

# Gastric cancer in Ukraine: epidemiologic data and its nosological structure between 2003 and 2020

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## Abstract

**Introduction:** Gastric cancer is one of the world's leading causes of death due to oncological diseases. Gastric cancer comprises a diverse group of diseases that includes several oncological units.

**Aim:** To analyse the nosological structure of epidemiological data related to gastric cancer in Ukraine and compare it with global trends from 2003 to 2020.

**Material and methods:** The data were retrieved from the National Cancer Registry of Ukraine and analysed using MedCalc for Windows, version 20.218 (MedCalc Software, Ostend, Belgium).

**Results:** Eight forms of gastric cancer were diagnosed every year. The lowest incidence rate was in 2020, with 8.99 per 100,000 people/year. This was a 33.71% drop compared to 2005 ( $p < 0.0001$ ). Adenocarcinoma constituted the largest part of the cases over the 2003 to 2020 period: 96.38% (95% CI: 95.02–97.05%). All the other types of gastric cancer together comprised 2.97% (95% CI: 2.34–3.76%) of the cases. The number of adenocarcinoma cases as well as its incidence rate decreased in 2003–2020 in Ukraine. The incidence rate of all types of gastric cancer was seen to decrease over the 2003–2020 timeframe in Ukraine. Adenocarcinoma was the leading form of gastric cancer in the country, and other types were uncommon in both Ukraine and the rest of the world. There was a change in the incidence rates of the other forms of gastric cancer, but those incidences did not notably affect the structure of the epidemiological data.

**Conclusions:** The total number of cases of gastric cancer, as well as its incidence rate, decreased in Ukraine from 2003 to 2020. This situation corresponds with global tendencies.

## Introduction

Gastric cancer is one of the main causes of death worldwide. In terms of cancer-related mortality, it is the fourth most common oncological disease. Gastric cancer requires healthcare expenses from society [1].

The main risk factors for gastric cancer are *Helicobacter pylori* (*H. pylori*) and Epstein-Barr virus (EBV) infection, smoking, the consumption of certain types of food (such as broiled, smoked, and salt-preserved food), and family history (familial gastric cancer incidence is higher in people with far-east Asian ethnicities, such as those from China and Japan) [1].

There are various, diverse forms of gastric cancer. They are classified and systematized in the International Classification of Diseases for Oncology (ICD-O-3, first revision) and the International Classification of Diseases (ICD), 11<sup>th</sup> edition [2, 3]. Aetiological, pathomorpho-

logical, and diagnostical characteristics are described in the WHO Classification of Digestive Systems Tumours (the latest edition refers to ICD-10) [4].

It was recently shown that the incidence of gastric cancer has been constantly dropping in most of the world [5].

The phenomenon of this decrease is rather difficult to understand. It includes several factors to be considered, such as health lifestyle trends, possibilities of diagnosis and prevention, identification of the genetic markers that are associated with a higher risk of gastric cancer, successful eradication of *H. pylori*, and updated understanding mechanisms of its persistent infection of the gastric epithelium [1, 5].

Adenocarcinoma not otherwise specified (adenocarcinoma NOS) is one of the most common types of gastric cancer in the world. It is a polyaetiological disease, and only 10% of cases have familial origin [4]. Authors

often refer to gastric adenocarcinoma as adenocarcinoma NOS [2, 4].

Analysis of the nosological structure of gastric cancer epidemiological data is helpful to understand the dynamics of the incidence rate and understand what measures should be taken for further effective disease prevention.

## Aim

The main aim is to analyse the nosological structure of the epidemiological data regarding gastric cancer in Ukraine from 2003 to 2020.

## Material and methods

Epidemiological data were requested and obtained from the National Cancer Registry of Ukraine [6]. The request contained the codes of oncological units according to ICD-O-3 [2, 4]. Only cases with “stomach” as the primary site of “cancer” localization were selected for the study; the primary diagnosis according to ICD-10 was gastric cancer. The incidence rate was calculated per 100,000 people-year, part for each nosological form

of the total number of cases, and the median was presented with 95% CI.  $R^2$  (coefficient of determination) was calculated to assess the trends with regression analysis using exponential regression. The data were analysed by use of MedCalc® Statistical Software version 22.009 (MedCalc Software Ltd, Ostend, Belgium; <https://www.medcalc.org>; 2023).

## Results

The highest incidence rate was noted in 2005, and the lowest rate was in 2020 (Tables I, III). The decrease in the incidence rate was 30.63% in 2020 compared to 2003, which is the beginning of the time frame ( $p < 0.0001$ ), and 33.70% compared to 2005 ( $p < 0.0001$ ). The lowest drop was observed between 2019 and 2020, when it reached 17.97% ( $p < 0.0001$ ) (Figure 1).

A total of 30 different forms of primary gastric cancer were identified in Ukraine from 2003 to 2020. In the tables shown, only the forms of gastric cancer that were diagnosed over this specific time frame have been listed. The following 8 permanently occurring forms of gastric cancer were identified: adenocarcinoma NOS

**Table I.** Incidence rates of stomach cancers in Ukraine from 2003 to 2008 per 100000 people-year

Morphological diagnosis	ICD-O-3	2003	2004	2005	2006	2007	2008
Adenocarcinoma NOS	8140	12.44	12.82	13.09	12.88	12.79	12.36
Adenocarcinoma scirrhous	8141	0.19	0.13	0.17	0.16	0.13	0.11
Linitis plastica	8142	0	0	0	0	0.002	0
Superficial spreading adenocarcinoma	8143	0.004	0.006	0.002	0.002	0.000	0.002
Intestinal type adenocarcinoma	8144	0.01	0.004	0.02	0.01	0.02	0.03
Diffuse type adenocarcinoma	8145	0.07	0.07	0.05	0.04	0.03	0.04
Malignant gastrinoma	8153	0	0	0.002	0.002	0.004	0.009
Hepatocellular carcinoma	8170	0	0	0.002	0	0	0
Adenocarcinoma trabecular	8190	0	0	0	0.002	0.002	0
Cribriform carcinoma	8201	0	0.002	0.002	0.004	0.002	0
Adenomatous polyp	8210	0.03	0.03	0.03	0.02	0.02	0.02
Adenocarcinoma tubular	8211	0.04	0.07	0.08	0.06	0.04	0.06
Parietal cell adenocarcinoma	8214	0	0	0	0	0.002	0
Solid adenocarcinoma	8230	0.10	0.07	0.04	0.07	0.06	0.08
Neuroendocrine tumour	8240	0.01	0.03	0.02	0.03	0.03	0.03
Argentaffin carcinoid	8241	0.002	0	0	0	0	0
Papillary adenocarcinoma	8260	0.03	0.03	0.03	0.03	0.02	0.03
Villous adenocarcinoma	8262	0	0	0	0	0	0.002
Adenocarcinoma in tubulovillous adenoma	8263	0.002	0.002	0.002	0.011	0.006	0.006
Clear cell adenocarcinoma	8310	0.01	0.02	0.01	0.01	0.01	0.01
Granular cell adenocarcinoma	8320	0	0	0.002	0	0	0.002
Mixed cell adenocarcinoma	8323	0.002	0	0	0	0	0
Total incidence rate of gastric cancer	–	12.96	13.29	16.56	13.32	13.18	12.79

**Table II.** Incidence rates of stomach cancers in Ukraine from 2009 to 2014 100000 people-year

Morphological diagnosis	ICD-O-3	2009	2010	2011	2012	2013	2014
Adenocarcinoma NOS	8140	12.09	12.49	12.34	12.23	12.00	12.36
Adenocarcinoma scirrhus	8141	0.15	0.13	0.06	0.08	0.07	0.08
Superficial spreading adenocarcinoma	8143	0	0.002	0.002	0	0	0
Intestinal type adenocarcinoma	8144	0.02	0.01	0.02	0.02	0.04	0.05
Diffuse type adenocarcinoma	8145	0.03	0.03	0.05	0.11	0.11	0.09
Malignant gastrinoma	8153	0	0.02	0.02	0.01	0.01	0.01
Adenocarcinoma trabecular	8190	0.002	0.002	0	0	0.002	0
Adenoid cystic carcinoma	8200	0	0	0	0.002	0	0
Adenomatous polyp	8210	0.03	0.02	0.01	0.02	0.01	0.01
Adenocarcinoma tubular	8211	0.05	0.05	0.09	0.04	0.03	0.04
Parietal cell adenocarcinoma	8214	0.002	0	0	0	0	0
Solid adenocarcinoma	8230	0.07	0.08	0.08	0.06	0.06	0.03
Neuroendocrine tumour	8240	0.03	0.03	0.03	0.03	0.01	0.02
Neuroendocrine carcinoma	8246	0	0.01	0.03	0.03	0.03	0.04
Neuroendocrine tumour, grade 2	8249	0	0	0	0	0.002	0.006
Papillary adenocarcinoma	8260	0.02	0.02	0.03	0.02	0.02	0.02
Villous adenocarcinoma	8262	0.002	0	0	0	0	0
Adenocarcinoma in tubulovillous adenoma	8263	0.01	0.02	0.007	0.009	0.004	0
Clear cell adenocarcinoma	8310	0.02	0.02	0.02	0.01	0.02	0.02
Granular cell adenocarcinoma	8320	0	0	0	0.002	0.002	0.006
Mixed cell adenocarcinoma	8323	0	0	0	0	0.002	0.003
Total incidence rate of gastric cancer	–	12.52	12.92	12.78	12.69	12.43	12.79

(8140), adenocarcinoma scirrhus (8141), intestinal type adenocarcinoma (8144), diffuse type adenocarcinoma (8145), adenocarcinoma tubular (8211), solid adenocarcinoma (8230), neuroendocrine tumour (8240), and papillary adenocarcinoma (8260) (Tables I–III). These forms were diagnosed every year from 2003 to 2020 in Ukraine.

The following 4 forms of gastric cancer were not diagnosed in some years: adenomatous polyp (8210) (no cases in 2018), neuroendocrine carcinoma (8246) (no cases in 2003–2009), adenocarcinoma in tubulovillous adenoma (8263) (no cases in 2014 and 2020), and clear cell adenocarcinoma (8310) (no cases in 2019) (Tables I–III).

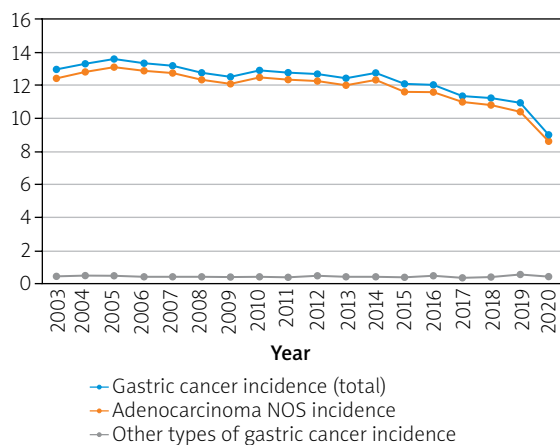
Among those 4 cases, the most interesting is neuroendocrine carcinoma. It was not diagnosed from 2003 to 2009, both years inclusive, but the incidence rate in 2010 was 0.01. This figure increased over time to over 9-fold higher in 2019 ( $p < 0.0001$ ). The increasing trend is reliable over the indicated time frame ( $R^2 = 0.82$ ;  $p < 0.0001$ ) (Tables II, III).

Most cases were of adenocarcinoma NOS (Tables I–III). Adenocarcinomas NOS reduced insignificantly from 96.03% of the total cases in 2003 to 95.20% of the total

in 2020. The highest incidence rate was noted in 2005 and the lowest in 2020. The lowest decrease in incidence rate was between 2019 and 2020 with a 17.85% drop ( $p < 0.0001$ ) (Tables I–III). The decreasing trend is reliable over the indicated time frame ( $R^2 = 0.66$ ;  $p < 0.0001$ ). This trend was similar to that of the total incidence rate of gastric cancer in Ukraine from 2003 to 2020 (Figure 1).

The collective incidence rate of all the gastric cancer types, other than adenocarcinoma NOS, was not higher than 0.55 and not lower than 0.34 in 2019 and 2017, respectively. The incidence rates of these types were largely stable without notable variability (Table III).

In the period 2003–2014, the second most common type of gastric cancer diagnosed in Ukraine, after adenocarcinoma NOS, was adenocarcinoma scirrhus (Tables I, II). However, it became the seventh most common type in 2015–2020 (Table III). It decreased from 1.5% of the total number of cases in 2003 to 0.47% of the total in 2020 ( $p < 0.0001$ ). The lowest percentage of this type of gastric cancer was noted in 2018, when it constituted 0.27% of the total number of cases. The difference between the highest and lowest incidence rate for this type of gastric



**Figure 1.** Annual incidence of gastric cancer in Ukraine per 100,000 people-year, 2003–2020

cancer was 6.33-fold ( $p < 0.0001$ ) (Tables I, III). This tendency to decrease is reliable ( $R^2 = 0.84$ ;  $p < 0.0001$ ).

During the time frame 2003–2008, the third most common type of gastric cancer was solid adenocarcinoma, and the fourth most common type was diffuse type adenocarcinoma (Table I). The incidence of rate of solid adenocarcinoma was stable over the period and showed minor fluctuations. In 2009–2020 it became the fourth most common form of gastric cancer, and diffuse type adenocarcinoma became the third most common. This indicated that the incidence rate of diffuse type adenocarcinoma grew insignificantly over this period (Tables II, III).

The incidence rate of adenocarcinoma tubular also grew insignificantly from 2003 to 2020, and it reached its maximum in 2019 (Tables I–III).

**Table III.** Incidence rates of stomach cancers in Ukraine from 2015 to 2020 100000 people-year

Morphological diagnosis	ICD-O-3	2015	2016	2017	2018	2019	2020
Adenocarcinoma NOS	8140	11.64	11.61	11.04	10.83	10.42	8.56
Adenocarcinoma scirrhus	8141	0.05	0.03	0.04	0.03	0.05	0.04
Superficial spreading adenocarcinoma	8143	0	0	0	0	0.008	0
Intestinal type adenocarcinoma	8144	0.06	0.05	0.03	0.04	0.05	0.05
Diffuse type adenocarcinoma	8145	0.11	0.09	0.09	0.09	0.07	0.04
Islet cell adenocarcinoma	8150	0	0	0	0	0.003	0.008
Malignant gastrinoma	8153	0.008	0.01	0.003	0.02	0.02	0.003
Adenocarcinoma trabecular	8190	0	0	0	0.003	0	0
Adenoid cystic carcinoma	8200	0	0.003	0	0	0	0
Cribriform carcinoma	8201	0.003	0	0	0.003	0	0
Adenomatous polyp	8210	0.01	0.01	0.003	0	0.008	0.003
Adenocarcinoma tubular	8211	0.04	0.05	0.02	0.07	0.14	0.09
Parietal cell adenocarcinoma	8214	0	0	0	0.003	0	0
Solid adenocarcinoma	8230	0.07	0.08	0.04	0.04	0.07	0.04
Neuroendocrine tumour	8240	0.02	0.02	0.03	0.02	0.02	0.06
Mucinous carcinoma	8243	0	0	0	0	0	0.006
Mixed adeno-neuroendocrine carcinoma	8244	0	0	0	0	0	0.003
Adenocarcinoid tumour	8245	0	0	0	0	0	0.003
Neuroendocrine carcinoma	8246	0.04	0.03	0.04	0.07	0.09	0.07
Neuroendocrine tumour, grade 2	8249	0	0	0.003	0	0.003	0
Adenocarcinoma with mixed subtypes	8255	0	0	0.003	0	0.003	0
Papillary adenocarcinoma	8260	0.02	0.03	0.02	0.003	0.02	0.01
Villous adenocarcinoma	8262	0	0	0	0	0	0.003
Adenocarcinoma in tubulovillous adenoma	8263	0.00	0.01	0.006	0.006	0.003	0
Clear cell adenocarcinoma	8310	0.01	0.02	0.01	0.003	0	0.006
Mixed cell adenocarcinoma	8323	0.003	0	0	0	0	0
Total incidence rate of gastric cancer	–	12.10	12.06	11.38	11.23	10.96	8.99

The part of intestinal type adenocarcinoma of the total number of cases increased over 18 times by 2020 from the minimum 0.03% seen in 2004 ( $p < 0.0001$ ) (Tables I–III).

Neuroendocrine tumour (8240) and papillary adenocarcinoma (8260) did not demonstrate significant fluctuation, and their incidence rates remained largely stable from 2003 to 2020 (Tables I–III).

Hepatocellular adenocarcinoma (8170) and linitis plastica (8142) were diagnosed only once each during the 2003–2020 period, in 2005 and 2007, respectively (Table I).

## Discussion

In general, the oncologic structure of gastric cancer in Ukraine from 2003 to 2020 resembled that of in the rest of the world at similar timeframes, with adenocarcinoma as the leading form of gastric cancer observed [1, 4, 5].

The other types of gastric cancer that were identified in Ukraine over this time period was not a common diagnosis in other countries. Such diseases are considered to be uncommon forms of gastric cancer [1, 4, 5], and their diagnosis can sometimes be difficult [1, 4]. It requires more advanced identification techniques that should be validated in every diagnostic centre [7]. The European and international healthcare standards for diagnostics and treatment have begun to be consistently implemented in recent decades. One example of consequent improvement in actions is the implementation of methodological recommendations for the pathomorphological departments in Ukrainian hospitals, which leads to continuous updates in the knowledge of how to approach the latest diagnostic tools and methods [8].

An overall decreasing tendency has been observed, especially in recent years. There are several factors that affect this trend [1, 4, 5].

First, there has been an improvement in genetic testing to identify people at risk for familial types of gastric cancer. This opens the possibility for the patients to undergo a gastrectomy. There were several mutations identified in the genes (*BRCA2*, *STK11*, *ATM*, *SDHB*, *PRSS1*, *MSR1*, *CTNNA1*, and *PALB2*) that can play a role in gastric cancer pathogenesis [1]. This was proven for patients who were carriers of germline alterations at the *CDH1* (E-cadherin) gene [9]. This is most important for populations that are proven to be at a higher risk for the development of familial forms of gastric cancer [1, 9]. It is difficult to conclude whether this is the case for Ukraine. On the one hand, data from the National Cancer Registry of Ukraine has limited capacity regarding the diagnostic and screening tests performed for each case. On the other hand, diagnostic laboratories

in Ukraine provide screening tests for genetic variations that are proven to be associated with a higher risk of gastric cancer [10].

Second, the use of proton pump inhibitors (PPIs) is becoming increasingly rational due to the new data on their role in gastric cancer development [11]. The sales of PPIs were seen to increase all over the world, and new medical substances and over-the-counter brands are constantly being introduced. In many countries, monitoring the use of drugs is well established, and healthcare providers are obliged to report all possible adverse drug reactions. The introduction of digital healthcare notes is also helpful to retrospectively identify the role of drugs, as well as other contributing factors, in the development of certain diseases [12]. It has also been demonstrated earlier that the use of PPIs is associated with the risk of gastric cancer, but the causality has not been proven. The propagation mechanism of *H. pylori* persistent infection by PPIs was proposed [13].

Third, there are practical implementations of the diagnosis and eradication of *H. pylori*. These methods have been considerably developed over recent years [10, 14]. The mechanisms of persistent infection with *H. pylori* as well as the mechanisms of carcinogenesis caused by *H. pylori* were studied. It was shown that *H. pylori* has several mechanisms to protect itself from the stomach's aggressive acidic environment. The adhesion properties of *H. pylori* are mediated by a repertoire of adhesins that the bacterium can turn on and off depending on the environment. Due to a high mutation rate, they can undergo quick adjustments, making *H. pylori* a unique microorganism in the sense of adaptation [13].

Fourth, a healthier way of life has become more popular all over the world. The trends associated with building a healthy lifestyle include reducing smoking, eating healthier food, controlling weight, and indulging in a higher level of physical activity [1, 5].

Finally, the consumption of widely used drugs is associated with a decrease in the risk of gastric cancer. For example, it has been demonstrated that the COX-2 enzyme plays an important role in the pathogenesis of *H. pylori*-induced gastric cancer [15]. Statins were shown to be associated with an increased risk of gastric cancer [5]. In experiments, acetylcysteine was shown to protect against *H. pylori*-associated carcinogenesis [16]. Further studies are required for the drug consumption patterns in the population of Ukraine.

## Conclusions

The incidence rate of gastric cancer was seen to decrease over the period 2003–2020. This was mostly due to the decrease of the incidence rate of adenocarcinoma NOS. The epidemiological tendency for gastric can-

cer to decrease corresponds with international trends of the disease. This tendency can be explained by several factors.

## Conflict of interest

The authors declare no conflict of interest.

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