Accuracy and Transparency in Medical English Terminology. A Focus on Suffixes, with Particular Reference to the Use of *-itis*

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Abstract

The prominent position of English in medical research makes term accuracy a very important feature in the successful transmission of meanings. Accuracy refers to the correctness of a term; it represents a very important feature of medical communication together with other principles, such as transparency. The latter is the possibility of immediately decoding the meaning of a term through an analysis of its surface form. Transparency does not always overlap with accuracy. In this respect, medical English terminology shows terms that, despite being transparent, are not used with the meaning an analysis of their form would suggest but are referred to different concepts. Starting from Tanchev's discussion regarding the misuse of osteoarthritis in orthopedic surgery, this paper investigated whether other cases exist in medical English of inaccurately used terms ending in -itis. A list of diseases and conditions referring to inflammatory diseases was retrieved from Wikipedia, and the PubMed database was queried by means of keywords to provide illustrative text strings. The International Classification of Diseases served as a reference tool for the analysis. The investigation was also supported by authoritative medical dictionaries. The results showed that even though most of the investigated English terminology ending in -itis is accurately used, cases exist of either improper use of the suffix or imprecision due to the lack of the suffix itself. Corrective terminology interventions should be carried out to guarantee accuracy and semantic precision in taxonomies of diseases to prevent any ambiguities and misleading uses in medical literature and practice.

Keywords: Medical English terminology, accuracy, transparency, affixation, terminology misuse

Introduction

The rapid and continuous progress of medical science entails a parallel renewal and development of its language. In this respect, if on the one hand the naming of new concepts is carried out in accordance with principles of

terminological standardization and systematization, on the other hand, the rapidity of medical knowledge does not always allow compliance with those principles.

Of the several important features of medical language at a lexical level, two are particularly important, accuracy and transparency. Accuracy refers to the correctness with which a given term is employed. Transparency is "the possibility to promptly access the meaning of a term through its surface form" (Gotti 2003: 37). A transparent term may not necessarily also be accurate. A term can be used with a meaning other than the one the analysis of its form refers to, or it can lack semantic components that are essential to obtain the thorough meaning with which that term is used. In medical language, terms are sometimes made up of two or more lexical components, which can be decoded separately, and by the union of all components, the meaning of the whole term is achieved. Thus, for example, the term *hysterosalpingo-oophorectomy* is composed of *hysteron* (uterus) + G. *salpinx* (trumpet/tube) + \bar{o} on (egg) + phoros (bearing) + ektomē (excision), forming the complete meaning "excision of the uterus, oviducts, and ovaries" (*Stedman's Medical Dictionary* 2006).

One of the strategies employed in medical discourse to ensure transparency is the use of conventional affixation. As a result of the need for systematization, affixes have assumed precise meanings. They generally refer consistently to the concepts with which they are conventionally associated. However, there are also cases where an affix is not used properly.

Affixation is the process where a bound morpheme, an affix (prefix, infix, and suffix) is attached to a root (or morphological base). The word "affix" comes from the Latin "affixus", the past participle of the verb "affigere", i.e. "to fasten to", ad- (to) + figere (fix). Affixation is a very important strategy in the terminology construction process in scientific texts and represents one of the main objects of investigation of derivational morphology (Ackema and Neeleman 2004; Lieber 2004; Montero-Fleta 2011; Manova 2016; O'Dell 2016; Carstairs-McCarthy 2018). Halliday (1978: 195) identifies affixation as one of the seven strategies in the word-formation process in specialized terminology:

- reinterpretation of existing words;
- creation of new words from a native stock;
- borrowing of words from foreign languages;
- calquing;
- invention of totally new words;
- creation of locutions:
- creation of new words from a non-native word stock.

Affixation, which in medical language is considerably manifest, is part of the second strategy listed above. This strategy includes several word-formation processes occurring thanks to inner mechanisms whereby a language uses existing resources to form neologisms. Montero-Fleta (2011) investigated the productivity of 14 affixes in two scientific English registers, medicine and

information science, and found out that affixation is a very productive resource in terminology production in both domains. Areej *et al.* (2018) highlight the importance of affixation in medical language and its role in changing the meaning and the grammatical function of terms. In their book on medical terminology, Cohen and Jones (2013) devote a large space to affixation, providing a comprehensive description of it. Suffixes, in particular, are given a broad account; they are classified according to the grammatical category they form, i.e. nouns and adjectives, and also include endings pertaining to diseases, treatments, and body systems.

The majority of medical affixes are of classical origin, Greek or Latin. The most common types of prefixes denote quantity, e.g. *hyper*- (excessive), as in the case of *hyperglycemia*; deviation from normality, e.g. *dys*- (difficult, painful, not functioning properly), as in *dyslipidemia*; site, e.g. *peri*- (around), as in *pericardium*; lack, e.g. *an*-, *a*-, as in *anemia*; time, e.g. *pre*- (before), as in *prenatal*. Suffixes usually indicate a test or a procedure, e.g. *-ectomy*, "removal of", as in *cholecystectomy*; a pathology, e.g. *-pnea*, "breathing", as in *dyspnea*; a specialty, e.g. *-ian*, which indicates someone who is a specialist or a practitioner, as in *pediatrician*; study of / science, i.e. *-ology*, as in *dermatology*, etc.

In medical language, the suffix of Greek origin -itis is conventionally added to anatomy terms to form nouns that denote the inflammation of the organ or tissue the terms refer to. Gingivitis, dermatitis, nephritis, blepharitis, and laryngitis are only some of the innumerable examples of terms where -itis is used to refer to an inflammatory condition. -Itis is often used as opposed to another common suffix, of Greek origin too, namely -osis (e.g. nephritis / nephrosis). - Osis deserves special attention as, unlike -itis, this suffix shows significant polysemy. The following is the definition given by Stedman's Medical Dictionary (2006) sub voce (s.v.) -osis:

Suffix meaning a process, condition, or state, usually abnormal or diseased; production or increase, physiologic or pathologic; an invasion or infestation; in the latter sense, it is similar to and often interchangeable with Greek *-iasis*, as seen in *trichinosis*, *trichiniasis*. [G.]

Merriam-Webster Medical Dictionary (https://www.merriam-webster.com/medical) registers the following definitions for *-osis*:

1. a) action; process; condition ex: *hypnosis*

b) abnormal or diseased condition ex: *leukosis*

2. increase: formation ex: *leukocytosis*

Both *Stedman's Medical Dictionary* (2006) and *Merriam-Webster Medical Dictionary* (https://www.merriam-webster.com/medical) display numerous meanings of *-osis*, ranging from generic definitions ('condition', 'process', 'state', 'action') to more specific meanings ('abnormal or diseased condition', 'production', 'increase', 'invasion', 'infestation'). Thus, *-osis* has not been given any systematicity. Although in the majority of the above-mentioned examples the underlying concepts of "condition" and/or "process" are present, *-osis* displays several other meanings referring to diseases/disorders of different nature and etiology.

The present study focused, in particular, on suffixes, with special attention to the use of *-itis*. More specifically, this study explored whether other cases exist of inaccurately used terms ending in *-itis* in medical English terminology. The starting point for the investigation was an article by Tanchev (2017), a Bulgarian orthopedic surgeon who examines the inaccuracy of *osteoarthritis*, a term that in the Anglo-Saxon literature and practice is used to refer to degenerative joint disease. In medical language, the suffix *-itis* is conventionally used to denote inflammation, and not a degenerative condition, which is usually referred to by the suffix *-osis*. Hence, the incorrectness of *osteoarthritis* as opposed to the appropriateness of *osteoarthrosis*, which is (or should be) the correct term to refer to degenerative joint disease.

Materials and Methods

To carry out the analysis for this work, the Wikipedia encyclopedia (https://www.wikipedia.org/) was initially searched for using the entry "inflammation." The search drove to the item "list of inflammatory disorders" and "list of types of inflammation by location." Both entries included a list of terms organized depending on the body system affected by the inflammation, i.e. Nervous System, further subdivided into CNS (Central Nervous System), including 5 entries; PNS (Peripheral Nervous System), 1 entry; Eye, 9 entries, and Ear, 4 entries; Cardiovascular System, 9 entries; Respiratory System, 11 entries; Digestive System, 32 entries; Integumentary System, 7 entries; Musculoskeletal System, 15 entries; Urinary System, 7 entries; Reproductive System, subdivided into Female, 16 entries, and Male, 8 entries; Endocrine System, 6 entries; Lymphatic System/Immune System, 4 entries, for a total of entries. these entries were searched in (https://pubmed.ncbi.nlm.nih.gov/) database to investigate whether the suffix itis was appropriately used, i.e. whether it was deployed with reference to inflammation or conditions of different nature. In this respect, strings of texts were retrieved as illustrative examples of terminology use.

The analysis was also supported by investigation of the World Health Organization (WHO) *International Classification of Diseases (ICD-11*, 2019), the global standard of health-related information, which contains more than one million terms referring to diseases and disorders, health-related conditions, causes of illness and death, medicines, vaccines, etc. Also, three authoritative medical dictionaries were consulted, viz. *Stedman's Medical Dictionary* (2006),

Dorland's Illustrated Medical Dictionary (2019), and Merriam-Webster Medical Dictionary (https://www.merriam-webster.com/medical).

Results

Investigation of terms referring to inflammation in *Wikipedia* yielded five cases worthy of attention, *osteoarthritis*, *cellulite*, *pneumonia*, *diphtheria*, and *pleurisy*.

As for *osteoarthritis*, this was found s.v. *arthritis* and introduced as follows: "There are over 100 types of arthritis. The most common forms are osteoarthritis (degenerative joint disease) and rheumatoid arthritis" (https://en.wikipedia.org/wiki/Arthritis). As can be seen from the description, and as already discussed by Tanchev (2017), *osteoarthritis* is not used to refer to an inflammatory disease, as its suffix would suggest, but to a degenerative process. In this respect, *PubMed* yielded innumerable examples of scientific articles where *osteoarthritis* is used in this way; some excerpts are reported below:

- 1. Osteoarthritis (OA), the most prevalent chronic joint disease, increases in prevalence with age, and affects majority of individuals over the age of 65 and is a leading musculoskeletal cause of impaired mobility in the elderly. Because the precise molecular mechanisms which are involved in the degradation of cartilage matrix and development of OA are poorly understood and there are currently no effective interventions to decelerate the progression of OA or retard the irreversible degradation of cartilage except for total joint replacement surgery. [...] (Xia *et al.* 2014: 495).
- 2. Osteoarthritis (OA) is a degenerative joint disease involving the cartilage and many of its surrounding tissues. Disease progression is usually slow but can ultimately lead to joint failure with pain and disability. OA of the hips and knees tends to cause the greatest burden to the population as pain and stiffness in these large weight-bearing joints often leads to significant disability requiring surgical intervention. [...] (Litwic *et al.* 2013: 185).
- 3. Osteoarthritis (OA), the syndrome of joint pain and dysfunction caused by joint degeneration, affects more people than any other joint disease. In most instances joint degeneration develops in the absence of an identifiable cause, but increasing age, excessive joint loading, and joint abnormalities and insults increase the risk of OA. [...] (Buckwalter and Martin 2019: 150).
- 4. Osteoarthritis (OA) is a disease associated to age or conditions that precipitate aging of articular cartilage, a post-mitotic tissue that remains functional until the failure of major homeostatic mechanisms. OA severely impacts the national health system costs and patients' quality of life because of pain and disability. [...] (D'Adamo *et al.* 2020: 1232).

As can be seen, there is no reference to inflammation in any of the above excerpts. Osteoarthritis is described as a disease characterized by joint degeneration (extracts 2 and 3) and is mostly associated with aging (extracts 1 and 4). This shows the incorrect use of the term, which should be more appropriately substituted with *osteoarthrosis*. To further confirm this, *Stedman's Medical Dictionary* (2006) and *Dorland's Illustrated Medical Dictionary* (2019) provide the following definitions s.v. *osteoarthritis*:

This word is a misnomer in that the dominant pathologic process is degeneration rather than inflammation. Arthritis characterized by erosion of articular cartilage, either primary or secondary to trauma or other conditions, which becomes soft, frayed, and thinned [...]; mainly affects weight-bearing joints, is more common in old people and animals. SYN arthrosis, degenerative arthritis, degenerative joint disease, osteoarthrosis (Stedman's Medical Dictionary 2006).

A non-inflammatory degenerative type of arthritis marked by degeneration of the articular cartilage, overgrowth of bone at the margins, and changes in the synovial membrane. [...] Also called degenerative joint disease (*Dorland's Illustrated Medical Dictionary* 2019).

However, it is important to say that even though not dominant, inflammation is a component of osteoarthrosis, and recent studies (Robinson *et al.* 2016; Marchev *et al.* 2017; Griffin and Scanzello 2019; Nees *et al.* 2019) have highlighted its important role in the development and progression of the disease. The fact that recent research has found out the important role that inflammation plays in what has always been considered as a degenerative non-inflammatory disease makes *osteoarthritis* – perhaps – not entirely incorrect.

Osteoarthritis (OA) has long been viewed as a degenerative disease of cartilage, but accumulating evidence indicates that inflammation has a critical role in its pathogenesis. [...] (Robinson *et al.* 2016: 580).

Although osteoarthritis (OA) was historically referred to as the non-inflammatory arthritis, it is now considered a condition involving persistent low-grade inflammation and activation of innate inflammatory pathways. [...] (Griffin and Scanzello 2019: 57).

Osteoarthritis (OA) is one of the major causes of chronic pain. Although OA has long been considered a non-inflammatory "wear and tear" disease leading to loss of articular cartilage, recent findings provide convincing evidence that inflammatory mechanisms play a pivotal role in the pathophysiology of OA. [...] (Nees *et al.* 2019)

Independently of common aspects, osteoarthritis and osteoarthrosis

remain two distinct processes due to fundamentally different causes (François *et al.* 1995: 616; Tanchev 2017: 46) and are diseases that affect different age groups; osteoarthrosis typically affects the elderly population, whereas osteoarthritis can also affect young people (see *Healthline*, https://www.healthline.com/health/arthrosis-vs-arthritis; *Humanitas*, https://www.humanitas.net/news/arthritis-arthrosis-difference/).

The misuse of *osteoarthritis* has also influenced medical Italian language, where *osteoartrite* has been employed with the meaning of degenerative disease for more than thirty years, as shown by *Churchill's Medical Dictionary* (1989):

osteoartrite Forma di artrite cronica caratterizzata da una degenerazione cartilaginea. [...]. Generalmente l'osteoartrite si verifica negli anziani, o in quei soggetti in cui le articolazioni si sono precedentemente deformate per qualsiasi ragione. Anche osteoartrosi, artrite atrofica, artrite degenerativa, artrosi deformante, malattia degenerativa articolare, reumatismo di Heberden.

[A form of chronic arthritis characterized by cartilage degeneration [...] Osteoarthritis usually occurs in the elderly, or in those subjects whose joints have previously deformed for any reason. Also *osteoarthrosis*, *atrophic arthritis*, *degenerative arthritis*, *deforming arthrosis*, *degenerative joint disease*, *Heberden's rheumatism*].¹

The use of *osteoartrite* as an equivalent for *osteoartrosi* is reported in the second definition provided by the *Treccani* encyclopedia (https://www.treccani.it/):

- 1. Processo infiammatorio, acuto, subacuto o cronico, a carico dei capi ossei articolari, osservabile nel corso di alcune malattie infettive.
 - [Inflammatory process, acute, subacute or chronic, affecting the joint bone heads, observable in the course of some infectious diseases.]
- 2. In adesione alla nomenclatura medica anglosassone, sinonimo di osteoartrosi o di artrosi.

[In compliance with the Anglo-Saxon medical nomenclature, synonym for *osteoarthrosis* or *arthrosis*.]

A research article clearly shows the use of *osteoartrite* as a synonym for *osteoartrosi* in medical Italian language:

Lo sviluppo dell'osteoartrite è associato alla presenza di determinati fattori di rischio come l'età avanzata, lo stato ormonale, la predisposizione genetica, l'obesità e la sindrome metabolica. [...] (Migliore and Picarelli 2018: 13)

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¹ The translations are by the author.

[The development of osteoarthritis is associated with the presence of specific risk factors such as old age, hormonal status, genetic predisposition, obesity, and metabolic syndrome].

As can be seen, osteoarthritis is referred to as a disease associated with several risk factors, the first of which is old age, which, as previously mentioned, is a characteristic of osteoarthrosis.

Another term about which there is confusion is cellulitis. Wikipedia includes this term in the list of types of inflammation pertaining to the integumentary system, and immediately specifies "not to be confused with cellulite." Leroy Young and DiBernardo (2021: 521) state that there is "frequent and inappropriate interchangeable use of the terms "cellulite" and "cellulitis" (a potentially serious infection) to describe the same condition." Both cellulite and cellulitis include the suffix conventionally used to refer to inflammation (although cellulite has a slightly different form as it has maintained its original Greek suffix), but the conditions the two terms refer to are completely distinct. Cellulitis is "the inflammation of subcutaneous, loose connective tissue" (Stedman's Medical Dictionary 2019), while cellulite describes "dimpled contour alterations of the skin that are present in approximately 85% to 90% of post pubertal females" (Young and DiBernardo 2021: 521). Cellulite was loaned by English from French in 1968 after its use mainly in fashion magazines for beauty treatments (*Online Etymology Dictionary*, https://www.etymonline.com). However, as Young and DiBernardo (2021: 521) report, the first clinical description of cellulite was provided in 1920, when it was described as "a noninflammatory mesenchymal disorder attributable to abnormal metabolism." The precise, scientific term for what is referred to as *cellulite* is, indeed, edematous-fibro-sclerotic panniculopathy, which shows no element referring to inflammation, as well as other synonymous terms, namely adiposis edematosa, nodular liposclerosis, gynoid lipodystrophy, and status protusus cutis (Leroy Young and DiBernardo 2021: 522).

The list of types of inflammation provided by Wikipedia includes another term that deserves attention, namely *pneumonia*. As can be immediately noticed, this term does not contain the suffix -itis, yet it is used to refer to an inflammatory condition of the lung. More precisely, Wikipedia reports two terms to refer to the inflammation of the lungs, pneumonia and pneumonitis. The analysis of the use of these terms seems to suggest that pneumonia has a more specific meaning as compared to pneumonitis, which shows a more generic use: "Pneumonitis is distinguished from pneumonia on the basis of causation as well as its manifestation" (https://en.wikipedia.org/wiki/Pneumonitis). In this respect, it emerges that pneumonitis is the "inflammation of the lung" (Dorland's Illustrated Medical Dictionary 2019), and pneumonia the "inflammation of the lung with consolidation and exudation" (ibid.). Dorland's Medical Dictionary (2019) also specifies that "while pneumonitis and pneumonia are often used synonymously, pneumonitis is typically used when the cause is a noninfectious agent (such as chemicals or radiation)." The distinct use of pneumonia and pneumonitis according to the cause of the inflammation –

whether it is an infection or not - is confirmed by research literature on the topic, as shown by the following article extracts:

Pneumonia remains the leading cause of death in children outside the neonatal period, despite advances in prevention and management. [...] New conjugate vaccines against Haemophilus influenzae type b and Streptococcus pneumoniae have contributed to decreases in radiologic, clinical and complicated pneumonia cases and have reduced hospitalization and mortality. [...] (le Roux and Zar 2017).

The clinically indistinguishable overlap between pneumonitis caused due to immune checkpoint inhibition (ICI) and pneumonia associated with COVID-19 has posed considerable challenges for patients with cancer and oncologists alike. [...] (Abid 2021).

Globally, infectious diseases, including pneumonia, diarrhoea and malaria, along with pre-term birth complications, birth asphyxia and trauma, and congenital anomalies remain the leading causes of death for children under 5 years. [...] (World Health Organization 2022, ICD-11).

The use of *pneumonia* and *pneumonitis* as distinct terms to refer to the inflammation of the lungs depending on the type of agent that caused the condition is an indicator of lexical accuracy; however, the lack of *-itis* in *pneumonia* makes the term inaccurate. *Pneumonia* represents what may be called an 'inaccurately transparent' term in that the analysis of its surface form allows immediate decoding of the meaning (*pneumonia* is formed by the Greek *pneumōn*, meaning "lung", and by the suffix *-ia*, typically forming nouns in scientific discourse) but no element referring to the concept of inflammation is displayed.

Similarly to *pneumonia*, a term that refers to inflammation but does not show the suffix -itis is diphtheria, a term which refers to a once-feared disease that has now become very rare thanks to vaccination. Diphtheria is not included in the list of the types of inflammation provided by Wikipedia, where it is displayed separately and described as an infectious disease. However, diphtheria is characterized by a strong inflammatory component, which manifests itself through the formation of a necrotic, thick membrane in the throat. This membrane is similar to the tanned leather of animals that in ancient Greece was used as a writing material and called diphthera. Hence, the name of the disease and of the bacterium that causes it, Corynebacterium diphtheriae. The lack of itis in diphtheria is due to the etymology of the term, which derives from French diphtérie, coined in 1855 by the physician Bretonneau; the latter had previously named the disease diphthérite (1821), anglicized as diphtheritis in 1826 (Online Etymology Dictionary, https://www.etymonline.com). It is worth noting that -itis is also absent in other languages, such as Spanish and German, where the denominations are, respectively, difteria and diphtherie, while in the Italian language the suffix has been maintained, as displayed in *differite*.

Finally, in the list of types of inflammation provided by *Wikipedia*, another term can be found that lacks the suffix *-itis*, i.e. *pleurisy*, which shows a linguistic anomaly. *Pleurisy* refers to the inflammation of the pleura, which is "the serous membrane enveloping the lungs and lining the walls of the pulmonary cavities" (*Stedman's Medical Dictionary* 2006). Medical English also displays another term to refer to the inflammation of the pleura, *pleuritis*. *Pleurisy* and *pleuritis* are used interchangeably, with *pleuritis* registering 5,704 occurrences in *PubMed*, and *pleurisy* 4,160. *Merriam-Webster Medical Dictionary* (https://www.merriam-webster.com/medical) reports the etymology of *pleurisy*, which seems to have been influenced by the Anglo-French *pleurisie*, afterward anglicized as *pleurisy*.

Conclusion

The present paper was inspired by Tanchev's (2017) discussion regarding the misuse of *osteoarthritis* in orthopedic surgery. It investigated whether other cases exist in medical English of inaccurately used terms ending in -itis. The prominent position of English in medical research makes term accuracy a very important feature in the successful transmission of meanings. Accuracy refers to the correctness of a term; it represents a very important feature of medical communication together with other principles, such as transparency. The latter is the possibility of immediately decoding the meaning of a term through an analysis of its surface form. Transparency does not always overlap with accuracy. In this respect, medical English terminology, despite being transparent, shows terms that are not used with the meaning an analysis of their form would suggest, but are referred to different concepts. Furthermore, the present investigation analyzed affixation in medical language, and the important role that it plays in the process of terminology systematization and standardization was highlighted. To address all the above issues, a list of diseases and conditions referring to inflammatory diseases was retrieved from Wikipedia, and the PubMed database was queried by means of keywords to provide illustrative text strings. The International Classification of Diseases (ICD-11, 2019) served as a reference tool for the analysis. The investigation was also supported by authoritative medical dictionaries. The results showed that even though most of the investigated English terminology ending in -itis is accurately used, cases exist of either improper use of the suffix or imprecision due to the lack of the suffix itself. Corrective terminology interventions should be carried out to guarantee accuracy and semantic precision in taxonomies of diseases to prevent any ambiguities and misleading uses in medical literature and practice.

Medical sciences are in continuous evolution parallel to the rapid progress of scientific knowledge. Scholars Areej *et al.* (2018: 2) state that learning medical terminology "may seem like learning the entire vocabulary of a foreign language." The rapidity with which medical language develops entails that the outcomes linguistic research can accomplish are extremely temporary but also that medical language is an endless source of investigation.

Although the principles of accuracy and precision in medical terminology

are generally respected to guarantee clear and effective communication, various factors can arise that lead to 'deviation from the rule'. There can be the case of a term that for tradition or inertia has been used improperly, and no remedial change has been made over time; on the contrary, its misuse has become so popular to be registered in dictionaries (e.g. osteoarthritis). There is also the unremitting progress of medicine, which leads to reinterpretation strategies whereby already existing linguistic elements are employed to create new meanings (e.g. -osis). Moreover, influences from other languages cannot be ignored. Medical English, in particular, has been intensely affected not only by Greek and Latin but also by French, which left important marks in its development. However, the fact remains that precise and accurate terminology is fundamental in medical language as it must ensure effective and safe communication. Medical terminology must refer unequivocally and accurately to the meaning with which it is used because it is directly related to practice, diagnostics, and treatment. In this respect, future research is needed to investigate whether other cases of inaccuracy and misuse of medical English terminology exist. Linguistic research can play a crucial role in identifying any critical issues and suggesting corrective interventions. This is crucial in the specific case of English, the chosen language for international scientific communication and therefore the most influential worldwide.

This article does not contain any studies with human participants performed by any of the authors.

This article does not contain any studies with animals performed by any of the authors.

Conflicts of interest.

The authors of this paper certify that they have NO affiliations with or involvement in any organization or entity with any financial or non-financial interest (such as honoraria; educational grants; membership, employment; affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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