

Non-Pharmacological Interventions: Nomenclature, Taxonomy, and a Working Definition

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Abstract

Many terms have been used to describe interventions that do not involve the use of pharmacological products in the setting of communicable diseases. Terminology has varied from physical, non-pharmaceutical, non-drug, non-pharmacologic, and non-pharmacological interventions, as well as public health measures and public health and social measures. Previous epidemics and pandemics, and especially the recent COVID-19 pandemic, have highlighted the importance of non-pharmacological interventions (NPIs), and the term is now recognized globally. The use of the terms public health measures or public health and social measures have variably also been inclusive of the use of vaccines which would be considered a pharmacological product. Given this background and confusion over terminology and descriptions, we sought to review this topic and provide clarity regarding nomenclature, taxonomy, and definitions with an aim to ensure an explicit shared understanding of any interventions that do not involve pharmacological products, given the importance of conducting NPI evaluations for future epidemics and pandemics. For clarity, we would define a NPI as a measure not involving a medicinal product, used in humans with the intent to treat or prevent disease. In this context, a medicinal product would be one which has intended effects on physiological bodily functions through any pharmacological, immunological or metabolic action, as outlined by the European Medicines Agency. The use of pharmacological interventions versus NPIs have different regulatory frameworks, different descriptors and different evaluation approaches. It has been well recognized that there was a dearth of high quality evidence generated for NPIs in the same manner as PIs such as vaccines and antivirals during the recent COVID-19 pandemic, which has been already termed a “pandemic tragedy” in late 2021.

Introduction

Many terms have been used in the published literature (1-8) and by multiple organizations to describe therapeutic interventions that do not involve pharmacological products, most often in the context of communicable diseases. Terms used have included physical, non-pharmaceutical, non-drug, non-pharmacologic, and non-pharmacological interventions, as well as public health measures and public health and social measures. Although “non-pharmaceutical interventions” has been the term used by the World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC) and other public health organizations and governments (2-8), the term “non-pharmacological interventions” is more often used in the scholarly literature (9), including the Academic Collaborative Platform on Assessment of Non-Pharmacological Interventions known as Plateforme CEPS (<https://plateformeceps.www.univ-montp3.fr/fr/english-0>).

Data from PubMed (<https://pubmed.ncbi.nlm.nih.gov/>) on the frequencies of variants of the terms “non/pharmacologic/al intervention/s” and “non/pharmaceutic/al intervention/s” (Appendix, Figure 1) show that until 2019 the former was used far more frequently than the latter. During the COVID-19 pandemic (2020–23) the frequencies of the latter increased markedly, although since 2023 this trend has started to reverse. Acknowledging transatlantic differences in the use of the terms “pharmacologic” and “pharmacological”, “pharmaceutic” and “pharmaceutical”, here we shall use the terms ending in –ical. (10)

The recent COVID-19 pandemic has highlighted the importance of non-pharmacological interventions (NPIs), and the term has entered common usage globally. Now the terms public health measures and public health and social measures (which may or may not be inclusive of vaccines) are also being used. Given this background and confusion over terminology and descriptions, and the paramount importance of conducting robust evaluations of any of these interventions, we sought to review the literature on this topic and provide clarity regarding nomenclature, taxonomy, and definitions, to ensure an explicit shared understanding of any interventions that do not involve pharmacological products, as planning is undertaken for managing future pandemics.

“Pharmacological” and “Pharmaceutical”

Although the terms “pharmaceutical” and “pharmacological” are often loosely used to mean the same thing, and some dictionary definitions equate a “pharmaceutical” with a drug, they are quite different in terms of their background and applications from a scientific perspective. The term “pharmaceutical” relates to the discovery, development, formulation, manufacture, and distribution of drugs or medicinal products. (11) In contrast, the term “pharmacological” (11) relates to the study of how drugs or medicinal products interact with the body, including their mechanisms of action, pharmacokinetics, pharmacodynamics, interactions with specific targets in living systems, therapeutic uses, and adverse effects. The distinction is highlighted in the names of two learned UK

societies, the British Pharmacological Society and the Royal Pharmaceutical Society. The former is primarily constituted on behalf of pharmacologists and clinical pharmacologists, the latter largely on behalf of pharmacists. The term “medicinal product”, according to the European Medicines Agency in one of its recent regulatory documents, is defined as “(a) any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or (b) any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.” (12, 13) They further define the terms “physiological” and “diagnosis” and provide specific examples, including vaccines, tetanus anti-serum, monoclonal antibodies, and CAR-T cells as medicinal products. (12)

The most recent (11th) edition of the International Pharmacopoeia (14), published by the WHO in 2023, represents “a collection of recommended procedures for analysis and specifications for active pharmaceutical ingredients, excipients and finished pharmaceutical products” and reflects work by the WHO Expert Committee on Specifications for Pharmaceutical Preparations. In the Pharmacopoeia, the monographs come under the title of “pharmaceutical substances”, (14) which is similar to the nomenclature of the European Medicines Agency and their use of the term “medicinal product”. In the most recent report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations, it was agreed to bring vaccines and in vitro diagnostic products within the scope of pharmaceutical products. (15) The database, which is compiled and maintained by a technical standards and specifications team at WHO related to the “quality assurance of medicines and regulatory aspects for medical products published in the related World Health Organization (WHO) Expert Committee reports”, also uses the terms “pharmaceutical product” or “pharmaceutical ingredient” most commonly in its definitions and rarely uses “pharmaceutical” as a stand-alone noun term. (16)

The term “drug” has social connotations, and although a drug may have “a pharmacological, immunological or metabolic action” when administered, it may or may not necessarily “treat or prevent disease in human beings” as described above and can refer to a substance that can be used legally or illegally. It is noteworthy that there are few references to the term “drug” in the documents referenced above.

The History of Non-Pharmacological Interventions

NPIs are not new, although they were not originally readily identifiable by the specific term used today. They have been used in various forms for millennia, not only to improve general health but also in the setting of contagious illnesses. For example, quarantine was used in the ancient Persian “Canon of Medicine” as early as 980 AD for control of contagion, with 40 days of separation, and centuries later it was used to control the spread of the plague during the Middle Ages. (17) There are records of the use of social distancing, isolation, handwashing, environmental controls, and later

masking for the plague, cholera, and influenza (17, 18). Many types of NPIs have been used for many different diseases. Although communicable diseases often come to mind, other conditions have included psychiatric disorders, addictions, cancers, respiratory conditions, cardiovascular diseases, musculoskeletal disorders, palliative care, sleep disorders, healthy ageing, and many others, which have been extensively reviewed in many books and published manuscripts over the years. (9, 19-23)

Historically, many diverse and heterogeneous interventions have been regarded as NPIs.

Defining Non-Pharmacological Interventions

Given what has been described above related to pharmacological effects, we define a NPI as a measure used in humans with the intent to treat or prevent disease, not involving a medicinal product, applying the definition of a medicinal product as outlined by the European Medicines Agency (12, 13). Thus, the use of any vaccine would not be considered an NPI. Many definitions have been applied over the years, but according to the Plateforme CEPS in 2017 (9), “NPIs are science-based and non-invasive interventions on human health. They aim to prevent, care for, or cure health problems. They may consist of products, methods, programs or services whose contents are known..... they have a measurable impact on health, quality of life, behavioural and socioeconomic markers.”

Examples of NPIs, which may be used alone or in combination with other non-pharmacological or pharmacological interventions, include exercise, dietary modifications, salt restriction, sleep pattern changes, behavioural and cognitive therapy, psychotherapy, certain natural remedies, supportive care, lifestyle modifications, public health actions, social influencing strategies, environmental measures, and some complementary treatments (e.g. acupuncture, chiropractic therapy). NPIs can be directed and implemented at the individual/personal level or the community or environmental levels, as described by the CDC, (7) and at the individual, institutional, community, and local and national governmental levels, and/or an international level, as described by the WHO. (2,4,5) Other descriptors divide NPIs into top-down and bottom-up, depending on the level of governmental involvement and the stringency of interventions that are applied. NPIs may also take on various orientations, including educational, operational, persuasive, or administrative, and may be simple or complex.

Non-Pharmacological Interventions Used During Epidemics and Pandemics

From an epidemiological perspective, interventions to reduce the spread of an epidemic or pandemic have been described as pharmacological (PIs) or non-pharmacological (NPIs). The general public most often heard these terms during the recent COVID-19 pandemic. The term “public health and social measures” (PHSMs) has been used more recently by the WHO in its descriptions and documents (24-26), which include both PIs

and NPIs. Other public health organizations and governments have continued to use the term NPIs or are migrating towards the term PHSMs. (6-8, 27)

The WHO, in its proposed glossary document, defined PHSMs as “actions or measures taken by individuals, institutions, communities, local and national governments to reduce the spread of covid-19. PHSMs include non-pharmaceutical interventions, physical distancing measures, pre- and post-exposure prophylaxis, and vaccines” (25). The WHO further indicated that “Public health and social measures (PHSMs) are a key strategy to reduce the transmission of pathogens with epidemic or pandemic potential. PHSMs include non-pharmaceutical [*sic*] interventions that can be taken by individuals, institutions, communities, local and national governments and international bodies to slow or stop the spread of an infectious disease, such as COVID-19.” (<https://www.who.int/activities/measuring-the-effectiveness-and-impact-of-public-health-and-social-measures>). The latter reference and other WHO documents are less clear in their nomenclature, and in two recent documents the WHO has seemed to imply that PHSMs do not refer to both PIs and NPIs, as in their published glossary (25), but rather only to NPIs, despite the inclusion of vaccines. The research agenda established at a global consultation meeting in 2021 explicitly stated that “public health and social measures refer to non-pharmaceutical [*sic*] interventions implemented by individuals, communities and governments at all levels”. It did not mention that PHSMs may include both PIs and NPIs and seemed to imply that PHSMs are synonymous with NPIs. (26) Another 2023 WHO document stated, “Medical countermeasures such as drug administration or vaccination are not included in this guidance. PHSMs are complementary, act in concert, and in combination with other measures required to ensure adequate control of a circulating pathogen, such as SARS-CoV-2. Some personal PHSMs, such as hand hygiene, respiratory etiquette and staying home when sick, should be considered basic measures practised and supported by governments and businesses at all times, irrespective of COVID-19” (28).

The terms NPIs and PHSMs have both been and not been considered synonymous in the literature to date. However, the current definitions and descriptions are confusing, and a distinct taxonomy and nomenclature is required to avoid future disparities in definitions, given that both terms apply to the setting of communicable micro-organisms with epidemic and pandemic potential. Given the confusion over current definitions and nomenclature identified in the literature on this topic, including how public health and social measures have been variably defined to date, the broad range of interventions not involving pharmacological products that are available (including those that fall outside the usual parameters traditionally used in the setting of communicable diseases), and to ensure precision and uniform understanding, the term non-pharmacological interventions with added descriptors may offer the best option.

Taxonomy

There are many classifications and organizational schemes for the available NPIs, and differing interpretations of the ways in which individual, community, local, national, and

international interventions may be applied, either alone or in combination and at different levels. Many interventions in studies have not been adequately described or have had poorly delineated descriptions, an area that needs additional nomenclatural focus (29, 30). The Plateforme CEPS (plateforme-ceps.fr) acknowledges that there is no definitive classification of NPIs but has presented five categories, which are practical, functional, and current in terms of the interventions they represent – psychological, physical, nutritional, digital, and elemental – and offer examples of NPIs belonging to each of the categories. Another suggested approach comes from the perspective of societal biosecurity risk management; using a solution-scanning approach, a group of authors provided a list of 519 societal biosecurity measures that could be used to reduce the transmission of SARS-CoV-2. (31) They listed eight key areas under which specific measures could be catalogued, including interventions such as physical distancing, reducing transmission via contaminated items, and enhancing cleaning and hygiene. Similar to others, these authors acknowledged that there was very little evidence on the effectiveness of specific measures that were used during the pandemic, which is a universal theme.

We have listed many, but not all, of the NPIs (Table 1: A Working Summary) used by several public health organizations and have added others of increasing importance that are not traditionally covered by public health organizations and governments. The additions are drawn from existing literature on the broader range of NPIs and those that may have been neglected as the pandemic progressed or have been recognized only over time and have the same potential to limit the spread of infectious pathogens of epidemic potential. The list should not be considered as complete in its current form. The nomenclature ascribed to NPIs should be a “living document”, so that novel and/or innovative interventions can be added as needed through regular updates. This living document should also aim to improve reporting of the description of NPIs, facilitating their implementation.

The additions to date that we have considered as relevant NPIs include behavioural and educational, psychosocial, lifestyle, and infodemic interventions. The presence of a parallel infodemic during COVID-19, especially with the emergence of social media and problems with misinformation and disinformation, may have interfered with or led to conflicting understanding of the pandemic and its responses globally. Managing these additional NPIs deserves as much attention as the more traditional interventions do.

Conclusions

We have attempted to provide some background, clarity, and uniformity regarding the nomenclature and taxonomy of interventions that do not involve pharmacological products, and which may be used in the context of communicable diseases. The importance of clarity in descriptions and definitions cannot be overstated, since pharmacological interventions and NPIs have different regulatory frameworks and different challenges to their evaluation. It has been well recognized that NPIs were not evaluated in the same manner as PIs such as vaccines and antivirals during the recent

COVID-19 pandemic. The lack of good research on “public health measures for COVID-19” was already being termed a “pandemic tragedy” in late 2021, (32) and the magnitude of the lack of any high-quality research such as randomized trials only worsened over the course of the pandemic. A scoping review published in 2021 showed that of >4000 registered trials worldwide, only 41 (~0.1%) randomized trials of NPIs to prevent COVID-19 could be identified. This review demonstrates the tragedy of the failure to adequately assess NPIs, which were among the most disruptive and divisive measures undertaken during the pandemic. The authors of the scoping review punctuated their point of view by drawing attention to the estimate that globally 1.5 billion students were affected by mandated school closures without the benefit of a randomized trial from which to draw high quality evidence. (33) A recent systematic review showed that “school settings do not substantially contribute to community incidence, hospitalisations, or mortality” related to COVID-19 (34) which suggests that school closures were unnecessary. The need for an agreed NPI terminology with descriptors attached is critical for facilitating and planning future high-quality research for future pandemics and epidemics, to ensure that evidence-based policy decisions may be made.

Table 1: A Working Summary of NPIs Applicable to Pathogens of Potential Epidemic and/or Pandemic Significance

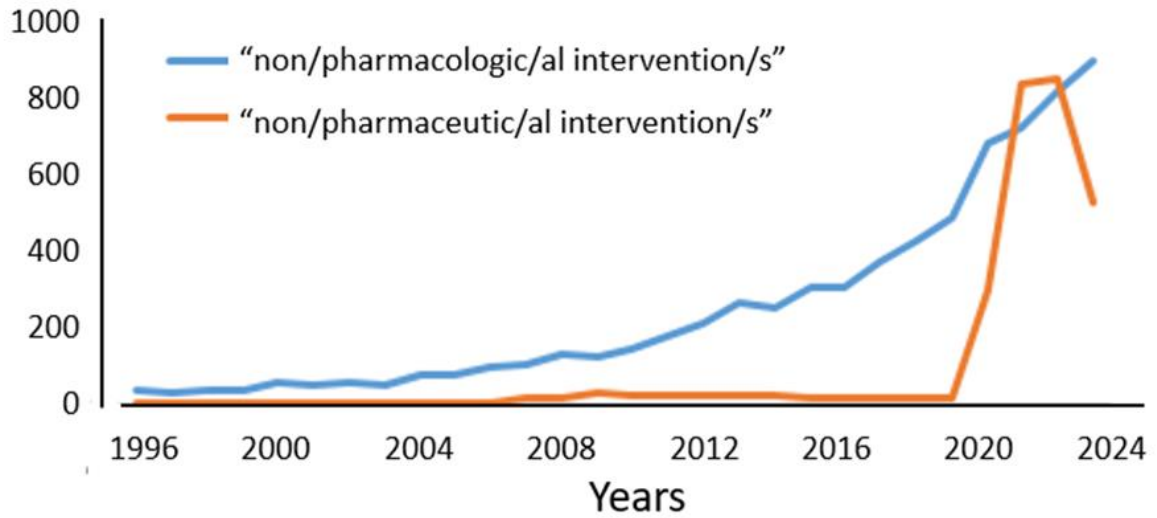
- Individual protective interventions
 - ✓ hand hygiene
 - ✓ glove use
 - ✓ face masks or coverings
 - ✓ respiratory etiquette
 - ✓ use of protective eyewear
 - ✓ use of gargles and nasal washes
 - ✓ general hygiene
 - ✓ avoidance of commonly shared objects
 - ✓ self-care
- Physical distancing interventions
 - ✓ staying a specified distance from others
 - ✓ avoiding crowded spaces
- Contact tracing interventions
 - ✓ notification and monitoring of all contacts to a known case
 - ✓ testing of contacts
 - ✓ quarantine of contacts
- Environmental interventions
 - ✓ cleaning and disinfection of contaminated surfaces
 - ✓ cleaning and disinfection of high-touch surfaces
 - ✓ improving ventilation
 - ✓ use of ultraviolet irradiation and/or air purification devices
 - ✓ humidification manipulations
 - ✓ use of physical barriers and structural changes
 - ✓ avoidance of opportunistic transmission-enhancing activities e.g. use of fans in the vicinity of infected ill persons
- Isolation interventions
 - ✓ staying at home if ill
 - ✓ use of private rooms in healthcare facilities and long-term care
 - ✓ avoiding all contact with others while ill
 - ✓ creation of social “bubbles”
 - ✓ unit or ward closures
- Quarantine interventions
 - ✓ isolation of healthy exposed persons, voluntary or mandatory
- Closure (partial or full) interventions
 - ✓ schools, colleges, universities
 - ✓ day-care centres
 - ✓ long-term care facilities
 - ✓ healthcare facilities
 - ✓ public gatherings

- ✓ public transport
- ✓ places of worship
- ✓ workplaces and businesses
- ✓ circuit breaker lockdowns
- ✓ total lockdowns of prolonged duration
- Border crossing interventions
 - ✓ notification at borders
 - ✓ border entry screening and testing
 - ✓ quarantine after border crossings
 - ✓ border closures
- Screening and testing
 - ✓ hospital entry
 - ✓ long term care entry
 - ✓ large gathering entry
 - ✓ workplace entry
- Travel related interventions
 - ✓ travel advisories
 - ✓ screening and testing with travel entry and exit
 - ✓ travel restrictions
 - ✓ travel suspension
- Behavioural and educational interventions
 - ✓ public health messaging
 - ✓ messaging of best practices
- Nutritional interventions
 - ✓ encourage proper dietary intake and proper nutrition
 - ✓ dietary supplements
 - ✓ avoidance of excessive drug and alcohol use
- Mental health and psychosocial interventions
 - ✓ maintaining psychological health
 - ✓ maintaining social interactions in a safe and appropriate manner
- Lifestyle interventions
 - ✓ maintaining appropriate sleep patterns
 - ✓ appropriate physical activity and exercise
 - ✓ physiotherapy, massage, yoga, and calisthenics
- Infodemic and digital interventions
 - ✓ handling of misinformation and disinformation in social and mainstream media
 - ✓ establishing appropriate communication channels
 - ✓ use of trusted social media platforms
 - ✓ use of apps, tracking sites, and other digital assets in real time to facilitate intervention adoption
 - ✓ adherence using self reporting and external monitoring

Appendix

Figure 1. Frequencies of variants of the terms “non[-]pharmacologic/al intervention/s” and “non[-]pharmaceutic/al intervention/s” in publications indexed in PubMed, 1996–2023

Numbers of publications



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