UK National Screening Committee

Screening for stomach cancer in adults

External review against programme appraisal criteria for the UK National Screening Committee

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The UK National Screening Committee secretariat is hosted by Public Health England.

About the UK National Screening Committee (UK NSC)

The UK NSC advises ministers and the NHS in the 4 UK countries about all aspects of population screening and supports implementation of screening programmes. Conditions are reviewed against evidence review criteria according to the UK NSC's evidence review process.

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Plain English summary

Stomach cancer is an important cause of death worldwide. In 2017 there were 6,595 people who were diagnosed with stomach cancer and 4,370 people who died from the disease in the UK. The numbers of people being diagnosed with stomach cancer has been decreasing in the UK for at least the past 30 years. Men are around twice as likely as women to develop stomach cancer and it is more common in older people over the age of 50.

One of the main reasons people develop stomach cancer is if they have a stomach infection caused by a bacterium *Heliobactoer pylori*. Tobacco smoking and being overweight or obese are also linked with people developing stomach cancer.

The UK NSC last looked at screening for stomach cancer in adults in 2016. The UK NSC decided not to recommend screening. There was too little evidence that screening the general population would be beneficial.

This report looks at new evidence about stomach cancer compared to the findings in the previous review in 2016, for 2 key questions. Question 1 is about changes in the number and type of people who develop stomach cancer and includes evidence published up to June 2020. Question 2 is about what type of evidence is available about screening tests for stomach cancer and includes evidence published up to August 2020.

For question 1 the review found that there was a lot of evidence about the number and type of people who develop stomach cancer but that the overall picture had not changed since 2016. There was evidence that in the future different types of people are likely to develop stomach cancer. It is recommended that these changes are monitored.

For question 2 a single publication was found about a screening test for stomach cancer so it is not recommended that a detailed review is carried out.

Executive summary

Purpose of the review

This document reviews the evidence on the epidemiology of stomach cancer in adults against the UK National Screening Committee (NSC) criterion about the understanding of the natural history of the condition. The document also maps the available evidence about the performance of screening tests for stomach cancer against the UK NSC criterion about the availability of a suitable accurate test. The purpose of the evidence map is to provide the basis for discussion by the UK NSC so an informed decision can be made about whether there is sufficient evidence to justify commissioning a more sustained review of the evidence about screening tests for stomach cancer.

Gastric adenocarcinoma accounts for 95% of all stomach cancer diagnoses in adults in the UK and in this document these 2 terms (stomach cancer and gastric adenocarcinoma) are used interchangeably to reflect the terminology used by the included studies.

Background

Stomach cancer is a major cause of mortality worldwide. There were 6,595 cases of stomach cancer diagnosed and 4,370 deaths from the condition in 2017 in the UK. Trends in the incidence and mortality of stomach cancer show a decline in many countries including the UK. The UK age-standardised incidence rate for stomach cancer has steadily decreased since the early 1990s, from 23.4 per 100,000 in 1993 to 10.3 per 100,000 in 2017.

Important non-modifiable risk factors that increase the risk of stomach cancer are age, gender, social deprivation and ethnic origin. The presence of the bacterium *Heliobactor pylori (H.pylori)* has been identified as the most important modifiable risk factor for developing stomach cancer. Diagnosis and treatment of people with *H.pylori* since the 1990's is thought to be instrumental in an overall decline in the incidence of stomach cancer seen in many countries including the UK. There is convincing evidence that tobacco smoking and being overweight or obese increases risk and probable evidence that alcohol is also a risk factor for developing stomach cancer.

There are 2 systems most often used to describe how gastric adenocarcinomas look and develop; the Lauren classification and the World Health Organisation (WHO) classification. The Lauren classification separates solid tumours from diffuse tumour cells scattered

throughout the stomach and the WHO classification separates 5 types of tumours by their morphology.

Gastric adenocarcinomas are usually classified by where they occur in the stomach. Non-cardia cancer, also known as distal stomach cancer, occurs in the lower portion of the stomach whereas, cardia stomach cancers occur at the top of the stomach, close to where the stomach joins the oesophagus. Despite the overall decline in gastric adenocarcinoma there is evidence that the incidence of cardia cancers in many countries including the UK, is increasing. There is a suggestion that some gastric adenocarcinomas of the cardia have a similar aetiology to oesophageal adenocarcinoma occurring near the junction of the oesophagus and the stomach. Increasing obesity is thought to be responsible for an increase in gastro-oesophageal reflux disease; a risk factor for oesophageal adenocarcinoma and this has also been implicated in the rise of stomach cardia cancer.

Screening for stomach cancer

Three pre-malignant stages have been identified that precede the development of gastric adenocarcinoma, these are; atrophic gastritis; intestinal metaplasia and dysplasia. Accurately identifying and treating people with these pre-malignant stages of the condition is important in improving survival rates. Some countries with a high incidence of gastric adenocarcinoma such as Japan (27.5 per 100,000 population in 2018) and South Korea (39.6 per 100,000 population in 2018) screen their populations for the pre-malignant stages of the condition. Screening tests used in population based screening programmes are either imaging procedures such as contrast radiography or endoscopy or detection of *H.pylori* or gastric tumour biomarkers.

Focus of the review

This evidence update about the epidemiology of stomach cancer and evidence map about screening tests for the condition has been prompted by more recent evidence of an increase in diagnoses of cancers of the stomach cardia. These link to UK NSC criteria 1 and 4, about understanding the natural history of the condition and the accuracy and validity of available screening tests.

Key question 1 is a review about the epidemiology of stomach cancer and has 4 sub questions:

Key question 1: What is the UK incidence and prevalence of Gastric adenocarcinomas?
Sub-questions:

1. What is the overall incidence and prevalence of Gastric adenocarcinomas in the UK?

2. What is the incidence and prevalence of different classifications of Gastric adenocarcinomas in the UK, such as Lauren or WHO classifications?
3. What is the incidence and prevalence of Gastric adenocarcinomas in the UK by anatomic sites (i.e. cardia or non-cardia, stomach, oesophagus or other locations)?
4. What is the incidence and prevalence of Gastric adenocarcinomas in the UK by risk factor or cause (i.e. *H.Pylori*, diet, smoking etc)?

The search for evidence about the epidemiology of stomach cancer included relevant studies up to June 2020.

Key question 2 is an evidence map about the type and volume of peer-reviewed publications available about tests for population screening for stomach cancer.

Key question 2: What is the test accuracy of screening tests for the detection of gastric and stomach cancer?

The search for evidence about screening tests for stomach cancer included relevant studies up to August 2020.

Recommendation under review

In the previous UK NSC review of screening for stomach cancer in 2016 there was sufficient evidence to meet criterion 1 about the natural history. The current review of this evidence aims to determine if the risk factors and who develops stomach cancer has changed since 2016. In the previous review there was not sufficient evidence to meet criterion 4 that a suitable screening test was available, and the current evidence map aims to determine the volume and type of evidence in this area published since 2016.

Findings and gaps in the evidence

The review for key question 1 focussed on the epidemiology of stomach cancer and found evidence from 5 peer reviewed studies and 2 data reports that were sufficient to meet the UK NSC criterion about understanding the prevalence and incidence of the condition. All the publications reported secondary analysis of national cancer registry data to determine the prevalence and/or incidence of people registered with an ICD 10 stomach cancer diagnosis in a complete year or period of years in the UK. The different publications reported incidence by different population characteristics and risk factors. Results extracted from the publications are similar to the findings of the previous UK NSC review in 2016 with the most important modifiable risk factor, *H.pylori* infection, continuing to account for around 40% of stomach cancer cases. When appraised the included studies were all of high quality

with no concerns about sample selection and estimation methods. There were concerns about the proportion of stomach cancers registered as ‘unspecified’ which means sub site specific trends (for example in cardia and non-cardia sub sites) are unreliable and difficult to interpret.

Early trends and future predictions of changes in the characteristics of the people who develop stomach cancer suggest that there will be a continued steep acceleration of people under 50 developing the condition over the next 20 years driven by exposure to risk factors other than *H.pylori,* such as being overweight or obese. There will also be a rise in stomach cancers in the age group 50 to 69 driven by similar factors to those in the younger age groups. It will be important to continue to monitor these changes by different population characteristics such as gender, age group, anatomical sub site, socioeconomic status and other risk factors in the future.

Key question 2 focussed on identifying the volume and type of publications available about tests for population screening for stomach cancer and found a single new study that met the inclusion criteria published since the last evidence summary by the UK NSC in 2016. There is considerable literature about outcomes of screening programmes in Asia in terms of improved survival and detecting cancers at an earlier stage but a dearth of studies about the performance of screening tests.

Recommendations on screening

This evidence update about the epidemiology of stomach cancer and evidence map about screening tests for the condition has been prompted by more recent evidence of an increase in diagnoses of cancers of the stomach cardia which may be linked to environmental risk factors other than *H.pylori.* For key question 1, the volume, quality and direction of new evidence is sufficient to ensure that UK NSC criterion 1 about understanding the natural history of stomach cancer continues to be met.
The findings of this evidence summary are similar to the last UK NSC review in 2016, however future changes in the natural history of stomach cancer are highly likely. It is recommended that these changes are monitored.

For key question 2, a single, small, prospective cohort study of screening in Chinese males was the only eligible study exploring the accuracy of tests for population based screening for stomach cancer identified since the last UK NSC update in 2016. A further review of the evidence in this key area is not currently justified.

Limitations

This rapid review process was conducted over a condensed period of time. Studies not available in the English language, abstracts and poster presentations, were not included.

Evidence uncertainties

The volume, quality and direction of new evidence is sufficient to ensure that the UK NSC criterion 1 about understanding the natural history of the condition continues to be met. However, it is likely that the natural history of stomach cancer will change in the future with predictions suggesting increased exposure to some risk factors will impact on the groups of people likely to develop the condition. It will be important to monitor future changes in the incidence of stomach cancer by age, gender, anatomical sub site, socio-economic status and other risk factors.

Introduction and approach

This document reviews the evidence on the epidemiology of a form of stomach cancer called gastric adenocarcinoma, against the UK National Screening Committee (NSC) criterion about the understanding of the natural history of the condition. The document also maps the available evidence about the performance of screening tests for stomach cancer against the UK NSC criterion about the availability of a suitable accurate test. The purpose of the evidence map is to provide the basis for discussion by the UK NSC so an informed decision can be made about whether there is sufficient evidence to justify commissioning a more sustained review of the evidence about screening tests for stomach cancer.

Gastric adenocarcinoma accounts for 95% of all stomach cancer diagnoses in adults in the UK and in this document these 2 terms (stomach cancer and gastric adenocarcinoma) are used interchangeably to reflect the terminology used by the included studies.

Background

Stomach cancer is a major cause of cancer mortality worldwide[1]. In 2017 it was the 5th most common cancer globally and the 17th most common in the UK[2,3]. In the same year there were 6,595 cases of stomach cancer diagnosed and 4,370 deaths from the condition in the UK[2]. Trends in the incidence and mortality of stomach cancer show a decline in many countries including the UK. The UK age-standardised incidence rate for stomach cancer has steadily decreased since the early 1990s, from 23.4 per 100,000 in 1993 to 10.3 per 100,000 in 2017[2].

There are a number of factors which are known to increase the risk of developing stomach cancer. The presence of the bacterium *Heliobactor pylori (H.pylori)* has been identified as the most important risk for developing stomach cancer[4]. The chronic inflammation in the stomach due to the presence of *H.pylori* induces cell changes in the stomach mucosa; a precursor to the development of the condition. Diagnosis and treatment of people with *H.pylori* since the 1990's is thought to be instrumental in an overall decline in the incidence of stomach cancer seen in many countries including the UK[5]. Treatment relies on the use of 1 or more of 5 antibiotics to eradicate the bacterium[6]. These include clarithromycin, metronidazole, levofloxacin, amoxicillin and tetracycline. *H.pylori* antibiotic resistance to these drugs suggests that this is associated with an increased risk of treatment failure[6]. In the UK. *H.pylori* antibiotic resistance to clarithromycin is 36%(95% confidence intervals(CI) 30-43), metronidazole is 57%(95% CI, 51-63), levofloxacin 11% (95% CI, 8-16), amoxicillin 2%(95% CI 1-5) and tetracycline is 2% (95% CI 1 -4)[6]. As antibiotic resistance exhibits

regional differences the World Health Organisation (WHO) recommend the selection of treatment based on local resistance patterns[6].

The other important population characteristics that increase the risk of gastric adenocarcinoma are age, sex, social deprivation and ethnic origin. Incidence rates rise steadily from around age 45-49 years with the highest rates in the 85 to 89 age group[2]. Males have a higher incidence of gastric adenocarcinoma than females accounting for 65% of all new cases in the UK[2]. Incidence rates in males are 86% higher and in females 93% higher in the most deprived areas compared with the least deprived[2]. A report by the National Cancer Intelligence Network in 2009 reported that people of Caucasian ethnicity were more likely to develop stomach cancer compared to people of Asian origin but less likely to develop the condition than those of a Black African or Caribbean origin[7].

The International Agency for Research on Cancer (IARC) have listed the particular environmental factors where there is convincing evidence that exposure increases the risk of developing gastric adenocarcinoma[8]. These include tobacco smoking, obesity, occupations involving rubber production and exposure to X-radiation or gamma radiation. Environmental factors with limited or probable evidence of increasing the risk of gastric adenocarcinoma include; asbestos; Epstein-Barr virus (a common virus in humans also known as glandular fever); inorganic lead compounds; nitrate or nitrite; traditional Asian pickled vegetables; processed meat; alcohol; and foods preserved by salting.

There are 2 systems most often used to describe how gastric adenocarcinomas look and develop; the Lauren classification[4] and the World Health Organisation (WHO) classification[9]. The Lauren classification divides adenocarcinomas into 2 main groups, solid tumours known as an intestinal type accounting for most stomach cancer diagnoses and diffuse type which are poorly differentiated tumour cells scattered throughout the stomach found in 1% to 3% of cases[4] . Some people can have a mix of intestinal and diffuse types of tumour. The WHO classification separates stomach cancers by their morphology; tubular adenocarcinoma is made up of branching tubules; papillary adenocarcinoma comprises finger like tumours growing out of the stomach wall; mucinous adenocarcinoma has a lot of mucin surrounding the cancer cells; poorly cohesive carcinomas are clumps of tumour cells and mixed carcinoma can be a mix of any of the 5 types[9].

Gastric adenocarcinomas are usually classified as cardia and non-cardia according to their anatomical site. Non-cardia cancer, also known as distal stomach cancer occurs in the lower portion of the stomach whereas, cardia stomach cancers occur at the top of the stomach, close to where the stomach joins the oesophagus[4]. Despite the overall decline in gastric adenocarcinoma there is evidence that the incidence of cardia cancers in many countries including the UK, is increasing[4]. There has been a particular focus of some studies on the link between obesity and development of gastric adenocarcinoma in the

stomach cardia adjacent to the oesophagus[4]. There is a suggestion that some gastric adenocarcinomas of the cardia have a similar aetiology to oesophageal adenocarcinoma occurring near the junction of the oesophagus and the stomach. Increasing obesity is thought to be responsible for an increase in gastro-oesophageal reflux disease; a risk factor for oesophageal adenocarcinoma and this has also been implicated in the rise of stomach cardia cancers[4].

Screening for stomach cancer

Three pre-malignant stages have been identified that precede the development of gastric adenocarcinoma, these are; atrophic gastritis; intestinal metaplasia and dysplasia. Accurately identifying and treating people with these pre-malignant stages of the condition is important in improving survival rates[10]. Some countries with a high incidence of gastric adenocarcinoma such as Japan (27.5 per 100,000 population in 2018)[3] and South Korea (39.6 per 100,000 population in 2018)[3] screen their populations for the pre-malignant stages of the condition and there is some evidence that these screening programmes have improved survival[10,11,12] . The incidence rate of stomach cancer in Japan and South Korea has been decreasing over past decades in a similar way to countries who have not implemented screening such as the UK. For example, in Japan the incidence of stomach cancer in males was 79.2 per 100,000 population in 1983 and had fallen to 70.2 in 1993 and 51.0 in 2002[13].

There are a range of different types of screening tests to identify people at high risk of developing stomach cancer. Procedures to visually detect stomach abnormalities using upper endoscopy or contrast radiography with barium meal are used in screening programmes in South Korea and Japan[12]. The previous UK NSC review concluded that the adverse outcomes of the endoscopy in terms of risk of haemorrhage, mortality and morbidity did not justify its use in routine population based screening in the UK.

Less invasive tests have been developed to screen for the presence of *H.pylori*. Serology tests employ enzyme linked immunosorbent assays to detect serum *H. pylori* specific immunoglobulin G and immunoglobulin A antibodies, whilst the fecal *H. pylori* antigen test is performed using either a monoclonal or polyclonal enzyme immunoassay[14].

The C^{13}-urea breath test is based on the ability of *H.pylori* to convert urea to carbon dioxide (CO^2) and ammonia[15]. Patients ingest urea labelled with the C^{13} isotope and 10 to 30 minutes later a breath test detects the waste products of the bacterium as ammonia and CO^2 labelled with C^{13}.

Another biomarker test involves detecting serum pepsinogen. Pepsinogen (PG), an inactive precursor of the enzyme pepsin, is produced in the stomach and has 2 main biochemically and immunologically different isozymes (PG I and PG II). In areas of the stomach with atrophic gastritis there is a reduction in PG I whilst the presence of *H.pylori* results in an increase in PG II. The serum levels and ratio of PG I to PG II is used to determine the presence of *H.pylori*[16]. Testing for gastrin-17 is often carried in conjunction with PG screening as high levels of serum gastrin often indicate chronic atrophic gastritis, the precursor to gastric cancer.

The monoclonal gastric cancer 7 antigen (MG7-Ag) biomarker has also been assessed for potential as a screening test. However, in the last UK NSC review a single study of a Chinese population had explored its suitability for screening for stomach cancer[17].

The previous UK NSC review concluded that there are currently no tests for *H.pylori*, or any other biomarkers or combinations of biomarkers that are sufficiently valid for use in a population-based screening programme.

This evidence update and map about the epidemiology and screening tests for stomach cancer has been prompted by more recent evidence of an increase in diagnoses of cancers of the stomach cardia which may be linked to environmental risk factors other than *H.pylori*.

Current guidance

In the most recent guideline about stomach cancer published by the British Society of Gastroenterology (BSG), endoscopic screening for gastric adenocarcinoma in the UK population is not recommended[1]. However, there was a consensus that screening could be considered for a sub group of the population with multiple risk factors for developing the condition such as people who are over the age of 50, male, with a family history of gastric adenocarcinoma and those who smoke and are obese[1].

Current policy context and previous reviews

The UK NSC currently recommends against screening for stomach cancer. The Committee based this recommendation on the evidence provided by the 2016 review carried out by Solutions for Public Health[17].

In 2016, the UK NSC recommended that a systematic population screening programme for stomach cancer is not recommended because the evidence at the time did not identify a screening test and treatment strategy that was appropriate for use in the UK. This review focused on gastric adenocarcinoma associated with *H.pylori* but as the epidemiology of the

condition may have changed due to a change in the proportion of people with risk factors, the conclusions drawn may no longer be applicable.

Objectives

This evidence summary was prompted by recent evidence of an increase in diagnoses of cancers of the stomach cardia which may be linked to environmental risk factors other than *H.pylori*. The aim of the evidence summary is to review the trends in the epidemiology of stomach cancer in the UK to determine if there have been changes in the incidence and characteristics of the populations diagnosed with the condition in the UK population since the last review.

The objective of mapping the evidence about the accuracy of screening tests for stomach cancer in adults is to gauge the volume and type of evidence available to inform a decision on whether commissioning a more in depth review is justified about this topic.

Table 1. Key questions for the evidence summary, and relationship to UK NSC screening criteria

	Criterion	Key questions	Studies included
	THE CONDITION	**Key review question**	
1	The condition should be an important health problem as judged by its frequency and/or severity. The epidemiology, incidence, prevalence and natural history of the condition should be understood, including development from latent to declared disease and/or there should be robust evidence about the association between the risk or disease marker and serious or treatable disease.	What is the incidence and prevalence of Gastric adenocarcinomas in the UK? Sub-questions: 1. What is the overall incidence and prevalence of Gastric adenocarcinomas in the UK? 2. What is the incidence and prevalence of different classifications of Gastric adenocarcinomas in the UK, such as Lauren or WHO classifications? 3. What is the incidence and prevalence of Gastric adenocarcinomas in the UK by anatomic sites (i.e. cardia or non-cardia, stomach, oesophagus or other locations)? 4. What is the incidence and prevalence of Gastric adenocarcinomas in the UK by risk factor or cause (i.e. H Pylori, diet, smoking etc)?	5 peer reviewed studies and 2 data reports
4	There should be a simple, safe, precise and validated screening test.	What is the test accuracy of screening tests for the detection of gastric and stomach cancer?	1

Methods

The current evidence summary was conducted by Solutions for Public Health in keeping with the UK National Screening Committee evidence review and evidence map processes.

Database searches (Medline and Embase) to identify studies relevant to key question 1 were conducted on 30th June 2020.

Systematic searches of 3 databases (Medline, Embase and Cochrane) were conducted on the 18th August 2020 to identify studies relevant to key question 2.

Eligibility for inclusion in the evidence summary

Key question 1: In order to review the evidence available about the recent trends in the prevalence and incidence of stomach cancer this process was followed:

1. Each title and abstract was reviewed against the inclusion/exclusion criteria by 1 reviewer. If applicability of the inclusion criteria was unclear, the article was included at this stage in order to ensure that all potentially relevant studies were captured
2. Full-text articles required for the full-text review stage were acquired
3. Each full-text article was reviewed against the inclusion/exclusion criteria by 1 reviewer, who determined whether the article was relevant to 1 or more of the review questions
4. Data extraction and critical appraisal was conducted by 1 reviewer
5. Any queries at the abstract, full-text, or data extraction stage were resolved through discussion with a second reviewer
6. The review was quality assured by a second senior reviewer, not involved with the writing of the review in accordance with SPH's quality assurance process.

Key question 2: In order to assess the volume of evidence available about screening tests for stomach cancer this process was followed:

1. Each title and abstract was assessed against inclusion/exclusion criteria by 1 reviewer and included publications were reviewed at abstract level though in some cases full texts were reviewed to clarify uncertainty.
2. To examine the volume and type of evidence available, the key information extracted and reported from the abstracts (or full text where necessary) includes:
    - type of study (systematic review, meta analysis, RCT etc),
    - country
    - number of studies (in systematic reviews) or participants (primary research)
    - search dates (systematic reviews)
    - study objective
    - population
    - intervention

    - comparator
    - study outcome measures or other type of results reported
3. Any queries were resolved through discussion with a second reviewer
4. The findings of the map question were quality assured by a second senior reviewer, who was not involved with the writing of the review in accordance with SPH's quality assurance process.

Eligibility criteria for the key questions are presented in **Error! Reference source not found.** and 3.

Table 2. Inclusion and exclusion criteria for key question 1

Key question	Inclusion criteria				Exclusion criteria
	Population	**Target condition**	**Outcome**	**Study type**	
1 What is the incidence and prevalence of gastric adenocarcinomas in the UK? Sub questions: • what is the overall incidence of Gastric adenocarcinomas in the UK? • what is the incidence and prevalence of different classifications of Gastric adenocarcinomas in the UK, such as Lauren or WHO classifications • what is the incidence and prevalence of Gastric adenocarcinomas in the UK by anatomic sites (i.e. cardia or non-cardia, stomach, oesophagus or other locations)? • what is the incidence and prevalence of Gastric adenocarcinomas in the UK by risk factor or cause (i.e. H Pylori, diet, smoking etc)?	Adult population	Gastric adenocarcinoma	Incidence, prevalence, and 95% confidence intervals	Cross sectional, cohort, systematic reviews and/or meta-analyses of these, any statistical reports from published or grey literature	Non-UK studies

Table 3. Inclusion and exclusion criteria for evidence map key question 2

Key question	Inclusion criteria						Exclusion criteria
	Population	**Target condition**	**Index test**	**Reference standard**	**Outcome**	**Study type**	
2. What is the test accuracy of screening tests for the detection of gastric and stomach cancer?	Asymptomatic adults in the general population	Gastric adenocarcinoma	Tests considered for use as part of a screening programme	As defined by the study	Sensitivity, specificity, positive predictive value, negative predictive value	Prospective and retrospective studies where patients are randomised to screening/no screening or randomised to different index tests with the same reference standard.	Case control studies, studies with longitudinal assessment of reference standard Studies not in the English language

Appraisal for quality

A critical appraisal tool for prevalence studies published by the Joanna Briggs Institute (JBI) was used to initially assess the quality and risk of bias for each of the publications included for key question 1[18]. The British Journal of General Practitioners (BJGP) has proposed key areas where there are likely to be challenges for researchers in carrying out secondary analysis of large databases[19]. These areas overlap to some extent with the JBI checklist criteria but with a specific focus on; process of selection of records from a general database; the use of different estimation methods to enable comparisons between countries; diagnostic coding accuracy; historic diagnostic coding changes; a lag in data availability; and completeness of records. All but one of the BJGP questions were incorporated within the JBI tool as appropriate and one question on incomplete data measurement of exposure was added to Table 8 that summarises the critical appraisal of the studies. Question 9 of the JBI tool about the response of the study population to the research questions is not applicable to the included studies as no response was required from these study populations.

For key question 2, a formal quality appraisal of the evidence was not required, given the scope of UK NSC evidence map questions.

Databases/sources searched (key question 1)

Systematic searches of 2 databases (Medline and Embase) were conducted to identify studies relevant to key question 1. We conducted additional targeted searches using NICE Evidence Search, the TRIPdatabase and Google for publications in the English language, reporting UK stomach cancer incidence and prevalence rates not listed in the above databases.

The searches were conducted on 30th June 2020 for key question 1 and the search strategy is presented in Appendix 1.

Evidence review key question 1: Question level synthesis

Criterion 1:

The condition should be an important health problem as judged by its frequency and/or severity. The epidemiology, incidence, prevalence and natural history of the condition should be understood, including development from latent to declared disease and/or there should be robust evidence about the association between the risk or disease marker and serious or treatable disease.

Question 1 – What is the incidence and prevalence of Gastric adenocarcinomas in the UK?

Sub questions:

- *what is the overall incidence of Gastric adenocarcinomas in the UK?*
- *what is the incidence and prevalence of different classifications of Gastric adenocarcinomas in the UK, such as Lauren or WHO classifications?*
- *what is the incidence and prevalence of Gastric adenocarcinomas in the UK by anatomic sites (i.e. cardia or non-cardia, stomach, oesophagus or other locations)?*
- *what is the incidence and prevalence of Gastric adenocarcinomas in the UK by risk factor or cause (i.e. H Pylori, diet, smoking etc)?*

The previous UK NSC review (2016) reported the overall incidence of stomach cancer in the UK and by age, gender, and the proportion that were likely to be caused by *H.pylori*. The review found that the UK age-standardised incidence rate for stomach cancer had been steadily decreasing since the early 1990s. The cancer was the 11th most common cancer in UK men and the 15th most common cancer in UK women. About 90% of new cases of stomach cancer occurred in people aged 55 and over, and approximately 50% of cases were diagnosed in people aged 75 and over. About 95% of cancers were reported as adenocarcinomas, of which 32% were estimated to be associated with *H.pylori*.

Eligibility for inclusion in the review

For this question we included peer-reviewed published studies about the overall incidence and prevalence of gastric adenocarcinoma in the UK, by Lauren or WHO classifications and by anatomic site. Studies examining stomach cancer by sociodemographic factors such as age, gender, ethnicity, socioeconomic status and modifiable risk factors such as *H.pylori*, smoking and obesity were also included. We also included ‘grey literature’ publications by organisations that reported national incidence and prevalence rates of stomach cancer.

Description of the evidence

Database searches yielded 1,074 unique results, of which 32 were judged to be relevant to this question. These comprised 28 peer-reviewed studies and 4 data reports.

After review of the full texts, 7 publications met the inclusion criteria for this question. These consisted of 5 peer-reviewed studies and 2 data reports carrying out secondary data analysis of nationally collected registry data about cancer incidence and prevalence in the UK.

Nationally collected cancer registry data is used by a range of researchers and national and international organisations who carried out secondary data analysis of cancer registrations of UK population based cohorts diagnosed with stomach cancer based on the International Disease Classification version 10 (ICD-10 disease category C16).

National organisations such as the Office for National Statistics (ONS) and Cancer Research UK (CRUK) and international groups such as International Agency for Research into Cancer (IARC), Cancer incidence of the 5 continents (Ci5) and the Global Burden of Disease (GBD) study, all access the same registry data and collate, model and compare cancer data for research and health planning purposes. The different data repositories employ different methods of standardisation and modelling of incidence and prevalence so there can be small variations in the results reported for the same time periods.

Of the relevant studies and reports relating to overall cancer incidence and prevalence (sub-question 1), 2 peer-reviewed studies and 2 data reports have been included.

No publications were identified that met the search criteria for sub-question 2 about the incidence of histopathological sub-types of stomach cancer using either the Lauren or WHO classification of stomach cancers in UK populations.

For sub-question 3 about stomach cancer incidence by anatomical sub site, 2 peer-reviewed publications and 1 data report have been included.

Of the relevant studies relating to the incidence of stomach cancer by risk factor (sub-question 4), a single peer-reviewed study has been included.

0contains a full PRISMA flow diagram (Figure 2), along with a table of the included publications (Table 11).

The exclusion of 25 peer reviewed studies or data reports was due either to studies only reporting data from 1 part of the UK when similar data was available for the whole of the UK, or when analysis of data for a more recent time period was available (Appendix 2 Table 12).

Discussion of findings

A study-level summary of data extracted from each included publication and data source is presented in the 'Summary and appraisal of individual studies' in **Error! Reference source not found.**' and are stratified by sub-question.

Sub-question 1: What is the overall incidence of Gastric adenocarcinomas in the UK?

For sub-question 1 about the overall prevalence and incidence of stomach cancer in the UK, studies that examined incidence by age, gender and longitudinal trends over a period of years are included.

The peer-reviewed studies by Arnold et al (2020)[20] and Fitzmaurice et al (2019)[21], and 2 data reports extracted from the Global Burden of Disease study[22] and Cancer Research UK[23] are included for this sub-question.

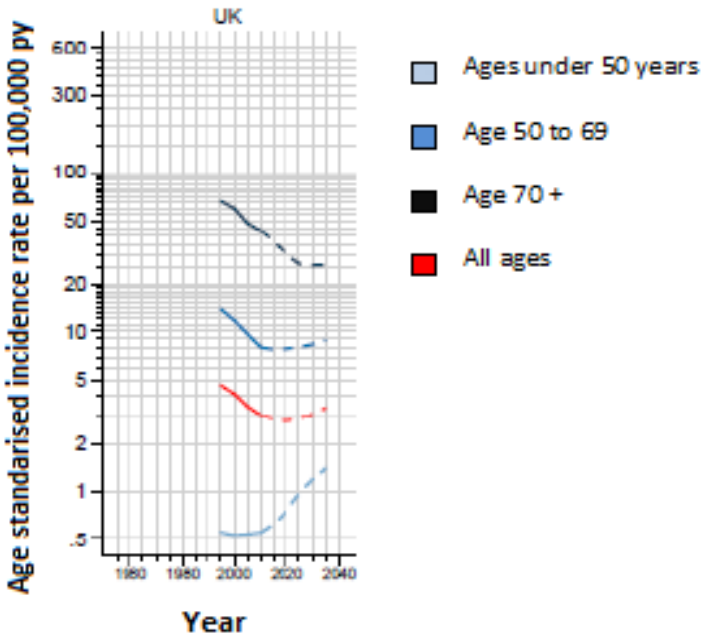
Arnold et al (2020)[20] carried out a secondary analysis of the UK National Cancer Registry Data extracted from the Ci15 Plus dataset held by IARC. This study examines historical gastric cancer trends from 2010 in 34 countries, including the UK and modelled the likely rates to 2035. The UK age standardised rates per 100,000 person years were 5.2 in 2010 and predicted to fall to 4.7 by 2035. Absolute numbers of cases in the UK were predicted to increase slightly from 7,446 in 2010 to 7,863 in 2035. The modelling largely attributed this change to a change in population rather than the presence of risk factors.

Predictions of the change in incidence for those aged under 50 were highlighted by Arnold et al (2020)[20] and suggest this part of the population will experience a steep rise in stomach cancer incidence. Numbers of stomach cancer cases in the UK in people under 50 were predicted to increase from 398 in 2010 to 832 in 2035, a doubling of the incidence rate from 0.7 to 1.4 per 100,000 population. The modelling attributed this change to an increase in the presence of environmental risk factors such as obesity.

Arnold et al (2020)[20] reported a comparison of predicted change in incidence by different age groups graphically only (Figure 1). This suggests that whilst the incidence of stomach cancer in people aged 70 and over will continue to fall and then plateau to 2035 there will be a steep rise in the incidence in stomach cancer in those aged under 50 and a less steep

rise in those aged 50 to 69. Overall, the incidence is predicted to fall with the impact of the rising incidence of stomach cancer in the younger age groups being masked by the decrease in older age groups. Despite the steep rise in stomach cancer in the younger age groups the predictions suggest that by 2035 those rates will still be lower than the rates of stomach cancer in older age groups.

Figure 1. Predicted change in age standardised incidence of stomach cancer per 100,000 person years in the UK by age group from 2010 to 2035 (Source: Arnold et al, 2020)[20]



The study by Fitzmaurice et al (2019)[21] describes the methods and high level results of carrying out secondary data analysis of cancer registry data which has now become part of the Global Burden of Disease study data repository. In order to access a more detailed output of the results from this secondary data analysis reviewers extracted data specific to stomach cancer in the 4 UK countries, as a data report from the GBD study[22]. The peer-reviewed study by Fitzmaurice et al (2019)[21] and the GBD study[22] data extract is treated together for the purposes of this review. The GBD study is a repository for data about the disease burden of 195 countries using data gathered by each nation[21]. Cancer registry data is submitted from each country and standardisation and secondary data analysis is carried out to provide comparable information to describe cancer incidence, prevalence, mortality, years of life lost, years lived with disability and disability-adjusted life years[21]. New data is submitted annually, and the secondary analysis process is updated with all years being

recalculated[21]. The study by Fitzmaurice et al (2019)[21] describes the methods and outcomes of carrying out the secondary data analysis for 29 cancers including gastric cancer by country using the latest available data for 2017. The reviewers downloaded the incidence (per 100,000 person years) and 10 year prevalence from the GBD dataset for 1992 and 2017 for the 4 countries of the UK[22].

Whilst the incidence overall for men and women has decreased considerably in the 25 years from 1992 to 2017 (15.18, 95% Uncertainty Interval (UI) 14.80 to 15.57 per 100,000 people in 1992 vs 10.33, 95% UI 10.06 to 10.65, in 2017), the 10 year prevalence has not changed appreciably (27.25, 95% UI 26.59 to 27.93 in 1992 to 27.08, 95% UI 26.34 to 27.93 per 100,000 population in 2017)[21,22].

Cancer Research UK[23] reported secondary data analysis of age and gender specific incidence rates for 2015 to 2017. Males and females had similar incidence rates up to age band 30 to 34 (0.8 and 0.7 per 100,000 person years respectively) and then rates increased in males compared to females in older age bands[23]. The largest difference between males and females was in the age group 65 to 69, when the age-specific incidence rate was 2.6 times lower in females than males (females,12.0 vs males, 31.3)[23].

Stomach cancer age standardised incidence rates in the UK decreased by 53% in females and 55% in males between 1993-1995 and 2015-2017.

Table 4 summarises the incidence and prevalence figures reported by each of the studies and data reports.

Table 4. Studies included reporting overall stomach cancer incidence and prevalence by age and gender in the UK

Study	Area	Time	Age	Gender	Incidence (95% UI)
Arnold (2020)[20]	34 countries including the UK	2010	All	All	5.2
		2035	All	All	4.7
		2010	<50 years	All	0.7
		2035	<50 years	All	1.4
Fitzmaurice et al (2019)[21] and the GBD data report[22]	195 countries including 4 countries of the UK	1992	All	All	15.18 (14.80-15.57)
		2017	All	All	10.33 (10.06-10.65)

		1992	All	Male	23.55 (22.74-24.39)
		2017	All	Male	14.84 (14.31-15.43)
		1992	All	Female	9.22 (8.92-9.56)
		2017	All	Female	6.55 (6.27-6.85)
CRUK[23]	4 countries of the UK	2015-17	30 to 34	Female	0.8
			35 to 39	Female	1.3
			40 to 44	Female	1.7
			45 to 49	Female	2.4
			50 to 54	Female	4
			55 to 59	Female	6.4
			60 to 64	Female	9
			65 to 69	Female	12
			70 to 74	Female	18.6
			75 to 79	Female	31.8
			80 to 84	Female	42.3
			85 to 89	Female	51.9
			90+	Female	43.2
			30 to 34	Male	0.7
			35 to 39	Male	1.4
			40 to 44	Male	2.5
			45 to 49	Male	4.4
			50 to 54	Male	8.1
			55 to 59	Male	12.9
			60 to 64	Male	21.2
			65 to 69	Male	31.3
			70 to 74	Male	48.1
			75 to 79	Male	76.8
			80 to 84	Male	100.6
			85 to 89	Male	117.2
			90+	Male	102
		1993	All	Female	14.8
		2017	All	Female	6.6
		1993	All	Male	36
		2017	All	Male	14.9

UI -Uncertainty interval, GBD – Global Burden of Disease

Sub-question 2: What is the incidence and prevalence of different classifications of Gastric adenocarcinomas in the UK, such as Lauren or WHO classifications?

No publications were identified that met the search criteria for this sub-question.

Sub-question 3: What is the incidence and prevalence of Gastric adenocarcinomas in the UK by anatomic sites (i.e. cardia or non-cardia, stomach, oesophagus or other locations)?

For this sub-question, 2 peer reviewed studies Deakhshan et al (2016)[24] and Coupland et al, (2012)[25] are included with both reporting the incidence of stomach cancer in parts or the whole of the UK by anatomical sub site. A data report by CRUK[23] reporting the results of secondary analysis of national cancer registration data by sub site for the years 2006 to 2010 is also included.

Derakhshan et al (2016)[24] reported the age standardised incidence rates of cardia and non-cardia stomach cancer per 100,000 person years in the UK in 2012. The incidence of cardia cancer vs non-cardia was higher in men (3.89 vs 2.55) but not in women (1.46 vs 1.69)[24].

The study also carried out an analysis of the trend in incidence of oesophageal and stomach cancer in the North West of England, the South West of England and Scotland over the period 1989 to 2007[24]. In the North West of England, the incidence rate per 100,000 person years of total stomach cancer decreased in men from 17.76 in 1989 to 10.12 in 2007 with a similar pattern in women (7.74 vs 4.08)[24]. In contrast the rates of oesophageal cancer increased in men from 3.70 in 1989 to 7.70 in 2007 and for women from 0.86 to 1.34[24]**Error! Bookmark not defined.**. Similar trends were seen in the South West of England and Scotland and all 3 areas had a highly significant inverse correlation between stomach cancer and oesophageal cancer (North West England correlation coefficient (CC) -0.800 $p<0.000$, South West England CC-0.774, $p<0.000$ and Scotland CC -0.913, $p<0.000$)[24].

Coupland et al (2012)[25] analysed 133,804 English patients diagnosed with oesophageal and stomach cancer between 1998 and 2007. They reported the incidence of cardia stomach cancer was much higher in males than females (M:F 4:1) and was higher in the most socioeconomically deprived quintiles(Q) (Q5:Q1 1.5:1 males; 1.7:1 females). Similarly, in non-cardia stomach cancers incidence was twice as high in males, than females and was also higher in more deprived areas (Q5:Q1 2.0:1 males; 1.9:1 females)[25].

Table 5 summarises the incidence figures reported by the studies and data report.

Table 5. Studies meeting the evidence review inclusion criteria reporting incidence of gastric cancer by anatomical subsite in part or the whole of the UK

Study	Area	Gender	Year	Anatomic subsite	Rate per 100,000 person years
Derakhshan et al (2016)[24]	38 countries including the regions of the UK	Males	2012	Total stomach cancer	6.44
				Cardia stomach cancer	3.89
				Stomach non cardia	2.55
		Females	2012	Total stomach cancer	3.15
				Cardia stomach cancer	1.46
				Non cardia Stomach cancer	1.69
Derakhshan et al (2016)[24]	North west England region	Males	1989	Total gastric cancer	17.76
				Oesophageal cancer	3.70
			2007	Total gastric cancer	7.74
				Oesophageal cancer	0.86
		Females	1989	Total gastric cancer	7.74
				Oesophageal cancer	0.86
			2007	Total gastric cancer	4.08
				Oesophageal cancer	1.34
	South West England Region	Males	1989	Total gastric cancer	14.79
				Oesophageal cancer	3.46
			2007	Total gastric cancer	7.04
				Oesophageal cancer	5.84
		Female	1989	Total gastric cancer	3.77
				Oesophageal cancer	0.48
			2007	Total gastric cancer	2.72
				Oesophageal cancer	1.11
	Scotland	Males	1989	Total gastric cancer	18.56
				Oesophageal cancer	3.42
			2007	Total gastric cancer	9.72
				Oesophageal cancer	7.47
		Females	1989	Total gastric cancer	7.90
				Oesophageal cancer	1.05
			2007	Total gastric cancer	4.57
				Oesophageal cancer	1.49
Coupland et al (2012)[25]	England	All	1998	Cardia stomach cancer	10.8
			2007	Cardia stomach cancer	9.2
			1998	Non cardia stomach cancer	11.4
			2007	Non cardia stomach cancer	9.4
			1998	Stomach cancer NOS	11.7
			2007	Stomach cancer NOS	8.9
			1998	Lower oesophageal cancer	8.6
			2007	Lower oesophageal cancer	11.2
			1998	Upper/mid oesophageal cancer	9.4
			2007	Upper/mid oesophageal cancer	10.4
			1998	Oesophageal cancer NOS	11.8
			2007	Oesophageal cancer NOS	8.2
			1998	Total stomach + oesophageal cancer	10.4
			2007	Total stomach + oesophageal cancer	9.7

CRUK[23] carried out secondary data analysis of anatomic sub site of stomach cancers in men and women from national cancer registry data collected between 2010 and 2012. The proportion of people with cardia stomach cancer is higher in males (34.0%) than females (19.7%) with cancers classified as unspecified or present in overlapping areas higher in women than in men (48.5% vs 39.1%)[23].

Table 5. Proportion of gastric cancers diagnosed by anatomical subsite (CRUK)

Study	Area	Gender	Year	Anatomic subsite (ICD 9 code)	Percentage diagnosis at each site
CRUK[23]	UK	Males	2010-2012	Cardia (16.0)	34.0%
				Fundus of Stomach (C16.1)	2.6%
				Body of Stomach (C16.2)	6.4%
				Pyloric Antrum (C16.3)	7.1%
				Pylorus (C16.4)	3.5%
				Lesser Curvature of Stomach, Unspecified (C16.5)	5.6%
				Greater Curvature of Stomach, Unspecified (C16.6)	1.8%
				Stomach, Overlapping and Unspecified (C16.8-C16.9)	39.1%
				Total	100.0%
		Females	2010-2012	Cardia (16.0)	19.7%
				Fundus of Stomach (C16.1)	2.7%
				Body of Stomach (C16.2)	7.3%
				Pyloric Antrum (C16.3)	9.5%
				Pylorus (C16.4)	4.7%
				Lesser Curvature of Stomach, Unspecified (C16.5)	5.1%
				Greater Curvature of Stomach, Unspecified (C16.6)	2.4%
				Stomach, Overlapping and Unspecified (C16.8-C16.9)	48.5%
				Total	100.0%

Sub-question 4: What is the incidence and prevalence of Gastric adenocarcinomas in the UK by risk factor or cause (i.e. H Pylori, diet, smoking)?

For this sub-question the focus of the search was to identify studies that had examined the role of modifiable risk factors on the incidence of stomach cancer in the UK. A single study is included by Brown et al (2018)[26] who calculated the population attributable fractions and attributable cases to the incidence of cancers by risk factor, by gender and UK country for 31 cancers including stomach cancer.

Brown et al (2018)[26] reported that the 3 modifiable risk factors that contributed most to the incidence of stomach cancer in 2015 were *H.pylori* infections (41.1%), tobacco smoking

(14.8%) and being overweight or obese (6.3%) (Table 6). Overall, 54.2% (3,649) of incident stomach cancer diagnoses were estimated to be due to modifiable risk factors. A higher proportion of stomach cancer in males was attributable to modifiable risk factors (57.3%) compared to females (48.6%). A higher proportion of stomach cancer cases were attributable to tobacco smoking in males (21.0%) compared to females (3.4%). Being overweight or obese contributed to 7.4% of cases in males and 4.3% in females and males had occupations that were more likely to expose them to the risk of stomach cancer (3.3%) than females (0.3%). Women were more likely to have stomach cancer from exposure to *H.pylori* infections than males (43.7% vs 39,7%).

Table 6. Table showing the fraction of stomach cancer attributable to modifiable risk factors by gender in the United Kingdom in 2015 Brown et al (2018)[26]

Males n= 4,353	**Risk factor**	**Population attributable fraction (%)**	**Attributable cases**
	Tobacco	21.0%	912
	Overweight and obesity	7.4%	320
	Infections (eg *H.pylori*)	39.7%	1,742
	Occupation	3.0%	131
	Radiation - ionising	0.4%	19
	All of the above	**57.3%**	**2,496**
Females n=2,383	**Risk factor**	**Population attributable fraction (%)**	**Attributable cases**
	Tobacco	3.4%	81
	Overweight and obesity	4.3%	102
	Infections (eg *H.pylori*)	43.7%	1,042
	Occupation	0.3%	7
	Radiation - ionising	0.9%	22
	All of the above	**48.6%**	**1,159**

Brown et al (2018)[26] also reported the data by individual UK country (Table 7) which shows that 48.2% of cases of stomach cancer can be attributable to combined modifiable risk factors in Wales whilst in Northern Ireland this rises to 65%.

Table 7. Table showing the fraction of stomach cancer attributable to modifiable risk factors combined in the United Kingdom in 2015 (Brown et al 2018)[26]

	Males		**Females**		**Persons**	
	PAF (%)	**Att. Cases**	**PAF (%)**	**Att. Cases**	**PAF (%)**	**Att. Cases**
England	56.4%	2,009	47.5%	921	53.1%	2,925
Scotland	67.6%	260	57.4%	129	64.0%	390
Wales	51.3%	137	43.7%	68	48.2%	203
Northern Ireland	66.0%	90	63.8%	41	65.0%	130
UK	57.3%	2,496	48.6%	1,159	54.2%	3,649

Att. Cases – Attributable cases, PAF – Population attributable fraction

The differences between the countries is largely due to the proportion of cases attributable to *H.pylori* infection rather than other modifiable risk factors with infections accounting for

37.7% of cases in women and 27.5% of cases in men in Wales whilst in Northern Ireland the figures are 60.3% and 53.0% respectively (Table 8).

Table 8. Table showing the fraction of stomach cancer attributable to *H.pylori* infection in the United Kingdom in 2015 (Brown et al 2018)[26]

	Males		Females		Persons	
	PAF (%)	**Cases**	**PAF (%)**	**Cases**	**PAF (%)**	**Cases**
England	38.6%	1,375	42.7%	827	40.0%	2,202
Scotland	53.6%	206	52.5%	118	53.2%	324
Wales	27.5%	73	37.7%	58	31.3%	132
Northern Ireland	53.0%	72	60.3%	39	55.3%	111
UK	39.7%	1,727	43.7%	1,042	41.1%	2,769

Att. Cases – Attributable cases, PAF – Population attributable fraction

Brown et al (2018)[26] limited the type of risk factors for stomach cancer to those with convincing evidence of a causal link as described by IARC but not risk factors with a probable or likely cause of some stomach cancers. This means that estimates of the risk of being overweight and obese and tobacco smoking were included in the analysis but not the of use of alcohol. It is likely that researchers underestimated the true population attribution fraction of risk factors as there may be limited evidence for some risk factor-cancer combinations.

Overall, there is a large volume of evidence describing the overall incidence and prevalence of stomach cancer and the modifiable and non-modifiable risk factors that contribute to the number of people diagnosed annually with the condition. The most recent analysis of incidence rates combined with evidence about risk factor exposure indicate that *H.pylori* is still the main modifiable risk factor for stomach cancer in the UK. There are early signs of an increasing incidence of stomach cancer in people under the age of 50 but the risk factors that might lead to this increase such as tobacco smoking and being overweight or obese still account for a much lower proportion of stomach cancer cases than *H.pylori* although this could change in the future.

Quality Appraisal

The combined critical appraisal of the studies using the JBI prevalence tool and BJGP questions are summarised in Table 9. Overall the included studies were at low risk of bias when assessed using the modified JBI and BJGP tool. All 6 studies met the JBI appraisal of quality criteria for questions 1 to 6 about identifying and sampling the population to be studied. There were some limited concerns about the accuracy of ICD 10 coding of stomach cancer anatomical subsites, the use of confidence intervals of the data and whether there was complete data for the exposure to risk factors. These are detailed below.

Table 9. Appraisal of quality for the included publications combining the JBI prevalence critical appraisal tool and BJGP database research questions

	Arnold et al (2020)[20]	CRUK[23]	Fitzmaurice et al (2019)[21] & GBD	Deakshan et al (2016)[24]	Coupland et al 2012)[25]	Brown et al (2018)[26]
1.Was the sample frame appropriate to address the target population?	Yes	Yes	Yes	Yes	Yes	Yes
2.Were study participants sampled in an appropriate way?	Yes	Yes	Yes	Yes	Yes	Yes
3.Was the sample size adequate?	Yes	Yes	Yes	Yes	Yes	Yes
4.Were the study subjects and the setting described in detail?	Yes	Yes	Yes	Yes	Yes	Yes
5.Was the data analysis conducted with sufficient coverage of the identified sample?	Yes	Yes	Yes	Yes	Yes	Yes
6.Were valid methods used for the identification of the condition?	Yes	Yes	Yes	Yes	Yes	Yes
7.Was the condition measured in a standard, reliable way for all participants?	Yes	Yes	Yes	Yes	No	Yes
8.Was there appropriate statistical analysis?	Yes	Unclear	Yes	Yes	Yes	Yes
9. Was there complete data or measurement of exposure to risk factors?	Yes	Yes	Yes	Yes	Yes	No

Selection bias (BJGP Process of the selection of records and data availability /JBI checklist questions 1 to 5)[18]

The studies included in the review were at low risk of selection bias. This is because all of the studies sampled a country or region in the UK using the same large scale international or national whole population cancer registry databases. These agencies standardise the data, which forms the basis of future estimates of incidence and prevalence. There were no concerns of attrition bias as the studies were not based on data collected from prospective cohorts of patients who may or may not respond to requests for information.

Similarly, the latest year data available about stomach cancer incidence is 2017 due to processing of data within the registries and the agencies that use the information. It is unlikely that this lag is concerning as researchers are able to predict future incidence based on 25 years of historic data collection and changes in incidence are relatively small year on year.

Analysis reporting bias (BJGP Estimation methods / JBI checklist questions 8)[18]

Estimation methods varied between the different agencies as they had different objectives. For example, Arnold et al (2020) developed a model to predict incidence rates in the future using the statistical package NORDPRED whilst the GBD study, re-estimated the entire time series with every new update of the database. Overall the studies were consistent in their results, for example, CRUK[23] reported an incidence of stomach cancer of 6.6 in women and 14.09 in men per 100,000 person years whilst for the same year the GBD study[22] reported an incidence rate with 95% uncertainty intervals of 6.55 (6.27-6.85) for women and 15.06 (14.47 - 15.68) for men.

Confidence intervals were not reported in all studies. The CRUK[23] data report did not report any confidence intervals and as a data report there was limited methodology to understand how the statistical analysis had been completed. The studies by Coupland et al (2012)[25,] Derakhshan et al (2016)[24] and Brown et al (2018)[26] calculated but did not report upper and lower confidence intervals. Brown et al (2018)[26] suggested that confidence intervals for the Population Attributable Fractions can be misleading as they do not take into account all the possible biases effecting the PAF calculations.

Overall the studies had a low risk of bias due to the statistical analysis undertaken. Of the 6 studies 1 publication by CRUK had an unclear risk of bias with no discussion about the methodology for analysing the data and the absence of confidence intervals.

Outcome measurement bias (BJGP Diagnostic coding accuracy / JBI checklist questions 6 and 7)[18, 19]

The ICD-9 diagnostic coding system implemented in 1979 was superseded by the ICD-10 system and first used in 1994. Stomach cancer coding maps exactly between the 2 systems so searching for a stomach cancer code across years is unlikely to uncover coding issues. Therefore, the risk of measurement bias across the studies is low. However, both Arnold et al (2020)[20] and Coupland et al (2012)[25] found that drilling down to the anatomic sub site of stomach cancer using these data sets was not always informative as historically high proportions of cancers were registered as unspecified which means sub site specific trends are unreliable and difficult to interpret increasing the risk of bias.

Incomplete data or measurement of exposure to risk factors (BJGP Completeness of records)[18,19]

The completeness of records of registry data is likely to be adequate for demographic details such as age and gender but may be not be complete for details such as height,

weight and ethnicity. This was not flagged as a concern by any of the studies and in order to establish estimates of the impact of risk factors, other sources of population based information were used.

For 2 of the peer-reviewed studies (Brown et al 2018)[26], Coupland et al 2012)[25] in addition to secondary data analysis of registry data, researchers needed to access other population level data about risk factors such deprivation indices, tobacco smoking rates and overweight and obesity rates by country. Brown et al (2018)[26] obtained prevalence of exposure to risk factors from nationally representative population surveys and where exposure prevalence data were not available data conversions or imputations were made. In order to ascertain deprivation indices Coupland et al (2012)[25] used linked postcode to 2007 indices of deprivation. These estimates will lead to uncertainty in the reliability of the results.

One limitation of the study by Brown et al (2018)[26] was that the included risk factors for stomach cancer were those with convincing evidence of a causal link as described by IARC but not risk factors with a probable or likely link to stomach cancer. This means that estimates of the risk of being overweight and obese and tobacco smoking were included in the analysis but not the of use of alcohol. It is also likely that researchers underestimated the true population attribution fraction of environmental risk factors as there is limited evidence for the synergistic effects of some risk factor-cancer combinations.

Overall where studies were reporting individual characteristics such as age and gender the risk of bias was low. However, when risk factors were included that are less readily measured and collected and the impact of exposure to multiple risk factors unclear, there is likely to be a greater risk of bias.

Summary of Findings Relevant to Criterion 1: Criterion met

For this review question about the epidemiology of stomach cancer 5 peer reviewed publications and 2 data reports were included. All the publications reported secondary analysis of national cancer registry data to determine the incidence of people registered with an ICD 10 stomach cancer diagnosis in a complete year or period of years in the UK. The different publications reported incidence by different population characteristics and risk factors.

There is a large volume of evidence based on the whole population of the UK, describing the incidence and prevalence of stomach cancer and the modifiable and non-modifiable risk factors that contribute to the number of people diagnosed annually with the condition in the UK. The evidence is consistent and applicable to the UK population. When appraised the included studies were all of high quality with no or limited concerns about sample selection and estimation methods. There were concerns about the proportion of stomach cancers registered as ‘unspecified’ which means sub site specific trends are unreliable and difficult to interpret.

This review found that in the UK the current epidemiology of stomach cancer is similar to the findings of the previous UK NSC review in 2016 with the most important risk factor, *H.pylori* infection continuing to account for around 40% of stomach cancer cases. Predictions of changes in the characteristics of the people who develop stomach cancer suggest that there will be an acceleration of people under 50 developing the condition over the next 20 years. It will be important to continue to monitor these changes in the future.

Evidence map key question 2: Screening test performance

Criterion 4: Screening test performance

Criterion 4: There should be a simple, safe, precise and validated screening test

Question 2 – What is the test accuracy of screening tests for the detection of gastric and stomach cancer?

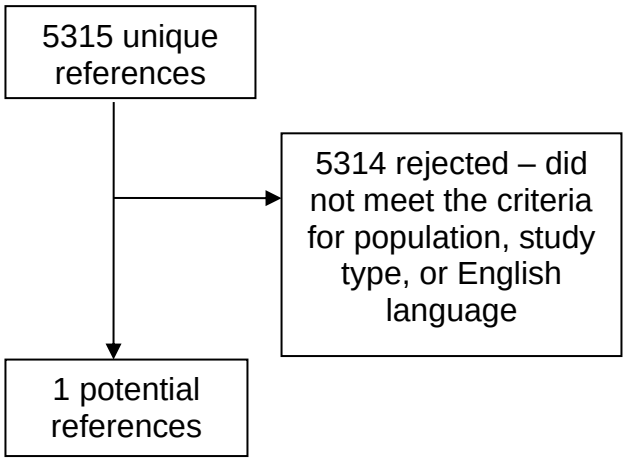
Search results

The search was conducted on 18th August 2020 on 3 databases: [Medline, Embase and Cochrane library]. The search period was restricted to 2014 – August 2020. The detailed search strategies, including exclusion and inclusion criteria are available in Appendix 1. The search returned a total of 5,315 unique references which were initially sifted by an information scientist for potential relevance. One reviewer assessed 570 titles and abstracts for further appraisal and possible inclusion in the evidence map. The full papers of 15 studies were checked to clarify whether they met the inclusion criteria for the evidence map. This clarification centered around the use of the word ‘screening’ in abstracts where either no description of the population screened was noted or there was an absence of screening test performance data. Once the full papers had been checked 1 study met the inclusion criteria set out in Table 3. The remaining studies did not meet 1 or more of the inclusion criteria because:

- no screening test performance outcomes were reported (7 studies)
- the systematic review included papers only from the time period covered by the previous UK NSC review (1 study)
- the study population was symptomatic (4 studies)
- the study was included in the previous review (1 study)
- the study was not in English (1 study)

A flow diagram summarising the number of studies included and excluded is presented in Figure 2.

Figure 2: Summary of included and excluded publications



Summary of findings

A single prospective cohort study met the inclusion criteria. This used faecal testing to identify *H.pylori* in asymptomatic older people (Han et al 2020)[27]. This small study of elderly (≥ 65 years of age), Chinese males, compared the *H.pylori* stool antigen (HpSA) index test with the C^{13} urea breath test as a reference standard. Two groups, those who had previously been diagnosed and treated for *H.pylori* (n=123) and those who had never been diagnosed with *H.pylori* (n=193) were tested. Sensitivity of the test to detect *H.pylori* was 65.1% and specificity was 98.7%, in the group with no previous *H.pylori* diagnosis. Rates were similar in the group with a previous *H.pylori* diagnosis (sensitivity 75.0%, specificity 96.0%)

Multivariate analysis indicated that constipation and colorectal polyps were independent factors for the sensitivity of HpSA in the group with no previous *H.pylori* diagnosis.

The abstract reporting table for this study is in Appendix 5.

In summary, there was a single new study about the accuracy of tests for population based screening for stomach cancer since the last UK NSC update in 2016.

At present there is an insufficient volume of evidence in this key area to justify commissioning an evidence summary.

Overall summary

Conclusions and implications for policy

The review focussed on the epidemiology of stomach cancer and found evidence from 5 peer reviewed studies and 2 data reports that were sufficient to meet the UK NSC criterion about understanding the prevalence and incidence of the condition. All the publications reported secondary analysis of national cancer registry data to determine the prevalence and/or incidence of people registered with an ICD 10 stomach cancer diagnosis in a complete year or period of years in the UK. The different publications reported incidence by different population characteristics and risk factors. Results extracted from the publications are similar to the findings of the previous UK NSC review in 2016 with the most important risk factor, *H.pylori* infection continuing to account for around 40% of stomach cancer cases.

Early trends and future predictions of changes in the characteristics of the people who develop stomach cancer suggest that there will be a continued steep acceleration of people under 50 developing the condition over the next 20 years driven by exposure to risk factors other than *H.pylori,* such as being overweight or obese. There will also be a rise in stomach cancers in the age group 50 to 69 driven by similar factors to those in the younger age groups. It will be important to continue to monitor these changes by different population characteristics such as gender, age group, anatomical sub site, socioeconomic status and other risk factors in the future.

A single study published since the last UK NSC review in 2016 was identified that met the inclusion criteria for the evidence map about accuracy of population based screening tests for stomach cancer. This was a small prospective cohort study of elderly Chinese males. Based on this limited evidence, a further review about the accuracy of screening tests for stomach cancer is not currently justified.

Limitations

This rapid review process was conducted over a condensed period of time. Studies not available in the English language, abstracts and poster presentations, were not included.

Appendix 1 — Search strategy

Electronic databases – key question 1

The search strategy included searches of the databases shown in Table 10. MEDLINE, MEDLINE In-Process, MEDLINE Daily, Epub Ahead of Print and Embase.

Table 10. Summary of electronic database searches and dates

Database	Platform	Searched on date	Date range of search
Embase	OvidSP	1974-present	30/06/2020
Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) 1946 to present	OvidSP	1946-present	30/06/2020

Search Terms – key question 1

Search terms included combinations of free text and subject headings (Medical Subject Headings [MeSH] for MEDLINE, and Emtree terms for Embase).

Search terms for MEDLINE, MEDLINE In-Process, MEDLINE Daily, and Epub Ahead of Print are shown in Table 11 and for Embase in 12.

Table 11. Search strategy for key question 1 - MEDLINE, MEDLINE In-Process, MEDLINE Daily, Epub Ahead of Print

# ▲	Searches	Results
1	Stomach Neoplasms/	96006
2	((gastric or stomach) adj3 (cancer? or carcinoma? or adenocarcinoma? or neoplas* or malignan* or tumo?r?)).ti,ab,kw.	97672
3	(gastro* adj3 (cancer? or carcinoma? or adenocarcinoma? or neoplas* or malignan* or tumo?r?)).ti.	16002
4	1 or 2 or 3	136911
5	prevalence/	290294
6	incidence/	261132
7	(prevalence or cross-section*).ti,ab,kw.	934044
8	incidence.ti,ab,kw.	746599
9	(epidemiolog* or risk factor?).ti.	232692
10	5 or 6 or 7 or 8 or 9	1911046

11	4 and 10	15056
12	Stomach Neoplasms/ep [Epidemiology]	5471
13	11 or 12	17591
14	exp United Kingdom/	364099
15	(national health service* or nhs*).ti,ab,in.	195481
16	(english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab.	94894
17	(gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jw,in.	2059789
18	(bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's " or st asaph or "st asaph's" or st davids or swansea or "swansea's").ti,ab,in.	55279
19	(aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in.	208524
20	(armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's").ti,ab,in.	26034
21	(bath or "bath's" or ((Birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) or (canterbury not zealand*) or ("canterbury's" not zealand*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or (durham not (carolina* or nc)) or ("durham's" not (carolina* or nc)) or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds* or leicester or "leicester's" or (lincoln not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or norwich or "norwich's" or nottingham or "nottingham's" or oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or (worcester not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachuse tts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*))))).ti,ab,in.	1402908
22	14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	2647240
23	(exp africa/ or exp americas/ or exp antarctic regions/ or exp arctic regions/ or exp asia/ or exp oceania/) not (exp great britain/ or europe/)	2861791
24	22 not 23	2499149
25	13 and 24	1076
26	(comment or letter or editorial or review).pt.	4490625
27	25 not 26	835
28	limit 25 to ("systematic review" or systematic reviews as topic or "reviews (maximizes specificity)")	86

29	27 or 28	890
30	limit 29 to (english language and yr="1994 -Current")	685

Table 12. Search strategy for key question 1 - Embase

# ▲	Searches	Results
1	exp *stomach cancer/	78780
2	((gastric or stomach) adj3 (cancer? or carcinoma? or adenocarcinoma? or neoplas* or malignan* or tumo?r?)).ti,ab,kw.	129735
3	(gastro* adj3 (cancer? or carcinoma? or adenocarcinoma? or neoplas* or malignan* or tumo?r?)).ti.	22339
4	1 or 2 or 3	155846
5	*prevalence/	64122
6	*incidence/ or cancer incidence/	92815
7	(prevalence or cross-section*).ti,ab,kw.	1278589
8	incidence.ti,ab,kw.	1063151
9	(epidemiolog* or risk factor?).ti.	291051
10	5 or 6 or 7 or 8 or 9	2439600
11	4 and 10	20752
12	exp stomach cancer/ep	4528
13	11 or 12	23286
14	exp United Kingdom/	416478
15	(national health service* or nhs*).ti,ab,in.	292437
16	(english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab.	43115
17	(gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jw,in.	3102921
18	(bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's " or st asaph or "st asaph's" or st davids or swansea or "swansea's").ti,ab,in.	98817
19	(aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in.	333976
20	(armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's").ti,ab,in.	44988
21	(bath or "bath's" or ((Birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) or (canterbury not zealand*) or ("canterbury's" not zealand*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or (durham not (carolina* or nc)) or ("durham's" not (carolina* or nc)) or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds* or leicester or "leicester's" or (lincoln not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or norwich or "norwich's" or nottingham or "nottingham's" or	2416768

	oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or (worcester not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachuse tts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*))))).ti,ab,in.	
22	14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	3786289
23	(exp africa/ or exp americas/ or exp antarctic regions/ or exp arctic regions/ or exp asia/ or exp oceania/) not (exp great britain/ or europe/)	2892459
24	22 not 23	3566407
25	13 and 24	1753
26	(conference* or editorial or letter or note or "review").pt.	9739442
27	25 not 26	1122
28	limit 25 to "reviews (maximizes specificity)"	109
29	27 or 28	1170
30	limit 29 to (english language and yr="1994 -Current")	926

Results were imported into EndNote and de-duplicated.

Electronic databases – key question 2

The search strategy included searches of the databases shown in Table 13. MEDLINE, MEDLINE In-Process, MEDLINE Daily, Epub Ahead of Print, Embase, Cochrane database of systematic reviews and Cochrane central register of controlled trials.

Table 13. Summary of electronic database searches and dates

Database	Platform	Searched on date	Date range of search
Embase	OvidSP	1974-present	14/08/2020
Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®)	OvidSP	1946-present	14/08/2020
Cochrane Database of Systematic Reviews	Cochrane Library, Wiley	Issue 8 of 12, August 2020	14/08/2020
Cochrane Central Register of Controlled Trials	Cochrane Library, Wiley	Issue 8 of 12, August 2020	14/08/2020

Search Terms – key question 2

Search terms included combinations of free text and subject headings (Medical Subject Headings [MeSH] for MEDLINE, and Emtree terms for Embase).

Search terms for MEDLINE, MEDLINE In-Process, MEDLINE Daily, and Epub Ahead of Print are shown in Table 14, for Embase in Table 15 and for Cochrane library databases in Table 16.

Table 14. Search strategy for key question 2 - MEDLINE, MEDLINE In-Process, MEDLINE Daily, Epub Ahead of Print

# ▲	Searches	Results
1	Stomach Neoplasms/	96429
2	(stomach adj4 cancer).ti,ab.	10051
3	(stomach adj4 neoplas$).ti,ab.	761
4	(stomach adj4 (tumor$ or tumour$)).ti,ab.	3761
5	(gastric adj4 cancer).ti,ab.	64456
6	(gastric adj4 neoplas$).ti,ab.	2336
7	(gastric adj4 (tumor$ or tumour$)).ti,ab.	10947
8	Helicobacter pylori/	34725
9	"h. pylori".ti,ab.	27099
10	helicobacter pylori.ti,ab.	40270
11	Helicobacter Infections/	30402
12	(helicobacter adj2 infection).ti,ab.	14310
13	((stomach or gastric) adj5 (pre-cancer$ or precancer$ or adenocarcinoma$ or carcinoma$ or metaplasia$ or dysplasia$ or malignan$ or pre-malignan$ or premalignan$)).ti,ab.	36862
14	or/1-13	163206
15	Mass Screening/	103573
16	Early Detection of Cancer/	25583
17	Early Diagnosis/	26578
18	screen$3.ti,ab.	749577
19	((early adj3 diagnos$) or detect$).ti,ab.	2434794
20	Population Surveillance/	59378
21	surveillance.ti,ab.	178274
22	(test or tests or testing).ti,ab.	2306470
23	exp Enzyme-Linked Immunosorbent Assay/	149136
24	enzyme linked immunosorbent assay.ti,ab.	80806
25	ELISA.ti,ab.	168279
26	exp Hematologic tests/	250486
27	exp Serologic Tests/	178311
28	(endoscop$ or photofluorography or "serum pepsinogen" or "gastrin 17").ti,ab.	208167

29	biomarkers/ or biomarkers, tumor/	421844
30	(biomarker$ or marker$).ti,ab.	974728
31	Risk factors/	827149
32	or/15-31	6896451
33	14 and 32	69776
34	Meta-Analysis as Topic/	18171
35	meta analy$.tw.	176993
36	metaanaly$.tw.	2109
37	Meta-Analysis/	118213
38	systematic review.pt. or (systematic adj (review$1 or overview$1)).tw.	198324
39	exp "Review Literature as Topic"/	14151
40	34 or 35 or 36 or 37 or 38 or 39	318979
41	cochrane.ab.	85663
42	embase.ab.	94319
43	(psychlit or psyclit).ab.	917
44	(psychinfo or psycinfo).ab.	36843
45	(cinahl or cinhal).ab.	29145
46	science citation index.ab.	3156
47	bids.ab.	540
48	cancerlit.ab.	631
49	41 or 42 or 43 or 44 or 45 or 46 or 47 or 48	154346
50	reference list$.ab.	18190
51	bibliograph$.ab.	18361
52	hand-search$.ab.	6997
53	relevant journals.ab.	1190
54	manual search$.ab.	4524
55	50 or 51 or 52 or 53 or 54	44160
56	selection criteria.ab.	30614
57	data extraction.ab.	21649
58	56 or 57	49938
59	Review/	2681145
60	58 and 59	29452
61	40 or 49 or 55 or 60	375767
62	Randomized Controlled Trials as Topic/	135270
63	Randomized Controlled Trial/	511146
64	Random Allocation/	103360
65	Double-Blind Method/	159244
66	Single Blind Method/	28900
67	Clinical trial/	524255
68	clinical trial, phase i.pt.	20672
69	clinical trial, phase ii.pt.	33251

70	clinical trial, phase iii.pt.	17099
71	clinical trial, phase iv.pt.	1929
72	controlled clinical trial.pt.	93798
73	randomized controlled trial.pt.	511146
74	multicenter study.pt.	277248
75	clinical trial.pt.	524255
76	exp Clinical Trials as Topic/	344404
77	(clinical adj trial$).tw.	371159
78	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	173714
79	Placebos/	35022
80	placebo$.tw.	216979
81	randomly allocated.tw.	28975
82	(allocated adj2 random$).tw.	32290
83	62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82	1646265
84	exp "Sensitivity and Specificity"/	585231
85	sensitivity.tw.	802374
86	specificity.tw.	464302
87	((pre-test or pretest) adj probability).tw.	2246
88	post-test probability.tw.	591
89	predictive value$.tw.	109209
90	likelihood ratio$.tw.	15670
91	84 or 85 or 86 or 87 or 88 or 89 or 90	1479026
92	33 and 61	1963
93	33 and 83	6135
94	33 and 91	8471
95	92 or 93 or 94	15090
96	(comment or editorial or historical article or letter).pt. or case control.ti. or case report.tw. or case report/	4198671
97	95 not 96	14596
98	exp animals/ not humans.sh.	4725270
99	97 not 98	14421
100	limit 99 to (english language and yr="2014 -Current")	4979

Table 15. Search strategy for key question 2 - Embase

# ▲	Searches	Results
1	exp *stomach cancer/	79712
2	(stomach adj4 cancer).ti,ab.	10254
3	(stomach adj4 neoplas$).ti,ab.	774
4	(stomach adj4 (tumor$ or tumour$)).ti,ab.	4401
5	(gastric adj4 cancer).ti,ab.	89600

6	(gastric adj4 neoplas$).ti,ab.	3601
7	(gastric adj4 (tumor$ or tumour$)).ti,ab.	15160
8	*Helicobacter pylori/	27363
9	"h. pylori".ti,ab.	38072
10	helicobacter pylori.ti,ab.	53722
11	*Helicobacter infection/	18717
12	(helicobacter adj2 infection).ti,ab.	19059
13	((stomach or gastric) adj5 (pre-cancer$ or precancer$ or adenocarcinoma$ or carcinoma$ or metaplasia$ or dysplasia$ or malignan$ or pre-malignan$ or premalignan$)).ti,ab.	48772
14	or/1-13	189284
15	screening/ or mass screening/ or screening test/ or cancer screening/	365878
16	early cancer diagnosis/	6827
17	Early Diagnosis/	107007
18	screen$3.ti,ab.	1049301
19	((early adj3 diagnos$) or detect$).ti,ab.	3106243
20	surveillance.ti,ab.	245623
21	(test or tests or testing).ti,ab.	3227034
22	exp enzyme linked immunosorbent assay/	368969
23	enzyme linked immunosorbent assay.ti,ab.	91760
24	ELISA.ti,ab.	267810
25	exp blood examination/	258125
26	exp serology/	204542
27	(endoscop$ or photofluorography or "serum pepsinogen" or "gastrin 17").ti,ab.	331644
28	biological marker/ or tumor marker/ or pepsinogen/ or gastrin/ or gastrin blood level/	405668
29	(biomarker$ or marker$).ti,ab.	1408653
30	*risk factor/	81767
31	or/15-30	8288194
32	14 and 31	91206
33	meta analy$.tw.	229617
34	metaanaly$.tw.	10032
35	Meta-Analysis/	193372
36	systematic review.pt. or (systematic adj (review$1 or overview$1)).tw.	218690
37	"systematic review"/	257007
38	33 or 34 or 35 or 36 or 37	451747
39	cochrane.ab.	110945
40	embase.ab.	119390
41	(psychlit or psyclit).ab.	996
42	(psychinfo or psycinfo).ab.	33605
43	(cinahl or cinhal).ab.	34094
44	science citation index.ab.	3637
45	bids.ab.	684

46	cancerlit.ab.	729
47	39 or 40 or 41 or 42 or 43 or 44 or 45 or 46	185727
48	reference list$.ab.	21203
49	bibliograph$.ab.	23215
50	hand-search$.ab.	8490
51	relevant journals.ab.	1414
52	manual search$.ab.	5442
53	48 or 49 or 50 or 51 or 52	53769
54	selection criteria.ab.	37199
55	data extraction.ab.	26607
56	54 or 55	61555
57	Review/	2493537
58	56 and 57	28191
59	38 or 47 or 53 or 58	511369
60	exp clinical trial/	1513423
61	(clinical adj trial$).tw.	530082
62	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	240664
63	Placebos/	296823
64	placebo$.tw.	311426
65	randomly allocated.tw.	35991
66	(allocated adj2 random$).tw.	39938
67	60 or 61 or 62 or 63 or 64 or 65 or 66	2044462
68	"Sensitivity and Specificity"/ or predictive value/ or diagnostic accuracy/	652162
69	sensitivity.tw.	1036092
70	specificity.tw.	597884
71	((pre-test or pretest) adj probability).tw.	4012
72	post-test probability.tw.	846
73	predictive value$.tw.	163645
74	likelihood ratio$.tw.	21270
75	68 or 69 or 70 or 71 or 72 or 73 or 74	1731612
76	32 and 59	2262
77	32 and 67	8352
78	32 and 75	11180
79	76 or 77 or 78	19750
80	(conference* or editorial or letter or note).pt. or case control.ti. or case report.tw. or case report/	9274806
81	79 not 80	13992
82	(exp animals/ or nonhuman/) not human/	6550380
83	81 not 82	13666
84	limit 83 to (english language and yr="2014 -Current")	4732

Table 16. Search strategy key question 2 - Cochrane Database of Systematic Reviews and Cochrane central register of controlled trials

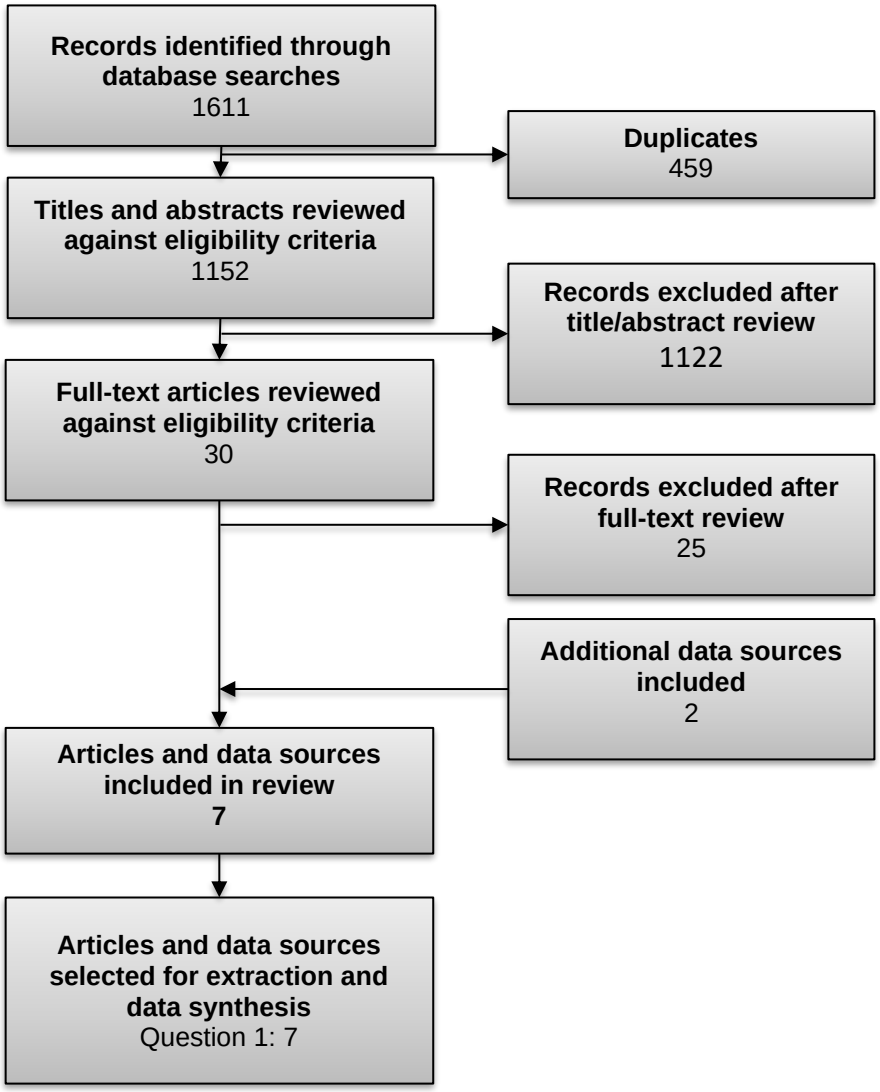
ID	Search
#1	MeSH descriptor: [Stomach Neoplasms] explode all trees
#2	(((stomach or gastric) NEAR/4 (cancer or tumor* or tumour* or neoplas*))):ti,ab,kw
#3	MeSH descriptor: [Helicobacter pylori] explode all trees
#4	MeSH descriptor: [Helicobacter Infections] explode all trees
#5	("h pylori" OR helicobacter):ti,ab,kw
#6	(((stomach or gastric) NEAR/5 (pre-cancer* or precancer* or adenocarcinoma* or carcinoma* or metaplasia* or dysplasia* or malignan*or pre-malignan* or premalignan*))):ti,ab,kw
#7	#1 or #2 or #3 or #4 or #5 or #6
#8	MeSH descriptor: [Mass Screening] explode all trees
#9	MeSH descriptor: [Early Diagnosis] explode all trees
#10	MeSH descriptor: [Population Surveillance] this term only
#11	(screen*):ti,ab,kw OR (((early NEAR/3 diagnos*) or detect*)):ti,ab,kw OR (test or tests or testing):ti,ab,kw OR (surveillance):ti,ab,kw
#12	MeSH descriptor: [Enzyme-Linked Immunosorbent Assay] explode all trees
#13	(elisa or "enzyme linked immunosorbent assay"):ti,ab,kw
#14	MeSH descriptor: [Hematologic Tests] explode all trees
#15	MeSH descriptor: [Serologic Tests] explode all trees
#16	((endoscop* or photofluorography or "serum pepsinogen" or "gastrin 17")):ti,ab,kw
#17	MeSH descriptor: [Biomarkers] explode all trees
#18	(marker* or biomarker*):ti,ab,kw
#19	MeSH descriptor: [Risk Factors] explode all trees
#20	#8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21	#7 and #20

Appendix 2 — Included and excluded studies

PRISMA flowchart – key question 1

Figure 2 summarises the volume of publications included and excluded at each stage of the review for key question 1. 7 publications were ultimately judged to be relevant to the review question and were considered for extraction. Publications that were included or excluded after the review of full-text articles are detailed below.

Figure 2. Summary of publications included and excluded at each stage of the review



Publications included after review of full-text articles – key question 1

The 7 publications included in key question 1 after review of full-texts are summarised in 2 below.
Studies were prioritised for extraction and data synthesis. It was planned *a priori* that the following approach would be taken to prioritise studies for extraction:

- Systematic reviews and meta-analyses would be considered the highest quality of evidence if any were found.
- Studies relating to epidemiology would be prioritised if they considered a UK population, followed by studies from individual, UK countries and regions.

In addition, the following criteria were applied after assessing the overall volume of evidence identified in the review:

- Epidemiology studies that were completed over 15 years before this review was conducted (ie. national registry data where the latest year of data was for 2005 or earlier, regardless of publication date) were not extracted.
- Data for a more recent time period was prioritised over older analysis of earlier years.

Publications not selected for extraction and data synthesis for key question 1 are clearly detailed in Table 17 below.

Table 17. Summary of publications and data sources included after review of full-text articles or most relevance to key question 1sub questions

Study	Sub question 1	Sub question 3	Sub question 4
Arnold et al (2020)[20]	X		
Cancer research UK (2020)[23]	X	X	
Fitzmaurice et al (2019)[21] and the Global burden of Disease Dataset (2020)[22]	X		
Brown et al (2018)[26]			X
Derakhshan et al (2016)[24]		X	
Coupland et al (2012)[25]		X	

Publications excluded after review of full-text articles for key question 1

Of the 32 publications included after the review of titles and abstracts, 25 were ultimately judged not to be relevant to this review. These publications, along with reasons for exclusion, are listed in
Table 18.

Table 18. Publications excluded after review of full-text articles

Reference	Reason for exclusion

1	Office for National Statistics Statistical bulletin: Cancer registration statistics 2017, England. Released April 2019.	England only – other publications include all countries within the UK.
2	de Jong R, Peeters P, Burden AM, de Bruin ML, Haak HR, Masclee AAM, et al. Gastrointestinal cancer incidence in type 2 diabetes mellitus; results from a large population-based cohort study in the UK. Cancer Epidemiology. 2018;54:104-11.	A more recent analysis of UK stomach cancer incidence is included in the review.
3	Fitzmaurice C, Allen C, Barber RM, Barregard L, Bhutta ZA, et al. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 32 Cancer Groups, 1990 to 2015: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncology. 2017;3(4):524-48.	A more recent update of the GBD analysis is included in the review.
4	Luo G, Zhang Y, Guo P, Wang L, Huang Y, Li K. Global patterns and trends in stomach cancer incidence: Age, period and birth cohort analysis. International Journal of Cancer. 2017;141(7):1333-44.	A more recent analysis of UK stomach cancer incidence is included in the review.
5	Carstensen B, Read SH, Friis S, Sund R, Keskimaki I, Svensson AM, et al. Cancer incidence in persons with type 1 diabetes: a five-country study of 9,000 cancers in type 1 diabetic individuals. Diabetologia. 2016;59(5):980-8.	A more recent analysis of UK stomach cancer incidence is included in the review.
6	Roberts SE, Morrison-Rees S, Samuel DG, Thorne K, Akbari A, Williams JG. Review article: The prevalence of Helicobacter pylori and the incidence of gastric cancer across Europe. Alimentary Pharmacology and Therapeutics. 2016;43(3):334-45.	A more recent analysis of UK stomach cancer incidence due to *H.Pylori* is included in the review.
7	Ali R, Barnes I, Cairns BJ, Finlayson AE, Bhala N, Mallath M, et al. Incidence of gastrointestinal cancers by ethnic group in England, 2001-2007. Gut. 2013;62(12):1692-703.	A more recent analysis of UK stomach cancer incidence is included in the review.
8	Coupland VH, Lagergren J, Konfortion J, Allum W, Mendall MA, Hardwick RH, et al. Ethnicity in relation to incidence of oesophageal and gastric cancer in England. British Journal of Cancer. 2012;107(11):1908-14.	A more recent analysis of UK stomach cancer incidence is included in the review.
9	Mistry M, Parkin DM, Ahmad AS, Sasieni P. Cancer incidence in the United Kingdom: projections to the year 2030. British Journal of Cancer. 2011;105(11):1795-803.	A more recent analysis of UK stomach cancer incidence is included in the review.
10	Steevens J, Botterweck AA, Dirx MJ, van den Brandt PA, Schouten LJ. Trends in incidence of oesophageal and stomach cancer subtypes in Europe. European Journal of Gastroenterology & Hepatology. 2010;22(6):669-78.	A more recent analysis of UK stomach cancer incidence is included in the review.
11	Derakhshan MH, Liptrot S, Paul J, Brown IL, Morrison D, McColl KE. Oesophageal and gastric intestinal-type adenocarcinomas show the same male predominance due to a 17 year delayed development in females. Gut. 2009;58(1):16-23.	Data collection was 1998-2002 so did not meet the criteria for data extraction (the last year of data collection should be 2005 or after)
12	Gajperia C, Barbiere JM, Greenberg D, Wright K, Lyratzopoulos G. Recent incidence trends and sociodemographic features of oesophageal and gastric cancer types in an English region. Alimentary Pharmacology & Therapeutics. 2009;30(8):873-80.	A more recent analysis of UK stomach cancer incidence is included in the review.

13	Gossage JA, Forshaw MJ, Khan AA, Mak V, Moller H, Mason RC. The effect of economic deprivation on oesophageal and gastric cancer in a UK cancer network. International Journal of Clinical Practice. 2009;63(6):859-64.	A more recent analysis of UK stomach cancer incidence is included in the review
14	National Cancer Intelligence Network Cancer Incidence and Survival By Major Ethnic Group,England, 2002 – 2006 London NCIN 2009.	A more recent analysis of UK stomach cancer incidence is included in the review.
15	Alston RD, Geraci M, Eden TO, Moran A, Rowan S, Birch JM. Changes in cancer incidence in teenagers and young adults (ages 13 to 24 years) in England 1979-2003. Cancer. 2008;113(10):2807-15.	A more recent analysis of UK stomach cancer incidence in adults is included in the review.
16	Downing A, Forman D, Gilthorpe MS, Edwards KL, Manda SO. Joint disease mapping using six cancers in the Yorkshire region of England. International Journal of Health Geographics [Electronic Resource]. 2008;7:41.	A more recent analysis of UK stomach cancer incidence is included in the review.
17	Carneiro F, Moutinho C, Pera G, Caldas C, Fenger C, Offerhaus J, et al. Pathology findings and validation of gastric and esophageal cancer cases in a European cohort (EPIC/EUR-GAST). Scandinavian Journal of Gastroenterology. 2007;42(5):618-27.	A more recent analysis of UK stomach cancer incidence is included in the review.
18	Fitzsimmons D, Osmond C, George S, Johnson CD. Trends in stomach and pancreatic cancer incidence and mortality in England and Wales, 1951-2000. British Journal of Surgery. 2007;94(9):1162-71.	A more recent analysis of UK stomach cancer incidence is included in the review.
19	Newnham A, Quinn MJ, Babb P, Kang JY, Majeed A. Trends in the subsite and morphology of oesophageal and gastric cancer in England and Wales 1971-1998. Alimentary Pharmacology & Therapeutics. 2003;17(5):665-76.	A more recent analysis of UK stomach cancer incidence is included in the review.
20	Byrne JP, Mathers JM, Parry JM, Attwood SE, Bancewicz J, Woodman CB. Site distribution of oesophagogastric cancer. Journal of Clinical Pathology. 2002;55(3):191-4.	A more recent analysis of UK oesophageal and stomach cancer incidence is included in the review.
21	Powell J, McConkey CC, Gillison EW, Spychal RT. Continuing rising trend in oesophageal adenocarcinoma. International Journal of Cancer. 2002;102(4):422-7.	A more recent analysis of UK oesophageal and stomach cancer incidence is included in the review.
22	Corley DA, Buffler PA. Oesophageal and gastric cardia adenocarcinomas: analysis of regional variation using the Cancer Incidence in Five Continents database. International Journal of Epidemiology. 2001;30(6):1415-25.	A more recent analysis of UK oesophageal and stomach cancer incidence is included in the review.
23	Kocher HM, Linklater K, Patel S, Ellul JP. Epidemiological study of oesophageal and gastric cancer in south-east England. British Journal of Surgery. 2001;88(9):1249-57.	A more recent analysis of UK oesophageal and stomach cancer incidence is included in the review.
24	Wayman J, Forman D, Griffin SM. Monitoring the changing pattern of esophago-gastric cancer: data from a UK 25regional cancer registry. Cancer Causes & Control. 2001;12(10):943-9.	A more recent analysis of UK oesophageal and stomach cancer incidence is included in the review.
25	Botterweck AA, Schouten LJ, Volovics A, Dorant E, van Den Brandt PA. Trends in incidence of adenocarcinoma of the oesophagus and gastric cardia in ten European countries. International Journal of Epidemiology. 2000;29(4):645-54	A more recent analysis of UK oesophageal and stomach cancer incidence is included in the review.

Appendix 3 — Summary and appraisal of individual studies

Data Extraction

Question 1: What is the incidence and prevalence of Gastric adenocarcinomas in the UK?

Sub question 1: What is the overall incidence of Gastric adenocarcinomas in the UK?:

Table 19. Arnold et al (2020)[20]

<table>
<tr><td>Publication</td><td>Arnold M, Park JY, Camargo MC, Lunet N, Forman D, Soerjomataram I. Is gastric cancer becoming a rare disease? A global assessment of predicted incidence trends to 2035. Gut. 2020;30:30.</td></tr>
<tr><td>Study details</td><td>Secondary analysis of national cancer registry data</td></tr>
<tr><td>Study objectives</td><td>To explore the decrease in incidence in gastric cancer in 34 countries from 2010 and predict future trends to 2035.</td></tr>
<tr><td>Inclusions</td><td>Registrations of ICD-10 stomach cancer diagnoses (C16) by year of diagnosis, gender and 5 year age group from the Cancer Incidence in Five Countries Plus (C15 Plus) database. UK registry data was included from the C15 Plus database if the registry had been providing data for 15 consecutive years.</td></tr>
<tr><td>Exclusions</td><td>None reported</td></tr>
<tr><td>Population</td><td>Gastric cancer registrations from 92 registries in 34 countries in 2010
Population estimates were obtained from the UN World Population Prospects 2017 revision by country, year, gender and age. Number of UK registrations extracted in 2010 =7,446.</td></tr>
<tr><td>Analysis</td><td>Future predicted incidence of gastric cancer to 2035 was calculated using a model using the cancer incidence prediction package NORDPRED.</td></tr>
<tr><td>Outcomes</td><td>Gastric cancer varies more than 8 fold across countries with highest rates for 2010 in Japan (Age standardised incidence rates (ASR) 36.3 per 100,000 person years) and Korea (ASR 40.6 per 100,000 PY) and lowest in Northern America (ASR 4.4 per 100,000 PY) and Denmark (ASR 4.9 per 100,000 PY). The overall trend of decreasing rates is predicted to continue with reductions in most countries including those with high incidence such as Japan (ASR 36 per 100,000 PY in 2010 vs ASR 30 2035 per 100,000 PY).

The UK ASR was 5.2 in 2010 and predicted for fall to 4.7 by 2035.
Absolute numbers of cases in the UK were predicted to increase slightly due to an increase in the population from 7,446 in 2010 to 7,863 in 2035. This change was 52.4% attributed to a change in population and -46.8% due to a change in the presence of risk factors.

The UK age standardised incidence rate per 100,000 person years and number of cases in 2010 and 2035 for all people and those under 50 years of age.
<table>
<tr><td></td><td colspan="2">All ages</td><td colspan="2">Age <50 years</td></tr>
<tr><td></td><td>Incidence</td><td>Cases</td><td>Incidence</td><td>Cases</td></tr>
<tr><td>2010</td><td>5.2</td><td>7446</td><td>0.7</td><td>398</td></tr>
<tr><td>2035</td><td>4.7</td><td>7863</td><td>1.4</td><td>832</td></tr>
</table>
Incidence in people under the age of 50 is increasing in countries with both high and low overall incidence while incidence in people aged over 50 was stable or decreasing. Cases were predicted to increase from 398 in 2010 to 832 in 2035 a doubling of the incidence</td></tr>
</table>

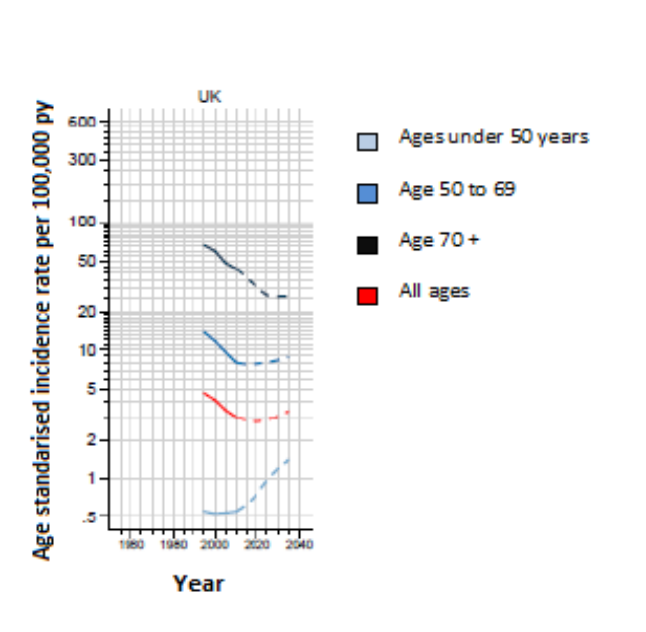
	rate from 0.7 to 1.4 per 100,000 population. This change was modelled to be -0.2% due to population a change and 109.2% due to change in risk factor. **Predicted change in age standardised incidence of stomach cancer per 100,000 person years in the UK by age group from 2010 to 2035** 
Quality appraisal	The study was assessed using the JBI checklist for prevalence studies and no concerns were identified using this tool Using the BJGP key points for the appraisal of database studies one concern was raised. There was a relatively large proportion of patients with an unspecified anatomical subsite. This meant these patients could not be assigned to either the cardia or non-cardia subgroup.

Table 20. Cancer Research UK (2020)[23]

Publication	Cancer Research UK https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/stomach-cancer/incidence Accessed August 2020.
Study details	Secondary analysis of national cancer registry data.
Study objectives	To provide an analysis of the latest data available for cancers in the UK
Inclusions	All stomach cancer registrations for the UK by age and sex by year (1993 to 2017) were accessed from the following sources: the National Cancer Registration, Analysis Service ISD Scotland, the Welsh Cancer Intelligence and Surveillance Unit, Public Health Wales and the Northern Ireland Cancer Registry.
Exclusions	None reported
Population	UK population of people with a registered stomach cancer (C16), Number of registrations extracted for 2017=6,363
Analysis	Age standardisation of incidence data and analysis by age, gender, year of registration, and UK country was carried out.
Outcomes	**Stomach cancer by gender** In females in the UK, stomach cancer is the 19th most common cancer (1% of all new female cancer cases). In males in the UK, it is the 13th most common cancer (2% of all new male cancer cases). 35% of stomach cancer cases in the UK are in females, and 65% are in males.

Stomach cancer incidence rates (European age-standardised (AS) rates) for persons are significantly higher than the UK average in Scotland, Wales and Northern Ireland, and similar to the UK average in England

Stomach Cancer (C16), Number of New Cases, Crude and European Age-Standardised (AS) Incidence Rates per 100,000 Population, UK, 2017

		England	Scotland	Wales	Northern Ireland	UK
Females	**Cases**	1,764	245	130	77	2,216
	Crude rate	6.3	8.8	8.2	8.1	6.6
	AS rate (95% CI)	6.2 (5.9-6.5)	8.4 (7.4-9.5)	7.4 (6.1-8.7)	8.8 (6.8-10.8)	6.6 (6.3-6.8)
Males	**Cases**	3,378	372	285	112	4,147
	Crude rate	12.3	14.1	18.5	12.2	12.7
	AS rate (95% CI)	14.4 (13.9-14.9)	16.3 (14.6-17.9)	19.3 (17.0-21.5)	15.3 (12.5-18.1)	14.9 (14.4-15.3)
Persons	**Cases**	5,142	617	415	189	6,363

AS – Age standardised CI – Confidence interval

Stomach cancer and age and gender
Stomach cancer incidence is strongly related to age, with the highest incidence rates being in older people.

In the UK in 2015-2017, on average each year around half of new cases (51%) were in people aged 75 and over.

Age-specific incidence rates rise steadily from around age 45-49 and more steeply from around age 65-69. The highest rates are in in the 85 to 89 age group for females and males.

Incidence rates are significantly lower in females than males in a number of (mainly older) age groups. The gap is widest at age 65 to 69, when the age-specific incidence rate is 2.6 times lower in females than males.

Average Number of New Cases Per Year and Age-Specific Incidence Rates per 100,000 Population, UK 2015 -2017

Age Range	Female Cases	Male Cases	Female Rates	Male Rates
0 to 04	0	0	0.0	0.0
05 to 09	0	0	0.0	0.0
10 to 14	0	0	0.0	0.0
15 to 19	1	0	0.1	0.0
20 to 24	5	5	0.2	0.2
25 to 29	7	5	0.3	0.2
30 to 34	17	16	0.8	0.7
35 to 39	27	29	1.3	1.4
40 to 44	37	52	1.7	2.5
45 to 49	55	99	2.4	4.4
50 to 54	94	184	4.0	8.1
55 to 59	131	259	6.4	12.9

60 to 64	163	368	9.0	21.2
65 to 69	222	543	12.0	31.3
70 to 74	281	664	18.6	48.1
75 to 79	372	763	31.8	76.8
80 to 84	387	699	42.3	100.6
85 to 89	317	445	51.9	117.2
90+	172	175	43.2	102.0
All Ages	2,288	4,306	6.8	15.8

Trends in incidence of stomach cancer by gender from 1993 to 2017

Stomach cancer European age-standardised (AS) incidence rates for females and males combined decreased by 53% in the UK between 1993-1995 and 2015-2017.

For females, stomach cancer AS incidence rates in the UK decreased by 53% between 1993-1995 and 2015-2017. For males, stomach cancer AS incidence rates in the UK decreased by 55% between 1993-1995 and 2015-2017.

Over the last decade in the UK (between 2005-2007 and 2015-2017), stomach cancer AS incidence rates for females and males combined decreased by 29%. In females AS incidence rates decreased by 28%, and in males rates decreased by 32%.

Age standardised stomach cancer incidence per 100,000 person years by gender from 1993 to 2017

Gender	1993	1995	1997	1999	2001	2003
Female	14.8	14.0	13.8	12.3	11.7	10.8
Male	36.0	34.0	33.7	31.2	28.6	25.5
Persons	23.4	22.3	21.9	20.1	18.8	17.0

Gender	2005	2007	2009	2011	2013	2015	2017
Female	9.6	9.5	8.6	8.1	7.9	7.2	6.6
Male	23.9	22.7	21.2	19.3	18.2	16.5	14.9
Persons	15.7	15.2	14.1	13.0	12.4	11.4	10.3

Quality appraisal	The study was assessed using the JBI checklist for prevalence studies. Using this tool one criterion was unclear concerning the type of statistical analysis carried out. This was a data report with no description of the data analysis. Using the BJGP key points for the appraisal of database studies one concern was raised. No confidence intervals were reported with some of the incidence rates relating to incidence trends over a period of years and by age band. It is unclear the level of confidence to attribute to these particular results**.**

Table 21. Fitzmaurice et al (2019)[21] and the Global Burden of Disease Dataset (2020)[22]

Publication	Fitzmaurice C, Abate D, Abbasi N, Abbastabar H, Abd-Allah F, et al. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2017: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncology. 2019;27:27. And: Institute for Health Metrics and Evaluation (IHME). GBD Compare. Seattle, WA: IHME,. University of Washington, 2020
Study details	Secondary analysis of national cancer registry data.

Study objectives	To describe cancer burden for 29 cancer groups in 195 countries from 1990 through 2017 by estimation of a range of measures to provide data needed for cancer control planning.
Inclusions	For the UK, inclusions comprised all people registered with an ICD-9 or ICD 10 diagnosis of cancer within one of the following registries.

Region	Years of data extraction
Ayrshire	1970-1972
East Anglia	1988-1997
East Midlands	1990-2014
East Scotland	1973-1987
East of England	1990-2014
England	1993-2016
England and Wales	1979-1990
Greater London	1990-2014
Merseyside and Cheshire	1959-2002
National Registry	2008-2012

Exclusions	Data were excluded if they were not representative of the coverage population (eg hospital-based registries), if they did not cover all malignant neoplasms as defined in ICD9 (140-208) or ICD10 (C00-C96) (eg, specialty cancer registry), if they did not include data for both sexes and all age groups, if the data were limited to years prior to 1980, or if the source did not provide details on the population covered.
Population	Populations from 195 countries with data available by country for age band, disease and gender. For the UK in 1992 n=14,667 and 2017 n=13,769
Analysis	GBD study estimation methods were used to describe cancer incidence, prevalence, mortality, years lived with disability, years of life lost, and disability-adjusted life-years. Results are presented at the national level.
Outcomes	In order to access the specific data required for this review the reviewers downloaded the relevant Global Burden of Disease data (https://vizhub.healthdata.org/gbd-compare/) compiled by this study. This included 10 year prevalence and incidence of stomach cancer for males, females and all persons for 1992 and 2017 for each of the countries of the UK.

Prevalence: Age standardised 10 year prevalence of stomach cancer for 1992 and 2017 (https://vizhub.healthdata.org/gbd-compare/)

	1992			2017		
	All persons (95% UI)	**Male (95% UI)**	**Female (95% UI)**	**All persons (95% UI)**	**Male (95% UI)**	**Female (95% UI)**
England	27.14 (26.37 to 27.93)	43.62 (41.94 to 45.34)	14.17 (13.65 to 14.17)	26.72 (25.94 to 27.58)	40.15 (38.61 to 41.78)	14.87 (14.23 to 15.55)
Wales	25.93 (24.32 to 27.96)	41.00 (37.63 to 45.13)	14.20 (13.13 to 15.53)	28.91 (25.45 to 32.21)	45.71 (38.90 to 52.60)	13.87 (11.71 to 16.41)
Scotland	28.34 (27.41 to 28.42)	42.61 (40.67 to 44.56)	17.51 (16.64 to 18.43)	27.62 (25.03 to 30.38)	40.23 (35.39 to 45.48)	16.48 (14.45 to 19.02)
Northern Ireland	29.26 (27.04 to 32.06)	46.22 (41.38 to 51.77)	16.00 (16.63 to 17.82)	32.59 (28.71 to 36.55)	48.42 (41.19 to 56.08)	18.70 (15.51 to 22.11)
United Kingdom	27.25 (26.59 to 27.93)	43.48 (42.03 to 44.91)	14.53 (14.08 to 15.00)	27.08 (26.34 to 27.93)	40.69 (39.29 to 42.27)	15.06 (14.47 to 15.68)

UI- Uncertainty Interval

Incidence: Age standardised stomach cancer rates per 100,000 person years for 1992 and 2017 (https://vizhub.healthdata.org/gbd-compare/)

	1992			2017		
	All persons (95% UI)	**Male (95% UI)**	**Female (95% UI)**	**All persons (95% UI)**	**Male (95% UI)**	**Female (95% UI)**
England	15.07 (14.62 to 15.51)	23.50 (22.56 to 24.49	9.03 (8.69 to 9.41)	10.20 (9.89 to 10.53)	14.64 (14.10 to 15.26)	6.46 (6.17 to 6.77)
Wales	15.75 (14.74 to 17.01)	24.64 (22.50 to 27.49)	9.39 (8.65 to 10.39)	11.22 (9.86 to 12.52)	16.66 (14.06 to 19.14)	6.54 (5.50 to 7.82)
Scotland	15.58 (15.10 to 16.10)	22.92 (21.91 to 23.97)	10.62 (10.11 to 11.15)	10.72 (9.76 to 11.78)	15.14 (13.30 to 17.12)	7.03 (6.13 to 8.10)
Northern Ireland	16.13 (14.85 to 17.67)	24.49 (21.82 to 27.85)	10.23 (9.31 to 11.57)	11.44 (10.15 to 12.74)	16.10 (13.71 to 18.59)	7.53 (6.22 to 8.91)
United Kingdom	15.18 (14.80 to 15.57)	23.55 (22.74 to 24.39)	9.22 (8.92 to 9.56)	10.33 (10.06 to 10.65)	14.84 (14.31 to 15.43)	6.55 (6.27 to 6.85)

UI – Uncertainty Interval

Quality appraisal	The study was assessed using the JBI checklist for prevalence studies which did not highlight any concerns. Using the BJGP key points for the appraisal of database studies, no concerns were identified.

Sub question 2: What is the incidence and prevalence of different classifications of Gastric adenocarcinomas in the UK, such as Lauren or WHO classifications

No studies were identified that met the search criteria for this sub question.

Sub question 3: What is the incidence and prevalence of Gastric adenocarcinomas in the UK by anatomic sites (i.e. cardia or non-cardia, stomach, oesophagus or other locations)?

Table 22. Derakhshan et al (2016)[24]

Publication	Derakhshan MH, Arnold M, Brewster DH, Going JJ, Mitchell DR, Forman D, et al. Worldwide Inverse Association between Gastric Cancer and Esophageal Adenocarcinoma Suggesting a Common Environmental Factor Exerting Opposing Effects. American Journal of Gastroenterology. 2016;111(2):228-39.
Study details	Secondary analysis of national cancer registry data.
Study objectives	To analyse the annual incidence trends of oesophageal cancer, stomach cancer of the cardia and stomach cancer of the non-cardia sub site between 1989 to 2007 in 38 countries.
Inclusions	Registrations of ICD-10 stomach cancer diagnoses (C16) by year of diagnosis, gender and 5 year age group from the Cancer Incidence in Five Countries Plus (C15plus) database volume X and GLOBOCAN 2012. Registry data was included from the C15 Plus database if the registry had been providing data for 15 consecutive years.
Exclusions	None reported

Population	Gastric cancer registrations for 38 countries in 2012. Number of cases was not reported in the main paper.
Analysis	Correlation analysis of oesophageal cancer, and stomach cancer of the cardia and stomach cancer of the non-cardia sub site were performed.
Outcomes	**Estimated age standardised (world standardisation) incidence rates of cardia and non-cardia stomach cancer per 100,000 person years in the UK in 2012**

Males			**Females**		
Total stomach cancer	Cardia	Non-cardia	Total stomach cancer	Cardia	Non-cardia
6.44	3.89	2.55	3.15	1.46	1.69

Estimated age standardised incident rates of gastric cancer and oesophageal cancer by region in 1989 and 2007 by gender per 100,000 person years

	Males				**Females**			
	1989	**2007**	**1989**	**2007**	**1989**	**2007**	**1989**	**2007**
	OAC	**OAC**	**TGC**	**TGC**	**OAC**	**OAC**	**TGC**	**TGC**
England, North West	3.70	7.70	17.76	10.12	0.86	1.34	7.74	4.08
England South West	3.46	5.84	14.79	7.04	0.48	1.11	3.77	2.72
Scotland	3.42	7.47	18.56	9.72	1.05	1.49	7.90	4.57

OAC – Oesophageal adenocarcinoma, TGC- Total gastric cancer

A highly significant negative correlation coefficient between oesophageal cancer and stomach cancer between 1989 and 2007 was reported for:
North West England = -0.800 p<0.000
South West England = -0.774, p<0.000
Scotland = -0.913, p<0.000

Quality appraisal	The study was assessed using the JBI checklist for prevalence studies which did not highlight any concerns..

Using the BJGP key points for the appraisal of database studies, one concern was identified. No confidence intervals were reported with some of the incidence rates so it was unclear the level of confidence to attribute to these particular results**.**

Table 23. Coupland et al (2012)[25]

Publication	Coupland VH, Allum W, Blazeby JM, Mendall MA, Hardwick RH, Linklater KM, et al. Incidence and survival of oesophageal and gastric cancer in England between 1998 and 2007, a population-based study. BMC Cancer. 2012;12:11.
Study details	Secondary analysis of national cancer registry data.
Study objectives	To describe the incidence and survival of patients with oesophago-gastric cancers in England using a national cohort of patients diagnosed between 1998 and 2007.
Inclusions	People diagnosed with oesophageal and gastric cancer in England between 1998 and 2007.
Exclusions	None reported
Population	Data on 133,804 patients (85,361 males; 48,443 females) diagnosed with oesophageal and gastric cancer in England between 1998 and 2007 were extracted from the National Cancer Data Repository.
Analysis	Using information on anatomical site and tumour morphology, data were divided into six groups; upper and middle oesophagus, lower oesophagus, oesophagus with an unspecified anatomical site, cardia, non-cardia stomach, and stomach with an unspecified anatomical site. Age-standardised incidence rates (per 100,000 European standard population) were calculated for each group by year of diagnosis and by socioeconomic deprivation.

Outcomes

The cases and percentage of the 6 groups of oesophago-gastric cancers by gender in England in 2007

	UMOAC Cases(%)	LOAC Cases(%)	OACNOS Cases(%)	CSC Cases(%)	NCSC Cases(%)	SCNOS Cases(%)	OAC+ SC Cases(%)
Male	8,228 (45.4)	26,495 (73.9)	4,323 (54.7	14,107 (75.3)	9,531 (62.1)	22,677 (59.9)	85,361 (63.8)
Female	9,900 (54.6)	9,354 (26.1)	3,575 (45.3)	4,621 (24.7)	5,809 (37.9)	15,184 (40.1)	48,443 (36.2)

%=percentage of male or female cases of total cases
CSC – Cardia stomach cancer, I - Incidence per 100,000 person years, LOAC – Lower, oesophageal adenocarcinoma, NCSC – Non-cardia stomach cancer, OACNOS - oesophageal adenocarcinoma not otherwise specified, , SC – Stomach cancer, SCNOS – stomach cancer not otherwise specified, OAC - oesophageal adenocarcinoma, UMOAC –Upper/middle oesophageal adenocarcinoma

Both lower oesophageal and cardia cancers had a much higher incidence in males compared with females (M:F 4:1). Incidence of non-cardia stomach cancer was twice as high in males, than females.

The cases and incidence per 100,000 person years of 6 groups of oesophago-gastric cancers in England in 1998 and 2007

	UMOAC Cases(I)	LOAC Cases(I)	OACNOS Cases(I)	CSC Cases(I)	NCSC Cases(I)	SCNOS Cases(I)	OAC+ SC Cases(I)
1998	1,702 (9.4)	3,067 (8.6)	929 (11.8)	2,022 (10.8)	1,752 (11.4)	4,446 (11.7)	13,918 (10.4)
2007	1,883 (10.4)	4,011 (11.2)	649 (8.2)	1,727 (9.2)	1,286 (8.4)	3,366 (8.9)	12,922 (9.7)

CSC – Cardia stomach cancer, I - Incidence per 100,000 person years, LOAC – Lower, oesophageal adenocarcinoma, NCSC – Non-cardia stomach cancer, OACNOS - oesophageal adenocarcinoma not otherwise specified, , SC – Stomach cancer, SCNOS – stomach cancer not otherwise specified, OAC - oesophageal adenocarcinoma, UMOAC –Upper/middle oesophageal adenocarcinoma

The incidence of lower oesophageal cancer increased between 1998 and 2002 and remained stable thereafter. The incidence of cancer of the cardia, non-cardia stomach, and stomach with an unspecified anatomical site declined over the 10 year period.

The cases and incidence per 100,000 person years of 6 groups of oesophago-gastric cancers by most affluent and least affluent deprivation quintile in England between 1998 and 2007

Deprivation quintile	UMOAC Cases(I)	LOAC Cases(I)	OACNOS Cases(I)	CSC Cases(I)	NCSC Cases(I)	SCNOS Cases(I)	OAC+ SC Cases(I)
1	1,503 (16.1)	3,589 (18.8)	592 (16.6)	1,554 (17.5)	1,058 (15.0)	2,607 (15.3)	10,903 (16.8
5	2,058 (22.1)	3,256 (17.0)	738 (20.7)	1,730 (19.5	1,561 (22.1)	4,180 (24.5)	13,523 (20.8)

CSC – Cardia stomach cancer, I - Incidence per 100,000 person years, LOAC – Lower, oesophageal adenocarcinoma, NCSC – Non cardia stomach cancer, OACNOS - oesophageal adenocarcinoma not otherwise specified, , SC – Stomach cancer, SCNOS – stomach cancer not otherwise specified, OAC - oesophageal adenocarcinoma, UMOAC –Upper/middle oesophageal adenocarcinoma

The incidence of cardia stomach cancers was higher in the most socioeconomically deprived quintiles(Q) (Q5:Q1 1.5:1 males; 1.7:1 females). The incidence of non-cardia stomach cancers was higher in more deprived areas (Q5:Q1 2.0:1 males;1.9:1 females).

Quality appraisal	The study was assessed using the JBI checklist for prevalence studies which did not highlight any concerns.. Using the BJGP key points for the appraisal of database studies, one concern was identified. There was a relatively large proportion of patients with an unspecified anatomical subsite, particularly for gastric cancers where over half (52.6%) fell into this group. This meant that these patients could not be assigned to either the cardia or non-cardia subgroup. No confidence intervals were reported with some of the incidence rates so it was unclear the level of confidence to attribute to these particular results.

Table 24 Cancer Research UK (2020)[23]

Publication	Cancer Research UK, Stomach Cancer Incidence in the UK https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/stomach-cancer/incidence Accessed August 2020
Study details	Secondary analysis of national cancer registry data.
Study objectives	To provide information to health professionals about cancer epidemiology, risk, diagnosis and treatment.
Inclusions	All registrations of stomach cancer in the UK between 2010 and 2012
Exclusions	None reported
Population	Registrations of stomach cancer between 2010-2012 from the National Cancer Data Repository.
Analysis	Age standardisation of incidence data and analysis by age, gender and anatomical sub site was carried out.
Outcomes	The largest proportion of stomach cancer cases occur in the cardia, with much smaller proportions of non-cardia stomach cancers in the pyloric antrum and body of the stomach. The proportion of cases in the cardia is higher in males (34.0%) than females (19.7%) and there are no marked gender differences in other parts of the stomach. A large proportion of cases did not have the specific part of the stomach recorded in cancer registry data or overlapped in more than one part.

Number of cases and proportion of stomach cancer diagnoses between 2010-2012 by anatomical sub site and gender

	Males		Females	
Stomach cancer anatomical sub site and ICD 10 diagnostic classification	**Average Cases per year**	**%**	**Average Cases per year**	**%**
Cardia (16.0)	1,576	34.0%	497	19.7%
Fundus of Stomach (C16.1)	119	2.6%	69	2.7%
Body of Stomach (C16.2)	295	6.4%	184	7.3%
Pyloric Antrum (C16.3)	327	7.1%	240	9.5%
Pylorus (C16.4)	163	3.5%	119	4.7%
Lesser Curvature of Stomach, Unspecified (C16.5)	261	5.6%	129	5.1%
Greater Curvature of Stomach, Unspecified (C16.6)	84	1.8%	61	2.4%
Stomach, Overlapping and Unspecified (C16.8-C16.9)	1,811	39.1%	1,222	48.5%

Total	4,637	100.0%	2,521	100.0%

Quality appraisal

The study was assessed using the JBI checklist for prevalence studies which did not highlight any concerns..

Using the BJGP key points for the appraisal of database studies, two concerns were identified. There was the relatively large proportion of patients with an unspecified anatomical subsite, (39.1% to 48.5%) fell into this group. This meant that these patients could not be assigned to either the cardia or non-cardia subgroup. Confidence intervals for these rates were not included with the reported data.

Sub question 4: What is the incidence and prevalence of Gastric adenocarcinomas in the UK by risk factor or cause (i.e. H.Pylori, diet, smoking etc)?

Table 25. Brown et al (2018)[26]

Publication	Brown KF, Rumgay H, Dunlop C, Ryan M, Quartly F, Cox A, et al. The fraction of cancer attributable to modifiable risk factors in England, Wales, Scotland, Northern Ireland, and the United Kingdom in 2015. British Journal of Cancer. 2018;118(8):1130-41.
Study details	Secondary analysis of national cancer registry data.
Study objectives	To provide 2015 population attributable fractions (PAFs) by cancer type and risk factor for the UK overall and for each constituent country.
Inclusions	Cancer incidence data for 2015 for each of the UK constituent countries from publications of cancer registry data.
Exclusions	None reported
Population	People diagnosed with stomach cancer and oesophageal cancer in the UK in 2015.
Analysis	Population attributable fractions (PAFs) were calculated for combinations of risk factor and cancer type with sufficient evidence of a causal association. Relative risks (RRs) were drawn from meta-analyses of cohort studies where possible. Prevalence of exposure to risk factors was obtained from nationally representative population surveys. Cancer incidence data for 2015 were sourced from national data releases and, where needed, personal communications. PAF calculations were stratified by age, sex and risk factor exposure level and then combined to create summary PAFs by cancer type, gender and country.
Outcomes	**Table showing the fraction of oesophagus and gastric cancer attributable to modifiable risk factors in the United Kingdom in 2015 by gender**

MALES	6,077		4,353	
Cancer Incidence in 2015 = 4,353	**PAF (%)**	**Att. Cases**	**PAF (%)**	**Att. Cases**
Tobacco	33.8%	2,053	21.0%	912
Overweight and obesity	31.3%	1,900	7.4%	320
Infections			39.7%	1,742
Alcohol	16.8%	499		
Occupation	3.3%	201	3.0%	131
Radiation - ionising	0.3%	21	0.4%	19
All of the above	**60.7%**	**3,691**	**57.3%**	**2,496**
FEMALES	2,963		2,383	
Cancer Incidence in 2015 =2,383	**PAF (%)**	**Att. Cases**	**PAF (%)**	**Att. Cases**
Tobacco	33.0%	977	3.4%	81
Overweight and obesity	16.7%	496	4.3%	102
Infections			43.7%	1,042
Alcohol	16.8%	499		

Occupation	1.1%	33	0.3%	7
Radiation - ionising	0.6%	19	0.9%	22
All of the above	**54.4%**	**1,612**	**48.6%**	**1,159**

Att. Cases – Attributable cases, PAF – Population attributable fraction

Table showing the fraction of stomach cancer attributable to *H.pylori* infection in each of the 4 countries of the United Kingdom in 2015

	Males		**Females**		**Persons**	
	PAF (%)	**Att. Cases**	**PAF (%)**	**Att. Cases**	**PAF (%)**	**Att. Cases**
England	38.6%	1,375	42.7%	827	40.0%	2,202
Scotland	53.6%	206	52.5%	118	53.2%	324
Wales	27.5%	73	37.7%	58	31.3%	132
Northern Ireland	53.0%	72	60.3%	39	55.3%	111
UK	39.7%	1727	43.7%	1042	41.1%	2769

Att. Cases – Attributable cases, PAF – Population attributable fraction

Table showing the fraction of stomach cancer attributable to tobacco smoking in each of the 4 countries of the United Kingdom in 2015

	Males		**Females**		**Persons**	
	PAF (%)	**Att. Cases**	**PAF (%)**	**Att. Cases**	**PAF (%)**	**Att. Cases**
England	20.9%	744	3.3%	64	14.7%	808
Scotland	21.0%	81	4.2%	9	14.8%	90
Wales	23.0%	61	3.6%	6	15.9%	67
Northern Ireland	19.7%	27	3.3%	2	14.4%	29
UK	21.0%	912	3.4%	81	14.8%	994

Att. Cases – Attributable cases, PAF – Population attributable fraction

Table showing the fraction of stomach cancer attributable to being overweight or obese in each of the 4 countries of the United Kingdom in 2015

	Males		**Females**		**Persons**	
	PAF (%)	**Att. Cases**	**PAF (%)**	**Att. Cases**	**PAF (%)**	**Att. Cases**
England	7.1%	252	4.1%	80	6.0%	332
Scotland	8.6%	33	5.3%	12	7.3%	45
Wales	9.6%	26	5.1%	8	8.0%	34
Northern Ireland	6.9%	9	4.5%	3	6.1%	12
UK	7.4%	320	4.3%	102	6.3%	423

Att. Cases – Attributable cases, PAF – Population attributable fraction

Quality appraisal

The study was assessed using the JBI checklist for prevalence studies and no concerns were identified.

Using the BJGP key points for the appraisal of database studies, one concern was identified. The study limited the type of risk factors for stomach cancer to those with convincing evidence of a causal link as described by IARC but not risk factors with a probable or likely cause of some stomach cancers. This means that estimates of the risk of being overweight and obese and tobacco smoking were included in the analysis but not the use of alcohol. It is likely that researchers underestimated the true population attribution fraction of risk factors as there may be limited evidence for some risk factor-cancer combinations. No confidence intervals were reported for the PAF rates although they were calculated. This was due to concerns that the ranges would suggest a precision that could be misleading as not all biases are known when calculating the estimates.

Appendix 4 - Evidence map - Abstract reporting tables

Question 2 - What is the test accuracy of screening tests for the detection of gastric and stomach cancer?

Table 26. Han et al (2020)[27]

TITLE	
Citation	Han Y, Dai W, Meng F, Gan X, Liu M, Deng X, et al. Diagnosis of Helicobacter pylori infection in the elderly using an immunochromatographic assay-based stool antigen test. Microbiology Open. 2020:e1102.
BACKGROUND	
Study type	Prospective cohort test
Objectives	To assess the diagnostic accuracy of the immunochromatographic assay-based *Helicobacter pylori* stool antigen (HpSA) tests in a male elderly cohort and identify factors affecting the accuracy.
Components of the study	Population: asymptomatic elderly male citizens (≥65 years old) who received health check ups the between July 2007 and November 2018 in a Chinese hospital (n=193) Index test: HpSA test Reference standard: 13C-urea breath test Outcomes: Sensitivity and specificity
RESULTS	
Results	Sensitivity: 65.1% (95% CI: 49.0%–78.5%) Specificity: 98.7% (95% CI: 94.8%–99.8%) Positive predictive value: 93.3% (95% CI: 76.5%–98.8%) Negative predictive value: 90.8% (95% CI: 85.0%–94.6%) Factors affecting accuracy of the test included the presence of constipation and colorectal polyps. The former decreased accuracy and the latter increased the accuracy of the test. (*From full text)*
Conclusions	In an observational study of an elderly male cohort, HpSA achieves high accuracy and specificity but suboptimal sensitivity when using 13C-UBT as a reference standard. There is limited applicability to the UK target population as this was a small, male, Chinese cohort.

Appendix 5 – UK NSC reporting checklist for evidence summaries

All items on the UK NSC Reporting Checklist for Evidence Summaries have been addressed in this report. A summary of the checklist, along with the page or pages where each item can be found in this report, is presented in Table 27.

Table 27. UK NSC reporting checklist for evidence summaries

	Section	Item	Page no.
1.	TITLE AND SUMMARIES		
1.1	Title sheet	Identify the review as a UK NSC evidence summary.	Title page
1.2	Plain English summary	Plain English description of the executive summary.	5
1.3	Executive summary	Structured overview of the whole report. To include: the purpose/aim of the review; background; previous recommendations; findings and gaps in the evidence; recommendations on the screening that can or cannot be made on the basis of the review.	6
2.	INTRODUCTION AND APPROACH		
2.1	Background and objectives	Background – Current policy context and rationale for the current review – for example, reference to details of previous reviews, basis for current recommendation, recommendations made, gaps identified, drivers for new reviews Objectives – What are the questions the current evidence summary intends to answer? – statement of the key questions for the current evidence summary, criteria they address, and number of studies included per question, description of the overall results of the literature search. Method – briefly outline the rapid review methods used.	11
2.2	Eligibility for inclusion in the review	State all criteria for inclusion and exclusion of studies to the review clearly (PICO, dates, language, study type, publication type, publication status etc.) To be decided *a priori*.	16
2.3	Appraisal for quality/risk of bias tool	Details of tool/checklist used to assess quality, e.g. QUADAS 2, CASP, SIGN, AMSTAR.	19
3.	SEARCH STRATEGY AND STUDY SELECTION (FOR EACH KEY QUESTION)		
3.1	Databases/ sources searched	Give details of all databases searched (including platform/interface and coverage dates) and date of final search.	19

3.2	Search strategy and results	Present the full search strategy for at least one database (usually a version of Medline), including limits and search filters if used. Provide details of the total number of (results from each database searched), number of duplicates removed, and the final number of unique records to consider for inclusion.	38
3.3	Study selection	State the process for selecting studies – inclusion and exclusion criteria, number of studies screened by title/abstract and full text, number of reviewers, any cross checking carried out.	17
4.	STUDY LEVEL REPORTING OF RESULTS (FOR EACH KEY QUESTION)		
4.1	Study level reporting, results and risk of bias assessment	For each study, produce a table that includes the full citation and a summary of the data relevant to the question (for example, study size, PICO, follow-up period, outcomes reported, statistical analyses etc.). Provide a simple summary of key measures, effect estimates and confidence intervals for each study where available. For each study, present the results of any assessment of quality/risk of bias.	52
5.	QUESTION LEVEL SYNTHESIS		
5.1	Description of the evidence	For each question, give numbers of studies screened, assessed for eligibility, and included in the review, with summary reasons for exclusion.	20
5.2	Combining and presenting the findings	Provide a balanced discussion of the body of evidence which avoids over reliance on one study or set of studies. Consideration of four components should inform the reviewer's judgement on whether the criterion is 'met', 'not met' or 'uncertain': quantity; quality; applicability and consistency.	22
5.3	Summary of findings	Provide a description of the evidence reviewed and included for each question, with reference to their eligibility for inclusion. Summarise the main findings including the quality/risk of bias issues for each question. Have the criteria addressed been 'met', 'not met' or 'uncertain'?	33
6.	REVIEW SUMMARY		
6.1	Conclusions and implications for policy	Do findings indicate whether screening should be recommended? Is further work warranted? Are there gaps in the evidence highlighted by the review?	37
6.2	Limitations	Discuss limitations of the available evidence and of the review methodology if relevant.	37

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