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How to improve microbiota to harness chronic inflammation and prevent cancer, cardiovascular or neurodegenerative diseases? A transversal qualitative review

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ABSTRACT

Background: Dysbiosis should be controlled since it is implicated in metabolic syndrome, cancer occurrence or prognosis, inflammatory bowel diseases, periodontitis, as well as in systemic, neurological, or cardiovascular chronic inflammation.

Eradication strategies with antibiotics are in conflict with new proposals of a diversified diet to magnify the diversity of the microbiome. Probiotic use does not meet expectations.

Objective: Reconcile the different – and sometimes divergent - medical recommendations. Suggest an integrative and preventive approach that uses as little antibiotic therapy as possible, to improve the flora and to reduce silent chronic inflammation (SCI). Elaborate a simple flow chart to be used in ambulatory practice.

Methods: Identify the most frequent life-threatening diseases associated (bidirectional perspective) with altered microbiota and SCI. Specify the bacteria or viruses involved.

Select the most appropriate methods to detect, to quantify and to follow such SCI-associated dysbiosis, in usual and ambulatory practice.

Suggest inexpensive and innocuous treatments of SCI induced by dysbiosis.

Build a general model that can optimize flora quality and inflammation control, while adapting to current official recommendations.

Results: Cancer, cardiovascular and neurodegenerative diseases are the most prevalent preventable causes of death. They are frequently associated with *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, herpes viruses (herpes simplex type 1, Epstein-Barr virus or cytomegalovirus) or human papillomavirus infections. A low diversity of microbiota with low levels of hydrogen sulphide may exacerbate SCI.

SCI and dysbiosis can be detected with a breath test, detection of calprotectine and pyruvate kinase M2 in saliva. A simple flow chart may be used in ambulatory practice to control SCI.

Treatment with diet, mouth cleaning, tiny amount of essential oils and natural immunostimulating agents could improve the oral and foregut microbiota and therefore SCI.

Conclusion: Cost-effective detection and prevention of SCI could be implemented in usual practice. Its usefulness could be evaluated in a second step according to the figures available in reliable meta-analyses.

Keywords: dysbiosis – Calprotectin – breath test – PKM2

List of abbreviations:

CLP: calprotectin;
CMV: cytomegalovirus;
COVID: coronavirus 19;
EBV: Epstein-Barr virus;
FN: *Fusobacterium nucleatum*;
FODMAP: low fermentable oligosaccharides, disaccharides, monosaccharides and polyols;
H2O2: hydrogen peroxide;
H2S: hydrogen sulphide;
HPV: Human Papillomavirus;
HSV1/2: herpes simplex virus types 1 or 2;
IU: international unit;
NDD: neurodegenerative diseases;
NLR: neutrophils/lymphocytes ratio;
NO: nitric oxide;
PDL1: Programmed death-ligand 1;
PG: *Porphyromonas gingivalis*;
PKM2: Pyruvate kinase M2;
SCI: Silent chronic inflammation.

Introduction

Silent chronic inflammation (SCI) is implicated in numerous local or systemic diseases.

The microbiota is defined as all the micro-organisms living on and in the human body. A pathogenic microbiota - dysbiosis - can harbour inappropriate bacteria, viruses, yeasts or parasites, leading to SCI.

Silent chronic inflammation is rarely restricted to a single organ and is rather a wide-spread issue. Therefore, in addition to its main target-organ, SCI frequently also involves the cardiovascular[1-3] or the central nervous system.[4]

For example, periodontitis is associated with SCI,[5] leading to many severe diseases.[6-12] It may concern up to 70% of US adults aged 65 years and older and is associated with more than 50 systemic inflammatory disorders and comorbidities, including cancers, neurodegenerative diseases (NDD) or cardiovascular diseases.[13] Causal relationships are not yet established. However a bidirectional effect is currently admitted.[14,15]

Cancers are largely attributable to at least 30 modifiable risk factors including nine infectious agents accounting for 10.2% of cases, just behind smoking (15.1%), however far ahead alcohol consumption (3.2%). Strengthening efforts to reduce modifiable exposures remain central to global cancer prevention.[16]

Alterations in the gut microbiota frequently exist in patients with autoimmunity such as multiple sclerosis,[17] lupus,[18] Sjögren's disease,[19] autoimmune thyroidis,[20] or inflammatory bowel diseases[21,22] and could contribute to the severity of inflammatory flare-ups.

Decreased diversity of microbiota can also be considered as a kind of dysbiosis and is frequently detected in inflammatory diseases.[23] disease,[24,25] overweight,[26,27] as well as neutrophilic[28] or eosinophilic diseases.[29,30]

Many diseases – such as Alzheimer's disease, Parkinson's disease or depression - are associated with small intestinal bacterial overgrowth, leaky gut syndrome and vagal-mediated inflammation currently classified as gut-brain axis disorders.[31-34]

Epstein-Barr virus (EBV) and human papillomaviruses (HPV) are known to favour many types of cancers.[35-38]

The association of viruses with bacteria triggers deleterious inflammation. For example, EBV may worsen Helicobacter pylori-induced SCI.[39] EBV, HPV and Helicobacter pylori are the most frequently reported infectious oncogenic germs.[40,41]

There is currently no attempt to identify and list all bacteria and viruses implicated in SCI and subsequently no attempt to treat oral dysbiosis in patients with cancer, cardiovascular, central nervous system or auto-immune diseases. Silent chronic inflammation is usually controlled with systemic and symptomatic anti-inflammatory or immunosuppressive drugs which may induce severe adverse events or favour immunosuppression and consequently opportunistic infections or cancers.[42-46]

The most frequent recognized types of chronic inflammation are: visceral fat,[47,48] chronic viral, or bacterial infections (periodontitis or dysbiosis).[49-51]

Etiological treatments of chronic infections - such as control of dysbiosis - should be started as early as possible in order to prevent alterations of specific organs: e.g. joints, heart, arteries, skin, central nervous system, etc..

Any alleviation or control of any type of chronic inflammation should be considered as an appropriate anti-inflammatory therapy, and therefore performed in parallel with classical medical care. In addition, destruction of inappropriate germs may have important consequences on anticancer or antiviral immunity.

For example encouraging results have been reported after the improvement of microbiota due to faecal graft in patients with melanoma, renal carcinoma or non-small cell lung cancer. These improvements are attributed to the destruction of inappropriate bacteria rather than actual implantation of beneficial germs.[52,53]

The severity of SCI is usually not quantified before immunosuppressant therapy and is not evaluated during or after immunosuppressive therapy.

More individualised clinical decision-making models should be explored. For example, white blood cell counts and exhaled-nitric oxide (NO) could be taken into account,[54] as well as neutrophils lymphocytes (NLR) ratio.[55-59]

Efficient, inexpensive and easy-to-use detection tools are now available to physicians who may evaluate dysbiosis and chronic inflammation.

Calprotectin (CLP) is a simple and inexpensive marker to detect oral neutrophil-induced inflammation.[60] Saliva CLP is increased in patients with periodontitis.[61]

Pyruvate kinase M2 (PKM2) has received increasing attention because of its role in tumour cell energy supply or proliferation, epithelial-mesenchymal transition, invasion and metastasis.[62] Its detection in saliva has been associated with colorectal polyps, dysplasia of the stomach or of the uterine cervix, as well as multiple sclerosis or Parkinson's disease.[63]

Hydrogen sulphite (H2S) is a gasotransmitter which could significantly reduce chronic and degenerative diseases especially, brain, cardiovascular or kidney diseases.[64,65]

Inducible-NO is a marker of mucosal inflammation.[66] Exhaled inducible-NO is a recognized marker of asthma, chronic cough or allergic chronic rhinitis.[67-69]

H2S and inducible-NO production, estimated through the H2S and inducible-NO levels in exhaled breath, are associated with CPL level and PKM2 detection.[70]

Increasingly precise and numerous guidelines are available to manage bacterial or viral infections, or chronic inflammatory diseases. However, they do not always take into consideration the quality of the microbiota or the respect for the environment. In addition they are specific to one single disease or organ system and they do not take transversal medical issues into consideration: e.g. destruction of diversity of flora after *Helicobacter pylor*'s eradication with an increased risk of multiple sclerosis[71] or Crohn's diseases.[72]

We intended to identify and list the main bacteria and viruses undoubtedly implicated in SCI, as well as in the most frequent and severe life-threatening diseases in Europe.

The scope of the study is deliberately as broad as possible since bacteria, virus or visceral fat can involve multiple organs, impair immunity or reach functional systems such as the cardiovascular system, the autonomic nervous system or the endocrine system. As a consequence, the study may include all specific or systemic diseases which have been associated with periodontitis.[13]

The approach is integrative and transversal. The red thread of the study is to identify the germs involved in the occurrence of life-threatening diseases associated with usually undiagnosed dysbiosis-induced chronic inflammation.

We investigated what could be the place of dietetic advices, sport, antibiotic therapy or antiviral therapy

to control chronic dysbiosis and how the currently available recommendations, quality of microbiota and environment could be merged respectfully.

We will try to build an algorithm for screening and management in ambulatory medicine that takes into account all the collected elements.

In a second time and in a second article, we will try to quantify the possible benefit of such a preventive global integrative approach.

Material and methods

Only medical issues associated with frequent (prevalence >1/10.000) and potentially life-threatening diseases were included. The most recent French and European statistics, from 2022, were used.[73,74]

Only diseases potentially induced by chronic bacterial or viral infections, or gut dysbiosis were included. We searched meta-analysis and review articles in PubMed database. Only recent articles (less than 5 years) were included. The literature search was conducted on February 2026.

Only diseases with detectable SCI during usual outpatient medical practice were included. It can be a blood or salivary test, as well as a breath test for the detection of intestinal dysbiosis.

Only preventable causes of SCI were considered. Decrease visceral fat (dietetic, physical activity, GLP1 agonists), treatment of periodontitis, treatment of dysbiosis (diet, tiny amount of essential oils, fibres), treatment of viruses such as herpes viruses (valaciclovir, immunostimulating agents), treatment of mycotoxins (decrease intake, inhibitors) will be suggested for each type of dysbiosis. We searched meta-analysis and randomized clinical trials in PubMed database. Only recent articles (less than 5 years) were included. The literature search was conducted on February 2026.

The scientific approach will be based on the following steps. See figure 1.

- Identify convincing reviews and/or meta-analyses on the most frequent life-threatening diseases which may be favoured by bacterial or viral dysbiosis.
- Identify convincing reviews and/or meta-analyses on SCI associated with such dysbiosis.
- Identify convincing reviews and/or meta-analyses on easily detectable and curable SCI in ambulatory practice. Infections which could be controlled with current innocuous and inexpensive therapy will be identified.
- Build an algorithm for screening and management of SCI in ambulatory medicine that takes into account all the collected elements. The algorithm should not lead to any lack of screening or management of at-risk condition according to available European guidelines.

Benefits which may be achieved as well as percentages of patients who may be concerned will be quantified in another work (part II).

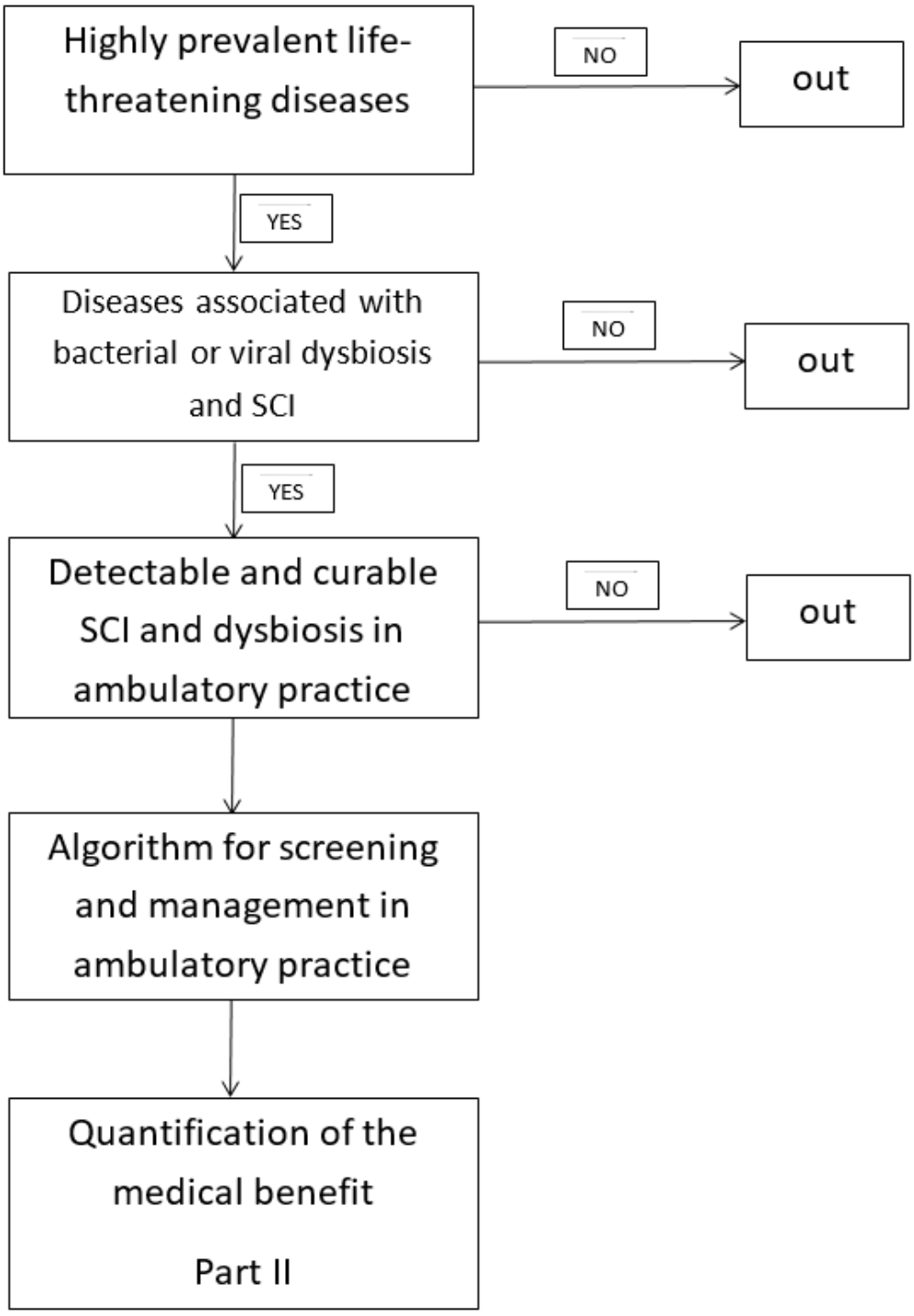

Figure 1: Steps and design of the study

Results

1. SELECTION OF THE MOST FREQUENT AND SEVERE DISEASES ASSOCIATED WITH SILENT CHRONIC INFLAMMATION AND DYSBIOSIS

The first cause of death in France and Europe is cancer, especially lung, colon-rectum or breast.[73,74]

Lung cancer is mainly attributed to tobacco or microparticles[75] and is poorly influenced by overweight.[76,77]

Some infectious diseases may favour its occurrence such as tuberculosis,[78,79] or some viruses. For example cytomegalovirus (CMV), EBV and HPV are frequently associated with adenocarcinoma or non-small cell lung cancer.[80-82] Polyomavirus is also frequently found in lung cancer,[83] as well as hepatitis C virus.[84]

A systematic review and meta-analysis demonstrated a significant association between periodontal disease and the incidence of lung cancer. Although further studies are required to eliminate confounding

factors, an implication of oral bacteria is possible.[85] *Fusobacterium nucleatum* (FN) has been particularly implicated.[86]

Since FN, EBV, CMV and HPV are implicated in lung cancer, this disease is selected for this study.

Colorectal cancer - occurrence or prognosis - is associated with dysbiosis, in particular with Periodontitis and FN which is now considered as the major drivers of malignant tumorigenesis in the distal colon.[87-91]

Fusobacterium nucleatum is probably also implicated in the occurrence of pancreatic cancer.[92,93]

Periodontitis is associated with the occurrence of colorectal cancer.[94]

In gastric cancers, a biphasic course may explain that *Helicobacter pylori* is found only at early stages of mild mucosal atrophy without dysplasia, whereas FN is found in later stages with dysplastic lesions.

Helicobacter pylori infection causes a decreased secretion of stomach acid, making it easier for oral bacteria to colonize the stomach. Solid evidences have revealed the association between oral and gastric commensal microbes other than *Helicobacter pylori* and the development of gastric cancer.[95,96]

The incidence of gastric cancer is decreasing over time in France and in Europe.

The role of *Helicobacter pylori* is currently debated although eradication guidelines remain similar. A test for *Helicobacter pylori* infection with a positive result in adults implies an indication of treatment. The decision regarding a possible eradication treatment is therefore made before requesting diagnostic tests.[97-100]

Eradication Guidelines only concern *Helicobacter pylori* despite the probable role of viruses such as HPV, EBV or CMV.[101-107] Eradication is based on antibiotic therapy despite the ineluctable antibiotic resistance over time.

The eradication recommendations are restricted to patients with atrophic or lymphocytic gastritis or gastric ulcer, malt-lymphoma, or thrombocytopenia. However, *Helicobacter pylori*-eradication is widely over-prescribed.

Periodontitis is associated with gastric cancer.[108,109]

Oral and other digestive cancers - Oesophageal carcinoma is also associated with high levels of FN.[110]

Porphyromonas gingivalis (PG) and FN, contribute to oral squamous cell carcinoma progression through mechanisms involving inflammation, epithelial-mesenchymal transition, and immune evasion.[111]

Fusobacterium nucleatum is more frequently detected and in higher abundance in oral/head and neck cancer samples when compared to non-cancer samples.[112]

Porphyromonas gingivalis could also play an important role in or oral squamous cell carcinoma development and could be involved in three different stages: epithelial-mesenchymal transition, neoplastic proliferation, and tumour invasion.[113]

Periodontitis is associated with an increase in oral,[114] oesophageal,[115] pancreatic,[116] hepatic,[117] and in general all digestive cancers.[118]

Most of digestive cancers are associated with oral bacteria or viruses (HPV, EBV, CMV and FN) and are therefore selected for further investigation. *Helicobacter pylori* has only been implicated in some types of gastric cancer, which is infrequent in Europe.

Breast cancers have been associated with viruses[119-126] (EBV, CMV, HPV, mouse mammary tumour virus), especially coinfection with HPV and EBV[124] or aggressive bacteria (FN, PG).[127]

Lack of anti-programmed death-ligand 1 (anti-PDL1) effect, attributed to inappropriate intestinal microbiota for example post-antibiotic therapy, is well-established.[128-130] Control of microbiota has been suggested to improve the efficacy of immunotherapy in oncological treatments.[131-132]

Periodontitis is associated with an increased risk of breast cancer.[133,134]

Because of the probable involvement of FN or PG, the impact of dysbiosis on the efficacy of treatment and HPV/EBV/CMV, breast cancer is selected for the study.

Prostatic cancer is associated with HPV,[135-137] not with Herpes simplex virus types 1 or 2 (HSV1/2) or CMV.[138]

Cancerous prostatic tissues are enriched with pro-inflammatory bacterial genera (e.g. FN, *Cutibacterium acnes*).[139-141]

Prostatic cancer will therefore be included in this study.

Human papillomavirus infections: a transversal oncological issue

A specific attention should be brought to HPV infections because it may favour several types of cancers which may spuriously be split into many subgroups: oropharyngeal, gastric, pulmonary, colorectal, anal, bladder, breast or uterine cervix, etc..[142-148] Human papillomavirus control or prevention with vaccination is therefore crucial.[149]

Synergies between FN and HPV, HSV2, EBV have been reported.[150-152]

Periodontitis has been associated with HPV.[153]

The role of HPV in ovarian cancer is controversial.[154,155]

No convincing study is available regarding herpes virus or FN. Ovarian cancer will not be included into the study. However a link between endometriosis and ovarian cancer is likely,[156,157] and endometriosis is potentially associated with periodontitis[158] and FN.[159]

Overweight is associated with a lack of diversity in the gut microbiota.[160-163]

Surprisingly, overweight is associated with better results of check-point inhibitors efficacy.[164-167] A role of chronic inflammation, of bacterial selection/ resistance and/or of viral reactivation is more likely than the paucity of diversity itself.

Accordingly, overweight has been attributed to chronic viral infections (CMV/HSV/hepatitis A[168] or adenovirus36[169-172]).

Overweight is associated with a decreased interferon-gamma synthesis, an increased diversity of influenza viruses,[173] as well as an increased rate of viral infection.[174]

Overweight is associated with an increased risk of breast[175] or colorectal cancer,[176] and a poorer prognosis of breast cancer patients.[177]

Bariatric surgery dramatically reduces the risk of breast cancer.[178] A role of aromatase from visceral tissues is not disputed, leading to anti-aromatase therapy in oestrogen+ breast cancer.[179]

Overweight is of course associated with cardiovascular accidents.[180]

Overweight is therefore selected for further analysis.

Cardiovascular diseases

Ischaemic heart disease (such as heart attacks) and cerebrovascular diseases (such as strokes) account respectively for 32.4% and 20.8% of deaths from circulatory diseases.

The predominant vascular complication in Europe is coronary artery disease (31.07%).[74]

Cardiovascular diseases could be partly attributed to chronic inflammation due to various metabolic conditions such as diabetes type2 or liver steatosis.[181,182]

Other systemic chronic inflammation such as endometriosis,[183] rheumatoid arthritis,[184,185] or psoriasis are associated with increased cardiovascular risks – mainly stroke.[186]

Periodontitis is attributed to anaerobic bacterial and viral oral chronic infections. The enterotype of periodontitis is Prevotella and includes HP, FN and PG.[187]

Patients with periodontitis have a significantly higher risk of stroke compared to the healthy population.[188-192]

Periodontitis is associated with carotid artery calcifications.[193]

Porphyromonas gingivalis and *Aggregatibacter actinomycetemcomitans* are detected in coronary atheromatous plaque specimens of myocardial infarction patients.[194]

Helicobacter pylori infection - especially cytotoxin-associated gene-A positive - is more frequently detected in patients with cardiovascular complications[195] such as coronary heart disease[196] or abdominal aneurysm.[197]

Porphyromonas gingivalis antibodies are more frequently detected in patients with atrial fibrillation.[198]

Periodontitis is associated with an increased risk of all-cause mortality: cardiovascular, cancer, coronary heart disease, cerebrovascular diseases.[199] Non-surgical periodontal therapy exerts beneficial effects on coronary artery disease.[200] However, invasive dental therapy without chronic infection does no increase the risk of cerebrovascular accident.[201]

Many publications report the role of acute viral infections followed with acute vascular complications: e.g. influenza, SARS-CoV-2, HIV, hepatitis C virus, and herpes zoster.[202]

Coronavirus19 (COVID) increases the risk of ischemic or haemorrhagic stroke,[203,204] myocardial infarction, venous thromboembolism, ischemic stroke, major bleeding, myocarditis and global mortality, especially in men.[205,206]

Herpes zoster is followed by an increased risk of stroke.[207,208]

Flu may favour heart failure, arrhythmia, myocarditis 2.56%, acute myocardial infarction and stroke.[209]

After a CMV infection, the estimated increased risk of future CV disease is 13.4%.[210-212]

Epstein-Barr virus is associated with coronary artery dilation, coronary artery aneurysm, myocarditis, arrhythmias, and heart failure.[213]

Ischaemic heart disease, cerebrovascular disease and metabolic syndrome are therefore included into the umbrella of complications driven by SCI due to chronic infections or dysbiosis. Periodontal dysbiosis (FN/PG, EBV, CMV), herpes zoster and flu appear particularly implicated in such cardiovascular complications.

Additional diseases to be considered. Neurodegenerative diseases (NDD)

Parkinson's disease (7367 deaths per year in Europe), Alzheimer's disease (16909 deaths per year in Europe) and dementia (18138 deaths per year in Europe) may be considered as the third cause of death instead of chronic lung disease (11 486 deaths per year in Europe). The classification of an acute lung infection with chronic obstructive pulmonary disease is not relevant for an etiological approach. These *two entities* represent *different clinical* and developmental charts.

Parkinson's disease. A role of dysbiosis is well documented in the occurrence of Parkinson's disease.[214]

Helicobacter pylori, hepatitis C virus and *Malassezia* have been implicated.[215-217] Treatments against Hepatitis C virus reduce the risk of Parkinson's disease.[215]

Influenza virus, herpes virus, hepatitis B virus, scarlet fever, mumps virus, chicken pox, pertussis, German measles, and measles were not associated with an increased risk of Parkinson's disease. [215,218]

An implication of COVID is unclear.[219] A direct role of periodontitis is unlikely.[220]

Alzheimer's disease.
Infections with CMV, severe COVID, hepatitis C virus, and in general human herpesvirus are associated with an increased risk of Alzheimer's disease.[221-225]

There is no statistically significant difference between the dementia group and the no dementia group regarding herpes zoster except with herpes zoster

ophthalmicus.[226] The benefit of herpes zoster vaccination is therefore still debated. [227-229]

There are respectively a ten-fold and a six-fold increased risk of Alzheimer's disease when oral bacteria and PG were found in the brain.[230]

Periodontitis increases the risk of Alzheimer's disease.[231,232]

Antiviral treatment or vaccination are currently discussed to prevent the occurrence of Alzheimer's disease.[233,234]

We concluded this first part by the observation that SCI is frequently associated with all top three life-threatening diseases and may be triggered by visceral fat, HSV1, HPV, EBV, CMV, FN or PG.

It is difficult to implicate *Helicobacter pylori* since it belongs to *Prevotella* enterotype and its eradication based on large spectrum antibiotic therapy is not specific. *Helicobacter pylori* is anyway restricted to fundus and antral carcinoma.

The causes of SCI may be entangled and bidirectional leading to vicious circles. As a consequence, eradication of a single infectious agent or any significant decrease of visceral fat may be sufficient to control chronic inflammation.

See table 1.

Table 1: Selected diseases and associated bacterial or viral dysbiosis. Identification of main pathogenic germs to be harnessed in order to control silent chronic inflammation.

Selected frequent life-threatening diseases	Associated bacterial dysbiosis	Associated viral dysbiosis
Lung cancer	Tuberculosis	HPV, EBV, CMV, hepatitis C
Colorectal, pancreatic, oesophageal cancers	*Fusobacterium nucleatum*	
Gastric cancer	*Helicobacter pylori*, *Fusobacterium nucleatum*	HPV, EBV, CMV
Oral squamous cell carcinoma	*Fusobacterium nucleatum*, *Porphyromonas gingivalis*	HPV
Breast cancer	*Fusobacterium nucleatum*, *Porphyromonas gingivalis*	HPV, EBV, CMV
Prostatic cancer	*Fusobacterium nucleatum*, *Cutibacterium acnes*	HPV, HSV1/2, CMV
Cervix uterine cancer	*Fusobacterium nucleatum*	HPV, HSV2, EBV
Overweight	Low diversity	CMV, HSV1/2, hepatitis A, adenovirus36
Cardiovascular diseases	*Helicobacter pylori*, *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*	EBV, CMV, influenza, SARS-Cov-2
Parkinson	*Helicobacter pylori*	Hepatitis C
Alzheimer/dementia	*Porphyromonas gingivalis*	HSV1, Herpes zoster ophthalmicus, CMV, hepatitis C, SARS-Cov-2
Cancers, cardiovascular diseases or NDD altogether	*Fusobacterium nucleatum*, *Porphyromonas gingivalis* **+/-** *Helicobacter pylori,* **when *Fusobacterium nucleatum* and herpes viruses are also involved**	**HPV, EBV, CMV, HSV1/2**

2. HOW TO DETECT AND QUANTIFY SILENT CHRONIC INFLAMMATION IN AMBULATORY USUAL PRACTICE? PROPOSED ALGORITHM.

Clinical anamnesis and examination

This part will not be developed since it relies on basic clinical knowledge.

The physician will look for a medical history of cancer, severe viral infections, herpetic flares, herpes zoster, HPV positive cervical smear, cardiovascular clinical signs of allergic, inflammatory or autoimmune diseases: polyarthritis, psoriasis, endometriosis, oral or genital lichen, asthma, chronic obstructive pulmonary disease, overweight with increased waist diameter, as well as periodontitis.

Chronic viral infections

The most reliable method would be the detection of replication of virus with quantitative Polymerase Chain Reaction. It is possible in research, for EBV, CMV and HSV1,[235-238] or HPV in routine.[239,240]

However, it is expensive and time consuming. It cannot be performed in usual practice especially for all previously pointed infectious agents (i.e. FN/PG, oral HPV, CMV or EBV, HSV1), particularly since viruses could be detected only a few days/month despite their implication, as it has been observed in periodontitis.[241]

On the contrary oral detection of HPV may spuriously generate anxiety although the virus is most likely transient and is, most of the time, not associated with an increased risk of oral cancer. For example, it appears that there is no established link between chronic HPV infection and oral cancer.[242]

The detection of oral HPV is therefore not recommended in usual practice.

Therefore, we suggest relying on a meticulous clinical examination and chairside tools. Quantification of inflammation and detection of dysbiosis will complete the screening.

Basic biology

For general inflammation

Absolute neutrophil count or the Systemic Immune-Inflammation Index, derived from platelet, neutrophil, and lymphocyte counts (platelets × neutrophils/ lymphocytes), could be used to evaluate obesity-related inflammation. Systemic Immune-Inflammation Index may better reflect the interplay between systemic inflammation and immune suppression.[243]

The NLR and the systemic Immune-Inflammation Index are derived from routine blood tests – cost-effective and accessible for resource-constrained settings – and capture complementary pathophysiological dimensions: The NLR reflects neuro-inflammation *via* neutrophil-lymphocyte balance, while SII integrates platelets to reflect inflammation-thrombosis crosstalk. These parameters are predictive of the outcome of stroke.[244]

The NLR predicts the cardiovascular outcome in diabetic patients,[245] peripheral artery diseases,[246] depression,[247] inflammatory bowel disease,[248] or patients with cancer.[55,57,249,250]

The NLR may serve as a convenient tool in monitoring psoriasis treatment and indicator of systemic inflammation.[251]

The NLR may be used to evaluate the risk of hip fracture[252] or of sarcopenia.[253]

The NLR may quantify the severity of periodontitis,[254] and is increased in patients with Alzheimer's disease.[255]

The NLR is therefore considered in this study. The cut-off value of 2.0 should be assumed as an alert threshold.[54,248,249,256,257]

For metabolic syndrome

Waist circumference or perhaps waist to hip ratio are very good parameters to quantify and follow a metabolic syndrome.[258] It is associated with the global risk of death.[259]

A large waist circumference is an independent factor of diabetes type 2.[260]

Glycosylated haemoglobin, glucosaemia), Insulin resistance (HOMA-IR), body mass index, triglyceride, total cholesterol, low-density lipoprotein, and high-density lipoprotein, along with inflammation factors such as C-reactive protein are the most classical parameters used to follow type 2 diabetic patients.[261]

Homocysteine belongs to hepatic inflammatory markers, linked with obesity,[26] and endothelial dysfunction.[263]

Usual metabolic markers appear sufficient to detect SCI.[261]

FibroScan® (elastometry) may be useful for staging liver fibrosis.

FibroScan® value greater than 7·0 kPa is considered to identify most adults with hepatitis B or C, or alcohol induced significant fibrosis.[265,266]

However a precise evaluation of liver histology by computerized morphometry shows that high level of steatosis induces misevaluation of liver fibrosis by Fibroscan.[267] As a consequence, FibroScan® cannot be used in metabolic dysfunction-associated fatty liver diseases and therefore, biological parameters are required.

Fibrosis-4 index appears particularly relevant to evaluate fatty liver diseases. A Cut-off value of 1.3 has been suggested.[268]

Detection of dysbiosis

Breath tests could be used for the detection of dysbiosis,[269-271] especially the dosage of inducible-NO and H2S.[70]

We previously suggested that H2S and inducible-NO could be reliably detected for the screening of SCI or oral/foregut dysbiosis in patients with clinical periodontitis. The suggested cut-of values were 0.11 ppm for inducible-NO and 0.10 ppm for H2S.[70]

New markers

Salivary calprotectine

Calprotectine is mainly synthesized by neutrophils[272] and is a good marker of neutrophil-induced inflammation.

Faecal CLP is a recognized marker of inflammatory bowel disease with an established cut-off around 50 international units (IU)/ml.[273,274]

Saliva CLP is increased in periodontitis,[60,61] and in numerous severe pathologies such as cancer,[6] metabolic syndrome,[7] psoriasis,[8] bone loss,[9] dementia,[10] or cardiovascular diseases,[11] rheumatoid arthritis,[275] inflammatory bowel disease [276] or oral lichen planus.[277] Oral CLP may also be increased in infant with *Helicobacter pylori* infection.[277]

The dosage of CLP in saliva can be carried out during a simple medical consultation. Although the threshold remains to be refined, the salivary CLP could already be recognized as a reliable marker of oral inflammation. Three previous observational studies identified 750 IU/ml as a possible threshold for severe inflammation and 450 IU/ml as a possible threshold for mild inflammation.[60,63,70]

Therefore, CPL appears to be an excellent new marker for the detection of SCI or to follow the therapeutic response.

Pyruvate kinase M2 (PKM2)

Pyruvate kinase M2 is a key enzyme for glycolysis and is closely related to tissue repair and regeneration. The switch to PKM2 modifies the glucose metabolism toward the Warburg effect which favours transformation, invasion, metastasis, and cell proliferation.[62]

Pyruvate kinase M2 in stools is a recognized marker of dysplastic polyps of the colon-rectum.[279]

Pyruvate kinase M2 switch could also be involved in gastric cancer development.[280]

Pyruvate kinase M2 can also be measured in the saliva and is strongly correlated with oral squamous cell carcinoma progression.[281] Pyruvate kinase M2 in saliva is also associated with colorectal polyps, dysplasia of the stomach or of the uterine cervix, as well as multiple sclerosis or Parkinson's disease.[60,63]

There is a clear association between PKM2 detection and high CLP or inducible-NO levels, or low H2S levels.[70]

The detection of PKM2 in saliva can also be carried out during a simple medical consultation. It is only qualitative. There is no published information on any quantitative approach in saliva. There is no evidence that a quantitative measure has a medical interest.

This measure might be reserved for patients with high levels of CLP in saliva.

Other tests

Oral quantitative polymerase chain reaction for oral bacteria or viruses (EBV, CMV, HSV1 or HPV) may be performed.[282,283]

However, no consensus has been yet accepted for their use in routine detection. In addition, they are expensive and cannot help for a quick decision of further screening.

Fusobacterium nucleatum or PG may be detected by clinical examination and simple fluorescence,[284] as well as *Cutibacterium acnes*.[285]

Endotest® is a very expansive test which cannot be used in routine ambulatory consultation. In France, Endotest® is only offered to few young women with a strong suspicion of endometriosis.[286]

Salivary proteins - such as IL1β, IL6, IL8 or TNF-α - can be used as inflammatory markers of the oral cavity.[287,288] However none of them can be measured by a simple inexpensive ambulatory test.

We therefore suggest relying on a thorough clinical examination with a Wood lamp and a blue light, a breath test, as well as low-cost CLP and PKM2 kits for all outpatients with a history of periodontitis.

Proposed algorithm for the detection of silent chronic inflammation

We previously suggested a practical ambulatory approach in all patients with oral or digestive symptoms in order to detect SCI.[70] See figure 2.

First step: Breath test and oral examination should be performed in all patients with abdominal complaints.

Second step: Salivary CLP dosage should be performed in all patients with periodontitis and abnormal breath test results.

Third step: The detection of PKM2 will be reserved for patients with CLP levels ≥750 IU/l.

This screening is innocuous and inexpensive. It may enable early detection of severe ongoing inflammatory stage and stop there evolution toward cancers, cardiovascular/metabolic or neurodegenerative diseases.

It may also have beneficial effects on other severe dysbiosis-associated diseases. For example, FN and PG control may reduce the risk of inflammatory bowel disease, especially of haemorrhagic colitis,[289] of endometriosis,[290] of periodontitis and all associated diseases.[291,292]

The control of viruses may also decrease the risk of transformation of asymptomatic monoclonal gammapathies in myeloma or lymphoma.[293]

Joint pain[294] or depression[295,296] may also be alleviated by the improvement of gut microbiota.

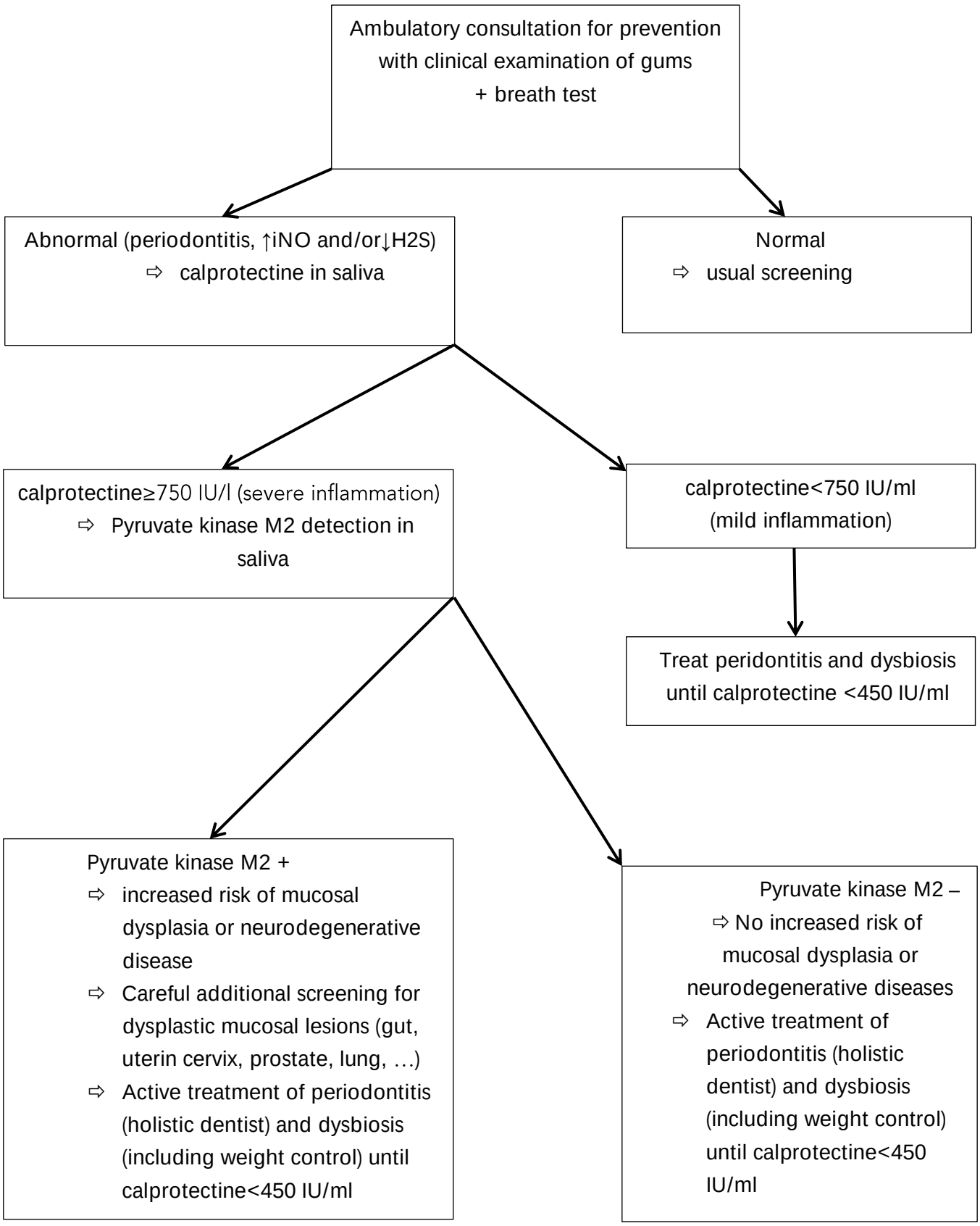

Figure 2: Proposed algorithm for the early detection of mucosal or brain chronic inflammation based on breath test, and calprotectine or pyruvate kinase M2 detection in saliva.

3. IDENTIFICATION OF INNOCUOUS AND INEXPENSIVE THERAPY TO CONTROL SILENT CHRONIC INFLAMMATION. PROPOSED GLOBAL INTEGRATED TREATMENT.

Treatments to be selected should have a very favourable risk/benefit ratio for the patients, for the environment and low cost because they should be used on a long term period, for a large part of the population, without severe life-threatening diseases yet. The treatments should not induce germ-resistance or any destruction of the microbiota which may end to low diversity, decreased immunity or overweight.

Goals are entangled: clear periodontitis, reduce visceral fat and improve diversity of microbiota with an increase of NO (without inducible-NO increase) and H2S, as well as PDL1 inhibition. This will decrease chronic inflammation, immunosuppression and chronic systemic damages. The stimulation of immunity will help to control herpes viruses or HPV.

Treatments should act synergically, based on firstly harmless tiny doses, secondly the same narrow target tackled simultaneously, thirdly adapted to a large diversity of situation which represents the diversity of enterotypes, immunotypes and systemic inflammation/organ defects encountered in real life medicine.

For all these prerequisites, we try to select natural products, considered as food, spices or aromatic natural products rather than medications or foods complements which may firstly induce adverse events, secondly contain excipients or contaminants and thirdly contain no or low amount of fibres and are devoid of natural beneficial endobiota.

Such products should be consumed in tiny amounts on a long term basis.

They should fit into a global lifestyle change with diet, brain training, decreased stress and increased physical activity.

Probiotics have failed to control cancer, overweight, cardiovascular diseases, NDD, viral infections. In addition they cannot be considered as natural products.

Clear periodontitis = Control *Fusobacterium nucleatum*, *Porphyromonas gingivalis* and herpes viruses

Fusobacterium nucleatum and PG are anaerobic bacteria implicated in periodontitis.[297]

Periodontitis can be controlled by non-surgical treatment with mechanical mouth cleaning,[53] photobiomodulation,[298] or mouth wash with 1% hydrogen peroxide (H2O2).[299-302]

Hydrogen peroxide is also efficacious against SARS-COV-2 and herpes simplex.[303-304]

Vitamin D supplementation may promote autophagy of PG.[305]

We selected personal mechanical mouth cleaning, hydrogen peroxide mouth wash and vitamin D supplementation.

Reduce visceral fat with diet or lipase inhibition

Low carb and low caloric diets are necessary to control visceral fat. Diet or the use of medications such as GLP1 agonist will not be discussed here. Intermittent fasting[306] with low fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) intake[307,308] could be suggested.

Overweight and visceral fat is associated with decreased microbial diversity. Increased diversity cannot be achieved by destruction of the remaining flora but with diversification of fibres and therefore vegetables.[309]

An increased intake of organic vegetables is a well-established recommended diet for body weight, CV diseases or cancer.[310-314]

The intake of fibres is also beneficial in Crohn's disease.[315]

Tiny amount of essential oils may decrease the amount of undesirable bacteria and increase diversity.[316,317]

For example, *Cinnamomum verum* or *Origanum vulgare* could be efficacious against FN and periodontitis at very low dose.[318,319]

Oral microbiota produces nitrite leading to the synthesis nitric oxide.[320,321]

Nitric oxide possesses antiviral (SARS-CoV-2, herpes, HPV).[322-329]

Altered endogenic NO production may favour breast[330] or prostatic cancer occurrence.[331]

An improvement of diversity will improve the efficacy of PDL1 inhibition.[131,132]

Laetiporus sulphureus or *Grifola frondosa* are documented inhibitors of lipase.[332,333]

We suggest a low-caloric diet, and low intake of FODMAPs in association with tiny amounts of essential oils such as *Origanum vulgare*, *Cinnamomum verum* or *Citrus lemon*, *zinziber officinale* in association with either *Grifola frondosa* (maitake) or *Laetiporus sulphureus*.

Stimulation of immunity will help to control herpes viruses or human papillomavirus.

Coriolus versicolor is a well-documented immunostimulating mushroom. It may increase the survival of patients with adenocarcinoma, especially of the stomach or of the colon.[334,335]

It has anti-viral properties against HPV, EBV, herpes simplex,[336-339] or even SARS-CoV-2.[340]

The association valaciclovir + *Coriolus versicolor* is associated with a decreased risk of myeloma or lymphoma in asymptomatic monoclonal gammapathy.[293] However the long term use of valaciclovir does not belong to usual recommendations.

Coriolus versicolor has also been reported to decrease Alzheimer's disease in a mouse model,[341,342] and clear prion or intracellular bacteria.[343-349]

It modulates Toll-Like Receptor,[346,347] and inhibits many mycotoxins.[348]

Phellinus linteus is also a strong immunostimulating agent with anticancer properties.[349] It is efficacious against periodontitis.[350,351]

Ganoderma lucidum could, when added to quercetin, control EBV in mice.[352]

Proposed global integrative treatment with low risk and low cost

According to the results, we suggest a very limited number of actions to control SCI.

Firstly, mechanical mouth cleaning with hydrogen peroxide mouth wash, *Coriolus versicolor* +/- *Ganoderma lucidum* or *Phellinus linteus*, vitamin D and tiny amounts of essential oils, especially *Origanum compactum*.

Secondly, decrease visceral fat with specific diet, *Grifola frondosa*, *Laetiporus sulphureus* and tiny amount of essential oils, especially *Origanum compactum*, *Cinnamomum verum*, *Citrus lemon* or *Zinziber officinale*.

Thirdly, increase organic food (especially green vegetables and fibres), which probably contains endobiota and natural polyphenols. Please note that food complements do not contain endobiota and cannot increase microbiota diversity.

Periodontitis, body weight, waist diameter, NLR, breath test, CLP and when needed PKM2 appear valuable parameters for annual or biannual surveillance.

Discussion

The most frequent causes of death are undisputedly cancers, cardiovascular diseases and neurodegenerative diseases.

The currently used classifications may lead to spurious conclusion regarding aetiology. Some diseases are classified according to organs (heart disease), others according to the pathology (cancer), others according to clinical signs (neurodegenerative diseases).

In order to prevent disease, it is necessary to tackle the causes. Therefore, an etiological approach is suggested.

We focussed on the causes of chronic inflammation, e.g. frequent viral or bacterial infections and/or visceral fat.

Tobacco or alcohol abuse, although largely implicated in cancer and cardiovascular diseases does not belong to dysbiosis related causes.

The most frequent causes of death are at least partly explained by chronic infections and/or dysbiosis

Surprisingly a very limited number of infectious agents are implicated: few oral bacteria, herpes viruses or HPV, dysbiosis-related visceral fat.

According to the "Consortium milieu intérieur", the quality of immunity could be evaluated from only three main factors, tobacco, CMV serology and BMI.[353]

However, oral inflammation appears to be a corner-stone of SCI and foregut dysbiosis.

Periodontitis is associated with silent chronic inflammation and many severe diseases.[6-12] It may concern up to 70% of US adults aged 65 years and older and is associated with more than 50 systemic inflammatory disorders and comorbidities.[13]

Considering that periodontitis treatment or prevention could decrease the frequency and the severity of many systemic infections or chronic diseases, oral evaluation of SCI appears mandatory in all patients. It could start with clinical examination of gums, maybe with the help of a Wood lamp and a blue light.[284,285]

Oral bacteria build biofilms and conjugate their competence to destroy proteins and to generate permeability, inflammation and immunosuppression leading to excessive repair involving epithelial–mesenchymal transition.[354]

Viral infections - especially EBV or HPV are able to induce mutations and therefore to increase the risk of tumor.[355]

Global Mechanism of destruction and inflammation. The need of synergic enzymes of deleterious infectious agents

Fusobacterium nucleatum does not possess protease and cannot induce chronic inflammation alone.

The destructive process requires proteases from PG[356] or *Aggregatibacter actinomycetemcomitans*[357] in the mouth or from *Gardnerella vaginalis* on the cervix to alter the mucosa. This cutting of mucus enables a cross-feeding which supports mutualism.[150]

When protease are inhibited, the pathogenic process is disrupted.[358]

Aggregatibacter actinomycetemcomitans protects PG[359] from H2O2 produced by commensal beneficial bacteria.[360]

Phellinus species are mushrooms which contain strong protease inhibitors,[361,362] and therefore may protect the gingiva.[350,351]

Coriolus versicolor[363] inhibits Toll-Like-Receptor4 which is a key receptor implicated in oral inflammation induced by anaerobic bacteria.[364,365]

Fusobacterium nucleatum may co-aggregate with *Candida albicans*, *Cutibacterium acnes*, or *Streptococcus cristatus* leading to mutual attenuation of virulence, which promotes a long-term persistence within the oral cavity, especially in endodontic lesions. Long lasting lesions are therefore able to survive to short term treatments.[366-368]

Fusobacterium nucleatum favours the occurrence of HPV-induced intraepithelial neoplasia on the cervix.[369-371]

Fusobacterium nucleatum is able to target sugars of numerous tumours (stomach, prostate, ovary, colon, uterus, pancreas, breast, lung, and oesophagus)[372] and favour tumour spread.[373]

Fusobacterium nucleatum in excess is frequently found in patients with severe haemorrhagic colitis.[374] This latter disease dramatically increase the risk of digestive tumours (odd ratio between 3.0 to 6.0).[375]

Concomitant CMV infection may lead to methylation of the gene of interferon-gamma[376] and herpes simplex flares may favours the appearance of anti-interferon-gamma antibodies.[377] Both mechanisms end to immunosuppression.

Protection by gasotransmitters (hydrogen sulphide and nitric oxide) and diversified gut microbiota

The diversity of microbiota of the foregut could be estimated with the exhaled-H2S level. Hydrogen sulphide is a gasotransmitter with supposed anti-aging properties and which could significantly reduce progressive, chronic, and degenerative diseases especially, brain, cardiovascular or kidney disease.[64]

Accumulative data suggest that H2S may have biphasic effects. At low levels it has anti-inflammatory and antioxidant roles. However, it has pro-inflammatory effects under certain conditions where rapid release of H2S in tissues occurs, such as sepsis.[378]

In healthy conditions, H2S-related enzymes are expressed in human lungs, where they have mucolytic, antioxidant, anti-inflammatory, and antibacterial roles, thus contributing to airway epithelium homeostasis.[379]

In published studies, the mean H2S levels range from 0.01 ppm in chronic pulmonary disease or type 2 diabetes mellitus[380,381] to 0.08 ppm in patients with digestive diseases including colorectal cancers.[382] We previously published results within the same range in patients with colonic polyps.[383]

Hydrogen sulphide works with NO to induce vasodilation and angiogenesis in a cooperative manner.[65,384]

Nitric oxide production depends mainly on oral flora and of the transformation of nitrate to nitrite.[320,321]

In lung, NO reacts with oxyhaemoglobin with high affinity and is rapidly scavenged in red blood.[385] Therefore, the low levels of NO produced locally are not exhaled.

However, a biphasic effect has been described. High levels of NO can be produced by immune cells and is called inducible-nitric oxide (inducible-NO). Inducible-NO reacts with superoxide, resulting in peroxynitrite formation and cellular toxicity.[386] It is a marker of mucosal inflammation.[61]

In recent reviews of literature, exhaled inducible-NO ranges from 0.02 ppm to more than 0.05 ppm when chronic inflammation is expected.[48,387] It is increased in many inflammatory diseases such as systemic lupus erythematosus,[388] asthma,[389] psoriasis,[390] heart failure[391] or inflammatory bowel diseases.[392] The cut-off could be 0.11 ppm for iNO.[60]

Dysbiosis of the foregut may be split into two groups: decreased diversity or overgrowth of undesirable bacteria named small intestinal bacterial overgrowth.

Small intestinal bacterial overgrowth usually develops in the ileum, not in the foregut. It can be diagnosed with the detection of hydrogen in exhaled air.[269] The measurement is performed after a fasting period longer than 10 hours. After fasting, hydrogen level should be very low except in case of ongoing mucosal destruction (e.g. celiac disease or ongoing viral infection). Hydrogen is not increased in case of silent chronic inflammation.[270]

Accordingly, ambulatory consultations should mainly focus on oral bacteria linked to periodontitis and to decreased global diversity.

Markers of decreased diversity

Decreased diversity is associated with overweight[393] or inflammatory bowel diseases.[394] Cancer may also be associated with decreased amount of small chain fatty acids – attributed to low diversity in the colon.[395] A decrease in diversity - for example after antibiotic therapy – has also been implicated in the attenuation of checkpoint inhibitor efficacy.[396]

Less community richness was also observed in the poststroke patients, with consequences on the prognosis.[397]

Small chain fatty acids levels can be low and associated with decreased diversity.[398] They can be high and associated with gut dysbiosis, gut permeability,

excess adiposity, and cardio-metabolic risk factors[399] or with periodontitis.[400] However, contradictory results have been reported with periodontitis.[401] Small chain fatty acids measures are therefore difficult to interpret.

Furthermore, measurement of small chain fatty acids requires complicated and expensive devices such as Xpid-9500® which cannot be easily implemented in usual practice.[402] Dosage of small chain fatty acids will not be considered

Decreased endogenous NO impairs gastric emptying[403] which is almost always found in patients with overweight.[404]

Glucagon-Like-Peptide1 agonists are known to worsen gastric emptying which may reduce food intake.[405]

Overweight is associated with altered microbiota and low diversity.[165,167,406]

The efficacy of GLP1 agonists is correlated with increased diversity of the microbiome.[407]

It would appear that *Akkermansia muciniphila*, and other bacteria producing short-chain fatty acids enhance GLP-1 agonists' efficacy by improving insulin sensitivity and stimulating endogenous GLP-1 secretion. Conversely, dysbiosis characterized by reduced microbial diversity and increased lipopolysaccharide-producing pro-inflammatory bacteria correlates with poor therapeutic response. Furthermore, GLP-1 agonists may exert beneficial modulatory effects on the gut microbiota itself, indicating a bidirectional relationship.[407]

We hypothesize that the increase in the diversity of microbiota is a key factor influencing body weight loss. We therefore consider that oral cleaning in order to increase oral diversity and decrease *Prevotella* dominance is required for weight control.

The most important targets are FN and PG. They are anaerobic and sensitive to H2O2.

Fusobacterium nucleatum and PG are sensitive to tiny amounts of essential oils.[319,408-412]

Suggested integrative innocuous therapeutic approach to control oral and digestive viruses

All targeted viruses (HPV, HSV1, CMV or EBV) are at least partly sensitive to *Coriolus*, *Phellinus* or *Ganoderma*.

Coriolus versicolor possesses well documented immunostimulating[314,315] and anti-viral properties.[316-340] Its efficacy against HPV is demonstrated.

It may be associated with *Ganoderma lucidum* against HSV1, HPV or EBV.[337-339]

Ganoderma lucidum could, when added to quercetin further control EBV.[352]

Phellinus is also be added since it is efficacious against periodontitis,[350,351] may inhibit catalase (which destroys H2O2) produced by *Aggregatibacter actinomycetemcomitans*.[413] Phellinus may also protect against flu (H5N1).[363,414,415]

Previous observational studies suggest that the efficacy of these natural therapy are close to 80% for EBV,[338] 88% for HPV,[337] 95% for HSV,[336] and 95% for inflammatory bowel disease.[317]

Additional plants which are considered as food products could be added to control HSV1: such as *Geum urbanum*,[416] *Prunella vulgaris*,[417] or *Rumex acetosa*.[418,419]

Please remember that diversification of diet with organic green vegetables which contains fibres and endobiota are expected to increase the diversity of microbiota, whereas H2O2 will kill undesirable bacteria.

Cruciferous vegetable intake appears to decrease the risk of breast cancer.[420]

Please note that shiitake is excluded since it may induce severe allergic reaction[421-428] and is overpassed by *Coriolus*, *Ganoderma* and *Phellinus* species.

We therefore consider that natural antibacterial oral agents and natural antiviral agents may enable to control all the agents and pathological biofilms

which are associated with the three majors causes of death in Europe: cancers, cardiovascular diseases and neurodegenerative disease.

The quantity of these natural food products to be ingested per day and the duration of diet remain to be defined. However 400 mg appears to be enough according to yet available observational studies involving several thousands of patients.

The duration should last several months or even years per principal to modify immunity, microbiota, visceral fat and the autonomic nervous system.

How to detect silent chronic inflammation and to quantify improvement

Neutrophils/lymphocytes ratio is probably the most cost-effective and accessible blood test.[243]

Only basic blood tests and fibrosis-4 index are required for detection an quantification of metabolic syndrome.[263,268]

Paucity of diversity and inflammation will be assessed by a breath test with the measurement of H2S and inducible-NO.

A previous observational study confirms that higher inducible-NO levels are associated with high CLP levels while a higher H2S levels - assumed to be associated with diverse flora – is a marker of mild or lack of inflammation and that the Xam-8000® device can be used to detect H2S and iNO for the screening of silent chronic inflammation or oral/foregut dysbiosis in patients with clinical periodontitis.[70]

This first step (clinical examination + breath test) allows deciding when a CLP dosage in the saliva should be carried out.

These markers will complete the clinical examination in ambulatory medicine.

Salivary calprotectine and oral evaluation of neutrophilic chronic inflammation

Periodontitis is associated with an increased level of CLP in saliva.[60,61]

Serum CPT is an excellent marker of COVID severity, prognosis or recovery.[430-439]

Although the thresholds remain to be refined, the salivary CLP level could be acknowledged as a reliable marker. We previously suggested the threshold of 750 IU/ml.[70]

Pyruvate kinaseM2 detection in saliva: the risk of cancer or of neuro-inflammation

Pyruvate kinase is a key enzyme for glycolysis and is closely related to tissue repair and regeneration. The switch to PKM2 modifies the glucose metabolism toward the Warburg effect which favours transformation, invasion, metastasis, and cell proliferation.[63]

Pyruvate kinase M2 can be measured in the saliva and is strongly associated with oral squamous cell carcinoma progression,[280] with colorectal polyps, dysplasia of the stomach or of the uterine cervix, as well as multiple sclerosis or Parkinson's disease.[60,63]

Pyruvate kinase M2 in stools is a recognized marker of dysplastic polyps of the colon-rectum.[278]

Pyruvate kinase M2 switch could be involved in gastric cancer development.[279] *Helicobacter pylori* is a recognized cause of non-cardia gastric cancer.[440]

We suggest that the detection of PKM2 could be reserved for patients with high levels of CLP in saliva, as well as low H2S and high iNO levels in breath. All three items are markers of mucosal chronic inflammation associated with predictable atrophy/dysplasia.

Practical suggested global and integrative ambulatory approach

We propose the following algorithm to detect SCI in ambulatory usual practice. See figure 2.

First step: Breath test and oral examination should be performed in all patients with abdominal complaints or clinical periodontitis.

Second step: Salivary CLP dosage should be performed in any patients with abnormal breath test

results or in any patients with systemic inflammatory disease or risks factor for cancer or NDD.

Third step: The detection of PKM2 will be reserved for patients with increased CLP levels, and abnormal breath test results or clinical periodontitis.

This screening is innocuous and inexpensive. It may enable early detection of severe ongoing inflammatory stage and stop there evolution toward cancer of Parkinson or Alzheimer or osteoporosis.[60,63]

Clinical implications and future directions

This work confirms the hypothesis that high salivary CLP is associated with foregut dysbiosis and PKM2 switch with possible severe consequences such as dysplastic lesions of gut or uterine cervix or NDD.

After breath test, we suggest that salivary CLP could be an adequate pre-screening marker for oral or digestive cancers in patients with periodontitis and *Fusobacterium nucleatum/Porphyromonas gingivalis*.

The flow chart depicted in figure 2 is not time consuming, and appears reliable to detect silent chronic inflammation which may spread down-ward or to the brain.

This part could be completed with the quantification of the medical benefit related to the control of SCI induced by oral bacteria or viruses which could be controlled by currently available inexpensive and innocuous medications or dietary supplements.

Conclusion

Silent chronic inflammation is not due to a single cause, entanglement is almost constant.

Several organs are concerned: nervous central system + cardiovascular system + specific organ.

A simple flow chart for early detection of dangerous chronic inflammation of the mouth or of the foregut can be applied in ambulatory medicine.

We suggest its application in all patients with oral or digestive symptoms.

This early detection is essential because treatments to reduce oral inflammation or methods to detect complications are available.

Neglecting this simplistic approach could signify heavy loss of chance for a large proportion of the population.

However, further studies are required to refine the threshold levels for CPL or H2S/NO levels for example according to the age, underlying vascular conditions or perhaps gastric emptying and gastroesophageal reflux.

Long-term observational studies could assess the value of reducing salivary CLP through local care and see the preventive effect of the control of inflammation on gut dysbiosis, body weight, dysplastic mucosal lesions, some cancers, osteoporosis, alveolar bone loss, anxiety-depression episodes, etc.

Conflict of interest:

DFN sarl. Farming business. Production of organic natural flavors

References:

1. Asenjo-Lobos C, González L, Bulnes JF, Roque M, Muñoz Venturelli P, Rodríguez GM. Cardiovascular events risk in patients with systemic autoimmune diseases: a prognostic systematic review and meta-analysis. *Clin Res Cardiol*. 2024; 113(2):246-259. doi:10.1007/s00392-023-02291-4

2. Bhagavathula AS, Bentley BL, Woolf B, Dissanayaka TD, Rahmani J. Increased risk of stroke among patients with ankylosing spondylitis: A systematic review and meta-analysis. *Reumatol Clin (Engl Ed)*. 2023;19(3): 136-142. doi:10.1016/j.reumae.2023.02.002

3. Patrick MT, Li Q, Wasikowski R, et al. Shared genetic risk factors and causal association between psoriasis and coronary artery disease. *Nat Commun*. 2022;13(1):6565. Published 2022 Nov 2. doi:10.1038/s41467-022-34323-4

4. Long S, Chen Y, Meng Y, et al. Peripheral high levels of CRP predict progression from normal cognition to dementia: A systematic review and meta-analysis. *J Clin Neurosci*. 2023;107:54-63. doi:10.1016/j.jocn.2022.11.016

5. Cardisciani M, Di Nicolantonio S, Altamura S, Ortu E, Del Pinto R, Pietropaoli D. Temporal dynamics of early inflammatory markers after professional dental cleaning: a meta-analysis and spline-based meta-regression of TNF-α, IL-1β, IL-6, and (hs)CRP. *Front Immunol*. 2025;16:1634622. Published 2025 Aug 28. doi:10.3389/fimmu.2025.1634622

6. Sulaiman Y, Pacauskienė IM, Šadzevičienė R, Anuzyte R. Oral and Gut Microbiota Dysbiosis Due to Periodontitis: Systemic Implications and Links to Gastrointestinal Cancer: A Narrative Review. *Medicina (Kaunas)*. 2024;60(9):1416. Published 2024 Aug 29. doi:10.3390/medicina60091416

7. Nibali L, Tatarakis N, Needleman I, et al. Clinical review: Association between metabolic syndrome and periodontitis: a systematic review and meta-analysis. *J Clin Endocrinol Metab*. 2013;98(3):913-920. doi:10.1210/jc.2012-3552

8. Dalmády S, Kemény L, Antal M, Gyulai R. Periodontitis: a newly identified comorbidity in psoriasis and psoriatic arthritis. *Expert Rev Clin Immunol*. 2020;16(1):101-108. doi:10.1080/1744666X.2019.1700113

9. Zhang M, Liu Y, Afzali H, Graves DT. An update on periodontal inflammation and bone loss. *Front Immunol*. 2024;15:1385436. Published 2024 Jun 11. doi:10.3389/fimmu.2024.1385436

10. Lee YT, Lee HC, Hu CJ, et al. Periodontitis as a Modifiable Risk Factor for Dementia: A Nationwide Population-Based Cohort Study. *J Am Geriatr Soc*. 2017;65(2):301-305. doi:10.1111/jgs.14449

11. Schulze-Späte U, Wurschi L, van der Vorst EPC, et al. Crosstalk between periodontitis and cardiovascular risk. *Front Immunol*. 2024;15:1469077. Published 2024 Dec 9. doi:10.3389/fimmu.2024.1469077

12. Ferrillo M, Giudice A, Migliario M, et al. Oral-Gut Microbiota, Periodontal Diseases, and Arthritis: Literature Overview on the Role of Probiotics. *Int J Mol Sci*. 2023;24(5):4626. Published 2023 Feb 27. doi:10.3390/ijms24054626

13. Pai SI, Matheus HR, Guastaldi FPS. Effects of periodontitis on cancer outcomes in the era of immunotherapy. *Lancet Healthy Longev*. 2023;4(4): e166-e175. doi:10.1016/S2666-7568(23)00021-1

14. Zhang Z, Wen S, Liu J, et al. Advances in the relationship between periodontopathogens and respiratory diseases (Review). *Mol Med Rep*. 2024; 29(3):42. doi:10.3892/mmr.2024.13166

15. Lin EC, Chiang YC, Lin HY, et al. Unraveling the Link between Periodontitis and Coronavirus Disease 2019: Exploring Pathogenic Pathways and Clinical Implications. *Biomedicines*. 2023;11(10):2789. Published 2023 Oct 14. doi:10.3390/biomedicines11102789

16. Fink H, Langselius O, Vignat J, et al. Global and regional cancer burden attributable to modifiable risk factors to inform prevention. *Nat Med*. Published online February 3, 2026. doi:10.1038/s41591-026-04219-7

17. Deng X, Gong X, Zhou D, Hong Z. Perturbations in gut microbiota composition in patients with autoimmune neurological diseases: a

systematic review and meta-analysis. *Front Immunol*. 2025;16:1513599. Published 2025 Feb 6. doi:10.3389/fimmu.2025.1513599

18. Wang Y, Wu H, Yan C, et al. Alterations of the microbiome across body sites in systemic lupus erythematosus: A systematic review and meta-analysis. *Lupus*. 2024;33(12):1345-1357. doi:10.1177/09612033241281891

19. Shen Y, Yu X, Wang Q, et al. Association between primary Sjögren's syndrome and gut microbiota disruption: a systematic review and meta-analysis. *Clin Rheumatol*. 2024;43(2):603-619. doi:10.1007/s10067-023-06754-x

20. Gong B, Wang C, Meng F, et al. Association Between Gut Microbiota and Autoimmune Thyroid Disease: A Systematic Review and Meta-Analysis. *Front Endocrinol (Lausanne)*. 2021;12:774362. Published 2021 Nov 17. doi:10.3389/fendo.2021.774362

21. Sarkar D, Roy P, Saha S. Meta-analysis of faecal microbiome studies followed by machine learning to identify intestinal disease-specific taxonomic signatures. *Microb Pathog*. 2026;211:108221. doi:10.1016/j.micpath.2025.108221

22. Chulenbayeva L, Jarmukhanov Z, Kaliyekova K, Kozhakhmetov S, Kushugulova A. Quantitative Alterations in Short-Chain Fatty Acids in Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis. *Biomolecules*. 2025;15(7):1017. Published 2025 Jul 15. doi:10.3390/biom15071017

23. Wagenaar CA, van de Put M, Bisschops M, et al. The Effect of Dietary Interventions on Chronic Inflammatory Diseases in Relation to the Microbiome: A Systematic Review. *Nutrients*. 2021;13(9):3208. Published 2021 Sep 15. doi:10.3390/nu13093208

24. Spiller AL, Costa BGD, Yoshihara RNY, et al. Ultra-Processed Foods, Gut Microbiota, and Inflammatory Bowel Disease: A Critical Review of Emerging Evidence. *Nutrients*. 2025;17(16):2677. Published 2025 Aug 19. doi:10.3390/nu17162677

25. Starz E, Wzorek K, Folwarski M, et al. The Modification of the Gut Microbiota via Selected Specific Diets in Patients with Crohn's Disease. *Nutrients*. 2021;13(7):2125. Published 2021 Jun 22. doi:10.3390/nu13072125

26. Wang S, Bao Z, Li Z, Zhao M, Wang X, Liu F. The impact of very-low-calorie ketogenic diets on gut microbiota in individuals with obesity: a systematic review and meta-analysis. *Gut Microbes*. 2025;17(1):2566305. doi:10.1080/19490976.2025.2566305

27. Ojo O, Feng QQ, Ojo OO, Wang XH. The Role of Dietary Fibre in Modulating Gut Microbiota Dysbiosis in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomised Controlled Trials. *Nutrients*. 2020;12(11):3239. Published 2020 Oct 23. doi:10.3390/nu12113239

28. Zhao Y, Li L, Zhang W, et al. Associations of indoor airborne microbiome with systemic inflammation in the context of indoor particulate matter pollution and the metabolic mechanisms. *J Environ Sci (China)*. 2026;159:187-198. doi:10.1016/j.jes.2025.04.022

29. Barchi A, Massimino L, Mandarino FV, et al. Microbiota profiling in esophageal diseases: Novel insights into molecular staining and clinical outcomes. *Comput Struct Biotechnol J*. 2023;23:626-637. Published 2023 Dec 27. doi:10.1016/j.csbj.2023.12.026

30. Sharma A, Laxman B, Naureckas ET, et al. Associations between fungal and bacterial microbiota of airways and asthma endotypes. *J Allergy Clin Immunol*. 2019;144(5):1214-1227.e7. doi:10.1016/j.jaci.2019.06.025

31. Lin D, Howard A, Raihane AS, et al. Traumatic Brain Injury and Gut Microbiome: The Role of the Gut-Brain Axis in Neurodegenerative Processes. Curr Neurol Neurosci Rep. 2025;25(1):23. Published 2025 Mar 15. doi:10.1007/s11910-025-01410-0

32. Braak H, de Vos RA, Bohl J, Del Tredici K. Gastric alpha-synuclein immunoreactive inclusions in Meissner's and Auerbach's plexuses in cases staged for Parkinson's disease-related brain pathology. Neurosci Lett. 2006;396(1):67-72. doi:10.1016/j.neulet.2005.11.012

33. Pravin V, Vellapandian C, Naveen Kumar V. The oral-gut-brain axis in periodontitis: microbial signaling

in systemic and neuroinflammatory disease. Brain Res. 2026;1875:150168. doi:10.1016/j.brainres.2026.150168

34. Zainal Abidin Z, Hein ZM, Che Mohd Nassir CMN, Shari N, Che Ramli MD. Pharmacological modulation of the gut-brain axis: psychobiotics in focus for depression therapy. Front Pharmacol. 2025;16:1665419. Published 2025 Sep 26. doi:10.3389/fphar.2025.1665419

35. Karen AA, Elkhalaf AS, Tluli O, et al. Global Prevalence and Cancer Risk of Epstein-Barr Virus and Human Papillomavirus Coinfection in Breast Cancer: A Systematic Review and Meta-Analysis. Viruses. 2025;17(12):1592. Published 2025 Dec 8. doi:10.3390/v17121592=108

36. Bui NN, Huang SC, Tran TNL, et al. Association between Helicobacter pylori and Epstein-Barr virus co-infection and gastric cancer risk: a systematic review and meta-analysis. QJM. 2025;118(8):584-591. doi:10.1093/qjmed/hcaf092

37. de Moraes FCA, Wagner PHS, da Silva ABN, Magalhães MCF, Burbano RMR. Does Epstein-Barr Virus Contribute to Breast Cancer Risk Worldwide? A Systematic Review and Meta-Analysis. Clin Breast Cancer. 2026;26(1):229-246.e22. doi:10.1016/j.clbc.2025.07.017=109

38. Yang M, Huo Y, Huang Y, He W, Luo Q, Zhang L. Human papillomavirus (HPV) infection and prevalence of colorectal cancer: an updated systematic review and meta-analysis of global data. Int J Surg. 2026;112(1):1815-1825. doi:10.1097/JS9.0000000000003426

39. Cárdenas-Mondragón MG, Carreón-Talavera R, Camorlinga-Ponce M, Gomez-Delgado A, Torres J, Fuentes-Pananá EM. Epstein Barr virus and Helicobacter pylori co-infection are positively associated with severe gastritis in pediatric patients. PLoS One. 2013;8(4):e62850. Published 2013 Apr 24. doi:10.1371/journal.pone.0062850

40. Moon S, Choi J, Sung S, et al. Preventable Cancers Caused by Infection in Korea From 2015 to 2030. J Korean Med Sci. 2025;40(26):e143. Published 2025 Jul 7. doi:10.3346/jkms.2025.40.e143

41. Collatuzzo G, La Vecchia C, Parazzini F, et al. Cancers attributable to infectious agents in Italy. Eur J Cancer. 2023;183:69-78. doi:10.1016/j.ejca.2023.01.010

42. Chupin A, Perduca V, Meyer A, Bellanger C, Carbonnel F, Dong C. Systematic review with meta-analysis: comparative risk of lymphoma with anti-tumour necrosis factor agents and/or thiopurines in patients with inflammatory bowel disease. *Aliment Pharmacol Ther*. 2020;52(8):1289-1297. doi:10.1111/apt.16050

43. Wang JL, Yin WJ, Zhou LY, et al. Risk of non-melanoma skin cancer for rheumatoid arthritis patients receiving TNF antagonist: a systematic review and meta-analysis. *Clin Rheumatol*. 2020;39(3):769-778. doi:10.1007/s10067-019-04865-y

44. Sundaram K, Vajravelu LK, Velayutham R, Mohan U. Progression of tuberculosis among patients with rheumatic diseases - A systematic review and meta-analysis. *Indian J Tuberc*. 2025;72(2):174-182. doi:10.1016/j.ijtb.2023.07.001

45. Minozzi S, Bonovas S, Lytras T, et al. Risk of infections using anti-TNF agents in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis: a systematic review and meta-analysis. *Expert Opin Drug Saf*. 2016;15(sup1):11-34. doi:10.1080/14740338.2016.1240783

46. Borren NZ, Ananthakrishnan AN. Safety of Biologic Therapy in Older Patients With Immune-Mediated Diseases: A Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol*. 2019;17(9):1736-1743.e4. doi:10.1016/j.cgh.2018.12.032

47. Zalagkitis C, Philippou A, Karatzanos E, Metsios G, Dinas PC. Combined effects of physical activity and diet on chronic inflammation of overweight/obese children and adolescents: A systematic review and meta-analysis. *J Sports Sci*. 2025;43(22):2841-2857. doi:10.1080/02640414.2025.2561349

48. Bulmer C, Avenell A. The effect of dietary weight-loss interventions on the inflammatory markers interleukin-6 and TNF-alpha in adults with obesity: A systematic review and meta-analysis of randomized controlled clinical trials. *Obes Rev*. 2025;26(7):e13910. doi:10.1111/obr.13910

49. Dornas W, Reis JP, Belilo TE, et al. Persistent inflammatory cytokine signature in long Covid-19 patients: a meta-analysis. *Inflammopharmacology*. 2026;34(1):1-16. doi:10.1007/s10787-025-02033-0

50. Mostafaei S, Sayad B, Azar MEF, et al. The role of viral and bacterial infections in the pathogenesis of IPF: a systematic review and meta-analysis. *Respir Res*. 2021;22(1):53. Published 2021 Feb 12. doi:10.1186/s12931-021-01650-x

51. Zhang Y, Jia R, Zhang Y, et al. Effect of non-surgical periodontal treatment on cytokines/ adipocytokines levels among periodontitis patients with or without obesity: a systematic review and meta-analysis. *BMC Oral Health*. 2023;23(1):717. Published 2023 Oct 5. doi:10.1186/s12903-023-03383-3

52. Porcari S, Ciccarese C, Heidrich V, et al. Fecal microbiota transplantation plus pembrolizumab and axitinib in metastatic renal cell carcinoma: the randomized phase 2 TACITO trial. Nat Med. Published online January 28, 2026. doi:10.1038/s41591-025-04189-2

53. Duttagupta S, Messaoudene M, Hunter S, et al. Fecal microbiota transplantation plus immunotherapy in non-small cell lung cancer and melanoma: the phase 2 FMT-LUMINate trial. Nat Med. Published online January 28, 2026. doi:10.1038/s41591-025-04186-5

54. Meulmeester FL, Mailhot-Larouche S, Celis-Preciado C, et al. Inflammatory and clinical risk factors for asthma attacks (ORACLE2): a patient-level meta-analysis of control groups of 22 randomised trials. *Lancet Respir Med*. 2025;13(6):505-516. doi:10.1016/S2213-2600(25)00037-2

55. Alshahrani AM, Kaur K, Saini RS, Heboyan A. Hematological parameters as predictors of oral cancer prognosis: a systematic review and meta-analysis. *J Cancer Res Clin Oncol*. 2025;152(1):11. Published 2025 Dec 16. doi:10.1007/s00432-025-06394-5

56. Yang Y, Fang H, Cai Z, Xu Q. Prognostic Significance of Neutrophil-to-Lymphocyte Ratio in Melanoma: A Systematic Review and Meta-Analysis. *J Surg Oncol*. 2025;132(3):456-464. doi:10.1002/jso.70039

57. Yang Y, Shao B, Wei C, Zhang X. Prognostic Value of Immune-Inflammation Indexes for Breast Cancer Patients Undergoing Endocrine Therapy: A Systematic Review and Meta-analysis. *Clin Breast Cancer*. 2025;25(7):e968-e978.e2. doi:10.1016/j.clbc.2025.05.010

58. Saeed R, McSorley S, Cascales A, McMillan DC. The prognostic/ predictive value of the systematic inflammatory response in patients receiving immunotherapy for non-small cell lung cancer: a systematic review and meta-analysis. *BMC Cancer*. 2025;25(1):994. Published 2025 Jun 4. doi:10.1186/s12885-025-13822-9

59. Worapongpaiboon R, Siranart N, Pajareya P, Phutinart S. Inflammatory markers in predicting survival in pancreatic cancer: A Systematic review and Meta-Analysis. *Pancreatology*. 2025;25(3):385-395. doi:10.1016/j.pan.2025.02.014

60. Donatini Bruno. Salivary Calprotectin is a Marker for Periodontitis, Osteoporosis or Chronic Inflammation of Brain, Joints, Liver or Skin. *J Case Rep Stud* 2025;13(1): 103. Published online 2025 Jan 15

61. Kim HD, Karna S, Shin Y, Vu H, Cho HJ, Kim S. S100A8 and S100A9 in saliva, blood and gingival crevicular fluid for screening established periodontitis: a cross-sectional study. *BMC Oral Health*. 2021;21(1):388. Published 2021 Aug 9. doi:10.1186/s12903-021-01749-z

62. Zhang Z, Deng X, Liu Y, Liu Y, Sun L, Chen F. PKM2, function and expression and regulation. *Cell Biosci*. 2019;9:52. Published 2019 Jun 26. doi:10.1186/s13578-019-0317-8

63. Donatini B. Salivary Calprotectin and Pyruvate Kinase M2 Are Markers for Mucosal Dysplastic Lesions, Multiple Sclerosis or Parkinson Disease, J Case Rep Stud 2025;13(2): 201. Published online 2025 Oct 24

64. Piragine E, Malanima MA, Lucenteforte E, Martelli A, Calderone V. Circulating Levels of Hydrogen Sulfide (H_2S) in Patients with Age-Related Diseases: A

Systematic Review and Meta-Analysis. *Biomolecules*. 2023;13(7):1023. Published 2023 Jun 21. doi:10.3390/biom13071023

65. Farrugia G, Szurszewski JH. Carbon monoxide, hydrogen sulfide, and nitric oxide as signaling molecules in the gastrointestinal tract. *Gastroenterology*. 2014;147(2):303-313. doi:10.1053/j.gastro.2014.04.041

66. Facchin BM, Dos Reis GO, Vieira GN, et al. Inflammatory biomarkers on an LPS-induced RAW 264.7 cell model: a systematic review and meta-analysis. *Inflamm Res*. 2022;71(7-8):741-758. doi:10.1007/s00011-022-01584-0

67. Tsurumaki H, Abe Y, Oishi K, Nagasaki T, Tajiri T. Assessing the utility of fractional exhaled nitric oxide-guided management in adult patients with asthma: A systematic review and meta-analysis. *Respir Investig*. 2025;63(1):118-126. doi:10.1016/j.resinv.2024.12.010

68. Ambrosino P, Accardo M, Mosella M, et al. Performance of fractional exhaled nitric oxide in predicting response to inhaled corticosteroids in chronic cough: a meta-analysis. *Ann Med*. 2021;53(1):1659-1672. doi:10.1080/07853890.2021.1979242

69. Dahlan AF, Islam MA, Shukri NM, Abdullah B. Nasal nitric oxide measurement in allergic rhinitis and non-allergic rhinitis: a meta-analysis. *Acta Otorhinolaryngol Ital*. 2024;44(2):100-112. doi:10.14639/0392-100X-N2634

70. Donatini Bruno, Le Blaye Isabelle. High Salivary Calprotectin is Associated with Low Exhaled Levels of Hydrogen Sulphide (H2S) and High Exhaled Inducible-Nitric Oxide (iNO). J Case Rep Stud 2026;14(1): 101. Published 2026 Feb 01

71. Jaruvongvanich V, Sanguankeo A, Jaruvongvanich S, Upala S. Association between Helicobacter pylori infection and multiple sclerosis: A systematic review and meta-analysis. *Mult Scler Relat Disord*. 2016;7:92-97. doi:10.1016/j.msard.2016.03.013

72. Zhong Y, Zhang Z, Lin Y, Wu L. The Relationship Between *Helicobacter pylori* and Inflammatory Bowel Disease. *Arch Iran Med*. 2021;24(4):317-325. Published 2021 Apr 1. doi:10.34172/aim.2021.44

73. Fouillet A, Cadillac M, Rivera C, Coudin E. Leading causes of death in France in 2022 and recent trends. *Bull Épidémiol Hebd*. 2024;(18):388-404. Published 2024 Jun 18.

74. eurostat 2022. https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Causes_of_death_statistics

75. Thandra KC, Barsouk A, Saginala K, Aluru JS, Barsouk A. Epidemiology of lung cancer. *Contemp Oncol (Pozn)*. 2021;25(1):45-52. doi:10.5114/wo.2021.103829

76. Georgakopoulou VE, Lempesis IG, Trakas N, Sklapani P, He Y, Spandidos DA. Lung cancer and obesity: A contentious relationship (Review). *Oncol Rep*. 2024;52(5):158. doi:10.3892/or.2024.8817

77. Wen H, Deng G, Shi X, et al. Body mass index, weight change, and cancer prognosis: a meta-analysis and systematic review of 73 cohort studies. *ESMO Open*. 2024;9(3):102241. doi:10.1016/j.esmoop.2024.102241

78. Sodeifian F, Kian N, Atefi A, et al. Pulmonary Tuberculosis and Risk of Lung Cancer: A Systematic Review and Meta-Analysis. Respiration. 2025;104(5):360-376. doi: 10.1159/000543319.

79. Luczynski P, Poulin P, Romanowski K, Johnston JC. Tuberculosis and risk of cancer: A systematic review and meta-analysis. *PLoS One*. 2022;17(12):e0278661. Published 2022 Dec 30. doi:10.1371/journal.pone.0278661

80. Harabajsa S, Šefčić H, Klasić M, et al. Infection with human cytomegalovirus, Epstein-Barr virus, and high-risk types 16 and 18 of human papillomavirus in EGFR-mutated lung adenocarcinoma. *Croat Med J*. 2023;64(2):84-92. doi:10.3325/cmj.2023.64.84

81. Karnosky J, Dietmaier W, Knuettel H, et al. HPV and lung cancer: A systematic review and meta-analysis. *Cancer Rep (Hoboken)*. 2021;4(4):e1350. doi:10.1002/cnr2.1350

82. Nakra T, Mehta A, Bal A, et al. Epidermal growth factor receptor mutation status in pulmonary adenocarcinoma: Multi-institutional data discussion

at national conference of "Lung Cancer Management in Indian context". *Curr Probl Cancer*. 2020;44(3):100561. doi:10.1016/j.currproblcancer.2020.100561

83. Saadh MJ, Mustafa AN, Taher SG, et al. Association of polyomavirus infection with lung cancer: A systematic review and meta-analysis. *Pathol Res Pract*. 2024;262:155521. doi:10.1016/j.prp.2024.155521

84. Ponvilawan B, Charoenngam N, Rujirachun P, et al. Chronic Hepatitis C Virus Infection is Associated with an Increased Risk of Lung Cancer: A Systematic Review and Meta-analysis. *Lung*. 2020;198(4):705-714. doi:10.1007/s00408-020-00365-y

85. Wang J, Yang X, Zou X, Zhang Y, Wang J, Wang Y. Relationship between periodontal disease and lung cancer: A systematic review and meta-analysis. *J Periodontal Res*. 2020;55(5):581-593. doi:10.1111/jre.12772

86. Zhang K, He C, Qiu Y, Li X, Hu J, Fu B. ASSOCIATION OF ORAL MICROBIOTA AND PERIODONTAL DISEASE WITH LUNG CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS. *J Evid Based Dent Pract*. 2023;23(3):101897. doi:10.1016/j.jebdp.2023.101897

87. Zepeda-Rivera M, Minot SS, Bouzek H, et al. A distinct Fusobacterium nucleatum clade dominates the colorectal cancer niche. *Nature*. 2024;628(8007):424-432. doi:10.1038/s41586-024-07182-w

88. Sameni F, Elkhichi PA, Dadashi A, et al. Global prevalence of Fusobacterium nucleatum and Bacteroides fragilis in patients with colorectal cancer: an overview of case reports/case series and meta-analysis of prevalence studies. *BMC Gastroenterol*. 2025;25(1):71. Published 2025 Feb 10. doi:10.1186/s12876-025-03664-x

89. Reitano E, de'Angelis N, Gavriilidis P, et al. Oral Bacterial Microbiota in Digestive Cancer Patients: A Systematic Review. *Microorganisms*. 2021;9(12):2585. Published 2021 Dec 14. doi:10.3390/microrganisms9122585

90. Chen WD, Zhang X, Zhang YP, et al. Fusobacterium Nucleatum Is a Risk Factor for Metastatic Colorectal Cancer. *Curr Med Sci*. 2022;42(3):538-547. doi:10.1007/s11596-022-2597-1

91. Straka M, Borecová P, Straka M. Periodontitis, Fusobacterium nucleatum, and Colorectal Carcinoma. A Review. *Neuro Endocrinol Lett*. 2025;46(4):232-248.

92. Liang M, Liu Z, Zhang R, Yang JH, Wang XW, Zhang N. Changes in intestinal microbiota in patients with pancreatic cancer: a systematic review and meta-analysis. *Front Microbiol*. 2025;16:1619323. Published 2025 Sep 1. doi:10.3389/fmicb.2025.1619323

93. D'Antonio DL, Zenoniani A, Umme S, Piattelli A, Curia MC. Intratumoral *Fusobacterium nucleatum* in Pancreatic Cancer: Current and Future Perspectives. *Pathogens*. 2024;14(1):2. Published 2024 Dec 26. doi:10.3390/pathogens14010002

94. Momen-Heravi F, Babic A, Tworoger SS, et al. Periodontal disease, tooth loss and colorectal cancer risk: Results from the Nurses' Health Study. *Int J Cancer*. 2017;140(3):646-652. doi:10.1002/ijc.30486

95. Li Y, Hu Y, Zhan X, et al. Meta-analysis reveals *Helicobacter pylori* mutual exclusivity and reproducible gastric microbiome alterations during gastric carcinoma progression. *Gut Microbes*. 2023;15(1):2197835. doi:10.1080/19490976.2023.2197835

96. Liu C, Ng SK, Ding Y, et al. Meta-analysis of mucosal microbiota reveals universal microbial signatures and dysbiosis in gastric carcinogenesis. *Oncogene*. 2022;41(28):3599-3610. doi:10.1038/s41388-022-02377-9

97. Update S2k-Guideline Helicobacter pylori and gastroduodenal ulcer disease of the German Society of Gastroenterology, Digestive and Metabolic Diseases (DGVS). August 2023 – AWMF-Registernummer: 021 – 001.

98. Zagari RM, Romano M, Ojetti V, et al. Guidelines for the management of Helicobacter pylori infection in Italy: The III Working Group Consensus Report 2015. *Dig Liver Dis*. 2015;47(11):903-912. doi:10.1016/j.dld.2015.06.010

99. Malfertheiner P, Megraud F, Rokkas T, et al. Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report. *Gut*. Published online August 8, 2022. doi:10.1136/gutjnl-2022-327745

100. Haute Autorité de Sant. HAS. Helicobacter pylori : recherche et traitement. Publisher online 2019 Mar 26

101. Wang R, Liu K, Chen XZ; SIGES research group. Associations between gastric cancer risk and virus infection other than Epstein-Barr virus: The protocol of a systematic review and meta-analysis based on epidemiological studies. *Medicine (Baltimore)*. 2019; 98(32):e16708. doi:10.1097/MD.0000000000016708

102. Bae JM. Human papillomavirus infection and gastric cancer risk: A meta-epidemiological review. *World J Virol*. 2021;10(5):209-216. doi:10.5501/wjv.v10.i5.209

103. Bozdayi G, Dinc B, Avcikucuk H, et al. Is Human Papillomavirus and Helicobacter pylori Related in Gastric Lesions?. *Clin Lab*. 2019;65(10):10.7754/Clin.Lab.2019.181244. doi:10.7754/Clin.Lab.2019.181244

104. Zeng ZM, Luo FF, Zou LX, et al. Human papillomavirus as a potential risk factor for gastric cancer: a meta-analysis of 1,917 cases. *Onco Targets Ther*. 2016;9:7105-7114. Published 2016 Nov 17. doi:10.2147/OTT.S115053

105. Fattahi S, Nikbakhsh N, Taheri H, et al. Prevalence of multiple infections and the risk of gastric adenocarcinoma development at earlier age. *Diagn Microbiol Infect Dis*. 2018;92(1):62-68. doi:10.1016/j.diagmicrobio.2018.04.015

106. Del Moral-Hernández O, Castañón-Sánchez CA, Reyes-Navarrete S, et al. Multiple infections by EBV, HCMV and Helicobacter pylori are highly frequent in patients with chronic gastritis and gastric cancer from Southwest Mexico: An observational study. *Medicine (Baltimore)*. 2019;98(3):e14124. doi:10.1097/MD.0000000000014124

107. Sarshari B, Mohebbi SR, Ravanshad M, Shahrokh S, Aghdaei HA, Zali MR. Detection and quantification of Epstein-Barr virus, cytomegalovirus, and human herpesvirus-6 in stomach frozen tissue of chronic gastritis and gastric cancer patients. *Microbiol Immunol*. 2022;66(8):379-385. doi:10.1111/1348-0421.13013

108. Wang Q, Gu WJ, Ning FL, et al. Association between Periodontal Diseases and the Risk of Site-Specific Gastrointestinal Cancers: A Systematic Review and Meta-Analysis. *J Dent Res*. 2024;103 (10):962-972. doi:10.1177/00220345241263768

109. Aguiar FJN, Menezes FDS, Fagundes MA, et al. Gastric adenocarcinoma and periodontal disease: A systematic review and meta-analysis. *Clinics (Sao Paulo)*. 2024;79:100321. Published 2024 Jan 31. doi:10.1016/j.clinsp.2023.100321

110. Chen JC, Hsu MH, Hu SW, Lin YY. Exploring the Diagnostic and Predictive Value of Oral Microbiome in Esophageal Cancer: A Systematic Review and Meta-Analysis. *Int J Mol Sci*. 2025;26(19):9457. Published 2025 Sep 27. doi:10.3390/ijms26199457

111. Pigossi SC, Oliveira JA, de Medeiros MC, Soares LFF, D'Silva NJ. Demystifying the link between periodontitis and oral cancer: a systematic review integrating clinical, pre-clinical, and in vitro data. *Cancer Metastasis Rev*. 2025;44(3):67. Published 2025 Sep 9. doi:10.1007/s10555-025-10285-z

112. Bronzato JD, Bomfim RA, Edwards DH, Crouch D, Hector MP, Gomes BPFA. Detection of Fusobacterium in oral and head and neck cancer samples: A systematic review and meta-analysis. *Arch Oral Biol*. 2020;112:104669. doi:10.1016/j.archoralbio.2020.104669

113. Lafuente Ibáñez de Mendoza I, Maritxalar Mendia X, García de la Fuente AM, Quindós Andrés G, Aguirre Urizar JM. Role of Porphyromonas gingivalis in oral squamous cell carcinoma development: A systematic review. *J Periodontal Res*. 2020;55(1):13-22. doi:10.1111/jre.12691

114. Ye L, Jiang Y, Liu W, Tao H. Correlation between periodontal disease and oral cancer risk: A meta-analysis. *J Cancer Res Ther*. 2016;12 (Supplement): C237-C240. doi:10.4103/0973-148 2.200746

115. Michaud DS, Kelsey KT, Papathanasiou E, Genco CA, Giovannucci E. Periodontal disease and risk of all cancers among male never smokers: an updated analysis of the Health Professionals Follow-up Study. *Ann Oncol*. 2016;27(5):941-947. doi:10.1093/annonc/mdw028

116. Maisonneuve P, Amar S, Lowenfels AB. Periodontal disease, edentulism, and pancreatic cancer: a meta-analysis. *Ann Oncol*. 2017;28(5): 985-995. doi:10.1093/annonc/mdx019

117. Yang B, Petrick JL, Abnet CC, et al. Tooth loss and liver cancer incidence in a Finnish cohort. *Cancer Causes Control*. 2017;28(8):899-904. doi:10.1007/s10552-017-0906-y

118. Madugula S, Dhamodhar D, D P, et al. Oral dysbiosis and risk of gastrointestinal cancers: A systematic review and meta-analysis of longitudinal studies. *Indian J Gastroenterol*. 2024;43(4):729-739. doi:10.1007/s12664-024-01546-w

119. Rossi C, Inzani FS, Cesari S, et al. The Role of Oncogenic Viruses in the Pathogenesis of Sporadic Breast Cancer: A Comprehensive Review of the Current Literature. *Pathogens*. 2024;13(6):451. Published 2024 May 25. doi:10.3390/pathogens13060451

120. Li N, Bi X, Zhang Y, Zhao P, Zheng T, Dai M. Human papillomavirus infection and sporadic breast carcinoma risk: a meta-analysis. *Breast Cancer Res Treat*. 2011;126(2):515-520. doi:10.1007/s10549-010-1128-0

121. Karen AA, Elkhalaf AS, Tluli O, et al. Global Prevalence and Cancer Risk of Epstein-Barr Virus and Human Papillomavirus Coinfection in Breast Cancer: A Systematic Review and Meta-Analysis. *Viruses*. 2025;17(12):1592. Published 2025 Dec 8. doi:10.3390/v17121592

122. de Moraes FCA, Wagner PHS, da Silva ABN, Magalhães MCF, Burbano RMR. Does Epstein-Barr Virus Contribute to Breast Cancer Risk Worldwide? A Systematic Review and Meta-Analysis. *Clin Breast Cancer*. 2026;26(1):229-246.e22. doi:10.1016/j.clbc.2025.07.017

123. Farahmand M, Monavari SH, Shoja Z, Ghaffari H, Tavakoli M, Tavakoli A. Epstein-Barr virus and risk of breast cancer: a systematic review and meta-analysis. *Future Oncol*. 2019;15(24):2873-2885. doi:10.2217/fon-2019-0232

124. Huo Q, Zhang N, Yang Q. Epstein-Barr virus infection and sporadic breast cancer risk: a meta-analysis. *PLoS One*. 2012;7(2):e31656. doi:10.1371/journal.pone.0031656

125. El Baba R, Haidar Ahmad S, Vanhulle C, et al. Formation of polyploid giant cancer cells and the transformative role of human cytomegalovirus IE1 protein. *Cancer Lett*. 2025;630:217824. doi:10.1016/j.canlet.2025.217824

126. Gomes de Oliveira G, Gonçalves AK, Eleutério J, Pinheiro LGP. Systematic review and meta-analysis of the papillomavirus prevalence in breast cancer fresh tissues. *Breast Dis*. 2022;41(1):123-132. doi:10.3233/BD-201032

127. Li S, Wang T, Ren Y, Liu Z, Gao J, Guo Z. Prognostic impact of oral microbiome on survival of malignancies: a systematic review and meta-analysis. *Syst Rev*. 2024;13(1):41. Published 2024 Jan 25. doi:10.1186/s13643-023-02419-7

128. Luo Z, Hao S, Li Y, et al. The negative effect of antibiotics on RCC patients with immunotherapy: A systematic review and meta-analysis. *Front Immunol*. 2022;13:1065004. Published 2022 Nov 23. doi:10.3389/fimmu.2022.1065004

129. Yu Y, Zheng P, Gao L, et al. Effects of Antibiotic Use on Outcomes in Cancer Patients Treated Using Immune Checkpoint Inhibitors: A Systematic Review and Meta-Analysis. *J Immunother*. 2021;44(2):76-85. doi:10.1097/CJI.0000000000000346

130. Tsikala-Vafea M, Belani N, Vieira K, Khan H, Farmakiotis D. Use of antibiotics is associated with worse clinical outcomes in patients with cancer treated with immune checkpoint inhibitors: A systematic review and meta-analysis. *Int J Infect Dis*. 2021;106:142-154. doi:10.1016/j.ijid.2021.03.063

131. Thomas AM, Fidelle M, Routy B, et al. Gut OncoMicrobiome Signatures (GOMS) as next-generation biomarkers for cancer immunotherapy. *Nat Rev Clin Oncol*. 2023;20(9):583-603. doi:10.1038/s41571-023-00785-8

132. Mittal N, Singh S, Mittal R, Kaushal J, Kaushal V. Immune checkpoint inhibitors as neoadjuvant therapy in early triple-negative breast cancer: A systematic review and meta-analysis. *J Cancer Res Ther*. 2022;18(6):1754-1765. doi:10.4103/jcrt.jcrt_1867_20

133. Shi T, Min M, Sun C, Zhang Y, Liang M, Sun Y. Periodontal disease and susceptibility to breast cancer: A meta-analysis of observational studies. *J Clin Periodontol*. 2018;45(9):1025-1033. doi:10.1111/jcpe.12982

134. Wang K, Zhang Z, Wang Z. Assessment of the association between periodontal disease and total cancer incidence and mortality: a meta-analysis. *PeerJ*. 2022;10:e14320. Published 2022 Nov 7. doi:10.7717/peerj.14320

135. Tsydenova IA, Ibragimova MK, Tsyganov MM, Litviakov NV. Human papillomavirus and prostate cancer: systematic review and meta-analysis. *Sci Rep*. 2023;13(1):16597. Published 2023 Oct 3. doi:10.1038/s41598-023-43767-7

136. Moghoofei M, Keshavarz M, Ghorbani S, et al. Association between human papillomavirus infection and prostate cancer: A global systematic review and meta-analysis. *Asia Pac J Clin Oncol*. 2019;15 (5):e59-e67. doi:10.1111/ajco.13124

137. Russo GI, Calogero AE, Condorelli RA, Scalia G, Morgia G, La Vignera S. Human papillomavirus and risk of prostate cancer: a systematic review and meta-analysis. *Aging Male*. 2020;23(2):132-138. doi:10.1080/13685538.2018.1455178

138. Caini S, Gandini S, Dudas M, Bremer V, Severi E, Gherasim A. Sexually transmitted infections and prostate cancer risk: a systematic review and meta-analysis. *Cancer Epidemiol*. 2014;38(4):329-338. doi:10.1016/j.canep.2014.06.002

139. Pei X, Liu L, Han Y. Advances in human microbiome and prostate cancer research. *Front Immunol*. 2025;16:1576679. Published 2025 Apr 14. doi:10.3389/fimmu.2025.1576679

140. Ladoukakis E, Oliver T, Wilks M, et al. Exploring the Link Between Obligate Anaerobe-Related Dysbiosis and Prostate Cancer Development: A Pilot Study. *Cancers (Basel)*. 2024;17(1):70. Published 2024 Dec 29. doi:10.3390/cancers17010070

141. Alluri LSC, Paes Batista da Silva A, Verma S, et al. Presence of Specific Periodontal Pathogens in Prostate Gland Diagnosed With Chronic Inflammation and Adenocarcinoma. *Cureus*. 2021;13(9):e17742. Published 2021 Sep 5. doi:10.7759/cureus.17742

142. Chao G, Hong X, Chen X, Zhang S. The prevalence of human papillomavirus in colorectal cancer and adenoma: A meta-analysis. *J Cancer Res Ther*. 2020;16(7):1656-1663. doi:10.4103/jcrt.JCRT_636_20

143. Li X, Gao L, Li H, et al. Human papillomavirus infection and laryngeal cancer risk: a systematic review and meta-analysis. *J Infect Dis*. 2013;207 (3):479-488. doi:10.1093/infdis/jis698

144. Li N, Yang L, Zhang Y, Zhao P, Zheng T, Dai M. Human papillomavirus infection and bladder cancer risk: a meta-analysis. *J Infect Dis*. 2011;204 (2):217-223. doi:10.1093/infdis/jir248

145. Simões PW, Medeiros LR, Simões Pires PD, et al. Prevalence of human papillomavirus in breast cancer: a systematic review. *Int J Gynecol Cancer*. 2012;22(3):343-347. doi:10.1097/IGC.0b013e31823c712e

146. Koshiol J, Lindsay L, Pimenta JM, Poole C, Jenkins D, Smith JS. Persistent human papillomavirus infection and cervical neoplasia: a systematic review and meta-analysis. *Am J Epidemiol*. 2008;168(2): 123-137. doi:10.1093/aje/kwn036

147. Wang M, Zou X, Wang Z. Meta-analysis about correlation between the human Papillomavirus infection and the incidence of cervical intraepithelial Neoplasia. *J Pak Med Assoc*. 2025;75(Suppl 2)(7): S158-S161. doi:10.47391/JPMA.SRPH-27

148. Reynders C, Lerho T, Goebel EA, et al. Prevalence and genotype distribution of human papillomavirus in cervical adenocarcinoma (usual type and variants): A systematic review and meta-analysis. *J Med Virol*. 2023;95(10):e29190. doi:10.1002/jmv.29190

149. Bergman H, Henschke N, Arevalo-Rodriguez I, et al. Human papillomavirus (HPV) vaccination for the prevention of cervical cancer and other HPV-related diseases: a network meta-analysis. *Cochrane Database Syst Rev*. 2025;11(11):CD015364. Published 2025 Nov 24. doi:10.1002/14651858.CD015364.pub2

150. Agarwal K, Robinson LS, Aggarwal S, et al. Glycan cross-feeding supports mutualism between Fusobacterium and the vaginal microbiota. *PLoS Biol*. 2020;18(8):e3000788. Published 2020 Aug 25. doi:10.1371/journal.pbio.3000788

151. Chen Y, Qiu X, Wang W, et al. Human papillomavirus infection and cervical intraepithelial neoplasia progression are associated with increased vaginal microbiome diversity in a Chinese cohort.

BMC Infect Dis. 2020;20(1):629. Published 2020 Aug 26. doi:10.1186/s12879-020-05324-9

152. Zhang H, Cai S, Xia Y, et al. Association between human herpesvirus infection and cervical carcinoma: a systematic review and meta-analysis. *Virol J*. 2023;20(1):288. Published 2023 Dec 4. doi:10.1186/s12985-023-02234-5

153. Ali A, Lassi ZS, Kapellas K, Jamieson L, Rumbold AR. A systematic review and meta-analysis of the association between periodontitis and oral high-risk human papillomavirus infection. *J Public Health (Oxf)*. 2021;43(4):e610-e619. doi:10.1093/pubmed/fdaa156

154. Ibragimova MK, Kokorina EV, Tsyganov MM, Churuksaeva ON, Litviakov NV. Human papillomavirus and ovarian cancer (review of literature and meta-analysis). *Infect Genet Evol*. 2021;95:105086. doi:10.1016/j.meegid.2021.105086

155. Cherif S, Amine A, Thies S, et al. Prevalence of human papillomavirus detection in ovarian cancer: a meta-analysis. *Eur J Clin Microbiol Infect Dis*. 2021;40(9):1791-1802. doi:10.1007/s10096-021-04282-7

156. Chiaffarino F, Cipriani S, Ricci E, Esposito G, Parazzini F, Vercellini P. Histologic Subtypes in Endometriosis-Associated Ovarian Cancer and Ovarian Cancer Arising in Endometriosis: A Systematic Review and Meta-Analysis. *Reprod Sci*. 2024;31(6):1642-1650. doi:10.1007/s43032-024-01489-9

157. Ye L, Chen J, Guo W, et al. TCGA molecular subtypes in endometriosis-associated ovarian cancer: a systematic review and meta-analysis. *Ann Med*. 2025;57(1):2583543. doi:10.1080/07853890.2025.2583543

158. Marcickiewicz J, Jamka M, Walkowiak J. A Potential Link Between Oral Microbiota and Female Reproductive Health. *Microorganisms*. 2025;13(3):619. Published 2025 Mar 7. doi:10.3390/microorganisms13030619

159. Hicks C, Leonardi M, Chua XY, et al. Oral, Vaginal, and Stool Microbial Signatures in Patients With Endometriosis as Potential Diagnostic Non-Invasive Biomarkers: A Prospective Cohort Study. *BJOG*. 2025;132(3):326-336. doi:10.1111/1471-0528.17979

160. Hu X, Yu C, He Y, et al. Integrative metagenomic analysis reveals distinct gut microbial signatures related to obesity. *BMC Microbiol*. 2024;24(1):119. Published 2024 Apr 5. doi:10.1186/s12866-024-03278-5

161. Chanda D, De D. Meta-analysis reveals obesity associated gut microbial alteration patterns and reproducible contributors of functional shift. *Gut Microbes*. 2024;16(1):2304900. doi:10.1080/19490976.2024.2304900

162. Gong J, Shen Y, Zhang H, et al. Gut Microbiota Characteristics of People with Obesity by Meta-Analysis of Existing Datasets. *Nutrients*. 2022;14(14):2993. Published 2022 Jul 21. doi:10.3390/nu14142993

163. Gamba G, Colonetti T, Uggioni MLR, et al. Gut microbiota and breast cancer: systematic review and meta-analysis. *Breast Cancer*. 2025;32(2):242-257. doi:10.1007/s12282-024-01658-3

164. Nie RC, Chen GM, Wang Y, et al. Association Between Body Mass Index and Survival Outcomes In Patients Treated With Immune Checkpoint Inhibitors: Meta-analyses of Individual Patient Data. *J Immunother*. 2021;44(9):371-375. doi:10.1097/CJI.0000000000000389

165. Saowapa S, Polpichai N, Siladech P, et al. BMI Association With Treatment Outcomes in Head and Neck Cancer Patients Receiving Immunotherapy: A Comprehensive Review and Meta-Analysis. *Cancer Rep (Hoboken)*. 2025;8(2):e70147. doi:10.1002/cnr2.70147

166. Zhang T, Li S, Chang J, Qin Y, Li C. Impact of BMI on the survival outcomes of non-small cell lung cancer patients treated with immune checkpoint inhibitors: a meta-analysis. *BMC Cancer*. 2023;23(1):1023. Published 2023 Oct 23. doi:10.1186/s12885-023-11512-y

167. An Y, Wu Z, Wang N, et al. Association between body mass index and survival outcomes for cancer patients treated with immune checkpoint inhibitors: a systematic review and meta-analysis. *J*

Transl Med. 2020;18(1):235. Published 2020 Jun 12. doi:10.1186/s12967-020-02404-x

168. Schooling CM, Jones HE, Leung GM. Lifecourse infectious origins of sexual inequalities in central adiposity. *Int J Epidemiol*. 2011;40(6): 1556-1564. doi:10.1093/ije/dyr128

169. Marjani A, Khatami A, Saadati H, et al. Association of adenovirus 36 infection and obesity; An updated meta-analysis of community-based studies. *Rev Med Virol*. 2022;32(1):e2255. doi:10.1002/rmv.2255

170. da Silva Fernandes J, Schuelter-Trevisol F, Cancelier ACL, et al. Adenovirus 36 prevalence and association with human obesity: a systematic review. *Int J Obes (Lond)*. 2021;45(6):1342-1356. doi:10.1038/s41366-021-00805-6

171. Xu MY, Cao B, Wang DF, et al. Human Adenovirus 36 Infection Increased the Risk of Obesity: A Meta-Analysis Update. *Medicine (Baltimore)*. 2015; 94(51):e2357. doi:10.1097/MD.0000000000002357

172. Yamada T, Hara K, Kadowaki T. Association of adenovirus 36 infection with obesity and metabolic markers in humans: a meta-analysis of observational studies. *PLoS One*. 2012;7(7):e42031. doi:10.137 1/journal.pone.0042031

173. Honce R, Karlsson EA, Wohlgemuth N, et al. Obesity-Related Microenvironment Promotes Emergence of Virulent Influenza Virus Strains. *mBio*. 2020;11(2):e03341-19. Published 2020 Mar 3. doi:10.1128/mBio.03341-19

174. Lontchi-Yimagou E, Feutseu C, Kenmoe S, et al. Non-autoimmune diabetes mellitus and the risk of virus infections: a systematic review and meta-analysis of case-control and cohort studies. *Sci Rep*. 2021;11(1):8968. Published 2021 Apr 26. doi:10.1038/s41598-021-88598-6

175. Motuma A, Mussa I, Deressa A, Regassa LD, Birhanu A. Central obesity increases the risk of breast cancer irrespective of menopausal status in women: Systematic review and meta-analysis. *Cancer Treat Res Commun*. 2025;44:100965. doi:10.1016/j.ctarc.2025.100965

176. Azimi A, Jolfayi AG, Rezayifar V, et al. The association between metabolic-associated fatty liver diseases and risk of colorectal polyps, neoplasia, and cancer: A systematic review and meta-analysis of over 56 million individuals. *Clin Res Hepatol Gastroenterol*. 2025;49(8):102652. doi:10.1016/j.cl inre.2025.102652

177. Kong YH, Huang JY, Ding Y, Chen SH, Li QS, Xiong Y. The effect of BMI on survival outcome of breast cancer patients: a systematic review and meta-analysis. *Clin Transl Oncol*. 2025;27(2):403-416. doi:10.1007/s12094-024-03563-9

178. Clifford JT, Ryan OK, Donnelly M, et al. From obesity to oncology; bariatric surgery and the impact on breast cancer- what is the link? - A systematic review and meta-analysis. *Eur J Surg Oncol*. 2025;51 (12):110478. doi:10.1016/j.ejso.2025.110478

179. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Electronic address: bc.overview@ndph.ox.ac.uk; Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Extending the duration of endocrine treatment for early breast cancer: patient-level meta-analysis of 12 randomised trials of aromatase inhibitors in 22 031 postmenopausal women already treated with at least 5 years of endocrine therapy. *Lancet*. 2025; 406(10503):603-614. doi:10.1016/S0140-6736(25) 01013-X

180. Wang R, Liu J, Fang G, Shi J, Zhang C, Huang Y. Association between visceral adiposity index and cardiovascular disease: A systematic review and meta-analysis. *Nutr Metab Cardiovasc Dis*. 2025; 35(12):104216. doi:10.1016/j.numecd.2025.104216

181. Rashidian P, Mirchandani M, Somu KP, et al. Association between atherogenic index of plasma and various metabolic conditions: an umbrella review on meta-analyses. *BMC Cardiovasc Disord*. 2025;26(1):41. Published 2025 Dec 11. doi:10.1186/s12872-025-05409-w

182. Bhatia MK, Garg A, Ali J, et al. Association of NAFLD and Cardiovascular Events: A Systematic Review and Meta-analysis. *J Clin Gastroenterol*. 2026;60(2):101-114. Published 2026 Feb 1. doi:10.1097/MCG.0000000000002232

183. Cavadias I, Maitrot-Mantelet L, Perol S, et al. Risk of cardiovascular disease and mortality among

women with endometriosis: A systematic review and meta-analysis. *Acta Obstet Gynecol Scand*. 2026;105(2):225-237. doi:10.1111/aogs.70104

184. Yang L, Liu X, Yang G, et al. Rheumatoid arthritis and stroke risk: a systematic review and meta-analysis. *PeerJ*. 2026;14:e20568. Published 2026 Jan 29. doi:10.7717/peerj.20568

185. Ausserwinkler M, Gensluckner S, Voelkerer A, et al. Genetic relationship between rheumatoid arthritis and cardiovascular diseases : A systematic review of Mendelian randomization studies. *Wien Klin Wochenschr*. 2025;137(9-10):272-278. doi:10.1007/s00508-024-02392-8

186. Yang Y, Zhang Q, Huang A, et al. All-cause and cause-specific mortality in psoriasis patients: a systematic review and meta-analysis. *Front Immunol*. 2025;16:1610499. Published 2025 Jul 24. doi:10.3389/fimmu.2025.1610499

187. Arumugam M, Raes J, Pelletier E, et al. Enterotypes of the human gut microbiome. *Nature*. 2011;473(7346):174-180. doi:10.1038/nature09944

188. Zhang Y, Bian CE, Yu C, et al. THE ASSOCIATION BETWEEN PERIODONTAL DISEASE AND STROKE RISK: A SYSTEMATIC REVIEW AND META-ANALYSIS. *J Evid Based Dent Pract*. 2025;25(4):102172. doi:10.1016/j.jebdp.2025.102172

189. Zheng Q, Xu T, Luo S, et al. The contribution of oral infectious diseases in lacunar stroke based on meta-analysis and Mendelian randomization study. *Sci Rep*. 2025;15(1):17062. Published 2025 May 16. doi:10.1038/s41598-025-99742-x

190. Fagundes NCF, Almeida APCPSC, Vilhena KFB, Magno MB, Maia LC, Lima RR. Periodontitis As A Risk Factor For Stroke: A Systematic Review And Meta-Analysis. *Vasc Health Risk Manag*. 2019;15:519-532. Published 2019 Nov 6. doi:10.2147/VHRM.S204097

191. Leira Y, Seoane J, Blanco M, et al. Association between periodontitis and ischemic stroke: a systematic review and meta-analysis. *Eur J Epidemiol*. 2017;32(1):43-53. doi:10.1007/s10654-016-0170-6

192. Guo X, Li X, Liao C, Feng X, He T. Periodontal disease and subsequent risk of cardiovascular outcome and all-cause mortality: A meta-analysis of prospective studies. *PLoS One*. 2023;18(9):e0290545. Published 2023 Sep 8. doi:10.1371/journal.pone.0290545

193. Wang W, Yang Z, Wang Y, Gao H, Wang Y, Zhang Q. Association between Periodontitis and Carotid Artery Calcification: A Systematic Review and Meta-Analysis. *Biomed Res Int*. 2021;2021:3278351. Published 2021 Sep 4. doi:10.1155/2021/3278351

194. Joshi C, Bapat R, Anderson W, Dawson D, Hijazi K, Cherukara G. Detection of periodontal microorganisms in coronary atheromatous plaque specimens of myocardial infarction patients: A systematic review and meta-analysis. *Trends Cardiovasc Med*. 2021;31(1):69-82. doi:10.1016/j.tcm.2019.12.005

195. Yaslianifard S, Sameni F, Kazemi K, et al. Beyond the gut: a comprehensive meta-analysis on Helicobacter pylori infection and cardiovascular complications. *Ann Clin Microbiol Antimicrob*. 2025;24(1):18. Published 2025 Mar 18. doi:10.1186/s12941-025-00788-6

196. Sun L, Zheng H, Qiu M, et al. Helicobacter pylori infection and risk of cardiovascular disease. *Helicobacter*. 2023;28(3):e12967. doi:10.1111/hel.12967

197. Arain M, Karnatapu J, Moradi I, et al. Association between helicobacter pylori infection and abdominal aortic aneurysm: a systematic review and meta-analysis. *BMC Cardiovasc Disord*. 2025;25(1):676. Published 2025 Sep 26. doi:10.1186/s12872-025-05148-y

198. Cannavo A, Babajani N, Saeedian B, et al. Anti-Porphyromonas gingivalis Antibody Levels in Patients With Stroke and Atrial Fibrillation: A Systematic Review and Meta-Analysis. *Clin Exp Dent Res*. 2024;10(6):e70041. doi:10.1002/cre2.70041

199. Romandini M, Baima G, Antonoglou G, Bueno J, Figuero E, Sanz M. Periodontitis, Edentulism, and Risk of Mortality: A Systematic Review with Meta-analyses. *J Dent Res*. 2021;100(1):37-49. doi:10.1177/0022034520952401

200. Su Y, Cao Y, Bing X, et al. Effect of nonsurgical periodontal therapy on coronary artery disease or metabolic syndrome: a systematic review and meta-analysis. *J Evid Based Dent Pract*. 2025;25 (3):102136. doi:10.1016/j.jebdp.2025.102136

201. Luthra S, Orlandi M, Leira Y, et al. Invasive dental treatment and acute vascular events: A systematic review and meta-analysis. *J Clin Periodontol*. 2022;49(5):467-479. doi:10.1111/jcpe.13600

202. Kawai K, Muhere CF, Lemos EV, Francis JM. Viral Infections and Risk of Cardiovascular Disease: Systematic Review and Meta-Analysis. J Am Heart Assoc. 2025 Nov 4;14(21):e042670. doi: 10.1161/JAHA.125.042670.

203. de Souza AMLB, de Araújo EF, Junior NC, Raimundo ACS, Pereira AC, de Castro Meneghim M. Association between SARS-CoV-2 and stroke: perspectives from a metaumbrella-review. *BMC Neurol*. 2025;25(1):97. Published 2025 Mar 7. doi:10.1186/s12883-025-04041-7

204. Romero Starke K, Kaboth P, Rath N, et al. Cardiovascular disease risk after a SARS-CoV-2 infection: A systematic review and meta-analysis. *J Infect*. 2024;89(3):106215. doi:10.1016/j.jinf.2024.106215

205. Abubasheer TM, Abubasheer HMA, Odat RM, Elgenidy A, Afifi AM. Sex-Based Differences in Cardiovascular Outcomes Associated With COVID-19: A Systematic Review and Meta-Analysis. *Rev Med Virol*. 2025;35(3):e70022. doi:10.1002/rmv.70022

206. Zuin M, Rigatelli G, Bilato C, et al. One-Year Risk of Myocarditis After COVID-19 Infection: A Systematic Review and Meta-analysis. *Can J Cardiol*. 2023;39(6):839-844. doi:10.1016/j.cjca.2022.12.003

207. Lu P, Cui L, Zhang X. Stroke risk after varicella-zoster virus infection: a systematic review and meta-analysis. *J Neurovirol*. 2023;29(4):449-459. doi:10.1007/s13365-023-01144-0

208. Heiat M, Salesi M, Peypar MH, Ramazani A, Abdorrashidi M, Yeganeh AV. A comprehensive, updated systematic review and meta-analysis of epidemiologic evidence on the connection between herpes zoster infection and the risk of stroke. *Rev Med Virol*. 2024;34(4):e2556. doi:10.1002/rmv.2556

209. Ouranos K, Vassilopoulos S, Vassilopoulos A, Shehadeh F, Mylonakis E. Cumulative incidence and mortality rate of cardiovascular complications due to laboratory-confirmed influenza virus infection: A systematic review and meta-analysis. *Rev Med Virol*. 2024;34(1):e2497. doi:10.1002/rmv.2497

210. Wang H, Peng G, Bai J, et al. Cytomegalovirus Infection and Relative Risk of Cardiovascular Disease (Ischemic Heart Disease, Stroke, and Cardiovascular Death): A Meta-Analysis of Prospective Studies Up to 2016. *J Am Heart Assoc*. 2017;6(7):e005025. Published 2017 Jul 6. doi:10.1161/JAHA.116.005025

211. Roberts ET, Haan MN, Dowd JB, Aiello AE. Cytomegalovirus antibody levels, inflammation, and mortality among elderly Latinos over 9 years of follow-up. *Am J Epidemiol*. 2010;172(4):363-371. doi:10.1093/aje/kwq177

212. Savva GM, Pachnio A, Kaul B, et al. Cytomegalovirus infection is associated with increased mortality in the older population. *Aging Cell*. 2013;12(3):381-387. doi:10.1111/acel.12059

213. Chen X, Li Y, Deng L, et al. Cardiovascular involvement in Epstein-Barr virus infection. *Front Immunol*. 2023;14:1188330. Published 2023 May 22. doi:10.3389/fimmu.2023.1188330

214. Bai F, You L, Lei H, Li X. Association between increased and decreased gut microbiota abundance and Parkinson's disease: A systematic review and subgroup meta-analysis. *Exp Gerontol*. 2024;191: 112444. doi:10.1016/j.exger.2024.112444

215. Wang H, Liu X, Tan C, et al. Bacterial, viral, and fungal infection-related risk of Parkinson's disease: Meta-analysis of cohort and case-control studies. *Brain Behav*. 2020;10(3):e01549. doi:10.1002/brb3.1549

216. Meng L, Shen L, Ji HF. Impact of infection on risk of Parkinson's disease: a quantitative assessment of case-control and cohort studies. *J Neurovirol*. 2019;25(2):221-228. doi:10.1007/s13365-018-0707-4

217. Narváez-Bandera I, Suárez-Gómez D, Castro-Rivera CDM, et al. Hepatitis C virus infection and Parkinson's disease: insights from a joint sex-stratified BioOptimatics meta-analysis. *Sci Rep*. 2024;14(1):

22838. Published 2024 Oct 1. doi:10.1038/s41598-024-73535-0

218. Yaow CYL, Hong ASY, Chong NZ, Chong RIH, Mai AS, Tan EK. Risk of Parkinson's disease in hepatitis B and C populations: a systematic review and meta-analysis. *J Neural Transm (Vienna)*. 2024; 131(6):609-616. doi:10.1007/s00702-023-02705-7

219. Rahmati M, Yon DK, Lee SW, et al. New-onset neurodegenerative diseases as long-term sequelae of SARS-CoV-2 infection: A systematic review and meta-analysis. *J Med Virol*. 2023;95(7):e28909. doi:10.1002/jmv.28909

220. Chen Y, Jin Y, Li K, et al. Is There an Association Between Parkinson's Disease and Periodontitis? A Systematic Review and Meta-Analysis. *J Parkinsons Dis*. 2023;13(7):1107-1125. doi:10.3233/JPD-230059

221. Liu RY, Yin KF, He SY, et al. Viral infections and the risk of neurodegenerative diseases: a comprehensive meta-analysis and systematic review. *Transl Psychiatry*. 2025;15(1):388. Published 2025 Oct 10. doi:10.1038/s41398-025-03639-2

222. Wu D, Wang C, Pang P, et al. The association between herpes simplex virus type 1 infection and Alzheimer's disease. *J Clin Neurosci*. 2020;82(Pt A):63-70. doi:10.1016/j.jocn.2020.10.044

223. Feng H, Pan K, Shabani ZI, Wang H, Wei W. Association between herpesviruses and alzheimer's disease: a meta-analysis based on case-control studies. *Mol Cell Biochem*. 2025;480(7):4079-4090. doi:10.1007/s11010-025-05263-6

224. Bastan F, Saeedi-Moghaddam F, Rashidian M, Mirhosseini F, Mozhgani SH. Human herpesvirus 6 (HHV-6) infection and risk of Alzheimer's disease: a systematic review and meta-analysis. *BMC Neurol*. 2025;25(1):516. Published 2025 Nov 22. doi:10.1186/s12883-025-04500-1

225. Ou YN, Zhu JX, Hou XH, et al. Associations of Infectious Agents with Alzheimer's Disease: A Systematic Review and Meta-Analysis. *J Alzheimers Dis*. 2020;75(1):299-309. doi:10.3233/JAD-191337

226. Elhalag RH, Motawea KR, Talat NE, et al. Herpes Zoster virus infection and the risk of developing dementia: A systematic review and meta-analysis. *Medicine (Baltimore)*. 2023;102(43): e34503. doi:10.1097/MD.0000000000034503

227. Marra F, Gomes K, Liu E, Vadlamudi NK, Richardson K, Cragg JJ. Effects of herpes zoster infection, antivirals and vaccination on risk of developing dementia: A systematic review and meta-analysis. *Hum Vaccin Immunother*. 2025;21 (1):2546741. doi:10.1080/21645515.2025.2546741

228. Yin Y, Deng J, Liu J. The association between herpes zoster vaccination and the decreased risk of dementia: A systematic review and meta-analysis of cohort studies. *J Alzheimers Dis*. 2025;106(4): 1232-1241. doi:10.1177/13872877251351593

229. Shah S, Dahal K, Thapa S, et al. Herpes zoster vaccination and the risk of dementia: A systematic review and meta-analysis. *Brain Behav*. 2024;14 (2):e3415. doi:10.1002/brb3.3415

230. Liu S, Dashper SG, Zhao R. Association Between Oral Bacteria and Alzheimer's Disease: A Systematic Review and Meta-Analysis. *J Alzheimers Dis*. 2023;91(1):129-150. doi:10.3233/JAD-220627

231. Hu X, Zhang J, Qiu Y, Liu Z. Periodontal disease and the risk of Alzheimer's disease and mild cognitive impairment: a systematic review and meta-analysis. *Psychogeriatrics*. 2021;21(5):813-825. doi:10.1111/psyg.12743

232. Nadim R, Tang J, Dilmohamed A, et al. Influence of periodontal disease on risk of dementia: a systematic literature review and a meta-analysis. *Eur J Epidemiol*. 2020;35(9):821-833. doi:10.1007/s 10654-020-00648-x

233. Drinkall NJ, Siersma V, Lathe R, Waldemar G, Janbek J. Herpesviruses, antiviral treatment, and the risk of dementia - systematic review and meta-analysis. *Alzheimers Res Ther*. 2025;17(1):201. Published 2025 Sep 2. doi:10.1186/s13195-025-01838-z

234. Maggi S, Fulöp T, De Vita E, et al. Association between vaccinations and risk of dementia: a systematic review and meta-analysis. *Age Ageing*. 2025;54(11):afaf331. doi:10.1093/ageing/afaf331

235. Maulani C, Auerkari EI, C Masulili SL, Soeroso Y, Djoko Santoso W, S Kusdhany L. Association

between Epstein-Barr virus and periodontitis: A meta-analysis. *PLoS One*. 2021;16(10):e0258109. Published 2021 Oct 7. doi:10.1371/journal.pone.0258109

236. Vincent-Bugnas S, Vitale S, Mouline CC, et al. EBV infection is common in gingival epithelial cells of the periodontium and worsens during chronic periodontitis. *PLoS One*. 2013;8(12):e80336. Published 2013 Dec 19. doi:10.1371/journal.pone.0080336

237. Botero JE, Rodríguez-Medina C, Jaramillo-Echeverry A, Contreras A. Association between human cytomegalovirus and periodontitis: A systematic review and meta-analysis. *J Periodontal Res*. 2020;55(4):551-558. doi:10.1111/jre.12742

238. Arduino PG, Cabras M, Lodi G, Petti S. Herpes simplex virus type 1 in subgingival plaque and periodontal diseases. Meta-analysis of observational studies. *J Periodontal Res*. 2022;57(2):256-268. doi:10.1111/jre.12968

239. Phillips SA, Denoël S, Wentzensen N, Arbyn M. Accuracy of HPV Self-Collection Compared with Clinician-Collected HPV Testing and Cytology: A Meta-analysis. *Cancer Epidemiol Biomarkers Prev*. 2025;34(9):1467-1471. doi:10.1158/1055-9965.EPI-25-0362

240. Thomas J, Mazzara E, Guller M, et al. Methodology of cfHPV-DNA Detection in Head and Neck Cancer: A Systematic Review and Meta-analysis. *Otolaryngol Head Neck Surg*. 2025;172(3):798-810. doi:10.1002/ohn.1056

241. Griffin E, Krantz E, Selke S, Huang ML, Wald A. Oral mucosal reactivation rates of herpesviruses among HIV-1 seropositive persons. *J Med Virol*. 2008;80(7):1153-1159. doi:10.1002/jmv.21214

242. de la Cour CD, Sperling CD, Belmonte F, Syrjänen S, Verdoodt F, Kjaer SK. Prevalence of human papillomavirus in oral epithelial dysplasia: Systematic review and meta-analysis. *Head Neck*. 2020;42(10):2975-2984. doi:10.1002/hed.26330

243. Gomez-Casado G, Jimenez-Gonzalez A, Rodriguez-Muñoz A, et al. Neutrophils as indicators of obesity-associated inflammation: A systematic review and meta-analysis. *Obes Rev*. 2025;26(3):e13868. doi:10.1111/obr.13868

244. Ma X, Zhou Y, Li Z, Mao G, Wei H, Zhao T. Comparison of the predictive performance of systemic immune-inflammation index and neutrophil-to-lymphocyte ratio for three-month poor functional outcome in ischemic stroke: a systematic review and meta-analysis. *Ann Med*. 2026;58(1):2612820. doi:10.1080/07853890.2026.2612820

245. Ghasempour Dabaghi G, Rabiee Rad M, Mortaheb M, et al. The Neutrophil-to-Lymphocyte Ratio Predicts Cardiovascular Outcomes in Patients With Diabetes: A Systematic Review and Meta-Analysis. *Cardiol Rev*. 2025;33(3):202-211. doi:10.1097/CRD.0000000000000820

246. Kurniawan RB, Siahaan PP, Saputra PB, et al. Neutrophil-to-lymphocyte ratio as a prognostic biomarker in patients with peripheral artery disease: A systematic review and meta-analysis. *Vasc Med*. 2024;29(6):687-699. doi:10.1177/135 8863X24128 1699

247. Zhou Y, Jiang X, Hu Y, et al. The Relationship Between Neutrophil-to-Lymphocyte Ratio and the Prevalence and Clinical Outcomes of Depressive Disorders: A Systematic Review and Meta-Analysis. *Harv Rev Psychiatry*. 2025;33(6):289-304. doi:10.1097/HRP.0000000000000444

248. Tan S, Yang X, Mu X, et al. The predictive role of peripheral serum inflammatory markers NLR, PLR, and LMR in ulcerative colitis and Crohn's disease: a systematic review and meta-analysis. *Front Immunol*. 2025;16:1623899. Published 2025 Jul 25. doi:10.3389/fimmu.2025.1623899

249. Savioli F, Morrow ES, Dolan RD, et al. Prognostic role of preoperative circulating systemic inflammatory response markers in primary breast cancer: meta-analysis. *Br J Surg*. 2022;109(12):1206-1215. doi:10.1093/bjs/znac319

250. Qian M, Ma P, Zhao Y, et al. Immune checkpoint inhibitor therapy in advanced cancer: clinical association of irAEs type, inflammatory markers and efficacy. *Front Immunol*. 2025;16:1662333. Published 2025 Nov 26. doi:10.3389/fimmu.2025.1662333

251. Shen YH, Ho PY, Huang YC. Evaluating Psoriasis Severity Using the Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio: A Systematic Review and Meta-Analysis. *Exp Dermatol*. 2026; 35(1):e70214. doi:10.1111/exd.70214

252. Xu Y, He X, Zhang X, et al. The predictive value of immune inflammation indexes for the risk of fracture in patients with osteoporosis: a systematic review and meta-analysis. *Front Endocrinol (Lausanne)*. 2025;16:1650895. Published 2025 Nov 3. doi:10.3389/fendo.2025.1650895

253. Wang J, Wang X, Li X, et al. Association Between Neutrophil-to-Lymphocyte Ratio and Sarcopenia: A Systematic Review and Meta-Analysis. *J Am Med Dir Assoc*. 2026;27(1):105977. doi:10.1016/j.jamda.2025.105977

254. Ghasemi S, Mortezagholi B, Movahed E, et al. Systematic review and meta-analysis of the association of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio with periodontitis. *Eur J Med Res*. 2024;29(1):581. Published 2024 Dec 18. doi:10.1186/s40001-024-02175-x

255. Mohammadi A, Mohammadi M, Almasi-Dooghaee M, Mirmosayyeb O. Neutrophil to lymphocyte ratio in Alzheimer's disease: A systematic review and meta-analysis. *PLoS One*. 2024;19(6): e0305322. Published 2024 Jun 25. doi:10.1371/journal.pone.0305322

256. Sharifi A, Rahbar R, Simoneau T, et al. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in asthmatic children: a systematic review with meta-analysis. *Eur J Pediatr*. 2026;185 (2):112. Published 2026 Jan 30. doi:10.1007/s00431-026-06743-7

257. Zou P, Yang E, Li Z. Neutrophil-to-lymphocyte ratio is an independent predictor for survival outcomes in cervical cancer: a systematic review and meta-analysis. *Sci Rep*. 2020;10(1):21917. Published 2020 Dec 14. doi:10.1038/s41598-020-79071-x

258. Darbandi M, Pasdar Y, Moradi S, Mohamed HJJ, Hamzeh B, Salimi Y. Discriminatory Capacity of Anthropometric Indices for Cardiovascular Disease in Adults: A Systematic Review and Meta-Analysis. *Prev Chronic Dis*. 2020;17:E131. Published 2020 Oct 22. doi:10.5888/pcd17.200112

259. Pischon T, Boeing H, Hoffmann K, et al. General and abdominal adiposity and risk of death in Europe. *N Engl J Med*. 2008;359(20):2105-2120. doi:10.1056/NEJMoa0801891

260. Jayedi A, Soltani S, Motlagh SZ, et al. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. *BMJ*. 2022;376: e067516. Published 2022 Jan 18. doi:10.1136/bmj-2021-067516

261. Guo J, Chen H, Zhang X, et al. The Effect of Berberine on Metabolic Profiles in Type 2 Diabetic Patients: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Oxid Med Cell Longev*. 2021;2021:2074610. Published 2021 Dec 15. doi:10.1155/2021/2074610

262. Pinheiro Volp AC, Santos Silva FC, Bressan J. Hepatic inflammatory biomarkers and its link with obesity and chronic diseases. *Nutr Hosp*. 2015;31(5): 1947-1956. Published 2015 May 1. doi:10.3305/nh.2015.31.5.8525

263. Wiseman S, Marlborough F, Doubal F, Webb DJ, Wardlaw J. Blood markers of coagulation, fibrinolysis, endothelial dysfunction and inflammation in lacunar stroke versus non-lacunar stroke and non-stroke: systematic review and meta-analysis. *Cerebrovasc Dis*. 2014;37(1):64-75. doi:10.1159/000356789

264. Liguori A, Zoncapè M, Casazza G, Easterbrook P, Tsochatzis EA. Staging liver fibrosis and cirrhosis using non-invasive tests in people with chronic hepatitis B to inform WHO 2024 guidelines: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2025;10(4):332-349. doi:10.1016/S2468-1253(24)00437-0

265. Nguyen-Khac E, Thiele M, Voican C, et al. Non-invasive diagnosis of liver fibrosis in patients with alcohol-related liver disease by transient elastography: an individual patient data meta-analysis. *Lancet Gastroenterol Hepatol*. 2018;3(9): 614-625. doi:10.1016/S2468-1253(18)30124-9

266. Boursier J, de Ledinghen V, Sturm N, et al. Precise evaluation of liver histology by computerized morphometry shows that steatosis influences liver stiffness measured by transient elastography in chronic hepatitis C. *J Gastroenterol*. 2014;49(3): 527-537. doi:10.1007/s00535-013-0819-9

267. Petroff D, Blank V, Newsome PN, et al. Assessment of hepatic steatosis by controlled attenuation parameter using the M and XL probes: an individual patient data meta-analysis. *Lancet Gastroenterol Hepatol*. 2021;6(3):185-198. doi:10.1016/S2468-1253(20)30357-5

268. Patil A, Mungase SB, Nadella M, Adela R. Diagnostic performance of non-invasive markers for distinguishing MASLD/MASH: insights from meta-analysis and real-world data. *Clin Chim Acta*. 2026;582:120787. doi:10.1016/j.cca.2025.120787

269. Eisenmann A, Amann A, Said M, Datta B, Ledochowski M. Implementation and interpretation of hydrogen breath tests. *J Breath Res*. 2008;2(4): 046002. doi:10.1088/1752-7155/2/4/046002

270. Ledochowski M and Ledochowski L (2011). Hydrogen Breath Test (2nd Edn) Austria: Verlag Akademie für Ehrnarungsmedizin GmbH, Austria

271. Donatini B. Pullulation bactérienne de l'intestin grêle. Intérêt du test respiratoire à l'hydrogène et au méthane après lactulose. *Revue Inist Hegel*. 2015;5(2) :92-99. doi:10.4267/2042/56632

272. Stríz I, Trebichavský I. Calprotectin - a pleiotropic molecule in acute and chronic inflammation. *Physiol Res*. 2004;53(3):245-253.

273. Dajti E, Frazzoni L, Iascone V, et al. Systematic review with meta-analysis: Diagnostic performance of faecal calprotectin in distinguishing inflammatory bowel disease from irritable bowel syndrome in adults. *Aliment Pharmacol Ther*. 2023;58(11-12):1120-1131. doi:10.1111/apt.17754

274. Witarto BS, Visuddho V, Witarto AP, Sampurna MTA, Irzaldy A. Performance of fecal S100A12 as a novel non-invasive diagnostic biomarker for pediatric inflammatory bowel disease: a systematic review and meta-analysis. *J Pediatr (Rio J)*. 2023; 99(5):432-442. doi:10.1016/j.jped.2023.03.002

275. Kim M, Kim YI, Lee YA, Hong SJ. Potential Utility of Combined Salivary Calprotectin and Anti-Cyclic Citrullinated Peptide in Rheumatoid Arthritis Assessment. *Diagnostics (Basel)*. 2025;16(1):23. Published 2025 Dec 21. doi:10.3390/diagnostics16010023

276. Santos KO, Sassaki LY, Brusco De Freitas M, et al. Salivary Biomarkers in Crohn's Disease and Ulcerative Colitis: A Scoping Review and Evidence Map. *Int J Mol Sci*. 2025;26(22):11195. Published 2025 Nov 19. doi:10.3390/ijms262211195

277. El-Sadek HM, Mohamed EES, Risha BEM, Rageh MA. Estimation of salivary myeloid-related protein (calprotectin) level in patients with oral lichen planus: a case-control study. *Oral Maxillofac Surg*. 2025;29(1):167. Published 2025 Oct 8. doi:10.1007/s10006-025-01461-0

278. Zakrzewski M, Gornowicz A, Zakrzewska M, Bielawska A, Maciorkowska E. Selected Markers of Inflammation in the Saliva of Children Infected with *Helicobacter pylori*. *Int J Mol Sci*. 2024;25(23): 12780. Published 2024 Nov 28. doi:10.3390/ijms252312780

279. Nasir Kansestani A, Zare ME, Tong Q, Zhang J. Comparison of faecal protein biomarkers' diagnostic accuracy for colorectal advanced neoplasms: a systematic review and meta-analysis. *Sci Rep*. 2022;12(1):2623. Published 2022 Feb 16. doi:10.1038/s41598-022-06689-4

280. Shiroki T, Yokoyama M, Tanuma N, et al. Enhanced expression of the M2 isoform of pyruvate kinase is involved in gastric cancer development by regulating cancer-specific metabolism. *Cancer Sci*. 2017;108(5):931-940. doi:10.1111/cas.13211

281. Shiroki T, Yokoyama M, Tanuma N, et al. Enhanced expression of the M2 isoform of pyruvate kinase is involved in gastric cancer development by regulating cancer-specific metabolism. *Cancer Sci*. 2017;108(5):931-940. doi:10.1111/cas.13211

282. Ergün E, Toraman E, Barış Ö, Budak H, Demir T. Quantitative investigation of the bacterial content of periodontal abscess samples by real-time PCR. *J Microbiol Methods*. 2023;213:106826. doi:10.1016/j.mimet.2023.106826

283. Usui M, Miyagi S, Yamanaka R, et al. Measuring the Invisible: Microbial Diagnostics for Periodontitis-A Narrative Review. *Int J Mol Sci*. 2025;26(20):10172. Published 2025 Oct 19. doi:10.3390/ijms262010172

284. Lee MA, Kang SM, Kim SY, Kim JS, Kim JB, Jeong SH. Fluorescence change of Fusobacterium nucleatum due to Porphyromonas gingivalis. *J Microbiol*. 2018;56(9):628-633. doi:10.1007/s12275-018-7515-7

285. Shu M, Kuo S, Wang Y, et al. Porphyrin metabolisms in human skin commensal Propionibacterium acnes bacteria: potential application to monitor human radiation risk. *Curr Med Chem*. 2013;20(4):562-568. doi:10.2174/0929867311320040007

286. Ferrier C, Bendifallah S, Suisse S, et al. Saliva microRNA signature to diagnose endometriosis: A cost-effectiveness evaluation of the Endotest®. *BJOG*. 2023;130(4):396-406. doi:10.1111/1471-0528.17348

287. Zhang Y, Li L, Guo Y. Differential Association of Salivary Proinflammatory Mediators with Type 2 Diabetes: A Network Meta-Analysis. *Iran J Public Health*. 2024;53(12):2613-2624.

288. Carlucci AR, Bergo BR, Silva RNB, Bressane GD, Baeza M, Santos NCD. Effects of host modulation through omega-3 dietary supplementation on inflammatory outcomes in periodontitis: a scoping review. *Einstein (Sao Paulo)*. 2024;22:eRW0936. Published 2024 Dec 9. doi:10.31744/einstein_journal/2024RW0936

289. Koyyala VPB, Kantharia C, Darooka N, et al. Inflammatory Bowel Disease and Colorectal Cancer: An Eternal Fire in a Beautiful Garden. *South Asian J Cancer*. 2025;13(4):300-304. Published 2025 Jan 28. doi:10.1055/s-0045-1802335

290. Muraoka A, Suzuki M, Hamaguchi T, et al. *Fusobacterium* infection facilitates the development of endometriosis through the phenotypic transition of endometrial fibroblasts. *Sci Transl Med*. 2023;15(700):eadd1531. doi:10.1126/scitranslmed.add1531

291. Alavi SE, Ebrahimi Shahmabadi H, Sharma LA, Sharma A. The Role of the Oral Microbiome in Periodontal Disease: A Systematic Review of Microbial Associations and Therapeutic Implications. *Curr Microbiol*. 2025;83(1):64. Published 2025 Dec 9. doi:10.1007/s00284-025-04648-6

292. Xiao L, Zhang Q, Peng Y, Wang D, Liu Y. The effect of periodontal bacteria infection on incidence and prognosis of cancer: A systematic review and meta-analysis. *Medicine (Baltimore)*. 2020;99(15):e19698. doi:10.1097/MD.0000000000019698

293. Donatini B. Valaciclovir and/or Coriolus Versicolor Decreases the Risk of Transformation of Asymptomatic Monoclonal Gammapathies into Proliferative Disorders, J Case Rep Stud 2024;12 (2): 204. Published online 2024 Oct 14

294. Meléndez-Oliva E, Martínez-Pozas O, Sinatti P, et al. Relationship Between the Gut Microbiome, Tryptophan-Derived Metabolites, and Osteoarthritis-Related Pain: A Systematic Review with Meta-Analysis. *Nutrients*. 2025;17(2):264. Published 2025 Jan 12. doi:10.3390/nu17020264

295. Nikolova VL, Smith MRB, Hall LJ, Cleare AJ, Stone JM, Young AH. Perturbations in Gut Microbiota Composition in Psychiatric Disorders: A Review and Meta-analysis. *JAMA Psychiatry*. 2021;78(12):1343-1354. doi:10.1001/jamapsychiatry.2021.2573

296. Meyrel M, Varin L, Detaint B, Mouaffak F. Le microbiote intestinal : un nouvel acteur de la dépression ? [The intestinal microbiota: A new player in depression?]. *Encephale*. 2018;44(1):67-74. doi:10.1016/j.encep.2017.03.005

297. Meuric V, Le Gall-David S, Boyer E, et al. Signature of Microbial Dysbiosis in Periodontitis. *Appl Environ Microbiol*. 2017;83(14):e00462-17. Published 2017 Jun 30. doi:10.1128/AEM.00462-17

298. Mylona V, Anagnostaki E, Chiniforush N, Barikani H, Lynch E, Grootveld M. Photobiomodulation Effects on Periodontal Ligament Stem Cells: A Systematic Review of *In Vitro* Studies. *Curr Stem Cell Res Ther*. 2024;19(4):544-558. doi:10.2174/1574888X17666220527090321

299. Kim YM, Ha AN, Kim JW, Kim SJ. Double-blind Randomized Study to Evaluate the Safety and Efficacy of Over-the-counter Tooth-whitening Agents

Containing 2.9% Hydrogen Peroxide. *Oper Dent*. 2018;43(3):272-281. doi:10.2341/16-379-C

300. Muniz FWMG, Cavagni J, Langa GPJ, Stewart B, Malheiros Z, Rösing CK. A Systematic Review of the Effect of Oral Rinsing with H_2O_2 on Clinical and Microbiological Parameters Related to Plaque, Gingivitis, and Microbes. *Int J Dent*. 2020;2020: 8841722. Published 2020 Oct 31. doi:10.1155/2020/8841722

301. Žekonis G, Šadzevičienė R, Balnytė I, et al. Clinical and Microbiological Effects of Weekly Supragingival Irrigation with Aerosolized 0.5% Hydrogen Peroxide and Formation of Cavitation Bubbles in Gingival Tissues after This Irrigation: A Six-Month Randomized Clinical Trial. *Oxid Med Cell Longev*. 2020;2020:3852431. Published 2020 Jul 31. doi:10.1155/2020/3852431

302. Tanthanuch S, Kukiattrakoon B, Naiyanart C, Promtong T, Yothinwatthanabamrung P, Pumpua S. Effect of Mouthwashes for COVID-19 Prevention on Surface Changes of Resin Composites. *Int Dent J*. 2023;73(4):511-517. doi:10.1016/j.identj.2022.10.004

303. Ionescu AC, Brambilla E, Manzoli L, Orsini G, Gentili V, Rizzo R. Efficacy of personal protective equipment and H_2O_2-based spray against coronavirus in dental setting. *Oral Dis*. 2022;28 Suppl 1(Suppl 1):1010-1012. doi:10.1111/odi.13736

304. O'Donnell VB, Thomas D, Stanton R, et al. Potential Role of Oral Rinses Targeting the Viral Lipid Envelope in SARS-CoV-2 Infection. *Function (Oxf)*. 2020;1(1):zqaa002. doi:10.1093/function/zqaa002

305. Niu L, Chen S, Yang X, et al. Vitamin D decreases Porphyromonas gingivalis internalized into macrophages by promoting autophagy. *Oral Dis*. 2021;27(7):1775-1788. doi:10.1111/odi.13696

306. Wang B, Wang C, Li H. The impact of intermittent fasting on body composition and cardiometabolic outcomes in overweight and obese adults: a systematic review and meta-analysis of randomized controlled trials. *Nutr J*. 2025;24 (1):120. Published 2025 Jul 30. doi:10.1186/s12937-025-01178-6

307. Chu P, He Y, Hu F, Wang X. The effects of low FODMAP diet on gut microbiota regulation: A systematic review and meta-analysis. *J Food Sci*. 2025;90(3):e70072. doi:10.1111/1750-3841.70072

308. Mo C, Zhou S, Du Z, Huang X. Impact of fructooligosaccharides on gut microbiota composition and metabolite production: implications for childhood obesity. *PeerJ*. 2025;13:e19894. Published 2025 Aug 25. doi:10.7717/peerj.19894

309. Satija A, Malik V, Rimm EB, Sacks F, Willett W, Hu FB. Changes in intake of plant-based diets and weight change: results from 3 prospective cohort studies. *Am J Clin Nutr*. 2019;110(3):574-582. doi:10.1093/ajcn/nqz049

310. Kesse-Guyot, E., Rebouillat, P., Payrastre, L. *et al.* Prospective association between organic food consumption and the risk of type 2 diabetes: findings from the NutriNet-Santé cohort study. *Int J Behav Nutr Phys Act* **17,** 136 (2020). https://doi.org/10.1186

311. Baudry J, Assmann KE, Touvier M, et al. Association of Frequency of Organic Food Consumption With Cancer Risk: Findings From the NutriNet-Santé Prospective Cohort Study. *JAMA Intern Med*. 2018;178(12):1597-1606. doi:10.1001/jamainternmed.2018.4357

312. Monteiro CA, Louzada ML, Steele-Martinez E, et al. Ultra-processed foods and human health: the main thesis and the evidence. *Lancet*. 2025;406 (10520):2667-2684. doi:10.1016/S0140-6736(25)01565-X

313. Mendoza K, Smith-Warner SA, Rossato SL, et al. Ultra-processed foods and cardiovascular disease: analysis of three large US prospective cohorts and a systematic review and meta-analysis of prospective cohort studies. *Lancet Reg Health Am*. 2024;37:100859. Published 2024 Sep 2. doi:10.1016/j.lana.2024.100859

314. Oyebode O, Gordon-Dseagu V, Walker A, Mindell JS. Fruit and vegetable consumption and all-cause, cancer and CVD mortality: analysis of Health Survey for England data. *J Epidemiol Community Health*. 2014;68(9):856-862. doi:10.1136/jech-2013-203500

315. Serrano Fernandez V, Seldas Palomino M, Laredo-Aguilera JA, Pozuelo-Carrascosa DP,

Carmona-Torres JM. High-Fiber Diet and Crohn's Disease: Systematic Review and Meta-Analysis. *Nutrients*. 2023;15(14):3114. Published 2023 Jul 12. doi:10.3390/nu15143114

316. Donatini B, Le Blaye I. Weight loss associated with maitake or tiny amounts of essential oils. *Annals of Case Reports and Reviews.* Published online 2021 Jun 17. doi: 10.39127/2574/5747/ACRR:246.

317. Donatini B, Le Blaye I. Medicinal Sulphur Polypore Mushroom Laetiporus sulphureus (Agaricomycetes) Plus Tiny Amounts of Essential Oils Decrease the Activity of Crohn Disease. *Int J Med Mushrooms*. 2019;21(3):267-273. doi:10.1615/IntJMedMushrooms.2019030122

318. Lu QY, Summanen PH, Lee RP, et al. Prebiotic Potential and Chemical Composition of Seven Culinary Spice Extracts. *J Food Sci*. 2017;82(8):1807-1813. doi:10.1111/1750-3841.13792

319. Radu CM, Radu CC, Zaha DC. SmartGel OV: A Natural *Origanum vulgare*-Based Adjunct for Periodontitis with Clinical and Microbiological Evaluation. *Medicina (Kaunas)*. 2025;61(8):1423. Published 2025 Aug 7. doi:10.3390/medicina61081423

320. Hezel MP, Weitzberg E. The oral microbiome and nitric oxide homoeostasis. *Oral Dis*. 2015;21(1):7-16. doi:10.1111/odi.12157

321. Koch CD, Gladwin MT, Freeman BA, Lundberg JO, Weitzberg E, Morris A. Enterosalivary nitrate metabolism and the microbiome: Intersection of microbial metabolism, nitric oxide and diet in cardiac and pulmonary vascular health. *Free Radic Biol Med*. 2017;105:48-67. doi:10.1016/j.freeradbiomed.2016.12.015

322. Ferrari M, Santini A, Protti A, et al. Inhaled nitric oxide in mechanically ventilated patients with COVID-19. *J Crit Care*. 2020;60:159-160. doi:10.1016/j.jcrc.2020.08.007

323. Tavazzi G, Pozzi M, Mongodi S, Dammassa V, Romito G, Mojoli F. Inhaled nitric oxide in patients admitted to intensive care unit with COVID-19 pneumonia. *Crit Care*. 2020;24(1):508. Published 2020 Aug 17. doi:10.1186/s13054-020-03222-9

324. Abou-Arab O, Huette P, Debouvries F, Dupont H, Jounieaux V, Mahjoub Y. Inhaled nitric oxide for critically ill Covid-19 patients: a prospective study. *Crit Care*. 2020;24(1):645. Published 2020 Nov 12. doi:10.1186/s13054-020-03371-x

325. Safaee Fakhr B, Di Fenza R, Gianni S, et al. Inhaled high dose nitric oxide is a safe and effective respiratory treatment in spontaneous breathing hospitalized patients with COVID-19 pneumonia. *Nitric Oxide*. 2021;116:7-13. doi:10.1016/j.niox.2021.08.003

326. Garren MR, Ashcraft M, Qian Y, Douglass M, Brisbois EJ, Handa H. Nitric oxide and viral infection: Recent developments in antiviral therapies and platforms. *Appl Mater Today*. 2021;22:100887. doi:10.1016/j.apmt.2020.100887

327. Yu L, Sun B, Liu X, et al. Nitric oxide inhibits the transcription of E6 gene of human papillomavirus. *Acta Virol*. 2018;62(4):447-453. doi:10.4149/av_2018_414

328. Ellermann-Eriksen S. Macrophages and cytokines in the early defence against herpes simplex virus. *Virol J*. 2005;2:59. Published 2005 Aug 3. doi:10.1186/1743-422X-2-59

329. Tyring SK, Rosen T, Berman B, Stasko N, Durham T, Maeda-Chubachi T. A Phase 2 Controlled Study of SB206, a Topical Nitric Oxide-Releasing Drug for Extragenital Wart Treatment. *J Drugs Dermatol*. 2018;17(10):1100-1105.

330. Gao X, Wang J, Wang W, Wang M, Zhang J. eNOS Genetic Polymorphisms and Cancer Risk: A Meta-Analysis and a Case-Control Study of Breast Cancer. *Medicine (Baltimore)*. 2015;94(26):e972. doi:10.1097/MD.0000000000000972

331. Nikolić ZZ, Pavićević DLj, Romac SP, Brajušković GN. Genetic variants within endothelial nitric oxide synthase gene and prostate cancer: a meta-analysis. *Clin Transl Sci*. 2015;8(1):23-31. doi:10.1111/cts.12203

332. Slanc P, Doljak B, Mlinaric A, Strukelj B. Screening of wood damaging fungi and macrofungi for inhibitors of pancreatic lipase. *Phytother Res*. 2004;18(9):758-762. doi:10.1002/ptr.1548

333. Donatini B. Le Grifola frondosa (maïtaké): un régulateur du syndrome métabolique: poids, cholestérol, glycémie et hypertension artérielle; accessoirement un immunostimulant. *Phytothérapie* 2011;9:376-379. doi.org/10.1007/s10298-011-0669-7

334. Eliza WL, Fai CK, Chung LP. Efficacy of Yun Zhi (Coriolus versicolor) on survival in cancer patients: systematic review and meta-analysis. *Recent Pat Inflamm Allergy Drug Discov*. 2012;6(1):78-87. doi:10.2174/187221312798889310

335. Zhong L, Yan P, Lam WC, Yao L, Bian Z. *Coriolus Versicolor* and *Ganoderma Lucidum* Related Natural Products as an Adjunct Therapy for Cancers: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Front Pharmacol*. 2019;10:703. Published 2019 Jul 3. doi:10.3389/fphar.2019.00703

336. Donatini B. Prévention des récurrences d'herpès par l'association Ganoderma lucidum + Coriolus versicolor. *Phytothérapie* 2010;8:259-260. doi.org/10.1007/s10298-010-0564-7

337. Donatini B. Control of oral human papillomavirus (HPV) by medicinal mushrooms, Trametes versicolor and Ganoderma lucidum: a preliminary clinical trial. *Int J Med Mushrooms*. 2014;16(5):497-498. doi:10.1615/intjmedmushrooms.v16.i5.80

338. Donatini B. Diminution de l'expression du virus d'Epstein Barr (EBV) dans la muqueuse gingivale par la prise durant deux mois de Ganoderma lucidum, Coriolus versicolor et Lentinus edodes . *Phytothérapie* 2015;13:231–233. doi.org/10.1007/s10298-015-0952-4

339. Palacios S, Losa F, Dexeus D, Cortés J. Beneficial effects of a Coriolus versicolor-based vaginal gel on cervical epithelization, vaginal microbiota and vaginal health: a pilot study in asymptomatic women. *BMC Womens Health*. 2017;17(1):21. Published 2017 Mar 16. doi:10.1186/s12905-017-0374-2

340. Donatini B, Le Blaye I. Preventive Effect of Food Mushrooms against Herpetic or SARS-Cov-2 Infections. *Annals of Case Reports and Reviews*. Published online 2021 Mar 08. doi: 10.39127/2574/5747/ACRR:1000204

341. Trovato A, Siracusa R, Di Paola R, et al. Redox modulation of cellular stress response and lipoxin A4 expression by Coriolus versicolor in rat brain: Relevance to Alzheimer's disease pathogenesis. *Neurotoxicology*. 2016;53:350-358. doi:10.1016/j.neuro.2015.09.012

342. Trovato Salinaro A, Pennisi M, Di Paola R, et al. Neuroinflammation and neurohormesis in the pathogenesis of Alzheimer's disease and Alzheimer-linked pathologies: modulation by nutritional mushrooms. *Immun Ageing*. 2018;15:8. Published 2018 Feb 14. doi:10.1186/s12979-017-0108-1

343. Hamanaka T, Sakasegawa Y, Ohmoto A, Kimura T, Ando T, Doh-ura K. Anti-prion activity of protein-bound polysaccharide K in prion-infected cells and animals. *Biochem Biophys Res Commun*. 2011;405(2):285-290. doi:10.1016/j.bbrc.2011.01.030

344. Pramudya M, Wahyuningsih SPA. Immunomodulatory potential of polysaccharides from *Coriolus versicolor* against intracellular bacteria *Neisseria gonorrhoeae*. *Vet World*. 2019;12(6):735-739. doi:10.14202/vetworld.2019.735-739

345. Shi SH, Yang WT, Huang KY, et al. β-glucans from Coriolus versicolor protect mice against S. typhimurium challenge by activation of macrophages. *Int J Biol Macromol*. 2016;86:352-361. doi:10.1016/j.ijbiomac.2016.01.058

346. Wang Z, Dong B, Feng Z, Yu S, Bao Y. A study on immunomodulatory mechanism of Polysaccharopeptide mediated by TLR4 signaling pathway. *BMC Immunol*. 2015;16:34. Published 2015 Jun 2. doi:10.1186/s12865-015-0100-5

347. Rodríguez-Valentín M, López S, Rivera M, Ríos-Olivares E, Cubano L, Boukli NM. Naturally Derived Anti-HIV Polysaccharide Peptide (PSP) Triggers a Toll-Like Receptor 4-Dependent Antiviral Immune Response. *J Immunol Res*. 2018;2018:8741698. Published 2018 Jul 15. doi:10.1155/2018/8741698

348. Scarpari M, Reverberi M, Parroni A, et al. Tramesan, a novel polysaccharide from Trametes versicolor. Structural characterization and biological effects. *PLoS One*. 2017;12(8):e0171412. Published 2017 Aug 22. doi:10.1371/journal.pone.0171412

349. Lee SH, Hwang HK, Kang CM, Lee WJ. Potential Impact of Phellinus linteus on Adherence to Adjuvant Treatment After Curative Resection of Pancreatic Ductal Adenocarcinoma: Outcomes of a Propensity Score-Matched Analysis. *Integr Cancer Ther*. 2019;18:1534735418816825. doi:10.1177/1534735418816825

350. Mishra A, Ganeshpurkar A, Dubey N. In Silico Interaction of Phellilane L with HmuY: A Promising Therapeutic Strategy against Porphyromonas gingivalis in Chronic Periodontitis. *Int J Med Mushrooms*. 2025;27(7):31-43. doi:10.1615/IntJMedMushrooms.2025058014

351. Kim JE, Takanche JS, Yun BS, Yi HK. Anti-inflammatory character of Phelligridin D modulates periodontal regeneration in lipopolysaccharide-induced human periodontal ligament cells. *J Periodontal Res*. 2018;53(5):816-824. doi:10.1111/jre.12570

352. Huh S, Lee S, Choi SJ, et al. Quercetin Synergistically Inhibit EBV-Associated Gastric Carcinoma with *Ganoderma lucidum* Extracts. *Molecules*. 2019;24(21):3834. Published 2019 Oct 24. doi:10.3390/molecules24213834

353. Saint-André V, Charbit B, Biton A, et al. Smoking changes adaptive immunity with persistent effects. *Nature*. 2024;626(8000):827-835. doi:10.1038/s41586-023-06968-8

354. Pigossi SC, Oliveira JA, de Medeiros MC, Soares LFF, D'Silva NJ. Demystifying the link between periodontitis and oral cancer: a systematic review integrating clinical, pre-clinical, and in vitro data. *Cancer Metastasis Rev*. 2025;44(3):67. Published 2025 Sep 9. doi:10.1007/s10555-025-10285-z

355. Gulbahce N, Yan H, Dricot A, et al. Viral perturbations of host networks reflect disease etiology. *PLoS Comput Biol*. 2012;8(6):e1002531. doi:10.1371/journal.pcbi.1002531

356. Dong WB, Jiang YL, Zhu ZL, et al. Structural and enzymatic characterization of the sialidase SiaPG from Porphyromonas gingivalis. *Acta Crystallogr F Struct Biol Commun*. 2023;79(Pt 4):87-94. doi:10.1107/S2053230X23001735

357. Wahasugui TC, Nakano V, Piazza RM, Avila-Campos MJ. Phenotypic and genotypic features of Aggregatibacter actinomycetemcomitans isolated from patients with periodontal disease. *Diagn Microbiol Infect Dis*. 2013;75(4):366-372. doi:10.1016/j.diagmicrobio.2012.12.013

358. Frey AM, Satur MJ, Phansopa C, et al. Characterization of *Porphyromonas gingivalis* sialidase and disruption of its role in host-pathogen interactions. *Microbiology (Reading)*. 2019;165(11):1181-1197. doi:10.1099/mic.0.000851

359. Zhu B, Macleod LC, Newsome E, Liu J, Xu P. Aggregatibacter actinomycetemcomitans mediates protection of Porphyromonas gingivalis from Streptococcus sanguinis hydrogen peroxide production in multi-species biofilms. *Sci Rep*. 2019;9(1):4944. Published 2019 Mar 20. doi:10.1038/s41598-019-41467-9

360. Herrero ER, Boon N, Bernaerts K, et al. Clinical concentrations of peroxidases cause dysbiosis in in vitro oral biofilms. *J Periodontal Res*. 2018;53(3):457-466. doi:10.1111/jre.12534

361. Kim JY, Kim DW, Hwang BS, et al. Neuraminidase Inhibitors from the Fruiting Body of Phellinus igniarius. *Mycobiology*. 2016;44(2):117-120. doi:10.5941/MYCO.2016.44.2.117

362. Hwang BS, Lee IK, Choi HJ, Yun BS. Anti-influenza activities of polyphenols from the medicinal mushroom Phellinus baumii. *Bioorg Med Chem Lett*. 2015;25(16):3256-3260. doi:10.1016/j.bmcl.2015.05.081

363. Impellizzeri D, Fusco R, Genovese T, et al. Coriolus Versicolor Downregulates TLR4/NF-κB Signaling Cascade in Dinitrobenzenesulfonic Acid-Treated Mice: A Possible Mechanism for the Anti-Colitis Effect. *Antioxidants (Basel)*. 2022;11(2):406. Published 2022 Feb 17. doi:10.3390/antiox11020406

364. Baty JJ, Stoner SN, Scoffield JA. Oral Commensal Streptococci: Gatekeepers of the Oral Cavity. *J Bacteriol*. 2022;204(11):e0025722. doi:10.1128/jb.00257-22

365. Lima HR, Gelani V, Fernandes AP, et al. The essential role of toll like receptor-4 in the control of Aggregatibacter actinomycetemcomitans infection in mice. *J Clin Periodontol*. 2010;37(3):248-254. doi:10.1111/j.1600-051X.2009.01531.x

366. Bor B, Cen L, Agnello M, Shi W, He X. Morphological and physiological changes induced by contact-dependent interaction between Candida albicans and Fusobacterium nucleatum. *Sci Rep*. 2016;6:27956. Published 2016 Jun 14. doi:10.1038/srep27956

367. Wu T, Cen L, Kaplan C, et al. Cellular Components Mediating Coadherence of Candida albicans and Fusobacterium nucleatum. *J Dent Res*. 2015;94(10):1432-1438. doi:10.1177/0022034515593706

368. Zakaria MN, Takeshita T, Shibata Y, et al. Microbial community in persistent apical periodontitis: a 16S rRNA gene clone library analysis. *Int Endod J*. 2015;48(8):717-728. doi:10.1111/iej.12361

369. Chen Y, Qiu X, Wang W, et al. Human papillomavirus infection and cervical intraepithelial neoplasia progression are associated with increased vaginal microbiome diversity in a Chinese cohort. *BMC Infect Dis*. 2020;20(1):629. Published 2020 Aug 26. doi:10.1186/s12879-020-05324-9

370. Di Paola M, Sani C, Clemente AM, et al. Characterization of cervico-vaginal microbiota in women developing persistent high-risk Human Papillomavirus infection. *Sci Rep*. 2017;7(1):10200. Published 2017 Aug 31. doi:10.1038/s41598-017-09842-6

371. Zhang Z, Zhang D, Xiao BB, et al. *Zhonghua Fu Chan Ke Za Zhi*. 2018;53(7):471-480. doi:10.3760/cma.j.issn.0529-567x.2018.07.006

372. Abed J, Maalouf N, Parhi L, Chaushu S, Mandelboim O, Bachrach G. Tumor Targeting by *Fusobacterium nucleatum*: A Pilot Study and Future Perspectives. *Front Cell Infect Microbiol*. 2017;7:295. Published 2017 Jun 30. doi:10.3389/fcimb.2017.00295

373. Liao K, Wen J, Liu Z, et al. The role of intratumoral microbiome in the occurrence, proliferation, metastasis of colorectal cancer and its underlying therapeutic strategies. *Ageing Res Rev*. 2025;111:102820. doi:10.1016/j.arr.2025.102820

374. Li DH, Li ZP, Yan Zhang, et al. Fecal Fusobacterium nucleatum harbored virulence gene fadA are associated with ulcerative colitis and clinical outcomes. *Microb Pathog*. 2021;157:104964. doi:10.1016/j.micpath.2021.104964

375. Jung YS, Han M, Park S, Kim WH, Cheon JH. Cancer Risk in the Early Stages of Inflammatory Bowel Disease in Korean Patients: A Nationwide Population-based Study. *J Crohns Colitis*. 2017;11(8):954-962. doi:10.1093/ecco-jcc/jjx040

376. Luetke-Eversloh M, Hammer Q, Durek P, et al. Human cytomegalovirus drives epigenetic imprinting of the IFNG locus in NKG2Chi natural killer cells. *PLoS Pathog*. 2014;10(10):e1004441. Published 2014 Oct 16. doi:10.1371/journal.ppat.1004441

377. Valour F, Perpoint T, Sénéchal A, et al. Interferon-γ Autoantibodies as Predisposing Factor for Nontuberculous Mycobacterial Infection. *Emerg Infect Dis*. 2016;22(6):1124-1126. doi:10.3201/eid2206.151860

378. Suzuki Y, Saito J, Munakata M, Shibata Y. Hydrogen sulfide as a novel biomarker of asthma and chronic obstructive pulmonary disease. *Allergol Int*. 2021;70(2):181-189. doi:10.1016/j.alit.2020.10.003

379. Viegas J, Esteves AF, Cardoso EM, Arosa FA, Vitale M, Taborda-Barata L. Biological Effects of Thermal Water-Associated Hydrogen Sulfide on Human Airways and Associated Immune Cells: Implications for Respiratory Diseases. *Front Public Health*. 2019;7:128. Published 2019 Jun 5. doi:10.3389/fpubh.2019.00128

380. Katopodis S, Stylianakis E, Koufargyris P, et al. Hydrogen sulfide to modulate Glycated hemoglobin and gut microbiome in type 2 diabetes mellitus. *Metabol Open*. 2025;28:100405. Published 2025 Oct 11. doi:10.1016/j.metop.2025.100405

381. Sun Y, Wang XM, Chen YH, Zhu RX, Liao CC. Exhaled hydrogen sulfide in patients with chronic obstructive pulmonary disease and its correlation with exhaled nitric oxide. *Chin Med J (Engl)*. 2013;126(17):3240-3244.

382. Du P, Tseng Y, Liu P, et al. Role of exhaled hydrogen sulfide in the diagnosis of colorectal cancer. *BMJ Open Gastroenterol*. 2024;11(1): e001229. Published 2024 Feb 20. doi:10.1136/bmjgast-2023-001229

383. Donatini B, Le Blaye I. Exhaled Volatile Organic Compounds in Patients with Colonic Polyps. J Case Rep Stud 2022;10(3):301. Published online 2022 sept.

384. Altaany Z, Yang G, Wang R. Crosstalk between hydrogen sulfide and nitric oxide in endothelial cells. *J Cell Mol Med*. 2013;17(7):879-888. doi:10.1111/jcmm.12077

385. Yu B, Ichinose F, Bloch DB, Zapol WM. Inhaled nitric oxide. *Br J Pharmacol*. 2019;176(2): 246-255. doi:10.1111/bph.14512

386. Kurhaluk N, Kołodziejska R, Kamiński P, Tkaczenko H. Integrative Neuroimmune Role of the Parasympathetic Nervous System, Vagus Nerve and Gut Microbiota in Stress Modulation: A Narrative Review. *Int J Mol Sci*. 2025;26(23):11706. Published 2025 Dec 3. doi:10.3390/ijms262311706

387. Liao W, Ye T, Liu H. Prognostic Value of Inducible Nitric Oxide Synthase (iNOS) in Human Cancer: A Systematic Review and Meta-Analysis. *Biomed Res Int*. 2019;2019:6304851. Published 2019 Jun 4. doi:10.1155/2019/6304851

388. Pan L, Yang S, Wang J, Xu M, Wang S, Yi H. Inducible nitric oxide synthase and systemic lupus erythematosus: a systematic review and meta-analysis. *BMC Immunol*. 2020;21(1):6. Published 2020 Feb 17. doi:10.1186/s12865-020-0335-7

389. Kiss H, Örlős Z, Gellért Á, et al. Exhaled Biomarkers for Point-of-Care Diagnosis: Recent Advances and New Challenges in Breathomics. *Micromachines (Basel)*. 2023;14(2):391. Published 2023 Feb 4. doi:10.3390/mi14020391

390. Damiani G, Pacifico A, Rizzi M, et al. Patients with psoriatic arthritis have higher levels of FeNO than those with only psoriasis, which may reflect a higher prevalence of a subclinical respiratory involvement. *Clin Rheumatol*. 2020;39(10):2981-2988. doi:10.1007/s10067-020-05050-2

391. Schuster A, Thakur A, Wang Z, Borowski AG, Thomas JD, Tang WH. Increased exhaled nitric oxide levels after exercise in patients with chronic systolic heart failure with pulmonary venous hypertension. *J Card Fail*. 2012;18(10):799-803. doi:10.1016/j.cardfail.2012.08.356

392. Protopapas AA, Vradelis S, Karampitsakos T, Steiropoulos P, Chatzimichael A, Paraskakis E. Elevated Levels of Alveolar Nitric Oxide May Indicate Presence of Small Airway Inflammation in Patients with Inflammatory Bowel Disease. *Lung*. 2019;197(5):663-670. doi:10.1007/s00408-019-00253-0

393. Dao MC, Everard A, Aron-Wisnewsky J, et al. Akkermansia muciniphila and improved metabolic health during a dietary intervention in obesity: relationship with gut microbiome richness and ecology. *Gut*. 2016;65(3):426-436. doi:10.1136/gutjnl-2014-308778

394. Li X, Guo G, Shi Q, Chen Q, Li L. Association study between intestinal microbiota dysbiosis in inflammatory bowel disease and the global disease burden growth trend. *Front Med (Lausanne)*. 2025; 12:1635242. Published 2025 Nov 26. doi:10.3389/fmed.2025.1635242

395. Niccolai E, Baldi S, Ricci F, et al. Evaluation and comparison of short chain fatty acids composition in gut diseases. *World J Gastroenterol*. 2019;25 (36):5543-5558. doi:10.3748/wjg.v25.i36.5543

396. Routy B, Le Chatelier E, Derosa L, et al. Gut microbiome influences efficacy of PD-1-based immunotherapy against epithelial tumors. *Science*. 2018;359(6371):91-97. doi:10.1126/science.aan3706

397. Zhang X, Wang X, Zhao H, Cao R, Dang Y, Yu B. Imbalance of Microbacterial Diversity Is Associated with Functional Prognosis of Stroke. *Neural Plast*. 2023;2023:6297653. Published 2023 May 8. doi:10.1155/2023/6297653

398. Huang KC, Lin CY, Chuang PY, et al. Microbiota diversity and its influence on diabetic osteoporosis development. *Biochem Biophys Res Commun*. 2025;790:152884. doi:10.1016/j.bbrc.2025.152884

399. de la Cuesta-Zuluaga J, Mueller NT, Álvarez-Quintero R, et al. Higher Fecal Short-Chain Fatty Acid Levels Are Associated with Gut Microbiome Dysbiosis, Obesity, Hypertension and Cardiometabolic Disease Risk Factors. *Nutrients*. 2018;11(1):51. Published 2018 Dec 27. doi:10.3390/nu11010051

400. Takeuchi-Hatanaka K, Shirahase Y, Yoshida T, et al. Salivary short chain fatty acids serve as biomarkers of periodontal inflammatory burden. *Sci Rep*. 2025;16(1):1786. Published 2025 Dec 21. doi:10.1038/s41598-025-31364-9

401. Yang W, Zhang Y, Xu Y, Diao J, Zheng S, Yuan C. Gut Microbial Metabolite Butyrate Regulates Treg/Th17 Cell Balance to Alleviate Diabetic Periodontitis. *J Clin Periodontol*. 2026;53(2):321-333. doi:10.1111/jcpe.70041

402. Donatini B, Le Blaye I (2020) Exhaled Volatile Organic Compounds in Patients with a Medical History of Cancer/Dysplasia. *J Case Rep Stud* 2020; 8(3):303. Published online 2020 Dec 21

403. Sivarao DV, Mashimo H, Goyal RK. Pyloric sphincter dysfunction in nNOS-/- and W/Wv mutant mice: animal models of gastroparesis and duodenogastric reflux. *Gastroenterology*. 2008; 135(4):1258-1266. doi:10.1053/j.gastro.2008.06.039

404. Donatini B. Intérêt de l'échographie abdominale pour l'analyse des vidanges, des reflux et de la tonicité gastro-duodéno-jéjuno-iléale. *Revue Inist Hegel* 2019;9:1-7. doi.org/10.4267/2042/70441

405. Camilleri M. The role of gastric function in control of food intake (and body weight) in relation to obesity, as well as pharmacological and surgical interventions. *Neurogastroenterol Motil*. 2024;36 (2):e14660. doi:10.1111/nmo.14660

406. Enache RM, Profir M, Roşu OA, Creţoiu SM, Gaspar BS. The Role of Gut Microbiota in the Onset and Progression of Obesity and Associated Comorbidities. *Int J Mol Sci*. 2024;25(22):12321. Published 2024 Nov 16. doi:10.3390/ijms252212321

407. Ganamurali N, Sabarathinam S. Bidirectional interplay between the gut microbiota and GLP-1 receptor agonists: towards Microbiome-Mediated therapeutics in type 2 diabetes mellitus. *J Diabetes Metab Disord*. 2026;25(1):44. Published 2026 Jan 27. doi:10.1007/s40200-025-01834-y

408. Oliveira MS, Paula MSA, Cardoso MM, et al. Exploring the antimicrobial efficacy of tea tree essential oil and chitosan against oral pathogens to overcome antimicrobial resistance. *Microb Pathog*. 2024;196:107006. doi:10.1016/j.micpath.2024.107006

409. Lotfy WA, Matar MA, Alkersh BM. Evaluation of the antibacterial activity of cinnamon essential oil and its individual compounds on Aggregatibacter actinomycetemcomitans isolated from black extrinsic tooth stain: an in vitro study. *Eur Arch Paediatr Dent*. 2023;24(5):661-674. doi:10.1007/s40368-023-00841-y

410. Maggini V, Semenzato G, Gallo E, Nunziata A, Fani R, Firenzuoli F. Antimicrobial Activity of *Syzygium aromaticum* Essential Oil in Human Health Treatment. *Molecules*. 2024;29(5):999. Published 2024 Feb 25. doi:10.3390/molecules29050999

411. Kouidhi B, Al Qurashi YM, Chaieb K. Drug resistance of bacterial dental biofilm and the potential use of natural compounds as alternative for prevention and treatment. *Microb Pathog*. 2015; 80:39-49. doi:10.1016/j.micpath.2015.02.007

412. Lakhdar L, Hmamouchi M, Rida S, Ennibi O. Antibacterial activity of essential oils against periodontal pathogens: a qualitative systematic review. *Odontostomatol Trop*. 2012;35(140):38-46.

413. Choi DJ, Cho S, Seo JY, Lee HB, Park YI. Neuroprotective effects of the Phellinus linteus ethyl acetate extract against H2O2-induced apoptotic cell death of SK-N-MC cells. *Nutr Res*. 2016;36(1): 31-43. doi:10.1016/j.nutres.2015.11.005

414. Song AR, Sun XL, Kong C, et al. Discovery of a new sesquiterpenoid from Phellinus ignarius with antiviral activity against influenza virus. *Arch Virol*. 2014;159(4):753-760. doi:10.1007/s00705-013-1857-6

415. Ichinohe T, Ainai A, Nakamura T, et al. Induction of cross-protective immunity against influenza A virus H5N1 by an intranasal vaccine with extracts of mushroom mycelia. *J Med Virol*. 2010;82(1):128-137. doi:10.1002/jmv.21670

416. Zaharieva MM, Dimitrova LL, Philipov S, et al. In Vitro Antineoplastic and Antiviral Activity and In Vivo Toxicity of *Geum urbanum* L. Extracts. *Molecules*. 2021;27(1):245. Published 2021 Dec 31. doi:10.3390/molecules27010245

417. Zhang Q, Li Y, Zhong X, et al. Polyphenolic-protein-polysaccharide conjugates from Spica of Prunella vulgaris: Chemical profile and anti-herpes simplex virus activities. *Int J Biol Macromol*. Published online December 3, 2021. doi:10.1016/j.ijbiomac.2021.11.200

418. Gescher K, Hensel A, Hafezi W, Derksen A, Kühn J. Oligomeric proanthocyanidins from Rumex acetosa L. inhibit the attachment of herpes simplex virus type-1. *Antiviral Res*. 2011;89(1):9-18. doi:10.1016/j.antiviral.2010.10.007

419. Maffei ME, Salata C, Gribaudo G. Tackling the Future Pandemics: Broad-Spectrum Antiviral Agents (BSAAs) Based on A-Type Proanthocyanidins. *Molecules*. 2022;27(23):8353. Published 2022 Nov 30. doi:10.3390/molecules27238353

420. Romanos-Nanclares A. Cruciferous vegetable intake, dietary glucosinolate and risk of breast cancer in 2 large prospective studies. SABCS 2025: RF1-07.

421. Talour K, Abasq C, Sassolas B, Le Ru Y, Jannou V, Misery L. DRESS-like syndrome induced by shiitake mushroom. *Eur J Dermatol*. 2011;21(4):640-641. doi:10.1684/ejd.2011.1398

422. Hamer SE, Kulkarni K, Cohen SN. Shiitake dermatitis with oral ulceration and pustules. *Clin Exp Dermatol*. 2015;40(3):332-333. doi:10.1111/ced.12500

423. Goikoetxea MJ, Fernández-Benítez M, Sanz ML. Food allergy to Shiitake (Lentinus edodes) manifested as oesophageal symptoms in a patient with probable eosinophilic oesophagitis. *Allergol Immunopathol (Madr)*. 2009;37(6):333-334. doi:10.1016/j.aller.2009.05.002

424. Levy AM, Kita H, Phillips SF, et al. Eosinophilia and gastrointestinal symptoms after ingestion of shiitake mushrooms. *J Allergy Clin Immunol*. 1998;101(5):613-620. doi:10.1016/S0091-6749(98)70168-X

425. Kusumoto M, Koganemaru M, Nakayama G, Iwamoto R. Dietary small bowel obstruction. *BMJ Case Rep*. 2013;2013:bcr2012007950. Published 2013 Jan 25. doi:10.1136/bcr-2012-007950

426. Karanovic S, George S, Topham E. Don't miss shiitake dermatitis: a case report. *Br J Gen Pract*. 2014;64(625):426-427. doi:10.3399/bjgp14X681193

427. Adriano AR, Acosta ML, Azulay DR, Quiroz CD, Talarico SR. Shiitake dermatitis: the first case reported in Brazil. *An Bras Dermatol*. 2013;88(3):417-419. doi:10.1590/abd1806-4841.20131849

428. Ampere A, Delhaes L, Soots J, Bart F, Wallaert B. Hypersensitivity pneumonitis induced by Shiitake mushroom spores. *Med Mycol*. 2012;50(6):654-657. doi:10.3109/13693786.2012.658091

429. Boucher J, Gilbert C, Bose S, Tessier PA. S100A9: The Unusual Suspect Connecting Viral Infection and Inflammation. *J Immunol*. 2024;212(10):1523-1529. doi:10.4049/jimmunol.2300640

430. Hetland G, Fagerhol MK, Mirlashari MR, et al. Elevated NET, Calprotectin, and Neopterin Levels Discriminate between Disease Activity in COVID-19, as Evidenced by Need for Hospitalization among Patients in Northern Italy. *Biomedicines*. 2024;12(4):766. Published 2024 Mar 30. doi:10.3390/biomedicines12040766

431. Shokri-Afra H, Moradi M, Musavi H, et al. Serum calprotectin can indicate current and future severity of COVID-19. *J Clin Lab Anal*. 2023;37(1):e24809. doi:10.1002/jcla.24809

432. Gatselis NK, Lyberopoulou A, Lygoura V, et al. Calprotectin serum levels on admission and during follow-up predict severity and outcome of patients with COVID-19: A prospective study. *Eur J Intern Med*. 2024;122:78-85. doi:10.1016/j.ejim.2023.11.001

433. Al-Kuraishy HM, Al-Gareeb AI, Al-Niemi MS, Alexiou A, Batiha GE. Calprotectin: The Link Between Acute Lung Injury and Gastrointestinal Injury in Covid-19: Ban or Boon. *Curr Protein Pept Sci*. 2022;23(5):310-320. doi:10.2174/1389203723666220610124303

434. Didriksson I, Lengquist M, Spångfors M, et al. Increasing plasma calprotectin (S100A8/A9) is associated with 12-month mortality and unfavourable

functional outcome in critically ill COVID-19 patients. *J Intensive Care*. 2024;12(1):26. Published 2024 Jul 9. doi:10.1186/s40560-024-00740-4

435. Zhang H, Zhang Q, Liu K, Yuan Z, Xu X, Dong J. Elevated level of circulating calprotectin correlates with severity and high mortality in patients with COVID-19. *Immun Inflamm Dis*. 2024;12(3):e1212. doi:10.1002/iid3.1212

436. Cardiero G, Palma D, Vano M, et al. Calprotectin Levels and Neutrophil Count Are Prognostic Markers of Mortality in COVID-19 Patients. *Diagnostics (Basel)*. 2022;12(10):2554. Published 2022 Oct 20. doi:10.3390/diagnostics12102554

437. Francavilla B, Velletrani G, Fiorelli D, et al. Circulating calprotectin as a potential biomarker of persistent olfactory dysfunctions in Post-COVID-19 patients. *Cytokine*. 2024;181:156688. doi:10.1016/j.cyto.2024.156688

438. Abu Hussein N, Machahua C, Ruchti SC, et al. Circulating calprotectin levels four months after severe and non-severe COVID-19. *BMC Infect Dis*. 2023;23(1):650. Published 2023 Oct 3. doi:10.1186/s12879-023-08653-7

439. Mao Q, Wang C, Wen W, et al. A meta-analysis of the association between calprotectin and the severity of COVID-19. *J Infect*. 2022;84(3):e31-e33. doi:10.1016/j.jinf.2022.01.022

440. Gu J, He F, Clifford GM, et al. A systematic review and meta-analysis on the relative and attributable risk of *Helicobacter pylori* infection and cardia and non-cardia gastric cancer. *Expert Rev Mol Diagn*. 2023;23(12):1251-1261. doi:10.1080/14737159.2023.2277377