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CSIRO

RMIT UNIVERSITY

Solving Plastic Waste
Cooperative Research Centre
Growing the circular economy for plastics

GASTROENTEROLOGY
Northern Health

Microplastics and Human Gut Health

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Aims

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- Basic GI anatomy and physiology
- Increasing rates of GI disease
- Pathogenesis of IBD
- Gastrointestinal exposure to micro and nanoplastics
- Postulated mechanisms of micro and nanoplastic-associated disease

Basic Gastrointestinal Anatomy

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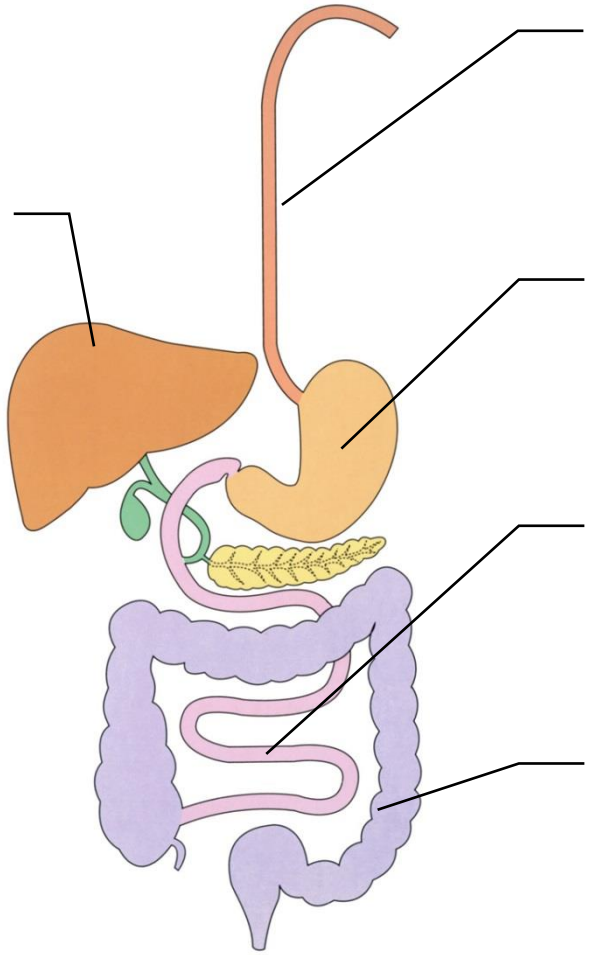

Liver

Oesophagus

Stomach

Small intestine: duodenum, jejunum and ileum

Large intestine: colon and rectum

Inflammatory Bowel Disease (IBD)

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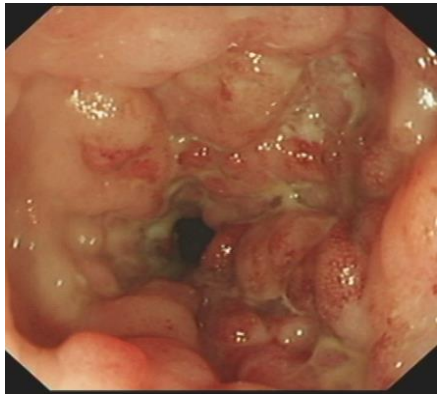
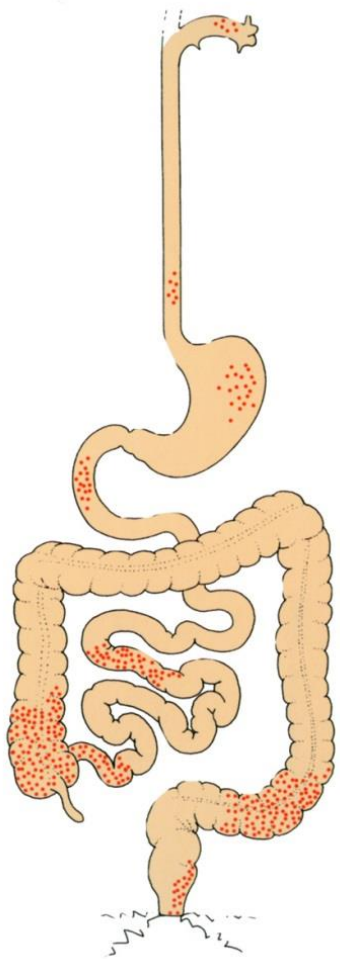
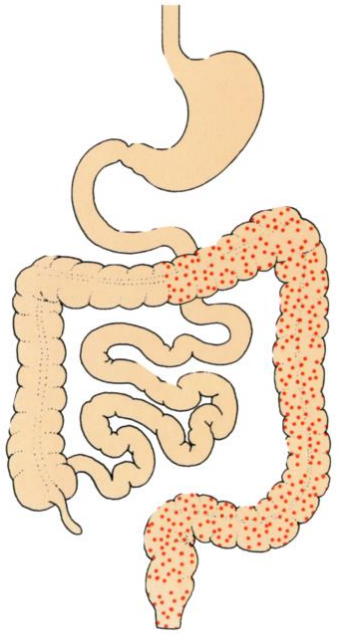
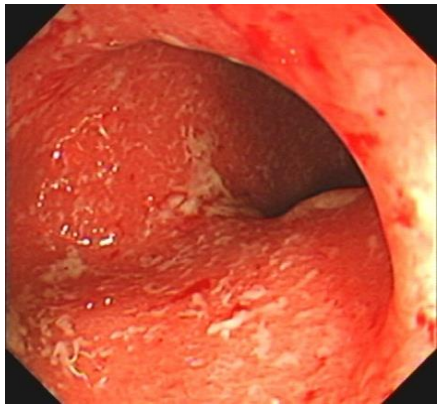
Crohn's disease (CD)





Ulcerative colitis (UC)





Increasing global burden of IBD

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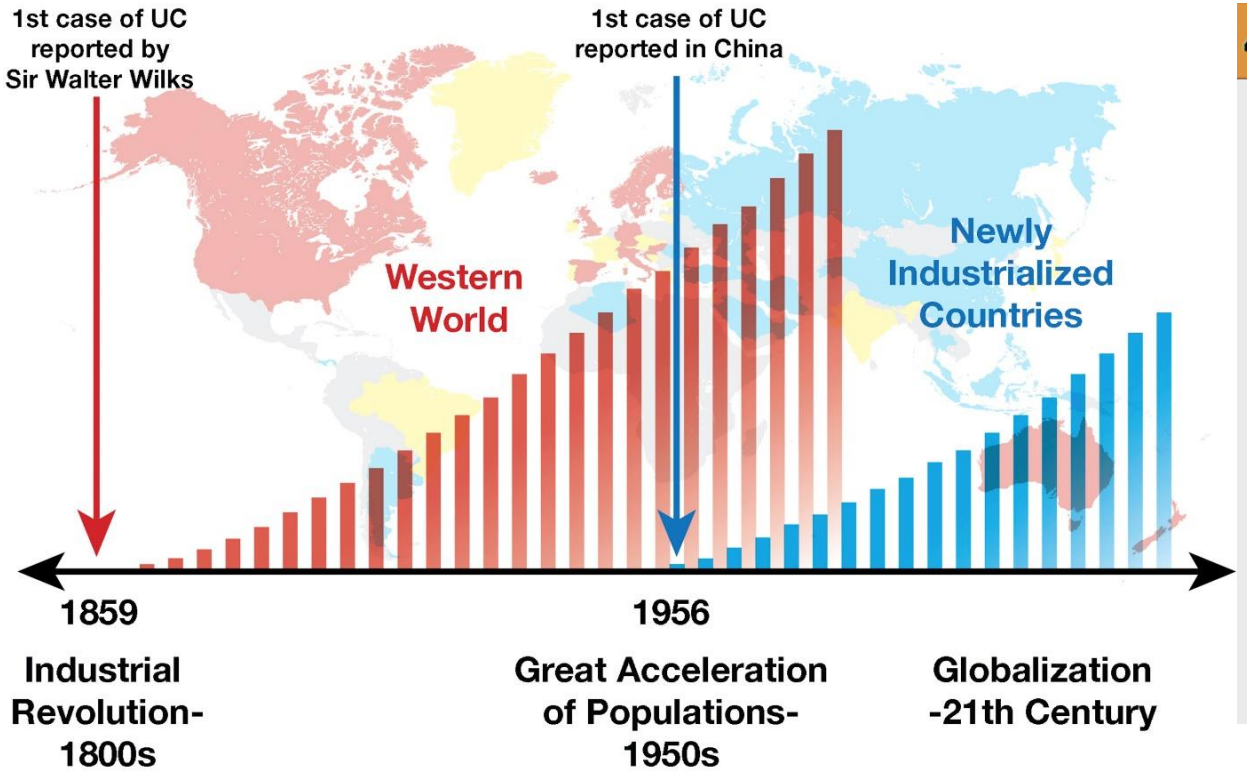
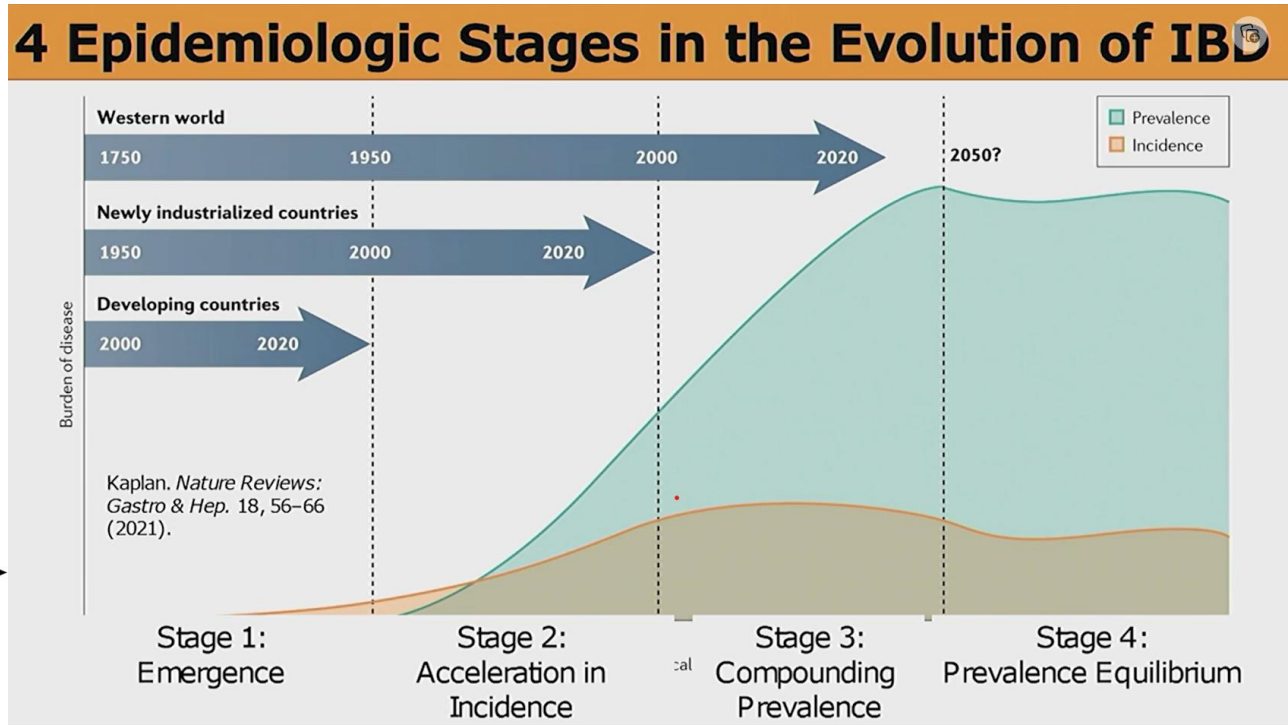
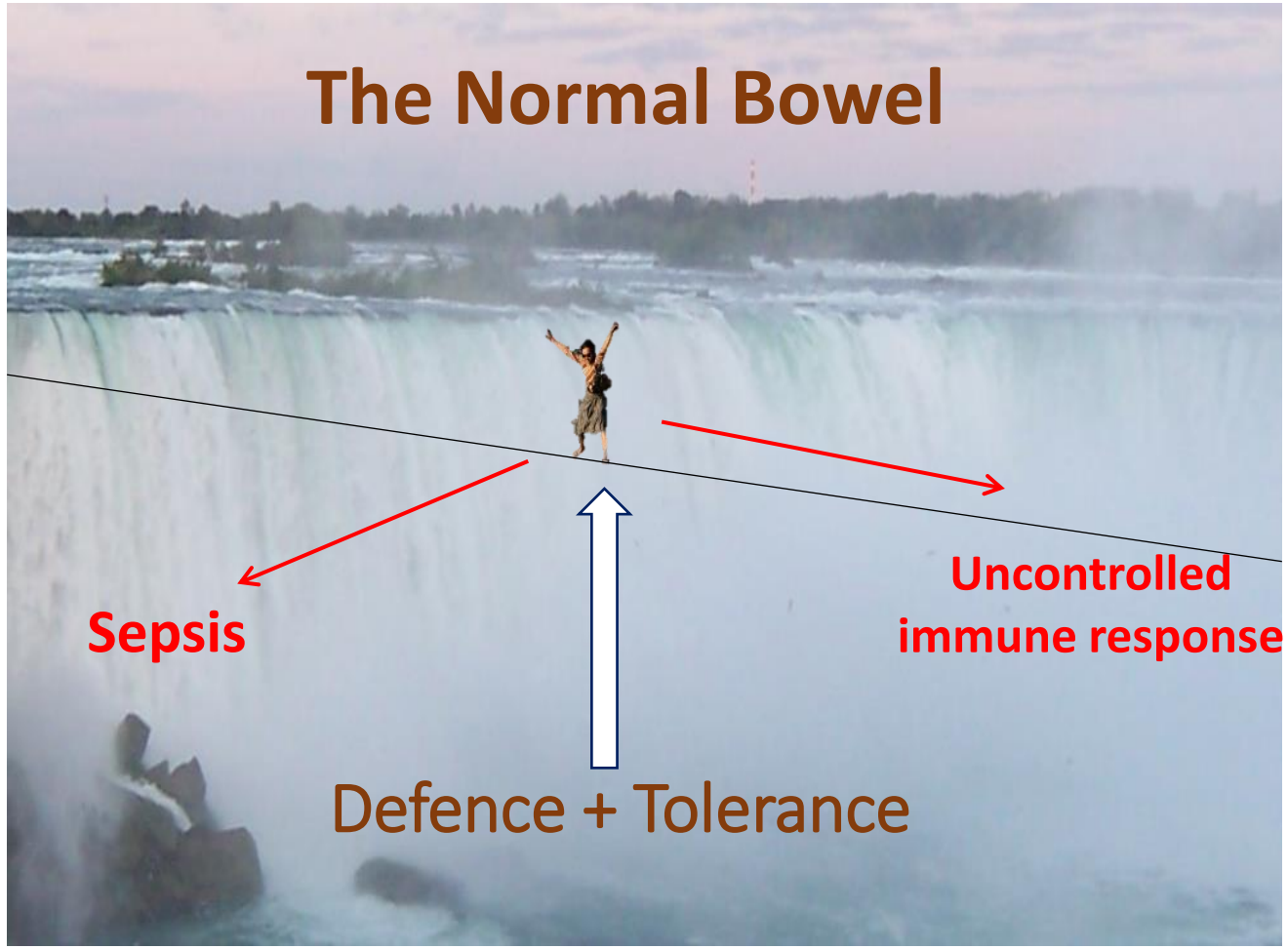




Kaplan. *Gastroenterology* 2017;152:313–321; Kaplan *Nature Rev Gas Hep* 2021;18:56-66

IBD: Pathogenesis



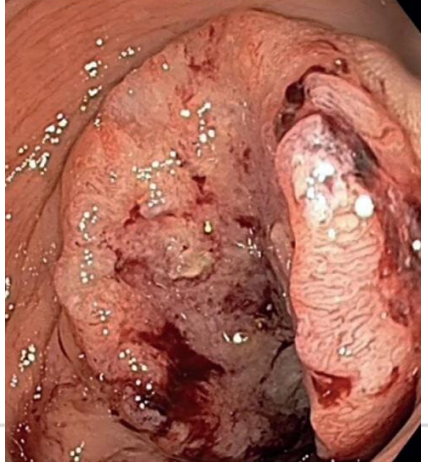
Dysregulated immune response

to intestinal microorganisms

in a genetically predisposed host

with a possible environmental trigger

Colorectal cancer



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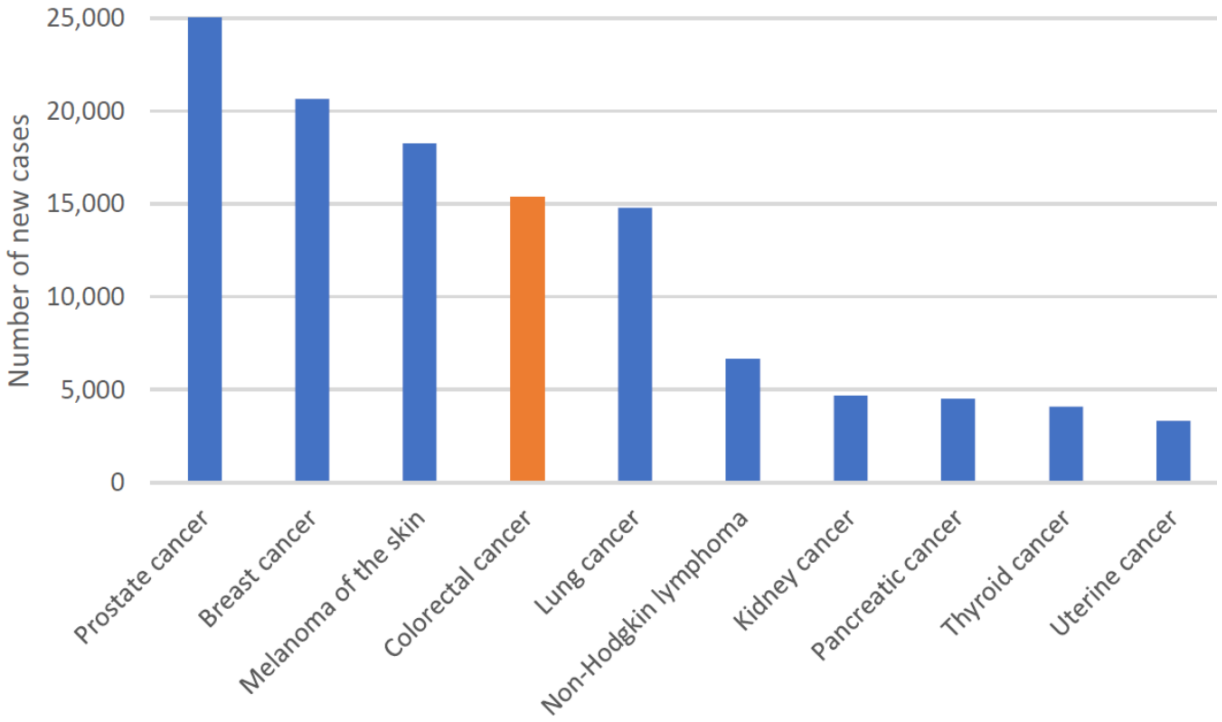

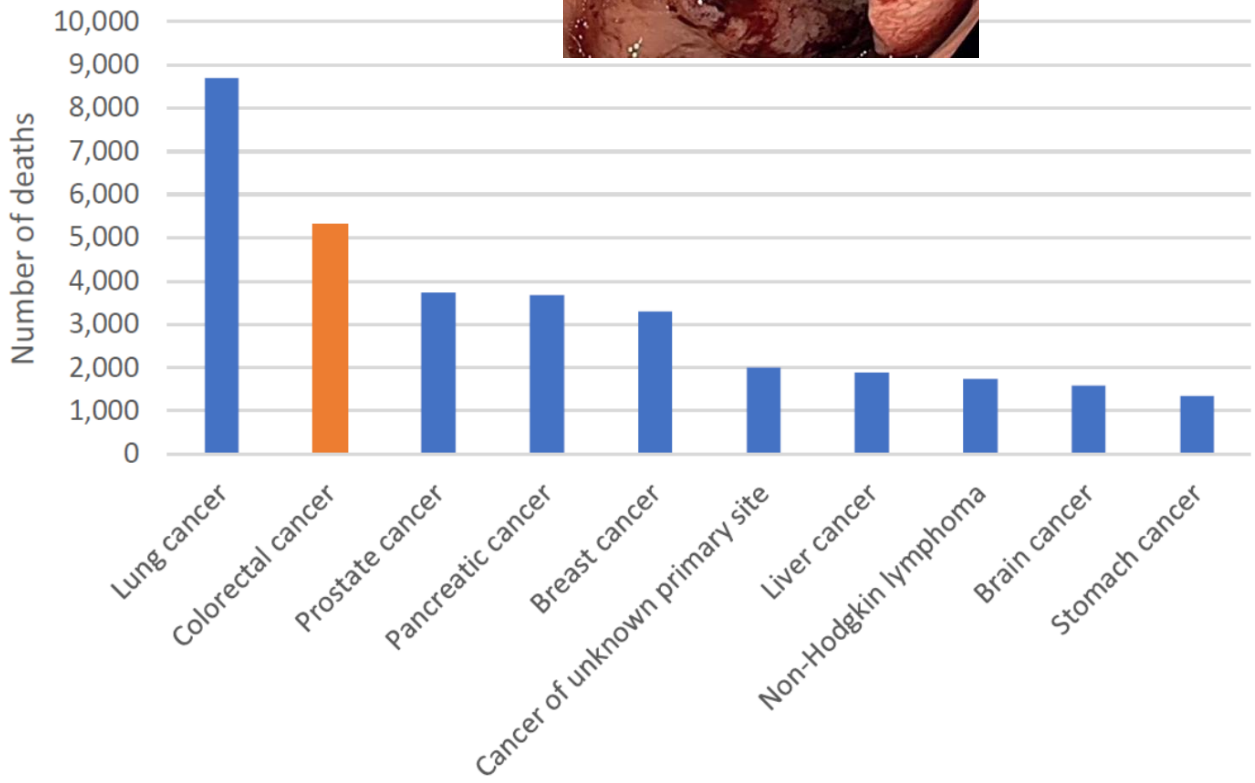

Figure 1. Estimated cancer incidence in Australia, 2023

Increasing incidence in younger adults, esp in Australia

Australian Institute of Health and Welfare. https://www.canceraustralia.gov.au/cancer-types/bowel-cancer/statistics; accessed 30/07/2024

Disorders of Gut-Brain Interaction (DGBIs)

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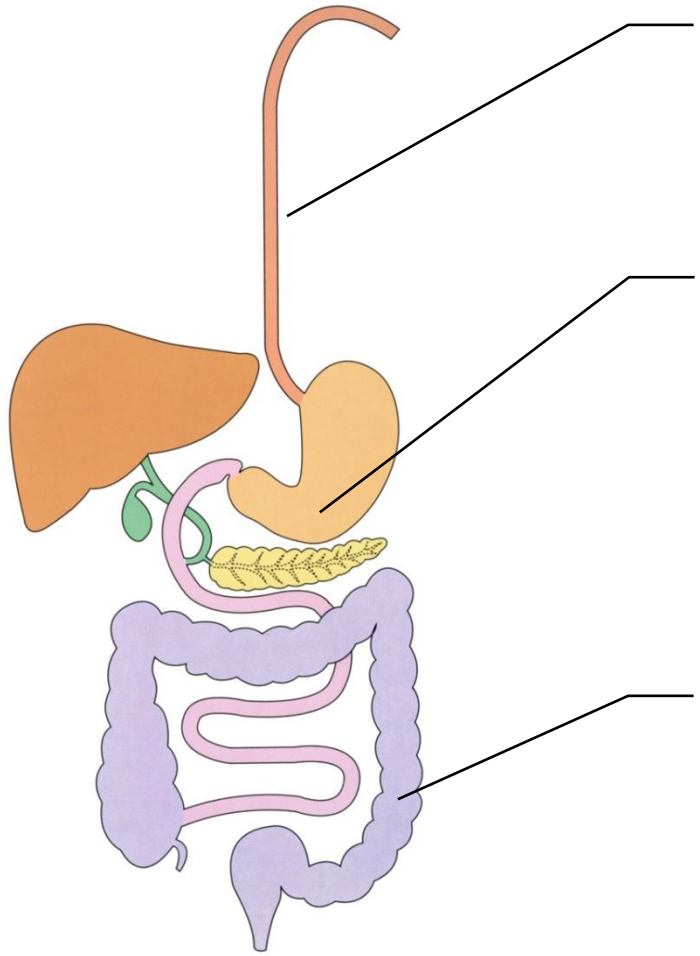

Functional heartburn, functional chest pain, reflux hypersensitivity syndrome

Functional dyspepsia, chronic idiopathic nausea, functional vomiting, cyclical vomiting, rumination syndrome, cannabinoid hyperemesis syndrome

Irritable bowel syndrome (IBS),
Functional constipation,
Functional diarrhoea,
Functional bloating,
Functional abdominal pain,
Functional incontinence,
Evacuatory disorders

Micro- and nanoplastics: GI exposure

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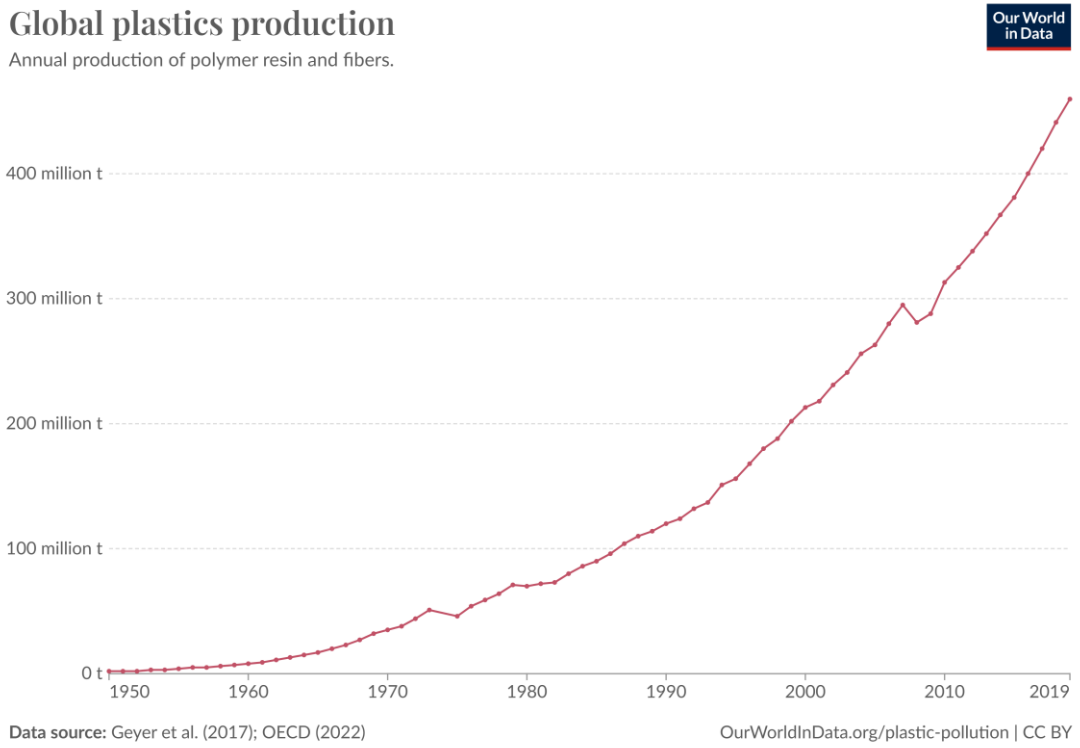
- Micro (1µm – 5 mm), nanoplastics (1nm – 1µm)
- Ingestion (or inhalation)

- Consumables and packaging
  - Table salt, tap water, and seafood
  - Packaged beverages (plastic bottled mineral water, beverage cartons)
    - Identical to the plastic polymers used to make the caps, bottle and lining of containers

- Consumption
  - Children – median 184 ng/day
  - Adults – median 583 ng/day
  - Overall, 22.5 mg over a lifetime (average life expectancy 83 years).



Karami. *Sci Rep.* 2017;7:46173; Rochman. *Sci Rep.* 2015;5:14340; Kosuth. PLoS One. 2018;13(4):e0194970. Schymanski. *Water Res*. 2018;129:154-62. OECD, Our World in Data https://ourworldindata.org/grapher/global-plastics-production accessed 05 Aug 2024

Absorption of micro- and nanoplastics

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- Emerging literature
- Exact amount ingested, metabolised, absorbed and then excreted in humans remains unclear
- In humans, absorption of MP <0.3%
  - Only particles < 150 µm in size able to cross the gut epithelium
- Faecal loss in 96-100% of participants
  - 20 microplastics (50 to 500 µm in size) per 10 g of human stool
  - 9 plastic types: most commonly polypropylene and polyethylene terephthalate

EFSA. *European Food Safety Authority Journal*. 2016;14(6); Zhang *Sci Total Environ*. 2021;767:144345. Schwabl *Ann. Intern. Med*., 171 (2019), pp. 453-457

Intestinal and Systemic deposition

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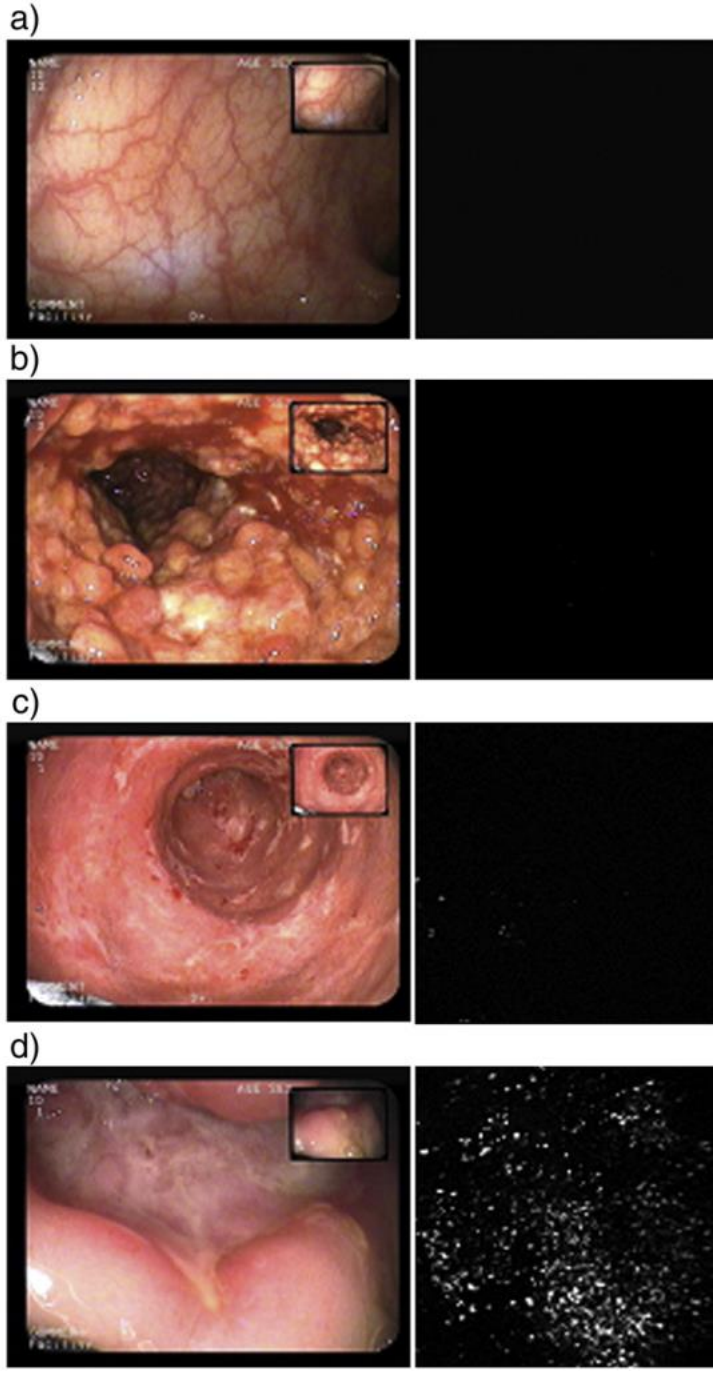
- Intestinal wall accumulation
  - 100% of colectomy specimens (n=11, undertaken for reasons including colon cancer, bleeding, perforation, trauma)
  - Presence of microplastics, predominantly larger in size (between 0.8 to 1.6 mm)
    - 90% polycarbonate, 50% polyamide and 40% polypropylene
- Human testes
- Cirrhotic liver

Ibrahim. *JGH Open.* 2021;5(1):116-21; Zhao. *Sci Total Environ*. 2023;877:162713; Horvatits. *EBioMedicine*. 2022;82:104147



Mucosal accumulation in inflammation

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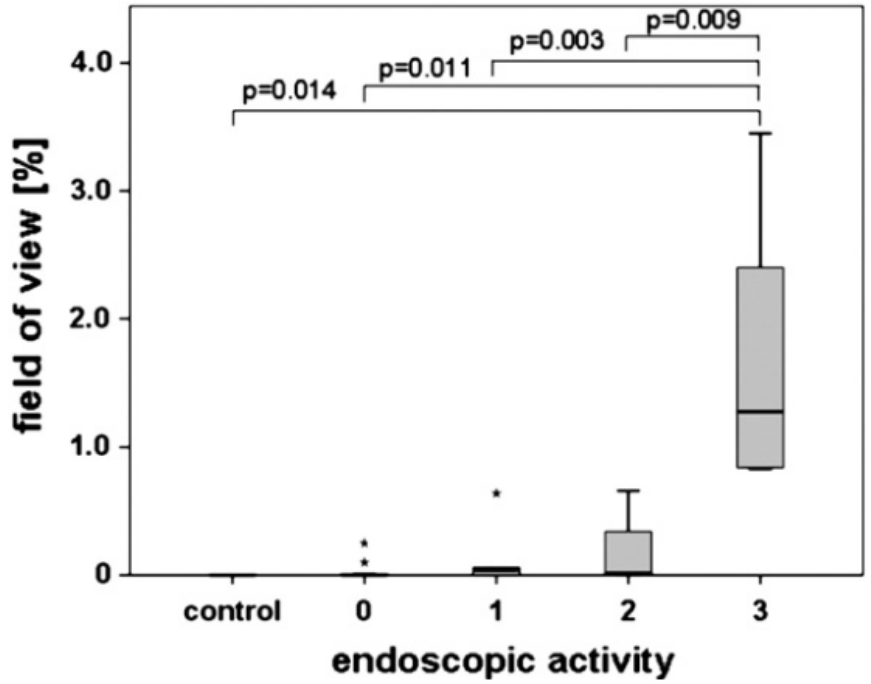

- Enema delivered microparticles accumulate in inflamed/ulcerated tissue more than normal
- Nanoparticles more likely to be absorbed across epithelium

Schmidt. *Journal of Controlled Release* 165 (2013) 139–145

Association with mucosal inflammation

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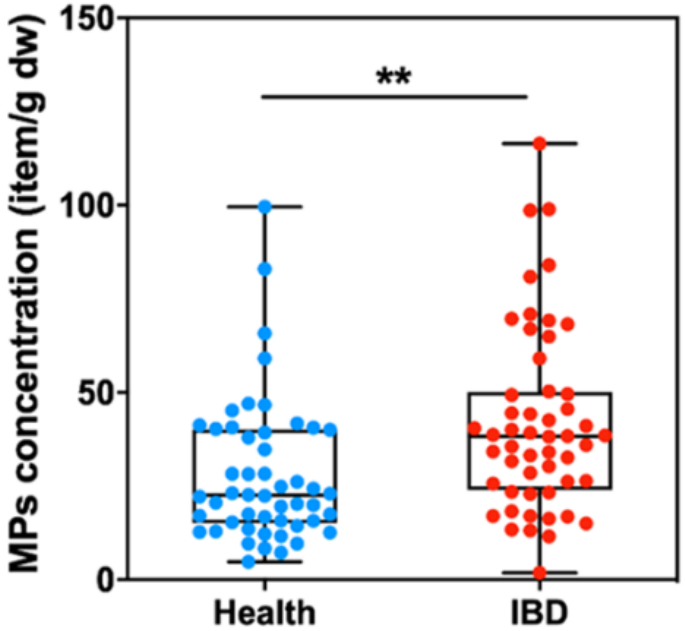

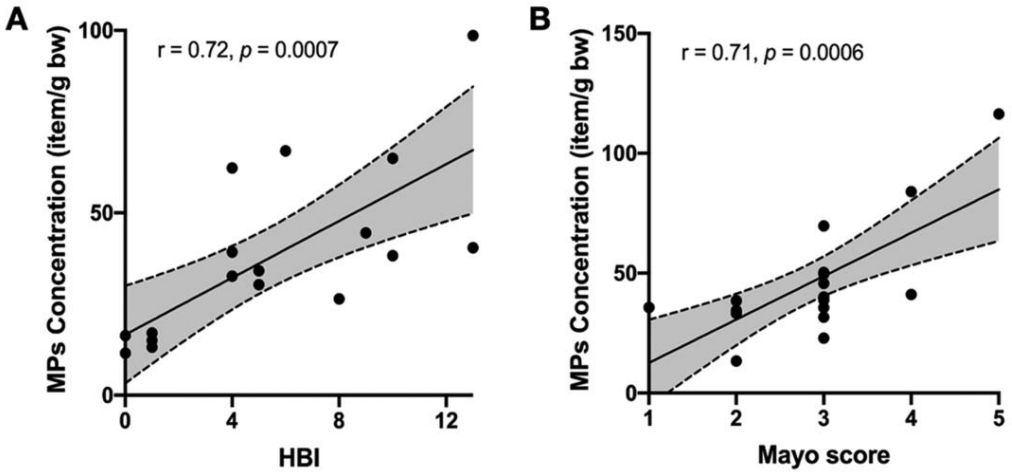

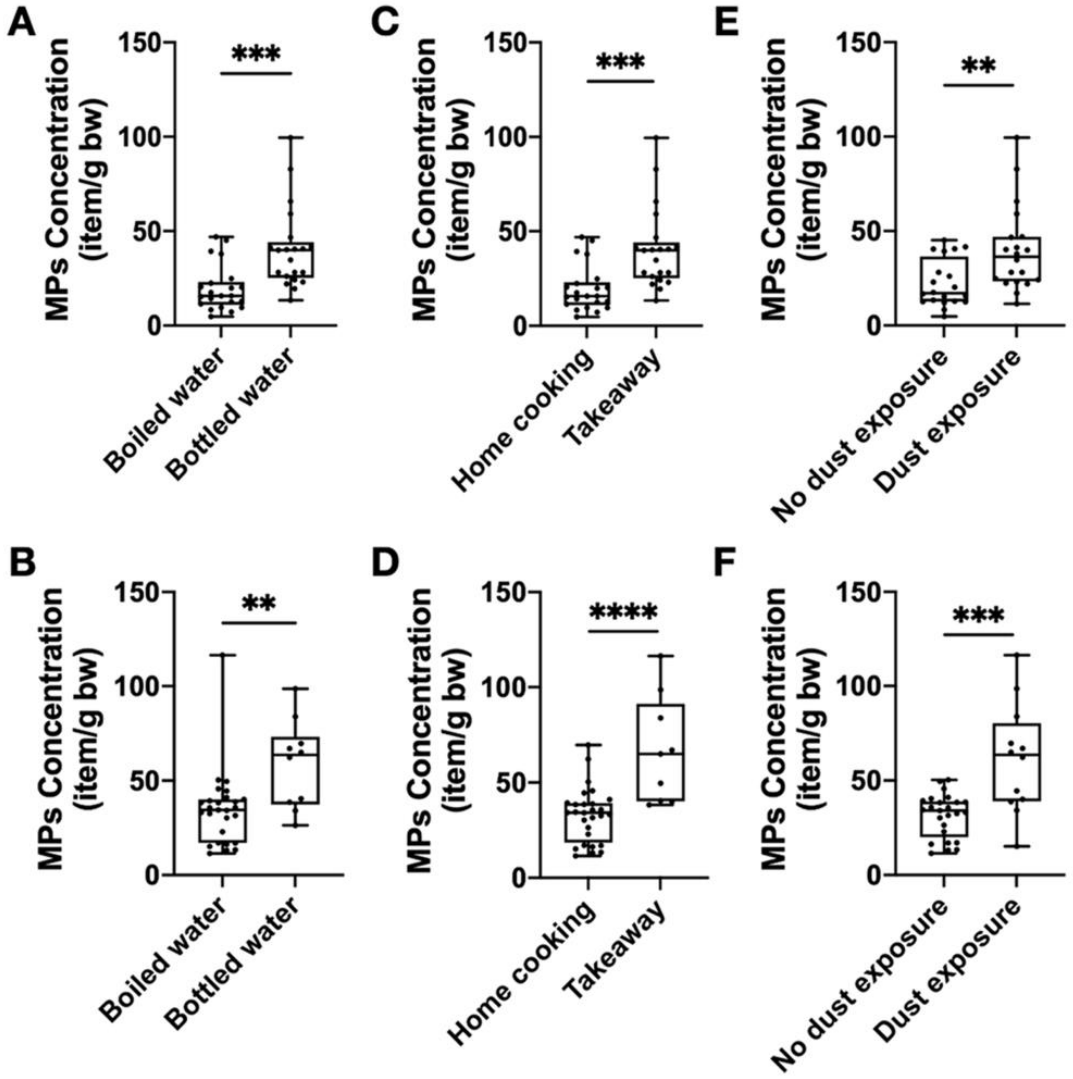

Yan. *Environ Sci Technol.* 2022;56(1):414-21.

Putative immunoregulatory mechanisms

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- Derived from murine studies
- Increased inflammatory signalling (IL-1β, IL-6, TNF-α) (Polystyrene)
- Alteration of innate protective factors
  - Decrease in gut mucin secretion following exposure to polystyrene MP;
  - Decrease in goblet cells;
  - Damage to colon tight junctions;
- Upregulation of pro-apoptotic markers eg Bax, cleaved caspase-9, cleaved caspase-3, with concurrent downregulation of anti-apoptosis factor Bcl-2
- Structural alterations
  - Decreased mucosa and muscle thickness
  - Disruption of villous architecture
- Conflicting data re microbiota modulation

Domenech. *Biomolecules.* 2021;11(10). Lin. *Chemosphere.* 2024;358:142275. Jia *Toxics*. 2023;11(2). Choi. *Lab Anim Res*. 2021;37(1):31. Lu. *Sci Total Environ*. 2018;631-632:449-58. Su *PLoS One*. 2024;19(6):e0304686.

Potential carcinogenesis

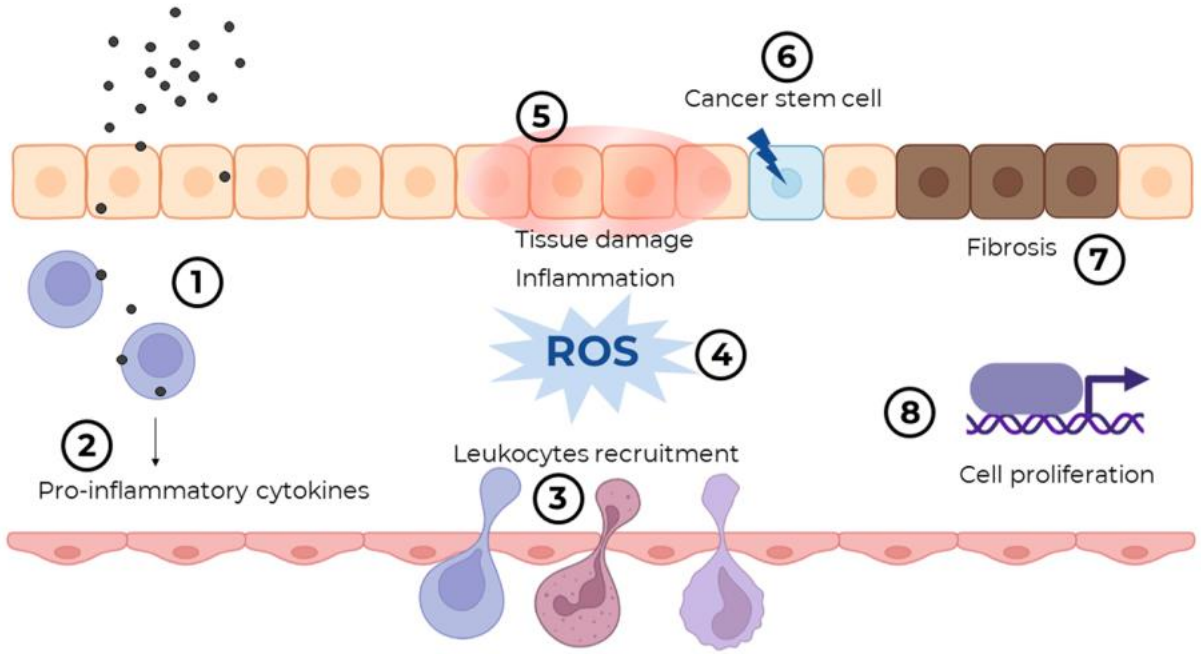
Groups	Number of microplastic particles (in per 1 g colon tissue)	Particle size (μm) (min.–max.)
Tumoral colon tissues ($n = 16$)	702.68 ± 504.26	1–613
Non-tumoral colon tissues ($n = 16$)	207.78 ± 154.12	1–743
Control tissues ($n = 15$)	218.28 ± 213.05	1–1299

- No excess cancer risk in workers employed in plastics manufacturing (1990s)

Cetin. *Environmental Chemistry Letters*. 2023;21(2):639-46. Lagast. *Occup Med*.45(2):69-74. Kim. *Theranostics*. 2022;12(7):3217-36

Potential carcinogenesis: mechanisms

- Increased inflammation;
- Alterations in gut innate defences (mucin) and dysbiosis;
- Generation of reactive oxygen species;
- Increased ASGR2 gene expression;
- Cell proliferation and migration;
- Decreased E-cadherin and increased N-cadherin.



Domenech. *Research-Reviews in Mutation Research* 791 (2023):108453. Lagast. *Occup Med*.45(2):69-74. Kim. *Theranostics*. 2022;12(7):3217-36

Conclusions

- Rapid increase in incidence and prevalence of multiple GI diseases and conditions
- Environmental factors remain incompletely elicited
- Increased micro- and nanoplastic exposure, association with GI accumulation and inflammation
- Biological plausibility from animal studies to date
- Further study regarding causality and role in pathogenesis of GI diseases warranted