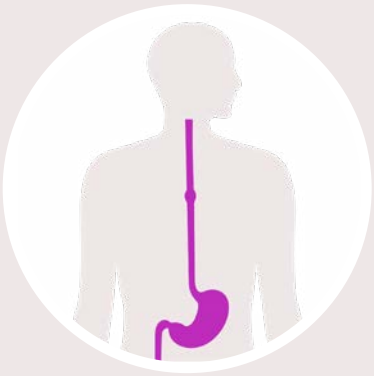
Consider oesophagogastric (OG) cancer



A review and practical aide for understanding risk and urgency of investigations for OG cancer in primary care

Developed in consultation with:

***A/Prof. Ralph Audehm**, General Practitioner and Honorary Clinical Associate Professor, University of Melbourne, Department of General Practice, VIC.*

***Dr Warren Joubert,** Medical Oncologist, Greenslopes Private Hospital, QLD.*

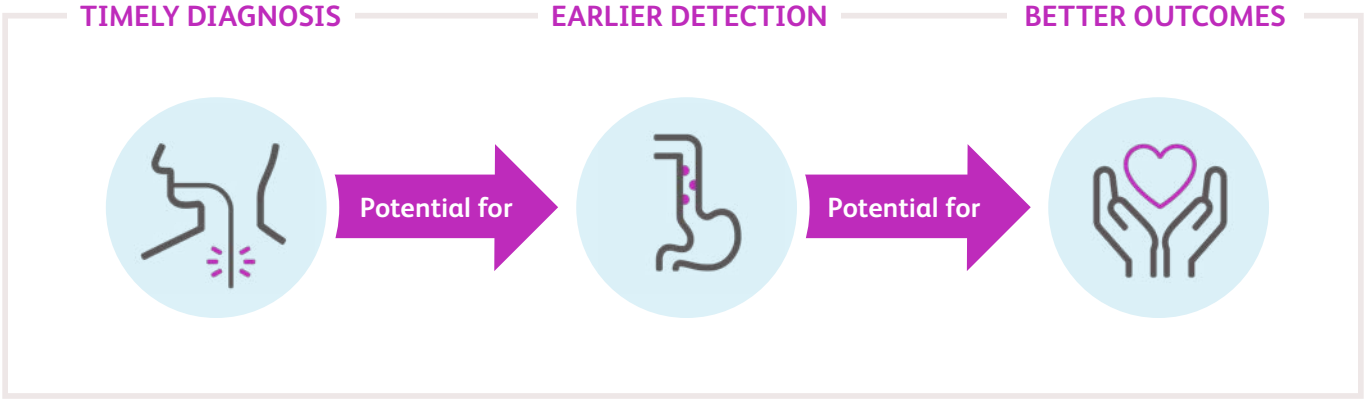
***Dr David Liu,** Upper Gastrointestinal Surgeon, Surgical Associates Melbourne, Latrobe Private Hospital, Peter MacCallum Cancer Centre, and Austin Health, VIC.*

Importance of timely diagnosis

- Diagnosis of OG cancer predominantly arises through symptomatic presentation to primary care.[1,2]

Early detection and diagnosis is associated with better clinical and patient-reported outcomes,[3,4] with stage at diagnosis strongly predictive of survival.[5,6]

- Data from the United Kingdom, indicates that nearly a quarter of patients require three or more consultations with their general practitioner before a hospital referral.[7]

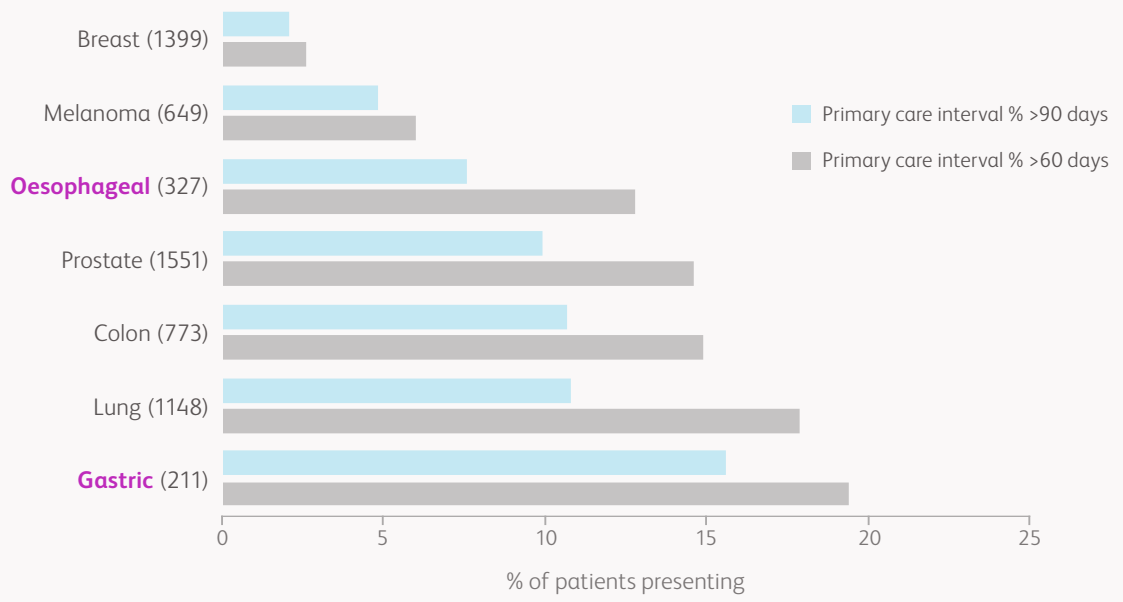


Importance of timely diagnosis

- Intra-luminal growth of OG cancers occurs late in the disease course and patients can present with poorly defined, broad symptomology which, in the case of general practice, occurs in a situation where the individual risk of cancer is low.[2,4,8]
- This can contribute to delays in diagnosis (Figure 1).[9]

Understanding signs and symptoms of greatest significance could assist in clinical evaluation and consideration for additional investigation or referral.[4,10]

Figure 1: Primary care interval (data from United Kingdom)[9]



Approximately 85% of patients with OG cancer present with **red-flag symptom/s** that are strongly predictive of cancer.[4,7,11] OG cancer symptoms usually reflect one or more of the **4 Bs**:

1. Blockage: Dysphagia, early satiety, regurgitation, nausea, vomiting, bloating, weight loss

2. Bleeding: Iron deficiency, melena

3. Burrowing: Dyspepsia, back pain

4. Bursting: Acutely unwell, severe abdominal pain, peritonitis

The presence of these symptoms and signs without a clear explanation should prompt consideration for endoscopic and gastrointestinal specialist referral.

At the referral stage, it is helpful for GPs to advise the patient about their options for referral, waiting periods, expertise, if there are likely to be out-of-pocket costs and the range of services available.[8]

Oesophageal and gastric cancer in Australia

OG cancers can arise in the oesophagus, stomach or the junction between these organs. Oesophageal cancer is divided into two distinct subtypes**, oesophageal squamous cell carcinoma (OSCC)** and **oesophageal adenocarcinoma (OAC)**. Globally, OSCC remains the most common subtype particularly in Eastern Asia, but the incidence of OAC has risen in Western countries including Australia.[12,13]

Adenocarcinoma is the most common histological type of gastric cancer and gastro-oesophageal junction cancer, accounting for approx. 90% of these diagnoses. Young onset OG cancers, which include those diagnosed under the age of 50, while still uncommon, is rising in incidence.[14,15] In Australia, migrants from South America, North-East Asia, and Polynesia experience higher incidence rates of gastric cancer than the Australian-born population.[16]

Oesophageal cancer in Australia[17]

Estimated number of new oesophageal cancer cases in 2024

1,323 *Male* **462** *Female*

1,785

20th most commonly diagnosed cancer

13th most common cause of cancer death

25% chance of surviving at least 5 years *(compared with 71% survival for all cancers combined)*

3,156 people living with oesophageal cancer at the end of 2020 *(diagnosed in the 5-year period 2016 to 2020)*

Source: Australian Institute of Health and Welfare, 2024.

Gastric cancer in Australia[17]

Estimated number of new gastric cancer cases in 2024

1,662 *Male* **922** *Female*

2,584

15th most commonly diagnosed cancer

10th most common cause of cancer death

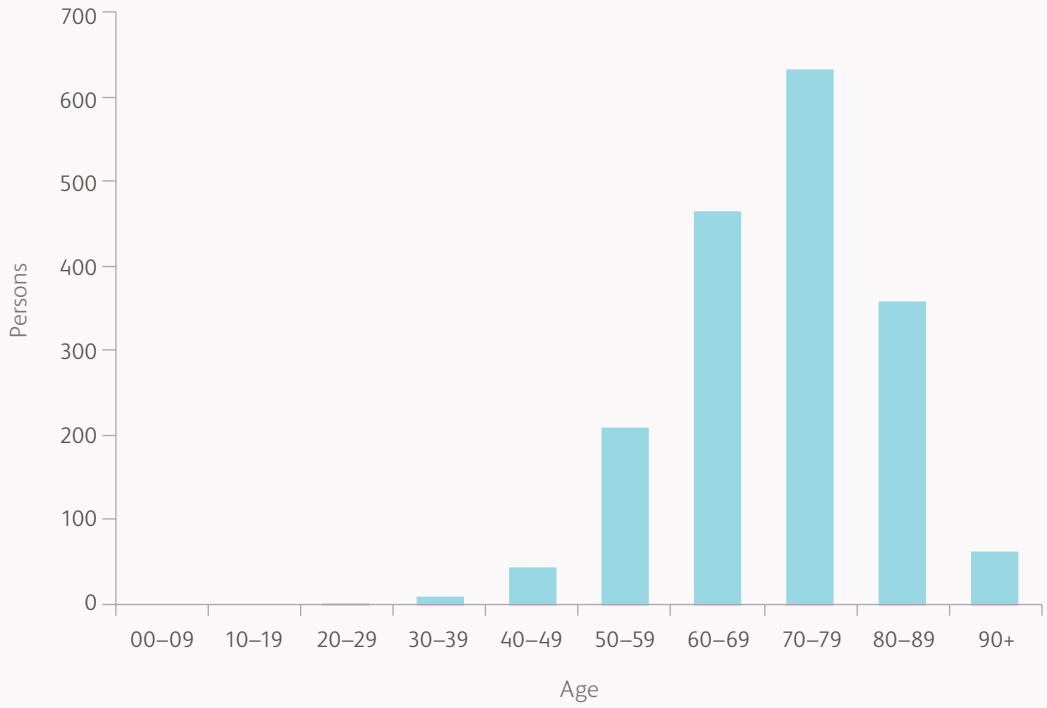
38% chance of surviving at least 5 years *(compared with 71% survival for all cancers combined)*

5,923 people living with gastric cancer at the end of 2020 *(diagnosed in the 5-year period 2016 to 2020)*

Source: Australian Institute of Health and Welfare, 2024.

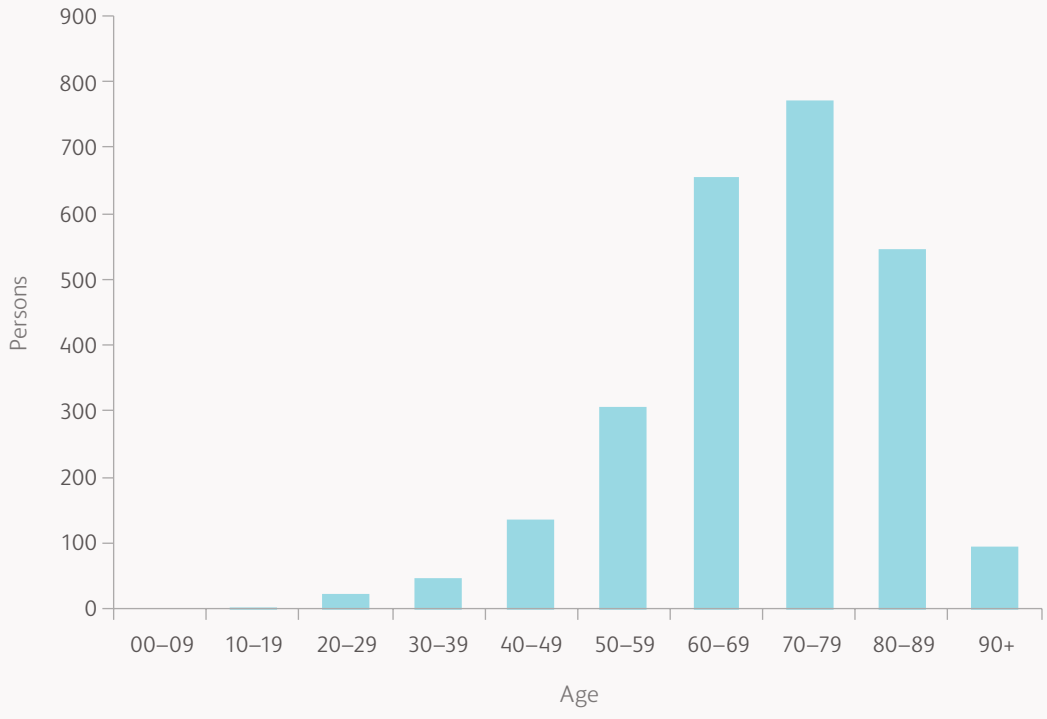
Oesophageal and gastric cancer in Australia

Oesophageal cancer, age distribution[17]



Source: Australian Institute of Health and Welfare, 2024.

Gastric cancer, age distribution[17]

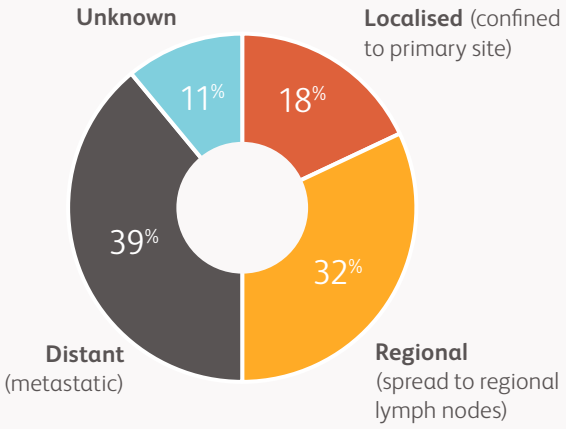


Source: Australian Institute of Health and Welfare, 2024.

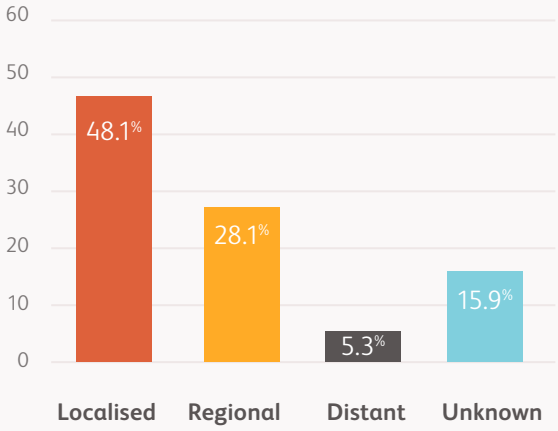
Staging at diagnosis and the importance of stage

Oesophageal cancer (data from USA)[5]

Percentage diagnosed by stage



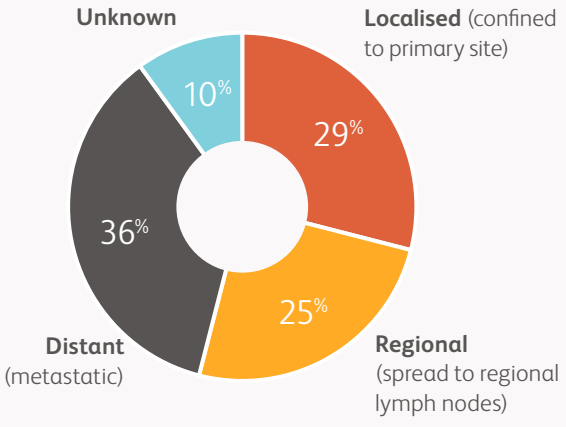
5-year relative survival



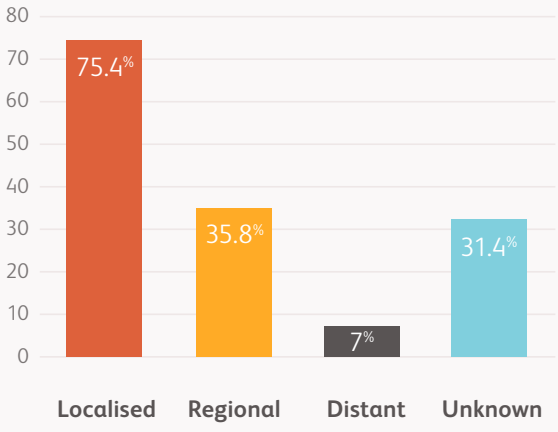
Source: SEER 2024.

Gastric cancer (data from USA)[6]

Percentage diagnosed by stage



5-year relative survival



Source: SEER 2024.

Risk factors associated with OG cancer[8]

- **Oesophageal squamous cell carcinoma – heavy alcohol consumption, tobacco smoking,** increasing age, caustic injury and achalasia.
- **Oesophageal adenocarcinoma – male gender, obesity, gastro-oesophageal reflux, Barrett's oesophagus,** tobacco smoking, alcohol consumption and increasing age.
- **Gastric cancer** – increasing age, helicobacter pylori bacteria (or current/historic peptic ulcer), previous partial gastrectomy (esp. more than 20 years ago), tobacco smoking, pernicious anaemia and family history of gastric cancer.

Most common risk factors are **bolded.*

Signs and symptoms associated with OG cancer[8]

Symptoms commonly associated with OG cancer include:

- **Dysphagia (difficulty swallowing)**[†]
- **Epigastric pain persisting for more than 2 weeks**[†]
- Persistent dyspepsia[#]
- Odynophagia (pain on swallowing)
- Food bolus obstruction
- Unexplained weight loss or anorexia
- Haematemesis or melena
- Early satiety
- Unexplained nausea/abdominal bloating or anaemia

*[†]**Red-flag symptoms** for which urgent – within 2 weeks – referral for endoscopy is urged.[8]*

[#]Treatment of dyspepsia with acid suppressants may hide symptoms of OG cancer and delay diagnosis.[1]

Figure 2: Two-way table of risks associated with OG cancers[1]

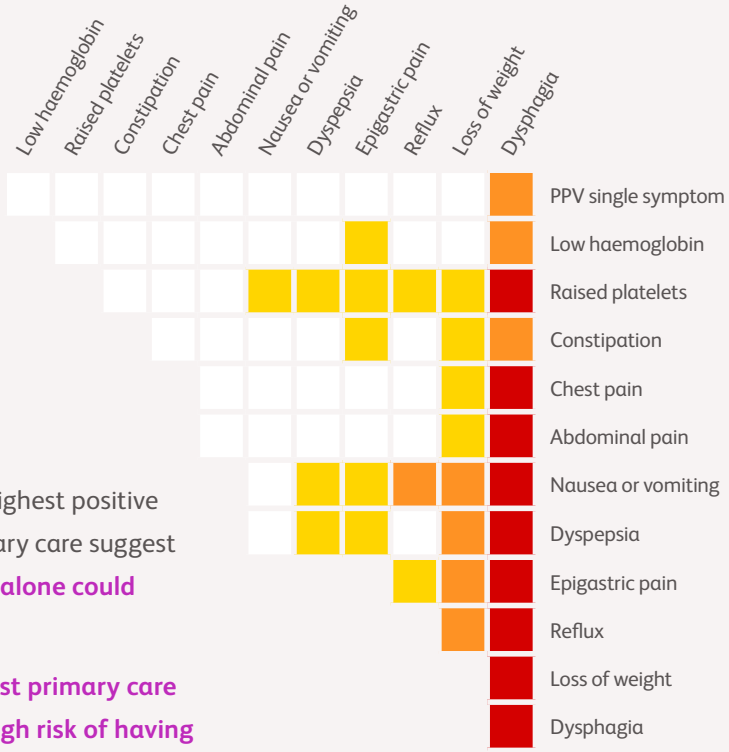
For patients aged 55 or over, the likelihood of positively predicting OG cancer is shown for individual risk markers (top row) and for pairs of risk markers (matrix).

- **PPV >1 but <2**
- **PPV >2 but <5**
- **PPV >5**

PPVs >1 indicate patients at highest risk of OG cancer in primary care and could signal for expediated referral and investigation.[1,3]

While dysphagia has been associated with the highest positive predictive value of OG cancer, studies from primary care suggest that **an approach focused on single symptoms alone could miss up to 40% of undiagnosed OG cancers.**[3]

Assessing symptoms in combination could assist primary care clinicians to assess and prioritise patients at high risk of having OG cancer for further investigation or referral (Figure 2).[1,3]



Triaging endoscopy in Australian hospitals

In Australian hospitals criteria are used to assist triaging clinicians assign urgency to endoscopy.[18–20]

Category 1 (appointment recommended within 30 days)

- Dysphagia alone, any age
- Mass/abnormal imaging, likely oesophageal or gastric cancer, any age.
- Haematemesis (vomiting blood) or melena, any age (assume haemodynamically stable and no acute bleed requiring immediate admission).
- Upper abdominal pain or persistent nausea/vomiting, age ≥45* years and unexplained weight loss (>10%) or abnormal blood test.
- Dyspepsia, any age and known intestinal metaplasia/gastric dysplasia.

- The presence of additional symptoms† and/or abnormal blood test and:
  - Unexplained weight loss, age ≥55*.
  - Unexplained iron deficiency +/- anaemia in men or non-menstruating women.
  - Unexplained dyspepsia, age ≥45* (or with atrophic gastritis or family history or upper GI cancer in 1st degree relative).
  - Non-responsive GORD (following 6–8 weeks of double dosage PPI treatment, age ≥55*, with known Barrett's.
  - Pernicious anaemia (endoscopically diagnosed), any age.

†Additional symptoms include dyspepsia, gastro-oesophageal reflux disease (GORD), upper abdominal pain, persistent nausea/vomiting, early satiety or unexplained loss of appetite. Abnormal blood tests include low Hb, low ferritin, microcytosis, hypochromia, raised platelets.

**Guidelines differ on age delineations (ranging from 45 to 55). Where there was discrepancy, the lowest age is summarised here.*

90 Category 2 (appointment recommended within 60–90 days)

- Dyspepsia, any age, and non-responsive to PPI and/or *H. pylori* therapy or *H. pylori* negative.
- *H. pylori* eradication failed (urea breath test) after standard first-line treatment.
- Non-responsive GORD (following 6–8 weeks of double dosage PPI treatment) age <55 and known Barrett's.
- Upper abdominal pain or persistent nausea/vomiting, age <45* years and unexplained weight loss (>10%) or abnormal blood test.
- Pernicious anaemia (serologically diagnosed), asymptomatic at time of diagnosis.
- Known coeliac disease with no exposure to gluten and persistent high titres after 12 months or persistent symptoms or persistent diarrhoea, abdominal pain, weight loss, fatigue or anaemia.
- Suspected coeliac disease with positive serology.

- The presence of additional symptoms[†] and/or abnormal blood test and:
  - Unexplained recent dyspepsia, age <45* (or with atrophic gastritis or family history or upper GI cancer in 1st degree relative).
  - Unexplained weight loss age <55*.
  - GORD recent onset age <55*.
  - Nausea/vomiting, persistent age <55*.

[†]Additional symptoms include dyspepsia, GORD, upper abdominal pain, persistent nausea/vomiting, early satiety or unexplained loss of appetite. Abnormal blood tests include low Hb, low ferritin, microcytosis, hypochromia, raised platelets.

Clinical judgement is critical

In the overall population, there are very few people at high risk of OG cancer (Thomas *et al.* 2021). **Having one or more risk factors does not mean that the patient will develop OG cancer, but it is important to consider risk factors along with symptoms and signs that may be consistent with OG cancer.**

Signs and symptoms for OG cancer can overlap with benign conditions, cancer types not specified in this material, and alternate aetiologies of varying severity.

Alternative diagnoses and appropriate investigations should be considered based on thorough consultation of current presentation and patient history.

**Guidelines differ on age delineations (ranging from 45 to 55). Where there was discrepancy, the lowest age is summarised here.*

GP Resources

- **Arterial Education** "Trust your gut" CPD — LEARN MORE
- **Pancare** (Pancare GP Education – Pancare Foundation) — LEARN MORE
- **Optimal Care Pathway for people with oesophagogastric cancer 2nd ed.** (oesophagogastric-cancer-optimal-cancer-care-pathway) — LEARN MORE
- **Cancer Australia** (Cancer Australia | Cancer Australia) — LEARN MORE

Patient Resources

- **Pancare Foundation** (We support Australians diagnosed with upper gastrointestinal (GI) cancers) — LEARN MORE
- **Cancer Council** (Cancer information and support | Cancer Council) — LEARN MORE

Plain language definitions

Abdominal bloating – uncomfortable sensation of fullness.
Adenocarcinoma – a type of cancer that starts in the glands that line your organs.
Anaemia – lack of enough red blood cells.
Anorexia – an abnormal loss of the appetite for food.
Gastric cancer – a cancer that forms in the cells lining the stomach.
Dysphagia – difficulty swallowing.
Dyspepsia – discomfort or pain in the upper abdomen.
Haematemesis – vomiting blood.
Incidence – proportion of new cases developed during a given time.
Melena – black, tarry stool (caused by internal bleeding).
Odynophagia – pain on swallowing.
Oesophagus – the muscular tube through which food passes from the throat to the stomach.
Oesophagus squamous cell carcinoma – a cancer that forms in the cells lining the inside of the oesophagus.
Positive predictive value (PPV) – likelihood that a person with a sign/symptom has the disease of interest.

References: 1. Stapley *et al. Br J Cancer* 2013;108;25–31. **2.** Venning & Emery. *Med J Aust* 2024;220:446–50. **3.** Hippisley-Cox & Coupland. *Br J Gen Pract* 2011;61:e707–14. **4.** Koo *et al. Neoplasia* 2018;20:165–74. **5.** SEER, Oesophageal Cancer. Available at: https://seer.cancer.gov/statfacts/html/esoph.html, accessed October 2024. **6.** SEER, Stomach Cancer. Available at: https://seer.cancer.gov/statfacts/html/stomach.html, accessed October 2024. **7.** Collins & Altman. *Eur J Cancer* 2013;49:1040–48. **8.** Thomas *et al. Optimal care pathway for people with oesophagogastric cancer,* 2nd edition (2021). **9.** Swann *et al. Br J Gen Pract* 2018;68:e63–e72. **10.** Emery & Chiang. *Aust Fam Physician* 2014;43:508–12. **11.** Stephens *et al. Br J Surg* 2005;92:840–6. **12.** Arnold *et al. Gut* 2020;69:1564–71. **13.** Sung *et al. CA Cancer J Clin* 2021;71:209–49. **14.** Codipilly *et al. Cancer Epidemiol Biomarkers Prev* 2021;30:142–9. **15.** Harrold *et al.* ASCO educational Book Vol 43 (2023). **16.** Yu *et al. Cancer Epidemiol Biomarkers Prev* 2022;31:1394–401. **17.** Cancer data in Australia. CDiA--2024-Book-1b, *Australian Institute of Health and Welfare* (2024), Available at: www.aihw.gov.au/reports/cancer/cancer-data-in-australia/data, accessed October 2024. **18.** A Direct Access Endoscopy Referral Guidelines (health.wa.gov.au). **19.** NSW Health Upper gastrointestinal dysfunction in adult patients (referral criteria) – Upper gastrointestinal dysfunction in adult patients – State-wide referral criteria (nsw.gov.au). **20.** Upper gastrointestinal endoscopy categorisation guidelines for adults 2018 (health.vic.gov.au).

Bristol-Myers Squibb Australia Pty Ltd, ABN 33 004 333 322, 4 Nexus Court, Mulgrave, VIC 3170.
1506-AU-2500014. February 2025. BRMSOY0292.

Bristol Myers Squibb®