



## SCIENTIFIC LETTER

## Characteristics of non-pharmacological non-commercial pediatric Spanish clinical trials completed in 2009–2024



### Características de los ensayos clínicos españoles no farmacológicos y no comerciales en pediatría completados en 2009–2024

Dear Editor:

We conducted a study with the aim of determining the characteristics of Spanish noncommercial clinical trials that evaluated nonpharmacological interventions in pediatrics, as this information was unavailable to date. This *post hoc* analysis was based on data from a systematic review of trials performed between September 1, 2009, and September 1, 2024.<sup>1</sup> To be included, the trials had to be registered in the registries that, according to a previous study,<sup>2</sup> are most commonly used by Spanish researchers: ClinicalTrials.gov (USA), ISRCTN (United Kingdom), DRKS (Germany), ReBEC (Brazil), or ANZCTR (Australia-New Zealand). We searched for trials in registries and, using the registry code, for the corresponding articles in PubMed and Google Scholar. The systematic review<sup>1</sup> provides a detailed explanation of the search process, the definition of certain study variables (eg, “multicomponent” intervention, “multidisciplinary” authorship, autonomous community where the principal investigators in the trial worked), and the limitations of the review itself. The articles considered relevant for the review were the earliest articles to describe the trial results and/or protocol; in the case of unpublished trials, we considered preprint releases.

Of 650 registered trials, the results or the protocol had been published for 499, out of which 33 described evaluations of pediatric interventions (Appendix B, Supplementary material). Of these 33 articles, 18 only reported the results, nine only the protocol, and six both the results and the protocol. In two trials, the results were published as preprints, and in one other, the protocol was published as preprint also.

Table 1 summarizes the main characteristics of the 33 trials. In 97% of cases, the authors reported that the trial had been approved by a research ethics committee (REC), and in 63.6%, the authors reported compliance with the principles of the Declaration of Helsinki (DoH). There were three pilot trials.

Table 2 shows the characteristics of the articles that reported trial results (n=24). Six of them, which included physicians among their authors, made no mention of adhering to the principles of the DoH. In 33.3% (15.6%–55.3%; 8/24) of the articles, there were no physicians among the authors: four were produced by multidisciplinary teams, three by psychologists, and one by sports science specialists. One trial, conducted by psychologists, did not mention REC approval or refer to the principles of the DoH. All were published in foreign journals except one—the only one that did not report on these ethical aspects. All had been cited, except two published in 2024 (8.3%; 1.0%–27.0%; 2/24). Two articles, both published in 2014, received more than 100 citations each, totaling 221 citations (39.3% of the total; 35.3%–43.5%; 221/562). In 54.5% of the trials, the participants were healthy children or adolescents, or parents of patients.

Spanish regulation requires that trials be approved by a REC, but it does not stipulate that they must meet the principles of the DoH.<sup>3</sup> This may have contributed to the nearly complete adherence to the process of obtaining approval from a REC. It is encouraging that 63.6% of articles reported that the trial adhered to the principles of the DoH; however, among the articles that did not report on this aspect, there were trials conducted by physicians, who have been ethically obligated to adhere to these principles for decades.<sup>4</sup> Still, not reporting adherence in these articles does not necessarily mean that the research was not conducted in adherence with the principles of the DoH. When we compared the 33 trials analyzed in our study to the 499 included in the complete series,<sup>1</sup> we found similar percentages of adherence: 97% vs 98%<sup>1</sup> in relation to approval by a REC and 61% vs 67%<sup>1</sup> in relation to the principles of the DoH.

With regard to the design of trials involving individual participants, there were similar percentages of randomized trials (83% vs 86%<sup>1</sup>), blinded trials (54% vs 53%<sup>1</sup>), and multicenter trials (38% vs 31%<sup>1</sup>), but the median number of participants per trial differed (86 vs 63<sup>1</sup>). There were no significant differences in the number of evaluated experimental interventions, but there were differences in the type, with behavioral interventions (27%) being most

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**Table 1** Main characteristics of the trials included in the study (N = 33, unless otherwise specified).

Characteristics	n	% (95% CI)
<i>Reported on compliance with ethical principles</i>		
Approval of study protocol by REC	32 <sup>a</sup>	97.0 (84.2–99.9)
Adherence to principles of the Declaration of Helsinki	20 <sup>b</sup>	60.6 (42.1–77.1)
<i>Design of trials that included individual participants (n = 24)<sup>c</sup></i>		
Randomized	20	83.3 (62.6–95.3)
Blinded	13	54.2 (32.8–74.4)
Assessor-blind	7	29.2 (12.6–51.1)
Double-blind	6	25.0 (9.8–46.7)
Multicenter	9	37.5 (18.8–59.4)
Parallel group	21	87.5 (67.6–97.3)
<i>Number of experimental interventions evaluated per trial</i>		
1	25	75.8 (57.7–88.9)
2	7	21.2 (9.0–38.9)
3	1	3.0 (0.1–15.8)
<i>Types of experimental interventions evaluated (alone or in combination)</i>		
Behavior	9	27.3 (13.3–45.5)
Exercise	8	24.2 (11.1–42.3)
eHealth <sup>d</sup>	6	18.2 (7.0–35.5)
Education	5	15.2 (5.1–31.9)
Dietary supplements	4	12.1 (3.4–28.2)
Other <sup>e</sup>	8	24.2 (11.1–42.3)
<i>Types of participants</i>		
Patients	15	45.5 (28.1–63.6)
Healthy children or adolescents	17 <sup>f</sup>	51.5 (33.5–69.2)
Parents of patients	1	3.0 (0.1–15.8)
<i>Trials conducted in primary care setting</i>		
	0	0.0 (0.0–10.6)
<i>External funding</i>		
Funded	27	81.8 (64.5–90.3)
Public funding from Spain	13	39.4 (22.9–57.9)
Public funding from Spain and EU	7	21.2 (9.0–38.9)
Private funding from Spanish organizations/institutions	1	3.0 (0.1–15.8)
All other	6	18.2 (7.0–35.5)
No funding	4	12.1 (3.4–28.2)
Not reported	2	6.1 (0.7–20.2)

Abbreviations: EU, European Union; ISCIII: Instituto de Salud Carlos III; REC, research ethics committee.

<sup>a</sup> Excluding one that had only published results.

<sup>b</sup> Excluding 6 of the trials that had only published results, 4 that had only published the protocol, 3 with both types of articles (results and protocol).

<sup>c</sup> Excluding 9 trials, (clusters).

<sup>d</sup> Including mobile health, health care information and communication technologies, mobile devices, telehealth and telemedicine.

<sup>e</sup> Such as multicomponent interventions (n = 3), medical devices (n = 2), and other (n = 2).

<sup>f</sup> Children in 14 trials, adolescents in 3.

frequent in pediatric trials compared to rehabilitation interventions (25%) in the total 499 trials.<sup>1</sup> Pediatric trials were funded more frequently (82%) than trials in the complete series of 499 trials (63%).<sup>1</sup> Authors working in Catalonia conducted a higher percentage of the trials in the pediatric trial subset (46% vs 25%).<sup>1</sup> The median number of citations did not differ significantly (8 vs 13<sup>1</sup>). It is worth noting that none of the pediatric trials was conducted at the primary care setting, compared to 9%<sup>1</sup> of the 499 trials. It is discouraging to see how few of the pediatric trials make their data available to other researchers: 46% (vs 59%<sup>1</sup>) did not publish the data, while the authors of 42% (vs 29%<sup>1</sup>) state that the data

will be made available upon request, but there is evidence that, of the researchers that make such a statement, only 7% actually end up sharing requested data.<sup>5</sup>

In conclusion, Spanish noncommercial trials evaluating nonpharmacological interventions in the pediatric population do not differ substantially from the other trials of this type in terms of design and ethical aspects. In this regard, future trials should be blinded and multicenter design whenever possible, as this would increase their internal validity and, possibly, their external validity as well. We ought to highlight the need to conduct more trials in pediatric patients, since more than half of those com-

**Table 2** Main characteristics of the trials with articles that reported the results (N = 24, unless otherwise specified).

<i>Year of publication</i>		
2011–2017	5	20.8 (7.1–42.2)
2018–2024	19	79.2 (57.8–92.9)
Range (IQR)	2011–2024	
Mean	2021	
Median	2022	
<i>Autonomous community where the principal investigators worked<sup>a</sup></i>		
Catalonia	11	45.8 (25.6–67.2)
Community of Madrid	3	12.5 (2.7–32.4)
Castilla-La Mancha	2	8.3 (1.0–27.0)
Valencian Community	2	8.3 (1.0–27.0)
Navarre	2	8.3 (1.0–27.0)
Other <sup>b</sup>	4	16.7 (4.7–37.4)
<i>Number of participants in trials that included individual participants (n = 19)<sup>c</sup></i>		
Total	3974	
Range (IQR)	22–856 (44–225)	
Mean	209	
Median	86	
<i>Number of citations received by articles</i>		
Total	562	
Range (IQR)	0–117 (3.8–26.5)	
Mean	23.4	
Median	8.0	
<i>Number of citations/year received by the articles</i>		
Range (IQR)	0–10.6 (1.8–7.5)	
Mean	4.2	
Median	3.7	
<i>Data availability</i>		
Upon request	10	41.7 (22.1–63.4)
Not available	2	8.3 (1.0–27.0)
Uncertain	1	4.2 (0.1–21.1)
No statement regarding availability	11	45.8 (25.6–67.2)

<sup>a</sup> Publication identified which authors were considered the principal investigators in the trial.<sup>1</sup>

<sup>b</sup> There were authors leading a trial conducted in the Canary Islands, Balearic Islands, Basque Country and Region of Murcia.

<sup>c</sup> Excluding 5 cluster trials.

pleted in 2009–2024 were in healthy children or adolescents. Although the difficulty of conducting pediatric trials in primary care is acknowledged, this is a goal that we should strive to achieve as soon as possible. Finally, professional pediatric societies should consider educating their members on the importance of making de-identified data from trial participants available to third parties—if possible in a public repository—to enable the performance of secondary analyses and meta-analyses.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.anpedi.2025.504085>.

## Declaration of competing interest

The authors have no conflicts of interest to declare.

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