YOU SHOULD KNOW

A Patient's Guide to Cancer Risk in IBD

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Contents

IBD & Cancer

5 KEY POINTS

The highest risk patients have extensive disease and active inflammation. But they are not the only patients with risk. Even patients with limited disease that is well-controlled by medication have cancer risk.

Colon cancer is the leading cause of cancer-related death for IBD patients.

Cancer risk steadily increases over time. It increases further, by large jumps, if dysplasia is detected or if a new abnormality develops, such as a stricture.

Colon cancer is usually fatal if detected late, but it is treatable if caught early. Symptoms do not tend to develop early, which makes surveillance so important.

The safest patients manage their cancer risk with the same determination that they manage their IBD. The key elements are getting inflammation under control and regular colonoscopy surveillance.

KNOWING YOUR RISK

The average person with IBD has

2- to 4-times more cancer risk

than an average person without IBD

The most frequently cited statistics estimate cancer risk in IBD at:

2% after 10 years
8% after 20 years
18% after 30 years

But these are just averages

Individual people with IBD may have somewhat **lower** risk…
or **much higher** risk

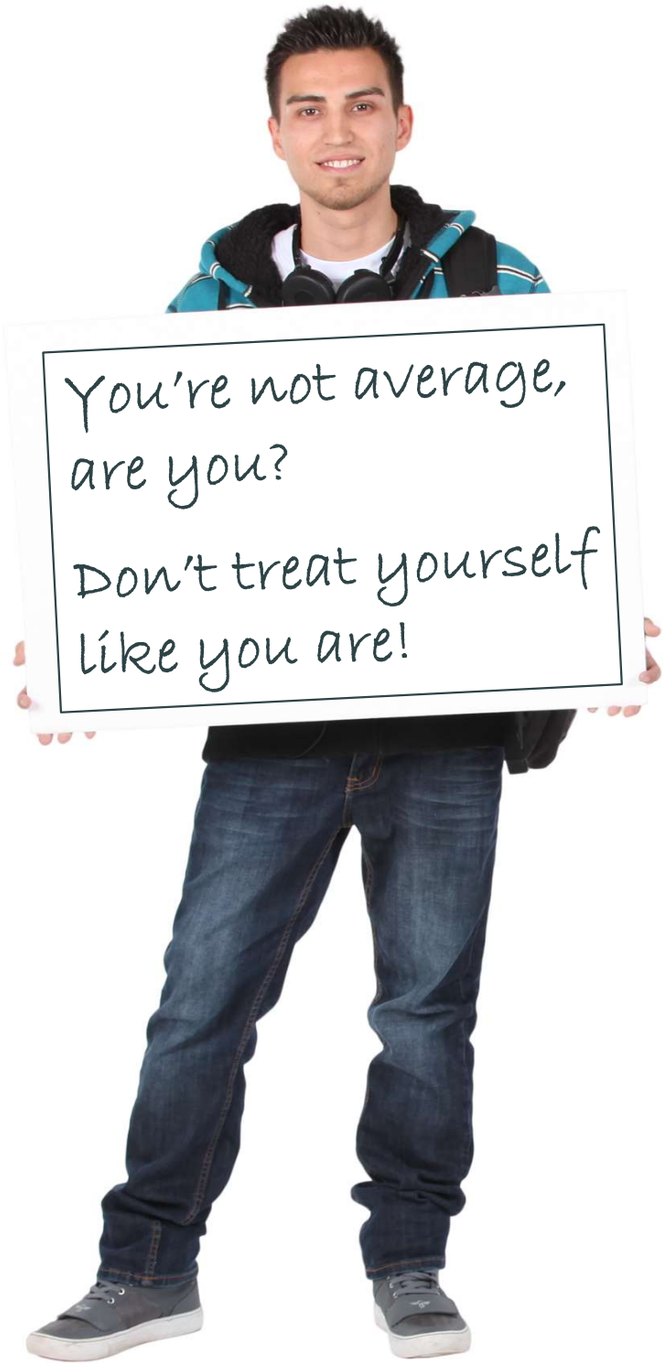
The **risk grows over time** and varies by person based on their own disease history

IBD Cancer Risk Drivers

Factors specific to you affect your personal risk of cancer. Smoking, for example, causes cancer by damaging lung tissue. A similar process takes place in the colon with IBD-related inflammation

Luck also plays a role. Luck is the reason some smokers never develop lung cancer while some non-smokers do. But luck has its limits. Smokers develop a lot more lung cancer than non-smokers!!

	Risk →			
IBD Extent	Rectum 	Left Side 	Full Colon 	
IBD Duration	Under 8 Years	8 to 12 Years	Over 12 Years	
IBD Severity		Mild 	Moderate 	Severe 
Tissue Damage		Pseudo-polyp	Shortened / Tubular Colon	Dysplasia or UC Stricture
Non-IBD Factors		Older Age	Family History	Genetic Syndrome or PSC



MANAGING YOUR RISK

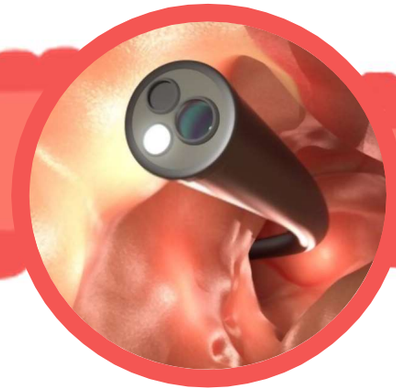
The actions you take directly affect the likelihood you will develop cancer

Reducing IBD-related cancer risk has two parts: inflammation control and regular colonoscopies

Inflammation Control

Bringing inflammation under control is by far the most important cancer prevention strategy. Controlling inflammation improves quality of life and reduces cancer risk.

Patients who don't successfully control inflammation, whether that is because they are avoiding medication or it has failed to work for them, are at significantly higher cancer risk.



Regular Colonoscopy

Patients who get regular colonoscopies are more likely to have pre-cancer removed (often without surgery) than patients who skip surveillance. They are also more likely to have a cancer detected at an early stage when it can be treated successfully, than later, why it is more likely to be fatal.

Healthy Living

In addition to controlling inflammation and getting regular colonoscopies, following good living habits can reduce non-IBD-related risk:

- Maintaining a healthy weight
- Exercising regularly
- Eating a high fiber diet
- Limiting red meat intake
- Managing stress

REAL TALK ABOUT COLONOSCOPIES

Early detection is critical for survival in colon cancer

90%

survive when caught **early**

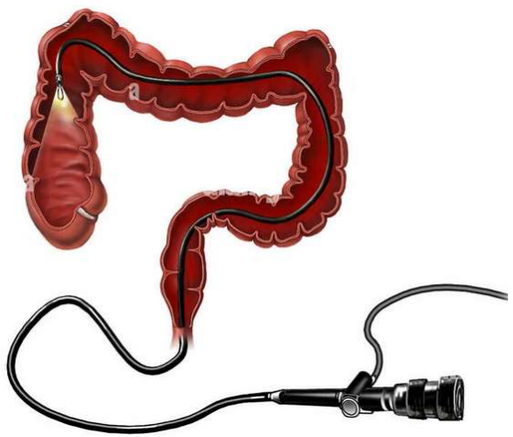
14%

survive when caught **late**

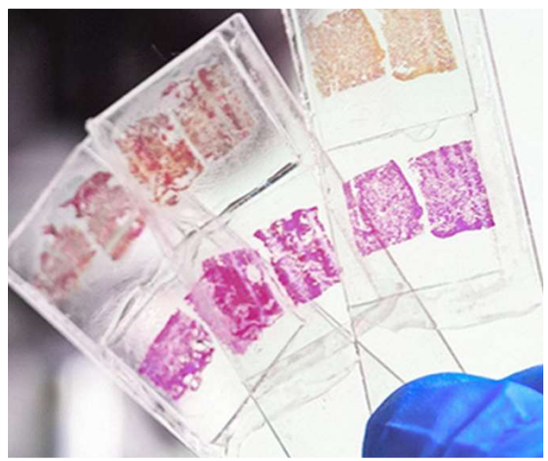
Colonoscopies consist of two components: visual inspection and microscopic inspection

An **endoscope** transmits video to visually detect polyps or dysplasia

Biopsies are sliced very thin for a **pathologist** to review under a **microscope**



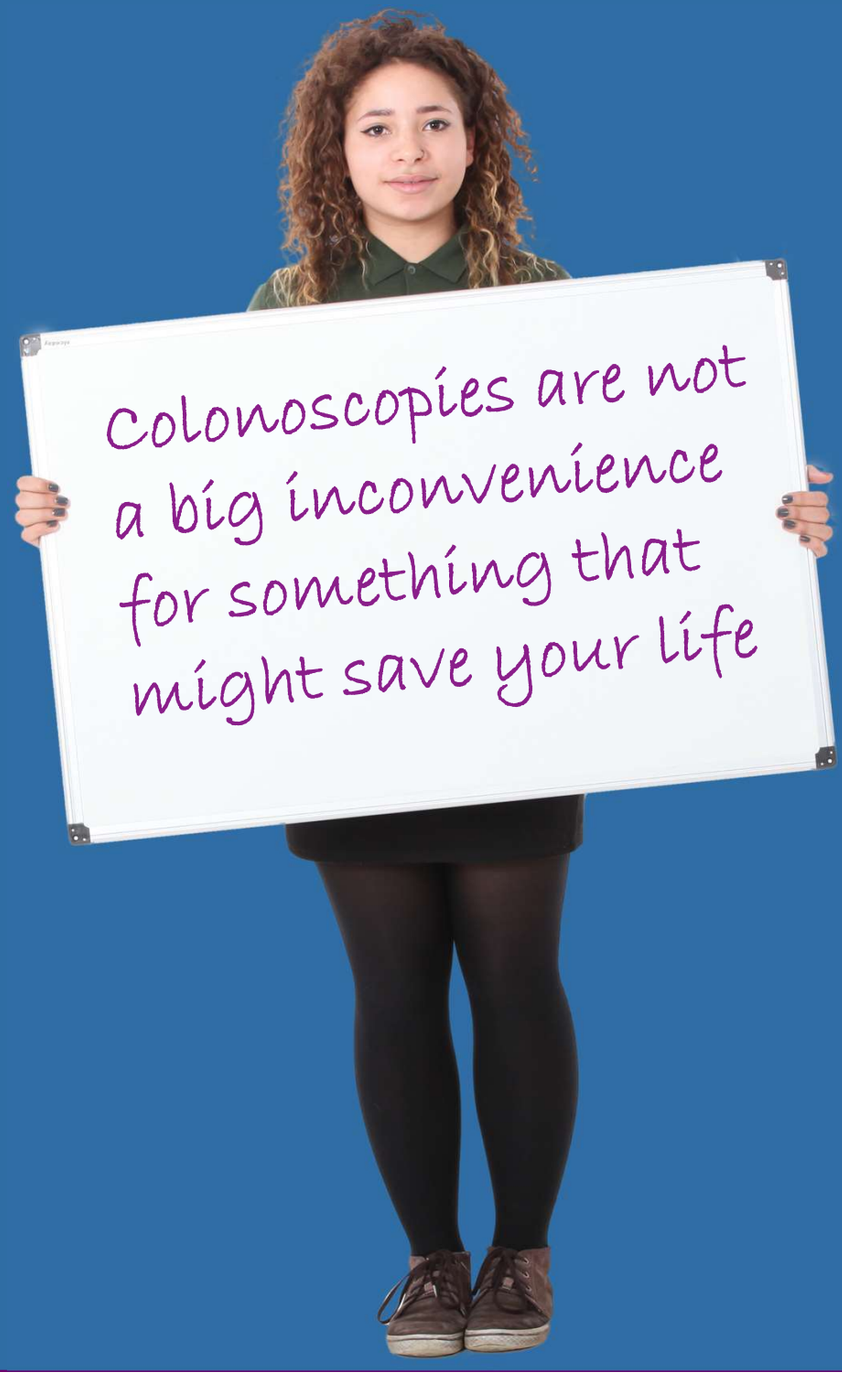
A claw on the endoscope snips **biopsies** (bits of tissue)



Most people with IBD will not develop colon cancer, but many others will.

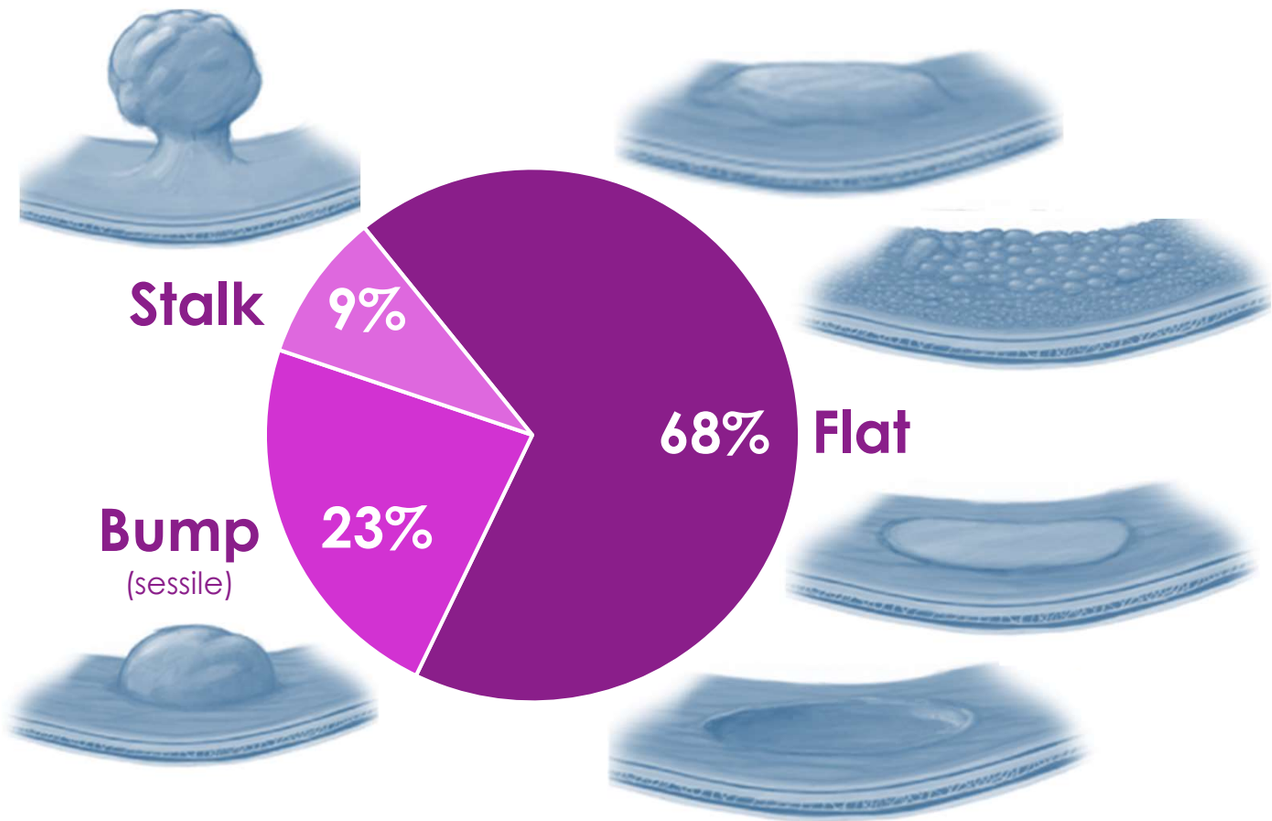
Those who follow surveillance guidelines are **more likely to have a pre-cancer removed** (often without surgery).

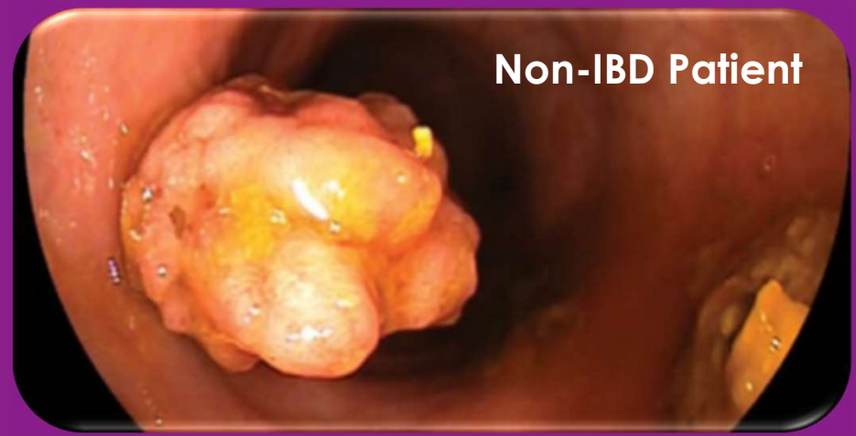
Among patients who develop colon cancer, those who undergo regular surveillance are **more likely to have it detected at an earlier, more treatable stage.**

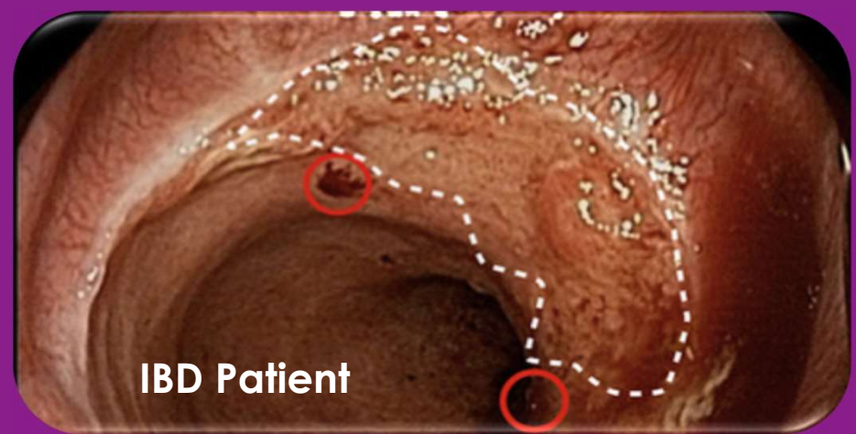


Expert Endoscopy is Mandatory

In IBD, 70% of dysplasia is flat. This makes it more difficult for a non-expert to detect. It also makes **good bowel prep** and **inflammation control** to improve visibility even more important.







The IBD cancer above was **missed**; biopsies (red) were taken outside the margins of the growth (white).

This meant a delayed diagnosis for the patient. A single biopsy only covers **1/20th of 1%** of the colon.

Questions for Your Endoscopist

What's your adenoma detection rate?

The national benchmark is 25% for men and 15% for women

In what percent of patients can you get to the cecum?

They should reach the cecum (the far end of the colon near the small intestine) in at least 95% of exams to get full coverage of the colon

How long do you plan to take to get in and out?

Withdrawal time should be at least 15 minutes to ensure inspection

Will I get a written report that clearly documents the findings?

Photos, comments on bowel prep, notes on insertion and withdrawal time, and a description of examination behind the folds, inflammation, and chronic tissue damage

Do you use chromoendoscopy for the exam or for a follow up if there are abnormal findings?

Chromo is the gold standard for dysplasia detection and should be automatic follow up when there are any suspicious findings

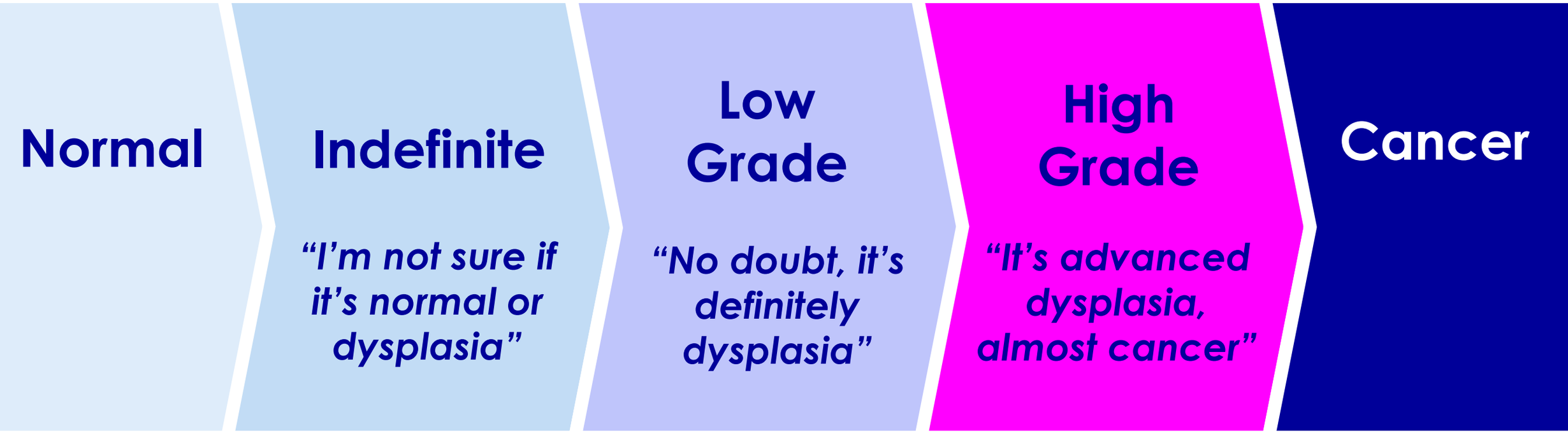
Do you use targeted or random biopsies and how many do you take?

Targeted biopsies focus on abnormal tissue, but in patients with higher risk, random biopsies should also be taken – at a minimum every 10 centimeters with additional random biopsies around any areas of concern.

DYSPLASIA: WHAT NEXT?

Grades of Dysplasia

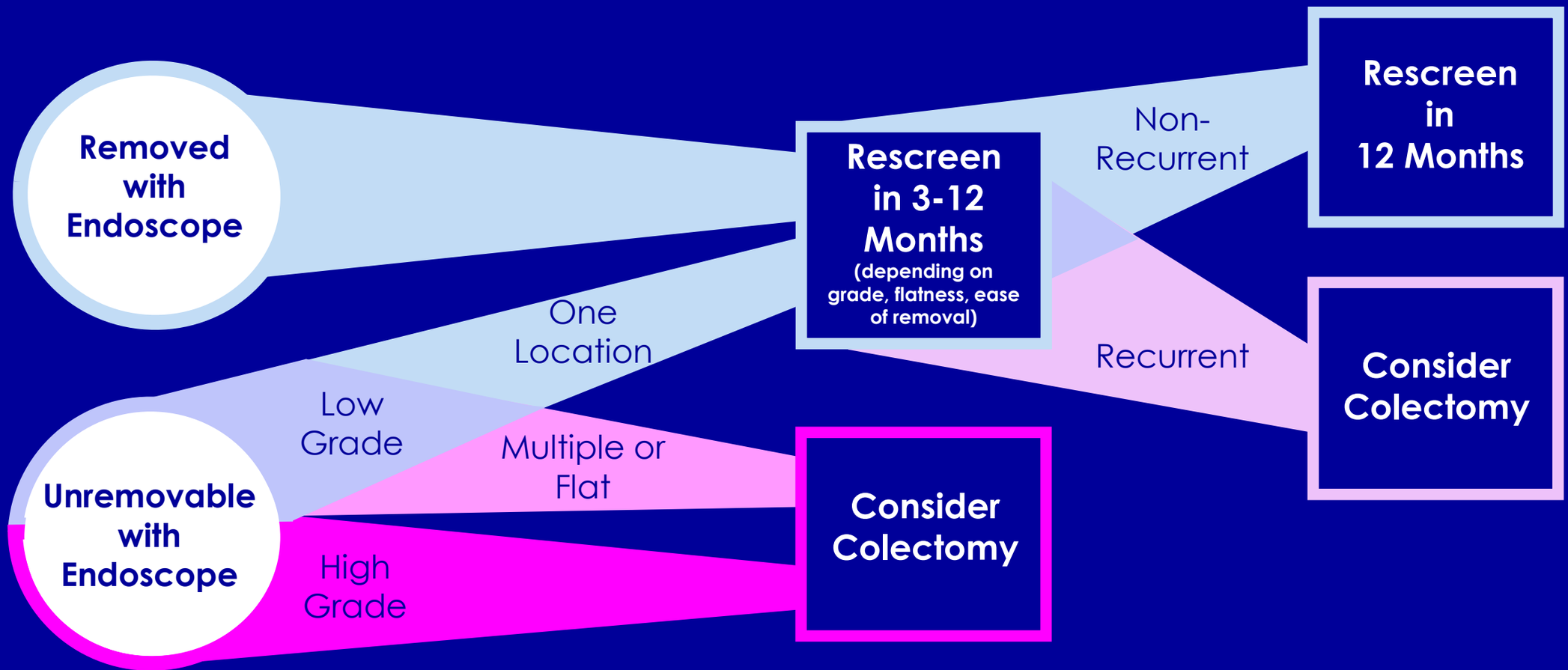
Pathologists classify dysplasia into categories, called **grades**, to indicate the degree of abnormality.



A challenge is that **active inflammation** can render biopsies **unreadable**, making pre-cancer more **difficult to identify**. This underscores the importance of high-quality bowel prep and inflammation control ahead of a colonoscopy.

There is no universally agreed upon framework for managing dysplasia.

Strategies depend on factors such as whether the dysplasia can be removed, how high the grade is, how large it is, where it is located, whether you have had dysplasia before, how flat it is, and whether it was visible or detected on a random biopsy.



WARNING SIGNS

Colon cancer symptoms often overlap with IBD symptoms, causing some people to miss them.

The appearance of any of the warning signs merits an immediate conversation with your healthcare provider – particularly if flare-like symptoms seem **different**, **worse**, or **more persistent** than usual.

Changes in the consistency, frequency, or size of bowel movements

Rectal bleeding or blood in stool (bright red or very dark)

Unusual fullness or sense the bowel is not emptying completely

Abdominal cramps, bloating, or inability to pass gas

Unintended or rapid weight loss

Feeling constantly weak or tired or developing anemia

Vomiting

APPENDIX: WHAT CAUSES IBD CANCER?

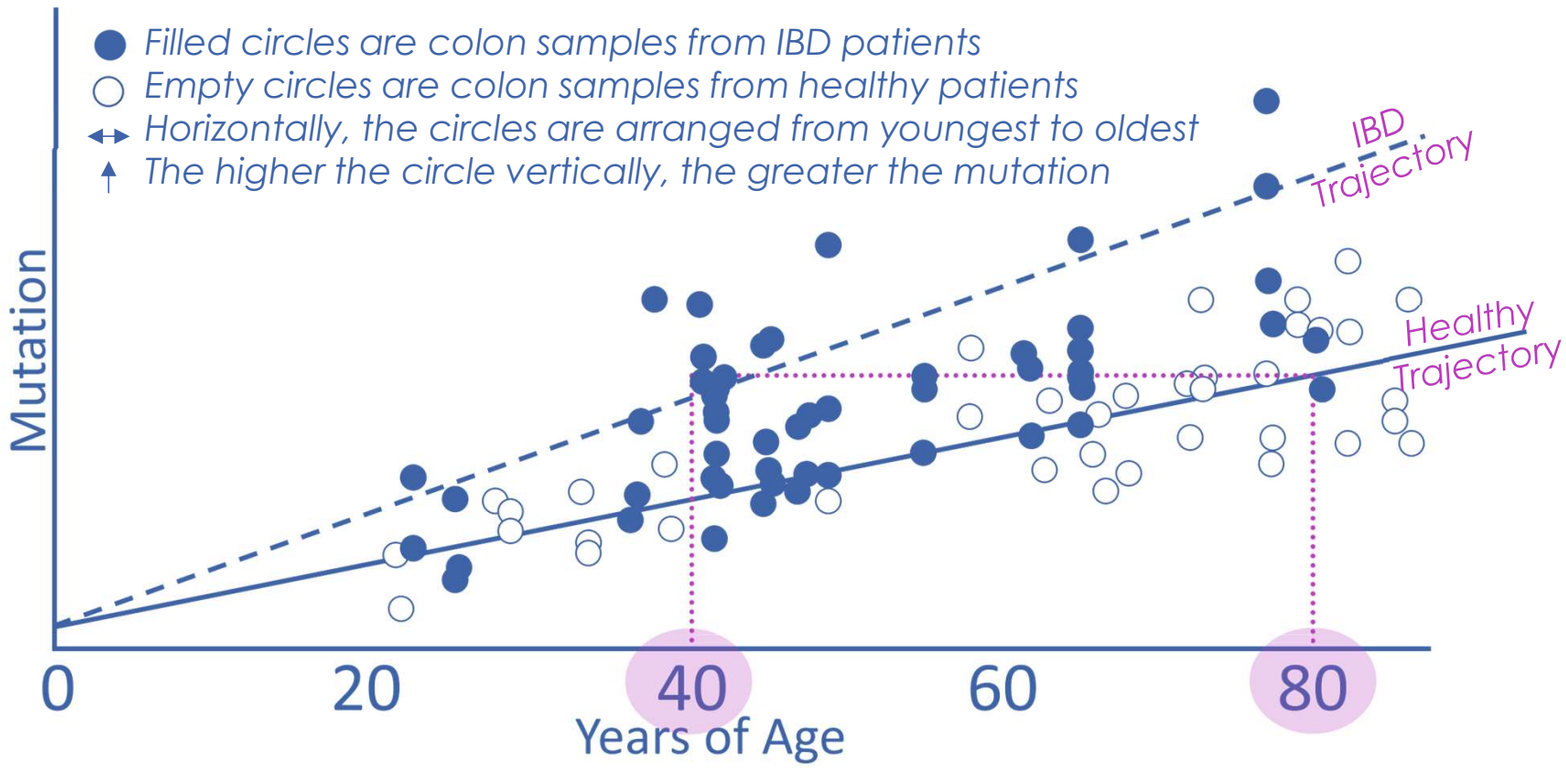
IBD increases cancer risk by accelerating the aging of the colon. The acceleration is directly tied to inflammation: how long, how extensive, and how severe.

By the age of 40, a person with colitis may have a colon that is "biologically" older than a person without colitis at age 80

Accelerated aging takes the form of DNA damage in cells. This damage, called **mutation**, causes cancer.

Some mutations originate at conception, but many more accumulate over time. This is why older people have more cancer than young people.

Just as smoking causes increased DNA damage in lung tissue, IBD causes increased DNA damage in the tissue of the gut.

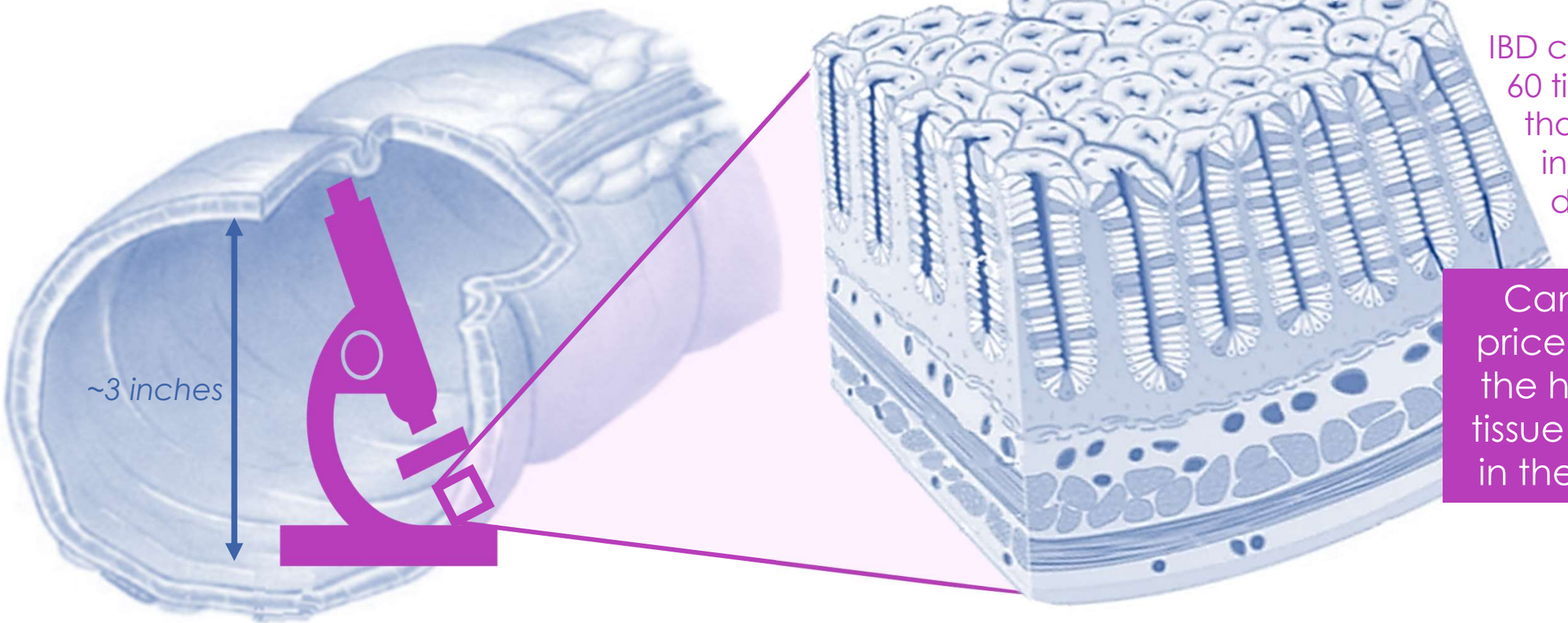


The colon is lined by millions of U-shaped glands, called crypts. Crypt cells secrete mucus and absorb water and nutrients.

These are the cells under attack by the immune system in IBD. They are also where colon cancer starts.

Virtually all of the **billions** of crypt cells die every 2-5 days and are replaced. Over a life, these cells divide **trillions** of times. Each division is an opportunity for mutations to develop.

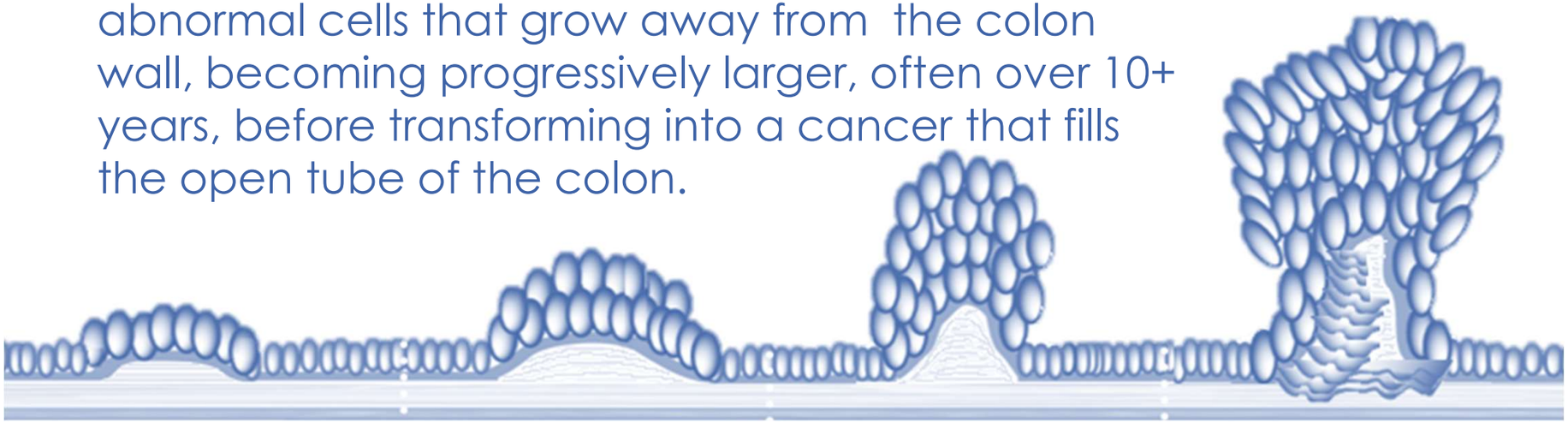
IBD crypts expand 60 times more rapidly than normal crypts in an effort to repair damaged tissue.



Cancer is the price we pay for the hyperactive tissue repair work in the IBD colon.

IBD Cancer is Different

Typical colon cancer arises from **polyps**, piles of abnormal cells that grow away from the colon wall, becoming progressively larger, often over 10+ years, before transforming into a cancer that fills the open tube of the colon.



IBD-related cancer begins with **dysplastic** tissue damage. This damage usually spreads along the colon wall or invades down, lying **flat** rather than popping up, making it more difficult to detect. It can develop into cancer as fast as 1-3 years.

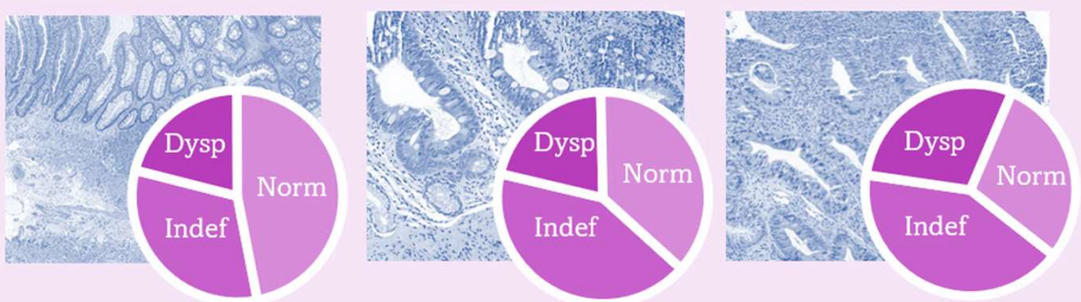
- Younger Patients
- More Difficult to Detect
- More Aggressive
- More Resistant to Treatment

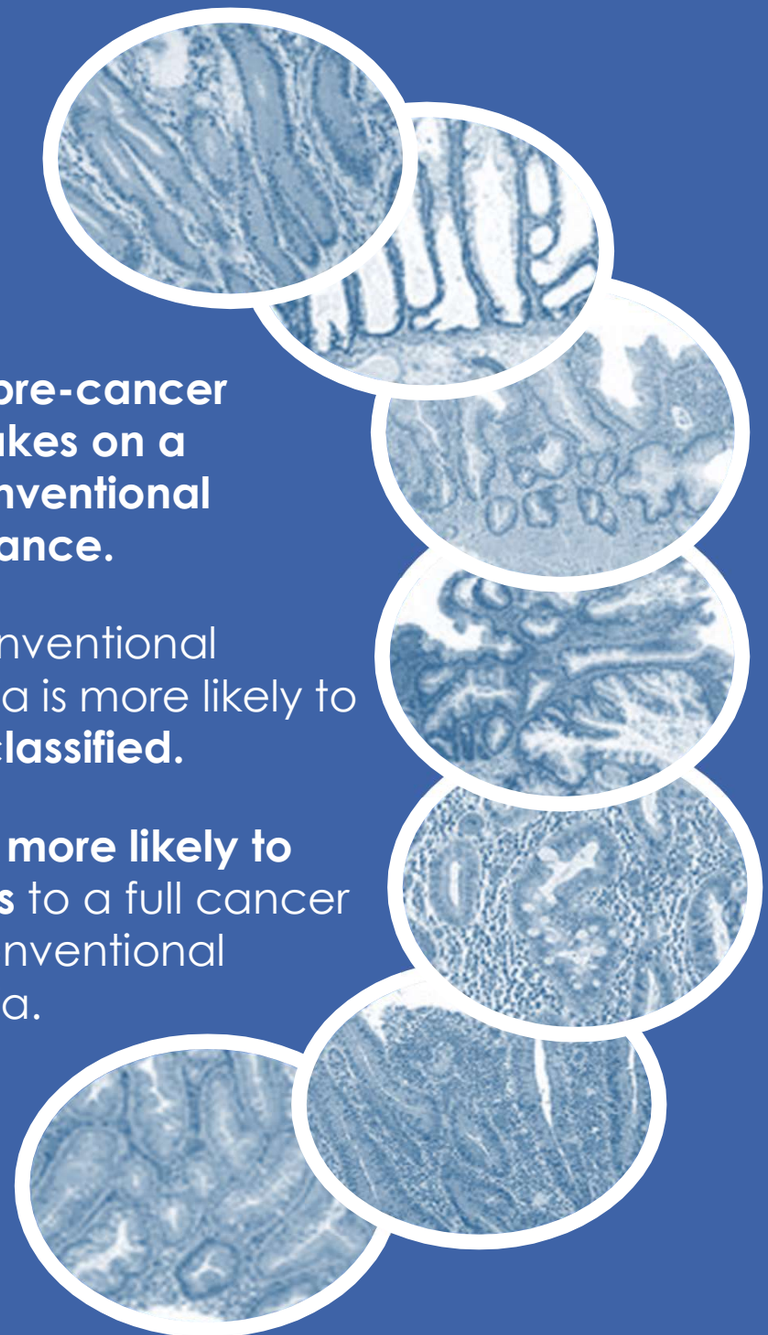
Dysplasia Differences

Grading dysplasia is subjective and experts can disagree.

The dysplasia samples below were reviewed independently by 20 expert pathologists. The pie charts highlight the **interobserver variability**.

Failure to correctly identify dysplasia can be an important issue. Even a single finding of "indefinite" dysplasia significantly changes a patient's risk.





40% of pre-cancer in IBD takes on a non-conventional appearance.

Non-conventional dysplasia is more likely to be **misclassified.**

It is also **more likely to progress** to a full cancer than conventional dysplasia.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