Cancers are complex and multifactorial diseases and considered a global problem, each year, approximately 9 million people die because of cancer in the world.\(^1\)\(^,\)\(^2\) In recent years, although significant advances have been made in prevention and treatment options for some cancer types, the number of cancer patients is still increasing due to the aging global population, as well as risk factors such as smoking, obesity and diet.\(^3\) Incidence of cancer is estimated to increase two times more in 2035. It is expected to affect especially in low-income and middle-income countries [LMICs].\(^3\) Of course not all cancers can be prevented, but prevention is very important and need long-term strategy.\(^4\) Besides surgery and radiotherapy systemic treatment options such as cytotoxic chemotherapy, hormonal

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**Abstract**

**Objectives:** Dialister is the genus classified within Veillonellaceae family in Firmicutes phylum. Dialister genus has been detected in patients with oral infections and healthy people in their oral cavity, as well as in clinical samples in different parts of the body. Cancers are complex and multifactorial diseases and considered a global problem. End products of Dialister such as acetate, lactate and propionate seem to be important in the mechanism of carcinogenesis. Although it is reported that the composition of Dialister has changed in articles investigating the microbiome relationship with cancer patients, it is seen that it is not taken into consideration. The aim of this review was to investigate cancer studies in humans on the association of microbiome with composition changes in Dialister.

**Methods:** A systematic literature search was performed using in Pubmed. In vitro and animal studies were excluded. After database search, 510 articles were found. 484 article were excluded based on the exclusion criteria. The remaining 26 articles were identified and analysed for Dialister. Meta-Mar online software was used for metaanalysis results.

**Results:** The meta-analysis included 26 studies with 1649 control samples and 1961 cancer samples. Compared to healthy controls, Dialister were significantly elevated in samples from cancer patients (Hedges'g=0.907, p<0.05, 95%CI [13.19 - 16.746]. Statistical heterogeneity was found high (I²=99.6%).

**Conclusion:** This review showed that a relationship between different cancer types and Dialister composition of microbiome. However, these data still seem very weak to reveal the Dialister and cancer relationship. Dialister can be an important genus especially in solid tumors but, more comprehensive and wider studies are needed to understand the relationship between Dialister and cancer. In addition, due to rapidly developing new bioinformatics analysis techniques, massive data should be added to public databases by the authors in studies of microbiome or microbiota disease relationship. Thus, it is valuable in terms of detecting different strains such as Dialister, which can be ignored by re-evaluating these data in the future.

**Keywords:** Cancer, Dialister, microbiome, microbiota, next generation sequencing
therapy, immunotherapy and targeted therapies are used for the treatment of cancer patients.\[5\] While many types of cancer cannot be cured, when they detect upper stages, early detection of cancerous and precancerous lesions are very important in order to reduce mortality, morbidity, psychological and economical burdens.\[6\] Despite the complex structure of cancers, technological techniques including medical imaging or minimally invasive biomarkers are used as reliable techniques in the diagnosis, treatment and follow-up of cancers patients. On the other hand, the interpretation of the big data obtained by these techniques is a new challenge.\[7\]

Many recent studies showed that symbiotic microorganisms that colonize body surfaces in the host are play important role in health or diseases such as cancer and associated with these conditions. The largest symbiotic microorganism concentration is found in the intestine, skin and oral cavity. Our system evolves together with these microorganisms, allowing our immune system to be regulated.\[8\] In recent years, advances in sequencing technology and bioinformatic techniques have enabled complex symbiotic microorganism communities to be detected in the host. Big data including these techniques such as the Human Microbiome Project, allowed us to understand the metabolic and metagenomic potentials of these symbiotic microorganisms. These data caused a very important change in our perspective. We no longer think of microorganisms as just a cause of disease, but we also believe that microorganisms contribute to the state of health.\[9\] The term microbiome refers to all habitats containing microorganisms, their genomes and environmental conditions.\[10\] The main purpose in human microbiome studies is to identify and characterize bacterial taxa and their functions.\[11\] With the use of culture-independent approaches based methods such as high-throughput sequencing, new culturable or non-culturable bacteria in the microbiome were detected. Thus, it was possible to determine the identity, activities and functional roles of these bacteria in the microbiome. Detection of a conserved fragment of the 16S rRNA gene by the amplification of universal primers using the High-throughput sequencing method is considered the standard method for detecting the complex microbiome profile.\[12\]

_Dialister_ is the genus classified within Veillonellaceae family in Firmicutes phylum. Although it is in Gram positive phylum, it has Gram negative cell wall. It is nonmotile, non-spore forming, nonfermentative small coccobacilli shaped cells. _Dialister_ are obligatory anaerobic or microaerophilic bacteria. _Dialister pneumosintes, Dialister microaerophilus, Dialister propionicifaciens, Dialister succinatiphilus_ and _Dialister invius species_ were identified according to their main cellular content and using with 16S rRNA sequencing techniques. _Dialister_ genus has been detected in patients with oral infections and healthy people in their oral cavity, as well as in clinical samples in different parts of the body. Acetate, lactate and propionate have been reported as metabolic end products.\[13\]-\[17\] In addition to being such important end products for carcinogenesis, it is seen that although the composition of _Dialister_ has changed in the articles investigating the microbiome relationship in cancer patients, it is not taken into consideration.

The present systematic review aims to examine and discuss all available microbiome studies such as case-control, cross-sectional, prospective cohort, observational, interventional, experimental or clinical trials in humans on the association of cancer with changes in _Dialister_.

### Methods

The main questions for this review was; How did changed the amount of _Dialister _ spp in microbiome of cancer patients? The PRISMA guidelines was used to design this systematic review.\[18\]

### Searching Strategy

A thorough systematic literature search was performed (March 13, 2020) using the following databases: Pubmed, BioMed Central, Cochrane Library, EBMR, EMBASE, Informa Healthcare. The systematic literature search was structured by means of the PICO\(s\) acronym (participants, interventions, comparators, outcome measures, study design). The following query was created by using the Boolean Search Operator: _((dialister[All Fields] AND (“microbiota”[MeSH Terms] OR “microbiota”[All Fields] OR “microbiome”[All Fields])) AND (“microbiota”[MeSH Terms] OR “microbiota”[All Fields]) AND (“neoplasms”[MeSH Terms] OR “neoplasms”[All Fields] OR “cancer”[All Fields])_.

### Eligibility Criteria

Eligibility criteria of this review were I) Articles in english, II) research articles which included studies of case-control, cross-sectional, prospective cohort, observational, interventional, and experimental or clinical trials III) articles focus on patients diagnosed with cancer, IV) microbiome or microbiota studies using with next generation sequencer. V) reported _Dialister_ result. In vitro and animal studies were excluded.

### Data Extraction

The following information was extracted from each article: author, published time, target cancer type, study population (number of participants) total study population, LDA Score (log10), sample type, sequencer, sequencing protocol, cancer patients age, gender, BMI, country, enrollment...
time of study, Dialister result from study and Dialister status.

Statistical Analysis

Meta-Mar online metaanalysis software was used for the statistical analysis and foresplot figure and p<0.05 value was being considered statistically significant. Effect estimation was performed Hedges’g value (small = 0.2 – 0.49, medium = 0.5 - 0.79 and large ≥ 0.8). Statistical heterogeneity were calculated with I² test (0-40% small, 40-70% medium, 70-90% high).

Results

After database search, 510 articles were found. 484 article were excluded based on the exclusion criteria. The remaining 26 studies were identified as using with next generation sequencing to analyse microbiome of cancer patients and mentioned about Dialister and then fully reviewed, The process for selecting studies for inclusion in this review is detailed in Figure 1. Main characteristics of studies included in this systematic review showed that in Table 1.

The meta-analysis included 26 studies with 1649 control samples and 1961 cancer samples. Compared to healthy controls, Dialister were significantly elevated in samples from cancer patients (Hedges’g=-0.907, p<0.05, 95%CI [13.19 - 16.746]. Statistical heterogeneity was found high (I²=99.6%) (Table 2, Table 3, Figure 2).

Wang et al.,[19] (2015), Walther-António et al.,[20] (2016), and Sims et al. [21] (2019) examined the microbiome of cervical cancer patients using with stool, swab & scrape and stool samples respectively. Walther-António et al., (2016), Sims et al. (2019) reported Dialister were found to be significantly elevated in cancer patients (p=0.0061; p<0.05 respectively).[20,21] Wang et al.,[19] (2015) reported had increased abundance of Dialister.

Eight studies were found for association of colorectal cancer with changes in Dialister.[22-27] Different sample types such as stool or tissue samples were used in these studies. Six of these studies reported Dialister were found to be significantly elevated in cancer patients, however, two of these studies reported Dialister were found decrease in cancer patients.[25,27] Zhang et al. 2018, which also showed increased Dialister pneumosintes.[26] Chen et al., (2012) reported specifically Dialister pneumosintes.[22] While the microbiome results of cancer patients generally were compared with the healthy control group, only the Loke et al., (2018) and Chen et al., (2012) studies compared the microbiome results of the cancerous and non-cancerous tissues of cancer patients.[22,27]

Chen et al., (2015) and Elliot et al., (2017) reported for association of esophageal cancer with changes in Dialister. saliva and tissue samples were used in these studies respectively.[28,29] Chen et al., (2015) reported a decrease in cancer patients compared to healthy controls,[28] while Elliot et al., (2017) reported an increase in cancer patients compared to healthy controls.[29]

Six studies were found for association of gastric cancer with changes in Dialister.[30-34] In all of these studies except Liang et al.,[31] (2019), Dialister were found elevated in microbiome results of cancer patients compared to control. In all of these studies except Liang et al.,[31] (2019), also performed from tissue samples, but Liang et al., (2019) performed their study with stool samples.[31] Interestingly, Liang et al., (2019) reported Dialister were found reduced in microbiome results of cancer patients compared to healthy controls. They also found Dialister were increased postoperative samples from gastric cancer patients compared to preoperative samples from gastric cancer patients.[31]

Eight studies were found for association of head and neck cancer with changes in Dialister.[35-41] Gong et al. performed two different studies in 2014 and 2017 association of laryngeal carcinoma with Dialister and other studies association of head and neck squamous cell carcinoma with Dialister.[35,37] Different sample types such as oral rinse sample, oral swab sample, tissue biopsy sample for buccal mucosa or saliva were used in these studies. All of these studies reported that Dialister were increased in the head and neck cancer patient group compared with the control subjects. Yang et al., (2018), reported specifically Dialister pneumosintes.[40]
### Table 2. Metaanalysis results

| Study name             | Control n | Cancer n | Control LDA g | Cancer LDA g | Proportion g | SEg | g_lower | g_upper | Weight (%) |
|------------------------|-----------|----------|---------------|--------------|--------------|-----|---------|---------|------------|
| Wang et al., 2015      | 4         | 11       | 0.001         | 2.001        | 1882.352941  | 343.669495 | 1208.76073 | 2555.94515 | 0.000697   |
| Walther-António et al., 2016 | 10       | 21       | 0.001         | 1.201        | 1168.695652  | 148.429468 | 877.782715 | 1459.60859 | 0.003736   |
| Sims et al., 2019      | 46        | 42       | 0.001         | 4.001        | 3965.01477   | 298.874294 | 3379.22096 | 4550.80819 | 0.000921   |
| Chen et al., 2012      | 56        | 46       | 0.001         | 0.405        | 400.962406   | 28.073678  | 345.937997 | 455.98615 | 0.104426   |
| Hibberd et al., 2017   | 21        | 15       | 0.001         | 1.281        | 1251.555556  | 147.497607 | 962.460246 | 1540.65087 | 0.003783   |
| Xu et al., 2017        | 61        | 99       | 0.001         | 3.101        | 3085.26149   | 172.471437 | 2747.21747 | 3423.30551 | 0.002767   |
| Flemer et al., 2018    | 103       | 131      | 0.341         | 2.881        | -338.899676  | 331.869188 | 2165.53639 | 3466.46361 | 0.000747   |
| Zhang et al., 2018     | 192       | 218      | 0.001         | 0.201        | 199.632128   | 6.972156  | 185.96701 | 213.297554 | 1.693068   |
| Loke et al., 2018      | 17        | 17       | 0.03          | 0.001        | -28.314961   | 3.449986  | -35.076934 | -21.552998 | 6.91471    |
| Chen et al., 2015      | 85        | 87       | 0.101         | 0.001        | -99.558174   | 5.369964  | -110.0833 | -89.033044 | 0.177498   |
| Elliot et al., 2017    | 20        | 66       | 0.001         | 0.201        | 198.208955   | 15.115408 | 168.582756 | 227.835155 | 0.360221   |
| Castaño-Rodríguez et al., 2017 | 4         | 32       | 0.001         | 2.881        | 2816         | 331.869188 | 2165.53639 | 3466.46361 | 0.000747   |
| Liang et al., 2019     | 22        | 20       | 0.401         | 0.001        | -392.45283   | 42.821187 | -476.382357 | -308.523303 | 0.044884 |
| Coker et al., 2018     | 168       | 19       | 0.001         | 1.901        | 1893.04093   | 93.08023  | 1710.68577 | 2075.39482 | 0.009508   |
| Ling et al., 2019      | 64        | 64       | 0.001         | 6.001        | 5964.21472   | 372.763461 | 5233.59833 | 6694.8311  | 0.005929   |
| Liu et al., 2019       | 230       | 216      | 0.001         | 0.811        | 809.136194   | 56.395002 | 742.739991 | 1020.5428  | 0.025878   |
| Gong et al., 2014      | 28        | 27       | 0.001         | 0.601        | 591.469194   | 6.847418  | 585.62993 | 697.30834 | 0.000747   |
| Guerrero-Preston et al., 2016 | 25       | 17       | 0.001         | 0.01         | 8.830189     | 1.011618  | 6.847418  | 10.812959 | 0.000747   |
| Gong et al., 2017      | 32        | 31       | 0.001         | 0.901        | 888.888889   | 79.18907 | 733.678631 | 1044.09915 | 0.013124   |
| Zhao et al., 2017      | 40        | 40       | 0.001         | 3.001        | 2971.061093  | 234.833017 | 2510.6902 | 3041.4619 | 0.01492   |
| Börnigen et al., 2017  | 242       | 121      | 0.001         | 1.01         | 99.7921     | 3.705298 | 92.529715 | 107.054845 | 0.004274   |
| Yang et al., 2018      | 51        | 197      | 0.001         | 3.101        | 3090.539166  | 138.769339 | 2818.55116 | 3362.52718 | 0.004274   |
| Zhang et al., 2019     | 50        | 50       | 0.001         | 0.321        | 317.544757   | 22.454682 | 273.53358 | 361.55934 | 0.163228   |
| Liu et al., 2018a      | 18        | 24       | 0.301         | 0.001        | -294.339623  | 32.116543 | -357.288046 | -231.391199 | 0.07979   |
| Liu et al., 2018b      | 44        | 40       | 0.001         | 1.631        | 1615.045872  | 124.603682 | 1370.82265 | 1859.26909 | 0.005301   |
| Liu et al., 2019       | 16        | 30       | 0.001         | 0.101        | 98.285714    | 10.25151 | 78.192754 | 118.378674 | 0.783128   |

**Fixed Effect Model**
- p<0.05

**Random Effect Model**
- p<0.05

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Test for heterogeneity: $I^2 = 99.6\%$, $Chi^2 = 6938.02$, df = 25, $Tau^2 = 16555.81$

Test for overall effect: $z = 1.645$ (p<0.05)
Three studies were found for association of lung cancer with changes in Dialister.[42-44] In these three lung cancer microbiome studies, they used different types of samples and were protected specimen brushing (PSB) samples, tissue biopsies and stool, respectively. Except PSB samples. [42] other samples. [43,44] reported Dialister were elevated in cancer compared to controls. But in PSB samples, Liu et al. (2018a) found Dialister was reduced in the microbiome of lung cancer patients. [42] Liu et al., (2018b) reported that patients with lung cancer plus emphysema had the highest Dialister amounts compared only emphysema or only lung cancer patients. [43]

**Discussion**

The interaction between microorganisms, cancer and immune response has not yet been fully discovered. Nevertheless, the evidence on the roles of microbiome studies in carcinogenesis and immunotherapy reveals that the microbiome should be examined. [45] The effect of microbiome changes on the formation of the immune response is indisputable. [46] An important way that the microbiome affects the host is bacterial metabolites. They can reach the target cells by participating in the circulation. These metabolites can affect the host through mitochondrial metabolism and can also regulate important metabolic processes such as lipid metabolism. [47]

Short chain fatty acids (SCFAs) are the ones that are considered to be the most important among the bacterial metabolites that affect the cellular or immunological mechanisms of the host. SCFAs are mainly accepted as butyrate, propionate and acetate and these are essential to maintain intestinal homeostasis, especially in the anaerobic environment of the intestine. SCFAs may have opposite effects that induce or inhibit autophagy and thus inhibit proliferation of cancer cells or induce apoptosis of cancer cells. [48]

Acetate, lactate and propionate have been reported as metabolic end products of Dialister. [13,14] Acetate has been reported as an important energy source for the development of solid tumors. [50] Similar to acetate, lactate has been reported as an important component of primary and metastatic cancer metabolism. [51] Propionate has been reported as an anti-tumor effective prebiotic, unlike acetate and lactate. [52]

Recently, articles also have been published about the relationship between Dialister and different diseases other than cancer such as depression, [53] obesity [54] or ankylosing spondylitis. [55] The data in these studies draw attention to the Dialister.

Yost et al., 2018 reported, Dialister were more active in the tumour sites. [56] Ling et al., 2019 reported, Dialister genus positively correlated with Forkhead box protein P3 (FoxP3)+ T regulatory cells (Tregs). [53] FoxP3+ Tregs cell elevations showed both prognostic effect and a positive correlation with poor clinical outcomes in cancer patients. [57] End products of Dialister may also be at play here. Jimma et al., 2010 reported acetate [58] and Angelin et al., 2017 reported lactate [59] induce FoxP3+ Treg cells.

In this review, there are some limitations such as different types of cancer, different sample types in analysis, different gene regions and different number of patients. Despite all these limitations, it is important to reach important conclusions about Dialister and cancer relationship.

**Conclusion**

In a conclusion, although there are interesting results related to Dialister in different cancer-microbiome relationship studies, it is not much emphasized. Generally, it is seen that the amount of Dialister is elevated in the microbiome of cancer patients. We think that due to the effects of bacterial metabolites on host cells, Dialister can be an important genus especially in solid tumors. Nevertheless, more comprehensive and wider studies are needed to understand this relationship between Dialister and cancer. In addition, although high-throughput data are obtained with constantly developing new molecular sequencing techniques, some genus with low levels such as Dialister can be overlooked among these data. For this reason, these raw data
must be uploaded to public databases by the authors in microbiome or microbiota - disease relationship studies. Thus, raw data will have the chance to be re-evaluated with continuously developing bioinformatics techniques.

**Disclosures**

**Ethics Committee Approval:** Not required.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

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| Author                  | Published time | Target cancer type | Study population | Total LDA scores (log10) | Sample type        | Sequencer | Sequencing protocol | Cancer patients mean age | Cancer patients gender (F/M) | Cancer patients BMI | Country | Enrolment time | Dialister status in cancer patients |
|-------------------------|----------------|-------------------|------------------|--------------------------|---------------------|-----------|---------------------|--------------------------|--------------------------|-------------------|---------|----------------|-----------------------------------|
| Wang et al.[19]         | 2015           | Cervical cancer   | Before and after pelvic radiotherapy for Pelvic Cancer patients (n=11), and healthy control (n=4) | 15 | 2 | Stool | Roche/454, GS-FLX | V3 region of 16s rRNA | 51 | 9/2 | 21.5 | China | N/A | Elevated |
| Walther-António et al.[20] | 2016          | Cervical cancer   | Benign gynecologic condition (control cohort) (n=10), endometrial hyperplasia (n=4), and endometrial cancer (n=17) patients | 31 | 1.2 | Vaginal and cervical swab and scrape samples | Illumina MiSeq | V3-V5 region of 16s rRNA | 64 | 17/0 | 32.1 | USA | N/A | Elevated |
| Sims et al.[21]        | 2019           | Cervical cancer   | Cervical cancer patients (n=42) and healthy controls (n=46) | 88 | 4 | Stool | Illumina MiSeq | V4 region of the 16s rRNA | 48.9±10.4 | 42/0 | 29.0±6.6 | USA | between 2015 to 2017 | Elevated |
| Chen et al.[22]        | 2012           | Colorectal cancer (CRC) | Colorectal cancer patients (CRC, n=46) and healthy controls (n=56) | 102 | 0.404 | Swab, stool and tissue samples | Roche/454, GS-FLX | V1-V3 region of 16s rRNA | 65 | N/A | N/A | China | N/A | Elevated |
| Hibberd et al.[23]     | 2017           | Colorectal cancer (CRC) | Colon cancer patients (n=15), and non-cancer healthy controls (n=21) | 36 | 1.28 | Tissue and stool samples | Illumina MiSeq | V4 region of the 16s rRNA | 77 | 9/6 | 24.1 | Sweden | between 2010 to 2016 | Elevated |
| Xu et al.[24]          | 2017           | Colorectal cancer (CRC) | Colorectal adenomas (n=47), invasive adenocarcinomas (n=52), and healthy control (n=61) | 160 | 3.1 | Tissue biopsies | Roche/454, GS-FLX | V1-V4 region of 16s rRNA | 67.85±13.18 | N/A | N/A | China | N/A | Elevated |
| Flemer et al.[25]      | 2018           | Colorectal cancer (CRC) | Colorectal cancer (CRC n=99), colorectal polyps (n=32) and healthy controls (n=103) | 234 | -0.34 | Oral swabs, colonic mucosae and stool | Illumina MiSeq | V3-V4 region of 16s rRNA | 65 | N/A | N/A | Ireland | N/A | Reduced |
| Zhang et al.[26]       | 2018           | Colorectal cancer (CRC) | Initially diagnosed CRC patients (n=130), advanced | 410 | 0.2 | Stool | Illumina MiSeq | V3-V4 region of 16s rRNA | 60.5 | 65/65 | N/A | China | Between 2014 to 2015 | Elevated |
| Author            | Published time | Target cancer type | Study population                                                                 | Total population | LDA scores (log10) | Sample type | Sequencer | Sequencing protocol | Cancer patients | Cancer patients | Cancer patients | Country       | Enrolment time | Dialister status in cancer patients |
|------------------|----------------|-------------------|-----------------------------------------------------------------------------------|------------------|-------------------|-------------|-----------|---------------------|----------------|----------------|----------------|--------------|---------------|-------------------------------|
| Loke et al. [27] | 2018           | Colorectal cancer (CRC) | Tumor and tumor-free tissues from colorectal cancer patients (CRC, n=17) and healthy controls (n=130) | 17 | -0.029 | Tissue biopsies | Illumina | V3-V4 region of 16s rRNA | N/A | 10/7 | N/A | Malaysia | Between 2013 to 2014 | Reduced |
| Chen et al. [28] | 2015           | Esophageal cancer | Esophageal squamous cell carcinoma (ESCC n=87), and healthy control (n=85) | 235 | -0.1 | Saliva | Roche/454, GS-FLX | V3-V4 region of 16s rRNA | 64.8±8.0 | 28/59 | N/A | China | Between 2010 to 2012 | Reduced |
| Elliot et al. [29] | 2017          | Esophageal cancer | Non-dysplastic (n=24), dysplastic Barrett’s oesophagus (n=23), and oesophageal adenocarcinoma (n=19) | 86 | 0.2 | Tissue biopsies | Illumina MiSeq | V1-V2 region of 16s rRNA | 70 | 4/15 | N/A | UK | N/A | Elevated |
| Castaño-Rodríguez et al. [30] | 2017 | Gastric cancer (GC) | Gastric cancer (n=12) and controls (functional dyspepsia (FD), n=20), and gastric ulcers (n=4) | 36 | 2.88 | Tissue biopsies | Illumina MiSeq | N/A | N/A | N/A | Australia | N/A | Elevated |
| Liang et al. [31] | 2019           | Gastric cancer (GC) | Gastric cancer patients (n=20) and healthy controls (n=22) & microbiota shifts of the patients with | 6 | -0.4 | Stool | Illumina MiSeq | 16s rRNA | 61.3±5.8 | 2/4 | 20.8±1.81 | China | Between 2017 to 2018 | Reduced |
| Author                  | Published time | Target cancer type | Study population                                                                 | Total population (log10) | Sample type | Sequencer | Sequencing protocol | Cancer patients mean age (range) | Cancer patients gender (F/M) | Cancer patients BMI | Country | Enrolment time | Dialister status in cancer patients |
|------------------------|----------------|--------------------|-----------------------------------------------------------------------------------|--------------------------|-------------|-----------|--------------------|-------------------------------|--------------------------|------------------|---------|----------------|----------------------------------|
| Coker et al.[32]       | 2018           | Gastric cancer (GC)| GC (n=6) before and after the radical distal gastrectomy (RDG)                    | 207                      | Tissue biopsies | Illumina MiSeq | V4 region of the 16s rRNA | N/A                          | N/A                      | N/A              | China   | N/A             | Elevated                                                  |
|                       |                |                    | Superficial gastritis (SG) (n=77), atrophic gastritis (AG) (n=74), intestinal     |                          |              |           |                    |                               |                          |                      |                   |         |                |                                                                 |
|                       |                |                    | metaplasia (IM) (n=17) and gastric cancer (GC) (n=39) patients                   |                          |              |           |                    |                               |                          |                      |                   |         |                |                                                                 |
| Ling et al.[33]        | 2019           | Gastric cancer (GC)| Tumor and tumor-free tissues from Gastric cancer patients (n=64)                 | 64                       | Tissue biopsies | Illumina MiSeq | V3 region of 16s rRNA | 60.30±12.75                  | 24/40                    | 22.37±3.25         | China   | between 2014 to 2017 | Elevated                                                  |
|                       |                |                    | primary gastric cancer tumoral tissues (n=229), peritumoral tissues (n=247) and  |                          |              |           |                    |                               |                          |                      |                   |         |                |                                                                 |
|                       |                |                    | normal tissues (n=230)                                                           |                          |              |           |                    |                               |                          |                      |                   |         |                |                                                                 |
| Liu et al.[34]         | 2019           | Gastric cancer (GC)| Tumor and tumor-free tissues from Gastric cancer patients (n=64)                 | 276                      | Tissue biopsies | Illumina MiSeq | V3 region of 16s rRNA | 61.11±11.82                  | 81/195                   | 22.46±3.32         | China   | Between 2009 to 2013 | Elevated                                                  |
|                       |                |                    | primary gastric cancer tumoral tissues (n=229), peritumoral tissues (n=247) and  |                          |              |           |                    |                               |                          |                      |                   |         |                |                                                                 |
|                       |                |                    | normal tissues (n=230)                                                           |                          |              |           |                    |                               |                          |                      |                   |         |                |                                                                 |
| Gong et al.[35]        | 2014           | Head and neck cancer| Laryngeal carcinoma patients (n=27) and subjects with vocal cord polyps (n=28) | 55                       | Swab and tissue samples | Roche/454, GS-FLX | V1-V3 region of 16s rRNA | N/A                          | 2/25                     | N/A              | China   | Between 2011 to 2012 | Elevated                                                  |
|                       |                |                    | Laryngeal carcinoma patients (n=27) and subjects with vocal cord polyps (n=28)  |                          |              |           |                    |                               |                          |                      |                   |         |                |                                                                 |
| Guerrero-Preston et al.[36] | 2016          | Head and neck cancer| Normal Mucosa (Control) HPV Negative (n=25), HNSCC patients (n=17) | 42                       | Saliva       | Roche/454, GS Junior | V3-V5 region of 16s rRNA | 66                          | 7/10                     | N/A              | USA     | between 2000 to 2011 | Elevated                                                  |
|                       |                |                    | Normal Mucosa (Control) HPV Negative (n=25), HNSCC patients (n=17) [Oropharynx |                          |              |           |                    |                               |                          |                      |                   |         |                |                                                                 |
|                       |                |                    | Squamous cell carcinoma (OPSCC) HPV Negative (n=4), Oropharynx Squamous cell     |                          |              |           |                    |                               |                          |                      |                   |         |                |                                                                 |
|                       |                |                    | carcinoma (OPSCC) HPV Positive (n=7), and Oral Cavity Squamous cell               |                          |              |           |                    |                               |                          |                      |                   |         |                |                                                                 |
| Author          | Published time | Target cancer type | Study population                                                                 | Total population | LDA scores (log10) | Sample type        | Sequencer          | Sequencing protocol | Cancer patients mean age | Cancer patients gender | Cancer patients BMI | Country | Enrolment time | Dialister status in cancer patients |
|-----------------|----------------|--------------------|----------------------------------------------------------------------------------|------------------|-------------------|--------------------|-------------------|---------------------|-----------------------|-----------------------|-------------------|---------|---------------|----------------------------------|
| Gong et al.[37] | 2017           | Head and neck cancer | carcinoma (OSCC) HPV Negative (n=61) Tumor and tumor-free tissues from laryngeal carcinoma patients (n=31) and subjects with vocal cord polyps (n=32) | 63               | 0.9               | Tissue biopsies    | Roche/454, GS-FLX | V3 region of 16S rRNA | 56.4                  | N/A                   | N/A               | China   | Between 2011 to 2012 | Elevated                  |
| Zhao et al.[38] | 2017           | Head and neck cancer | Oral squamous cell carcinoma (OSCC) patients (n=40) Oral cancer patients (n=121), oral cavity (n=43), oropharynx (n=64), or unknown primary (n=5) squamous cell carcinoma and healthy controls (n=242) | 40               | 3                 | Swabs of oral lesions Illumina MiSeq and anatomically matched normal sites | V4-V5 region of 16S rRNA | 62                  | 16/24                | N/A                   | N/A               | China   | N/A           | Elevated                  |
| Börnigen et al.[39] | 2017     | Head and neck cancer | Oral squamous cell carcinoma (OSCC, n=197) Oral squamous cell carcinoma (OSCC, n=197), Oral squamous cell carcinoma (OSCC, n=197), and OSCC stage 4 (n=90) healthy controls (n=51) | 363              | 0.1               | Oral rinse samples Illumina MiSeq | V4 region of 16S rRNA | 58                  | 27/94                | N/A                   | USA                | Between 2011 to 2013 | Elevated                  |
| Yang et al.[40]  | 2018           | Head and neck cancer | Oral squamous cell carcinoma (OSCC, n=197) Oral squamous cell carcinoma (OSCC, n=197), Oral squamous cell carcinoma (OSCC, n=197), and OSCC stage 4 (n=90) healthy controls (n=51) | 248              | 3.1               | Oral rinse samples Illumina MiSeq | V3-V4 region of 16S rRNA | 53                  | 20/177               | N/A                   | Taiwan             | N/A                | Elevated                  |
| Zhang et al.[41] | 2019           | Head and neck cancer | Tumor and tumor-free tissues from Oral squamous cell carcinoma patients (OSCC, n=50) | 50               | 0.32              | Buccal mucosa      | Illumina MiSeq | V3-V4 region of 16S rRNA | 60.7                  | 18/32                | N/A               | China   | Between Jan to July 2018 | Elevated                  |
| Liu et al.[42]    | 2018           | Lung Cancer (LC)    | Lung cancer patients (n=24) | 42               | -0.3              | Protected specimen Illumina MiSeq brushing (PSB) | V3-V4 region of 16S rRNA | 60.5±1.275          | 8/16                 | N/A                   | N/A                | China   | N/A           | Reduced                  |
| Author          | Published time | Target cancer type | Study population                                                                 | Total population | LDA scores (log10) | Sample type       | Sequencer        | Sequencing protocol | Cancer patients mean age | Cancer patients gender (F/M) | Cancer patients BMI | Country | Enrolment time | Dialister status in cancer patients |
|----------------|----------------|--------------------|----------------------------------------------------------------------------------|------------------|--------------------|--------------------|------------------|----------------------|--------------------------|------------------------|---------------------|---------|----------------|-----------------------------------|
| Liu et al.[43] | 2018           | Lung Cancer (LC)   | and healthy controls (n=18) Lung Cancer (n=40) (Emphysema-only (n=10), LC-only (n=11), LC with emphysema (n=19), and heavy smoker (n=44)) | 84               | 1.63               | Tissue biopsies    | Illumina MiSeq   | V4 region of 16s rRNA | 65                       | 4/36                   | N/A                 | USA     | N/A            | Elevated                        |
| Liu et al.[44] | 2019           | Lung Cancer (LC)   | newly diagnosed lung cancer patients (n=30), and healthy control (n=16)          | 46               | 0.1                | Stool              | Illumina Hiseq   | V4 region of 16s rRNA | 60                       | 9/21                   | N/A                 | China   | N/A            | Elevated                        |

N/A: Not available.