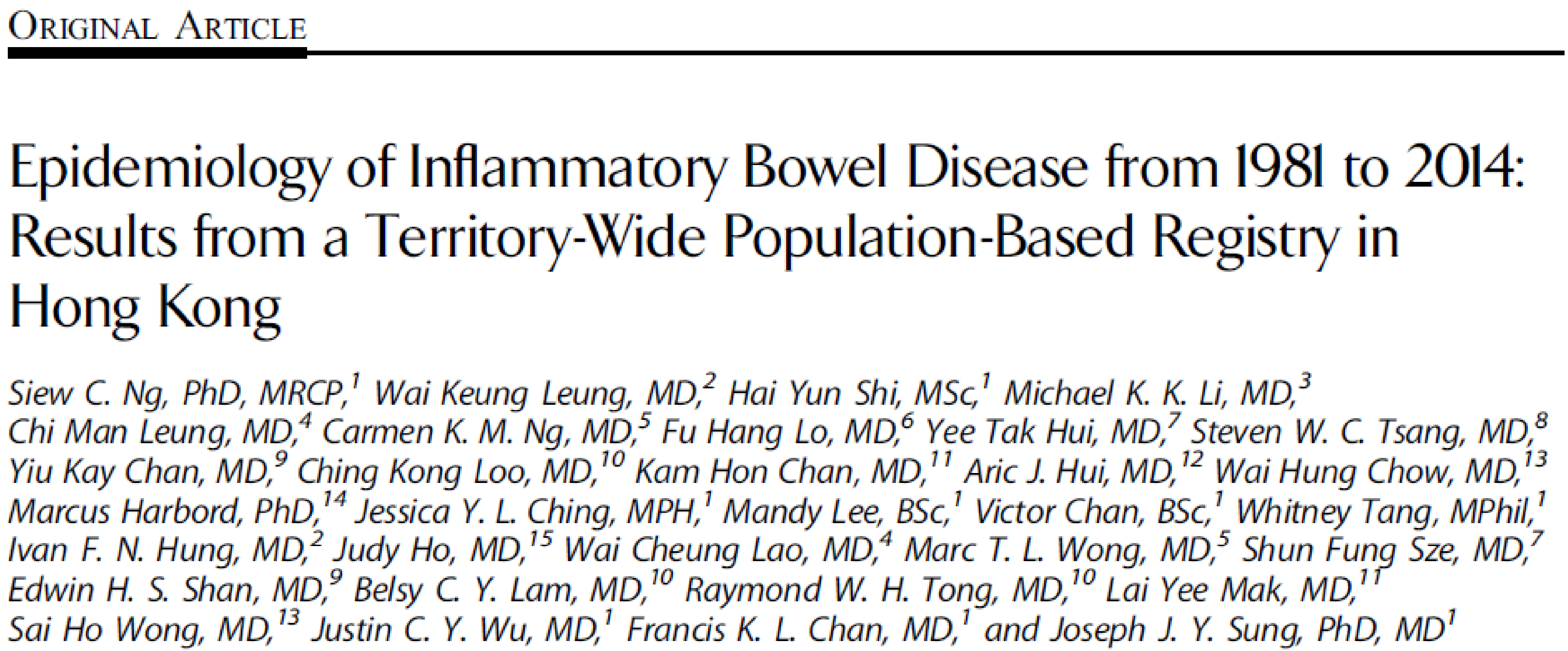
	Registry or database	Key advantages	Key disadvantages
University of Manitoba IBD Epidemiology Database	Canadian provincial database	• Population based • Long duration Comprehensive longitudinal health • contact follow up • Comprehensive prescription drug database	• Limited clinical data • Unable to phenotype • Disease activity state uncertain
Swedish regional health databases	Swedish, Database	• National health service provides population-based data • Comprehensive for longitudinal health care follow up • Can function as registry as clinical data can be accessed • Disease phenotype and activity and prescription drug use over time can be assessed	• Uncertain how well these data can be extrapolated to countries without universal health care access and with more fragmented insurance models

Examples of Databases and Registries in Use to Explore Epidemiology and Outcomes in IBD

	Registry or database	**Key advantages**	**Key disadvantages**
Danish Crohn Colitis Database	Danish , Database	• Comprehensive for longitudinal health care follow up of members • Can function as registry as clinical data can be accessed • Disease phenotype and activity and prescription drug use over time can be assessed	• Uncertain how well these data can be extrapolated to countries without universal health care access and with more fragmented insurance models
UK IBD Registry	UK, registry	• Comprehensive for longitudinal health care follow up of members • Can function as registry as clinical data can be accessed • Disease phenotype and activity and prescription drug use over time can be assessed	
Asia-Pacific Crohn's and Colitis Epidemiology Study (ACCESS)	Registry	• Comprehensive for longitudinal health care follow up of members • Disease phenotype and activity and prescription drug use over time can be assessed	

How does the IBD Registry help patients?

- Analyse information about IBD and use this to inform hospitals, and health-related organisations on how they can improve patient care, including better treatments and improved knowledge about medicines.
- Research studies using data from the Registry; for example, to compare different treatments and outcomes, or to monitor the safety and effectiveness of medications.
- Information collected and published by the Registry will help in improving professional and public awareness by presenting a more accurate and complete picture of the number of people who have IBD and the impact on their lives



ORIGINAL ARTICLE

Epidemiology of Inflammatory Bowel Disease from 1981 to 2014: Results from a Territory-Wide Population-Based Registry in Hong Kong

Siew C. Ng, PhD, MRCP,[1] Wai Keung Leung, MD,[2] Hai Yun Shi, MSc,[1] Michael K. K. Li, MD,[3] Chi Man Leung, MD,[4] Carmen K. M. Ng, MD,[5] Fu Hang Lo, MD,[6] Yee Tak Hui, MD,[7] Steven W. C. Tsang, MD,[8] Yiu Kay Chan, MD,[9] Ching Kong Loo, MD,[10] Kam Hon Chan, MD,[11] Aric J. Hui, MD,[12] Wai Hung Chow, MD,[13] Marcus Harbord, PhD,[14] Jessica Y. L. Ching, MPH,[1] Mandy Lee, BSc,[1] Victor Chan, BSc,[1] Whitney Tang, MPhil,[1] Ivan F. N. Hung, MD,[2] Judy Ho, MD,[15] Wai Cheung Lao, MD,[4] Marc T. L. Wong, MD,[5] Shun Fung Sze, MD,[7] Edwin H. S. Shan, MD,[9] Belsy C. Y. Lam, MD,[10] Raymond W. H. Tong, MD,[10] Lai Yee Mak, MD,[11] Sai Ho Wong, MD,[13] Justin C. Y. Wu, MD,[1] Francis K. L. Chan, MD,[1] and Joseph J. Y. Sung, PhD, MD[1]

Original Article

JCC
JOURNAL of CROHN'S and COLITIS

A 30-year Trend Analysis in the Epidemiology of Inflammatory Bowel Disease in the Songpa-Kangdong District of Seoul, Korea in 1986–2015

Sang Hyoung Park,[a] Ye-Jee Kim,[b] Kyoung Hoon Rhee,[c] Young-Ho Kim,[d] Sung Noh Hong,[d] Kyung Ho Kim,[e] Seung In Seo,[e] Jae Myung Cha,[f] Sun Yong Park,[g] Seung Kyu Jeong,[h] Ji Hyun Lee,[i] Hyunju Park,[j] Joo Sung Kim,[k] Jong Pil Im,[k] Hyuk Yoon,[l] Sung Hoon Kim,[m] Jisun Jang,[m] Jeong Hwan Kim,[n] Seong O Suh,[o] Young Kyun Kim,[p] Byong Duk Ye,[a] Suk-Kyun Yang[a]; on behalf of the Songpa-Kangdong Inflammatory Bowel Disease [SK-IBD] Study Group

Journal of Digestive Diseases 2018; **19**; 395–403 doi: 10.1111/1751-2980.12641

Original article

Rapid rise in the incidence and clinical characteristics of pediatric inflammatory bowel disease in a South–East Asian cohort in Singapore, 1994–2015

Christina ONG,* Marion M AW,† Maria J LIWANAG,* Seng H QUAK† & Kong B PHUA*

Singapore IBD Registry

Participating hospitals

- SGH
- CGH
- SKH
- NUH
- TTSH
- NTFGH
- KKH
- NUH paeds

Grant support from: Rotary Club

Singapore IBD Registry

- Approved by
  - **SingHealth** - Centralised Institutional Review Board (CIRB)
  - **National Healthcare Group** (NHG)- Domain Specific Review Board (DSRB)
- Guided by
  - Ethical principles outlined in the Belmont Report and
  - Legal mandates outlined in the International Conference for Harmonisation Guidelines for Good Clinical Practice (ICH GCP), Human Biomedical Research Act (HBRA) and its regulations.

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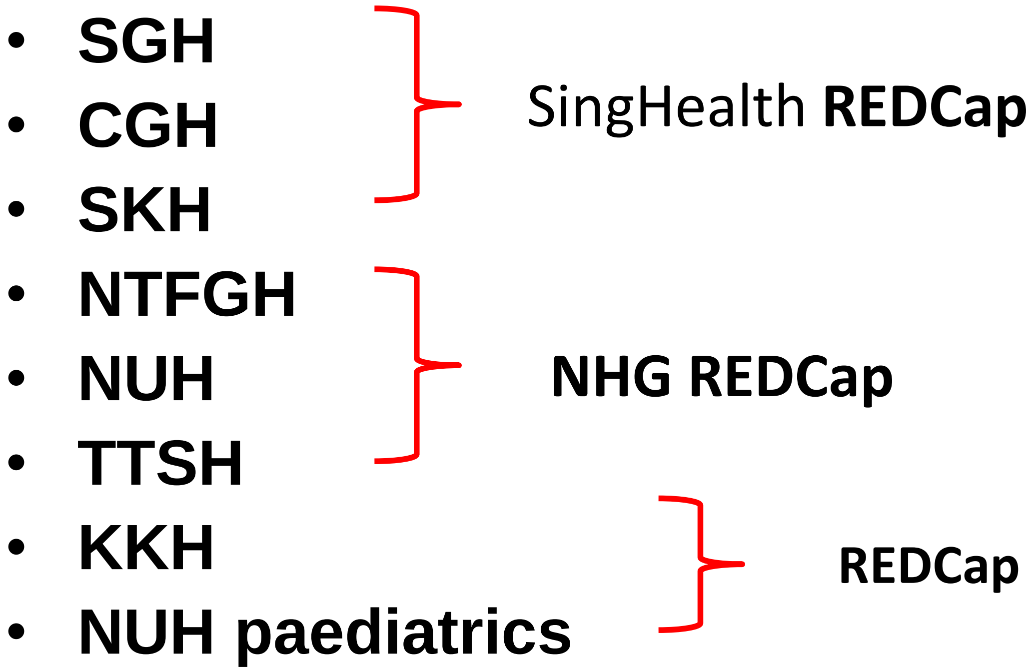
Where is the data stored?

- A secure web application for building and managing online surveys and databases
- SingHealth **Health Services Research Centre** (HSRC) manage applications for the creation and renewal of REDCap projects

Where is the data stored?



- **SGH**
- **CGH**
- **SKH**
- **NTFGH**
- **NUH**
- **TTSH**
- **KKH**
- **NUH paediatrics**

SingHealth **REDCap**

NHG REDCap

REDCap

How can you help with the IBD Registry?

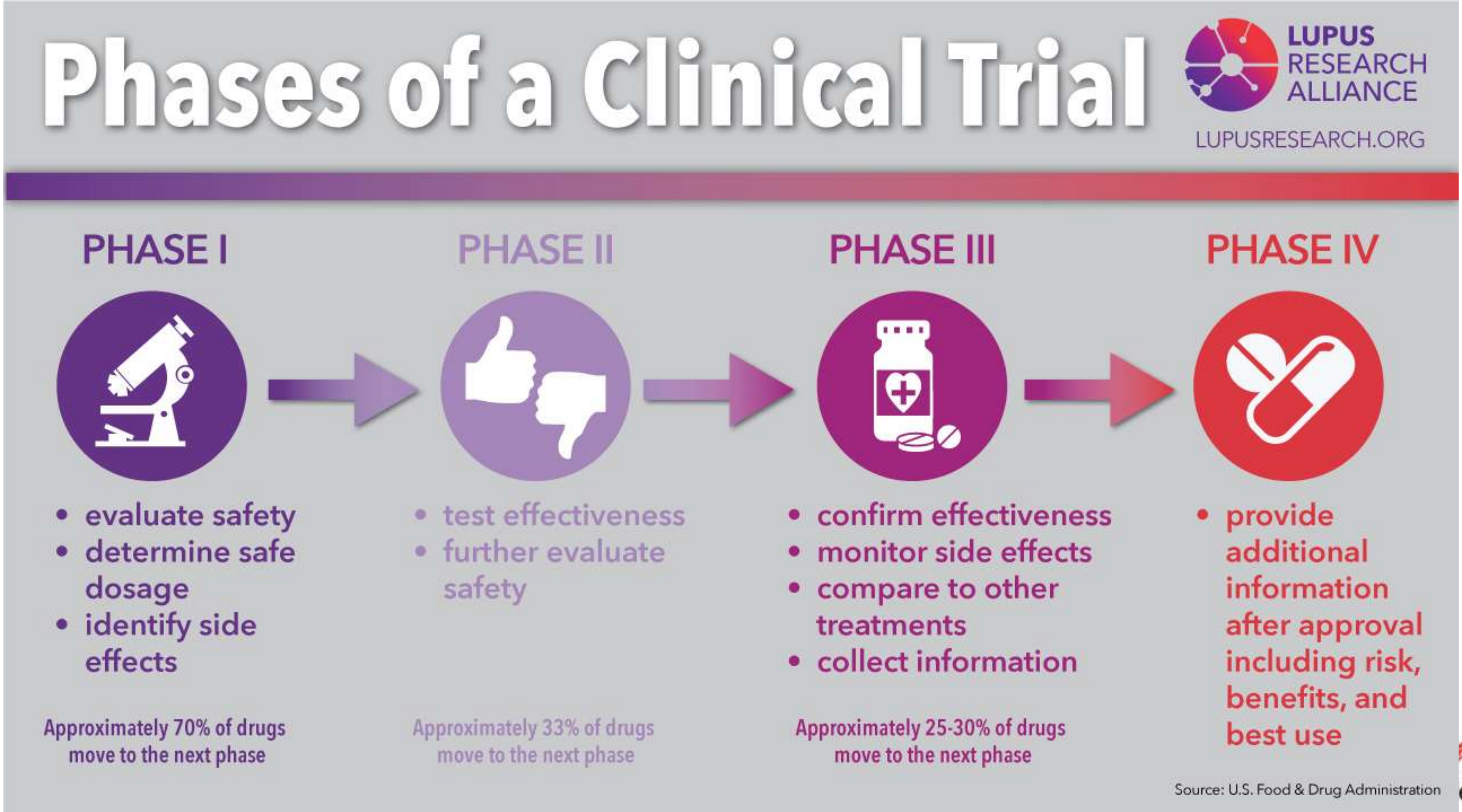
- Allow us to take consent for your data related to IBD be captured

What is Clinical trial?

Clinical trials - definition

- A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

National Institutes of Health –definition of clinical trials



Phases of a Clinical Trial

LUPUS RESEARCH ALLIANCE

LUPUSRESEARCH.ORG

PHASE I

- evaluate safety
- determine safe dosage
- identify side effects

Approximately 70% of drugs move to the next phase

PHASE II

- test effectiveness
- further evaluate safety

Approximately 33% of drugs move to the next phase

PHASE III

- confirm effectiveness
- monitor side effects
- compare to other treatments
- collect information

Approximately 25-30% of drugs move to the next phase

PHASE IV

- provide additional information after approval including risk, benefits, and best use

Source: U.S. Food & Drug Administration

Common terms about clinical trials

- **Investigational treatment**
  - That is currently under clinical study but does not have permission from the regulatory body to be legally marketed and sold

Common terms about clinical trials

- **Standard of care**
  - A treatment that is accepted by medical experts as a proper treatment for a certain type of disease that is widely used by healthcare professionals.
  - Also referred as best practice, standard medical care, and standard therapy

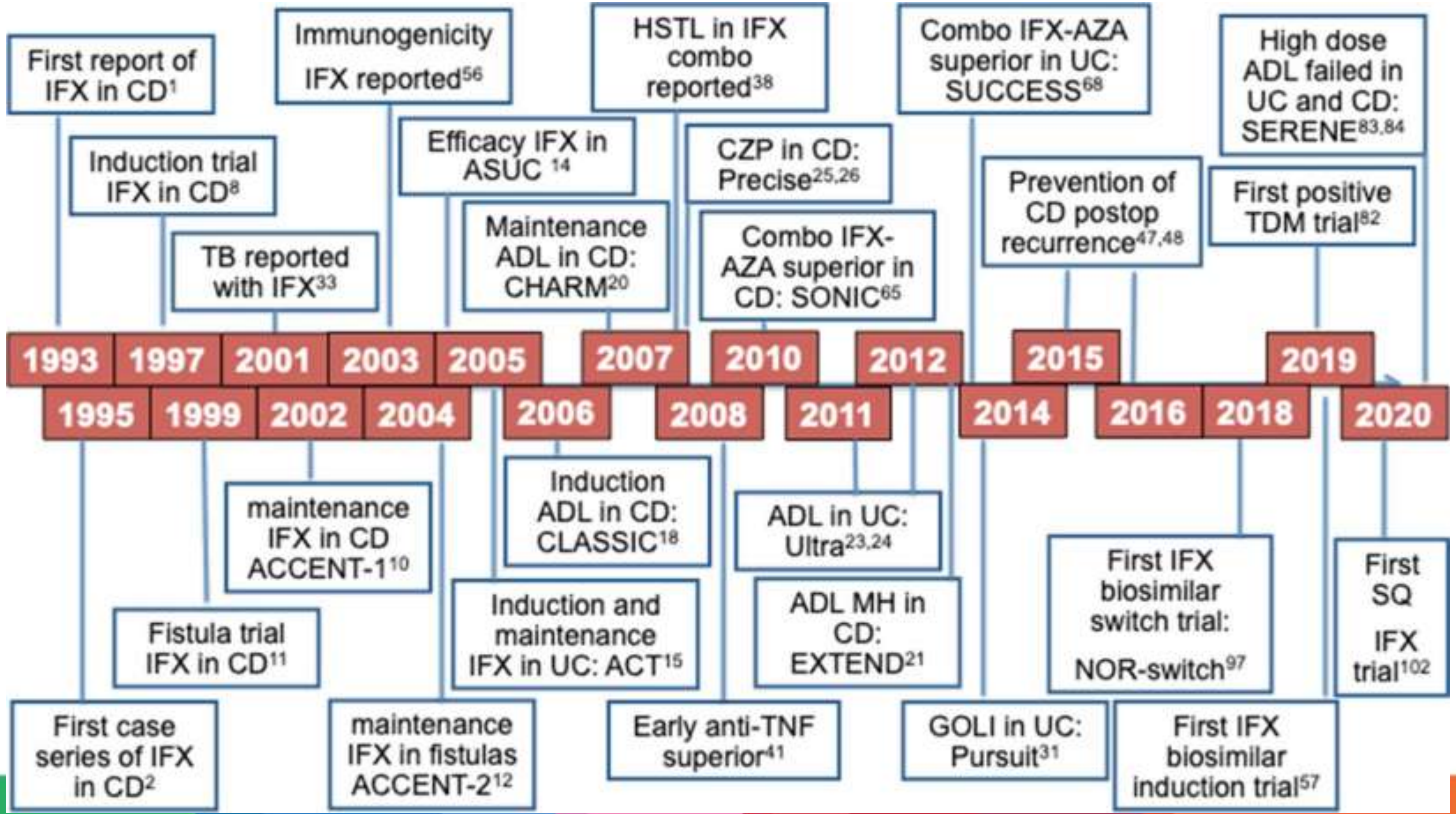
Common terms about clinical trials

- **Randomized clinical trial**
  - A study in which people are chosen at random to receive the treatment being studied.

Common terms about clinical trials

- **Placebo**
  - A pill or liquid which often looks like the real medical treatment being studied in a clinical trial, except it does not contain the active medication.

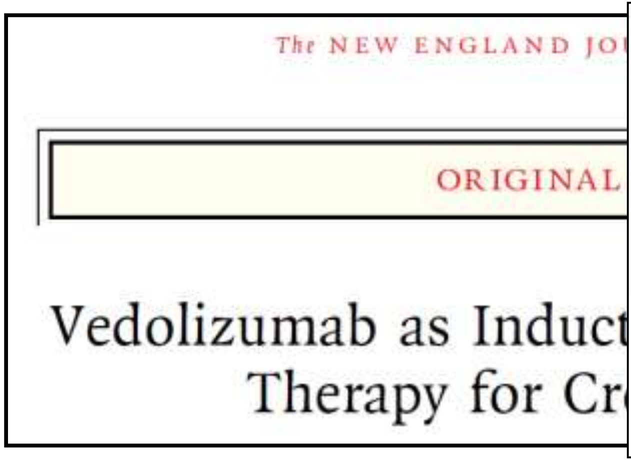
Anti-TNF studies in IBD



First report of IFX in CD[1]
Induction trial IFX in CD[8]
TB reported with IFX[33]
Immunogenicity IFX reported[56]
Efficacy IFX in ASUC [14]
Maintenance ADL in CD: CHARM[20]
HSTL in IFX combo reported[38]
CZP in CD: Precise[25,26]
Combo IFX-AZA superior in CD: SONIC[65]
Combo IFX-AZA superior in UC: SUCCESS[68]
Prevention of CD postop recurrence[47,48]
High dose ADL failed in UC and CD: SERENE[83,84]
First positive TDM trial[82]

1993 1997 2001 2003 2005 2007 2010 2012 2015 2019
1995 1999 2002 2004 2006 2008 2011 2014 2016 2018 2020

First case series of IFX in CD[2]
Fistula trial IFX in CD[11]
maintenance IFX in CD ACCENT-1[10]
maintenance IFX in fistulas ACCENT-2[12]
Induction ADL in CD: CLASSIC[18]
Induction and maintenance IFX in UC: ACT[15]
Early anti-TNF superior[41]
ADL in UC: Ultra[23,24]
ADL MH in CD: EXTEND[21]
GOLI in UC: Pursuit[31]
First IFX biosimilar switch trial: NOR-switch[97]
First IFX biosimilar induction trial[57]
First SQ IFX trial[102]



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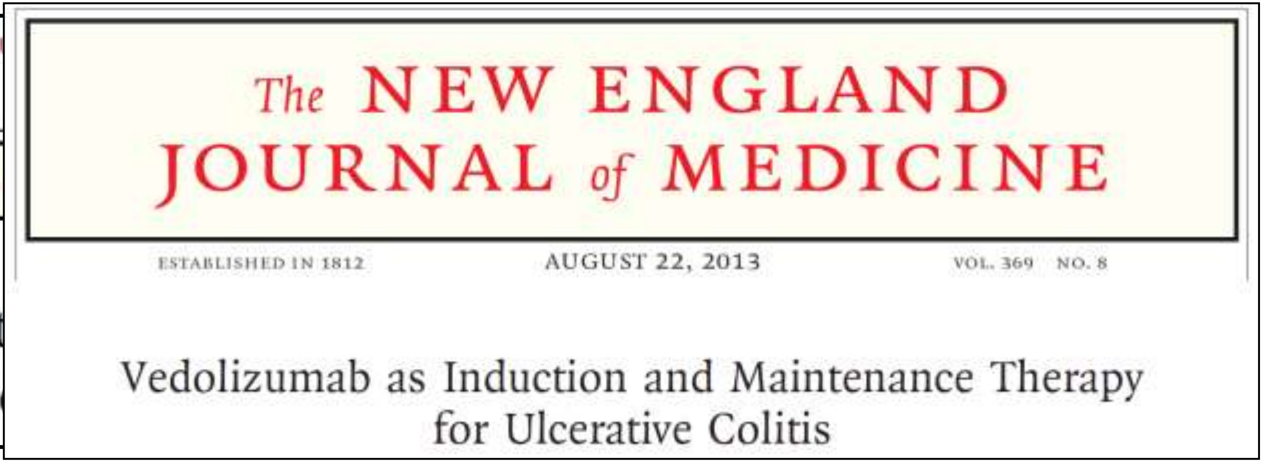
Vedolizumab as Induct

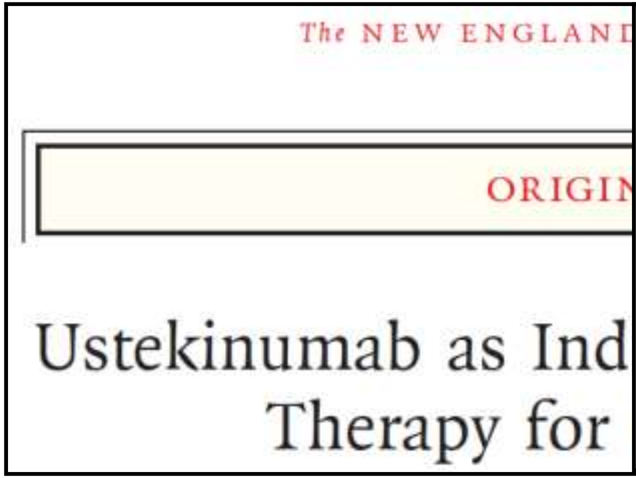
Therapy for Cr



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 22, 2013 VOL. 369 NO. 8

Vedolizumab as Induction and Maintenance Therapy for Ulcerative Colitis



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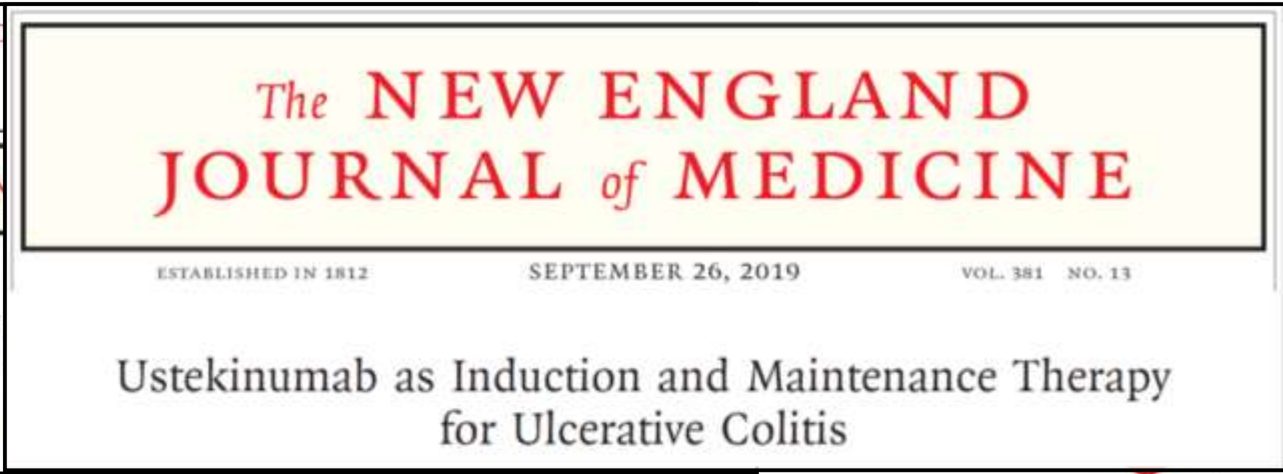
Ustekinumab as Ind

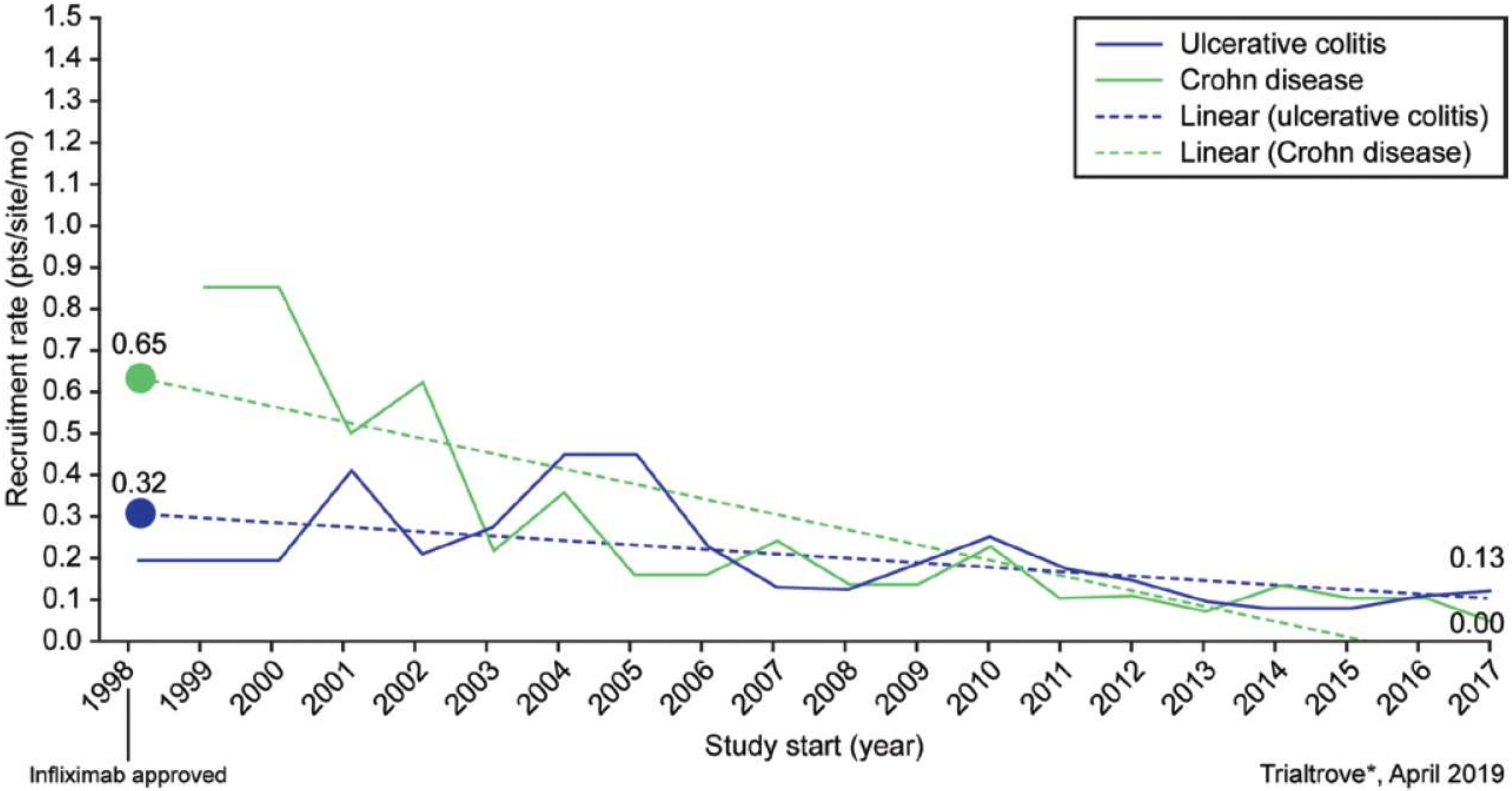
Therapy for



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 26, 2019 VOL. 381 NO. 13

Ustekinumab as Induction and Maintenance Therapy for Ulcerative Colitis



Trialtrove*, April 2019

Concerns in IBD Clinical Trials and Potential Solutions

Concern	Potential Solution
Receiving placebo or less effective treatment	Comparative efficacy trials; historical placebo data from completed trials; platform trials to reduce number of placebo arms
Lack of access to investigational treatment	Extension studies/access programs
Restrictive inclusion/exclusion criteria	Broadening inclusion/exclusion criteria; considering studies in underserved patient groups
Invasive end points/measures	Testing for biomarkers or validating noninvasive surrogate end points

How do I get involved in clinical trial?

- Talk to your doctor about whether participating in a clinical trial may be right for you

What questions should I ask my doctor about getting involved in a clinical trial?

- Do you know of any trials looking at new therapies or treatments?
- Can you tell me why this trial is being done?
- What are the possible advantages and risks of taking part in this trial?
- How many patients are in the trial?
- How long will the trial last?
- What will I have to do if I take part?

How do I know if I am eligible for a clinical trial?

- Each clinical trial has a set of guidelines for who can or cannot participate in the study (eligibility criteria)
- You could discuss with your doctor about participating in a clinical trial

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What are the costs of clinical trials to me?

- Majority of clinical trials are privately or institution funded, so there is typically no cost to the participant.
- Travel, parking, and arranging for child care/time off work are other possible costs associated with participating in a trial.
  - Trial sponsor will cover these costs.

Your help is appreciated

- By participating into clinical trials!

Thank you