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# **NPI Model: Standardised Framework for Evaluating Non-Pharmacological Interventions in the French Health Context**

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## **Competing interest**

None declared.

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## **Supplemental material**

<https://npisociety.org/modele-evaluation-inm/>

## **Background**

The term non-pharmacological interventions (NPIs) refers to health prevention and care protocols predominantly with a physical, nutritional or psychosocial focus supervised by a healthcare professional. Unlike drugs and medical devices, no consensual model for evaluating these complex interventions existed prior to the present study because of the heterogeneity in intervention content and study protocols. This heterogeneity limited the transferability of good practices and led to a great deal of mistrust in NPIs among professionals and healthcare users alike. The present study involved the co-construction of a consensual framework for the evaluation of NPIs, which meets both the specificity of these types of interventions and international standards for research in the field of health.

## **Method**

The study involved all concerned stakeholders in France, including academic and non-academic, researchers, healthcare users, health practitioners, health operators, scientific societies and health authorities. The framework was co-constructed under the direction of a multidisciplinary committee of 22 experts through iterative, open and tracked exchanges, in four successive stages: work performed by a select committee, work performed by a larger committee, open vote by college, and finally, consultation with health authorities and scientific societies.

## **Results**

The framework for evaluating NPIs, called the 'NPI Model', includes 14 ethical invariants and 63 methodological invariants distributed between five types of study: mechanistic, observational, prototypical, intervention, and implementation. It received the support of 28 scientific societies and three French health authorities.

## **Conclusion**

The creation of a standardized framework for evaluating NPIs in the French context has several advantages, as follows: i) it harmonises and clarifies epistemological, methodological and ethical expectations of NPI evaluation studies for researchers; ii) it ensures greater transferability of study results to real-world clinical use of the relevant NPI; iii) it guarantees that programs for professionals in the healthcare, prevention and social assistance sectors are more operational; iv) it facilitates efficient and safer practices for healthcare users; v) it helps to provide decision-makers and regulators with a greater understanding of NPIs; vi) it ensures more traceable interventions for health operators; vii) it provides solutions that can be better integrated into the financing strategies of insurance and social solidarity systems.

## **Key words**

Non-pharmacological interventions, complex interventions, health, prevention, care, framework, epistemology, methodology, ethics

## Introduction

The number of non-pharmacological interventions (NPIs) for human health - sometimes qualified in the literature as complex interventions<sup>1</sup> - has grown considerably since the beginning of the century.<sup>2</sup> These health interventions are increasingly used in prevention and care for chronic diseases, mental health, child care, addiction, occupational medicine, disability, gerontology, and end-of-life care.<sup>2</sup> NPIs can be prescribed by physicians, and may be recommended by other healthcare and prevention professionals, as well as professionals from the social sector. Moreover, patients themselves can follow an NPI without consulting a healthcare professional.

After ten years of preliminary work on a collaborative university platform in France, an international scientific society on NPIs was created in 2021 called the Non-Pharmacological Intervention Society (NPIS).<sup>2</sup> The large diversity between approaches, methods and techniques used, constrained the NPIS to create its own definition of NPIs in order to delineate their objective and scope. This definition limits NPIs to predominantly bodily (e.g., manual therapies, physiotherapy protocols, adapted physical activity programs), psychosocial (e.g., psychotherapies, therapeutic education programs, music therapies) and nutritional practices. Specifically, it defines an NPI as an evidence-based, effective, personalized, non-invasive health prevention or care protocol, registered and supervised by a qualified professional.

An NPI is therefore a non-invasive health solution with a clearly described protocol, whose main aim is to prevent, care or cure a health problem known in Western medicine. It is not a diagnostic procedure; it is part of a personalized health strategy, consistent with public health regulations. Where appropriate, an NPI is used to complement medications, surgeries and/or medical devices. It uses multiple systemic and dynamic mechanisms that can be rationally explained and presents identified risks. An NPI is therefore neither a product nor a discipline, an esoteric practice, a way of life, or an organization (e.g., office, establishment, platform, network).

Unlike medicines and medical devices, no consensual framework for evaluating NPIs currently exists at a national or supranational level. Furthermore, the *Enhancing the Quality and Transparency Of health Research (Equator)* library does not have a specific paradigm on NPIs. While the library does propose recommendations on how to create a control group in a clinical trial or a mechanistic study for physical, psychological, and self-management therapies<sup>3</sup>, and on how to conduct a randomized controlled trial<sup>4</sup>, these recommendations are not integrated into an overall framework. A systematic review identified 46 suggested frameworks for evaluating NPIs (as of April 2019), with a greater number of frameworks being proposed in recent years.<sup>5</sup> All these proposals (i.e., recent or not) were built by researchers for researchers, most of them using a mono-disciplinary approach. Some, such as ORBIT<sup>6</sup> and CONSORT<sup>7</sup>, are inspired by the drug evaluation model, and prioritize internal validity (i.e., absolute comparability of groups). However external validity for NPIs is of major importance (i.e., capacity to validate the results found for the target population). Other proposed frameworks are based on theories of behavioural change<sup>8</sup> or were inspired by engineering which uses an iterative and sequenced process for improving the quality of interventions.<sup>9</sup> Still others propose hybridizations such as MOST<sup>10</sup> and the *Complex Interventions model*.<sup>11</sup> This growing diversity hinders the adoption of a single framework.

The absence of a consensual evaluation framework on NPIs undermines the justification and the sequencing of studies. In turn, this *i*) leads to doubts about the effectiveness of NPIs (e.g., benefits, risks, relevance, mechanism, cost-effectiveness, dose, acceptability), *ii*) hampers study approval (e.g., ethics committee, reviewing process), and *iii*) forces systematic reviews to urge caution when interpreting their findings, and to frequently highlight study methodological and ethical limitations including design bias (e.g., specific vs. non-specific effect, context effects, insufficient sample size), selection bias, measurement bias (e.g., non-validated instruments, missing data, insufficient measurement of adverse effects), comparison bias (heterogeneity in the type of control group used), insufficiently-described NPIs<sup>11</sup>, analysis bias (e.g., attrition bias, erroneous statistical analyses), follow-up bias (e.g., taking into account concomitant practices, loss to follow-up, dropout rate, non-compliance rate, non-adherence rate), and conflicts of interest. The biases in this list have deleterious effects on published results; one author even estimated that 85% of research

resources in the field of health are wasted<sup>12</sup>. All these shortcomings lead to contradictions in recommendations proposed by authorities and medical societies at the national and supranational levels.<sup>2</sup> Academic institutions bemoan the lack of a standardized model to evaluate NPIs, as illustrated in a report from the French High Authority of Health: “*With regard to the criteria usually considered for evaluating drugs, studies evaluating the efficacy of non-pharmacological interventions for the most part have methodological inadequacies*” (p.13).<sup>13</sup> In other words, in the absence of a consensual and specific evaluation framework, only the drug evaluation model is applied.

The absence of a specific framework also hinders the sharing of relevant knowledge and the dissemination of good practices. In particular, it would suggest that each practitioner must reinvent his/her practices for each new patient, and that the only effect perceived by practitioners to be of benefit is therapeutic alliance.<sup>2</sup> It also tends to leave the way open to traditional and esoteric medicines, and more generally, to alternative offers of health and well-being with widely-publicized associated health risks (at-risk interactions, interrupting conventional treatment, psychological impact, etc.).<sup>14</sup> This tendency is making headway in particular in the United States in the field of oncology, leading to two juxtaposed offers of medicine; one is evidence-based medicine (EBM), while the other is integrative medicine, which is based on experience and tradition.<sup>15</sup>

Given that current EBM research focuses on health solutions that are both preventive and curative in nature, only a concerted, transdisciplinary and participatory approach can establish a standardized framework for the evaluation of NPIs. The revolution in medical drugs in the 1960s came about through epistemological work conducted by all the actors concerned, with science being the driving force.<sup>16</sup> As Bouvenot put it, “*Until the 1960s, many drugs did not yet have, as their sole justification the force of routine, the credulous attachment to traditions, or the generalization from a few occasional and anecdotal examples incorrectly called professional experience*” (p.13).<sup>17</sup> A similar validation approach has been recently adopted by the medical device sector.<sup>18</sup>

Given all this context, a common paradigm, making it possible to distinguish NPIs from everyday consumer products and services, medical products and devices, public health actions and environmental strategies, is needed (Figure 1). Although NPIs cannot be evaluated in exactly the same way as drugs, researchers<sup>2, 19-21</sup> and authorities<sup>13,22</sup> nonetheless expect a rigorous and standardized scientific approach in studies evaluating NPIs.

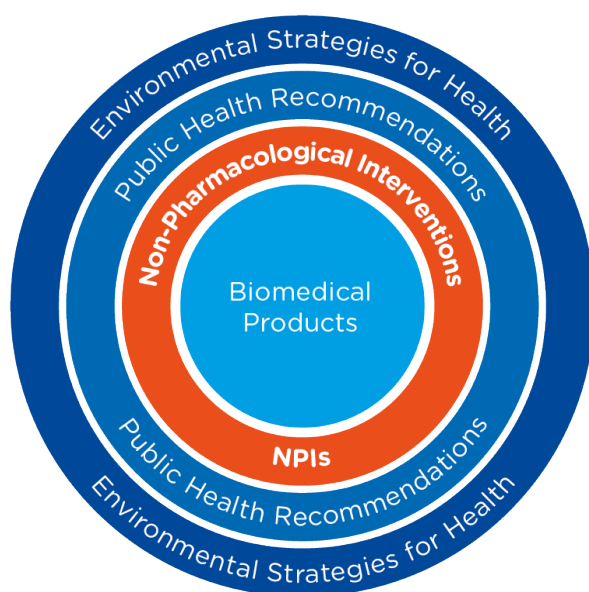


Figure 1: Evidence-based health solutions

The objective of the present study was to co-construct - with all concerned stakeholders - a consensual framework of scientific validation of NPIs which would be applicable in the context of the French health system, and which would follow contemporary epistemological and ethical international recommendations in the field of health.

**Methods**

*General principle*

Preliminary epistemological work on an NPI evaluation framework was conducted from 2011 to 2020 as part of a university collaborative platform in Montpellier, France. Starting in 2021, the NPIS extended this work with the goal of establishing a pragmatic and global model for evaluating NPIs based on the principles of EBM (Figure 2). To do this, the reflection process was structured around five types of study: (i) mechanistic studies, which aim is to highlight the biological mechanisms and active psychosocial processes of an NPI, (ii) observational studies, which aim to monitor the evolution of practices related to an NPI (iii) prototypical studies, which aim to describe all the characteristics of an NPI, (iv) intervention studies, which aim to determine the effectiveness of an NPI on health markers of a target population, and finally, (v) implementation studies, which aim to verify the conditions for deploying an NPI in a specific setting, and related modalities to adapt the intervention depending on the context.

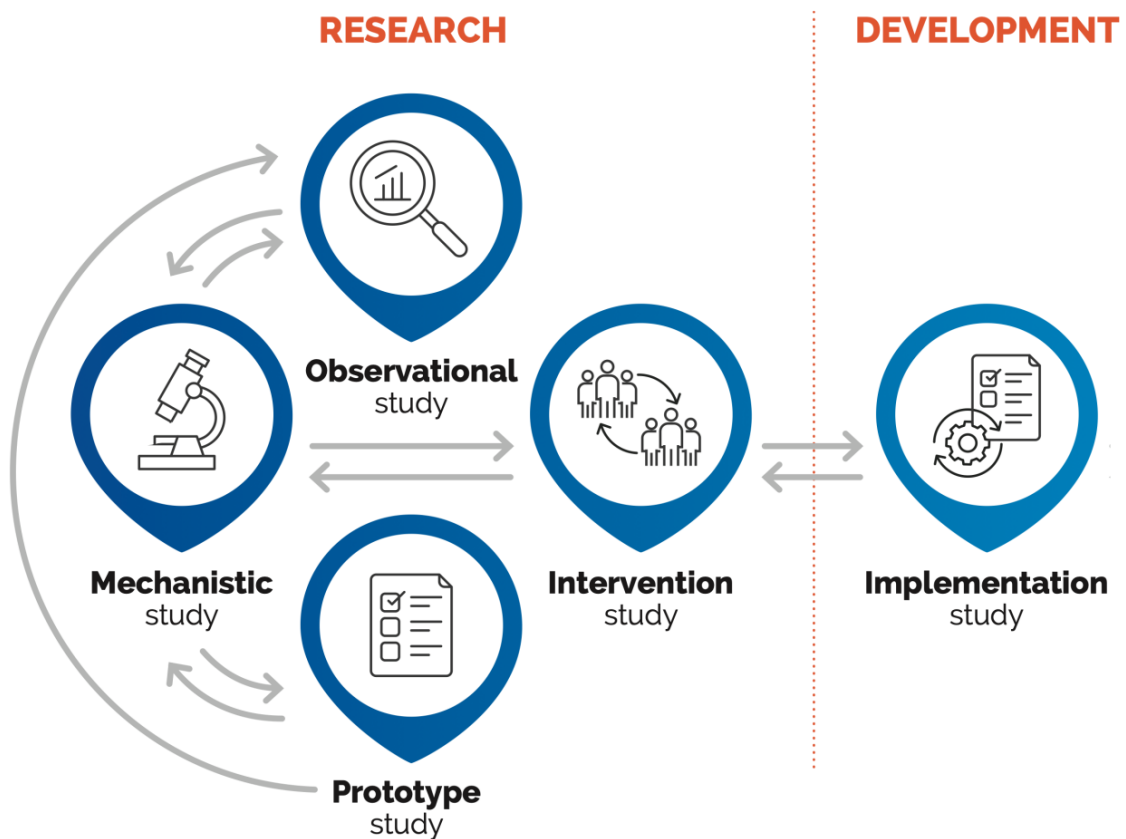


Figure 2: NPI Model, standardized framework for evaluating non-pharmacological interventions



Table 1 describes the characteristics of an NPI according to the different types of studies presented and the related research expectations, in the field of health.<sup>11,21</sup>

a.	Designation	Name (abbreviation if applicable)	[3, 4]
b.	Main health benefit	Health problem prevented, cared or cured	[4]
c.	Secondary benefits	Benefits for other health markers (biological and/or psychosocial)	[4, 5]
d.	Risks	Side effect(s), risky interaction(s)	[1, 2, 4, 5]
e.	Mechanisms	Biological mechanism(s) of action, and/or active psychosocial process(es) explaining the benefits for the health markers of interest	[2]
e.	Target population	Public responder, contraindication(s)	[1, 3, 4, 5]
g.	Protocol	Components (e.g., ingredients, techniques, gestures), procedure (e.g., duration, number and frequency of sessions, dose), equipment (e.g., physical, digital) required to guarantee the reproducibility of the effects on health	[3, 4]
h.	Professional	Required qualifications	[3, 4, 5]
i.	Context of use	Places of practice, good implementation practices, precautionary measures, regulatory characteristics, initiators	[3, 4, 5]

- [1] observational study reference published in a peer-reviewed scientific journal
- [2] mechanistic study reference published in a peer-reviewed scientific journal
- [3] prototypical study reference published in a peer-reviewed scientific journal
- [4] intervention/clinical study reference published in a peer-reviewed scientific journal
- [5] implementation study reference published in a peer-reviewed scientific journal

*Table 1: Descriptive characteristics of an NPI*

The consensus process leading to the pragmatic and global framework for evaluating NPIs followed the Equator recommendations.<sup>23</sup> It was also based on the Appraisal of Guidelines, Research and Evaluation II checklist<sup>24</sup>. Specifically, the process consisted of pointing out the methodological and ethical invariants already present in the literature for different health fields by adapting them to the specificities of NPIs. Designing the model involved all types of stakeholders: academic and non-academic actors, researchers, healthcare users, health practitioners and operators. Scientific societies and authorities were informed upstream of the project and were consulted downstream for their opinions. The recommendations made by the model were co-constructed through iterative, open exchanges, and were drawn up with a view to their application to the French health system. However, from the outset, the project was developed with a European and international vision in mind.

The development of the NPI Model was divided into four successive stages between 2022 and 2023; these are described below.

### *Step 1: Development of preliminary recommendations by a select committee*

This step consisted in the development of preliminary methodological and ethical invariants with an open call to members of the NPIS. Seven interdisciplinary and intersectoral consultations during online meetings were organized in 2022 over a total duration of 12 hours. These meetings led to the development of a shared working document and relevant scientific articles. They were monitored by a steering committee led by GN and ED. The recommendations in the NPI model were inspired by the STrengthening the Reporting of Observational Studies in Epidemiology guidelines (STROBE)<sup>25</sup>, the Standard Protocol Items: Recommendations for Interventional Trials 2013 document and its 2022 extension (SPIRIT)<sup>26-27</sup>, the Template for Intervention Description and Replication checklist and guide (TIDieR)<sup>28</sup>, the evidence-based reporting CONSORT statement for trials assessing nonpharmacologic treatments<sup>4</sup>, and the Standards for Reporting Implementation Studies statement and checklist for implementation studies (STaRI).<sup>29</sup> The presentation of the methodological recommendations followed the PICO criteria *population, intervention, comparison, and outcomes*. A website dedicated to the project was created.<sup>30</sup>

### *Step 2: Adjustment of recommendations by people living in France*

Step 2 consisted in improving the preliminary recommendation items through consensus meetings. It was initiated via a request to all persons living in France to participate, and was communicated by email and posts on social networks. Each person was attached to one of the four colleges, namely the college of researchers, the college of healthcare users, the college of practitioners, and the college of health operators. Nine interdisciplinary and intersectoral consultation meetings on each study type were scheduled between January and March 2023. The bibliographic resources were freely accessible on a webpage. The working document from Step 1 (see above) on the recommendations was shared before each meeting and then read and corrected live by the steering committee (GN, ED, GA). Each participant could make suggestions between meetings in revision mode in the working document. The 22-expert committee verified the intelligibility of all the recommended methodological and ethical items. The updated working document was presented at the NPIS international congress on March 22, 2023 in Montpellier to collect suggestions for modifications. A final meeting of the expert committee took place to verify each recommendation to be put to collegial vote.

### *Step 3: Collegial vote*

Step 3 comprised an online vote with individual registration of voters distributed among the four colleges mentioned above. It was initiated via a request for participation through email, posts and videos on social networks. All details could be found on the webpage. Each participant could vote only once between April and May 2023. To ensure single entry votes, the details for each participant were manually validated by checking the surname, first name, profession, organization, and email. Voters could only be people living in France (i.e., including overseas territories). A threshold of 80% agreement for each college per item was retained, in accordance with the rules of scientific societies. Each item had three possible response options (*agree, disagree, no answer*). Voters who responded *no answer* were considered not to have voted for the relevant item. This choice was justified by the fact that depending on the college, certain items were not relevant for the voter. Accordingly, his/her choice could be considered as reflecting a lack of opinion or competence, but not opposition. Therefore, for each item, the 80% threshold was calculated by considering the formula:  $agree / (agree + disagree) * 100$ .

### *Step 4: Consultation of French health authorities and scientific and medical societies*

Step 4 consisted in collecting the opinions of French authorities and scientific societies in the health sector about each recommendation. This was conducted between June 15 and September 17, 2023. The opinions deemed relevant by the expert committee were integrated into the methodological and ethical recommendations of the final version of the NPI Model after two two-hour videoconference meetings on August 28 and September 18, 2023.

## Results

Step 1 brought 70 contributors together and produced 41 recommendations (8 ethical and 33 methodological) to create version 1 of the NPI Model.

Stage 2 brought together 300 contributors living in France who were grouped into the four colleges: 110 researchers, 25 healthcare users, 116 practitioners, and 49 health operators. The total duration of the nine scheduled meetings was 15 hours, leading to version 2 of the NPI Model which comprised 77 recommendations (14 ethical and 63 methodological).

Step 3 included 503 voters from the four colleges: 80 researchers, 76 healthcare users, 315 practitioners and 32 health operators. Figure 3 presents the percentages of agreement for each of the 77 recommendations (i.e., online questionnaire items) according to the specific college. As all items exceeded the 80% threshold for all colleges, all were included in the NPI Model.

We tested the impact of item position in the questionnaire. The total number of *no answer* votes for the first item was 22 and 17 for the last item. The total number for the first ten items was 331 compared to 257 for the last ten items. Accordingly, we did not observe a significant impact of the item position.

Voters responded to the large majority of the 77 items: 34% responded to all items, 76% responded to at least 70 items, and 95% responded to at least 60 items. The lowest response rate was 69%. The number of voters who voted to *agree* or *disagree* met the minimum threshold value for all colleges for each item, and agreement was greater than 80% for all the items (Figure 3). Accordingly, version 3 of the NPI Model comprised 77 recommendations (14 ethical and 63 methodological).

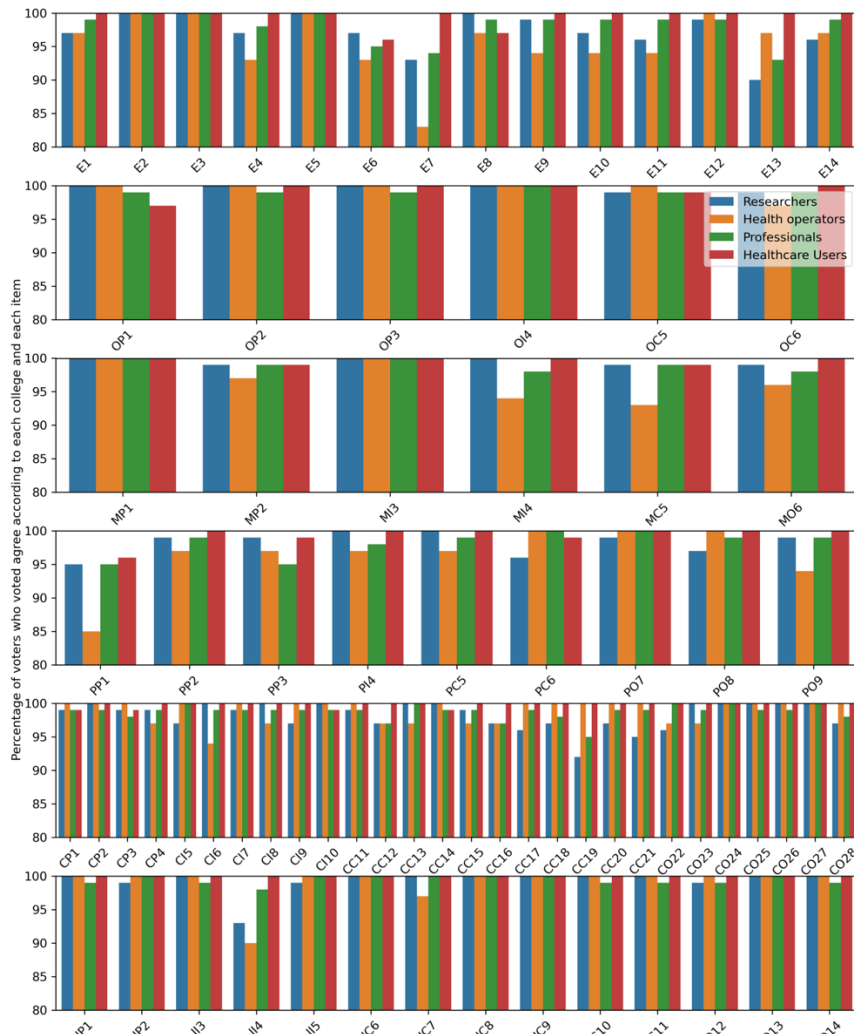


Figure 3: Percentage of voters who voted agree according to each college and each item. The y-axis begins at the 80% threshold.

With regard to Step 4, 28 scientific societies in the field of health and three authorities participated. Their support letters can be consulted on the project website. One scientific society for cancer redirected the demand for their opinion to the French society of supportive care in oncology, which also endorsed the model. Geriatrics and Physical and Rehabilitation Medicine societies redirected the demand for their opinion to their respective European Scientific Societies. The National College of General Practitioner Teachers (CNGE) made one request for the rewording of an item. This was accepted by the expert committee during its first meeting. Specifically, the text “if possible with a minimal clinically important difference” was added to item CO22 “Use objective and subjective criteria (e.g., patient-reported outcomes) employing the SMART approach (Specific, Measurable, Achievable, Realistic, and Timely)”. The National Cancer Institute (INCa), the National Centre for Palliative and End-of-Life Care, and the French Clinical Research Infrastructure Network (F-CRIN) also supported the model. The Ministry of Prevention and Health, the French National Authority for Health (HAS), and the French Health Insurances responded that they were not authorized to produce a support letter to a scientific society. Following a question by the French college of ethics committees, the second expert committee meeting focused on the sustainability of the data. However, no modification was made to any of the recommendations. Accordingly, the final version (i.e., version 4) of the online and freely accessible NPI Model includes 77 recommendations, 14 of which are ethical and 63 methodological in nature. Of the latter, six are for observational studies, six for mechanistic studies, nine for prototypical studies, 28 for intervention studies and 14 for implementation studies. Finally, given the size of this multidisciplinary endeavour, both a freely accessible interdisciplinary glossary and FAQs section are available on the NPI Model website. The results were presented in the French Senate on October 6, 2023. All related videos are freely accessible online.

## **Discussion**

The NPI Model’s definition of NPIs covers bodily, psychosocial and nutritional protocols administrated by healthcare professionals. The aim of this scientific consensus study was to improve the quality of research assessing NPIs for the health of the general population. The participatory, transdisciplinary, intersectoral, independent, pragmatic, and rigorous approach used followed the principles of honesty, scientific integrity and responsibility, three cornerstones on which the public bases its trust in research. This made it possible to develop a consensual and coherent model for the evaluation of NPIs called the NPI Model. This hybrid model comprises 14 ethical recommendations and 63 methodological recommendations. It was endorsed by three health authorities and 28 French scientific and medical societies. It facilitates the design, implementation and dissemination of studies evaluating NPIs, and consolidates the provision of coherent and convergent evidence through research and the dissemination of good practices when designing and implementing NPIs.<sup>1-5</sup> The 77 recommendations adapt the principles of EBM to the specificities of NPIs.

The NPI Model recommends that mechanistic studies measure multiple processes simultaneously. Furthermore, it recommends the development of prototypical studies using mixed methods to accurately describe intervention protocols<sup>21,28</sup>, instead of being limited to the evaluation of an approach that is too global and vague (e.g., psychotherapy or physical activity in the broad sense), or the evaluation of a component that is too restrictive (e.g., a technique such as a massage gesture or a muscle stretching exercise, an ingredient such as a food, or a piece of equipment such as a virtual reality headset). Moreover, the NPI Model recommends that intervention studies evaluating NPIs be pragmatic in nature<sup>31</sup> by examining data using intention-to-treat analyses: biological and self-reported markers of effectiveness as well as adverse effects.<sup>32</sup> It also recommends conducting implementation studies to assess NPIs in order to optimize the dissemination of the latter in a real-world situation, respecting cultural habits and individual preferences. Finally, the NPI Model recommends ethical and scientific integrity by researchers and study promoters.

From a scientific and sanitary point of view, the recognition of the NPI Model by relevant authorities may make it possible to ensure that the epistemological, methodological and ethical expectations of studies assessing NPIs are more readable for researchers and the results of such studies more transferable for practitioners and trainers. It may also make such studies more relevant for promoters, and the benefits of participation in them more obvious for study participants. One possible development of the model is the creation of a scoring system indicating the methodological and ethical quality of each study.

From an economic point of view, the recognition of the NPI Model by relevant authorities may facilitate returns on investment in research, the creation of local jobs to manage NPIs, the financing of effective practices for health insurance and social systems, and a reduction in avoidable healthcare and hospitalization expenses. Investments in effective interventions against chronic diseases such as chronic obstructive pulmonary disease could have substantial economic benefits in the future.<sup>33</sup>

From a societal point of view, the recognition of the NPI Model by relevant authorities may help promote better information for citizens, the sustainable engagement of users in safer practices (e.g., empowerment), the traceability of NPIs in the personalized pathways of healthcare operators, the reduction of social and territorial health inequalities, and the standardization of practices and of the practitioners implementing them. Furthermore, the accumulation of publications of standardized studies would facilitate the identification and comparison of NPIs. A register of NPIs could be built and made accessible to researchers as well as to practitioners and citizens. Each labelled NPI could have a unique code facilitating its traceability, particularly for massive data analyses. Once validated by an independent expert committee, an experimental *non-pharmacological intervention* could become a *normalized person-centred intervention*, thereby becoming an effective solution to ensure human health that is patient-proactive and sustainable human health.

### **Study limitations**

This work takes into account the ethical and methodological requirements of the French health system. Only after similar work is conducted at the European – and perhaps wider – level, will the NPI Model be able to show its full worth.

### **Conclusion**

This two-year participatory-based scientific study mobilized more than 1,000 researchers, healthcare practitioners, healthcare users and health operators. Furthermore, it was endorsed by 21 scientific societies and three French health authorities. The study led to the creation of a transdisciplinary and intersectoral framework for evaluating NPIs that is consensual and balanced in terms of study coherence, validity, reproducibility and transferability. The NPI Model - which is currently targeted at the French health system - will serve as a framework to justify new studies, consolidate scientific knowledge on NPIs, and disseminate good practices. The model clearly erases ambiguities between the NPI research domain and other evaluation frameworks in the field of health (e.g., drugs, medical devices, surgery, public health strategies). We plan to enhance and expand this model at the European level.

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