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# A Meta-Analysis of the Association Between Human Papillomavirus and Oesophageal Squamous Cell Cancer

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**Aim:** to systematise the data of available studies related to the association of papillomavirus infection with oesophageal squamous cell cancer.
**Methods.** A literature search was conducted in PubMed and Google Scholar databases. All full-text articles from 1995 to 2023 were included. The language of the studies was not a barrier to inclusion in this meta-analysis. A total of 130 literature sources were analysed. The meta-analysis was based on data from 17 case-control studies, which together account for 1912 oesophageal squamous cell tumour tissue samples and 2206 control samples of normal oesophageal tissue.
**Key points.** There is a growing body of research on the importance of human papillomavirus as a risk factor for oesophageal squamous cell cancer. However, the association of human papillomavirus with the risk of oesophageal cancer, despite the large number of studies on this topic, is still controversial.
**Conclusions.** The resulting relative risk (RR) of oesophageal squamous cell cancer in papillomavirus infection was 1.22 (95 % confidence interval (95 % CI): 1.11–1.35; $p = 0.000023$). Meanwhile, stratification of the data according to the ethnicity of the patients showed that the highest risk of oesophageal squamous cell cancer in papillomavirus infection was observed in patients of Asian ethnic group (RR = 1.34; 95 % CI: 1.26–1.42; $p = 0.042$). In the Arab ethnic group, the risk of oesophageal squamous cell cancer with papillomavirus infection was 1.27 (95 % CI: 1.09–1.48; $p = 0.005$), while in Europeans it does not reach statistically significant values ($p = 0.232$).
**Keywords:** oesophageal cancer, human papillomavirus, meta-analysis
**Conflict of interest:** the authors declare no conflict of interest.

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## Метаанализ связи вируса папилломы человека и плоскоклеточного рака пищевода

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**Цель:** систематизировать данные имеющихся исследований, связанных с вопросом ассоциации папилломавирусной инфекции с плоскоклеточным раком пищевода.
**Методы.** Поиск литературы был проведен в базах данных PubMed и Google Scholar. В исследование были включены полнотекстовые статьи за 1995–2023 гг. Язык исследований не являлся преградой для включения в данный метаанализ. Всего проанализировано 130 литературных источников. Метаанализ проводился на основе данных из 17 исследований «случай-контроль», которые в сумме учитывают 1912 образцов опухолевой ткани плоскоклеточного рака пищевода и 2206 контрольных образцов нормальной ткани пищевода.
**Основные положения.** На сегодняшний день встречается все больше исследований, касающихся определения значения вируса папилломы человека в качестве фактора риска развития плоскоклеточного рака

пищевода. Однако вопрос об ассоциации вируса папилломы человека с риском развития рака пищевода, несмотря на большое количество исследований по данной теме, по-прежнему является спорным.
**Выводы.** Результирующий относительный риск (RR) развития плоскоклеточного рака пищевода при папилломавирусной инфекции составил 1,22 (95 %-ный доверительный интервал (95 % ДИ): 1,11–1,35; $p = 0,000023$). При этом стратификация данных в зависимости от этнического происхождения пациентов показала, что наибольший риск развития плоскоклеточного рака пищевода при папилломавирусной инфекции наблюдается у пациентов азиатской этнической группы (RR = 1,34; 95 % ДИ: 1,26–1,42; $p = 0,042$). У арабской этнической группы риск развития плоскоклеточного рака пищевода при папилломавирусной инфекции составил 1,27 (95 % ДИ: 1,09–1,48; $p = 0,005$), в то время как у европейцев он не достигает статистически значимых значений ($p = 0,232$).
**Ключевые слова:** рак пищевода, вирус папилломы человека, метаанализ
**Конфликт интересов:** авторы заявляют об отсутствии конфликта интересов.

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## Introduction

Today, oesophageal cancer is the sixth leading cause of oncological mortality and the seventh leading cause of cancer incidence worldwide [1]. According to GLOBOCAN estimates, 604,000 cases of oesophageal cancer and 544,000 deaths from this oncopathology are diagnosed annually [2]. Moreover, in 70 % of cases, it is men who are affected [2, 3]. Oesophageal squamous cell carcinoma (88 % of cases) and adenocarcinoma (12 % of cases) are the two main histological subtypes of oesophageal cancer [3]. In most patients, oesophageal cancer is characterised by late presentation, while the lack of biomarkers for early cancer detection makes the diagnosis of the disease more difficult [4].

It is worth noting that oesophageal squamous cell cancer has highly variable geographical features: 80 % of the total cases occur in developing countries [5]. Meanwhile, the list of countries with the highest oesophageal cancer incidence includes South Africa, Japan, India, Iran and China [6, 7]. In particular, the Eastern Cape of South Africa, northern China and the Caspian coast of Iran have been identified as the regions with the highest risk of developing oesophageal squamous cell cancer in the world

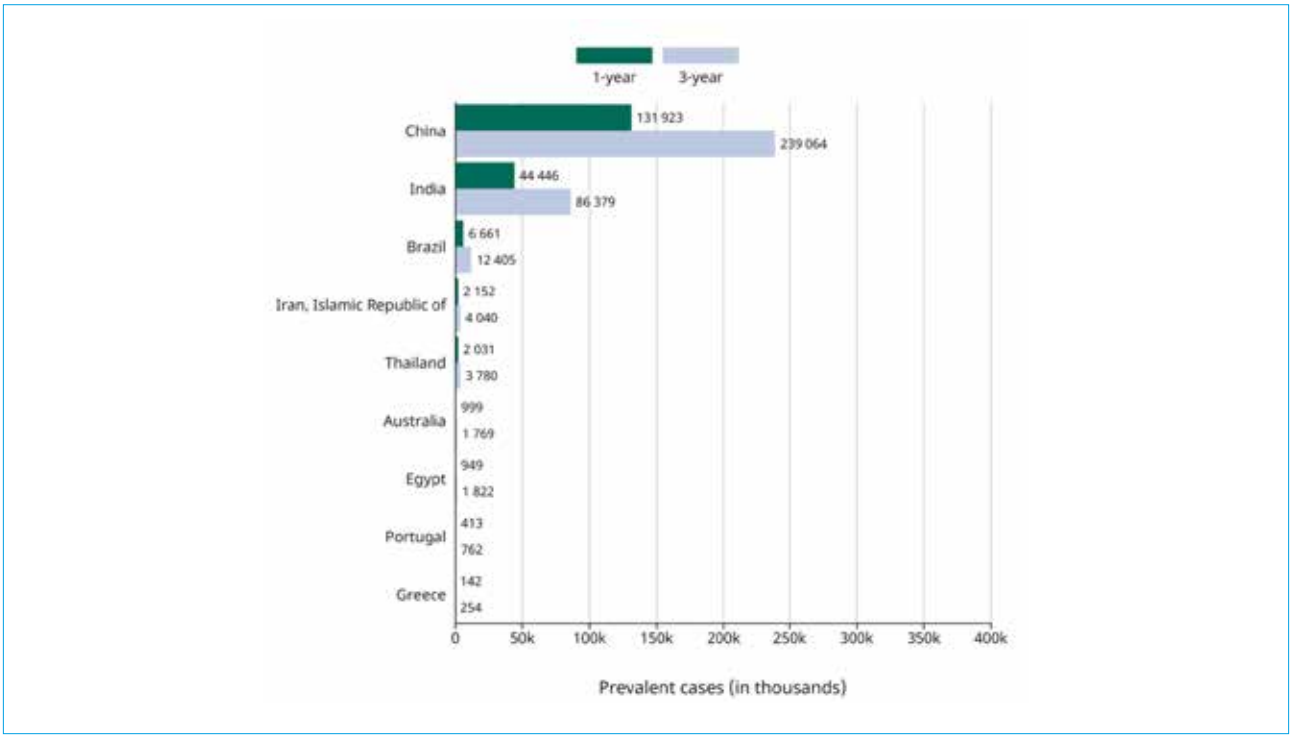


***Figure 1.*** Oesophageal cancer incidence statistics from 2020 to 2022 according to WHO

***Рисунок 1.*** Статистика заболеваемости раком пищевода за 2020–2022 гг. по данным ВОЗ

(incidence rate of 246 cases per 100,000 people) [6]. The comparison of the reported cases number of diagnosed oesophageal squamous cell cancer for the period 2020–2022 according to the World Health Organisation (WHO) in the countries included in the presented meta-analysis is shown in Figure 1.

These features of oesophageal squamous cell carcinoma prevalence can be explained by tobacco smoking, alcohol consumption, as well as dietary (rough and hot food, low content of vegetables and fruits in the diet, which correlates with vitamin deficiency), cultural and environmental (radiation and industrial chemicals) factors [1].

Also, multiple genetic mutations may be a risk factor for oesophageal squamous cell cancer (OSCC). For example, mutations of the tumour growth suppressor protein p53 (*TP53* gene product) can be observed in more than 83 % of OSCC cases [8]. Meanwhile, overexpression of epidermal growth factor receptor (EGFR), cyclin D1 (CCND1), cyclin-dependent kinase 4/6 (CDK4/CDK6) and *MDM2* proto-oncogene is observed in 76 %, 46 %, 24 % and 6 % of cases, respectively [8]. Epigenetic risk factors for the development of OSCC include DNA methylation, histone modification and loss of genome imprinting [8]. For example, hypermethylation of p16 is associated with p53 overexpression [9]. Polymorphisms in *TP53, MDM2, CASP8* (caspase 8) and *COX2* (cyclooxygenase 2) genes are also associated with the risk of oesophageal squamous cell cancer [8].

The role of human papillomavirus (HPV) in squamous cell carcinoma of the oropharynx and upper digestive tract began to be investigated in the early 1980s [10]. However, the International Agency for Research on Cancer (IARC) recognised the HPV involvement in the development of head and neck tumours, especially in oropharyngeal and oral squamous cell cancers due to the high infection rate (80–90 % for oropharyngeal cancer and up to 61 % for oral cancer) [10–12]. OSCC predominantly affects the upper and middle oesophagus, with metastasis usually to peri-oesophageal lymph nodes, liver and lungs, there is still no causal relationship between HPV and OSCC [13]. Although the etiology of the disease remains unclear, there is a growing body of research on the oncogenic types of HPV contributing to the development of OSCC [1].

To date, more than 200 HPV genotypes have been identified [1]. Based on propensity to transform host cells, there are two main groups: HPV of high carcinogenic risk and HPV of low carcinogenic risk [3]. HPV is currently recognised as an etiological factor in cervical cancer, oropharyngeal malignancies and anal neoplasia. OSCC associated with HPV is diagnosed in 0–78 % of cases [14]. Meanwhile, it is widely known that the most common high carcinogenic risk HPV genotypes in OSCC are HPV 16 and HPV 18 [5, 15, 16]. However, in a study by G. Georgantis et al., the predominant HPV types were types 11 and 31, which are known to have a low malignancy potential in OSCC [17].

There are also a number of studies in which HPV type 73 was detected: in 98.3 % of OSCC cases in the study by A.B. West et al., and in 10.6 % — in the study by Z. Szentirmay et al. [18, 19]. Meanwhile, HPV type 73 is still not classified as a carcinogenic type [20]. Another controversial study is the work of Chinese scientists, where no correlation was found between HPV of types 16, 18 and 73 in OSCC, even though the territory of China is included in the risk group for this oncopathology [20]. Also, no correlation between oesophageal squamous cell carcinoma and human papillomavirus was found in a study by M. Saegusa et al.: all oesophageal tumour tissue samples were HPV-negative [21]. By analysing the available data, it can be concluded that the role of HPV in oesophageal cancer is still unclear [3].

Thus, there is a large pool of contradictory studies in the literature evaluating the HPV association in the carcinogenesis of OSCC, nevertheless, this question remains open and the contribution of human papillomavirus to the development of oesophageal squamous cell carcinoma is still to be investigated [7]. It was necessary to perform a meta-analysis of these controversial studies, which was done in the present article.

## Oesophageal cancer and human papillomavirus

In 1982, human papillomavirus was first proposed as an epidemiological factor in the development of oesophageal cancer by K. Syrjänen et al. [22]. Since then, many studies have been conducted to investigate this issue [23–33]. According to the data obtained, the prevalence of HPV in OSCC varies in a wide range, and ranges from 0 to 78 % [34].

In the presented study, a literature search was conducted in PubMed and Google Scholar databases using the keywords “oesophageal cancer”, “esophageal cancer”, “human papillomavirus”, “human papilloma virus”, in different variations. All full-text articles from 1995 to 2023 were included in the study. The language of the studies was not a barrier to inclusion in this meta-analysis. A total of 130 literature sources were analysed.

Inclusion criteria for the meta-analysis were as follows: the study was a case-control study; tissue samples of OSCC were used as study material; normal oesophageal tissue samples were used as controls; HPV detection was performed using PCR technology. Exclusion criteria were failure to meet at least one inclusion criterion: the study was not a case-control study; the study material was esophageal adenocarcinoma samples or blood serum;

the study did not include a control group; human papillomavirus detection was performed by ELISA, Hybrid Capture II (HC2) or sequencing.

A total of 17 case-control studies fulfilling all the above criteria were selected, with a total inclusion of 1912 oesophageal cancer tumour tissue samples and 2206 control samples (all included studies used normal oesophageal tissue as a control).

Figure 2 presents a flowchart describing the study selection for inclusion in the meta-analysis. The studies in chronological order collected for this meta-analysis are summarised in Table 1. Meta-analysis was performed using Meta-Essentials_1.5 software. The results of meta-analysis are presented in Figure 3.

The pooled risk ratio (RR) of the risk of OSCC with papillomavirus infection was shown to be 1.22 (95 % confidence interval (95 % CI): 1.11–1.35; $p = 0.000023$. The sample heterogeneity index $I^2$ made 88.3 %, Cochrane $Q$-test was $p_Q = 2.6 \times 10^{-21}$, at the required level of $p < 0.1$, so Random model was used. The funnel plot shows no significant asymmetry (Fig. 3), and according to Begg's test there was no significant systematic publication error in this meta-analysis ($p = 0.621$). However, the result of Egger's test was not significant ($p = 0.294$).

At the next stage, subgroup analysis of the data was performed according to the ethnicity of the patients (Table 2).

The highest risk of OSCC with papillomavirus infection was found to be in patients of Asian ethnic groups with RR equal to 1.34 (95 % CI: 1.26–1.42; $p = 0.042$). In the Arab ethnic group, the risk of developing OSCC with papillomavirus infection was statistically significant (RR = 1.27; 95 % CI: 1.09–1.48; $p = 0.005$). In European ethnic group patients, the risk of developing OSCC with papillomavirus infection did not reach statistically significant values (RR = 1.02; 95 % CI: 0.99–1.06; $p = 0.232$). Thus, the risk of OSCC in papillomavirus infection has obvious ethnic features.

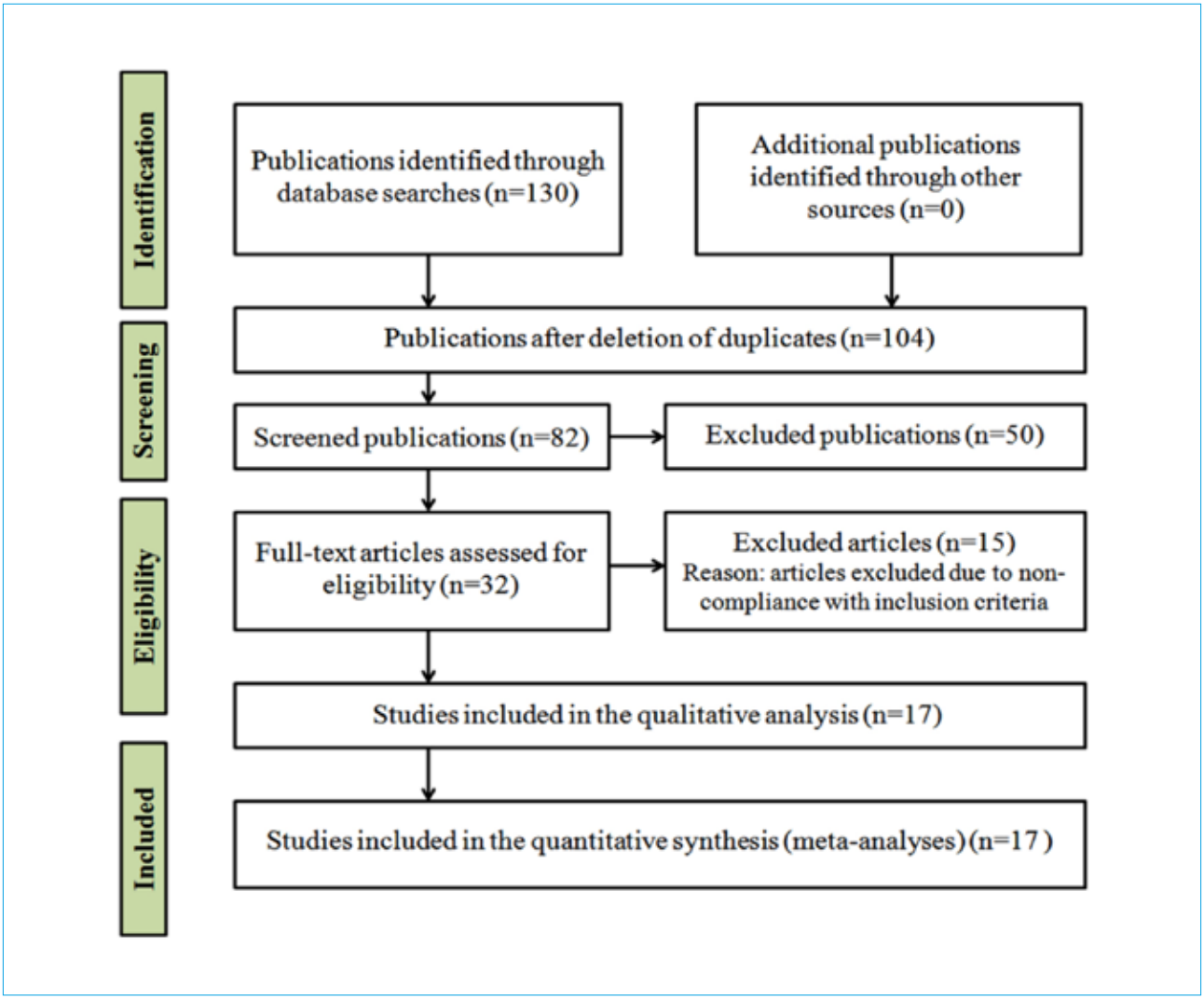


***Figure 2.*** Flow chart for selecting studies for inclusion in meta-analysis

***Рисунок 2.*** Блок-схема выбора исследований для включения в метаанализ

***Table 1.*** Human papilloma virus prevalence in oesophageal squamous cell cancer with normal tissue as control

***Таблица 1.*** Распространенность вируса папилломы человека при плоскоклеточном раке пищевода с нормальной тканью в качестве контроля

| Author, year of publication *Автор, год публикации* | Country *Страна* | Genotype of HPV *Генотип ВПЧ* | Tumor tissue *Опухолевая ткань* | | Controls *Контроль* | | *p* |
|---|---|---|---|---|---|---|---|
| | | | Total *Всего* | HPV+ *ВПЧ+* | Total *Всего* | HPV+ *ВПЧ+* | |
| Fidalgo P.O. et al., 1995 [15] | Portugal *Португалия* | 16, 18 | 17 | 9 | 8 | 5 | 0.695 |
| Cao B. et al., 2005 [16] | China *Китай* | 16, 18 | 265 | 207 | 357 | 203 | $3.627 \times 10^{-8}$ |
| Bahnassy A.A. et al., 2005 [26] | Egypt *Египет* | 16, 18, 11 | 50 | 27 | 50 | 12 | 0.004 |
| Katiyar S. et al., 2005 [27] | India *Индия* | 16, 18 | 101 | 19 | 26 | 1 | 0.073 |
| Moradi A. et al., 2006 [24] | Iran *Иран* | 6, 16, 18, 66, 52, | 85 | 42 | 31 | 18 | 0.529 |
| Zhang D. et al., 2010 [23] | China *Китай* | 16, 18, 58 | 70 | 35 | 60 | 19 | 0.049 |
| Antonsson A. et al., 2010 [25] | Australia *Австралия* | 16, 35 | 222 | 8 | 55 | 0 | 0.218 |
| Guo F. et al., 2012 [35] | China *Китай* | 16, 18, 58, 57, 3, 94, 27 | 300 | 93 | 900 | 61 | $1 \times 10^{-24}$ |
| Hu J.M. et al., 2013 [33] | China *Китай* | 16 | 150 | 55 | 150 | 24 | 0.000072 |
| Liyanage S.S. et al., 2014 [6] | Australia *Австралия* | 16 | 99 | 1 | 100 | 0 | 1 |
| Cui X. et al., 2014 [28] | China *Китай* | 16, 18, 35, 52, 6, 11, 43 | 183 | 58 | 89 | 8 | 0.000035 |
| Georgantis G. et al., 2015 [17] | Greece *Греция* | 11, 31 | 19 | 2 | 30 | 0 | 0.145 |
| Yahyapour Y. et al., 2016 [31] | Iran *Иран* | 11, 16, 45, 35, 52, 39, 45, 59, 33, 56, 58 | 51 | 16 | 45 | 20 | 0.210 |
| Pastrez P.R.A. et al., 2017 [29] | Brazil *Бразилия* | 51, 31, 66, 56, 18, 16, 26 | 87 | 10 | 87 | 2 | 0.032 |
| Mohammadpour B. et al., 2019 [30] | Iran *Иран* | 16, 18, 31, 33 | 43 | 15 | 43 | 8 | 0.143 |
| Sadeghian Z. et al., 2022 [32] | Iran *Иран* | 16, 18 | 70 | 20 | 70 | 0 | $3.9142 \times 10^{-7}$ |
| Burassakarn A. et al., 2023 [5] | Thailand *Таиланд* | 16, 18, 58 | 100 | 45 | 105 | 23 | 0.0006 |
| Total / *Всего* | | | 1912 | 662 | 2206 | 404 | 0.000023 |

***Note:*** *HPV — human papillomavirus.*
***Примечание:*** *ВПЧ — вирус папилломы человека.*

## Discussion

The results of the meta-analysis showed that the prevalence of HPV in oesophageal tumour tissue was 34.6 % of cases, while in control group samples HPV was detected in 18.3 % of cases. The data obtained are consistent with the results of previously published studies. Thus, in the work by S.S. Liyanage et al. HPV was detected in 35 % of tumour tissue samples and in 27 % of control samples [36]. At the same time, in the study by J.L. Petrick et al. the prevalence of HPV differed depending on the method of detection and was 17.6–32.2 % [37]. However, there are papers that have not demonstrated an association between papillomavirus infection and OSCC [38]. The contradictions between studies indicate the importance of resolving this issue. This is why it is important to take into account the results of the

| № | Study name | Risk Ratio | CI Lower limit | CI Upper limit | Weight |
|---|---|---|---|---|---|
| 1 | Guo F. et al, 2012, China | 1,35 | 1,25 | 1,46 | 8,57% |
| 2 | Liyanage S. S. et al, 2014, Australia | 1,01 | 0,98 | 1,04 | 9,26% |
| 3 | Burassakarn A. et al, 2023, Thailand | 1,42 | 1,16 | 1,74 | 5,69% |
| 4 | Zhang D. et al, 2010, China | 1,37 | 1,02 | 1,83 | 4,05% |
| 5 | Fidalgo P. O. et al, 1995, Portugal | 0,80 | 0,27 | 2,36 | 0,54% |
| 6 | Moradi A. et al, 2006, Iran | 0,83 | 0,52 | 1,33 | 2,15% |
| 7 | Antonsson A. et al, 2010, Australia | 1,03 | 0,99 | 1,07 | 9,19% |
| 8 | Cao B. et al, 2005, China | 1,97 | 1,52 | 2,55 | 4,63% |
| 9 | Bahnassy A. A. et al, 2005, Egypt | 1,65 | 1,17 | 2,33 | 3,38% |
| 10 | Katiyar S. et al, 2005, India | 1,18 | 1,05 | 1,34 | 7,63% |
| 11 | Cui X. et al, 2014, China | 1,33 | 1,18 | 1,50 | 7,70% |
| 12 | Pastrez P. R. A. et al, 2017, Brazil | 1,10 | 1,02 | 1,20 | 8,48% |
| 13 | Mohammadpour B. Et al, 2019, Iran | 1,25 | 0,96 | 1,63 | 4,55% |
| 14 | Yahyapour Y. et al., 2016, Iran | 0,81 | 0,59 | 1,12 | 3,61% |
| 15 | Georgantis G. et al., 2015, Greece | 1,12 | 0,94 | 1,34 | 6,43% |
| 16 | Sadeghian Z. et al, 2022, Iran | 1,40 | 1,20 | 1,62 | 6,96% |
| 17 | Hu J. M. et al, 2013, China | 1,33 | 1,15 | 1,53 | 7,18% |
| | **Total** | **1,22** | **1,11** | **1,35** | |

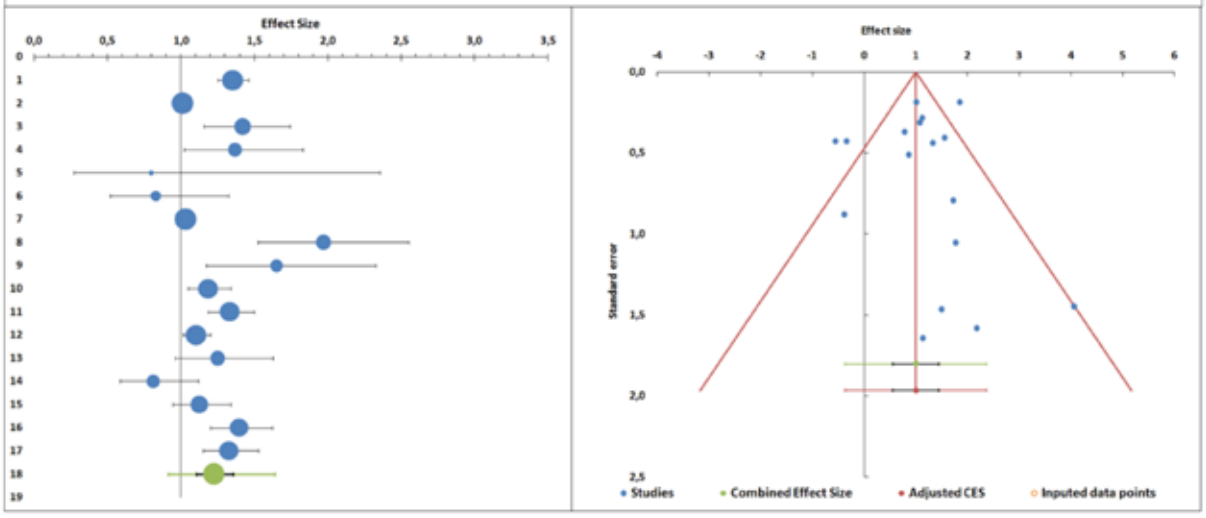


***Figure 3.*** Results of a meta-analysis of the association of papillomavirus infection with oesophageal squamous cell cancer risk

***Рисунок 3.*** Результаты метаанализа связи наличия папилломавирусной инфекции с риском развития плоскоклеточного рака пищевода

presented meta-analysis, which was conducted with strict inclusion and exclusion criteria. This analysis allows for a more accurate interpretation of the available data and an understanding of the importance of HPV in the development of OSCC.

During the analysis, it was observed that the most common human papillomavirus genotype is HPV type 16, with HPV type 18 being the second most common. The findings were consistent with previously published studies. It has been shown that HPV type 16 is the most frequently detected HPV genotype [37–40]. Moreover, HPV type 16 is detected more than twice as often as HPV genotype 18 [37, 40]. Together, these two genotypes account for a large percentage of prevalence, more than 80 % of HPV in infected oesophageal cancer specimens [40]. In a study by G. Georgantis et al., HPV type 31 and HPV type 11 were prevalent [17]. This feature can be explained by the fact that Greece is a region with a low risk of HPV-related OSCC and by the small sample of patients included in the presented study. According to this study, it can be assumed that HPV is not a significant etiological factor for OSCC in the Greek population [17].

Considering the data from the studies included in the meta-analysis, it can be said that the incidence

***Table 2.*** Results of meta-analysis of the association of papillomavirus infection with the risk of oesophageal squamous cell cancer according to ethnicity

***Таблица 2.*** Результаты метаанализа связи наличия папилломавирусной инфекции с риском развития плоскоклеточного рака пищевода в зависимости от этнической принадлежности

| No. *№* | Authors, year / Subgroup name *Авторы исследования, год / Название подгруппы* | Country *Страна* | Risk Ratio *Отношение рисков* | 95 % CI *95 % ДИ* | Weight *Масса* | $p_Q$ |
|---|---|---|---|---|---|---|
| 1 | Moradi A. et al., 2006 [10] | Iran *Иран* | 0.83 | 0.52–1.33 | 5.62 % | |
| 2 | Bahnassy A.A. et al., 2005 [13] | Egypt *Египет* | 1.65 | 1.17–2.33 | 10.59 % | |
| 3 | Mohammadpour B. et al., 2019 [17] | Iran *Иран* | 1.25 | 0.96–1.63 | 17.75 % | |
| 4 | Yahyapour Y. et al., 2016 [18] | Iran *Иран* | 0.81 | 0.59–1.12 | 11.80 % | |
| 5 | Sadeghian Z. et al., 2022 [20] | Iran *Иран* | 1.40 | 1.20–1.62 | 54.24 % | |
| Arab ethnic group *Арабская этническая группа* | | | 1.27 | 1.09–1.48 | 3.02 % | 0.005 |
| 6 | Guo F. et al., 2012 [4] | China *Китай* | 1.35 | 1.25–1.46 | 40.65 % | |
| 7 | Burassakarn A. et al., 2023 [6] | Thailand *Таиланд* | 1.42 | 1.16–1.74 | 5.91 % | |
| 8 | Zhang D. et al., 2010 [8] | China *Китай* | 1.37 | 1.02–1.83 | 2.91 % | |
| 9 | Cao B. et al., 2005 [12] | China *Китай* | 1.97 | 1.52–2.55 | 3.73 % | |
| 10 | Katiyar S. et al., 2005 [14] | India *Индия* | 1.18 | 1.05–1.34 | 16.72 % | |
| 11 | Cui X. et al., 2014 [15] | China *Китай* | 1.33 | 1.18–1.50 | 17.58 % | |
| 12 | Hu JM. et al., 2013 [21] | China *Китай* | 1.33 | 1.15–1.53 | 12.49 % | |
| Arab ethnic group *Арабская этническая группа* | | | 1.34 | 1.26–1.42 | 14.87 % | 0.042 |
| 13 | Liyanage S.S. et al., 2014 [5] | Australia *Австралия* | 1.01 | 0.98–1.04 | 57.58 % | |
| 14 | Fidalgo P.O. et al., 1995 [9] | Portugal *Португалия* | 0.80 | 0.27–2.35 | 0.04 % | |
| 15 | Antonsson A. et al., 2010 [11] | Australia *Австралия* | 1.03 | 0.99–1.07 | 34.28 % | |
| 16 | Pastrez P.R.A. et al., 2017 [16] | Brazil *Бразилия* | 1.10 | 1.02–1.20 | 6.58 % | |
| 17 | Georgantis G. et al., 2015 [19] | Greece *Греция* | 1.12 | 0.94–1.34 | 1.51 % | |
| Europoid ethnic group *Европеоидная этническая группа* | | | 1.02 | 0.99–1.06 | 82.11 % | 0.232 |

***Note:*** *CI — confidence interval.*
***Примечание:*** *ДИ — доверительный интервал.*

of OSCC varies greatly from region to region [39, 41]. The incidence of this oncopathology worldwide is shown in Figure 4.

Although geographical differences in the prevalence of papillomavirus infection observed in this oncopathology are notable, it cannot be expected that HPV can fully explain them, as to date there are several putative risk factors for OSCC, including dietary habits, tobacco and alcohol use, environmental pollution, various genetic factors, and family history [39].

In the current meta-analysis, a high risk of developing this oncopathology due to papillomavirus infection was found in Asians (RR = 1.34; 95 % CI: 1.26–1.42) and Arabs (RR = 1.27; 95 % CI: 1.09–1.48). A similar pattern of OSCC risk score for Asian countries (odds ratio (OR) — 1.63; 95 % CI: 1.29–2.04) was shown in a 2016 meta-analysis [39]. There was no systematic publication error indicating high reliability of the results [39]. In a 2019 meta-analysis, it was shown that in Iran, which belongs

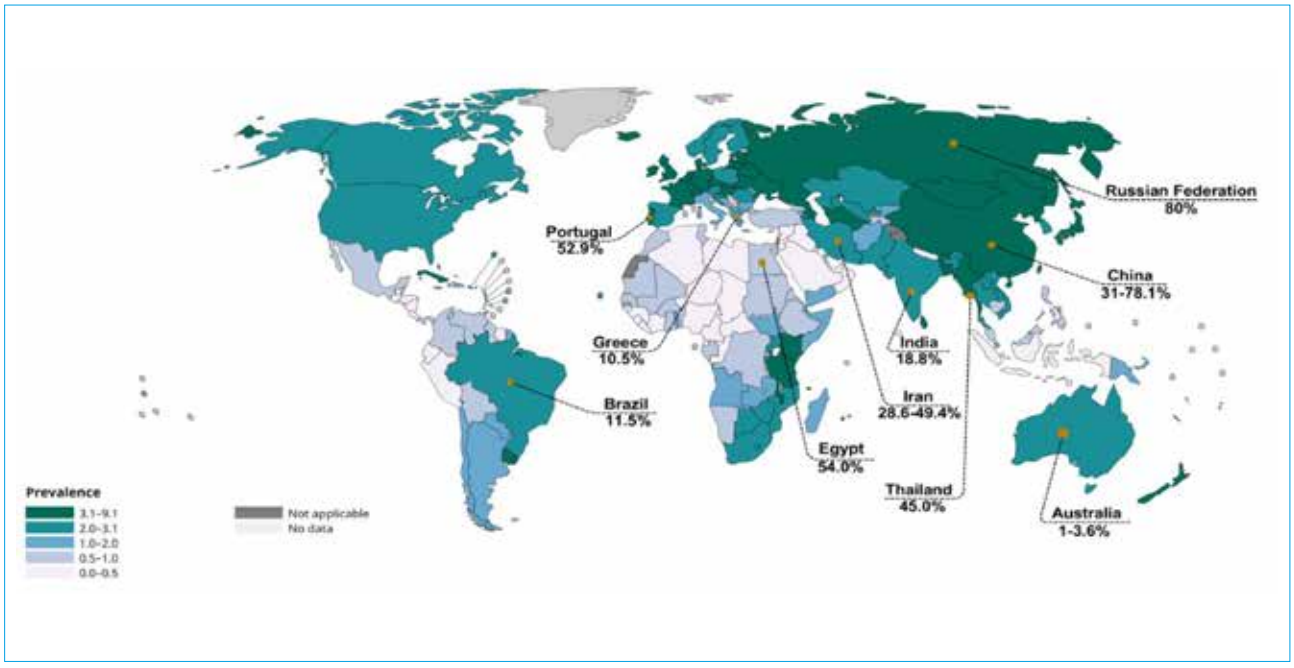


***Figure 4.*** Incidence of oesophageal cancer worldwide (percentages indicate the average incidence of cancer in the countries presented in Table 1)

***Рисунок 4.*** Частота встречаемости рака пищевода в мире (процентами обозначена средняя частота встречаемости данной онкопатологии в странах, представленных в таблице 1)

to Arab countries, the OR was 3.03 (95 % CI: 1.42–6.45) [41]. Such inconsistencies in HPV detection rates between studies may also be due to the different methods of HPV detection, and the fact that these analyses used an odds ratio (OR), which is always higher than risk ratio (RR). According to the data presented, it is important to note that papillomavirus infection is a significant factor in the incidence of OSCC in regions at high risk of developing this oncopathology. Especially, based on findings in our meta-analysis, the risk of OSCC with papillomavirus infection is statistically significant in Asian and Arab ethnic groups.

## Conclusion

Despite contradictory data on the role of papillomavirus infection in the occurrence and progression of oesophageal squamous cell cancer, the meta-analysis makes a significant contribution towards answering the question of the association of HPV with oesophageal squamous cell cancer. The meta-analysis confirmed that this association is ethnically specific. Based on these findings, papillomavirus infection should be considered as a potential risk factor for oesophageal squamous cell cancer.

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