



Original article

[Translated article] Profile of clinical trials with drugs for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in Spain



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A B S T R A C T

Background: On 11 March 2020, World Health Organisation declared COVID-19 a pandemic. During the early stages, treatments lacking scientific evidence, such as hydroxychloroquine and later remdesivir, were used; meanwhile, clinical trials were being conducted in Spain to evaluate new therapies with greater scientific rigor. This article analyses the study profile, publication rate and completion of studies during the COVID-19 pandemic in Spain.

Methods: Meta-epidemiological, analytical, and retrospective study analyzing the characteristics and rate of completion of clinical trials with SARS-CoV-2-related drugs authorized in Spain between March 2020 and March 2021, focusing on treatment and prophylaxis. 179 clinical trials were reviewed using sources such as Registro Español de Estudios Clínicos, ClinicalTrials.gov, PubMed, Embase and TESEO. Statistical analysis was performed with SPSS v.26.

Results: 67.0% of the trials were national and 71.0% multicentre, with non-commercial sponsors (64.8%) and phase II (44.7%) and phase III (48.0%) studies being the most common. The majority employed a comparative design (93.9%), preferentially focused on treatment (91.1%) versus prophylaxis of SARS-CoV-2 disease, with a predominance of therapeutic repositioning (72.1%). Notably, studies initiated during the first wave of the pandemic (March–June 2020) were mostly non-international, non-commercial, non-placebo-controlled and aimed at drug repositioning. Some 21.2% of the clinical trials closed prematurely, mainly due to recruitment problems, involuntary discontinuation or failure to achieve expected efficacy. By the end of the study, 41.1% of the clinical trials had a final report and 31.3% published their results, most of them (71.9%) in first quartile journals. Statistically significant associations were found between the publication of results and variables such as multicentre, not having closed prematurely, having a final report, and phase III trials.

The fact that a large number of clinical trials were not published (68.7%) represents a missed opportunity in terms of knowledge.

Conclusion: We conclude that there is a need to improve transparency, record all results– including negative ones– and review key aspects of design and funding, as recommendations for future research, including in health emergencies.

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Perfil de los ensayos clínicos con medicamentos para la infección por coronavirus del síndrome respiratorio agudo grave de tipo 2 (SARS-CoV-2) en España

R E S U M E N

Palabras clave:
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Estudios clínicos como tema
Diseño de investigación
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Pandemias

Introducción: El 11 de marzo de 2020, la Organización Mundial de la Salud declaró la COVID-19 como pandemia. Durante las primeras etapas se utilizaron tratamientos sin evidencia científica, como la hidroxicloroquina y, más adelante, el remdesivir. En paralelo, en España, se realizaban ensayos clínicos para evaluar nuevas terapias con mayor rigor científico. Este artículo analiza el perfil de los estudios, la tasa de publicación y la finalización de estos durante la pandemia por COVID-19 en España.

Métodos: Se realizó un estudio metaepidemiológico, analítico y retrospectivo sobre las características, la tasa de publicación de resultados y la tasa de finalización de los ensayos clínicos con medicamentos relacionados con SARS-CoV-2, autorizados en España, entre marzo de 2020 y agosto de 2021, enfocados en el tratamiento y la profilaxis de la enfermedad. Se revisaron 179 ensayos clínicos utilizando el Registro Español de Estudios Clínicos, ClinicalTrials.gov, PubMed, Embase y TESEO. Se realizó el análisis estadístico con SPSS v.26.

Resultados: el 67,0% de los ensayos fueron nacionales y el 71,0% multicéntricos, destacando los promotores no comerciales (64,8%) y los estudios en fases II (44,7%) y III (48,0%). La mayoría empleó un diseño comparativo (93,9%), enfocado preferentemente en el tratamiento (91,1%) frente a la profilaxis de la enfermedad por SARS-CoV-2, con predominio del reposicionamiento terapéutico (72,1%). Particularmente, los estudios iniciados durante la primera ola de la pandemia (marzo-junio de 2020) fueron, en su mayoría, no internacionales, no comerciales, sin comparación con placebo y destinados al reposicionamiento de medicamentos. Un 21,2% de los ensayos clínicos cerró de forma prematura, principalmente por problemas de reclutamiento, de interrupción involuntaria o de falta de eficacia esperada. Hasta la fecha del final del estudio, el 41,1% de los ensayos disponía de informe final y el 31,3% publicó sus resultados, la mayoría de ellos (71,9%) en revistas del primer cuartil. Se hallaron asociaciones estadísticamente significativas entre la publicación de resultados y variables como el carácter multicéntrico, el no haber cerrado prematuramente, el contar con informe final y ensayos fase III.

El hecho de que un gran número de los ensayos clínicos no llegara a publicarse (68,7%) supone una pérdida de oportunidad en términos de conocimiento.

Conclusión: Se concluye la necesidad de mejorar la transparencia, registrar todos los resultados —incluidos los negativos— y revisar aspectos clave del diseño y financiación, como recomendaciones para futuras investigaciones, incluso en situaciones de urgencia sanitaria.

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Introduction

On 11 March 2020, the World Health Organisation (WHO) declared the disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) a pandemic, stating that it was “deeply concerned by the alarming levels of spread and severity of the disease, and the equally alarming levels of inaction¹. The WHO had already issued a warning about the disease in a report on the joint WHO-China mission, which was published in February 2020². This report provided a series of recommendations for preventing, detecting, and isolating cases, monitoring disease progression, carrying out public health prevention activities, and managing media coverage. This report only refers to nonpharmacological support measures, except in the recommendations made to China, in which it suggests “establish a centralized research program to fast-track the most promising rapid diagnostics and serologic assays, the testing of potential antivirals and vaccine candidates, and Chinese engagement in selected multi-country trials”.

Before the pandemic was officially recognised as such, very few studies had been published on the use of drug therapy in coronavirus infection³. At that time, several antivirals and other drugs were tested in clinical trials (CTs) in China, but no significant scientific evidence of their efficacy was achieved.

When the first cases of SARS-CoV-2 infection appeared in Spain, the healthcare professionals' approach to treating these patients was characterised by uncertainty and a focus solely on clinical aspects. As in other European countries (e.g. France and Italy), off-label drugs were administered in Spain without robust evidence of their efficacy. These drugs included hydroxychloroquine, lopinavir/ritonavir, azithromycin and, later, remdesivir, in line with recommendations

from the scientific community and health authorities. These drugs are used in routine clinical practice to treat various diseases and have well-known safety profiles, in terms of both adverse reactions and potential drug interactions. Some of these effects are serious, particularly given that many of the patients treated were elderly or had pre-existing conditions^{4–6}. In line with these recommendations, the Spanish Agency for Medicines and Health Products (AEMPS) made great efforts to ensure that these drugs were available in Spanish hospitals, as they were already being used to treat affected patients.

Controlled CTs are the most reliable method to yield high-quality scientific evidence. The results obtained from scientific research help determine optimal therapeutic strategies. This information is disseminated through national registries (e.g. the Spanish Clinical Trials Registry in Spain) and by publishing the results, which is legally required by Royal Decree 1090/2015⁷. For this reason, health authorities in all countries, particularly in Spain and the United Kingdom, urged the initiation of CTs, initially using drugs that were already being employed empirically. Noteworthy initiatives included the WHO Solidarity trial⁸ and the UK National Health Service's Recovery trial⁹, the results of which were published shortly after completion. In addition, new research projects involving other drugs were initiated that, from the outset, called for the inclusion of as many patients as possible. The main objectives were to provide patients with new therapeutic options and to obtain drug efficacy and safety data that would confirm favourable risk-benefit ratios.

In Spain, approximately 17% of drug research is noncommercial or academic in nature¹⁰. However, during the COVID-19 pandemic, numerous independent or noncommercial CTs were conducted, sponsored by collaborative groups, scientific societies, hospital foundations, or

independent researchers. All those involved made great efforts to evaluate, authorise, implement, and develop the CTs, with the work of independent researchers being particularly noteworthy. This effort was not only financial, requiring significant public funding, but also organisational, involving the rapid evaluation and approval of protocol submissions and the rushed initiation of CTs in hospitals. The CT units played a decisive role by quickly adapting their standard operating procedures and participating in resource allocation^{11,12}.

According to the Organisation for Economic Co-operation and Development and major pharmaceutical companies, Spain was among the countries that conducted the most CTs on SARS-CoV-2 at the height of the pandemic¹². Now that some time has passed, a number of questions remain. How many of these trials have been completed? How many studies have published their results, even if they were negative? What problems arose during their implementation? In short, was the effort involved in setting them up worthwhile? Against this backdrop, the present study aimed to analyse CTs involving drugs for SARS-CoV-2 infection that were conducted in Spain during the pandemic, and to describe the publication and completion rates of these trials.

Materials and methods

A meta-epidemiological, analytical, retrospective study of the characteristics, completion rates, and publication of CTs involving drugs intended for the prophylaxis and treatment of SARS-CoV-2 infection approved in Spain between March 2020 and August 2021.

Eligibility criteria

Inclusion criteria

We included all Spanish CTs authorised by the AEMPS between March 2020 and August 2021 (18 months) that were entered in the Spanish Clinical Trials Registry (SCTR) and aimed at the prophylaxis and treatment of SARS-CoV-2 infection and its symptoms. As a quality assurance measure, only studies published in indexed journals were included.

Exclusion criteria

We excluded CTs of vaccines aimed at preventing infection, as well as phase I CTs in the paediatric population. We also excluded scientific opinion articles, letters to the editor, and conference publications.

Sources of information

A peer review was conducted between November 2024 and March 2025 based on the main sources of information on CTs: the SCTR; the US CT registry (clinicaltrials.gov); and the equivalent European registry (clinicaltrialsregister.eu). The PubMed and Embase databases were also consulted. The Spanish TESEO doctoral thesis data registry was reviewed to ensure a comprehensive search. Other databases were discarded due to duplication of results. All study data were recorded using the REDCap platform, which meets legal requirements regarding the integrity, accuracy, reliability, and consistency of data.

Search strategy

The previously defined eligibility criteria were used to select the CTs found in the research registries. The search strategy combined MeSH and DeCS terms, using the Boolean operators 'AND' and 'OR'. For each database, the review filter was applied (see [Table 1](#)).

Data extraction

Data extraction was conducted independently by pairs of researchers using a standardised form that collected the following

Table 1

Search strategies in the selected databases.

Database	Search strategy (November 2024)
PubMed	[("Clinicaltrial"[MeSH]) OR (research)] AND (((((((((((("COVID-19" OR ("2019 novel coronavirus disease")) OR ("COVID19")) OR ("COVID-19 pandemic")) OR ("SARS-CoV-2 infection")) OR ("COVID-19 virus disease")) OR ("2019 novel coronavirus infection")) AND ("spain")
Embase	'covid-19'/exp. OR 'sars-related coronavirus'/exp., 'therapy'/exp. AND 'therapy'/exp. AND 'clinical trial'/exp. OR 'randomisedcontrolled trial'/exp. AND 'spain'/exp

information: study code, EudraCT number, National Clinical Trial number, geographical coverage, sponsor, study design, type of control, experimental treatment, premature closure and reason for closure, study objective, communication of results, trial start, recruitment, and closure times, and percentage and place of publication of results.

Clinical trials by intervention

Therapeutic repurposing: trials evaluating drugs that have current marketing authorisation by the AEMPS for treating diseases other than COVID-19.

New molecule: trials investigating drugs that do not have prior marketing authorisation from the AEMPS for any indication.

Cell therapy: trials that administered cells prepared through prior manipulation for therapeutic purposes.

Statistics

All statistical analyses were performed using SPSS v.26 (IBM, Armonk, NY). A *P*-value <0.05 was used as a cutoff for statistical significance. The characteristics of the CTs are expressed as descriptive statistics. Categorical variables are expressed as absolute and relative frequencies. In both cases, the number of observations and any missing data were specified.

Bivariate analysis was used to compare the characteristics of CTs that published the results with those that did not. Pearson's chi-squared statistic was used in the analysis.

Results

During the study period, 191 CTs involving drugs were approved, 12 of which were excluded because they were phase I studies of paediatric populations. Ten CTs involved vaccines as a therapeutic option. The principal objective of most of the 179 CTs was therapeutic repurposing (72.1%). In addition, 45 studies (25.1%) involved new drugs not previously approved by the AEMPS for any disease. One CT had a dual objective, combining drug repurposing and new molecules (WHO Solidarity Trial)⁸. Only 6 studies (2.8%) were conducted with drugs classified as cell therapies.

Of the 179 CTs, 67.2% were Spanish, 71.0% were multicentre, and 64.8% had noncommercial sponsors. Most CTs were phase III (48.1%) or phase II (44.7%) ([Table 2](#)). Regarding methodology, the comparative design stood out, having been employed in 93.9% of the studies. The majority of the trials focussed on treatment (91.1%) and 10.6% addressed disease prophylaxis. A total of 21.2% of trials were terminated prematurely. The main reasons were recruitment difficulties (36.6%), withdrawal of consent (26.8%), and lack of efficacy (21.9%). By the cut-off date of November 2024, 41.1% had issued a final report and 31.3% had published results in scientific journals (71.9% in the first quartile).

Statistically significant associations were found between the availability of the final report and the following variables: being an international study (54.7% vs 45.3%; *p* < 0.001); being a multicentre study (84.0% vs 16.0%; *p* = 0.002); having a commercial sponsor (64.2% vs 35.8%; *p* < 0.001); comparing treatment with placebo

Table 2
Distribution of CTs by phase and start date.

	I	II	III	IV	Total
1st wave ¹	3	31	35	13	82
2nd wave ²	1	29	25	7	62
3rd wave ³	0	3	5	3	11
4th wave ⁴	0	4	7	3	14
5th wave ⁵	0	4	6	0	10
Total	4	71	78	26	179

¹ March–June 2020.

² June–December 2020.

³ January–February 2021.

⁴ March–June 2021.

⁵ July–September 2021.

(54.7% vs 45.3%; $p = 0.001$); focussing on drug repurposing (57.3% vs 42.7%; $p < 0.001$); and not undergoing early closure (69.3% vs 30.7%; $p = 0.009$).

Only 49 of the 179 CTs were published in indexed journals. Associations were found between publication and variables related to the study design: being multicentre (85.7% vs 14.3%; $p = 0.004$), phase III (58.9% vs 41.1%; $p = 0.049$), and Spanish (53.6% vs 46.4%; $p = 0.01$). The majority of CTs published in the first quartile were international (58.5% vs 41.5%; $p = 0.002$).

Notable findings regarding outcome-related variables included the availability of a final report (64.3% vs 35.7%; $p < 0.001$) and the absence of premature termination (89.3% vs 10.7%; $p = 0.02$).

The main characteristics of the studies ($N = 82$) that began during the first wave of COVID (March–June 2020) were as follows: not being international (82.9% vs 17.1%; $p < 0.001$), having noncommercial sponsors (80.5% vs 19.5%; $p < 0.001$), not being placebo-controlled (73.2% vs 26.8%; $p < 0.001$), and focussing on drug repurposing (84.1% vs 15.9%; $p = 0.001$).

The characteristics of studies approved during the second wave ($N = 62$) were as follows: not being international (61.3% vs 38.7%; $p < 0.001$), having commercial sponsors (90.3% vs 9.7%; $p < 0.001$), being placebo-controlled (66.1% vs 33.9% $p = 0.04$), and focussing on drug repurposing (70.9% vs 29.1%; $p = 0.001$). The characteristics during the third, fourth, and fifth waves ($N = 35$) were as follows: being international studies (61.5% vs 38.5%; $p < 0.001$), having commercial

sponsors (68.8% vs 31.2%), being placebo-controlled (78.8% vs 21.2%; $p < 0.001$); and evaluating new molecules (59.4% vs 40.6%; $p = 0.003$) (Fig. 1; Table 2).

Discussion

The need for effective and safe treatments for COVID-19 led to the large-scale initiation of CTs. According to recent data, over 2700 CTs related to SARS-CoV-2 were registered globally on [ClinicalTrials.gov](https://clinicaltrials.gov)¹³. In Spain, 191 studies were registered in the SCTR. These figures reflect the effort undertaken by the scientific and healthcare community to advance knowledge in this field.

Various published reviews identified significant limitations in the quality, impact, design, and publication of CTs¹⁴. They found that many CTs had significant methodological limitations that compromised their scientific value. These limitations included inconsistent designs, small sample sizes, an absence of control groups, unblinded patients and physicians, and nonrandomised designs¹⁵. Another key factor in these studies was the lack of coordination between different bodies¹⁶. The lack of quality was most pronounced during the first wave, when there was an urgent need for additional knowledge and increased pressure on healthcare systems^{16,17}.

Dal-Ré and Mahillo-Fernández¹⁸ reviewed 159 CTs that were not sponsored by the pharmaceutical industry and were conducted across various Western European countries over 1 year (May 2020–May 2021). Overall, 44% of the CTs exhibited at least 1 indicator of low methodological quality. For this reason, the results obtained in these trials made it difficult to reproduce them and draw firm conclusions. For example, one CT evaluated the effectiveness of hydroxychloroquine combined with macrolides, but the results were not statistically rigorous¹⁹. Publications such as these contributed to the initial confusion regarding treatment, which ultimately forced numerous scientific journals to retract them due to weak methodological rigour and questionable ethical clarity²⁰.

In addition to the methodological shortcomings mentioned above, we found that a significant proportion (68.7%) of CTs registered in Spain did not publish their results in a scientific journal. This figure is similar to the results of other reviews, including that by Fincham et al., which reported a nonpublication rate of 70.1%²¹. It should be emphasised that failing to publicly share the results of a CT can be considered detrimental to healthcare professionals, regulatory authorities,

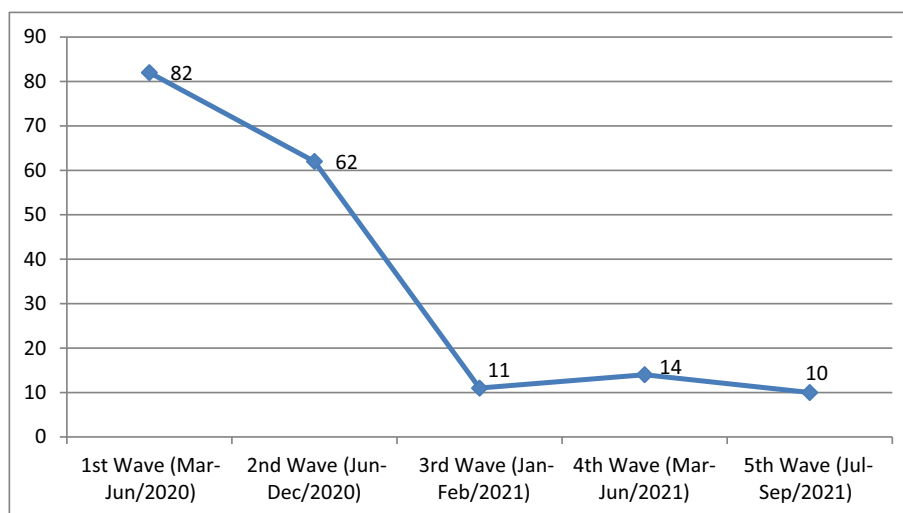


Figure 1. Number of CTs initiated in each wave of the pandemic.

and patients. Publication bias, whether positive or negative, hinders the accumulation of evidence.

The methodological characteristics of CTs conducted in Spain are similar to those of international research studies. Regarding design, most of the studies conducted during this period were controlled randomised CTs to ensure the internal validity of the results. One such design is exemplified by the WHO Solidarity trial⁸.

Regarding the treatment control arm, our results show that a placebo was used as the main comparator in 40.8% of the studies. This figure is higher than the 29.1% reported by Silva et al²².

The main barriers to the development of CTs were recruitment difficulties, lack of efficacy, and funding, much like those reported by Cook et al. in their Canadian study²³. In addition to the aspects mentioned above, consideration must also be given regarding the impact of publishing the CTs conducted. Of the studies analysed, only 31.3% published their results in a scientific journal, compared to the 53% reported by Showell et al²⁴. This percentage contrasts with the legal requirement to publish the results of CTs, whether positive or negative, as set out in current legislation⁷.

On the other hand, 89.2% of the published research appeared in first-quartile indexed journals. This figure is very similar to the 80% reported in the Annual Cancer Research Report²⁵. This situation raises ethical concerns regarding data transparency, as many studies remained unfinished or as preprint repositories²⁶. In turn, this research has the potential to influence decisions on healthcare policy. An example of this possibility was the prescription of dexamethasone to reduce mortality from SARS-CoV-2 respiratory infection as reported in the RECOVERY trial²⁷. The failure to publish data from scientific studies can raise significant mistrust.

Various authors and health authorities have pointed out the importance of the quality of the evidence produced by these trials. London and Kimmelman²⁸ proposed 5 conditions that clinical research must meet in the context of a health emergency in order to increase knowledge and be socially relevant. In March 2020, the European Medicines Agency and the US Food and Drug Administration published guidelines to support clinical research during the pandemic. The aim was to record any deviations from protocols and provide recommendations to ensure patient safety and maintain the integrity of CTs^{29,30}. The AEMPS published recommendations based on the European guidelines and adapted to Spanish legislation³¹.

This study was subject to a number of limitations. First, the time available for reviewing the publications was limited due to the acute nature of COVID-19 infection, and the time lag between selecting the studies (August 2021) and commencing the literature search (November 2024).

Another relevant limitation was the lack of detailed information regarding the early termination of certain CTs. Some studies were suspended, cancelled, or terminated prematurely, without providing clear explanations. In such cases, the information was supplemented using the scientific publications themselves or secondary sources, such as the SCTR maintained by the AEMPS. This lack of transparency made it difficult to correctly interpret the reasons behind these decisions and their potential impact.

Conclusion

During the COVID-19 pandemic, Spain experienced a moderate increase in the number of CTs involving drugs, driven by the worldwide urgency to identify effective alternatives. In the first wave of the epidemic, most CTs focused on drug repurposing, with the majority being

multicentre, Spanish, or sponsored by noncommercial bodies. As the pandemic progressed, research was dominated by complex, international studies involving commercial sponsors and designs focussed on new therapies.

The findings suggest that there were a substantial number of clinical studies that were never published in scientific journals. This results in research inefficiency, providing little scientific value and failing to advance knowledge, which is particularly critical in times of high uncertainty. In order to minimise lost opportunities, transparency must be improved by updating scientific registries and fulfilling the obligation to make the results publicly available. Finally, any limiting factors that could lead to failure to publish should be identified so that they can be minimised before studies are designed, funded, and scientifically evaluated. This approach can be applied in situations such as the SARS-CoV-2 pandemic as well as in routine clinical research.

Ethical responsibilities

All authors declare that this is an original work, has not been previously published, and is not under consideration by any other journal. They also confirm that they have each made a significant contribution to the manuscript and approved the final version. The applicable ethical standards for research have been followed. No data that could identify patients were used or published.

CRediT authorship contribution statement

Tejedor-Tejada Eduardo: Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Formal analysis, Data curation. **González-Pérez Cristina:** Writing – review & editing, Writing – original draft, Validation, Formal analysis, Data curation. **Goyache Goñi María del Puy:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation. **Suñé-Martín María Pilar:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Data curation, Conceptualization. **Serrano-Alonso María:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Data curation, Conceptualization. **Rafael Sánchez-del Hoyo:** Validation, Supervision, Methodology, Formal analysis.

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CRediT authorship contribution statement

Eduardo Tejedor-Tejada: Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Formal analysis, Data curation. **Cristina González-Pérez:** Writing – review & editing, Writing – original draft, Validation, Formal analysis, Data curation. **María del Puy Goyache Goñi:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation. **María Pilar Suñé-Martín:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Data curation, Conceptualization. **María Serrano-Alonso:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Data curation, Conceptualization. **Rafael Sánchez-del Hoyo:** Validation, Supervision, Methodology, Formal analysis.

Conflicts of interest

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.farma.2026.01.003>.

References

- World Health Organisation. Chronology of events. [Accessed 20 Dic 2024]. Available from: <https://www.who.int/es/news/item>.
- World Health Organisation. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). [Accessed 10 Nov 2024]. Available from: <https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf>.
- Ahn DG, Shin HJ, Kim MH, Lee S, Kim HS, Myoung J., et al. Current status of epidemiology, diagnosis, therapeutics, and vaccines for novel coronavirus disease 2019 (COVID-19). *J Microbiol Biotechnol.* 2020;30(3): 313–324. doi:10.4014/jmb.2003.03011.
- European Medicines Agency. Amsterdam: European Medicines Agency. Kaletra: EPAR – product information. [Accessed 10 Nov 2024]. Available from: https://www.ema.europa.eu/en/documents/overview/kaletra-epar-summary-public_en.pdf.
- Drug Information Center of the Spanish Agency of Medicines and Health Products. (AEMPS - CIMA). Madrid. Dolquine: Drug data sheet. Last review 2023. [Accessed 10 Nov 2024]. Available from: https://cima.aemps.es/cima/dohtml/p/74904/Prospecto_74904.html.
- Drug Information Center of the Spanish Agency of Medicines and Health Products. (AEMPS - CIMA). Madrid. Azithromycin: Drug data sheet Last review 2003. [Accessed 10 Nov 2024]. Available from: https://cima.aemps.es/cima/dohtml/ft/65600/FichaTecnica_65600.html.
- Real Decreto 1090/2015, de 4 de diciembre, por el que se regulan los ensayos clínicos con medicamentos. Boletín Oficial del Estado, núm. 307, 24 de diciembre de 2015, pp. 121069–121131. [Accessed 10 Feb 2025]. Available from: <https://www.boe.es/boe/dias/2015/12/24/pdfs/BOE-A-2015-14082.pdf>
- Pan H, Peto R, Henaó-Restrepo AM, Preziosi MP, Sathiyamoorthy V, et al, WHO Solidarity Trial Consortium. Repurposed antiviral drugs for Covid-19 - interim WHO Solidarity trial results. *N Engl J Med.* 2021;384(6): 497–511. doi:10.1056/NEJMoa2023184.
- Collaborative Group RECOVERY, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, et al. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med.* 2021;384(8):693–704. doi:10.1056/NEJMoa2021436.
- España, líder europeo en investigación clínica con medicamentos. Agencia Española del Medicamento. Feb 2025. [Accessed 9 May 2025]. Available from: https://www.aemps.gob.es/informa/espana-lider-europeo-en-investigacion-clinica-de-medicamentos/?utm_source=chatgpt.com#.
- Castro-Balado A., Varela-Rey I., Bandín-Vilar E.J., Busto-Iglesias M., García-Quintanilla L., Mondelo-García C., et al. Clinical research in hospital pharmacy during the fight against COVID-19. *Farm Hosp.* 2020;44(7):66–70. English. doi:10.7399/fh.11494.
- IQVIA. Assessing the clinical trial ecosystem in Europe. [Accessed 20 Dic 2024]. Available from: <https://www.farmaindustria.es/web/wp-content/uploads/sites/2/2024/10/EFPIA-Clinical-Trials-report-22.10.24.pdf>.
- Larson K, Sim I, von Isenburg M, Levenstein M, Rockhold F, Neumann S., et al. COVID-19 interventional trials: analysis of data sharing intentions during a time of pandemic. *Contemp Clin Trial.* 2022;115:106709. doi:10.1016/j.cct.2022.106709.
- Babaei F, Mirzababaei M, Nassiri-Asl M, Hosseinzadeh H. Review of registered clinical trials for the treatment of COVID-19. *Drug Dev Res.* 2021;82(4):474–493. doi:10.1002/ddr.21762.
- Mehta HB, Ehrhardt S, Moore TJ, Segal JB, Alexander GC. Characteristics of registered clinical trials assessing treatments for COVID-19: a cross-sectional analysis. *BMJ Open.* 2020;10(6):e039978. doi:10.1136/bmjopen-2020-039978.
- Jung RG, Di Santo P, Clifford C, Prosperi-Porta G, Skanes S, Hung A., et al. Methodological quality of COVID-19 clinical research. *Nat Commun.* 2021;12(1):943. doi:10.1038/s41467-021-21220-5.
- Johns Hopkins University Bloomberg School of Public Health. Majority of first-wave COVID-19 clinical trials have significant design short comings, study finds. Science Daily. [Accessed 20 Feb 2025]. Available from: www.sciencedaily.com/releases/2020/06/200609130006.htm.
- Dal-Ré R, Mahillo-Fernández I. Waste in COVID-19 clinical trials conducted in western Europe. *Eur J Intern Med.* 2020;81:91–93. doi:10.1016/j.ejim.2020.07.002.
- Schwartz IS, Boulware DR, Lee TC. Hydroxychloroquine for COVID19: the curtains close on a comedy of errors. *Lancet Reg Health Am.* 2022;11: 100268. doi:10.1016/j.lana.2022.100268.
- Gautret P., Lagier J.C., Parola P., Hoang V.T., Meddeb L., Mailhe M., et al. Retracted: Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents.* 2020 Jul;56(1):105949. Epub 2020 Mar 20. Retraction in: *Int J Antimicrob Agents.* 2025 Jan;65(1):107416. doi: 10.1016/j.ijantimicag.2024.107416. doi:10.1016/j.ijantimicag.2020.105949.
- Fincham L, Hohlfeld A, Clarke M, Kredt T, McCaul M. Exploring trial publication and research waste in COVID-19 randomised trials of hydroxychloroquine, corticosteroids, and vitamin D: a meta-epidemiological cohort study. *BMC Med Res Methodol.* 2024;24(1):19. doi:10.1186/s12874-023-02110-4.
- Silva P, Janjan N, Ramos KS, Udeani G, Zhong L, Ory M.G., et al. External control arms: COVID-19 reveals the merits of using real world evidence in real-time for clinical and public health investigations. *Front Med (Lausanne).* 2023;10:1198088. doi:10.3389/fmed.2023.1198088.
- Cook D, Taneja S, Krewulak K, Zytaruk N, Menon K, Fowler R., et al. Barriers, solutions, and opportunities for adapting critical care clinical trials in the COVID-19 pandemic. *JAMA Netw Open.* 2024;7(7): e2420458. doi:10.1001/jamanetworkopen.2024.20458.
- Showell M.G., Cole S., Clarke M.J., DeVito N.J., Farquhar C., Jordan V. Time to publication for results of clinical trials. *Cochrane Database Syst Rev.* 2024 Nov 27;11(11):MR000011. doi:10.1002/14651858.MR000011.pub3.
- Asociación Española contra el Cáncer. Comprometidos con la investigación en cáncer. [Accessed 9 May 2025]. Available from: https://observatorio.contraelcancer.es/sites/default/files/informes/Comprometidos%20con%20la%20investigacion%20en%20Cancer%20%20FINAL.pdf?utm_source=chatgpt.com.
- Maisonneuve H. COVID-19 as a source of poor publications. *Joint Bone Spine.* 2022;89(6):105427. doi:10.1016/j.jbspin.2022.105427.
- Collaborative Group RECOVERY, Horby P, Lim WS, Emberson JR, Mafham M, Bell J.L., et al. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med.* 2021;384(8):693–704. doi:10.1056/NEJMoa2021436.
- London AJ, Kimmelman J. Against pandemic research exceptionalism. *Science.* 2020;368(6490):476–477. doi:10.1126/science.abc1731.
- European Medicines Agency. Guidance on the management of clinical trials during the covid-19 (coronavirus) pandemic V5. [Accessed 3 Jul 2025]. Available from: https://health.ec.europa.eu/document/download/74386d75-e5fd-4d9c-9dfc-ec7d60758da9_en.
- Júarez-Gimenez JC, Suñé-Martín MP. Investigación en tiempos de pandemia. *El Farmacéutico Hospitalares.* [Accessed 15 Dic 2024]. Available from: <http://interactivos.elfarmacéuticohospitalares.es/EFH-222/index.html>.

31. Agencia Española de Medicamentos y Productos Sanitarios. Medidas excepcionales aplicables a los ensayos clínicos para gestionar los problemas derivados de la emergencia por COVID-19. [Accessed 3 Jul 2025]. Available from: [https://www.aemps.gob.es/informa/medidas-](https://www.aemps.gob.es/informa/medidas-excepcionales-aplicables-a-los-ensayos-clinicos-para-gestionar-los-problemas-derivados-de-la-emergencia-por-covid-19/)

[excepcionales-aplicables-a-los-ensayos-clinicos-para-gestionar-los-problemas-derivados-de-la-emergencia-por-covid-19/](https://www.aemps.gob.es/informa/medidas-excepcionales-aplicables-a-los-ensayos-clinicos-para-gestionar-los-problemas-derivados-de-la-emergencia-por-covid-19/).