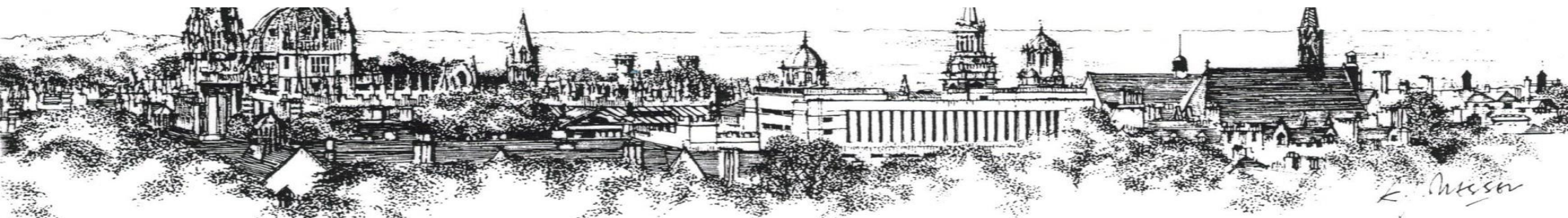


# Malignant Bowel Obstruction

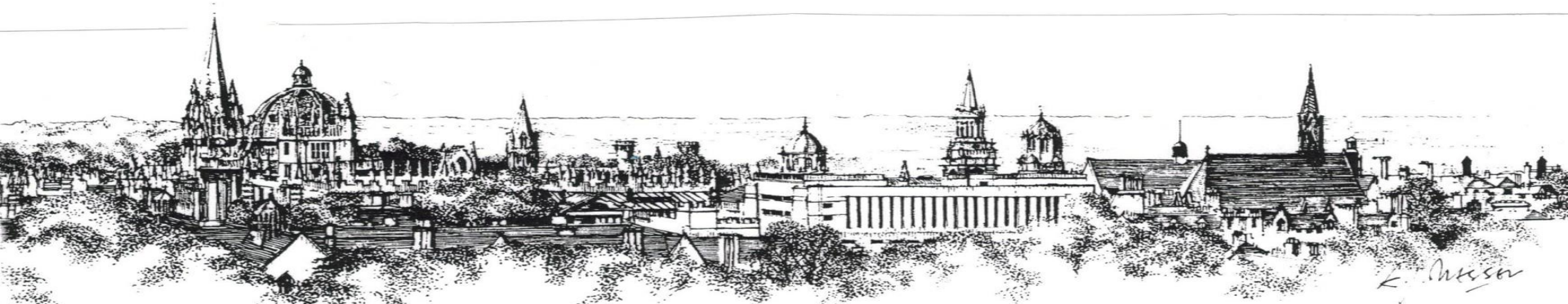
Dr Aoife Lowney

Consultant in Palliative Medicine

Oxford



1. An approach to management of malignant bowel obstruction (MBO)
2. The evidence base
3. New drugs/ Future considerations for management MBO



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# THE LANCET

Volume 326, Issue 8462, 2 November 1985, Pages 990-993

THE LANCET

"Under the direction of Sir  
Richard Doan, the journal  
of medicine, surgery, and  
general practice has been  
renewed from within."

Hospice Practice

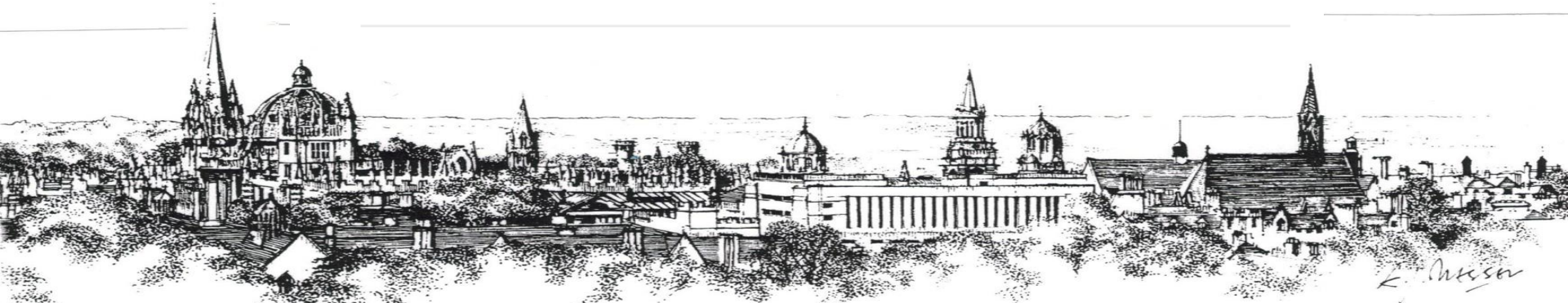
## MEDICAL MANAGEMENT OF INTESTINAL OBSTRUCTION IN PATIENTS WITH ADVANCED MALIGNANT DISEASE: A Clinical and Pathological Study

Mary Baines <sup>a, b</sup>, D.J. Oliver <sup>a, b</sup>, R.L. Carter <sup>a, b</sup>

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[https://doi.org/10.1016/S0140-6736\(85\)90534-3](https://doi.org/10.1016/S0140-6736(85)90534-3)

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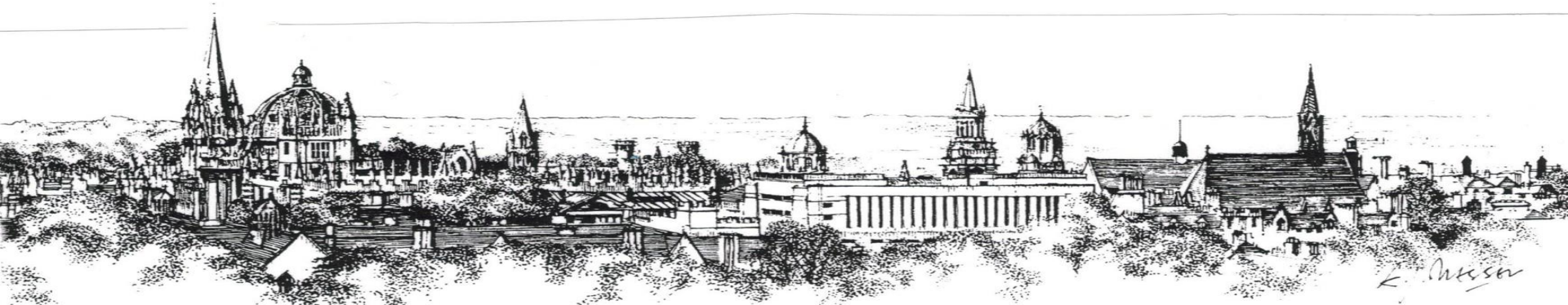


- GI Tract Function
  - To take in food/liquids, extract useful nutrients and expel waste
- Many enzymes, proteins, hormones, bacteria and muscles in a finely tuned balance
- Communicates with other organs
  - Brain
  - Liver
  - Gallbladder/Pancreas

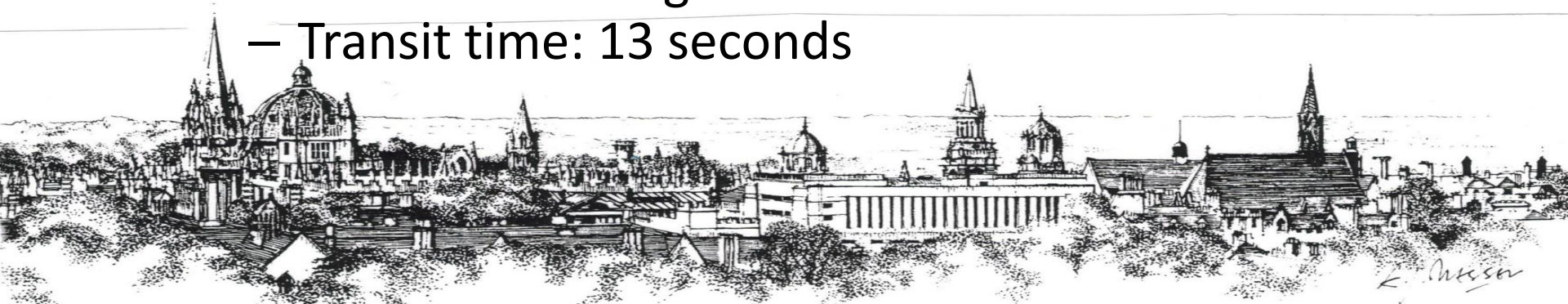




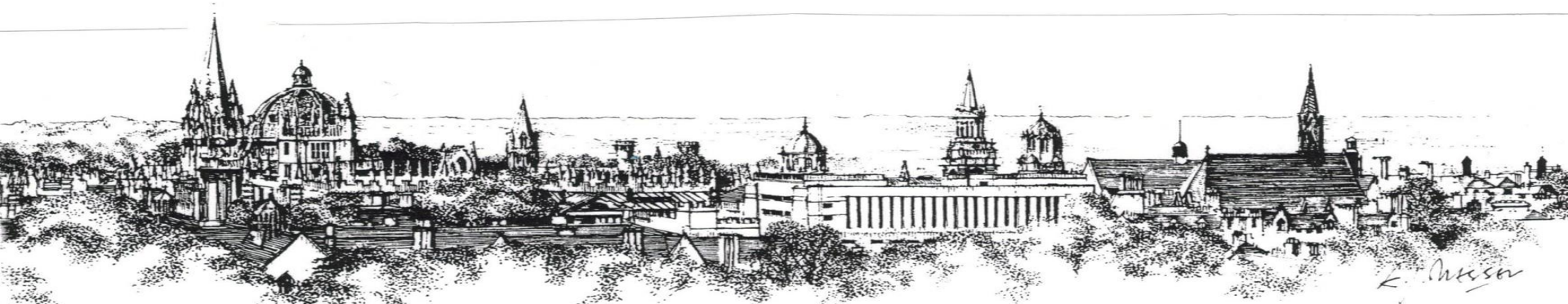
# Tour of the GI Tract



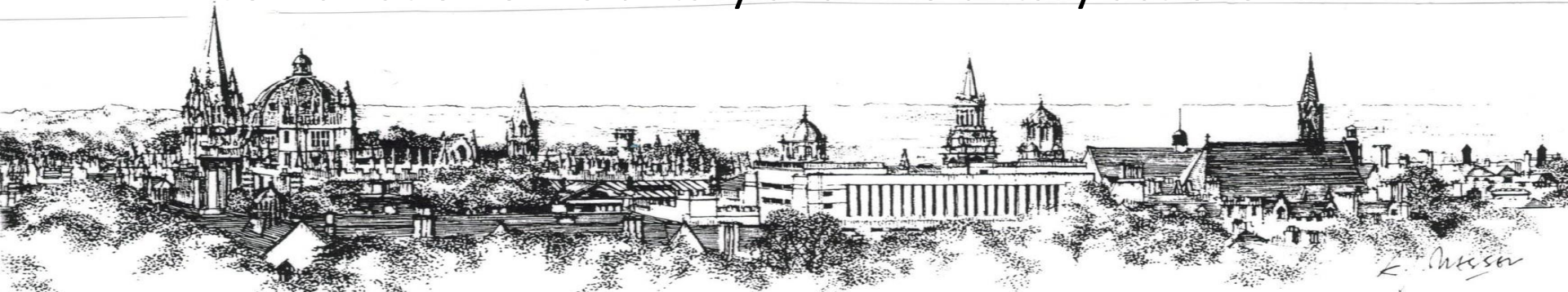
- Dentition
  - Initial break down of food
- Oropharynx
  - Saliva contains digestive enzymes that begin digestive process
- Oesophagus
  - First of muscular tubular structures
  - About 30cm long
  - Transit time: 13 seconds



- Stomach/Duodenal bulb
  - Stomach through to second portion of duodenum also approx 30cm
  - Strong muscular organ that mixes and threshes food
  - Acids to dissolve food and continue digestion
  - Transit time: 2-4 hours
- Small Intestine
  - 6-7.3m
  - Food moves via wave like contractions – much like a worm
  - Transit 1-3 hours
  - The “waste” is still liquid as it is delivered to....



- Large Bowel
  - Ileocecal valve to anal sphincter 1.2m
  - Extracts water/lubricates stool
  - Material is transported via segmenting contractions and propagating contractions
    - By 24 hours, stool has made it to transverse colon
    - By 48 hours, stool has made it to descending colon and sigmoid colon
- Rectum and Anus--The End!
  - Defecation is evacuation of faecal material from rectum
  - Combination of voluntary and involuntary actions





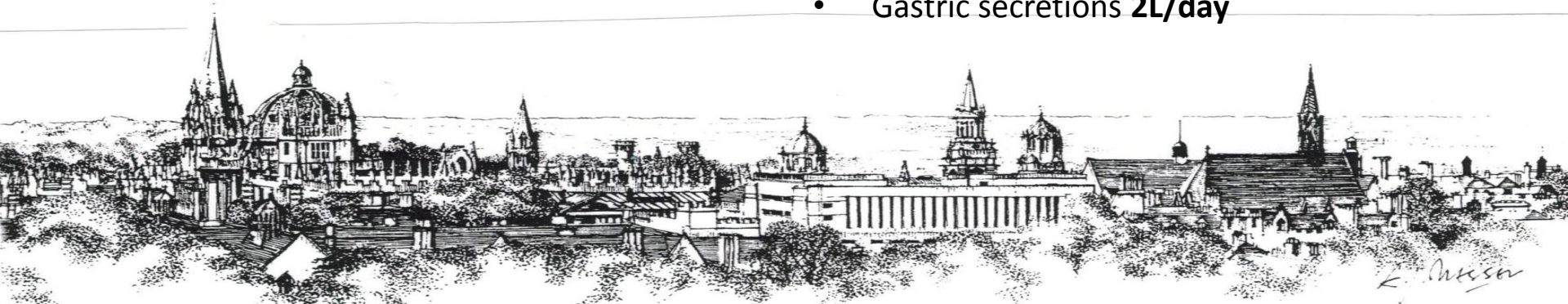
# Motility Control

## Intestinal Reflexes

- Gastroileal/Gastrocolic
  - increased gastric activity causes increased motility of the terminal ileum/colon
- Ileocolic
  - distension of the ileum causes a decrease in gastric motility
- Intestino-intestinal
  - overdistension of one intestinal segment causes relaxation throughout the rest of the intestine

## Hormones/Digestive Juices

- Cholecystokinin
- Secretin
- Motilin
- Somatostatin
- Vasointestinal Peptide
- Digestive enzymes from salivary glands, pancreas, gallbladder, small intestine
- Hydrochloric acid
- Bile (liver via GB)
- Mucus
- Gastric secretions **2L/day**



- Composition of faeces

- Water 73%

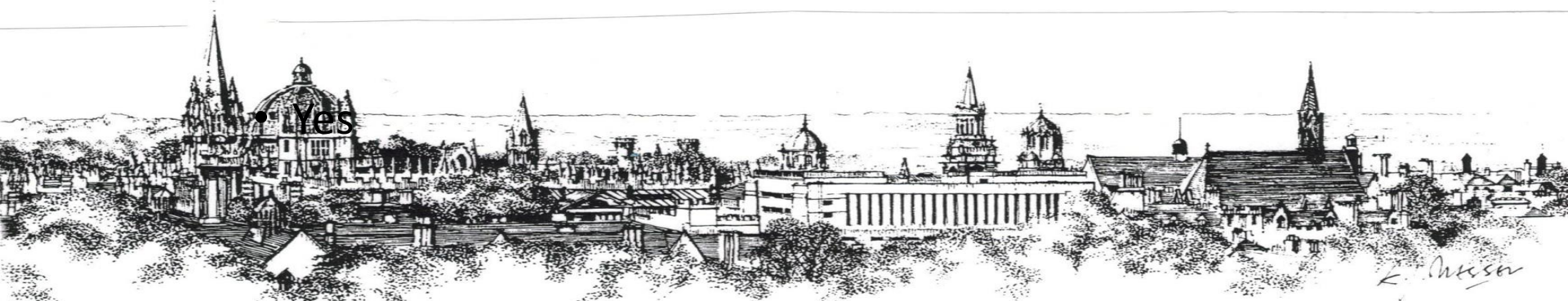
- Remainder:

- 1/3 dead bacteria
    - 1/3 residue (fibre)
    - 1/3 sloughed cells from intestine/bilirubin/fats/salts

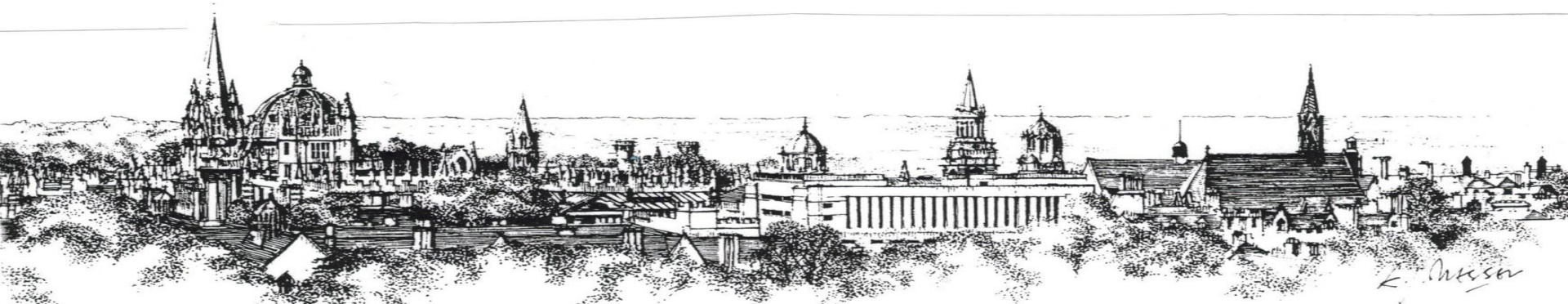


- If you don't eat will you still make poo?

- Yes

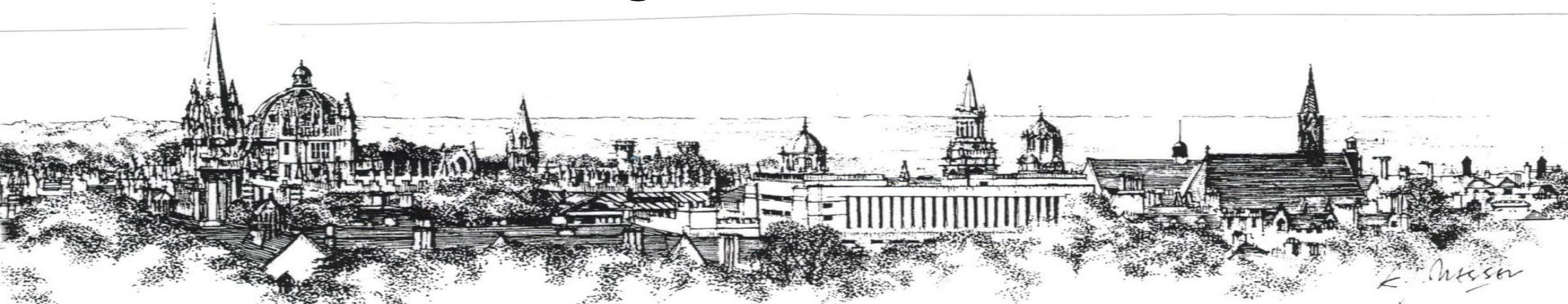


- The term “bowel obstruction” covers a range of clinical situations
- Permanent or intermittent; complete or partial; acute or chronic and can occur at any point along the gastro intestinal tract
- Many mechanisms; often not a single problem



# How common a problem is it?

- Common and distressing outcome in patients with abdominal or pelvic cancer
  - 5.5 to 42% ovarian cancer
  - 4.4% to 24% colorectal cancer
- Small bowel > large bowel 61% v 33%





- **Mechanical obstruction**

- Extrinsic occlusion

- From extra-luminal primary tumor or met, mesenteric and/or omental mets, adhesions, post-radiation fibrosis

- Intra-luminal occlusion

- Polypoidal lesions, narrowing due to disseminated disease

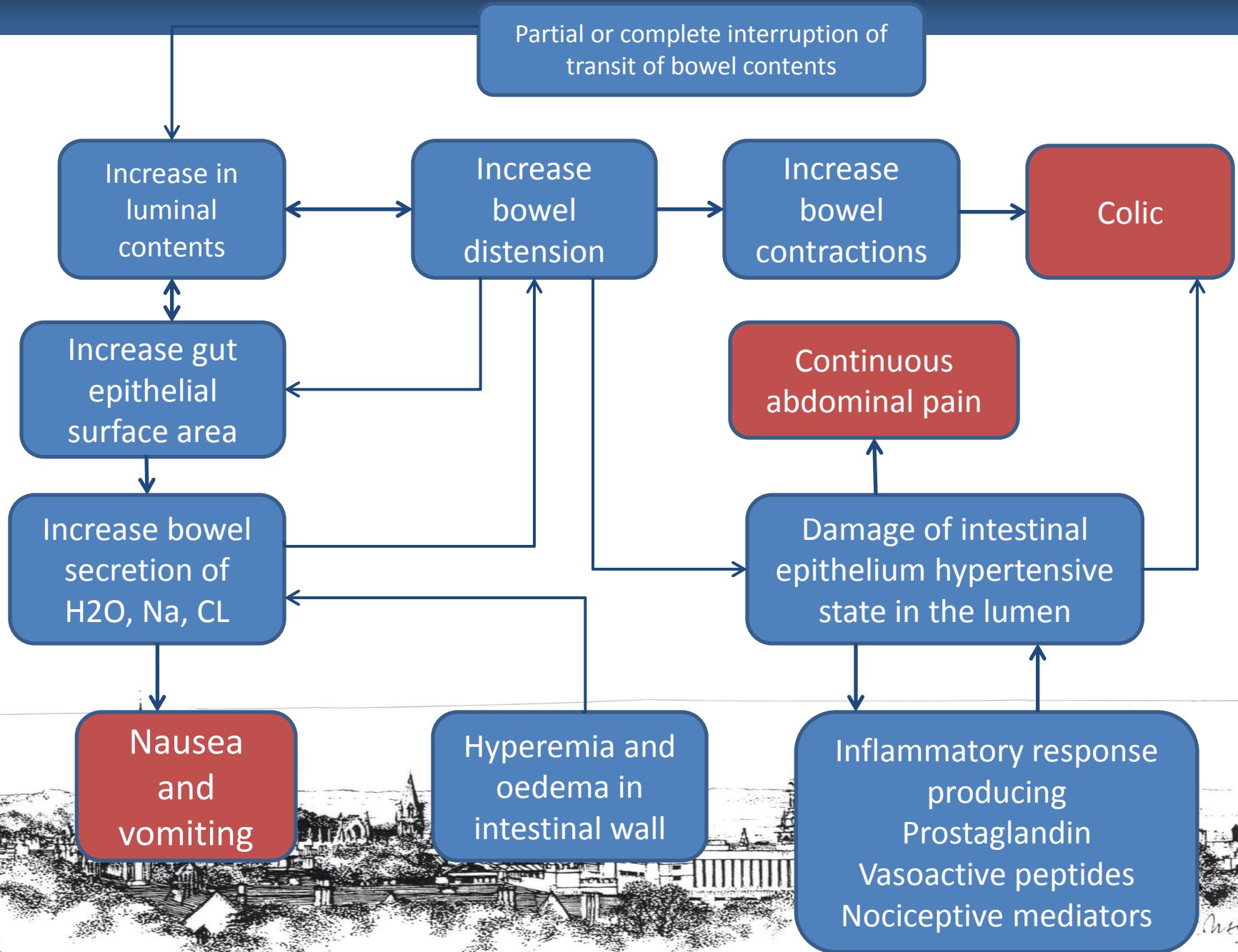
- Intramural disease

- Including intestinal linitis plastica, infiltration of intestinal musculature, inflammation

- **Functional obstruction**

- Motility disorders

- Tumour infiltration of enteric nervous system, malignant involvement of coeliac plexus, paraneoplastic neuropathy (particularly in lung ca), drugs....

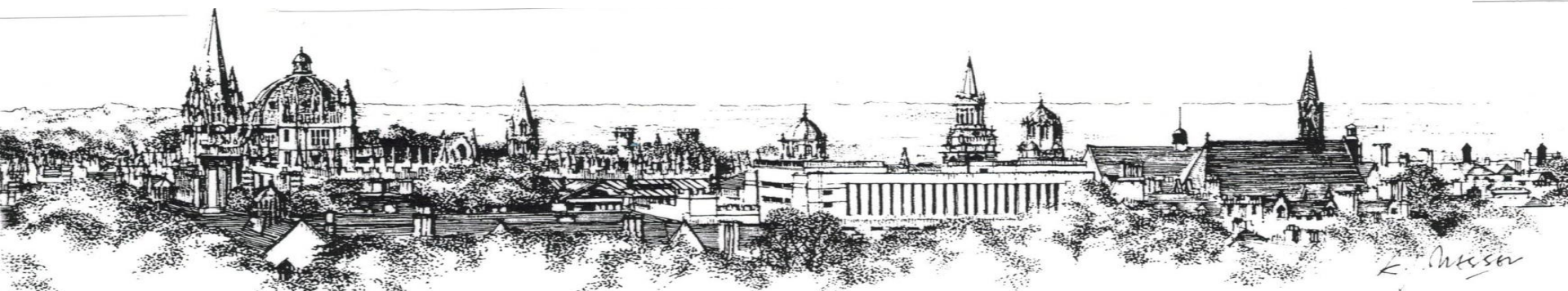


*Original Article*

# Malignant Bowel Obstruction: Natural History of a Heterogeneous Patient Population Followed Prospectively Over Two Years

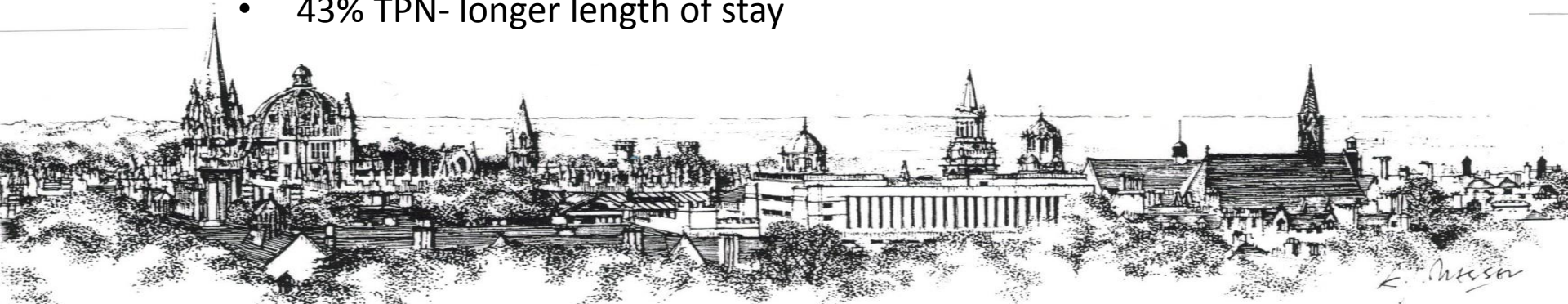
Anita Chakraborty, MD, Debbie Selby, MD, Kate Gardiner, BSc,  
Jeff Myers, MD, Veronika Moravan, BSc, and Frances Wright, MD

*Department of Palliative Medicine (A.C., D.S., K.G., J.M.) and Division of General Surgery (F.W.), Sunnybrook Health Sciences Centre; and Applied Statistician (V.M.), Toronto, Ontario, Canada*



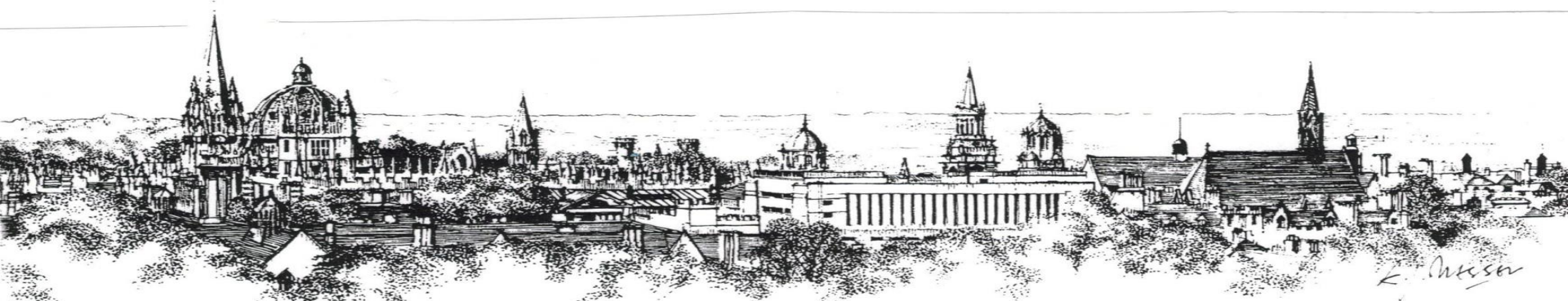
# Natural History

- 35 patients
- 2 years prospectively followed
- 1/2 had NGT
- 1/3 had surgery (Only operated if ecog 0-2)
- 1/4 had venting gastrostomy
- Only 1 was ecog 4
- 2 surgical patients had ascites and one had both carcinomatosis and ascites
- 43% offered chemo and 37% had it
- 43% TPN- longer length of stay





- Most significant factor affecting survival is ECOG performance status preceding obstruction.
  - Median survival:
    - ECOG 0-1: 222 days
    - ECOG 2: 63 days
    - ECOG 3-4: 27 days
- Other predictors of poor prognosis
  - low albumin, ascites, heavy tumour burden, aggressive disease, extensive previous treatment.



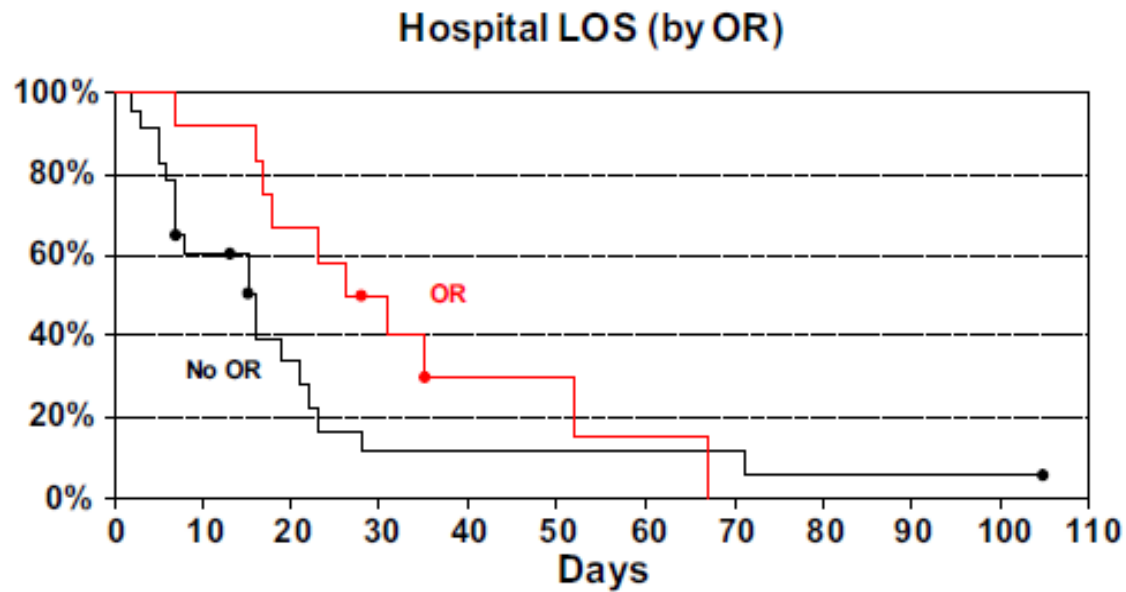
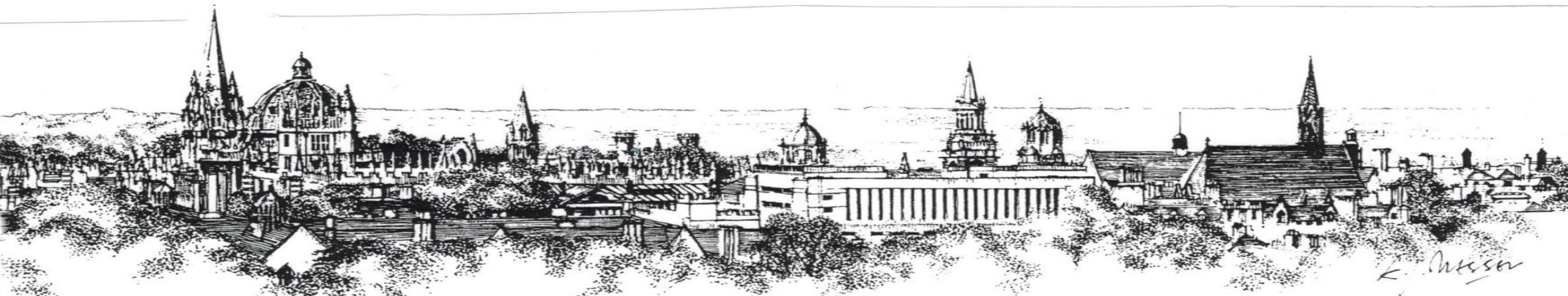
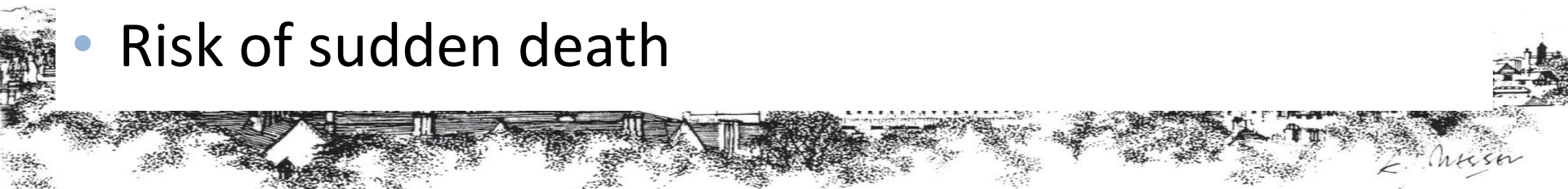


Fig. 2. Kaplan-Meier curves of hospital LOS by operative intervention.

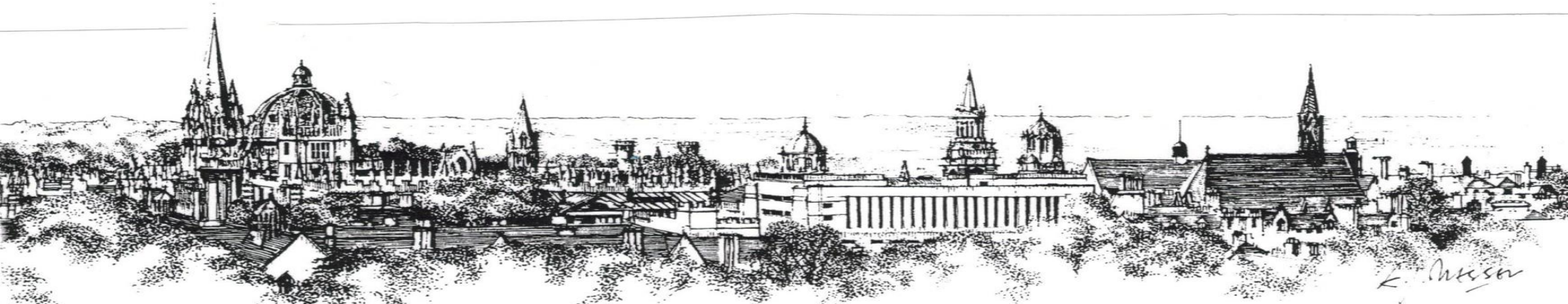


- Dynamic process
- Spontaneous resolution in as many as 40% medically managed cases
- Pts can live with partial bowel obstruction for some months, equates to gut failure
  - Psycho-social impact can be profound; inability to eat
  - TPN may impact on this ..
- Risk of sudden death

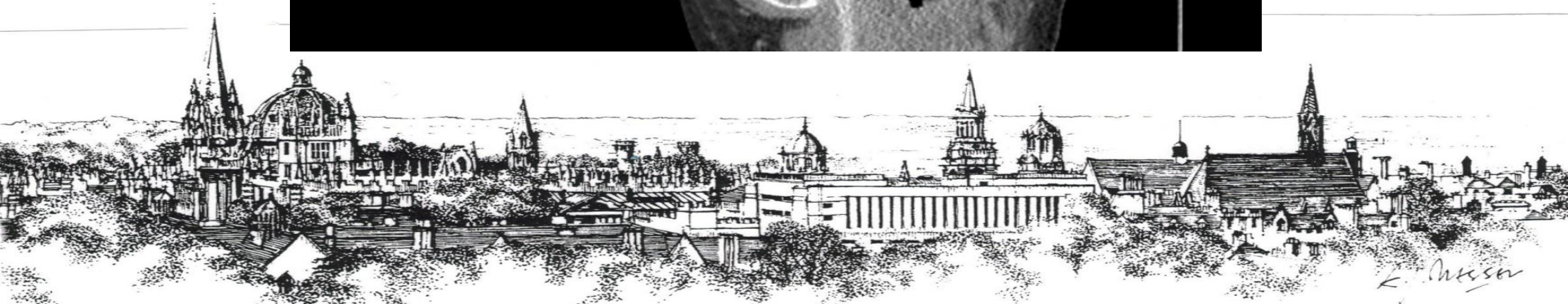


- Presentation

- Small bowel/high obstruction - likely to have vomiting and abdominal colic.
- Large bowel/low small bowel obstruction - likely to have the symptoms of abdominal distension and constipation







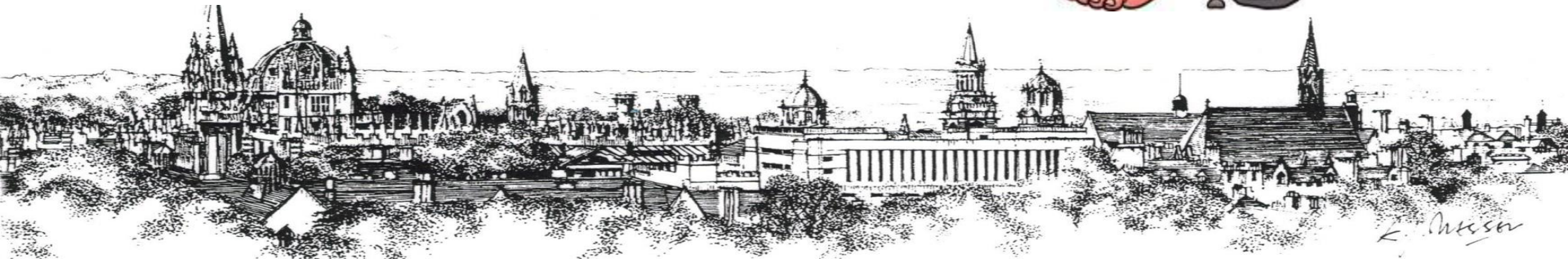
- **Nausea**
  - Mechanoreceptors triggered by local distention → vagus and splanchnic nerves to chemoreceptor trigger zone
- **Vomiting**
  - Following nausea or without warning
  - Faecalant
- **Obstipation**
  - Lack of flatus or stool suggests complete obstruction
  - Can also have liquefaction of stool by intestinal bacteria
- **Abdominal pain**
  - Colicky/waves/back pain
  - Localized pain worse with movement/ palpation suggests peritonitis
- **Abdominal distension**
  - From bowel distension +/- ascites



# Examination/Investigations

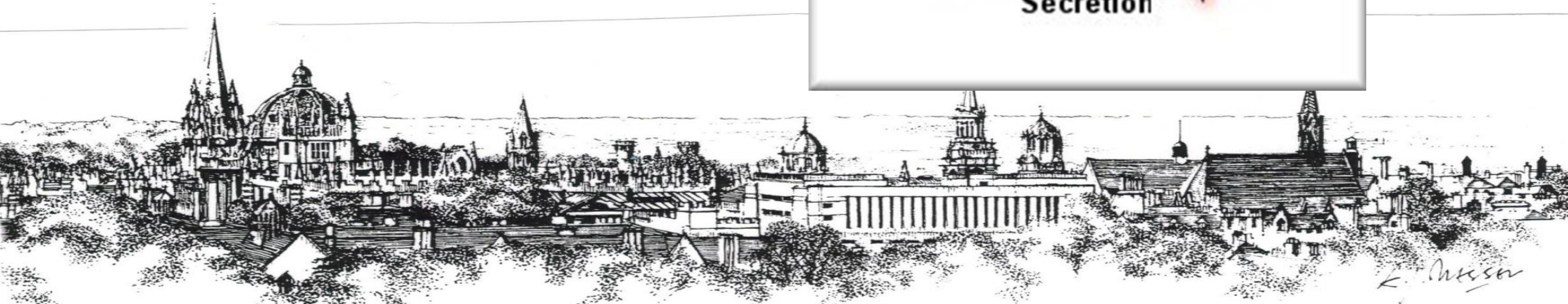
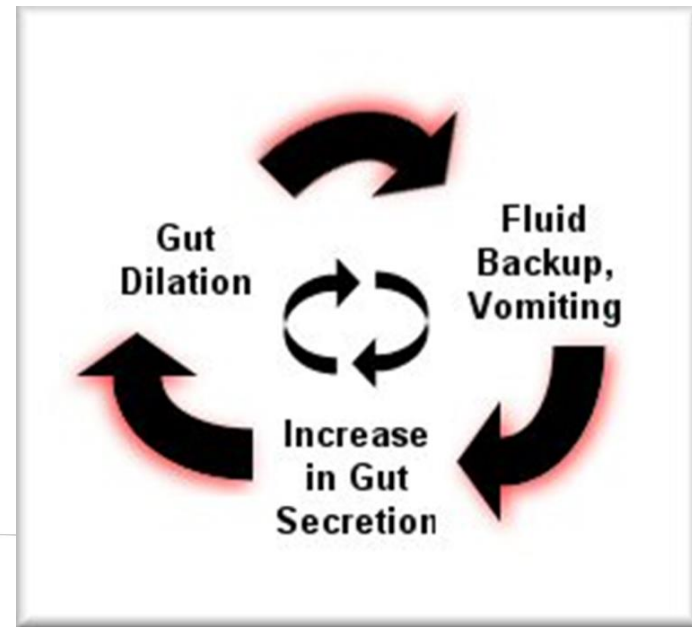
- Abdominal distension
  - Resonant to percussion (unless large volume ascites/high obstruction)
- Abnormal bowel sounds
  - Tinkling/quiet
- **PR**
  - May be full or if distended, may suggest stool higher up
- **AXR**
  - Dilated loops/ Faecal loading
- **CT scan** is the gold standard for diagnosis
  - Gastrograffin can sometimes help to clear an obstruction.....
  - Can identify presence and degree of obstruction
  - Can determine the pathological process(es)
    - 93% Se, 100% Sp, 94% accuracy in determining cause
    - *Carcinomatosis may be missed*. Accuracy for lesions <0.5cm is 20%.

- If the lumen of the gastrointestinal tract is occluded, fluid secreted by the bowel wall accumulates within the lumen. This results in bowel distention and stimulates release of further fluid from the gastrointestinal tract.
- This can be helpful for a food bolus but won't 'wash away' a tumour.

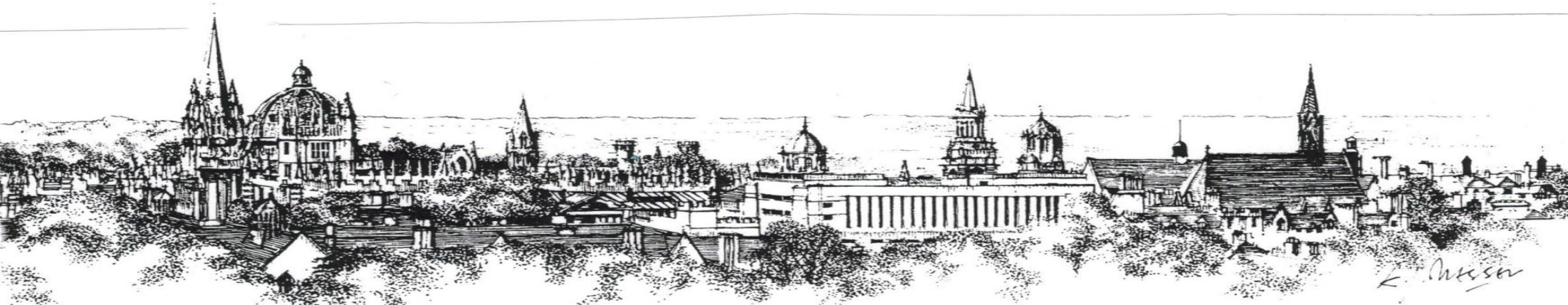




- The usual balance between fluid absorption and secretion shifts to secretion in MBO
- break the cycle



# Management

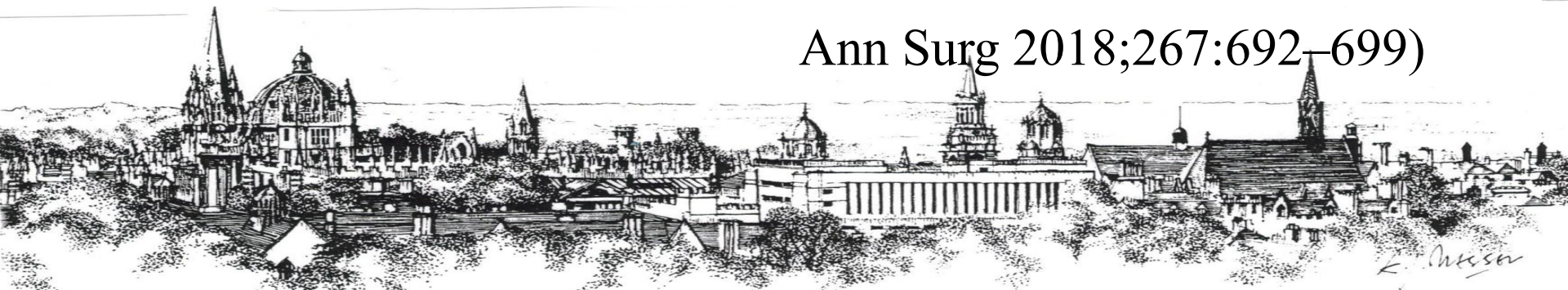


# Survival, Healthcare Utilization, and End-of-life Care Among Older Adults With Malignancy-associated Bowel Obstruction

## *Comparative Study of Surgery, Venting Gastrostomy, or Medical Management*

Elizabeth J. Lilley, MD, MPH,<sup>\*†</sup> John W. Scott, MD, MPH,<sup>\*‡</sup> Joel E. Goldberg, MD, MPH,<sup>‡</sup>  
Christy E. Cauley, MD, MPH,<sup>§¶</sup> Jennifer S. Temel, MD,<sup>¶</sup> Andrew S. Epstein, MD,<sup>||</sup> Stuart R. Lipsitz, ScD,<sup>\*</sup>  
Brittany L. Smalls, PhD, MHSA,<sup>\*\*</sup> Adil H. Haider, MD, MPH,<sup>\*‡</sup> Angela M. Bader, MD, MPH,<sup>\*††</sup>  
Joel S. Weissman, PhD,<sup>\*</sup> and Zara Cooper, MD, MSc<sup>\*‡§</sup>

Ann Surg 2018;267:692–699)



- 3500 patients
- Stage 4 disease
- Nonetheless, fewer than 5% had palliative care consultation.
- Patients treated with surgery at their first MBO admission had the longest survival.

Ann Surg 2018;267:692–699)



*Interser*



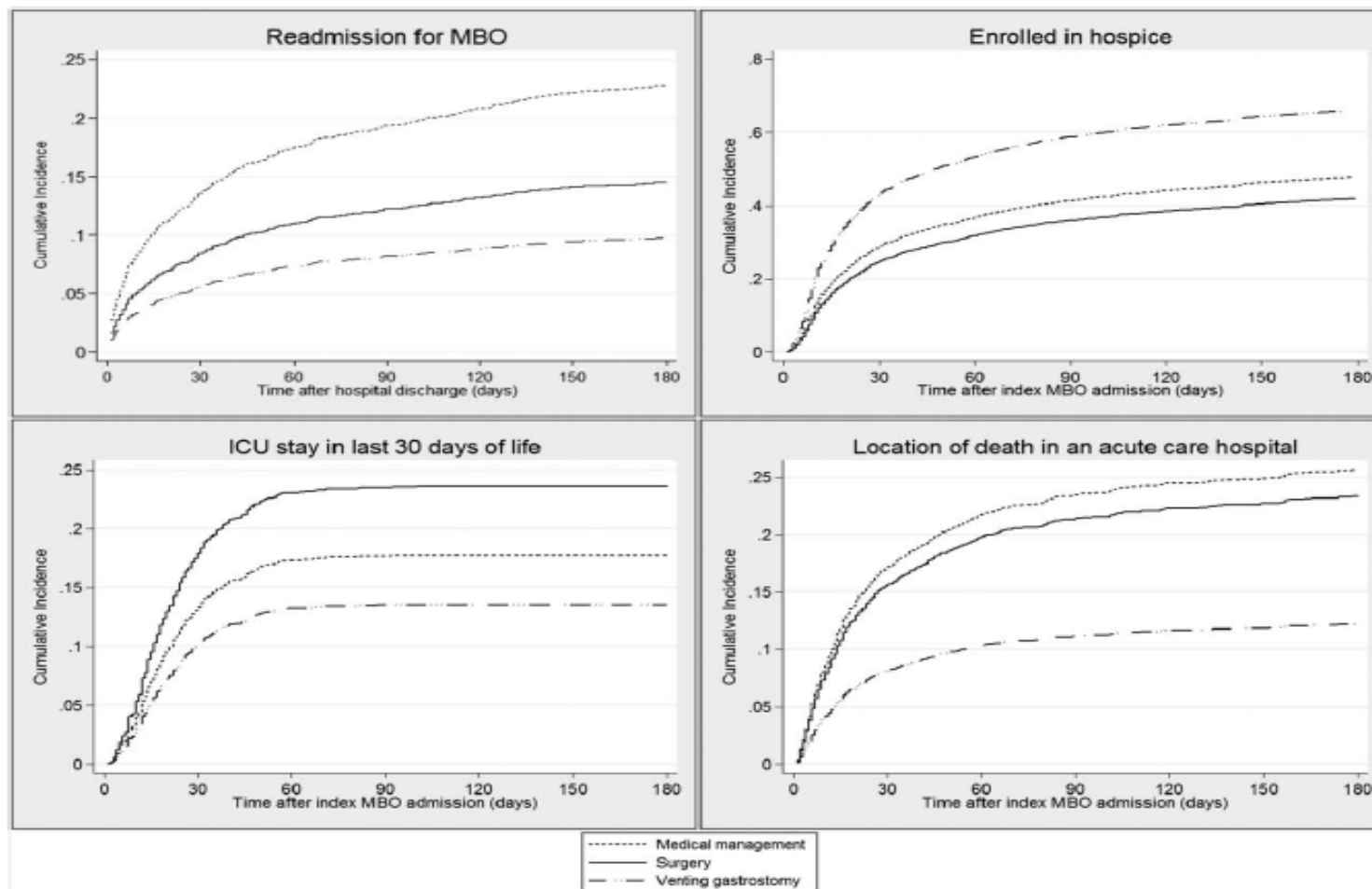
- Surgical options should be considered for all patients with MBO
  - High perioperative mortality rate (10%–20%) and post-op complication rate (20%–40%)
  - Not definitive: potential for re-obstruction
  - Risk of spending a lot of time in hospital/not where they wish to be...
- Remember MBO can spontaneously resolve
  - Might have 'time' to consider approach and not need to jump to surgery

*L. M. M. M.*

**FIGURE 2.** Survival after date of admission for the first malignancy-associated bowel obstruction admission occurring after cancer diagnosis.

### Limitations

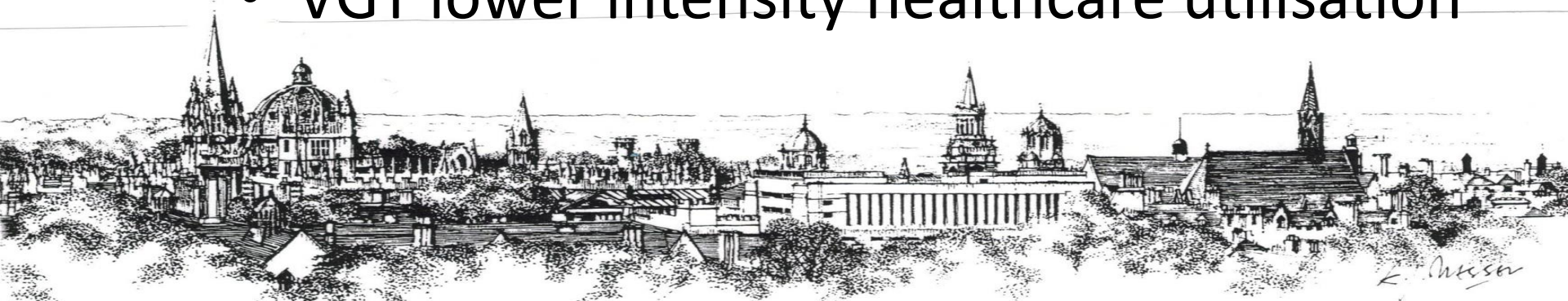
The present study had several important limitations. This study was retrospective and is limited by the unavailability of



**FIGURE 3.** Cumulative incidence estimates of malignancy-associated bowel obstruction readmission and end-of-life outcomes based upon treatment for malignancy-associated bowel obstruction.

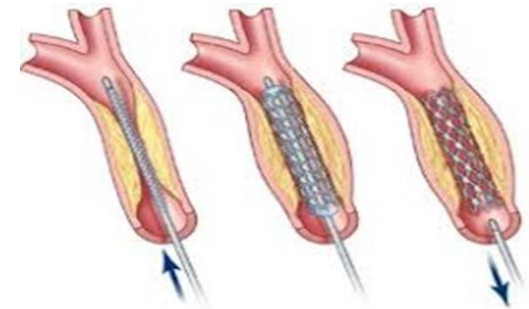
# Medical v Surgery v VGT

- MBO happens in the last months of life
- Patients treated with sx had longest survival
- Medical management associated with highest rate of re-admission
- VGT lower intensity healthcare utilisation



- Relative contraindications:
  - poor performance status
  - widespread disease/carcinomatosis
  - advancing age
  - extra-abdominal symptomatic metastases
  - poor nutritional status
  - previous radiotherapy/abdominal surgery

- Stents may be useful in proximal obstructions but risk of morbidity

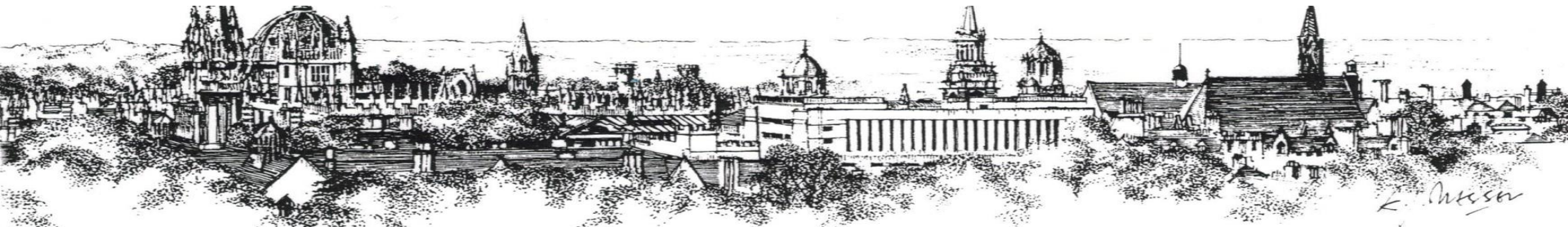


- Venting gastrostomy may be helpful for long-term/intermittent decompression
  - Cost effective with low morbidity/mortality

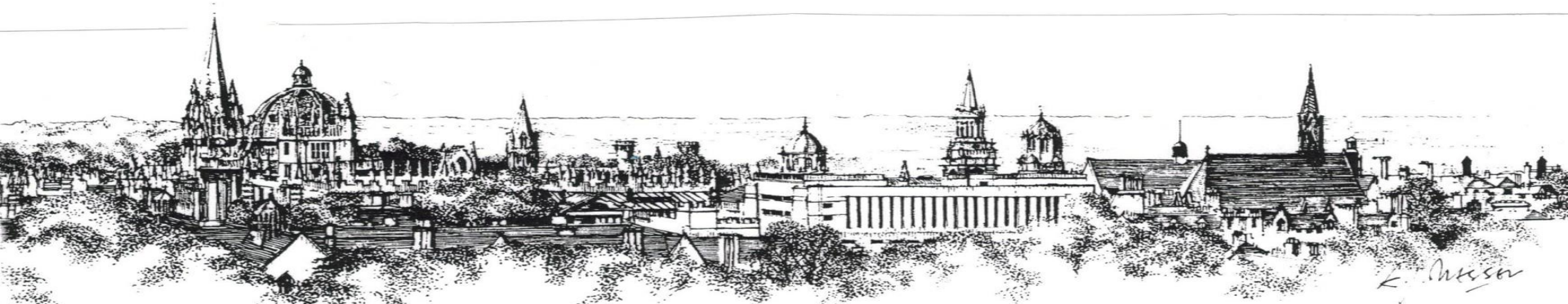




- Partial: Focus is to normalize gut function
- Complete or refractory obstruction: Focus is to rest the bowel
- Some medications used in both
- Be prepared to mix and match
  - Resting the bowel can allow recovery of MBO



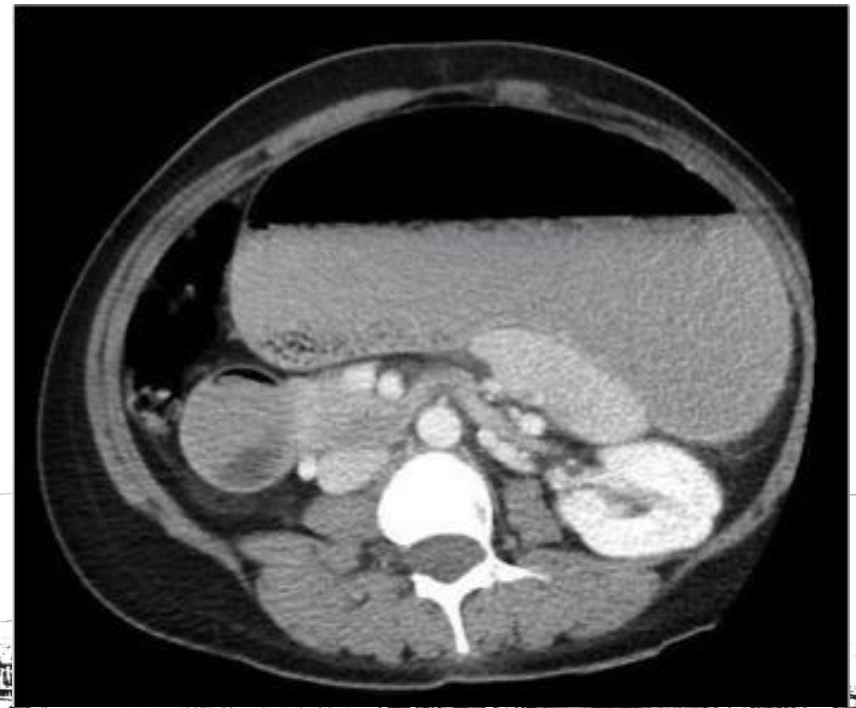
# Approaches for everyone



# Approaches for everyone

- Parenteral medications
  - Ensures absorption
- Consider opioids for pain relief
  - Generally pain management trumps motility management
  - Always individualise
  - ??Consider fentanyl to minimise opioid induced constipation
- If colic – stop stimulants before giving anti-spasmodics

# NG - Friend or Foe



Consider wide bore NG if large volume vomiting causing distress

*L. Mercer*



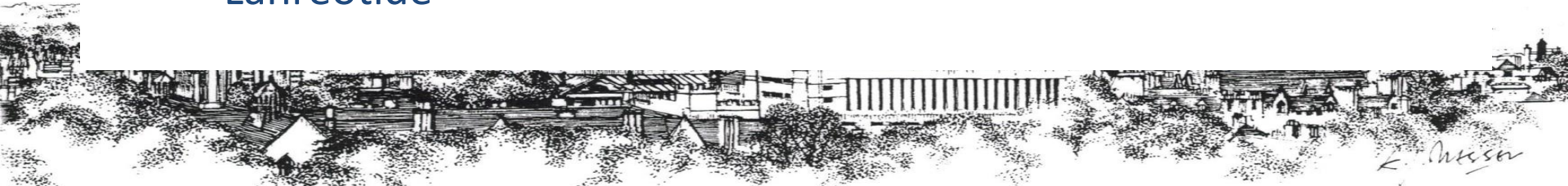
# Corticosteroids

- In general trial dexamethasone 8mg sc/iv for min 5 (7) days
  - Used in the hope of relieving obstruction by reducing swelling around obstructing growths
  - Efficacy is debatable.
    - One controlled study of the use of steroids in bowel obstruction
      - It showed no evidence that steroids were helpful in reducing obstruction
  - Steroids may nevertheless be useful in bowel obstruction by decreasing bowel and peritoneal inflammation and by acting as appetite stimulants.
    - Cochrane review: Trend towards resolution (NNT 6)
    - Short term use

# Consider anti-secretory

## 1. Octreotide

- Somatostatin analogue
- Reduces small bowel secretions
- Octreotide is generally well tolerated. It appears to have minimal effects on motility.
  - Effective in controlling vomiting in 60% malignant bowel obstruction cases regardless of type/level of obstruction
  - Octreotide is more effective than hyoscine butylbromide in relieving gastrointestinal symptoms of advanced cancer and should be considered as first-choice anti-secretory drug despite the cost (low level evidence, high risk of bias)
  - CSCI 300-1000mcg/24hrs
- Lanreotide

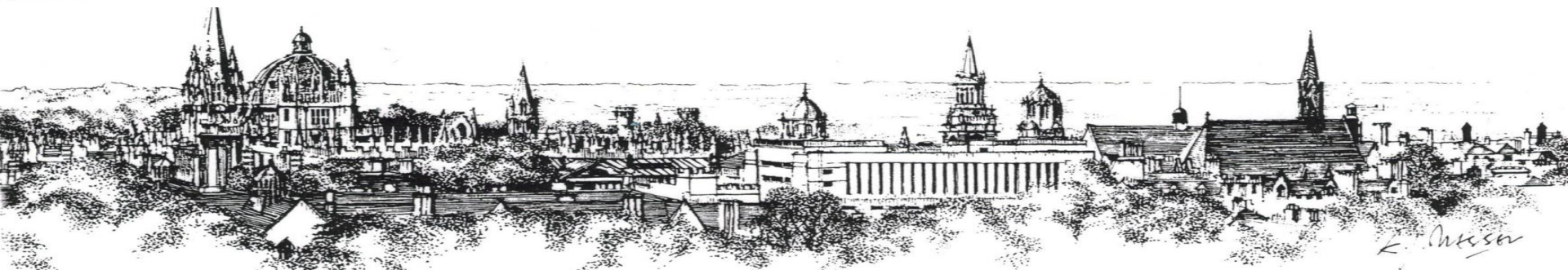


## *Original Article*

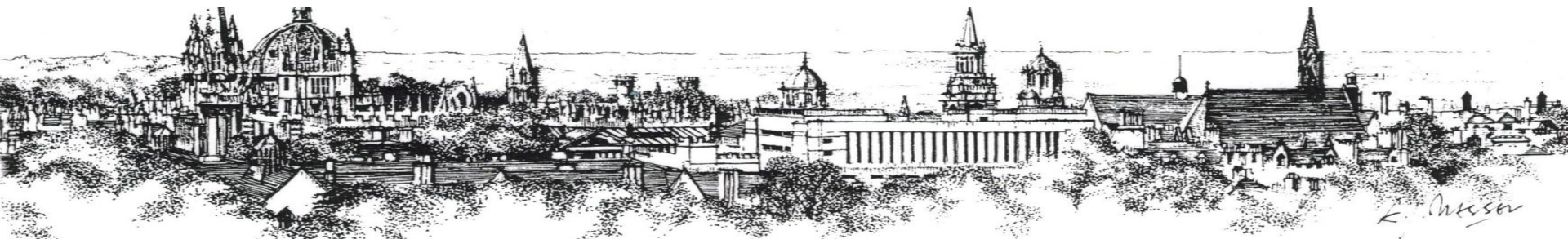
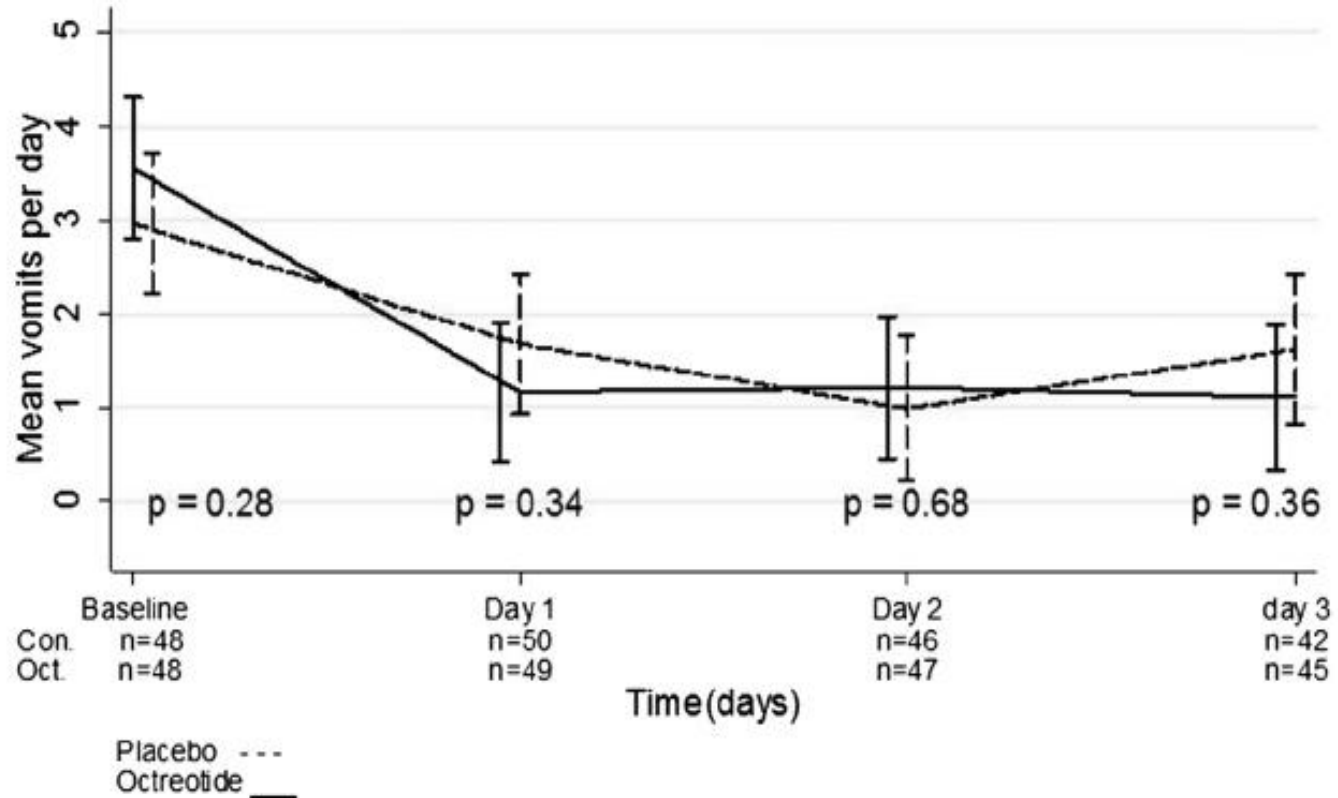
# Double-Blind, Placebo-Controlled, Randomized Trial of Octreotide in Malignant Bowel Obstruction

David C. Currow, FRACP, Stephen Quinn, PhD, Meera Agar, FRACP, Belinda Fazekas, GradDipCommHealth, Janet Hardy, FRACP, Nikki McCaffrey, MSc, Simon Eckermann, PhD, Amy P. Abernethy, MD, and Katherine Clark, FRACP

*Discipline, Palliative and Supportive Services (D.C.C., B.F., N.M., A.P.A.) and Flinders Clinical Effectiveness (S.Q., N.M.), Flinders University, Adelaide, South Australia; Sacred Heart Hospice (M.A.), Braeside Hospital, Sydney, New South Wales; Department of Palliative and Supportive Care (J.H.), Mater Health Services, South Brisbane, Queensland; Centre for Health Service Development (S.E.), Australian Health Services Research Institute, University of Wollongong, Wollongong, New South Wales, Australia; Duke University Medical Center (A.P.A.), Durham, North Carolina, USA; and Department of Palliative Care (K.C.), Calvary Mater Newcastle, Newcastle, New South Wales, Australia*



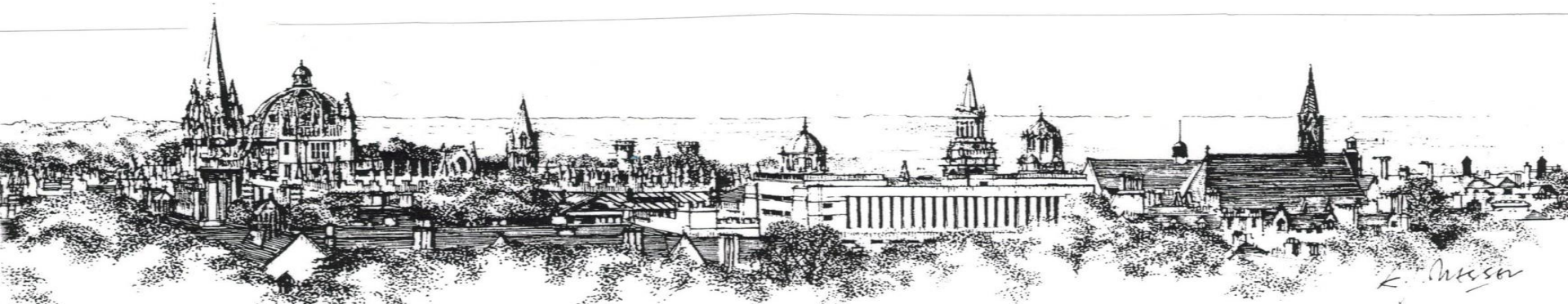
# Vomiting Episodes Baseline-Day 3





# Octreotide

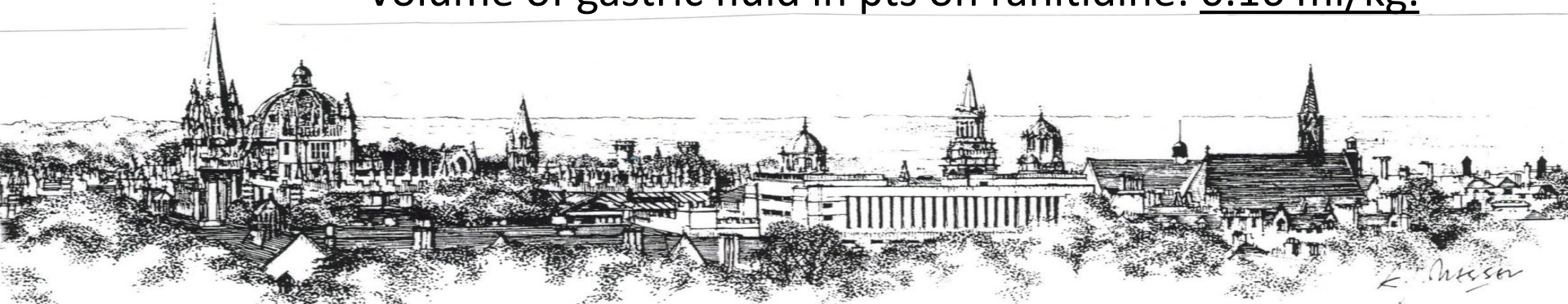
- Octreotide halved the overall number of vomiting episodes
- Reserve for instances in which regimen fails to reduce vomiting frequency
- Note ranitidine was part of standard care....



## 2. Ranitidine 50-200mg via syringe pump (does mix with metoclopramide and octreotide)

– Histamine 2 antagonist

- Meta-analysis of effects of ranitidine and PPIs on volume of gastric secretions prior to surgery:
  - Volume of gastric fluid in placebo arm: 0.54 ml/kg.
  - Volume of gastric fluid in pts on PPI: 0.410 ml/kg
  - Volume of gastric fluid in pts on ranitidine: 0.16 ml/kg.



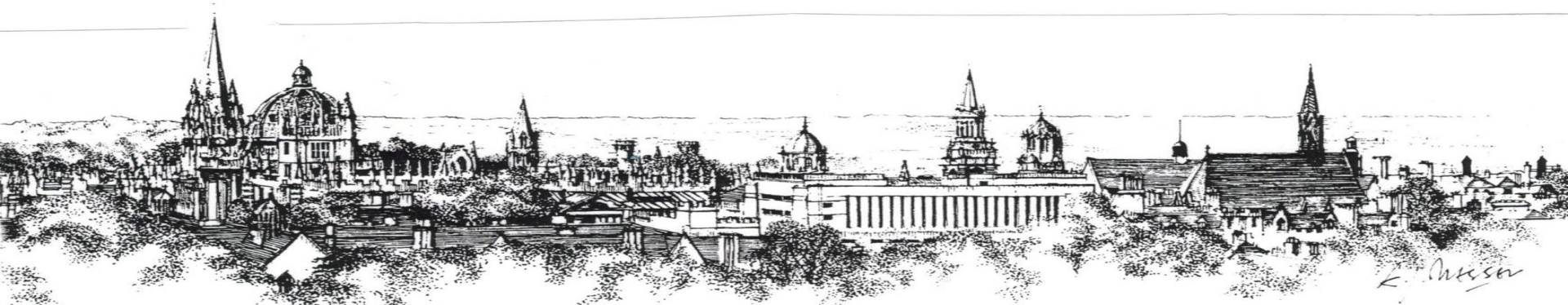
### 3. Hyoscine butylbromide

- Anti-cholinergic
- CSCI 60-360mg over 24hrs BUT
- Will slow GI motility
- Will limit normalisation of GI functioning
- More likely to be valuable if
  - Complete obstruction with colic
  - Severe colic not controlled by opioids



*L. H. H. H.*

# And now you subdivide

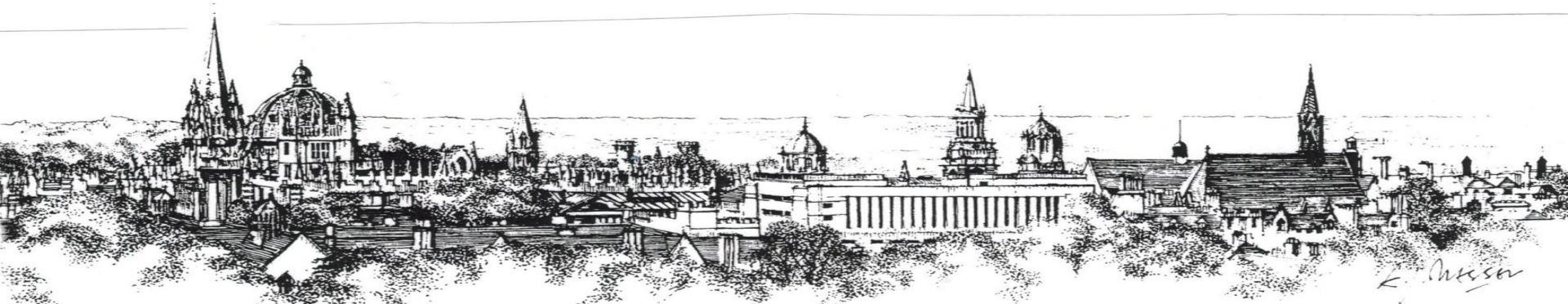




# And now you subdivide

Partial

Complete



# If Partial Obstruction

- Try to get things going – UNLESS colic present in which case manage as complete obstruction
  - If no/mild colic – prokinetic
    - Metoclopramide 30-100mg via syringe pump
    - Erythromycin 250mg bd either suspension po or IV – can be titrated
    - Softener such as docusate if able to tolerate oral meds
    - If low partial obstruction, **senna** may be worth adding
  - If in doubt re colic/setting doesn't allow monitoring
    - Consider non prokinetic anti-emetic
    - Resting the bowel can sometimes give time for obstruction to resolve
  - Not all colic is bad
    - No pain no gain
    - Remember remove prokinetics before adding anti-spasmodics



*L. Miller*

# Metoclopramide

- Dopamine antagonist
- Crosses blood brain barrier so some central anti-emetic effect
  - Inhibits gastric smooth muscle relaxation produced by dopamine, therefore increasing cholinergic response of the gastrointestinal smooth muscle
  - Accelerates intestinal transit and gastric emptying by preventing relaxation of the gastric body and increasing the phasic activity of antrum
  - Improves coordination between the body and antrum of the stomach and the upper small intestine by relaxation upper small intestine



*L. H. H. H.*

# Erythromycin

- Macrolide antibiotic – developed in 1952
- Abdominal cramping/diarrhoea commonly reported side effects
  - This can be to our advantage....
- Motilin agonist
  - Stimulates gastric/small bowel contractions and gastric emptying
  - Initiates migrating motor complex which begins in stomach and sweeps along small intestine

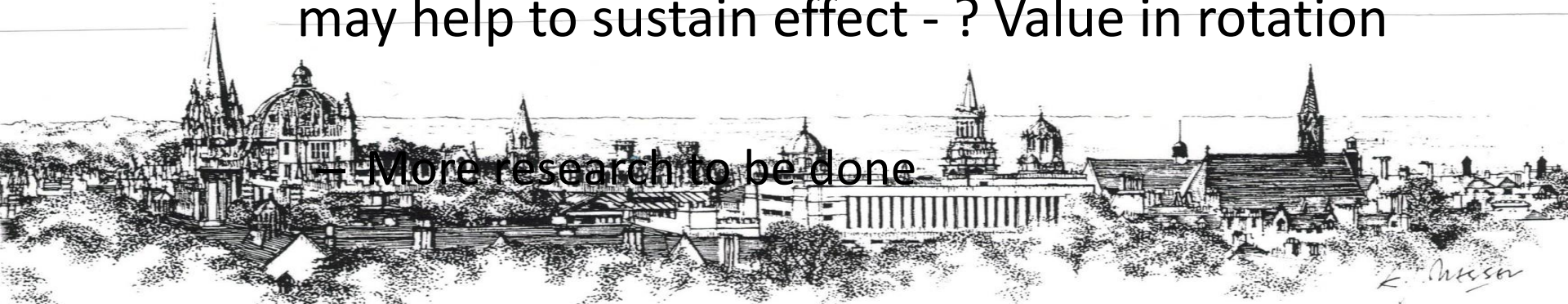


*L. H. H. H.*



- Erythromycin more effective than metoclopramide in enabling tolerance of feed at 24hrs 84% v 62%
- But – tachyphylaxis – both monotherapies significantly less effective at 3 days
- Combination erythromycin with metoclopramide may help to sustain effect - ? Value in rotation

— More research to be done —



- Azithromycin as potent motilin agonist as erythromycin
  - Clarithromycin lacks this effect
- Shelf life azithromycin suspension makes it less practical than erythromycin 10 days v 35 days
- Azithromycin used routinely for prophylaxis in chronic resp conditions
  - Erythromycin used less and hence may be less risk developing anti-biotic resistance



*L. H. H. H.*

- Erythromycin does have more significant drug interactions than azithromycin.
  - More potent inhibitor of CYP3A liver isoforms, which can lead to increased exposure to some drugs e.g. carbamazepine, methadone, sildenafil, simvastatin, tacrolimus, triazolam and vinblastine
  - QT-prolongation which can be problematic when used with drugs that also prolong the QT-interval e.g. amiodarone, methadone, haloperidol



*L. H. H. H.*



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## Case reports

# Erythromycin: prophylaxis against recurrent small bowel obstruction

Emily Rea<sup>1</sup> and Emma Husbands<sup>2</sup>

[Author affiliations](#)



PDF

## Abstract

We describe three cases where erythromycin suspension has been used successfully in preventing recurrence of small bowel obstruction in patients with terminal illness and for whom it proved more effective than standard preparations such as metoclopramide and domperidone. These patients also experienced a longer term benefit over some months. With recent alerts over longer term use of metoclopramide and domperidone, we demonstrate that erythromycin is a viable alternative prokinetic in patients with terminal illness at risk of small bowel obstruction instead of or alongside metoclopramide and domperidone. More research is required to establish the point at which erythromycin should be considered in the management of symptoms. In addition, research into the possibility of a viable alternative to erythromycin is needed.





- Marmite drug
- Use suspension form/consider IV form
  - Why suspension.....
- Consider as a second line prokinetic after metoclopramide
  - Generally commence alongside
- In subacute bowel obstruction, has helped stabilise episodes and been well tolerated on the whole
- Despite tachyphylaxis
  - Not always experienced



# Prokinetics around the corner

- Mitemincinal
  - Exhibits potent prokinetic action in the stomach and early results in diabetic gastroparesis promising.
- Ghrelin
  - A neuro-humoral transmitter secreted by the stomach, is believed to play a physiological role as a stimulant of food intake.
  - Recent preliminary investigations show a prokinetic action of ghrelin with stimulation of gastric emptying in patients with diabetic and idiopathic gastroparesis.



*L. H. H. H.*

# If Complete obstruction

- Rest the bowel
  - Non-prokinetic anti-emetic
    - Cyclizine/levomepromazine/ondansetron
  - Lower threshold for anti-spasmodics
    - If obstruction is complete, slowing gut less of a concern
    - Focus is on drying secretions/slowing GI motility to address large volume vomits and pain
- Consider continuing dexamethasone to optimise chance of reducing peri-tumour oedema BUT balance with appetite
- Surgery may be more valuable esp if distal lesion/transit point

Anti-emetic	Dose	Action	Effect
Levomepromazine	6.25-25mg s/c od or 24hrs via CSCI	D2 antagonist H1 antagonist Anti-cholinergic 5-HT4 antagonist	Central anti-emetic Mild reduction GI secretions and motility
Haloperidol	1.5-5mg 24hrs via CSCI	D2 antagonist	Central anti-emetic
Cyclizine	150mg s/c 24hrs via CSCI	H1 antagonist Anti-cholinergic	Central anti-emetic Mild reduction GI secretions and motility
Ondansetron	8-16mg s/c 24hrs via CSCI	5-HT3 antagonist	Central anti-emetic Reduces gut motility
Hyoscine Hydrobromide	1200-3600mcg via syringe pump	Anti-cholinergic	Central anti-emetic Reduction GI secretions and motility
Olanzapine	1.25-2.5mg sc (not in UK) 2.5-5mg orally if tolerated	D2 antagonist 5-HT2A antagonist	Central anti-emetic Mild reduction gut motility
Mirtazapine	15-45mg orally	H1 antagonist 5-HT1A antagonist 5-HT2/3 antagonist	Central antiemetic Relaxation gastric fundus



# Hydration

- Mouth care
  - Ice chips/lolly
  - Lubrication to the lips
  - Sips of fluid/ghee/olive oil
- IV/SC Fluids
  - Consider goals of a trial
  - Encourage oral intake esp if large bowel obstruction
    - May absorb enough
  - Can aid comfort
    - Psychological
    - Thirst
      - Patient may not be dying from disease but dehydrating to death with high obstruction

Are they not drinking because they are dying or dying because they are not drinking?

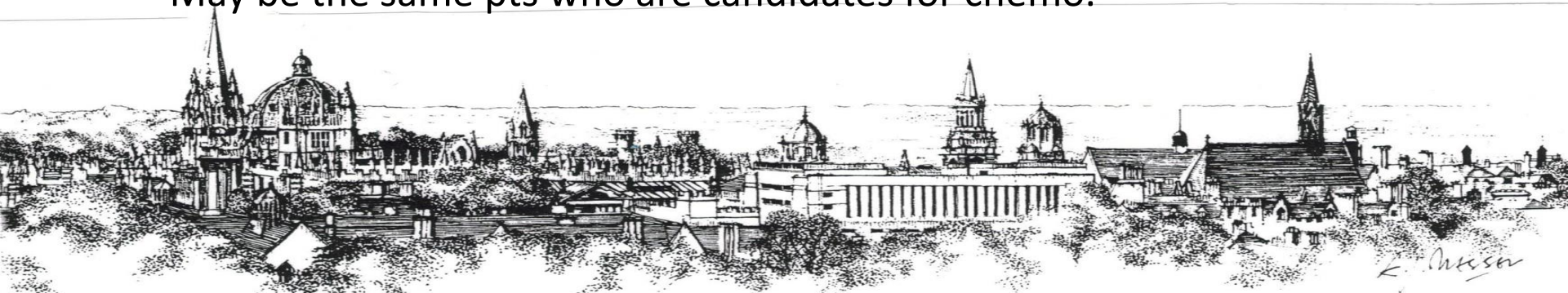
# Nutrition

- Most patients with bowel obstruction who are able to eat should be on a low-fibre/low-residue diet.
  - Essential if they are trying to eat with a total obstruction
- Patients with complete obstruction who do eat often vomit or regurgitate every few days
  - May be an acceptable trade-off
- Patient preference has a big part in choices over oral intake

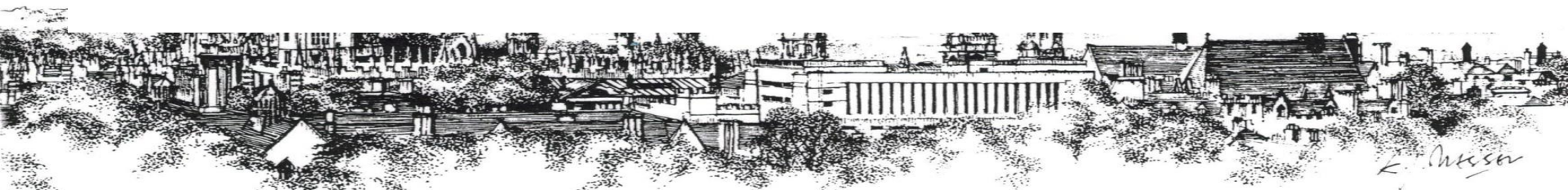


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- TPN should be considered carefully; routine use should be avoided.
  - High rate of complications (infection/electrolyte disturbance/thrombosis)
  - Cost
  - May prevent time in preferred location
  - Symptom exacerbation?
- Survival benefit in carefully selected patients
  - Suggested that TPN should be considered only if AKPS >50% and life expectancy >2 mths so that death from malnutrition is more likely than death due to other processes.
  - May be the same pts who are candidates for chemo.

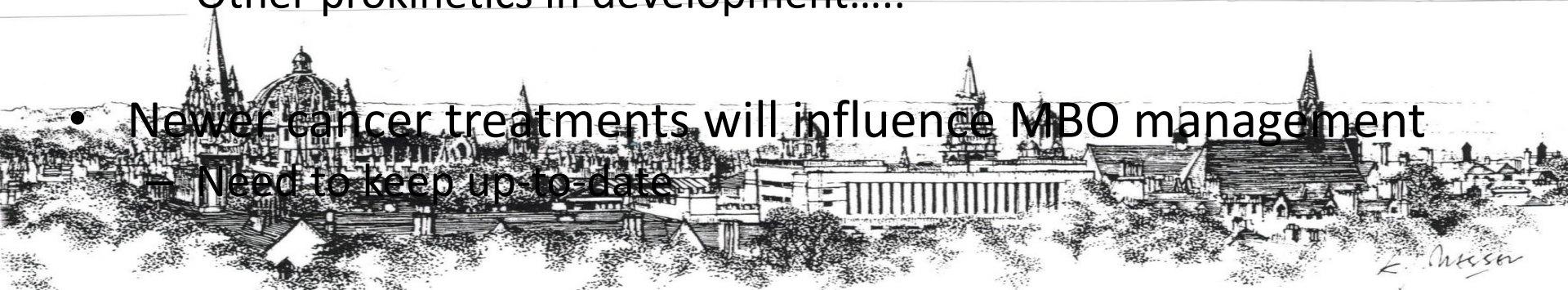


- Prognosis is poor
- Grief reaction to inability to eat and/or feed
- Fear around discontinuing NG tube/having another placed
  - Once you have vomited 'poo' unlikely you want to repeat it
- Altered body image
- *These decisions are complex*
- *Symptoms often distressing for staff as well as patients/families*

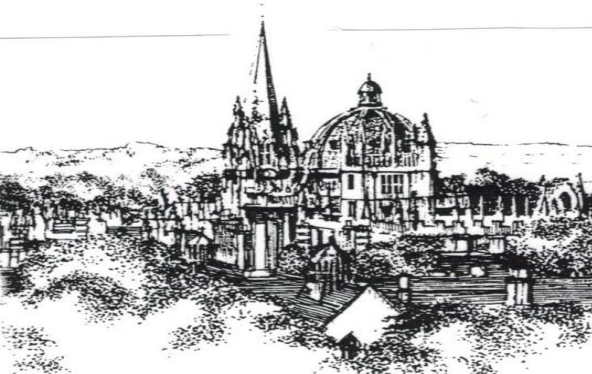


# Take Home

- One size doesn't fit all
  - GI tract is LOOOOONNG
  - Obstruction can spontaneously resolve
  - 'Where' the patient is will likely influence options
- Trying to normalise gut function
  - Reset balance of secretion and absorption
  - Improving/kick-starting motility where possible
- Erythromycin may be a useful adjunct for prokinesis
  - Other prokinetics in development.....
- Newer cancer treatments will influence MBO management
  - Need to keep up to date







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